# EMOTIONAL DYSREGULATION IN CHILDREN AND ADOLESCENTS

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# EMOTIONAL DYSREGULATION IN CHILDREN AND ADOLESCENTS

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EDITORIAL
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# Editorial: Emotional Dysregulation in Children and Adolescents

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**Keywords: emotion, self-regulation, disruptive mood dysregulation, emotion regulation, Emotion Dysregulation**

## Editorial on the Research Topic

## Emotional Dysregulation in Children and Adolescents

Emotional Dysregulation (ED) is defined as the inability to regulate and organize emotions to produce an appropriate emotional response and subsequent return to baseline. With regard to the intensity of reactions it partially overlaps with the concept of irritability (1), which is however regarded to be a more dispositional trait. ED represents a major health risk (2) and is associated with diverse forms of childhood psychiatric disorders and symptoms like attention deficit hyperactivity disorder, oppositional defiant- and conduct disorders (ODD and CD), personality disorders, self-injurious behavior and suicidality. In clinical settings, dysregulation problems are especially prominent (3), occurring in 26.0–30.5% of children admitted to child and adolescent psychiatric clinics or mental health facilities. A recent study could demonstrate that especially disturbed emotion regulation contributes to self-injurious behavior in a large group of adolescents presenting to a child and adolescent psychiatric emergency service (Kandsperger et al.). The occurrence of typical phenomena associated with ED, like severe tantrums, low frustration tolerance, aggression, negative mood and suicidality is even higher than the full syndrome of ED, with estimates of about 45% in child psychiatric patients between 6 and 18 years (4). An additional impact of Lockdown-related stressors on children and adolescents can also be discussed [e.g., (5)]. Thirty percentage of adults with emotional instability report having injured themselves at primary school age (6).

Several authors also mention emotionally dysregulated behavior as one of the leading symptoms of BPD and ADHD/DMDD (7). On the opposite note, emotion regulation capacity prevents the onset of multiple psychiatric and physical disorders and promotes successful social and professional development as described above (8). In connection with Emotion Dysregulation, large and rigorous studies (6) also emphasize that this behavior results in high costs for health and other services services.

In addition to biological vulnerability, epidemiological research suggests that the onset of most psychiatric disorders across the life course in nearly half of cases is attributable to adverse childhood experiences and stress related disorders (9, 10). Negative impact of adverse childhood experiences on general health seems to attributable partly to maladaptive strategies for emotion regulation, such as smoking, alcohol, overeating (11). Sleep problems related to the traumatic impact of adverse childhood experiences can be directly related (10, 12) and be an important target for treatment. Furthermore, early life trauma impairs neurobiological structures and functions related to emotion regulation, such as the orbitofrontal gyrus and frontolimbic connections (13). A challenge for clinical practice is the assumption that patients with ED remain notoriously difficult to treat (14).

Better equipment with psychotherapeutic tools for Emotion Regulation and characterization of the ecological contingencies, and an understanding of the developmental pathways through



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which early experience shapes later behavior, can help clinicians to tailor intervention efforts more precisely, to prevent future dysfunction (15).

Therefore, studies focusing on pathogenetic aspects of ED by addressing neurobiological underpinnings and childhood adversity are collected in this issue. Furthermore, interventions and therapies that give an overview on established therapeutic tools such as DBT and the younger "derivatives" and describe novel interventions developed from the recent ED-Framework, are included in this topic. Together with review articles on state of the art advancements in ED, research in this issue explores the adverse childhood experiences framework or describing empirical research on neurobiological associations.

With original articles and reviews on diagnosis and classification of ED our aim was to achieve with this issue a large transdiagnostic long-term benefit for research as well as clinical aspects since understanding and improving human emotion regulation capacity prevents the onset of multiple psychiatric and physical disorders and promotes successful social and professional development as will be shown in this issue.

## AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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ORIGINAL RESEARCH
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# Emotion Regulation as a Time-Invariant and Time-Varying Covariate Predicts Outcome in an Internet-Based Psychodynamic Treatment Targeting Adolescent Depression

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**Objective:** Although psychodynamic psychotherapy is efficacious in the treatment of depression, research on mechanisms of change is still scarce. The aim of this study was to investigate if and how emotion regulation affects outcome both as a time-invariant and a lagged time-varying predictor.

**Method:** The sample consisted of 67 adolescents diagnosed with major depressive disorder, attending affect-focused psychodynamic internet-based treatment (IPDT). Linear mixed models were used to analyze emotion regulation as a baseline predictor and to assess the effect of within-person changes in emotion regulation on depression.

**Results:** Analyses suggested that emotion regulation at baseline was a significant predictor of outcome, where participants with relatively larger emotion regulation deficits gained more from IPDT. Further, the results showed a significant effect of improved emotion regulation on subsequent depressive symptomatology. When not controlling for time, increased emotion regulation explained 41.23% of the variance in subsequent symptoms of depression. When detrending the results were still significant, but the amount of explained variance was reduced to 8.7%.

**Conclusion:** The findings suggest that patients with relatively larger deficits in emotion regulation gain more from IPDT. Decreased emotion regulation deficits seem to act as a mechanism of change in IPDT as it drives subsequent changes in depression.

**Clinical Trial Registration:** International Standard Randomised Controlled Trial Number (ISRCTN) 16206254, https://doi.org/10.1186/ISRCTN16206254.

**Keywords: emotion regulation, internet-based treatment, psychodynamic, psychotherapy process, adolescents, depression, mechanism of change**

## INTRODUCTION

Depression is the fourth leading cause of illness and disability among young people aged 15–19 years (1). Depression rates increase dramatically from childhood to adolescence (2), and many individuals will not receive any treatment for their condition (3, 4). Accordingly, there is a pressing need for accessible as well as cost- and time-efficient treatments for adolescent depression. One recent response to this need is the development and evaluation of internet-based treatments, which have the potential to reach and treat a larger number of patients (5). Internet-based cognitive behavioral therapy (ICBT) generally seems to perform on par with traditional face-to-face treatment delivered individually or in group (6), but to our knowledge no such head-to-head comparisons exist in the treatment of adolescent psychopathology. There are no studies where internet-based psychodynamic psychotherapy (IPDT) is compared to face-to-face PDT. Internet-based treatment for adolescent depression has been found effective when based on both ICBT (7, 8) and IPDT (9). However, little is known about the mechanisms of change in these treatments.

It has been suggested that emotion regulation deficits may underlie almost all psychiatric disorders (10, 11). Numerous studies have linked maladaptive emotion regulation skills to psychopathology across many different disorders (12), with evidence derived from both cross-sectional and longitudinal studies. Experimental studies have repeatedly shown that maladaptive emotion regulation strategies impair recovery from negative affect/mood (13–15).

In a longitudinal study, a lower capacity for emotion regulation predicted higher depressive symptomatology over five years (16). A recent meta-analysis (17) found that remitted and currently depressed research participants reported maladaptive emotion regulation strategies to a much higher extent when compared to healthy controls. Fortunately, research suggests that emotion regulation problems are not characterized by deficits in strategies per se. Depressed patients are able to use more adaptive emotion regulation skills if instructed to do so. Hence, the problem seems to be maladaptive selection of emotion regulation strategies rather than a lack of capacity (18).

Compared to younger children, adolescents are experiencing a process of individuation and rely more on internal emotion regulation strategies, rather than being regulated by parents (19, 20). A combination of rapid development and increased social and emotional demands makes adolescence a time of heightened emotional intensity, reactivity, and fluctuations. This means that adolescence could be considered a time that places extra demands on emotion regulation (21).

A current body of evidence suggests links between disruptions in emotion regulation and psychopathology in adolescents, even if results are mixed [for a review, see Young et al. (21)]. A meta-analysis (22) found that emotion regulation strategies had negative associations with anxiety and depression, while maladaptive emotion regulation had positive associations. Recently, Gonçalves et al. (23) determined that difficulties in emotion regulation in early adolescence predicted depressive symptoms both cross-sectionally and over time. Thus, it can be suggested that increasing the capacity of adaptive emotion regulation might be an important focus for both preventive and therapeutic interventions (e.g. 22, 24, 25).

There are several studies on the topic of emotion regulation and psychological treatment. Emotion regulation group therapy has been found to reduce dysregulated emotions in adults (26). This approach has also been tested as an internet-based treatment targeting adolescents suffering from deliberate self-harm tendencies with promising results regarding improvement in emotion regulation (27). Suveg et al. (28) found that cognitive behavioral therapy (CBT) had limited effects on emotion dysregulation in the treatment of anxious youths. Emotion dysregulation decreased in relation to worry, but not in relation to feelings of anger or sadness. Recently, an internet-based psychodynamic treatment targeting adolescent depression resulted in large improvements ($d$ = 0.92) in emotion dysregulation compared to a control condition (9). Several trials have also investigated emotion regulation as a predictor of outcome for CBT, rendering mixed results. Siegle, Carter, and Thase (29) found that depressed patients who exhibit deficits in emotion regulation may benefit more from CBT. This finding was corroborated by Niles et al. (30) for patients treated for social anxiety disorder. However, Nielsen et al. (31) found no evidence that emotion regulation at baseline predicted the rate of change among patients receiving group-delivered CBT for anxiety.

Several studies have found links between increased capacity for emotion regulation and improvement in depressive symptoms across treatments. Sauer-Zavala et al. (32) determined (using the Unified Protocol for the treatment for mixed emotional disorders) that changes in frequency of and reactivity to negative emotions, as well as awareness and acceptance of emotions, were related to change in depression. Increased capacity for emotion regulation predicted reductions in depressive symptoms through Affect Regulation Training (33) and CBT group treatment (34). Increased capacity for emotion regulation also had a mediating effect in an internet-based intervention for adolescents suffering from non-suicidal self-injury (27)

Even though the majority of research on the role of emotion regulation in psychological treatment has been conducted on treatments stemming from a CBT framework, emotion regulation has a prominent role in psychodynamic theory as well. The experiential-dynamic emotion-regulation model is grounded in both psychodynamic theory and affective neuroscience. It postulates that difficulties in emotion regulation either stem from dysregulated anxiety that has become a conditioned response to primary, adaptive feelings, and/or secondary, maladaptive emotions, which are products from defensive maneuvers (i.e. experiential avoidance) (35). According to psychodynamic theory, adaptive feelings can become conditioned to anxiety (fear of emotions) when they have been perceived as threatening to attachment relationships (36). This can happen when emotional expressions are dismissed, met with anger or leads to detachment from the significant other. These emotions will then be avoided through defensive maneuvers. Defenses solve the acute problem by repressing the emotions. However, in the long run they inhibit more adaptive ways of regulating and expressing one's emotions and may therefore create and perpetuate symptoms of depression and/or anxiety (37).

To the best of our knowledge, no prior studies have investigated emotion regulation as a time-invariant or time-varying predictor of change in psychodynamic treatments. Thus, the primary aim of the present study was to investigate whether entry levels of emotion regulation deficits would predict the rate of change in the treatment of adolescent depression. A second aim was to evaluate whether changes in emotion regulation during treatment could predict future change in depression using a time lagged model.

# METHOD

## Setting

Data from the present study were collected in the ERiCA-project, which evaluated internet-based treatment for adolescent depression and was conducted by Stockholm University in close collaboration with Linköping University. The trial was approved by the Regional Ethics Board of Stockholm, Sweden (number: 2018/2268-31/5). Participants submitted written informed consent via the online treatment platform and received treatment at no cost. The International Standard Randomized Controlled Trial Number (ISRCTN) registration ID is 16206254.

## Recruitment and Participants

Recruitment took place during January and February of 2019. Participants were recruited through social media, schools, youth centers, and from youth mental health care providers. Participants were required to be between 15 and 18 years of age, and had to fulfill a diagnosis of MDD according to the DSM-5 (38). This diagnosis resulted from an assessment using the MINI International Neuropsychiatric Interview [MINI 7.0 (39)] and by scoring ≥10 points on the Quick Inventory of Depressive Symptomatology—Adolescent Self-Rated Version [QIDS-A17-SR (40)]. The diagnosis of MDD had to be the primary diagnosis. Exclusion criteria included prior suicide attempts and/or substantial suicidality (i.e. intent and/or plans to commit suicide expressed during intake interview or on screening forms), ongoing psychotropic medication that was not stable ≥ 3 months, and partaking in other psychological treatments. Furthermore, participants fulfilling any of the following diagnoses were also excluded: any psychotic disorder, bipolar I/II disorder, antisocial personality disorder, autism-spectrum disorder, or any substance use disorder. In the original trial, 76 adolescents were randomized, of whom 4 never entered treatment after randomization and 5 never entered treatment after being in the control group. Accordingly, the sample in the present study (n = 67) only consisted of adolescents entering treatment, including participants who were crossed over to treatment after the initial allocation to the control group. Patients' demographics are presented in **Table 1**.

**TABLE 1** | Demographic data[a].

| | IPDT (n = 67) | |
|---|---|---|
| | n/M | %/SD |
| Female | 55 | 82.1 |
| Gender identity uncertain/other | 3 | 4.5 |
| Age | 16.63 | 1.10 |
| Major depressive disorder[b] | 67 | 100 |
| Any anxiety disorder[b] | 40 | 59.7 |
| PTSD[bc] | 4 | 6.0 |
| Eating disorder[bd] | 3 | 4.5 |
| Antidepressant medication | 4 | 6.0 |
| QIDS-A17-SR pretreatment | 14.56 | 4.37 |

*IPDT, Internet-based psychodynamic therapy; QIDS-A17-SR, quick inventory of depressive symptomatology adolescent version. [a]Diagnostic assessment was conducted at baseline for the main RCT, [b]Confirmed by the MINI-International Neuropsychiatric Interview. [c]Posttraumatic stress syndrome. [c]Bulimia nervosa/Binge-eating disorder.*

## Instruments

Eligible participants were contacted via phone to conduct the MINI 7.0 (39) to establish psychiatric diagnoses. The MINI 7.0 was slightly altered by adding the irritability criterion to the depression module as well as the separation anxiety module from the MINI for Children and Adolescents (MINI KID). We also replaced the section assessing suicidality with the Columbia-Suicide Severity Rating Scale [C-SSRS (41)]. The C-SSRS was chosen because it is more easily administered and is recommended for use in clinical trials by the United States Food and Drug Administration (42). The MINI and C-SSRS were conducted by experienced registered clinical psychologists (n = 3) from the research team, in addition to students from the clinical psychology master's program (n = 3) who received a full day of training in both instruments.

In the present study, two self-rated instruments were used for the analysis. Both were administered weekly as well as pre- and post-treatment via a secure internet platform. The primary outcome measure was QIDS-A17-SR, a reliable measure of depressive symptoms that has been found valid for both adult and adolescent populations (40, 43). Lindqvist et al. (9) reported an average Cronbach's alpha across all time points of $\alpha$ = .76 (range:.71–.85), suggesting acceptable internal consistency in the present sample. The Difficulties in Emotion Regulation Scale [DERS-16 (44)] was used as a measure of the capacity for emotion regulation. The original 36-item version of DERS is a comprehensive measure of emotion dysregulation encompassing six distinct (although related) dimensions of emotion regulation. These dimensions are lack of awareness, clarity of emotions, difficulties in controlling impulsive behavior, non-acceptance of emotions, engaging in goal-directed behaviors when distressed, and limited access to emotion regulation techniques that are perceived as effective (45). The DERS-16 is a short form, developed from the original DERS, measuring overall capacity for emotion regulation. Items from all subscales (except for lack of emotional awareness) have been retained in DERS-16. It should be noted that analyses have suggested only minor differences in convergent and discriminant validity between the scales (44). For the present study, DERS-16 was chosen over the original scale as its brevity allows for weekly measurement of emotion regulation. Lindqvist et al. (9) reported good internal consistency ($\alpha$ = .89) in the present sample.

## Intervention

The IPDT was eight weeks long and consisted of eight weekly-administered self-help modules consisting of texts, videos, and exercises (9). Exercises were reported on the platform and all

participants received weekly messages with feedback from their therapist. To reduce attrition and increase motivation, the intervention also contained a weekly 30-minute synchronous text chat session between therapist and participant. Due to limited resources, only the first group of patients (n = 34) received chat sessions. The remainder (n = 33) received the same treatment but without additional synchronous chat sessions. All communications between participants and their therapists were conducted through an encrypted online platform (46).

The treatment presents the possibility of inner, emotional conflicts triggering and maintaining symptoms of depression. The participants are introduced to theory about emotions and how and why they can be repressed with defenses. Through the treatment program participants learn to differentiate between different bodily symptoms of anxiety and how to regulate emotions and anxiety without using maladaptive defenses. This is done by enhancing their capacity for self-observation through acquired bodily awareness and by learning to observe their own emotional reactions, especially in relation to others. Furthermore, participants are encouraged to experience and express emotions that have been previously warded off. This gradual exposure will lead to the emotions being uncoupled from anxiety, and the use of maladaptive emotion regulation strategies (i.e. defenses) will no longer be needed.

## Statistical Analysis

The study used all available data on participants entering treatment (n = 67). The original outcome study (9) presents the main findings from the RCT. Data in the present study were analyzed based on all patients entering treatment, regardless of whether they dropped out (i.e. intent to treat). Growth curves were estimated using all available data. Model building started with estimating a basic time model including random intercepts and slopes for time. To account for possible non-linearity in the data a quadratic term ($TIME \times TIME$) and a cubic term ($TIME \times TIME \times TIME$) for time were tested and discarded as neither reached significance or improved model fit. All models were analyzed with full maximum likelihood and all statistical analyses were conducted using SPSS v.26 (IBM Corp., Armonk, NY).

### DERS-16 as a Time-Invariant Predictor

In this model, we analyzed whether pretreatment difficulties in emotion regulation predict within-group changes in the outcome variable during treatment. Within-group effect sizes were calculated using model estimated differences in pre- and postmeans and the observed pretreatment standard deviation, as recommended by Feingold (47).

A series of multilevel models of the trajectories of the QIDS-A17-SR were tested. First, an unconditional growth model was estimated to examine the average growth over time in treatment, represented by the following equations:

Level 1:

$$QIDS - A17 - SR_{it} = \beta_{0i} + \beta_{1i}(TIME_t) + \epsilon_{it}$$

Here, $QIDS - A17 - SR_{it}$ represents the depression score for individual $i$ at time $t$; $\beta_{0i}$ represents the intercept for individual $i$ at time 0 (i.e. at baseline); $\beta_{1i}$ represents the linear rate of growth for individual $i$ across each time point; and $\epsilon_{it}$ is the error term indicating the deviation of individual *i's* score from their own estimated regression line at each time point *(t)*.

Level 2:

$$\beta_{0i} = \gamma_{00} + u_{0i}$$

$$\beta_{1i} = \gamma_{10} + u_{1i}$$

Here, each individual's intercept, $\beta_{0i}$, is modeled as the grand mean of all individuals' scores at Time 0 ($\gamma_{00}$), plus each individual's deviation from that grand mean at time 0 ($u_{0i}$). Term $\beta_{1i}$ represents the linear rate of growth across all time points for each individual, $\gamma_{10}$ represents the average rate of change for all individuals across all time points, and $u_{1i}$ represents each individual's growth parameter deviation from that average.

Next, a conditional growth model was estimated to examine whether between-person differences in change over time were affected by initial levels of emotion dysregulation (DERS-16). Thus, equations on Level 2 are changed accordingly for the conditional model (while the equation on Level 1 is identical to the previous equation):

$$\beta_{0i} = \gamma_{00} + \gamma_{01}(DERS - 16) + u_{0i}$$

$$\beta_{1i} = \gamma_{10} + \gamma_{11}(DERS - 16) + u_{1i}$$

To assess the effect of DERS-16 scores on the individual intercept, $\gamma_{00}$ is the grand mean at time 0, $\gamma_{01}$ is the contribution of DERS-16 to the intercept value, and $u_{0i}$ represents each individual's deviation from the modeled intercept value. The second equation estimates the extent to which DERS-16 scores affect the rate of change in QIDS-A17-SR. Term $\gamma_{10}$ represents the average rate of change for all individuals across all time points, $\gamma_{11}$ depicts the influence of DERS-16 scores on the rate of change, and $u_{1i}$ represents each individual's growth parameter deviation from the estimated slope. Level 1 residuals were assumed independent and identically distributed. At Level 2, we used an unstructured covariance structure, allowing intercept and slope to correlate. As a post-hoc test, to control for potential confounders, gender and a centered variable measuring adherence to the treatment program (i.e. number of modules opened) were added in interaction with Time.

### DERS-16 as a Time-Varying Predictor in IPDT

To investigate whether within-person change in DERS-16 predicted change in depression the following week, we employed linear mixed effects modeling to analyze individual change over time (48). The time-lagged effects of DERS-16 scores on depression were analyzed as follows: the effect of DERS-16 the week before (time point t −1) was used to predict QIDS-A17-SR the following week (time point t). Patients providing at least one complete data point for both DERS-16 and the subsequent QIDS-A17-SR contributed to the models.

To separate within- and between-person effects, DERS-16 was divided into two predictors. The first predictor was a time-invariant variable consisting of the individual's total mean of all DERS-16 scores across all time points, from which the grand mean of all individual's DERS-16 scores during the entire treatment was subtracted. In other words, this predictor illustrates the difference between individuals on the pooled DERS-16 scores across all

assessment points (i.e. the grand mean centered between-person effect on DERS-16). The second predictor was calculated by subtracting each individual's mean DERS-16 value over all time points from their DERS-16 value at each time point. This within predictor, a so-called time-varying person-mean centered variable, was calculated to account for the within-person effect of DERS-16 scores on depression.

As a final step in the analysis, we included fixed and random effects of time in the model to control for general effects of time. Due to the autoregressive nature of the time series data, we used the first order autoregressive (AR[1]) structure for the within-person residuals in all analyses. On the between-person level, an unstructured covariance structure was chosen, which allowed intercept and slopes to correlate. The final analysis is illustrated using the following equation:

Level 1

$$QIDS-A17-SR_{it} = \beta_{00i} + \beta_{10}\left(DERS-16_{it-1} - \overline{DERS-16}_i\right) + \beta_{20i}(TIME_t) + \epsilon_{it}$$

Here, $QIDS-A17-SR_{it}$ is the individual's depression score at time point t. The equation also illustrates fixed effects on intercept ($\beta_{00i}$) and the fixed within-person effect of DERS-16 on QIDS-A17-SR the following week, i.e. the time lagged effect of person-mean centered DERS-16 $[\beta_{10}(DERS-16_{it-1} - \overline{DERS-16}_i)]$. Furthermore, this includes the fixed effect of time $\beta_{20i}$ on QIDS-A17-SR and $\epsilon_{it}$ represents the deviation of individual's *(i)* score from their own modeled line at each time point *(t)*.

Level 2

$$\beta_{00i} = \gamma_{00} + \gamma_{01}\left(\overline{DERS-16}_i - \overline{\text{DERS}-16}\right) + u_{0i}$$

$$\beta_{10} = \gamma_{10}$$

$$\beta_{20i} = \gamma_{20} + u_{1i}$$

Level 2 also includes random intercepts ($\beta_{00i}$), as illustrated in the first equation. Here, $\gamma_{00}$ is the grand mean at time 0, $\gamma_{01}(\overline{DERS-16}_i - \overline{\text{DERS}-16})$ is the between-person (grand mean centered) effect of DERS-16 on the intercept value, and $u_{0i}$ represents each individual's deviation from the modeled intercept value. $\gamma_{10}$ represents the fixed, time lagged effect of person-mean centered DERS-16.

This level also contains random slopes, as illustrated in the third equation. Here, $\beta_{20i}$ represents the linear rate of growth across all time points for each individual, $\gamma_{20}$ represents the average rate of change for all individuals across all time points and $u_{1i}$ represents each individual's growth parameter deviation from that average. As a post-hoc test, to control for potential confounders, gender and a centered variable measuring adherence to the treatment program (i.e. number of modules opened) were added in interaction with the lagged DERS-16.

### The Effect Sizes of DERS-16 as a Time-Invariant and Time-Varying Predictor

To make the results more easily interpretable, we also estimated pseudo-$R^2$, i.e. the proportion of residual variance explained by the within-person changes in DERS-16 (48). For DERS-16 as a time-varying predictor, pseudo-$R^2$ was calculated by dividing the difference in residual variance between models (with and without the within-person effects of DERS-16) by the residual variance from the model without the within-person predictor. However, in the calculations of DERS-16 as a time-invariant predictor, the residual variance actually increased when adding the predictor, resulting in negative explained variance. While this is a known phenomenon (49), it basically renders pseudo-$R^2$ uninterpretable; hence, we choose not to present the result.

## RESULTS

### Adherence and Attrition

The average participant opened 6.6 treatment modules (SD = 2.31), 64.2% (n = 43) opened all modules, 83.6% (n = 56) opened more than half, and 6% (n = 4) terminated treatment prematurely. **Table 2** presents observed values for QIDS-A17-SR and DERS-16 across treatment.

### Effects of Treatment

Results from the unconditional growth model for QIDS-A17-SR indicated that there was significant variance in the intercept (symptom level at baseline: 13.01, $p$ <.001) and in the slope (rate of decrease in QIDS-A17-SR scores over time: 0.15, $p$ <.001). This significant variance implies it might be worthwhile investigating possible predictors of change to further our understanding of treatment effects. The mean QIDS-A17-SR trajectory was estimated to start at 14.42 (at baseline) and the estimated average decrease was −0.46 per week in treatment. The effect size (Cohen's *d*), pre to post, for the treatment was 0.92, 95% CI [0.68, 1.16]. The correlation between intercept and slope was −0.16, indicating that patients starting with higher baseline scores on QIDS-A17-SR experienced a steeper decline of depressive symptomatology. While the correlation was statistically non-significant ($p$ = .559), we chose to retain the unstructured covariance structure to control for regression to the mean in the conditional growth model.

### Effects of Pretreatment Difficulties in Emotion Regulation on Outcome

In a conditional growth model, DERS-16 was added at Level 2 as a time-invariant predictor in interaction with intercept and with time. The $DERS-16 \times TIME$ interaction was statistically significant ($p$ = .041), indicating that relatively higher pretreatment DERS-16 scores significantly predicted increased growth rate in QIDS-A17-SR during treatment. Adding Gender in interaction with time did not reach statistical significance ($p$ = .88) and was dropped from the analysis. Adding centered adherence (modules opened) in interaction with time did reach statistical significance ($p$ = .04), indicating that participants taking part of more of the treatment material had larger effects. However, this did not affect the effects of pretreatment scores on DERS-16 on QIDS-A17-SR growth rates and was thus dropped from the analysis.

For more numerical details, see **Table 3**. **Figure 1** illustrates the different rates of growth in depression in patients presenting relatively high (+1 SD), average and relatively low scores (−1 SD) in the present sample on DERS-16.

**TABLE 2 |** Observed means, standard deviations, and number of observations for outcome and processes over the treatment period.

| Measure | Week | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| QIDS-A17-SR | | | | | | | | | | |
| *M* | 14.40 | 14.28 | 13.55 | 12.89 | 12.13 | 11.78 | 11.94 | 11.60 | 10.59 | 9.46 |
| *SD* | 4.52 | 4.08 | 4.6 | 4.52 | 4.14 | 4.20 | 4.31 | 4.60 | 5.02 | 4.98 |
| *n* | 67 | 67 | 65 | 57 | 55 | 55 | 50 | 55 | 46 | 59 |
| DERS-16 | | | | | | | | | | |
| *M* | 55.3 | 54.55 | 55.14 | 53.18 | 51.33 | 50.02 | 48.40 | 45.73 | 44.82 | 41.02 |
| *SD* | 11.73 | 12.55 | 12.13 | 11.66 | 11.84 | 12.26 | 11.62 | 12.27 | 13.86 | 14.21 |
| *n* | 67 | 67 | 65 | 57 | 55 | 55 | 50 | 55 | 45 | 57 |

*QIDS-A17-SR, quick inventory of depressive symptomatology adolescent self-rated version; DERS-16, difficulties in emotion regulation scale brief version.*

**TABLE 3 |** Effects of baseline scores of DERS-16 on rate of change in QIDS-A17-SR: parameter estimates, standard errors, 95% confidence intervals, and p-values (n = 67).

| Model estimates | Estimate *(SE)* | 95% CI | *P* value |
|---|---|---|---|
| **Fixed effects** | | | |
| $\gamma_{00}$ (model intercept) | 14.38 (0.38) | 13.60, 15.15 | <.001 |
| $\gamma_{01}$ (effect of grand mean centered DERS-16 on model intercept) | 0.20 (0.03) | 0.13, 0.27 | <.001 |
| $\gamma_{10}$ *(effects of time on outcome)* | –0.46 (0.06) | –0.58, –0.36 | <.001 |
| $\gamma_{11}$ (effect of DERS-16 on rate of change) | –0.01(0.00) | –0.02, –0.00 | .041 |
| **Random effects** | | | |
| $u_{0i}$ (variance intercept) | 7.79 (1.71) | 4.97, 12.21 | <.001 |
| $u_{1i}$ (variance slopes) | 0.14 (0.04) | 0.08, 0.25 | <.001 |
| Correlation between intercept and slope | –0.16 (0.21) | –0.25, 0.52 | .45 |
| $\epsilon_{it}$ (Residual variance) | 6.07 (0.41) | 5.32, 6.93 | <.001 |

*QIDS-A17-SR, quick inventory of depressive symptomatology adolescent self-rated version; DERS-16, difficulties in emotion regulation scale brief version.*

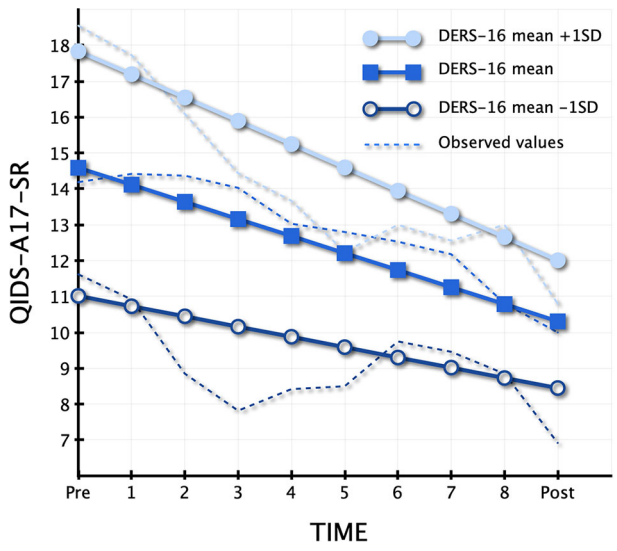


**FIGURE 1 |** Different trajectories of change depending on baseline value on Difficulties in Emotion Regulation Scale (DERS-16).

## Effects of Intraindividual Changes in Difficulties in Emotion Regulation on Outcome

Results from linear mixed effects models, examining within-person effects of DERS-16 on QIDS-A17-SR the following week, are presented in **Table 4**. The within-person effects of DERS-16 were significant through all analyses, even when controlling for effects of time (i.e. detrending). The time-lagged relationship was in the expected direction, meaning that lower scores on DERS-16 predicted lower scores on QIDS-A17-SR the subsequent week.

First, we estimated a model with fixed between- and within-person effects of DERS-16 without controlling for the effect of time. This model estimated a significant effect of within-person DERS-16, where a 1-point reduction in DERS-16 predicted a reduction of 0.11 points in QIDS-A17-SR the following week ($\gamma_{10}$ = 0.11; SE = 0.02; 95% CI [0.07 to 0.14]). Using the formula for pseudo-$R^2$, the added within-person effects of DERS-16 explained 41.23% of the variance in QIDS-A-17 the following week, which implies that approximately 41% of the change in QIDS-A17-SR stems from within-person changes in DERS-16.

In the final detrended model, controlling for the effect of time, the estimate of the time-lagged within-person DERS-16 was substantially lower, which was as expected. The parameter estimate for the within-person effect of DERS-16 indicates that a reduction of 1 point in DERS-16 predicted a reduction of 0.07 points in QIDS-A17-SR the following week. To illustrate this effect and make it more interpretable, we calculated pseudo-$R^2$: 8.70% of the variance in QIDS-A17-SR could be attributed to within-person changes of DERS-16.

Adding gender in interaction with lagged DERS-16 did not reach significance ($p$ = .35) and it was therefore dropped. However, centered treatment adherence (number of modules opened) in interaction with the lagged DERS-16 did reach significance ($p$ = .005), indicating that for each module opened during the entirety of the treatment, the effect of lagged DERS-16 on the following week QIDS-A17-SR increased by 0.03 points.

# DISCUSSION

The aim of the present study was to evaluate the role of emotion regulation, as measured by DERS-16, in IPDT for adolescent

**TABLE 4 |** Within-person effects of DERS-16 on QIDS-A17-SR: parameter estimates, standard errors, 95% confidence intervals, and p values (n = 67).

| | DERS-16 on QIDS-A17-SR (without controlling for time) | | | DERS-16 on QIDS-A17-SR (when controlling for time) | | |
|---|---|---|---|---|---|---|
| | **Estimates (*SE*)** | **95% CI** | **p-value** | **Estimates (*SE*)** | **95% CI** | **p-value** |
| **Fixed effects** | | | | | | |
| $\gamma_{00}$ (model intercept) | 12.15 (0.39) | 11.38, 12.93 | <.001 | 13.90 (0.39) | 13.12, 14.68 | <.001 |
| $\gamma_{10}$ (within-person effect, lagged process on outcome) | 0.11 (0.02) | 0.07, 0.14 | <.001 | 0.07 (0.02) | 0.03, 0.10 | <.001 |
| $\gamma_{20}$ (effect of time on outcome) | N/A | N/A | N/A | −0.39 (0.06) | −0.52, −0.27 | <.001 |
| $\gamma_{01}$ (between-person effect on outcome) | 0.26 (0.04) | 0.18, 0.33 | <.001 | 0.25 (0.03) | 0.18, 0.32 | <.001 |
| **Random effects** | | | | | | |
| $u_{0i}$ (variance intercept) | 7.64 (0.67) | 6.43, 9.07 | <.001 | 4.94 (1.78) | 2.44, 10.00 | <.01 |
| $u_{2i}$ (variance slopes for time) | N/A | N/A | N/A | 0.06 (0.05) | 0.01, 0.29 | .24 |
| Correlation intercept and slopes | N/A | N/A | N/A | 0.68 (0.66) | −0.91, 1.00 | .30 |
| $\epsilon_{it}$ (residual variance) | 8.29 | | | 6.19 | | |
| *Pseudo-*$R^2$ (explained variance) | 41.23% | | | 8.70% | | |

*Note. QIDS-A17-SR, quick inventory of depressive symptomatology adolescent self-rated; DERS-16, difficulties in emotion regulation scale brief version.*

depression. Emotion regulation was investigated as both a time-invariant and time-varying predictor of change in depression. Our findings suggest that emotion regulation indeed plays an important role in the treatment of adolescent depression with IPDT. Emotion regulation measured at baseline affected the rate of change in depression, where patients exhibiting more dysregulated affects made somewhat larger gains from treatment. Furthermore, our analyses imply that an increased capacity for emotion regulation might act as a mechanism of change in IPDT as within-person changes in emotion regulation during treatment predicted change in depression the following week.

The findings on emotion regulation as a baseline predictor imply that patients entering treatment with relatively larger deficits in emotion regulation benefit somewhat more from IPDT than patients with relatively less dysregulated emotions. Our results are in agreement with prior studies conducted on CBT (29, 30), suggesting that larger deficits in emotion regulation predict better treatment responses.

Our findings that intraindividual changes in emotion regulation predict outcome are in agreement with research on emotion-focused CBT (32), traditional CBT (34), and Affect Regulation Training (33), where increased emotion regulation has been shown to act as a potential mechanism of change. In fact, results from Berking et al. (33) suggest that increased capacity for emotion regulation might act as a common mechanism of change for treatments targeting depression, albeit with different theoretical underpinnings. This finding is corroborated by the present study.

The present study elucidates the process of change in the treatment of adolescent depression and presents an increased capacity for emotion regulation as a possible mechanism of change in IPDT. This raises the question whether this is also the case in experiential dynamic therapies (EDTs) in general. The model of psychopathology in IPDT is clearly based on psychodynamic principles (9). The treatment relies heavily on working with dysregulating defenses (i.e. unconscious strategies leading to experiential avoidance), while also targeting dysregulated anxiety through an increased capacity for self-observation and bodily awareness. These aims are often described as core elements in EDTs (50). This focus might be a possible explanation for our finding that greater difficulties in emotion regulation at baseline predicted treatment response. The treatment might target problems that are more relevant to young persons with relatively more severe emotion regulation problems, whilst depressed adolescents with less problems with emotion regulation would be helped more by interventions targeting other difficulties. Targeting emotion regulation might be particularly important in the treatment of young people as they are in a gradual process of learning to rely more on internal emotion regulation strategies, rather than depending on being regulated by significant others (19, 20). This is an area for future research. Further studies should also investigate if these results also apply to face-to-face PDT in the treatment of adolescent depression.

Another reason to look into further possible mechanisms of change in IPDT is the fact that increased intraindividual capacity for emotion regulation only predicted roughly 9% of variance in the outcome (after detrending, i.e. controlling for general effects of time). This implies there are probably several mechanisms of change yet to be empirically tested. Further studies on IPDT should investigate other theoretically sound concepts (i.e. mentalization, insight, and self-compassion) as mechanisms of change. Furthermore, future research should focus on investigating whether it is treatment components, common factors, or a combination of both that facilitate change in emotion regulation.

Because more difficulties in emotion regulation correlated with more severe depression, this could raise concerns about whether the extent of the effect of baseline emotion regulation on rate of change in depressive symptoms could merely be an effect of regression to the mean. However, by allowing intercept and slope to correlate, we controlled for the possible effect of regression to the mean.

Detrending of data to control for time is a debated subject in the context of analyses of within-person effects. On the one hand, this is an experimental study where we assume that changes in both emotion regulation and depression are caused by our experimental manipulation, i.e. the treatment. Detrending removes the effect of treatment, meaning that we actually risk

removing at least some of the effects we intended to study (51). On the other hand, since the current study only presents results for participants in treatment and not a control group, it could be argued that both effects are to some extent unrelated to treatment but caused merely by the passage of time (i.e. spontaneous remission). In this case, detrending for time would be necessary. Lindqvist et al. (9) showed that the treatment had large effects on both depressive symptoms and emotion regulation compared to a control condition ($d$ = 0.82 and $d$ = 0.97, respectively), rendering this explanation unlikely. However, one cannot be completely certain that there are no confounders associated with the time-trends in the data (52). This is why we chose to present results both with and without detrending. To explain this in relation to our results, the effect of intraindividual changes in DERS-16 remained significant (even when detrending for time), which strengthens claims for causality. However, it is also possible that the detrending leads to an underestimation of the effects of emotion regulation on depression.

## Strengths and Limitations

An apparent strength of the study is the multilevel framework, enabling us to separate within-and between-person variances, meaning that we could investigate effects on both the within- and between-person levels as well as make use of all available data. Weekly measurements of both predictor and outcome variables allowed us to investigate relationships between emotion regulation and depression over time in treatment, strengthening claims of causality.

One limitation of the study is the lack of a control group and random allocation. It could be argued that this prevents us from attributing the change process to the actual treatment. The significant, time-lagged and detrended results strengthens claims of causality, but it is still possible that confounders influenced our results and that this effect would have been seen in any remission from depression regardless of treatment. On the other hand, the treatment material and study therapists address many of the causes, as assumed in EDT, underlying emotion dysregulation (50). Furthermore, the post-hoc analysis indicating that participants who read more of the material had larger effects of emotion regulation on depression the following week strengthens the proposed pathway of treatment enhancing capacity for emotion regulation. Further research should be done comparing the processes in IPDT to control conditions and/or different internet-based treatments and their respective impact on depression through enhanced emotion regulation.

A higher frequency of assessments during treatment could have furthered our knowledge about the temporal relationships between emotion regulation and depression. In addition, the study only included one time-varying predictor measured weekly during treatment.

A final limitation worth mentioning is the relatively small sample size, possibly limiting the generalizability of the findings as well as making the estimates less precise. The present study should be replicated to establish increased emotion regulation as a mechanism of change in IPDT. As the present study investigates the role of emotion regulation in IPDT it is unclear to what extent the results can be generalized to the psychotherapeutic process in face-to-face PDTs.

## Conclusions

The results of the present study highlight the importance of emotion regulation as both a time-invariant and time-varying predictor of change in symptoms of depression in IPDT. The results imply that depressed patients expressing relatively higher degrees of dysregulated affect at intake experience larger treatment effects in IPDT. Also, an improved capacity for emotion regulation, presumably acquired through treatment, precedes improvement in depression. The effect of intraindividual changes in emotion regulation is in accordance with theory in EDTs. This theory postulates that recognizing and relinquishing defenses and regulating anxiety should lead to less dysregulated affective states and greater access to underlying adaptive emotions which in turn leads to symptom reduction. Further studies are needed to confirm these results, preferably on both IPDT and PDT delivered face-to-face.

# DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because participants are mostly minors and it contains sensitive data. Therefore, the dataset is available on reasonable requests as deemed by the principal investigator of the study. Requests to access the datasets should be directed to BP, bjorn.philips@psychology.su.se.

# ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Regional Ethics Board of Stockholm, Sweden (number: 2018/2268-31/5). Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

# AUTHOR CONTRIBUTIONS

All authors contributed to the article and approved the submitted version. JM, KL, and FF conducted the statistical analysis. JM and KL drafted the first version of the text while FF, GA, BP, and PC provided feedback and reviewed and revised the manuscript.

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# Psychological Mediators of the Association Between Childhood Emotional Abuse and Depression: A Systematic Review

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**Background:** A number of existing meta-analyses and narrative reviews have already addressed the relation between childhood adversity and depression, yet none of them has examined the specific link between emotional abuse and depression highlighted by previous research. It is no longer appropriate to regard childhood maltreatment as a unitary concept when considering its effects on subsequent depression; instead, subtypes of childhood maltreatment need to be scrutinized separately. This review addresses this significant gap by critically evaluating empirical studies examining psychological mediators of the relationship between childhood emotional abuse and subsequent depression.

**Methods:** A systematic search of nine electronic databases was conducted to identify eligible studies published in English between January 1980 and January 2020. Given the heterogeneous outcomes of eligible studies and the inconsistent reporting of indirect effects, a narrative synthesis, rather than a quantitative meta-analysis, was conducted. An appraisal of methodological quality was also included.

**Results:** We identified 34 papers, comprising 18,529 adults and 3,434 adolescents, including 888 clinical participants. Our synthesis suggests that studies on mediators in the emotional abuse–depression link have focused on five clusters of intervening variables: early maladaptive schemas, cognitive-personality variables, emotion dysregulation, interpersonal styles, and stressful negative events. Only 11 studies identified the unique contribution of emotional abuse to depression by controlling for other forms of childhood maltreatment.

**Conclusions:** Our findings support several routes with relative consistency (e.g., early maladaptive schemas, hopelessness, negative cognitive styles, brooding rumination, overall emotion dysregulation). Because psychological mediators function as a complex interrelated system, controlling for the interrelation between them is important. The evidence for the purported mediating role of the factors identified in this review should be considered with caution given the relative dearth of large-scale, adequately powered

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longitudinal studies. This review proposes a comprehensive multilevel theoretical framework as a basis for future research.

**Keywords: depression, emotional abuse, child maltreatment, psychological mechanisms, mediator, early maladaptive schemas, cognitive-personality variables, emotion dysregulation**

## INTRODUCTION

Both cross-sectional retrospective studies (1–3) and longitudinal studies (4–6) have provided evidence for the role of childhood maltreatment as a precursor to depression. Systematic reviews and meta-analyses (7–9) have consistently found childhood maltreatment to be strongly associated with clinical depression across the life course, an elevated risk of recurrent and persistent depressive episodes, and a lack of response or remission during treatment. In a recent meta-analysis of 184 studies totaling 255 effect sizes, maltreated individuals were found to be 2.66–3.73 times more likely to develop depression in adulthood, had an earlier onset of depression, and were twice more likely to develop chronic or treatment-resistant depression (10).

Whereas, the relation between childhood maltreatment and depression has been relatively well-established, much less is known about the relation between specific forms of maltreatment and depression. Historically, the more "obvious" forms of maltreatment, namely sexual and physical abuse, have attracted more attention when considering early adverse experiences associated with an increased risk of adolescent and adult depression (11, 12). Recently, however, researchers have started to examine particular types of childhood maltreatment as risk factors for depression, with an increasing focus on the more "silent" forms of maltreatment, such as emotional abuse. For example, studies have found that experience of parental physical abuse was least strongly associated with depressive symptoms (13), whereas self-reported childhood sexual abuse (14) and a history of emotional abuse have been more consistently associated with a wide range of psychopathology, and depression in particular (15–17). The term "childhood emotional abuse" has been used to describe exposure to spurning, terrorizing, isolating, exploiting or corrupting, and denying emotional responsiveness (18). Experiences of emotional abuse have been associated with powerful and enduring psychological sequelae, including shame, humiliation, anger, and feelings of worthlessness (19).

In a meta-analysis of 124 studies (20), emotional abuse was found to increase the risk of depression by an odds ratio of 3.06, whereas physical abuse increased the risk by an odds ratio of 1.5. In another meta-analysis of 184 studies (10), childhood emotional abuse was found to be most prominently linked to depression severity and was associated with the highest increase in the likelihood of depression in adulthood among all types of maltreatment. In addition, given that emotional abuse occurs in 90% of cases where the child is also physically or sexually abused and often precedes and persists beyond physical and sexual forms of abuse, it may be that the lasting psychological impact of different forms of abuse is largely explained by emotional abuse implicated in all forms of abuse (21). Although studies indicate that emotional abuse may play a key role in vulnerability for depression, emotional abuse is comparatively elusive, and its more "covert" nature often leads researchers and practitioners to focus on other more "tangible" forms of maltreatment in studying and treating depression (22, 23).

Relatively less is currently known about the potential psychological mechanisms linking emotional abuse and depression. Indeed, given that the time between exposure to abuse and onset of depression might be years or even decades, and that not all children who have experienced emotional abuse will go on to develop depression, the link between childhood emotional abuse and depression in adolescence and adulthood demands further explanation. Recent years have seen a vast increase in the number of studies investigating biological and psychosocial mechanisms addressing this issue (24). Biological mechanisms that have been investigated include genetic (25, 26) and neurobiological factors [e.g., impairments in HPA axis functioning; (27)]. Psychological mechanisms mainly involve maladaptive relationship and thinking styles, such as early maladaptive schemas (28), emotion dysregulation (29), hopelessness (30), insecure attachment styles (31), and interpersonal problems (32). Yet, the literature remains poorly integrated, and thus there is a need for a systematic review that has the potential to support the development of empirically supported models of depression vulnerability and maintenance and provides a platform for ensuring that psychological interventions target the most promising mechanisms, which may lead to improved treatment outcomes.

A number of existing meta-analyses and narrative reviews have already addressed the relation between adversity and depression, yet none of these meta-analyses focused on emotional abuse specifically. Braithwaite et al. (33) conducted a systematic review of longitudinal studies assessing the associations between childhood maltreatment in general and later depression. Interpersonal relationships (31, 34, 35), cognitive vulnerabilities (31, 36), and behavioral difficulties (37, 38) were found to mediate the relation between childhood maltreatment and depression. Hoppen and Chalder (24) conducted a systematic review of 214 studies on biopsychosocial mediating and moderating variables in the relationship between childhood adversity and affective disorders. They identified various psychological and social variables as mediators between childhood adversity in general and affective disorders in adulthood, including emotional dysregulation, attentional biases, psychoform dissociation, attachment anxiety, maladaptive cognitive styles, emotion-focused coping, lack of resilience, low self-esteem, trauma-related guilt, retraumatization, maladaptive personality types, anxious arousal, chronic interpersonal stress, and low social support. Fritz et al. (39) conducted a systematic review of social, emotional, cognitive, and behavioral resilience factors that may reduce the risk of psychopathology in young people

following childhood adversity. They found empirical support for resilience factors at the individual (e.g., high self-esteem, low rumination), family (e.g., high family cohesion, high parental involvement), and community (i.e., high social support) level that may benefit mental health in young people who have experienced childhood adversity. Most recently, Aafjes–van Doorn et al. (40) specifically examined the mediating role of cognitive factors in the relationship between childhood trauma and subsequent adult psychopathology across clinical and non-clinical populations in a systematic review of 98 empirical studies. They found that cognitive factors consistently mediated this relationship, with the vast majority of studies reporting a significant mediation effect (95%; of which 83% was full mediation), regardless of different measures of traumatic experiences, psychopathology, and cognitive mediators. However, as noted, none of these reviews has examined the specific link between emotional abuse and depression highlighted by previous research (10, 20).

As a more hidden and "silent" form of childhood maltreatment, emotional abuse may be difficult to distinguish from dysfunctional parenting in general (41) and is often unrecognized and unrecorded by professionals (and wider systems) as well as laypersons (42). Regardless, empirical studies have suggested that the incidence of emotional abuse in the absence of other forms of maltreatment is more common than often assumed (43, 44). In the U.S. National Child Traumatic Stress Network (NCTSN) Core Data Set (CDS), emotional abuse and neglect were found to be the most prevalent form of maltreatment, where nearly one quarter (24%) of maltreatment cases exclusively involved emotional maltreatment (45, 46). Not only is it the case that different forms of child maltreatment were reported to have equivalent psychiatric effects (47), but the occurrence of emotional abuse was found to be an equivalent or significantly greater predictor of 27 out of 30 negative outcomes compared with the co-occurrence of physical and sexual abuse (43). All of this points to the role that emotional abuse may play as a powerful form of childhood abuse in its own right. Given that emotional abuse constitutes a distinct form of maltreatment; misattributing its pernicious effects to other more "tangible" forms of maltreatment also has important implications for clinical practice (48). It is no longer appropriate to regard childhood maltreatment as a unitary construct; instead, subtypes of childhood maltreatment need to be scrutinized separately as well as in combination.

The current review aims to address this significant gap in the evidence base and provides a systematic review and synthesis of the empirical literature for the proposed psychological mechanisms of the relationship between childhood emotional abuse and subsequent depression, taking into consideration the robustness of the statistical mediation methods employed. Specifically, this review aims to (a) provide a comprehensive systematic review of quantitative studies investigating psychological mediators between childhood emotional abuse and depression in adolescence and in adulthood, and (b) evaluate the quality of the available evidence, including the relative strength of the statistical mediation analysis used to explain the emotional abuse–depression link.

# METHODS

## Search Procedure

The current review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (49, 50). Details of the protocol, including methods of the analyses and inclusion criteria, were specified in advance and documented on PROSPERO (PROSPERO registration: CRD42019127975). A systematic literature search was conducted twice by the first author, the first time in February 2019 when registering the study in PROSPERO, the second time in January 2020 to assure that more recent studies were also included. These two systematic searches identified the same set of 30 empirical studies to be included in this review and four additional studies that were published since the first review (51–54). Nine electronic databases—PsycINFO, Web of Science, MEDLINE, Scopus, and ProQuest (including PTSDpubs database, Health & Medical Collection, Research Library, Science Database, and Social Science Database)—were systematically searched using the following search terms: (depress OR internalizing OR Affective Disorder OR Mood Disorder) AND (emotional abuse OR emotional maltreatment OR verbal abuse OR emotional trauma OR psychological abuse OR child abuse OR child maltreatment). The search terms followed closely those of previously published meta-analyses of the relationship between childhood emotional abuse and depression. As different terms are used to describe mediators or mechanisms in different disciplines, we did not restrict our search to terms relating to psychological mediators. Duplicates were filtered out using EndNote Web. Examination of reference lists of eligible studies and a forward search was carried out in addition to the database search.

## Inclusion and Exclusion Criteria

Eligible studies were original empirical studies that investigated the relationship between childhood emotional abuse and depression and published between 1980 and 2020 in peer-reviewed journals. Eligible designs were cross-sectional, case-control, and prospective cohort (over any time period) studies that had assessed the association between childhood emotional abuse and depression symptoms and/or diagnosis of depression and the effect of one or more psychological mediating mechanisms on this relationship. Both a diagnosis of clinical depression and a continuous measure of depressive symptoms using scales with reported validity and reliability were considered eligible because there is evidence that depression can exist on a continuum of severity, ranging from mild, transient depressed mood states to severe, chronic forms.

Only reports that utilized mediation analysis or another suitable modeling approach to examine whether childhood emotional abuse had an indirect effect on depression outcomes via specific psychological processes were included. Our definition of psychological mechanisms was adapted from that of Harvey and Watkins (55) and considered any aspect of cognition, behavior, affective symptoms, or mood. Studies were regarded as eligible if the measures used to assess the variables under study (emotional abuse, symptoms/diagnoses,

and putative mediating mechanisms) were described as valid and reliable. However, where studies were epidemiological in nature, measures of variables using items created for the study without further additional validation were considered eligible given that population-based studies often employ extensive surveys, necessitating briefer means of assessing each variable of interest.

Participants were adolescents or adults from any background and in any setting, including inpatients. Studies that examined the mediating mechanisms between parental emotional abuse and current depression in a child sample or emotional abuse perpetrated by peers were excluded (56). Studies that used a single item from a validated scale were also excluded, as were studies that calculated the overall effect of childhood maltreatment only and not emotional abuse specifically (57–61). Studies in languages other than English were excluded, as were single-case studies, case series, qualitative studies without a quantitative element, review articles, book chapters, dissertations, discussion papers, non-research letters, editorials, and conference abstracts.

## Data Extraction and Analytic Plan

After the removal of duplicates, paper titles were analyzed by the first author. The majority of articles excluded at this stage had titles referring to either completely unrelated topics or did not meet the inclusion and exclusion criteria listed above. The abstracts of the remaining articles were then screened by the first author. All papers potentially meeting inclusion and exclusion criteria were included for full-text scrutiny. Uncertainties concerning whether a study should be included or excluded were resolved through discussions between the authors. To ensure that relevant papers were not missed, additional screening measures, consisting of conducting a citation search and screening the references of eligible studies, were conducted. The reference lists were manually checked for studies not retrieved via electronic searches.

Information about study design, sample, measures of variables, the statistical analysis used to test mediation, and outcomes of interest was extracted and integrated by using a narrative integration approach structured around the type of mediator examined (see **Table 1**). Given the heterogeneous outcomes of eligible studies (i.e., in terms of psychological mediators, adolescent and adult depression symptoms or diagnoses) and the inconsistent reporting of indirect effects, a narrative synthesis, rather than a quantitative meta-analysis, was conducted. Some studies did report model-related fit indices for mediation (e.g., Root Mean Square Error of Approximation) but the majority of the studies did not report mediator-related effect sizes. Hence, statistical comparison of effect sizes was not feasible.

In the present review, we grouped studies according to five types of psychological mediators in the emotional abuse–depression link: these were early maladaptive schemas, cognitive-personality variables, emotion dysregulation, interpersonal styles, and stressful negative events. These five types of mediating variables are neither necessarily independent nor mutually exclusive, but we considered them separately. In the Discussion we discuss to what extent these potential mediators might be hierarchically organized.

## Quality Assessment

The first author independently evaluated study quality. Uncertainties concerning study quality were resolved through discussions between the authors. Following methodological recommendations from PRISMA (49), a component approach to quality assessment was employed. The quality of eligible papers was assessed using the Effective Public Health Practice Project tool [EPHPP; (86)] adapted to enable assessment of the specific methodological features of the primary studies pertinent to the research question under scrutiny. Our quality assessment considered the following four domains: (a) selection bias, (b) study design, (c) confounders, (d) data collection methods, and (e) withdrawals and dropouts. The analytic approach employed was also assessed and rated as "strong," "moderate," or "weak" depending on its appropriateness in terms of testing for mediation effects. Regression methods (68) where mediational effects are inferred rather than based on direct statistical observation (87) were rated as weak. A moderate rating was assigned to analyses where regression methods with additional tests of indirect effects, such as the Sobel test, had been used in addition to regression analysis. Explicit analyses estimating direct and indirect effects with bootstrapping techniques (73, 88) and path analysis were assigned a strong rating. **Table 2** presents a summary of the quality of each eligible study.

# RESULTS

## Characteristics of the Primary Studies

The literature search yielded 24,563 articles. After electronically removing duplicates, the 6,290 remaining studies were screened based on title and abstract, and 6,090 articles were excluded as ineligible. The remaining 200 articles were assessed at full-text level, and 174 were excluded. An additional eight articles were included from a citation search and screening of the references of eligible studies. This resulted in 34 articles being included in the systematic review (see **Figure 1**). **Table 1** provides an overview of the studies reviewed, including details of the research measures employed. Papers were from the USA ($n = 18$), Canada ($n = 2$), Spain ($n = 2$), Germany ($n = 2$), the Netherlands ($n = 2$), Belgium ($n = 2$), Iran ($n = 2$), the UK ($n = 1$), Norway ($n = 1$), Japan ($n = 1$), and Turkey ($n = 1$). Cross-sectional ($n = 24$), longitudinal ($n = 9$), and case–control ($n = 1$) designs were included.

The age range of adult samples varied substantially across eligible studies from 18 to over 65 years, young adults from 16 to 29 years, older adults from 62 to 90 years, and adolescent samples from 11 to 19 years. Thus, there was no single definition of adolescent, young adult, older adult, and adult samples in this review, and these descriptions were instead based on how the original studies defined their samples. Overall, eligible articles comprised 14,332 adults, 4,116 young adults, 81 older adults, and 3,434 adolescents, with a total of 888 clinical participants involved. Eight studies used adolescent samples, 26 studies used adult samples, nearly half of which were young adults recruited from universities ($n = 11$), and only one (51) investigated older adults. Among all eligible studies, only seven used clinical samples (28, 63, 69, 74, 75, 80, 85). Most of the studies included

**TABLE 1 |** Overview of studies included in review.

| References; Country | Design | Sample | Measures Childhood emotional abuse | Measures Mediator(s) | Measures Depression | Analysis of mediation | Main relevant findings |
|---|---|---|---|---|---|---|---|
| Calvete (62); Spain | Longitudinal | 1,052 adolescents aged 13–17 years (499 girls, 553 boys, mean age = 13.43, *SD* = 1.29) | The 5-item Psychological Abuse Scale of the CTS-PC | YSQ-3 | CES-D | Structural equation modeling, autoregressive model, bootstrapping procedure (177) | Parental emotional abuse did not predict the worsening of early maladaptive schemas in the follow-ups but was directly associated with depressive symptoms |
| Carvalho Fernando et al. (63); Germany | Cross-sectional | 160 adults (49 BPD patients, 48 MDD patients, 63 controls) | CTQ | DERS, ERQ | BDI | Multiple regression analyses | No significant impact of self-reported childhood emotional abuse and emotion dysregulation on depressive symptoms was found |
| Christ et al. (32); The Netherlands | Cross-sectional | 276 female college students with a mean age of 21.7 years (*SD* = 2.38) | CTQ-SF | DERS, IIP-32 | Quick Inventory of Depressive Symptoms | Multiple regression analyses, the PROCESS tool (88) | The effect of childhood emotional abuse on depressive symptoms was mediated by emotion dysregulation and the following domains of interpersonal problems: cold/distant and domineering/controlling |
| Coates and Messman-Moore (64); USA | Cross-sectional | 771 female undergraduate students between the ages of 18 and 25 with a mean age of 18.78 (*SD* = 1.02) | The Computer Assisted Maltreatment Inventory | DERS, YSQ-SF | TSI | Structural equation modeling | Both emotion dysregulation and negative internalized beliefs significantly mediated the link between childhood psychological maltreatment and depressive symptoms, accounting for ∼68% of the variance in symptomatology |
| Courtney et al. (65); USA | Cross-sectional | 195 adolescent primary care patients (21.5% male, 78.5% female), aged 15–18 years (*M* = 16.30, *SD* = 1.07) | Three items adapted from CTQ that directly assess verbal and nonverbal emotional abuse | BHS | BDI | Multiple regression analyses | Hopelessness partially mediated the associations of emotional abuse with risk for depressive symptoms. Hopelessness accounted for 69.8% of the variance in the association between emotional abuse and depressive symptoms |
| Courtney et al. (30); USA | Longitudinal | 92 adolescent primary care patients (18.5% boys, 81.5% girls) between 15 and 18 years of age (*M* = 17.48, *SD* = 1.27) | Three items adapted from CTQ that directly assess verbal and nonverbal emotional abuse | BHS | BDI-II | Multiple regression analyses | Hopelessness partially mediated the association between T1 emotional abuse and T2 depressive symptoms. Hopelessness accounted for 87.3% of the variance in this association |
| Crow et al. (29); USA | Cross-sectional | 3,902 adults aged 18–81 years (*M* = 39.34, *SD* = 13.76, 68.9% women, 92.7% African American) | CTQ | EDS | BDI-II | (73) | Emotion dysregulation mediated the relationship between childhood emotional abuse and later depression |
| Gibb et al. (66); USA | Longitudinal | 297 university students (145 high cognitive risk, mean age = 18.92, 68.3% female; 152 low cognitive risk, mean age = 19.28, 68.4% female) | The maltreatment subscale of the LEQ | CSQ, DAS | BDI, BHS, SADS | Hierarchical regression analysis | Cognitive risk fully mediated the relation between reported levels of childhood emotional maltreatment and non-endogenous major depression as well as hopelessness depression |

*(Continued)*

**TABLE 1** | Continued

| References; Country | Design | Sample | Measures Childhood emotional abuse | Measures Mediator(s) | Measures Depression | Analysis of mediation | Main relevant findings |
|---|---|---|---|---|---|---|---|
| Gibb et al. (67); USA | Cross-sectional | 220 undergraduates aged 17–26 years (164 women, 56 men, mean age = 18.79, *SD* = 1.40) | LEQ | BHS | HDSQ | Path analyses using AMOS 4.0 | Hopelessness partially mediated the relation between childhood emotional maltreatment and symptoms of hopelessness depression |
| Hankin (31); USA | Study 1: Longitudinal (10 weeks) | Study 1: 652 undergraduate students aged 17–23 years (mean = 18.7, *SD* = 0.96, 210 males) | Study 1: LEQ | Study 1: CSQ, NLEQ, AAQ | Study 1: BDI, MASQ | Study 1: Path analyses (68), univariate and multivariate mediational analyses (178) | Study 1: An insecure attachment style and negative life events almost completely mediated the association between childhood emotional abuse and later depressive symptoms, while a negative cognitive style was minimized in the multivariate mediational model |
| | Study 2: Longitudinal (2 years) | Study 2: 75 undergraduate students aged 18–23 years (mean = 18.6, *SD* = 0.84, 34 males) | Study 2: CECA | Study 2: CSQ, NLEQ, AAQ | Study 2: BDI, MASQ | Study 2: Path analyses (68), univariate and multivariate mediational analyses (178) | Study 2: Only an insecure attachment style and negative life events remained partially accounted for the association between childhood emotional abuse and later depressive symptoms in the multivariate mediational model |
| Hayashi et al. (69); Japan | Cross-sectional | 113 untreated, newly diagnosed MDD patients aged 25–75 years (58 women and 55 men, mean age 41.91 years, *SD* = 11.20) | CATS | LES, NEO-FFI | BDI-II | Structural equation modeling | Childhood emotional abuse predicted the severity of depression indirectly through the mediation of personality: Neuroticism, Extroversion, and Conscientiousness. The negative life change was affected by childhood emotional abuse but did not predict the severity of depression |
| Jessar et al. (70); USA | Longitudinal | 204 early adolescents (52% African American, 54% female, mean age = 12.85 years) | The emotional abuse and emotional neglect subscales of the CTQ | ECQ | CDI | (73) | Emotional abuse did not significantly predict deficits in emotional clarity but did predict increases in depressive symptoms. Deficits in emotional clarity only mediated the relationship between emotional neglect and increases in depressive symptoms |
| Kaysen et al. (71); USA | Cross-sectional | 206 adult women who had been recently raped (*N* = 133) or physically assaulted (*N* = 73) (mean age = 31.21 years, *SD* = 8.58, range = 18–57) | HVQ | PBRS | BDI, SCID-MDD | (68) | No evidence for associations of childhood emotional abuse with either maladaptive cognitions or depression |
| Khosravani et al. (52); Iran | Cross-sectional | 350 males (age range = 18–61 years, *M* = 32.3) | CTQ-SF | DERS | BDI-II | Structural equation models (SEM), bootstrapping | A direct effect of emotional abuse on depressive symptoms and an indirect effect via emotion dysregulation |

*(Continued)*

**TABLE 1** | Continued

| References; Country | Design | Sample | Measures Childhood emotional abuse | Measures Mediator(s) | Measures Depression | Analysis of mediation | Main relevant findings |
|---|---|---|---|---|---|---|---|
| Krause et al. (72); USA | Cross-sectional | 127 adults aged 18–30 years (mean age = 20, *SD* = 2.76, 78 women, 76% Caucasian) | Psychological Abuse Scale (179) | WBSI, AEQ, CSQ, the 11-item avoidant reactions subscale of the Impact of Event Scale | BDI | Structural equation modeling, AMOS | Chronic emotional inhibition (including ambivalent expression, thought suppress, current and chronic avoid) fully mediated the relationship between childhood emotional invalidation (including emotional abuse) and depressive symptoms in adulthood |
| Li et al. (54); UK | Cross-sectional | 205 adults (80.5% female; mean age = 28.2, *SD* = 10.86) | 7-item Childhood Emotional Abuse Scale created and validated by Kent and Waller (180) | RFQ | 7 items of the Depression subscale in the DASS-21 | Multiple regression analyses, PROCESS macro (88) | Emotional abuse continued to exert a significant effect on adulthood depression after controlling for other forms of childhood maltreatment and mentalizing incapacity. A mediation effect between childhood emotional abuse and adulthood depression symptoms via mentalizing incapacity (both hypermentalizing and hypomentalizing) was established |
| Lumley and Harkness (28); Canada | Cross-sectional | 76 depressed adolescents meeting DSM-IV criteria for a current episode of a non-bipolar mood disorder, aged 13–19 years (24 boys, 52 girls) | The teenage version of the CECA | YSQ | MASQ, BDI-II, The child and adolescent version of the SADS | (68, 73) | A different set of early maladaptive schemas with contents, such as social isolation and self-sacrifice, mediated the relation of emotional maltreatment to anhedonic depression. But no specificity was found in the relation between emotional maltreatment and anhedonic depression |
| Lumley and Harkness (28); Canada | Cross-sectional | 91 young adults aged 17–21 years (21 men, 70 women, mean age = 18.10, *SD* = 0.84) | CECA.Q | YSQ, The Modified-Psychological Distance Scaling Task | BDI, the Mood Disorder Module of the SCID | (68), Sobel test | Depressotypic cognitive organization (i.e., tightly connected negative schema organization and loosely connected positive schema organization) mediated the relation between childhood emotional maltreatment and young adult depression |
| Maciejewski and Mazure (74); USA | Case-control | 50 adults (25 cases, 25 controls) aged 23–65 years (*M* = 39.6, *SD* = 10.3, 24 women, 42 European American descent) | ETI | The Fear of Criticism and Rejection subscale in Beck's Sociotropy-Autonomy Scale | SCID, CES-D, HRSD, the University of Michigan version of CIDI | Multiple logistic regression, multivariate analysis of covariance (MANCOVA) | Fear of criticism and rejection mediated the association between childhood emotional abuse and adult onset of major depression |
| O'Mahen et al. (21); USA | Cross-sectional | 140 pregnant women, age 18 or older, 24 or more weeks pregnant | CTQ | RRS, BADS | SCID-I, EPDS, BDI-II | Nested path models in AMOS 18.0, bootstrapping procedure (177) | Brooding partially mediated the relationship between childhood emotional abuse and depressive symptoms, whereas behavioral avoidance was not significantly correlated with childhood emotional abuse |

*(Continued)*

**TABLE 1** | Continued

| References; Country | Design | Sample | Measures Childhood emotional abuse | Measures Mediator(s) | Measures Depression | Analysis of mediation | Main relevant findings |
|---|---|---|---|---|---|---|---|
| Østefjells et al. (75); Norway | Cross-sectional | 261 patients aged 18–65 years with psychotic or bipolar disorders | CTQ-SF | The subscale measuring negative beliefs about the uncontrollability and danger of thoughts of the Metacognitions Questionnaire-30 items | Positive and Negative Syndrome Scale Score | Ordinary least-squares regressions with the PROCESS tool (88) | Metacognitive beliefs about thoughts being uncontrollable/dangerous significantly mediated the relationship between early emotional abuse and depression |
| Paredes and Calvete (36); Spain | Longitudinal | 998 adolescents (471 girls, 526 boys) between 13 and 17 years of age | The 6-item version of the Emotional Abuse Scale adapted from CTS-PC | CRSS, ACSQ | CES-D | Structural equation modeling, Sobel test | Only brooding partially mediated the relationship between emotional abuse by parents and depressive symptoms. Neither reflection nor negative inferential styles increased vulnerability to depression |
| Raes and Hermans (76); Belgium | Cross-sectional | 101 students (83 women, mean age = 19.64 years) | The emotional abuse subscale of the CTQ | RRS | BDI | Multiple regression analyses, Sobel test | Brooding partially mediated the relationship between emotional abuse and depression, even when reflection was partialed out |
| Rafi et al. (77); Iran | Cross-sectional | 492 middle school students (183 boys, mean age = 13.61 years, *SD* = 0.682, 309 girls mean age = 13.60, *SD* = 0.572) | Child Abuse Self Report Scale | SIC | The anxiety and depression subscales of the ASEBA | Path analysis | Early maladaptive schemas (i.e., loneliness, vulnerability to harm, and submission) mediated the relationship between childhood emotional maltreatment and depression |
| Reddy et al. (78); USA | Cross-sectional | 987 college undergraduates (52.5% males, 65% Caucasian, 93% below 22 years old) | FEQ | EAS, WBSI, Acceptance and Action Questionnaire | DASS-21 | Structural equation modeling | Experiential avoidance (examined by three measures) significantly mediated the relationship between childhood psychological abuse and current mental health symptoms (including depression, anxiety and stress), reducing the direct effect by 77% |
| Ross et al. (53); USA | Cross-sectional | 244 adults (53 males; mean age = 20.80, *SD* = 3.826) | CTQ | ISS, the 26-item Self-Compassion Scale | CESD-R | Path models, bootstrapping | A significant path from emotional abuse to depression, and a significant indirect path that passed through self-compassion and shame |
| Sachs-Ericsson et al. (79); USA | Cross-sectional | 5614 adults age range 15–54 years (*M* = 33.2 years, *SD* = 10.7) | A list of specific behaviors related to parental verbal abuse, including insulted, swore at, did or said something to spite, threatened to hit. | 4 items of self-criticism from the DEQ, Dependency and Emotional Reliance on Others Scale (181) | CIDI | Hierarchical linear regression analyses, Sobel test | Self-criticism fully mediated the relationship between parental verbal abuse and internalizing symptoms (including symptoms of depression), whereas dependency did not mediate the relationship between any abuse and internalizing symptoms |
| Schulz et al. (80); Germany | Longitudinal | 123 inpatients aged 18–65 years with current MDD diagnosis | The emotional abuse and emotional neglect subscales of the CTQ | PSDI, EAQ | BDI-II, Montgomery–Åsberg Depression Rating Scale | (73), Sobel test | Borderline personality traits and acceptance of pleasant emotions are significant mediators of the association between childhood emotional abuse and self-rated depression severity. Childhood emotional abuse is not correlated to expert-ratings of depression |

*(Continued)*

**TABLE 1** | Continued

| References; Country | Design | Sample | Measures Childhood emotional abuse | Measures Mediator(s) | Measures Depression | Analysis of mediation | Main relevant findings |
|---|---|---|---|---|---|---|---|
| Spasojevic and Alloy (81); USA | Longitudinal | 137 undergraduate students aged 16–29 years (88 females and 49 males, mean age = 19) | LEQ | RRS | BDI, Mod-SADS-L | Hierarchical regression analysis (68) | The relationship between childhood emotional maltreatment and the number of major depressive episodes was partially mediated by ruminative response style |
| Uhrlass and Gibb (82); USA | Longitudinal | 208 undergraduate students (mean age = 19.6 years, *SD* = 4.3, 148 females, 58.2% Caucasian) | LEQ | The 53-item Hassles subscale of the Hassles and Uplifts Scale | BDI-II | Path analysis, AMOS 5.0 | Changes in recent negative events fully mediated, rather than moderated, the link between reports of childhood emotional maltreatment and changes in depressive symptoms |
| Van Assche et al. (51); Belgium | Cross-sectional | 81 older adults age range 62–90 (36% males; *M* = 74.90, *SD* = 6.64) | CTQ-SF | ECR-R | GDS | Bootstrapping | Childhood emotional abuse was not significantly correlated with current depression or attachment. Both attachment anxiety and attachment avoidance showed a significant positive correlation with the current level of depression |
| van Harmelen et al. (83); The Netherlands | Cross-sectional | 2837 adults aged between 18 and 65 years (66.5% female, age *M* = 41.9 years, *SD* = 13.0) | The Netherlands Mental Health Survey and Incidence Study (NEMESIS) trauma interview | Implicit Association Test | CIDI, IDS | (73) | Both automatic and explicit negative self-associations partially mediated the relationship between childhood emotional maltreatment and depressive symptomatology |
| Wright et al. (84); USA | Cross-sectional | 301 undergraduate students (143 men, 158 women, mean age = 20.37, 94.4% Caucasian) | LEQ | YSQ | TSC-40 | Hierarchical regression analysis (68) | The schemas of vulnerability to harm, self-sacrifice, and defectiveness/shame mediated the relationship between childhood emotional abuse and adult symptoms of depression |
| Yigit et al. (85); Turkey | Cross-sectional | 325 participants in total (13–18 years old): 193 clinical adolescents (129 girls; mean age = 15.65, *SD* = 1.15); 132 non-clinical adolescents (94 girls; mean age = 15.05, *SD* = 1.07) | CTQ | YSQ-3 | CDI | Path analysis, bootstrapping | Disconnection/Rejection and Impaired Autonomy mediated significantly emotional abuse and depression in the non-clinical sample. Disconnection/Rejection significantly mediated the relationship between emotional abuse and depression in the clinical sample |

*CTQ, Childhood Trauma Questionnaire; CTQ-SF, Childhood Trauma Questionnaire-Short Form; BDI, Beck Depression Inventory; BDI-II, Beck Depression Inventory II; YSQ, Young Schema Questionnaire; YSQ-SF, Young Schema Questionnaire–Short Form; YSQ-3, Young Schema Questionnaire-3; CECA, Childhood Experience of care and Abuse; CECA.Q, Childhood Experience of Care and Abuse questionnaire; HADS, Hospital Anxiety and Depression Scale; ECR-R, Experiences in Close Relationships Questionnaire-Revised; CATS, Child Abuse and Trauma Scale; SCID, Structured Clinical Interview for DSM-IV; SCID-I, Structured Clinical Interview for DSM-IV Axis 1 Disorders-Patient Edition; SCID-MDD, Structured Clinical Interview for DSM-III-R Non-Patient Version; DERS, Difficulties in Emotion Regulation Scale; ERQ, Emotion Regulation Questionnaire; IIP-32, Inventory of Interpersonal Problems; CSQ, Cognitive Style Questionnaire; DAS, Dysfunctional Attitude Scale; TSI, Trauma Symptom Inventory; BHS, Beck Hopelessness Scale; EDS, Emotion Dysregulation Scale; LEQ, Lifetime Experiences Questionnaire; NLEQ, Negative Life Events Questionnaire; LES, Life Experiences Survey; NEO-FFI, Neuroticism Extroversion Openness Five Factor Inventory; ECQ, Emotional Clarity Questionnaire; DASS-21, Depression Anxiety Stress Scale−21item; MASQ, Mood and Anxiety Symptom Questionnaire; WBSI, White Bear Thought Suppression Inventory; AEQ, Ambivalence Over Emotional Expressiveness Questionnaire; HVQ, History of Victimization Questionnaire; RFQ, Reflective Functioning Questionnaire; CDI, Children's Depression Inventory; CES-D, Center for Epidemiological Studies Depression Scale; CESD-R, Center for Epidemiological Studies Depression Scale-Revised; SADS, Schedule for Affective Disorders and Schizophrenia; Mod-SADS-L, A modified Schedule for Affective Disorders and Schizophrenia – Lifetime; HDSQ, Hopelessness Depression Symptom Questionnaire; ETI, Early Trauma Inventory; RRS, Ruminative Responses Scale; BADS, Behavioral Activation for Depression Scale; EPDS, Edinburgh Postnatal Depression Screen; SIC, A Schema Inventory for Children; ASEBA, Achenbach System of Empirically Based Assessment; FEQ, Family Experiences Questionnaire; ISS, Internalized Shame Scale; EAS, Experiential Avoidance Scale; PBRS, Personal Beliefs and Reactions Scale; GDS, Geriatric Depression Scale; EAQ, Emotion Acceptance Questionnaire; PSDI, Personality Style and Disorder Inventory; DEQ, Depressive Experiences Questionnaire; HRSD, Hamilton Rating Scale for Depression; ACSQ, Adolescent Cognitive Style Questionnaire; CRSS, Children's Response Style Scale; CTS-PC, Conflict Tactics Scales-Parent-to-Child; TSC-40, Trauma Symptom Checklist-40; IDS, Inventory of Depressive Symptomatology; AAQ, Adult Attachment Questionnaire; CIDI, Composite International Diagnostic Interview.*

**TABLE 2 |** Quality assessment tool ratings.

| References; Country | Selection bias | Study design | Confounders | Data collection methods | | | Withdrawals and dropouts | Mediation analyses |
|---|---|---|---|---|---|---|---|---|
| | | | | IV | M | DV | | |
| Calvete (62); Spain | W | M | W | S | S | S | M | S |
| Carvalho Fernando et al. (63); Germany | M | W | S | S | S | S | M | W |
| Christ et al. (32); The Netherlands | W | W | S | S | Emotion dysregulation = S<br>Interpersonal problems = S | S | M | S |
| Coates and Messman-Moore (64); USA | W | W | W | S | Emotion dysregulation = S<br>Negative internalized beliefs = S | S | M | S |
| Courtney et al. (65); USA | M | W | W | S | S | S | M | W |
| Courtney et al. (30); USA | M | M | M | S | S | S | W | W |
| Crow et al. (29); USA | M | W | S | S | M | S | M | S |
| Gibb et al. (66); USA | W | M | M | S | S | S | S | W |
| Gibb et al. (67); USA | W | W | W | S | S | S | M | S |
| Hankin (31); USA Study 1 | W | M | S | S | Insecure attachment style = S<br>Negative cognitive style = S<br>Negative events = S | S | S | S |
| Study 2 | W | S | S | S | | S | S | S |
| Hayashi et al. (69); Japan | M | W | W | S | Personality = S<br>Stress of life events = S | S | M | S |
| Jessar et al. (70); USA | W | M | M | S | M | S | W | S |
| Kaysen et al. (71); USA | M | W | W | W | S | S | M | W |
| Khosravani et al. (52); Iran | M | W | S | S | S | S | M | S |
| Krause et al. (72); USA | W | W | W | W | S | S | M | S |
| Li et al. (54); UK | W | W | W | S | S | S | M | S |
| Lumley and Harkness (28); Canada | M | W | M | S | S | S | M | S |
| Lumley and Harkness (89); Canada | W | W | M | S | S | S | M | M |
| Maciejewski and Mazure (74); USA | M | M | S | S | S | S | M | W |
| O'Mahen et al. (21); USA | M | W | M | S | Brooding = S<br>Behavioral avoidance = S | S | M | S |
| Østefjells et al. (75); Norway | M | W | M | S | S | S | M | S |
| Paredes and Calvete (36); Spain | W | M | W | S | Brooding = S<br>Negative inferential styles = S | S | M | S |
| Raes and Hermans (76); Belgium | W | W | W | S | S | S | M | M |
| Rafi et al. (77); Iran | W | W | W | S | W | W | M | S |
| Reddy et al. (78); USA | W | W | S | W | S | S | M | S |
| Ross et al. (53); USA | W | W | W | S | Self-compassion = S<br>Shame = S | S | M | S |
| Sachs-Ericsson et al. (79); USA | S | W | S | W | Self-criticism = W<br>Dependency = W | S | M | M |
| Schulz et al. (80); Germany | M | M | S | S | Borderline personality = S<br>Low acceptance of pleasant emotions = W | S | W | S |
| Spasojevic and Alloy (81); USA | W | M | M | S | S | S | W | W |
| Uhrlass and Gibb (82); USA | W | M | W | S | S | S | W | S |
| Van Assche et al. (51); Belgium | M | W | S | S | S | S | M | S |
| van Harmelen et al. (83); The Netherlands | S | W | S | S | S | S | M | S |
| Wright et al. (84); USA | W | W | S | S | S | S | M | W |
| Yigit et al. (85); Turkey | M | W | M | S | S | S | M | S |

*S, strong; M, moderate; W, weak; IV, independent variable, M, mediator(s); DV, dependent variable.*

**TABLE 3 |** Summary of results and mediational analytic approaches.

| Cluster | Eligible studies | Percentage of studies supporting the pathway | Strength of the mediation analysis | | |
|---|---|---|---|---|---|
| | | | Strong | Moderate | Weak |
| Early maladaptive schemas (*N* = 8) | Calvete (62)<br>Coates and Messman-Moore (64)<br>Kaysen et al. (71)<br>Lumley and Harkness (28)<br>Lumley and Harkness (89)<br>Rafi et al. (77)<br>Wright et al. (84)<br>Yigit et al. (85) | 75% | *N* = 5 | *N* = 1 | *N* = 2 |
| Cognitive-personality variables (*N* = 14) | Courtney et al. (65)<br>Courtney et al. (30)<br>Gibb et al. (66)<br>Gibb et al. (67)<br>Hankin (31)<br>Hayashi et al. (69)<br>Li et al. (54)<br>Maciejewski and Mazure (74)<br>Østefjells et al. (75)<br>Paredes and Calvete (36)<br>Ross et al. (53)<br>Sachs-Ericsson et al. (79)<br>Schulz et al. (80)<br>van Harmelen et al. (83) | 92% (*N* = 12; cognitive vulnerability—the small bandwidth of cognitive-personality variables)<br>100% (*N* = 2; personality—the broader cognitive-personality variables) | *N* = 9 | *N* = 1 | *N* = 4 |
| Emotion dysregulation (*N* = 13) | Carvalho Fernando et al. (63)<br>Christ et al. (32)<br>Coates and Messman-Moore (64)<br>Crow et al. (29)<br>Jessar et al. (70)<br>Khosravani et al. (52)<br>Krause et al. (72)<br>O'Mahen et al. (21)<br>Paredes and Calvete (36)<br>Raes and Hermans (76)<br>Reddy et al. (78)<br>Schulz et al. (80)<br>Spasojevic and Alloy (81) | 85% | *N* = 10 | *N* = 1 | *N* = 2 |
| Interpersonal styles (*N* = 4) | Christ et al. (32)<br>Hankin (31)<br>Sachs-Ericsson et al. (79)<br>Van Assche et al. (51) | 50% | *N* = 3 | *N* = 1 | N/A |
| Stressful negative events (*N* = 3) | Hankin (31)<br>Hayashi et al. (69)<br>Uhrlass and Gibb (82) | 67% | *N* = 3 | N/A | N/A |

*Nine studies examined more than one mediating variable in their analyses so might be counted more than once in different clusters in this table.*

both men and women; four studies (21, 32, 64, 71) included female participants only and one study (52) included male participants only.

Sample sizes ranged from 50 to 5,614 participants. Twenty-nine studies had sample sizes larger than 100. We used a sample size of 100 as guideline for performing mediation analyses, as MacKinnon et al. (90) argued that a sample size of 100–200 was sufficient even for multiple mediator models in terms of power. Nine studies examined more than one mediating variable in their analyses (36, 79). Of the 34 studies that tested mediation, seven were rated as weak, three as moderate, and 24 as strong. More than one-third ($n = 13$) studies lacked information or did not provide an interpretation for potential confounding variables, such as age, gender, and socioeconomic status. Eleven studies controlled for other types of childhood maltreatment (e.g., sexual and physical abuse) in the mediation analyses to disentangle the independent contribution of emotional abuse.

Among all eligible studies, six (17.6%) found no association between childhood emotional abuse, mediating variables, and subsequent depression levels in their analyses. Van Assche et al. (51) reported that childhood emotional abuse was not significantly correlated with current depression or attachment

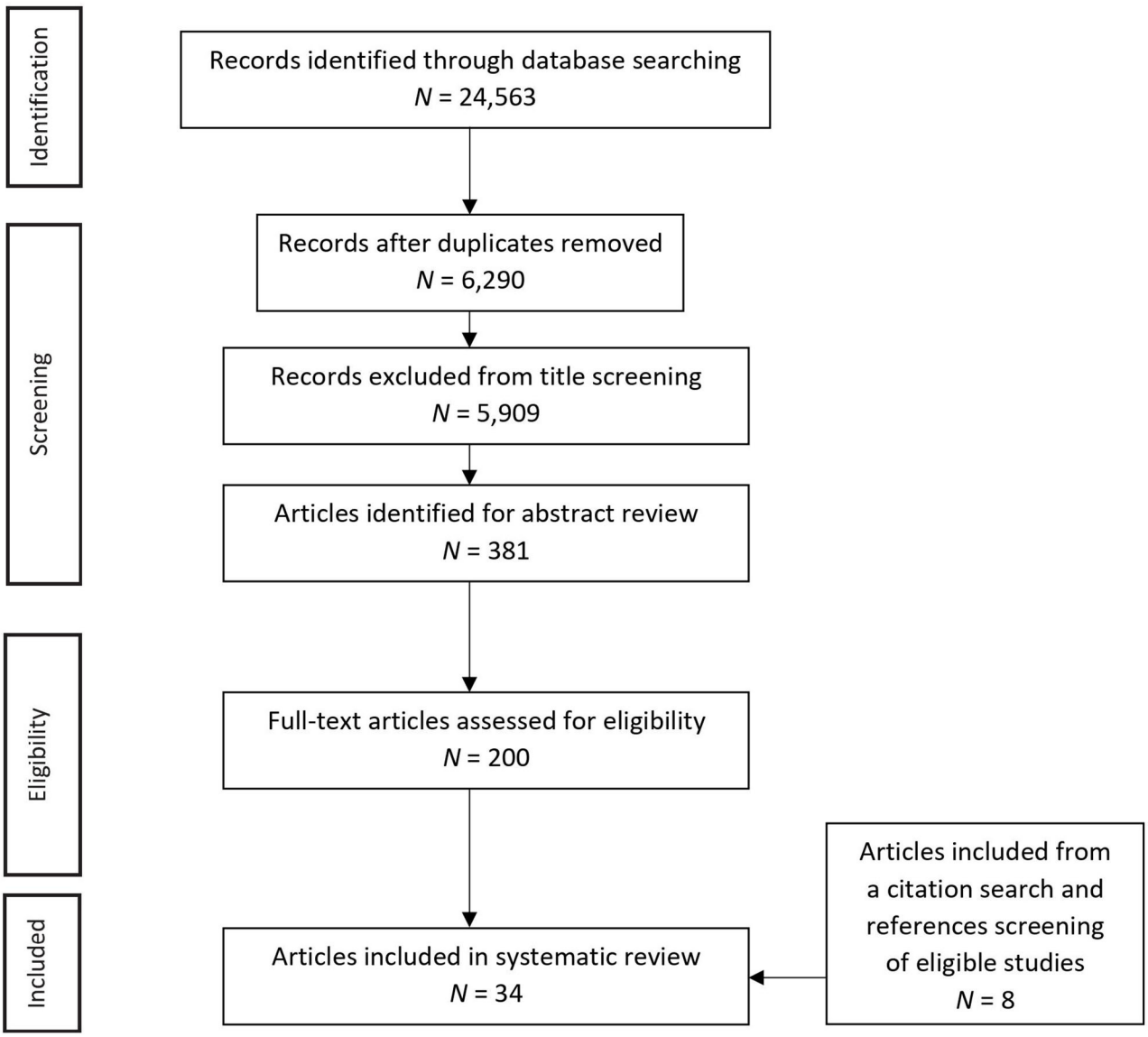


**FIGURE 1 |** Paper selection flow chart.

in a sample of community-dwelling older adults. Carvalho Fernando et al. (63) found no significant impact of self-reported childhood emotional abuse and emotion dysregulation on depressive symptoms. Hayashi et al. (69) reported that negative life events were affected by childhood abuse but did not predict the severity of depression. Kaysen et al. (71) showed no association of childhood emotional abuse with either adult depression or maladaptive cognitions. Calvete (62) reported that parental emotional abuse did not predict the worsening of early maladaptive schemas in adolescence, although it was directly associated with depressive symptoms. Jessar et al. (70) also indicated that emotional abuse did not significantly predict deficits in emotional clarity but did predict increases in depressive symptoms.

In addition, no specificity was found in the relation between emotional abuse and anhedonic depression in Lumley and Harkness's (28) analysis. Unexpectedly, Schulz et al. (80) reported that childhood emotional abuse was not correlated with expert ratings of depression, although it was correlated with self-rated depression severity. Some of these findings might be caused by the considerable co-occurrence of childhood sexual, physical, and emotional abuse in the studied samples. Any independent effects of emotional abuse on the development of depression might be diminished when severe physical or sexual abuse is also present. Therefore, we suggest that it would be important for future research to assess exposure to all forms of childhood maltreatment simultaneously, as multiple types of maltreatment may interact to produce varying outcomes, and to rule out other

forms of maltreatment that may have been contributing factors when examining the emotional abuse–depression link.

## Overview of the Measures Used in the Primary Studies

### Childhood Emotional Abuse

Following methodological recommendations from PRISMA (49), a component approach to quality assessment was employed. Regarding the measures used in the eligible studies, reliability and validity were taken into consideration. According to the EPHPP, (a) standard assessment tools with known reliability and validity were rated as strong; (b) data collection tools that have been shown to be valid but not shown to be reliable (or for which reliability is not described) were rated as moderate; and (c) measures that have not been shown to be valid (or for which both reliability and validity are not described) were rated as weak. Four studies obtained weak ratings for measures employed to capture childhood emotional abuse. The remaining studies employed valid and reliable measures of the independent variables being investigated. The most widely used retrospective measures of childhood emotional abuse were the CTQ (91, 92) ($n = 14$) and the LEQ (93) ($n = 6$). Research has provided considerable support for the reliability and validity of both scales. The CTQ is a 28-item self-report inventory developed to measure five types of abuse or neglect in childhood or adolescence. Five CTQ items directly assess verbal and non-verbal emotional abuse: (1) People in my family called me things like "stupid," "lazy," or "ugly"; (2) I thought that my parents wished I had never been born; (3) People in my family said hurtful or insulting things to me; (4) I felt that someone in my family hated me; (5) I believe that I was emotionally abused. Participants rate each item on a 5-point Likert-type scale with higher scores indicating more emotional abuse. The CTQ also provides cut-off scores for none to low, low to moderate, moderate to severe, and severe to extreme trauma exposure, and the cut-off scores for moderate to severe maltreatment are 13 or higher for emotional abuse (92). The LEQ scenarios describe specific examples of emotional, physical, and sexual abuse. Participants are instructed to indicate whether these events had occurred, the age of onset for each maltreatment event, cessation of the event, the frequency of occurrence, and the perpetrator, rather than reporting on global estimates of abuse. Twenty-seven items in the LEQ assess emotional abuse, including forms of belittling, ridiculing, spurning, humiliating, rejecting, extorting, and terrorizing. For example, "Did anyone humiliate or demean you in the presence of other people?" Only three studies adopted interview measures. Two studies (28, 31) used the CECA (94). The CECA is a semi-structured contextual threat interview that assesses childhood adversity, including the familial context of quality of care and relationship with parents or substitutes (i.e., antipathy, emotional neglect, discipline, discord) in addition to psychological, physical, and sexual abuse.

### Depression

The operationalization of depression varied greatly. Using EPHPP criteria, one study (77) obtained a weak rating for the measure employed to capture depression symptoms; the remaining studies employed valid and reliable measures of the dependent variables being investigated. Most studies examined symptoms of depression as the outcome variable in community samples. Among the 34 eligible studies, only seven were conducted with clinical samples (28, 63, 69, 74, 75, 80, 85). Seventeen studies used the BDI and the BDI-II (95, 96), four used the CES-D (97), two used the DASS-21 (98), two used the MASQ (99), and two used the CDI (100).

Nine studies (21, 28, 66, 71, 74, 79, 81, 83, 89) used interview measures to assess the severity of depression or diagnosis. Four studies (21, 71, 74, 89) were conducted with different versions of the SCID (101) to assess major depressive disorder (MDD) as defined in DSM-IV (102). Three studies (74, 79, 83) used the CIDI (103) also based on DSM-IV criteria for MDD (102). Three studies (28, 66, 81) used different versions of the SADS (104) to assess episodes of depression.

### Mediators

A range of potential mediators was assessed by various measures. According to the EPHPP, five studies obtained weak or moderate ratings for measures employed to capture the mediating variable; the remaining studies employed valid and reliable measures of the mediators being investigated.

## Synthesis of the Mediators of the Emotional Abuse–Depression Relationship

For the purposes of the review, we grouped studies according to the type of psychological mechanisms examined in the emotional abuse–depression link. These mediators were further grouped according to the five clusters of psychological mediators: early maladaptive schemas, cognitive-personality variables, emotion dysregulation, interpersonal styles, and stressful negative events (see **Figure 2**). These domains were created as part of the narrative integration approach we used to organize the findings from the literature. Eight studies had analytic approaches rated as weak (e.g., regression methods) on their appropriateness in terms of testing for mediation effects, three studies were rated as moderate (e.g., regression methods with additional Sobel test), and the remaining 23 studies were rated as strong (e.g., bootstrapping techniques; path analysis). **Table 3** provides a summary of results and mediational analytic approaches.

First, a large body of cross-sectional and prospective research has highlighted the role of negative schema contents in depression. Early maladaptive schemas (105) are defined as broad, dysfunctional, and pervasive patterns consisting of memories, emotions, cognitions, and bodily sensations about oneself and relationships with others and hypothesized to consolidate over time. Certain schema domains (disconnection/rejection, impaired autonomy and performance, and other directedness) have been found to be associated with depressive symptoms (106).

Second, theories that focus on personality dimensions include broad-bandwidth theories focusing on the Big Five dimensions (107), and narrower bandwidth theories focusing on more specific personality dimensions, such as sociotropy–autonomy (108, 109) and cognitive vulnerability as conceptualized in Beck's original formulation of the cognitive model of depression (108, 110). In this review, we grouped cognitive vulnerability

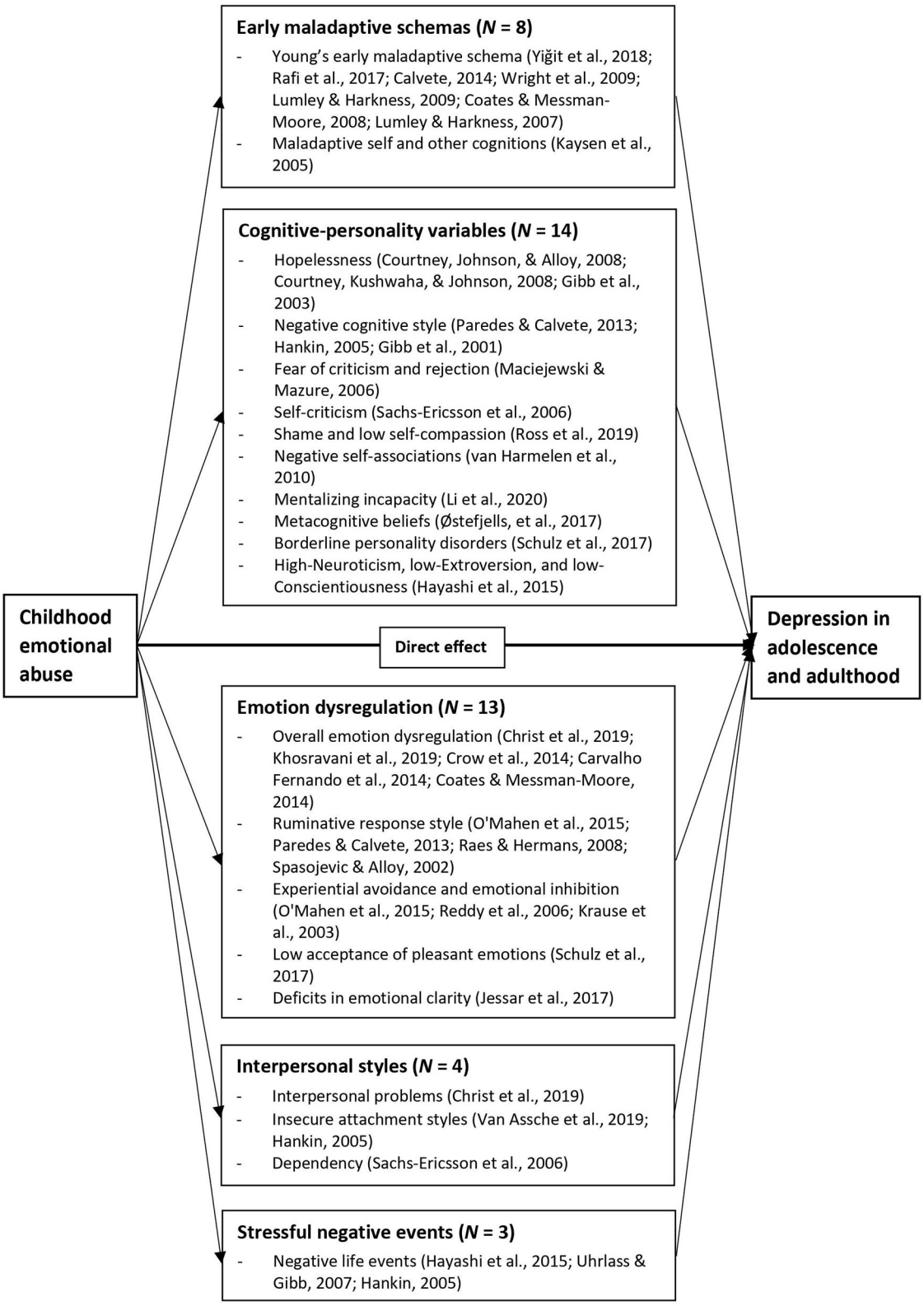


**FIGURE 2 |** Examined mediators in the emotional abuse–depression link.

with personality traits and dysfunctions as cognitive-personality variables. Cognitive theories of depression (111) have postulated that the impact of childhood maltreatment on subsequent psychopathology might be mediated by cognitive vulnerability (i.e., relatively stable, trait-like negative cognitive styles). People with chronic experiences of childhood emotional abuse, as opposed to physical or sexual abuse, are more likely to interpret current negative events in a similarly depressogenic manner (e.g., negative self-associations) because the depressogenic interpretations are directly supplied by the abusers (e.g., "you are such a stupid child"), which accounts for subsequent increases in depressive symptoms (61). A large number of studies have shown dysfunctional attributional styles and negative inferential styles for causes, consequences, and self-characteristics as predictors of depression in clinical and non-clinical samples (112–114). In addition, high Neuroticism, low Extroversion, and low Conscientiousness in the five-factor model of personality have been consistently linked to the onset of MDD (115). Although traits are considered to be largely genetically determined, neuroticism has been found to change over time as a result of childhood maltreatment (116). Several studies also revealed associations between childhood emotional abuse and different areas of personality dysfunction, including borderline, avoidant, and dependent pathology (117, 118). Given the high prevalence of comorbid personality disorders in inpatients with MDD (119), changes in personality functioning may mediate the emotional abuse–depression link. In Beck's (108) models of depression, these cognitive-personality characteristics have been shown not to be simply latent diatheses for depression; instead, they increase the probability of particular life events and one's vulnerability for the onset of depression with a diathesis-stress nature (120).

Third, chronic experiences of parental emotional abuse may increase children's internal focus and lead to emotion dysregulation, such as rumination. Individuals who tend to ruminate in response to negative life events are at high risk of developing and maintaining depressive symptoms. Treynor et al. (121) identified two distinct rumination components, labeled as brooding and reflection. There is a body of research consistently linking brooding rumination, but not reflection, with the onset and maintenance of depression (122).

Fourth, by definition, emotional abuse encompasses a repeated pattern of maladaptive interactions between the parent and child and has been described as a "pathogenic relational environment" [(123), p. 414]. Exposure to emotional abuse clearly threatens the security of attachment relationships and results in maladaptive models of self and self-in-relation-to-others, which may then impact on the quality of later interpersonal relationships. Individuals with a history of childhood maltreatment in general reported more dysfunctional relationships (124) and lower levels of social support (34) in adulthood. Recurring frustrated interpersonal dynamics, in turn, will render an individual more vulnerable to depression (125). Although empirical research is still scarce, interpersonal problems have been thought to be an underlying factor of the emotional abuse–depression link (126, 127).

Finally, Hammen's (128, 129) stress generation model of depression posited that a reciprocal relationship exists between negative life events and depression, whereby depressed individuals may generate additional negative stressors as they seek reassurance and comfort from others, only to be rejected by those they turned to for social support, and thus actively contribute to the occurrence of negative events in their lives. Importantly, Hammen's model suggests that childhood emotional abuse may set the stage for self-generated negative events and depressive symptoms in adolescence and adulthood (130).

### Early Maladaptive Schemas

In total, eight studies examined early maladaptive schemas as the pathway by which childhood emotional abuse may lead to subsequent depression symptoms. Both cross-sectional (28, 64, 71, 77, 84, 85, 89) and longitudinal (62) designs were employed. Five (28, 62, 64, 84, 89) used the YSQ (105) and two (77, 85) adapted the YSQ for Turkish or Iranian adolescents.

Four studies examined particular schema themes that may mediate the emotional abuse–depression link (28, 77, 84, 85). Lumley and Harkness (28) found that specific early maladaptive schemas of social isolation and self-sacrifice mediated the relation between early emotional maltreatment and anhedonic depression in depressed adolescents. Wright et al. (84) found that the schemas of vulnerability to harm, self-sacrifice, and defectiveness/shame mediated the relationship between childhood emotional abuse and symptoms of depression in a general population of young adults. In Turkish adolescents, Yigit et al. (85) found that both disconnection/rejection and impaired autonomy significantly mediated emotional abuse and depression in their non-clinical sample, whereas only disconnection/rejection significantly mediated the relationship between emotional abuse and depression in their clinical sample. In Iranian adolescents, Rafi et al. (77) reported that early maladaptive schemas of loneliness, vulnerability to harm, and submission mediated the relationship between childhood emotional maltreatment and depression. However, neither the Child Abuse Self Report Scale (CASRS) for assessing childhood emotional maltreatment nor the Schema Inventory for Children (SIC) for measuring early maladaptive schemas used in the study of Rafi et al. was validated. The CASRS was created in a master's thesis (131) and not peer-reviewed or published, and no further evidence of validity or reliability was found for the SIC.

In another two studies using the YSQ, Coates and Messman-Moore (64) found that general negative internalized beliefs significantly mediated the link between childhood psychological maltreatment and depressive symptoms. Lumley and Harkness (89) used a computer task, the Modified-Psychological Distance Scaling Task (M-PDST), whose stimuli (i.e., schema statements) were derived from the YSQ, to examine depressotypic schema organization as a mediator in young adults. They found that tightly connected negative schema statements mediated the relation between maternal and paternal emotional maltreatment and current depression, whereas loosely connected positive schema statements mediated the relation between maternal emotional maltreatment and current depression.

Unexpectedly, two studies (62, 71) found no association of parental emotional abuse with depression and/or maladaptive

schemas. Calvete (62) reported that parental emotional abuse predicted adolescents' depressive symptoms but not a worsening of early maladaptive schemas over time. Regardless, parental emotional abuse might have influenced the origin of early maladaptive schemas before their study. Kaysen et al. (71) found no association of childhood emotional abuse with depression or maladaptive cognitions in a sample of adult women who had recently been raped or physically assaulted. However, they used only three items (i.e., being called bad, dumb, or stupid; being threatened with a beating; being cursed at) of the HVQ to measure experiences of childhood emotional abuse in a recently traumatized population, and did not rule out other forms of maltreatment that are very likely to be contributing factors. This limits the individual effects of childhood emotional abuse on subsequent maladaptive cognitions and depressive symptoms.

Overall, six out of eight (75%) studies (28, 64, 77, 84, 85, 89) supported early maladaptive schemas as the pathway by which childhood emotional abuse may lead to subsequent depression symptoms. However, there is a lack of consistency in their findings concerning whether maladaptive schemas in general or specific schema themes act as the mediator. Only the schemas of vulnerability to harm and self-sacrifice appeared as the mediators in the emotional abuse–depression link more than once. Overall, two studies were rated as weak (71, 84), one as moderate (89), and five as strong, in terms of the relative strength of the statistical mediation analysis.

### Cognitive-Personality Variables

In total, 14 studies examined cognitive-personality variables as the pathway by which childhood emotional abuse may lead to subsequent depression symptoms. Within this domain, we split cognitive-personality variables into two subgroups (narrow bandwidth vs. broad bandwidth): one collection of studies ($n = 12$) has drawn on cognitive processes focusing on specific types of cognitive vulnerability, whereas another tradition has focused on broader cognitive-personality factors ($n = 2$).

In the subgroup of studies focusing on cognitive vulnerability, three studies (30, 65, 67) reported hopelessness as a mediator in the emotional abuse–depression link in adolescent or young adult samples using the BHS. Courtney et al. (65) found that the association of emotional abuse with depressive symptoms remained significant even after controlling for hopelessness, indicating that hopelessness was a partial mediator of the association between emotional abuse and depressive symptoms. In line with them, Gibb et al. (67) also indicated that the etiological chain of the hopelessness theory mediates only part of the relation between emotional maltreatment and symptoms of hopelessness depression. However, Courtney et al. (30) showed that hopelessness accounted for 87.3% of the variance in this association where the association of emotional abuse index scores with depression did not remain significant after controlling for hopelessness. Nonetheless, Courtney et al. (30) used only three items adapted from the CTQ that directly assess verbal and non-verbal emotional abuse and did not rule out other forms of maltreatment that may have been contributing factors, which limits the individual effects of emotional abuse on subsequent hopelessness and depressive symptoms.

Three studies (31, 36, 66) examined cognitive vulnerability as a potential mediating variable using the CSQ. Gibb et al. (66) found that cognitive risk fully mediated the relation of childhood emotional abuse to non-endogenous major depression and hopelessness depression, respectively, in a 2.5-years follow-up study. Hankin (31) also found that cognitive vulnerability helped account for the emotional abuse–depression link in two separate studies, a 10-weeks and a 2-years longitudinal study with undergraduate students. However, Paredes and Calvete (36) showed no evidence for negative inferential styles to be a mediator in their follow-up study. They reported that only negative inferential styles for consequences predicted depressive symptoms, which notably contrasts with studies showing that inferential style for causes of negative events is the most important element in the prediction of depressive symptoms (112, 113, 132). The CSQ employed in the above three studies is a self-report instrument assessing explicit cognitions. To include both explicit and automatic processes of cognitive functioning, van Harmelen et al. (83) had 2,837 adult participants complete a computer task, the Implicit Association Test (IAT). They found that childhood emotional maltreatment had the strongest link with enhanced explicit and automatic self-depression associations, compared with physical and sexual abuse; moreover, an increase in explicit and automatic negative self-associations partially mediated the relation between childhood emotional maltreatment and depressive symptomatology.

Three studies (53, 74, 79) assessed specific negative cognitive styles as mediators in the emotional abuse–depression link: fear of criticism and rejection (74), self-criticism (79), and shame and low self-compassion (53). Self-criticism, self-blame, and non-compassionate introjects may underlie the feelings of shame with a harsh internalized voice. All of them were found to significantly mediate the emotional abuse–depression link in adult samples. A significant path from emotional abuse to depression and a significant indirect path that passed through self-compassion and shame were reported by Ross et al. (53). However, after adjusting for fear of criticism and rejection, perceived childhood emotional abuse was no longer significantly associated with major depression in another study (74). Although Sachs-Ericsson et al. (79) also reported that verbal abuse no longer predicted depression once self-criticism was included in the analyses, they used specific behaviors of verbal abuse (e.g., insulted, swore at, did or said something to spite, threatened to hit) to estimate emotional abuse, which was neither validated nor shown to be reliable.

Finally, two studies (54, 75) examined metacognition as a mediator in the emotional abuse–depression link. Li et al. (54) found that childhood emotional abuse continued to exert a significant effect on adulthood depression after controlling for other forms of early maltreatment and current mentalizing incapacity in a general sample of 205 adults. A mediation effect between childhood emotional abuse and adulthood depression symptoms via current mentalizing incapacity (both hypermentalizing and hypomentalizing) was established in their analysis. Østefjells et al. (75) reported that specific beliefs about thoughts being uncontrollable and dangerous significantly mediated the relationship between early emotional abuse and

depression in 261 adult patients with psychotic or bipolar disorders. Although both studies examined metacognition-related mediators, Li et al. (54) introduced mentalizing to capture the interpersonal, cognitive, and developmental constructs of depression as an umbrella term for a group of basic psychological processes (e.g., theory of mind, reflective functioning), whereas metacognitive beliefs in Østefjells et al. (75) cover only specific beliefs about thoughts being uncontrollable and dangerous.

In the subgroup with broad bandwidth, two studies examined personality as a mediator in clinical adult samples by employing a cross-sectional (69) and a prospective observational (80) design. Hayashi et al. (69) found that childhood emotional abuse predicted the severity of depression indirectly through the mediation of high Neuroticism, low Extroversion, and low Conscientiousness in Japanese MDD patients. Schulz et al. (80) reported that elevated borderline personality traits mediated the association of childhood emotional abuse and self-rated MDD symptoms in German MDD patients; additionally, elevated passive-aggressive personality disorder traits mediated the link between childhood emotional abuse and lower self-rated symptom improvement. Although both studies examined personality as a potential mediator, Hayashi et al. (69) measured the five personality domains described in the five-factor model (107) using the NEO-FFI, whereas Schulz et al. (80) assessed personality traits using the PSDI. Unlike the NEO-FFI, the PSDI allows assessment of DSM-IV and ICD-10 personality traits as a dimensional approach in which characteristics of specific personality traits vary from adaptive to clinical levels and further reflect a personality disorder. Hayashi et al. (69) conducted structural equation modeling to examine the mediation model, and Schulz et al. (80) estimated direct and indirect effects using Preacher and Hayes (73) and the Sobel test; both were therefore rated as strong.

Overall, 11 of 12 (92%) studies drawing on cognitive processes established cognitive vulnerability, including hopelessness, general and specific types of negative cognitive styles, and metacognition, as mediators in the emotional abuse–depression link. Two studies assessing personality as a mediator potentially supported broader cognitive-personality factors as the pathway. There appears to be consistency of evidence supporting cognitive vulnerability (the small bandwidth of cognitive-personality variables; $n = 11$) as the pathway based on a noticeably greater number of studies, in contrast to personality (the broader cognitive-personality variables; $n = 2$). Although the above outcomes suggest that cognitive vulnerability may represent a common mediating mechanism in the emotional abuse–depression link, four were rated as weak (30, 65, 66, 74) and one as moderate (79) in terms of the analytic approach employed to test for mediation effects. Hence, further research is needed to replicate the abovementioned outcomes with explicit analyses estimating direct and indirect effects (e.g., bootstrapping techniques).

## Emotion Dysregulation

In total, 13 studies examined emotion dysregulation as a potential mediating variable in the emotional abuse–depression link. Overall emotion dysregulation was examined in five studies (29, 32, 52, 63, 64). Two studies (32, 64) reported that the effect of childhood emotional abuse on depressive symptoms was significantly mediated by emotion dysregulation measured by the DERS in emerging adult women. Khosravani et al. (52) reported a direct effect of emotional abuse on depressive symptoms and an indirect effect via emotion dysregulation, also measured by the DERS, in a sample of 350 treatment-seeking males with heroin dependence. Consistently, Crow et al. (29) found that emotion dysregulation partially mediated the relationship between childhood emotional abuse and later depression in a low-income African American sample of 3,902 adults, using the EDS. However, no significant impact of self-reported childhood emotional abuse and emotion dysregulation on depressive symptoms was found in a case–control sample by Carvalho Fernando et al. (63), although they reported that a history of emotional abuse was uniquely related to more frequent use of expressive suppression.

Eight studies examined specific dysfunctional emotion regulation strategies (e.g., rumination, emotional inhibition, experiential avoidance, low acceptance of pleasant emotions) as potential mediating variables. These dysfunctional emotional regulation strategies are largely overlapping and mutually influencing constructs. Reddy et al. (78) found that increased levels of experiential avoidance significantly mediated the relationship between childhood psychological abuse and current symptoms of depression in a cross-sectional sample of 987 undergraduates, reducing the direct effect by 77%. Experiential avoidance contains the elements of emotional inhibition and behavioral avoidance. In support of Reddy et al. (78), Krause et al. (72) found that chronic emotional inhibition fully mediated the relationship between a history of parental psychological abuse and adult depressive symptoms in a cross-sectional study. While employing an experientially avoidant coping style to inhibit thoughts and feelings may be temporarily adaptive as a means of escaping aversive emotional experiences, it often paradoxically leads to increased rumination on the thing sought to be avoided (78).

A ruminative response style was specifically examined as a potential mediating variable in four studies (21, 36, 76, 81). Spasojević and Alloy (81) first examined and found that rumination partially mediated the relationship between childhood emotional maltreatment and major depressive episodes in young adults who were followed prospectively for 2.5 years. The other three studies (21, 36, 76) all reported that brooding rumination (not reflection) partially mediated the relationship between emotional abuse and depressive symptoms in samples of adolescents, young adults, and low-income pregnant women. They suggested that the mediating role of rumination would be attributable to the brooding form, rather than to the more adaptive component of reflection. As the relationship between brooding and behavioral avoidance was hypothesized to be reciprocal (133), O'Mahen et al. (21) also examined behavioral avoidance in their study but found no correlation between childhood emotional abuse and behavioral avoidance.

Moreover, Schulz et al. (80) reported that low acceptance of pleasant emotions mediated the association between childhood

emotional abuse and self-rated depressive symptoms in a longitudinal study of 123 German MDD inpatients. Finally, Jessar et al. (70) assessed emotional clarity as a mediator between childhood emotional maltreatment and adolescent depression in a longitudinal study, but found that emotional abuse did not significantly predict deficits in emotional clarity.

In total, 11 of 13 (85%) studies in this cluster supported emotion dysregulation as a mediator in the emotional abuse–depression link. Overall emotion dysregulation ($n = 4$) and brooding rumination ($n = 4$) appeared to be the most consistent mediators in this link. In terms of the analytic approach employed to test for mediation effects, all studies in this cluster scored strong, except for two studies (63, 81) rated as weak, and one study (76) rated as moderate.

### Interpersonal Styles

Four studies (31, 32, 51, 79) examined interpersonal styles as the pathway by which childhood emotional abuse may lead to subsequent depression symptoms. Hankin (31) reported that a more insecure attachment style prospectively (over both 10-weeks and 2-years follow-up) mediated the association between a childhood history of emotional maltreatment and depressive symptoms in young adults. However, in a sample of older adults aged 62 and older, Van Assche et al. (51) found no significant correlation of childhood emotional abuse with either insecure attachment or current level of depression. Christ et al. (32) found that the effect of childhood emotional abuse on depressive symptoms was significantly mediated by two domains of interpersonal problems: cold/distant and domineering/controlling. Finally, Sachs-Ericsson et al. (79) unexpectedly found that dependent characteristics did not mediate the relationship between any parental abuse and depression symptoms in a large sample of adults, although a dependent interpersonal style has been constantly posited as a vulnerability marker for depression in literature. Three studies scored strong in their mediational analytic approaches (31, 32, 51) and one (79) was rated as moderate. Overall, only half of the studies in this cluster (31, 32) found expected outcomes supporting insecure attachment styles and specific interpersonal styles as potential pathways in the emotional abuse–depression link.

### Stressful Negative Events

Three studies examined stressful negative events as a potential mediating variable in the emotional abuse–depression link (31, 69, 82). Two studies (31, 82) employed a longitudinal design with path analysis in young adults. Uhrlass and Gibb (82) found that changes in recent negative events fully mediated, rather than moderated, the link between childhood emotional maltreatment and depressive symptoms; additionally, initial depressive symptoms contributed to prospective changes in negative life events. Instead of assessing major life events (e.g., deaths or unemployment), the Hassles Scale used in Uhrlass and Gibb's 7-weeks longitudinal study calculated the level of negative life events by summing the number of hassles endorsed during the past week. Hankin (31), described above, also assessed negative life events as a potential mediator using NLEQ which examines negative life events that typically occur for young adults. They found that experiencing a greater number of negative life events prospectively (over both 10-weeks and 2-years follow-up) mediated the association between a childhood history of emotional maltreatment and depressive symptoms in young adulthood. Unexpectedly, Hayashi et al. (69) found that negative life change affected by childhood emotional abuse did not predict the severity of depression. Although these three studies all scored strong in their mediational analytic approaches, only two of them supported stressful negative events as a potential mediating variable.

## DISCUSSION

Existing reviews (24, 33, 39, 40) have focused on the psychological mechanisms leading from childhood maltreatment in general to adult depressive symptoms, without considering the specific contributions of subtypes of maltreatment. The current systematic review goes beyond previous findings by examining potential mediating variables specifically in the emotional abuse–depression link. The aims of this review were to provide a comprehensive systematic review of quantitative literature investigating potential psychological mediators of the association between childhood emotional abuse and dimensional and categorical depression symptoms, with a focus on the quality of this evidence, including the relative strength of the statistical mediation analyses used to explain the emotional abuse–depression link. Our findings demonstrate several potentially causal mechanisms that might be involved in the relation between childhood emotional abuse and adolescent and adult depression. These psychological mediators fall into five clusters: (1) early maladaptive schemas, (2) cognitive-personality variables, (3) emotion dysregulation, (4) interpersonal styles, and (5) stressful negative events.

An important limitation of the eligible studies lies in the fact that not all of them addressed the unique impact of emotional abuse by accounting for the effects of the other types of childhood maltreatment. Only one-third of studies ($n = 11$) identified the unique contribution of emotional abuse to depression by statistically controlling for a history of other forms of childhood maltreatment (29, 31, 32, 53, 54, 63, 78–80, 83, 84). Emotional abuse was found to be uniquely associated with later depression after partialing out the effect of other forms of childhood maltreatment, and the findings of these 11 studies remained essentially unchanged when covariates were removed. Wright et al. (84) reported that the intercorrelations between all the abuse variables ranged from a low of 0.16 (between sexual abuse and emotional neglect) to a high of 0.63 (between physical abuse and emotional abuse), suggesting that different forms of child maltreatment do covary with each other and often co-occur in the same household. Given the co-occurring forms of childhood abuse, neglect, and other adverse family experiences, it would be of importance for future mediational studies to model the concurrent and possible additive effects of different types of abuse. In addition, a few studies (72) did not report the strength of the direct effect between the emotional abuse latent variable

and the depression latent variable without the mediator latent variable in the model. As such, a level of caution is required in interpreting the relative contributions of emotional abuse and mediators to ongoing depression.

Most eligible studies focused on examining a single mediator and indicated that this particular factor had the most impact in leading to depression following childhood emotional abuse. Nine studies included more than one variable in the mediational model of the emotional abuse-depression link (21, 31, 32, 36, 53, 64, 69, 79, 80), mainly involving emotion dysregulation, negative cognitive styles, stressful negative events, interpersonal styles, and personality, suggesting that the pathway from emotional abuse to depression is multi-determined and involves both cognitive and emotion-related factors. However, when integrating more than one mediator in a predictive model, not only effects and causal inferences might overlap with each other, but bidirectional relationships might also exist among contributing variables. For example, studies on stress generation (106, 134) have suggested that temperament may be related to stress-generation and increase interpersonal difficulties. Moreover, the cognitive and emotional deficits in the development of depression are not necessarily exclusive; studies have suggested an important role of cognitive processes underlying the regulation of emotion (135). Coates and Messman-Moore (64) reported that negative internalized beliefs increased vulnerability to emotion dysregulation and showed that the latter was an eventual outcome in mediating the emotional abuse-depression link.

Furthermore, as some mediating variables may be significant only when tested in isolation and not when entered simultaneously with other mediating variables, controlling for the interrelation between psychological mediators is important. Hankin (31), for instance, reported that an insecure attachment style and negative life events almost completely mediated the association between childhood emotional abuse and later depressive symptoms, while a negative cognitive style was minimized in their multivariate mediational model. Similarly, Coates and Messman-Moore (64) found that negative internalized beliefs no longer predicted depressive symptoms where emotion dysregulation appeared to be the stronger factor when the two were simultaneously entered into the same model. Likewise, a ruminative response style consistently appeared to be a stronger factor when entered simultaneously with cognitive vulnerability competing in the same mediational model (36, 81). Thus, our review supports the notion that not one mediator in isolation, but complex interrelations of psychological mediators, affect the relationship between childhood emotional abuse and subsequent depression.

Finally, although this review has shown specific pathways from exposure to childhood emotional abuse to later depression, the effects of childhood adversities are considered multivariate in their ultimate presentation (136). It has been suggested that childhood emotional abuse could first lead to the onset of depression in children and adolescents, and that depression in childhood and adolescence confer risk for depression in adulthood (137). A distal history of childhood maltreatment and context does not invariably contribute to depressive symptoms in adolescence and adulthood. Hamilton et al. (138) found that emotional abuse occurring during adolescence contributed to depressive symptoms in this period. Liu et al. (15) found that ongoing emotional maltreatment predicted shorter time to first onset of MDD in a sample of young adults. These findings together suggest that although childhood emotional abuse may have a specific depressogenic effect over a longer period of time, emotional abuse that occurs during that developmental stage may contribute to depression in a more immediate period. Further research is required to determine the specific contextual and process-related factors underlying this relationship.

## Toward a More Comprehensive Theoretical Model

In most eligible studies reporting mediations, childhood emotional abuse still significantly predicted depression symptoms after accounting for potential mediators, suggesting that each examined mediator is only one of many potential pathways in the emotional abuse–depression link. However, the psychological mediators examined in the emotional abuse–depression link in previous studies are largely dependent on researchers' preferences. Moreover, there are big differences in the conceptual and epistemological status of the various mediators that have been investigated. Person-dependent stressful life events, for instance, focus on the interplay between the individual and his/her environment, while rumination focuses on intrapsychic processes. Yet, it must be clear that rumination may also contribute to stress-generation processes, as do higher order theoretical constructs, such as personality. Hence, the current review suggests that there is a great degree of overlap in the investigated mediators between childhood emotional abuse and depression in adolescence and adulthood. Given that current theories on the pathways from childhood emotional abuse to subsequent depression (e.g., the hopelessness theory of depression and the stress generation theory of depression) are based on isolated investigations of researchers' interests rather than systematic empirical studies, this systematic review may contribute to a move to empirical research based on a more comprehensive theoretical model that incorporates the different potential psychological mediators and organizes them within a hierarchical multilevel theoretical framework.

In this model, childhood emotional abuse and various psychological mediators are considered to have direct and indirect effects on symptoms of depression (see **Figure 3**). Specifically, childhood emotional abuse is hypothesized to affect early schemas or attachment internal working models in childhood and/or adolescence, which in turn influence the development of broad and more specific personality dimensions, resulting in problems with emotional regulation and problems in person–environment exchanges (i.e., problems with salutogenesis), further expressed as (a) self-generated negative events, (b) heightened sensitivity to stressors, and (c) interpersonal problems in adolescence and adulthood.

In this integrated model, experiences of emotional abuse are thought to first affect early schemas or attachment internal working models in childhood and/or adolescence.

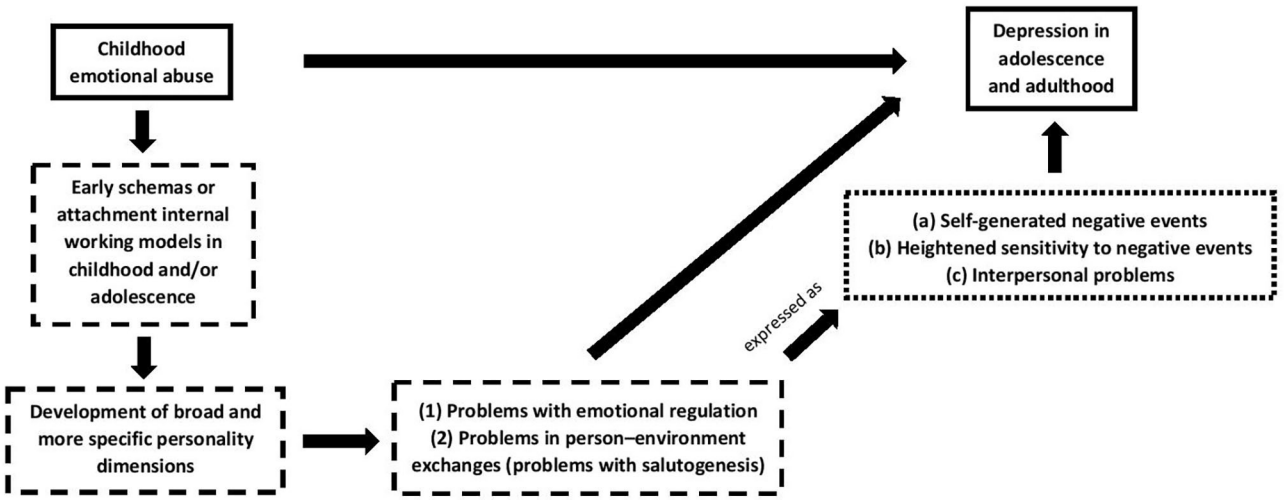


**FIGURE 3 |** A multilevel integrative model of the relationship between childhood emotional abuse and adult depression.

Studies included in the current review investigated the role of maladaptive schemas in the relation between emotional abuse and depression based on Young and colleagues' schema theory (105). Four studies addressed the pathways of particular schema themes that mediated the emotional abuse–depression link, including vulnerability to harm, self-sacrifice, social isolation, defectiveness and shame, disconnection and rejection, impaired autonomy, loneliness, and submission. It has been suggested that early maladaptive schemas might originate from unmet childhood needs for secure attachment (139). However, only two studies (31, 51) included in our review assessed attachment styles as a potential mediator, finding that insecure attachment styles prospectively mediated the association between a childhood history of emotional maltreatment and depressive symptoms in young adults, but were not significantly correlated with childhood emotional abuse or current depression in a small sample of community-dwelling older adults.

In this integrative theoretical model, we consider that early schemas and attachment internal working models in childhood and adolescence give rise to the development of broad and more specific personality dimensions (i.e., character tendencies and cognitive and emotion-related factors), resulting in problems with emotional regulation and problems in person–environment exchanges (problems with salutogenesis). The schemas of vulnerability to harm and self-sacrifice appeared as mediators in the emotional abuse–depression link in our review. The schema of vulnerability to harm highlights fear and helplessness about the future as a lasting sequel of emotional abuse, which might consolidate into a more pervasive negative cognitive style (31). There was robust evidence for a cognitive vulnerability pathway linking childhood emotional abuse and later depression. Especially consistent evidence was found for hopelessness mediating the emotional abuse–depression link (30, 65, 67). These findings fit with the hopelessness theory of depression developed by Abramson et al. (111), which postulates that chronic experiences of emotional abuse across different situations will induce hopelessness and lead to the development of an internal, stable, and global inferential style; this type of inference is generalized to other negative events, which accounts for subsequent increases in depressive symptoms. Gibb et al. (66) found that the relation between childhood emotional maltreatment and non-endogenous major depression was fully mediated by the presence vs. absence of negative cognitive styles; however, this was no longer the case when hopeless depression was controlled for. As such, it appeared that the etiological chain of the hopelessness theory accounted for only part of the emotional abuse–depression link. This assumption was also supported by Gibb et al. (67) who found that childhood emotional maltreatment led to negative attributions and inferences about specific experiences relating to emotional maltreatment, rather than cognitive vulnerability more generally.

In comparison, the schema of self-sacrifice refers to an excessive focus on others' desires and responses at the expense of one's own needs, so that individuals who are self-sacrificing typically believe that their own needs and emotions must be suppressed and inhibited (84). Hence, the schema of self-sacrifice might contribute to problems with emotional regulation as reflected in emotional inhibition and thought suppression, which are further demonstrated as experiential avoidance. Early maladaptive schemas refer not only to the content of one's thoughts but also to the repetitive and ruminative nature in which the person focuses on negative thoughts. Lumley and Harkness (89) found that tightly connected negative schema statements and loosely connected positive schema statements mediated the emotional abuse–depression link. This repetitive, ruminative nature of maladaptive schemas overlaps the cluster of emotion dysregulation in brooding rumination, consistent with the finding that brooding rumination was a mediator in the relation between early maladaptive schemas and symptoms of depression in adolescents (140). As such, the different clusters of mediators considered in the context of the present review

can overlap significantly, and most probably interact with and reinforce each other.

Yet, Young et al. (105) have argued that early maladaptive schemas originate as the result of the interaction between early experiences and the child's temperament. The influence of emotional abuse on maladaptive schemas and cognitive vulnerabilities might be particularly strong when early experiences interact with specific temperament dimensions, such as high Neuroticism and low Extroversion (141). Consistent with this assumption, high Neuroticism, low Extroversion, and low Conscientiousness have not only been consistently linked to the onset of MDD (115) but have also been found to be a mediator in the emotional abuse–depression link (69). Calvete (62) examined temperament as a moderator in a 1-year follow-up to test the hypothesis that parental emotional abuse interacting with temperament predicts a worsening of maladaptive schemas. However, emotional abuse and temperament seemed not to be related in their study. Thus, a direction for future research is to clarify the mechanism through which specific temperamental diatheses interact with early emotional abuse in the ongoing development of specific schema themes, thereby resulting in vulnerability to depression.

Finally, problems with emotional regulation and problems in person–environment exchanges (problems with salutogenesis) are expressed as (a) self-generated negative events, (b) heightened sensitivity to stressors, and (c) interpersonal problems in adolescence and adulthood. Both Hankin (31) and Uhrlass and Gibb (82) reported that stress associated with negative life events served as the mechanism linking childhood emotional abuse to current depression symptoms. Regarding stressful negative events, it is important to distinguish between (a) occurrence of life stress, which may be in part self-generated, and (b) subjective perception of life events. Hankin (31) measured a prospective increase in the number of negative life events that typically occur for young adults, from school/achievement to interpersonal/romantic difficulties. Uhrlass and Gibb (82) focused on hassles rather than major negative life events (e.g., deaths or loss of job) in their study, and levels of negative life events were calculated by summing the number of hassles endorsed rather than the subjective impact ratings. Thus, both studies fall into the category of occurrence of life stress, and are consistent with Hammen's model where childhood emotional abuse may set the stage for self-generated negative events and depressive symptoms, as well as the elaborated cognitive vulnerability–transactional stress model of depression (142). Hankin (31) claimed that childhood emotional maltreatment does not appear to serve merely as an additional risk factor for depression; rather, it may contribute to the onset of an ongoing cycle of negative events and depression in adulthood.

In respect of the subjective perception of life events, individuals with a history of childhood emotional abuse are at greater risk of developing depression through the proximal factor of a negative cognitive style for depression, which noticeably overlaps the cluster of cognitive-personality variables. This subjective perception of life events is highly intertwined with heightened sensitivity to stressors. Post's (143) stress sensitization hypothesis proposes that a history of childhood maltreatment lowers the threshold of stress necessary to trigger depression onset, so that individuals with a history of childhood maltreatment are more reactive and responsive to stressors (144–146). In addition, parental emotional abuse is likely to increase one's negative appraisal of stressful life events, and this relationship might be mediated by affective temperaments (147). Although Hayashi et al. (69) found no correlation between negative life events and personality, Monroe and Harkness (145) suggested that people with a characteristically negative style of interpersonal interactions tend to have more stressful life events. Future research should examine whether temperament interacts with stressful negative life events when integrated into the same structural model to help elucidate the common and specific etiological factors for depression.

With regard to problems with emotional regulation being manifested as interpersonal problems in adolescence and adulthood, Barthel et al. (148) have argued that emotion regulation is directly linked with one's ability to effectively navigate the social world. Engagement in emotion regulation often occurs interpersonally with trusted others helping to regulate one's emotions (148). One study included in our review, by Christ et al. (32), identified two specific domains of interpersonal problems—cold/distant and domineering/controlling—as particularly important in explaining the emotional abuse–depression link. Children with a history of emotional abuse are likely to develop negative internal working models of the self and others as well as maladaptive schemas that interfere with social functioning as the child matures, leading to experiential avoidance and a lack of trust in others (149). This avoidance, as an emotion regulation strategy, in interpersonal relationships and social situations can be seen as a cold/distant interpersonal style. By contrast, the examination of a domineering/controlling interpersonal style in depression has received inconsistent results (125, 127). In addition to cold/distant and domineering/controlling interpersonal styles, other interpersonal problems, such as self-sacrificing, non-assertive, intrusive/needy, and overly accommodating, also theoretically relate to the emotional abuse–depression link. However, Sachs-Ericsson et al. (79) found no evidence of a dependent interpersonal style as a mediator in this link, although the dependent characteristic reflects extreme distress in relation to a strong need for approval and has been posited as a vulnerability marker for depression. Future studies are needed to examine which specific interpersonal styles stem from childhood emotional abuse, and to what extent these types of interpersonal problems may be associated with a greater risk of depression.

## Directions for Future Research

Our findings support several potential psychological routes with relative consistency to adolescent and adult depression following a history of childhood emotional abuse (e.g., early maladaptive schemas, hopelessness, negative cognitive styles, brooding rumination, and overall emotion dysregulation). Further investigation is recommended to replicate the findings of those mediators that have been examined only a few times (e.g., personality traits, interpersonal styles). It is highly likely that considerable overlap exists between various mediating constructs and that several mediators may represent manifestations of

other underlying processes (e.g., the important role of cognitive processes underlying the regulation of emotion). There is a lack of clarity regarding the extent to which these processes are relatively independent from each other, as well as their relative contribution to explaining risk for depression in those who have experienced childhood emotional abuse. Future research is needed to (a) compare the effect size of different mediators, (b) explore the interrelation between various mediators, (c) determine the degree of overlap, to disentangle the independent contribution of these different processes, and (d) elucidate whether certain types of experiences are particularly likely to trigger certain mechanisms. It is also possible that some of the psychological variables reviewed in the current study have a moderating role, as opposed to a mediating one, in the emotional abuse–depression link. For example, Hoppen and Chalder (24) found that romantic attachment avoidance and low self-esteem served as moderators, rather than mediators, in the relationship of childhood adversity with affective disorders. It is therefore unwarranted to assume that factors that do not appear to mediate the emotional abuse–depression link in this review do not play a role in the development of depression.

Current theories and evidence explaining the emotional abuse–depression link are largely built on isolated investigations based on researchers' interests and constrained by research funding and sample sizes, which may at times narrow findings at the expense of the bigger picture. To scrutinize whether psychological mediators function as a complex interrelated system in the emotional abuse–depression link, this review proposes a multilevel integrative model. Such an approach would help to move isolated focuses forward to empirical research based on a more comprehensive theoretical model that incorporates the different potential psychological mediators. This future work will require larger sample sizes, longitudinal designs, and more complex modeling techniques, allowing the robust appraisal of different pathways from childhood emotional abuse to subsequent depression.

Future research should also take resilience and protective factors into consideration. Not all emotionally maltreated children develop lifelong maladaptation. A focus on the individual differences between childhood emotional abuse victims can help us understand how some people overcome the emotional challenges of growing up in such environments. Studied protective factors for childhood maltreatment include attributional style (e.g., attribute abuse to external causes), early childhood secure attachment, and environmental factors, such as school and the presence of supportive relationships (150, 151). This line of research will help establish protective factors across the family system, community, school, and peer group to moderate the effects of parental emotional abuse.

Finally, future research should involve neurobiological processes related to identified psychological mechanisms in investigating the paths. Childhood adversity has been shown to be particularly detrimental, with long-lasting effects, during early stages of brain development (152). The causes of depression are most likely to be multifactorial, with interplay between genetic, neurobiological, psychological, and social factors. This line of future work will benefit from the integration of neurobiological and psychosocial approaches to illuminate the pathways that lead from childhood emotional abuse to depression in adolescence and adulthood.

## Limitations

Findings should be considered in light of some limitations. Based on our quality assessment, more than half of the included studies ($n = 18$) were judged to be at high risk for selection bias, 13 studies did not control for the influence of potentially relevant confounders, such as age, gender, ethnicity, and socioeconomic status, and, importantly, eight studies were rated as weak in terms of the relative strength of the statistical mediation analysis. Given that the relationship between childhood maltreatment and later affective disorders has been found to be dependent on the age of exposure (153, 154), doses (2, 155), and severity (20, 156), a level of caution is required in the interpretation of the relative contribution of the mediators examined in the studies receiving weak ratings. In addition, more than two-third of the eligible studies ($n = 24$) were cross-sectional, where the relationship between the mediators and depressive symptoms is hard to disentangle as mediation is an inherently longitudinal process. Given that the quality of the studies might be impaired by the bidirectional relationship between risk factors for depression and depressive symptoms, the mediators identified in the cross-sectional studies should be accepted with caution.

An outstanding potential moderator that needs to be taken into consideration is the age of exposure. Twenty-six studies used adult samples (including one study investigating older participants), of which 11 used young adults recruited from universities, and eight studies used adolescent samples. Childhood emotional abuse might be more strongly predictive of depression onset in adolescence than in adulthood (157, 158), and the depressogenic effect of childhood maltreatment has also been shown to be stronger in adolescence than in adulthood (159). Considerable research has pointed to the dramatic increase in interpersonal stressful events and heightened sensitivity to social situations that occurs during adolescence as significant contributors to depressive symptoms. Affective processing (160) and top-down processes involved in understanding and identifying emotions are still developing during adolescence (161). Adolescence is a developmental period where individuals often experience their first depressive episode (162). The point prevalence of MDD in adolescence ranges from 3 to 8%, with lifetime rates reaching 20% by the end of adolescence (163). La Rocque et al. (164) examined the moderating role of age in the relation of childhood maltreatment with sensitization to stressors that occurred just before episode onset. They found that adolescents (but not adults) with a history of maltreatment reported a lower level of severity of life events before episode onset than those without such a history; moreover, this relation was specific to emotional abuse, not physical or sexual abuse. As such, adolescents with a history of childhood emotional abuse may be more strongly sensitized to stressful life events that are crucial to triggering depression than adults with a similar history. Moreover, given that childhood maltreatment is closer in time to depression onset for adolescents who may still be living in an environment characterized by family discord and parental cruelty than for adults (165), childhood emotional abuse is likely to have

a stronger etiological relation to depression onset in adolescence than in adulthood.

Notably, a majority of studies have samples composed of participants who are primarily Caucasian, women, university students, high-risk groups, low-income groups, or some combination thereof. One-third of included studies ($n = 11$) were conducted with young adult participants recruited from universities, who represent a fairly high-functioning sample with relatively homogeneous backgrounds. As such, the findings may be limited in generalizability to other populations. Nonetheless, well-educated young adult women have been shown to be an important high-risk group for developing depression (166). Not only are women twice as likely as men to experience MDD (167); a recent survey across eight countries demonstrated depressive disorder to be the most common mental disorder in first-year university students, with a 12-months prevalence of 18.5% (168). In addition, only a few mediators in eligible studies (e.g., early maladaptive schemas) have been examined in both clinical samples and non-clinical community samples. It will be important to examine whether the current findings of various mediators are replicated in both clinical and general samples and in more ethnically diverse samples.

Another limitation that has been repeatedly pointed out in the literature is the reliance on retrospective recall of childhood emotional abuse. There is a possibility of age and memory biases during affective episodes related to childhood maltreatment. As mentioned, some studies have reported that childhood maltreatment affected adolescents and young adults more strongly than middle-aged and older adults (164). However, some researchers found that childhood maltreatment had certain effects on older adults (169). Recent studies suggest the recall and mood effect can be negligible and retrospective reports can be highly consistent with prospective designs (170–172). In addition, as studies using a cross-sectional design do not allow any firm conclusions to be made regarding the direction of the present relationship between childhood emotional abuse, potential mediating factors, and later depression, in order to arrive at more solid ground it would be necessary for each potential mediator to be replicated in a longitudinal design.

There were also some limitations to the review itself. While our search strategy was sensitive and incorporated the screening of references and citations of eligible studies, included articles were restricted to those published in peer-reviewed English-language journals, which may have resulted in relevant evidence being overlooked. The exclusion of unpublished reports, including master's and doctoral theses, may impact on the current findings, as published sources may overrepresent outcomes where significant mediation via psychological processes is observed. However, our search strategy did not include the terms "mediator" or "mechanism" and therefore we were more likely to retrieve studies reporting diverse, rather than only positive, findings. Future evidence syntheses may include more thorough examination of gray literature or estimate the extent to which publication bias and other selection biases might affect the findings of the review. Despite these limitations, the current review represents an initial step in building a comprehensive multilevel theoretical framework to guide future more integrative research efforts in this field.

## Clinical Implications

Childhood maltreatment has been linked to treatment resistance in affective disorders (9, 173, 174) as well as greater functional impairment (175). Some researchers have claimed that childhood maltreatment-related affective disorders should be considered a clinically distinct subtype (176). Our results are in line with numerous studies arguing that early abusive experiences should be routinely assessed in clinical practice, and it is important for clinicians to recognize and assess any core dysfunctional beliefs. In comparison with other more "tangible" forms of maltreatment, a history of emotional abuse may be more elusive and subtle to detect in intervention. The very nature of emotional abuse contributes it the possibility that it may "hide in plain sight" from practitioners and help to explain the fact that few interventions exist that explicitly target a history of parental emotional abuse (43). Our findings represent potentially valuable intervention targets that clinicians should consider while developing prevention and treatment plans for victims of childhood emotional abuse who have distressing symptoms of depression. As these mediators are very likely to function as a complex interrelated system, clinical work should include work on identified pathways, with the awareness that addressing each one may also positively impact on the others.

Cognitive and emotion-related factors, sensitivity to stressors, emotion dysregulation, and interpersonal style are often explicitly targeted in therapeutic and preventive interventions that are already recommended for depression, such as cognitive-behavioral therapy, interpersonal psychotherapy, emotion-focused therapy, acceptance-based psychotherapeutic interventions, such as dialectical behavior therapy and acceptance and commitment therapy, as well as psychodynamic and mindfulness-based approaches. Schema therapy, which includes key strategies to modify early maladaptive schemas, such as emotional imagery, interpersonal techniques, cognitive restructuring, and self-empowerment exercises, would be helpful for victims of emotional abuse with chronic dysfunctional schemas. This review highlights the importance of personalized therapy plans, as well as preventive and public health interventions aimed at individuals with a history of childhood emotional abuse.

# CONCLUSIONS

The current systematic review demonstrates several potential mechanisms that might be involved in the relation between childhood emotional abuse and adolescent and adult depression. These psychological mediators fall into five clusters: (1) early maladaptive schemas, (2) cognitive-personality variables, (3) emotion dysregulation, (4) interpersonal styles, and (5) stressful negative events. However, the choice of examined variables to date has been limited and selective, suggesting that the conceptual framework guiding research in this field needs an integrative developmental cascade approach. Potentially significant elements of the emotional abuse–depression link may

remain invisible as relevant variables have not been sufficiently examined. For example, we found no study examining either guilt or anger/aggression as a mediator, although they are two central concepts in the psychodynamic understanding of depression. We also hope to see more research on resilience and protective factors that might buffer children who are at risk for emotional and behavioral maladjustments. Most importantly, our postulated multilevel integrative model aims to inspire future research that directly addresses a coherent and integrated developmental theory or model in the emotional abuse–depression link. Ultimately, we hope to see a shift from isolated focuses in this area toward empirical research based on a more comprehensive theoretical model that incorporates the different potential psychological mediators and organizes them within a hierarchical multilevel theoretical framework.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

## AUTHOR CONTRIBUTIONS

EL conducted the systematic search and data extraction. Uncertainties during this period were resolved through discussions among the authors. The initial writing up was performed by EL under the supervision of PL and NM. All authors contributed to the manuscript writing and further elaboration and approved the final manuscript.

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# The Association Between Adolescent Residential Mobility and Adult Social Anxiety, BDNF and Amygdala-Orbitofrontal Functional Connectivity in Young Adults With Higher Education

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**Background:** Large-scale epidemiological studies demonstrate that house moves during adolescence lead to an increase in anxiety and stress-sensitivity that persists into adulthood. As such, it might be expected that moves during adolescence have strong negative and long-lasting effects on the brain. We hypothesized that moves during adolescence impair fear circuit maturation, as measured by the connectivity between amygdala and orbitofrontal cortex, and expression of brain-derived neurotrophic factor (BDNF).

**Methods:** We examined young adults with middle and high economic status recruited from the community using clinical interviews, self-report questionnaires, functional magnetic resonance imaging during an emotional faces task and during a 10 min rest phase, and serum BDNF serum concentration.

**Results:** Out of 234 young adults, 164 did not move between ages 10 and 16 (i.e., moves with change of school), 50 moved once, and 20 moved twice or more than twice. We found relationships between adolescent moving frequency and social avoidance ($p_{corr} = 0.012$), right amygdala-orbitofrontal cortex connectivity ($p_{corr} = 0.016$) and low serum BDNF concentrations in young adulthood ($p_{corr} = 0.012$). Perceived social status of the mother partly mitigated the effects of moving on social avoidance and BDNF in adulthood.

**Conclusions:** This study confirms previous reports on the negative and persistent effects of residential mobility during adolescence on mental health. It suggests that these effects are mediated by impairments in fear circuit maturation. Finally, it encourages research into protecting factors of moving during adolescents such as the perceived social status of the mother.

**Keywords: residential mobility, connectivity, fMRI, BDNF, anxiety, stress**

## INTRODUCTION

There is growing evidence that moves, or residential mobility, in childhood and adolescence increase the risk of external behaviors such as impulsive and risky behaviors, and internalizing problems such as stress sensitivity, anxious temperament, and social withdrawal (1).

The impact of residential mobility on child development varies with the age of the child. A Danish national birth cohort study including 1.5 million participants examined moving during each age year between birth and 14 years (2). It demonstrated that the association between moving and health problems increased with age of moving. In addition, it showed that multiple moves during this sensitive time period were associated with worse outcomes than a single move. A follow-up examination of the cohort revealed that mental health problems related to moving in adolescence persisted into adult life.

Adolescence may be a particularly critical period for moving because of the loss of peer networks that are increasingly important in this period. Impairment of peer group socialization is a risk factor for stress-related disorders (3). Moreover, mobile adolescents experience less informal neighborhood control than their stable counterparts (4). As a result, residentially mobile adolescents are more frequently socially isolated, bullied, and affiliated with delinquent peers than residentially stable adolescents, and become less involved in prosocial and achievement-oriented activities (5). Even "upward" moves to wealthier, lower-risk and more prestigious neighborhoods were associated with more frequent school drop-outs (6).

Adolescence is the peak age of many psychiatric problems (7). In this critical phase, there are important changes in brain structure and brain function associated with synaptic reorganization and changes in neuroplasticity (8). Increased plasticity renders the brain highly vulnerable to environmental stress such as moving (9). The connection between the amygdala and the orbitofrontal cortex, a neural substrate of affect regulation, is particularly vulnerable in this period because it undergoes important changes in adolescence (10). The right amygdala-orbitofrontal connectivity is particularly relevant for fear conditioning and anxiety (11, 12).

Brain-derived neurotrophic factor (BDNF) plays a critical role in the development of the prefrontal-amygdala circuit during adolescence (13). Stress-induced reductions in BDNF bioavailability can compromise the integrity of this circuit and increase risk of social deficits. In rodents, chronic social defeat stress led to abnormal expression of BDNF by epigenetic modifications (14). Such modifications may lead to lasting impairments in neuroplasticity, which is widely implicated in psychiatric diseases including anxiety disorders, depression, bipolar disorders, schizophrenia, and addiction (15).

Most previous studies on residential mobility focused on subjects with low socioeconomic status and educational problems. Given that educational attainment is an important protective factor against stress-related disorders such as depression (16), it is important to investigate the effects of residential mobility in individuals with higher education. The majority of previous studies examined psychosocial outcomes and did not include biological measures. In this study, we used data from a community-based sample of young adults with middle and high socioeconomic status to examine psychiatry-relevant outcomes and their neurobiological correlates. Specifically, we hypothesized that moving in adolescence was associated with internalizing disorders, such as social anxiety and depression. Furthermore, lower social support, lower social status, abnormal amygdala-connectivity, and decreased serum BDNF concentration are supposed to be related to moving during this critical time period. We also hypothesized that multiple moves were associated with more pronounced behavioral problems and more abnormal biological markers than a single move (dose-response relationship).

## METHODS

### Subjects

Subjects were recruited using advertisements in local newspapers and University blackboard webpages. The recruitment in the student environment, the mentally challenging study procedures and the requirement to be fluent in German language provided us with a sample of predominantly young adults with relatively high educational attainment. Subjects were included into the study only after full explanation of the goals of the study and the risks of the study procedures. The study and the written consent were approved by the local ethics committee (Kantonale Ethikkommission Zürich). Individuals with severe psychiatric disorders such as schizophrenia, bipolar disorder, alcohol and drug dependence, and acute eating disorders were excluded.

The study is part of an ongoing neuroimaging study. We included 234 subjects who underwent MRI scanning and provided data on residential mobility in their adolescence. Out of the 234 subjects, 68 were diagnosed with lifetime major depressive disorder (MDD), including subjects in partial or full remission. **Table 1** displays the clinical characteristics of the study sample categorized by residential mobility.

### Clinical Assessments

Subjects underwent an extensive online survey. The Liebowitz Social Anxiety Scale (LSAS) (17), the Five-Factor Inventory (NEO-FFI) (18), the Obsessive Compulsive Inventory Revised (OCI-R) (19), and questions regarding sociodemographic characteristics, social status and social support were administered online before the MRI session. On the day of the MRI session, subjects filled out self-report questionnaires on acute psychiatric symptoms: Beck's Depression Inventory (BDI) (20) and Beck's Anxiety Inventory (BAI) (21). Psychiatric diagnoses were made based on the Structured Clinical Interview for DSM-IV (22). Adolescent residential mobility was assessed by a single question: "How many times did you move between the ages of 10 and 16 years (i.e., moves with change of school)."

### fMRI Data

All participants were scanned with a 3.0T GE Discovery MR750, using an 8-channel receive-only head coil. The same BOLD-fMRI sequence was acquired during an emotional faces task and for

**TABLE 1 |** Sociodemographic characteristics and residential mobility.

| | No moves | One move | Two or more moves | All | *p* (uncorr.) |
|---|---|---|---|---|---|
| *n* | 164 | 50 | 20 | 234 | |
| Female (%) | 107(65.2) | 35(70.0) | 16(80.0) | 158(67.5) | 0.378a |
| MDD (%) | 42(25.6) | 19(38.0) | 7(35.0) | 68(29.1) | 0.199a |
| Age [y] [M, (SD)] | 25.1(4.9) | 25.0(4.3) | 24.2(4.0) | 25.0(4.7) | 0.707b |
| Education [y] [M, (SD)] | 14.1(2.7) | 14.3(2.8) | 13.2(2.8) | 14.1(2.8) | 0.296b |
| Own income [1000SFR] [M, (SD)] | 21.8(29.3) | 18.4(17.9) | 20.5(21.3) | 21.0(26.6) | 0.726b |
| Parents' income [1000SFR] [M, (SD)] | 133(89) | 116(93) | 98(101) | 126(91) | 0.313b |
| Proportion of divorced parents (%) | 43(35.2) | 13(34.2) | 11(73.3) | 67(38.3) | 0.014a |
| Proportion of subjects in a partnership (%) | 86(54.1) | 23(46.0) | 10(52.6) | 119(52.2) | 0.607a |
| Social status subject [self-rated, M, (SD)] | 6.06(1.48) | 5.88(1.64) | 4.85(1.50) | 5.91(1.55) | 0.004b |
| Social status subject's mother, [rated by subject M, (SD)] | 6.23(1.78) | 6.04(1.77) | 4.95(2.06) | 6.08(1.80) | 0.014b |
| Subjects with regular alcohol consumption (at least once a week, %) | 66(40.2) | 21(42.0) | 9(45.0) | 96(41.0) | 0.909a |
| Subjects with regular drug consumption (mainly cannabis, at least once a month, %) | 9(5.5) | 3(6.0) | 0(0.0) | 12(5.1) | 0.548a |

*a, chisquare test; b, One-way ANOVA.*

a resting state sequence (eyes open, fixation). For both BOLD-fMRI sequences, the same T2*-weighted EPI image parameters were used (38 slices of 64 x 64 voxels, resulting in a resolution of 3.75 x 3.75 x 3.2 mm; TR = 1,925 ms, TE = 32 ms, flip angle = 90°; axial slices were tilted 20° from the AC-PC line forward to reduce potential signal dropouts in the amygdalae). The images were all warped to the MNI template and then smoothed with a 5 mm FWHM isotropic kernel (SPM12 for Matlab; https://www.fil.ion.ucl.ac.uk/spm/software/spm12). For four subjects, both task and resting state fMRI datasets could not be used; for the task fMRI, an additional 16 had to be excluded, for the resting state fMRI, an additional 3. Reasons for exclusion of fMRI datasets included: movement artifacts (5), sleepiness, e.g., with under 80% correct responses in the task (6), problems seeing the stimuli (4), software problems in the scanner or stimulus presentation pcs (4) or administrative reasons (lack of time after taking out the subject in the middle of the session in one subject, due to an artifact from a small metal drawstring tip recognized only during the scanning session); we had to exclude data from one subject because of a mild abnormality. The VOIs for the amygdalae were hand-drawn on a T2-weighted image coregistered with the normalized EPI-template. The VOIs for the orbitofrontal cortex were used from the conn toolbox (see below).

The fMRI task was programmed as closely as possible to the experiment used by Etkin et al. (23). It included unmasked fearful, masked fearful, and neutral faces to examine amygdala responses to threat cues. After five dummy scans, 243 volumes were collected over a duration of 467.8 s. Stimuli were presented on MR-compatible goggles (Nordic Neuro-Lab) by Cogent (Cogent2000v1.32) running on Matlab 2011b. fMRI contrasts were calculated according to the onsets of the blocks (block design folded with standard HRF using an autoregression model). For the present study, only the contrast "fearful faces vs. neutral faces" was used. All six movement parameters, as well as white matter and CSF-activations, were regressed out.

Resting state functional connectivities were calculated with the conn toolbox (https://www.nitrc.org/projects/conn), version 15 g. We concentrated on the functional connectivities of left-amygdala-left orbitofrontal cortex and right amygdala-right orbitofrontal cortex.

## Serum BDNF Concentration

Serum samples were collected between 10 h 24 min and 18 h 18 min [mean 14 h 06 min, SEM 6 min; the time of sampling did not differ between groups, ANOVA ($p = 0.512$)] and stored at −80°C before assaying BDNF content. BDNF concentrations in the serum were assessed with an enzyme-linked immunosorbent assay (ELISA) kit (Biosensis® Mature BDNF RapidTM ELISA Kit: Human, Mouse, Rat; Thebarton, SA, Australia). As described in the manufacturer's protocol, the samples were diluted (1:100) and detection of BDNF was carried out on pre-coated mouse monoclonal anti-mature BDNF 96-well plates. Within 5 min after addition of the stop solution, the absorbance was measured in a microplate reader set at 450 nm and a correction wavelength set to 690 nm, to determine BDNF concentrations according to the standard curve. All assays were carried out in duplicate and means were calculated.

## Statistical Analysis

We used group comparisons (Oneway ANOVAs and subsequent Tukey tests) and categorized the variable "moves during adolescents" into three categories, namely, zero moves, one move, and two or more moves (as to be expected, the number of moves followed a Poissonian-like distribution with a higher number of moves becoming extremely rare).

ANOVAs were possible because most variables tested could be interpreted on an interval scale, followed Gaussian distributions and showed approximately equal estimated population variances. The influence of third variables were assessed with ANCOVAs with a single control variable to minimize the impact of non-linearities and statistical dependencies among the control variables [control variables tested were sex (tested by looking at the sexes separately), age, education, alcohol consumption, Marijuana consumption; the self-rated social status of the

subject, the subject's father and the subject's mother were also tested]. We used a significance level of $p = 0.05$ as a threshold of a statistically meaningful result; for the correction of multiple comparisons, we used a Bonferroni-Holm correction (p(corrected)=p(uncorrected)*(n+1-k), where n is the number of independent comparisons and k is the number in the ranked list of results according to rising (uncorrected) $p$-values. For the psychiatric indices and the amygdala-orbitofrontal functional connectivities, we treated several measurements as one measurement, because they tended to be highly correlated.

To elaborate on the specificity of the main finding, subsequent ANCOVAs were used with an uncorrected $p = 0.05$ alpha error level.

## RESULTS

Out of the 234 subjects included in the study, 164 did not move between ages 10 and 16, 50 moved once, and 20 moved twice or more than twice. As shown in **Table 1**, objective indicators of social status such as educational achievement, personal income, and parental income were not associated with adolescent moving (all $p > 0.250$). However, moving was associated with lower subjective social status ($p = 0.004$) and lower ratings of the subject on the social status of the subject's mother ($p = 0.014$).

As shown in **Figure 1**, social anxiety as assessed using the LSAS was significantly associated with the three moving categories ($p = 0.028$ with Bonferroni-Holm correction) with non-movers having the lowest score of 13.4, followed by single-movers (23.7), and multi-movers (25.3) [in *post-hoc* Tukey tests, only the comparison 0 moves vs. 1 move turned out to be significant, p(uncorr) = 0.034]. Similarly, other anxiety/fear indicators also showed moving group differences, partly reaching significance (LSAS avoidance; BAI), partly as non-significant trends (neuroticism NeoFFI: OCD) (see **Table 2**).

As shown in **Figure 2**, there was a significant association between right amygdala-right orbitofrontal functional connectivity ($p = 0.016$ corrected with the Bonferroni-Holm method), between non-movers, single-movers and multi-movers. In response to suggestions from the reviewers, we calculated two MANOVAs, with the two "parallel" connectivities (left amygdala-left orbitofrontal cortex and right amygdala-right orbitofrontal cortex) or all four "parallel plus crossing" connectivities (left-left, right-right, left-right, right-left) as one dependent variable (all of them were significantly correlated) and in both cases found significant relationships with number of moves in adolescence ($p = 0.001$).

BOLD activations of the right amygdala in a fearful face task were not statistically significantly different among the groups ($p = 0.118$ corrected). As shown in **Figure 3**, there was

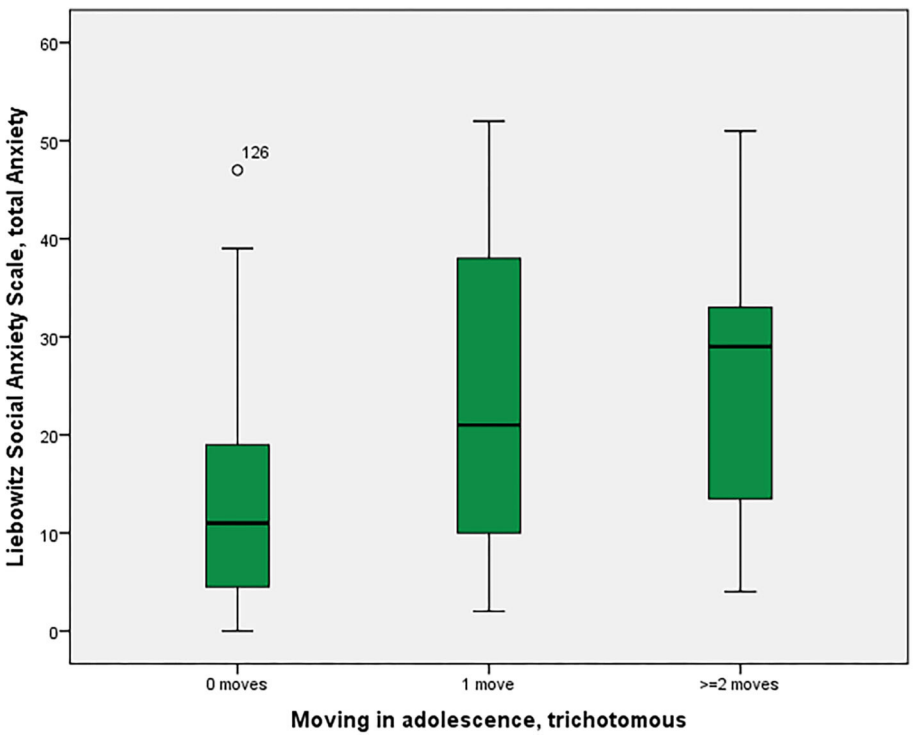


**FIGURE 1 |** Residential mobility in adolescence and social anxiety in adulthood. Boxplot for the group comparison in social anxiety (Liebowitz Social Anxiety Scale, Anxiety) between subjects who did not move during adolescence (M = 13.4, SEM = 1.5, $n = 52$) with subjects who moved one time (M = 23.7, SEM = 4.7, $n = 12$) and twice or more than twice (M = 25.3, SEM = 6.2, $n = 7$). The ANOVA for simultaneous 3-group comparison is significant ($p$ uncorrected = 0.007, with Bonferroni-Holm correction $p = 0.021$). Uncorrected *post-hoc* Tukey tests showed a significant result for zero moves vs. one move ($p = 0.034$), but not for the other comparisons (zero with two or more: $p = 0.055$; one with two or more: $p = 0.960$).

**TABLE 2 |** Detailed statistics for group comparisons.

| | No moves M(SEM) | One move M(SEM) | Two or more moves M(SEM) | ANOVA *p* (uncorr) | ANOVA *p* (corr) | Significant *post-hoc* tests (Tukey, $p < 0.05$ uncorr) |
|---|---|---|---|---|---|---|
| LSAS anxiety | 13.4(1.5) | 23.7(4.7) | 25.3(6.2) | 0.007 | 0.021 | 0 vs. 1 mvs |
| LSAS avoidance | 11.7(1.4) | 24.6(4.6) | 18.6(5.7) | 0.004 | 0.012 | 0 vs. 1 mvs |
| Neuroticism NeoFFI | 18.8(0.7) | 20.9(1.2) | 22.9(1.8) | 0.066 | 0.198 | |
| BAI | 4.77(0.41) | 5.45(0.82) | 9.60(2.63) | 0.005 | 0.015 | 0 vs. ≥ 2, 1 vs. ≥ 2 |
| Obsessive Compulsive Inventory Revised (OCI-R) | 8.80(0.59) | 12.00(1.33) | 9.85(1.87) | 0.050 | 0.150 | |
| Task fMRI BOLD-activation right amygdala | 0.09(0.02) | 0.07(0.03) | 0.18(0.06) | 0.118 | 0.118 | |
| Functional connectivity left amygdala - left OFC | 0.31(0.03) | 0.47(0.07) | 0.36(0.11) | 0.082 | 0.164 | |
| Functional connectivity right amygdala - right OFC | 0.21(0.03) | 0.42(0.06) | 0.21(0.11) | 0.008 | 0.016 | 0 vs. 1 mvs |
| BDNF (ng/ml) | 12.0(0.4) | 10.0(0.6) | 8.3(1.3) | 0.003 | 0.012 | 0 vs. 1 mvs |

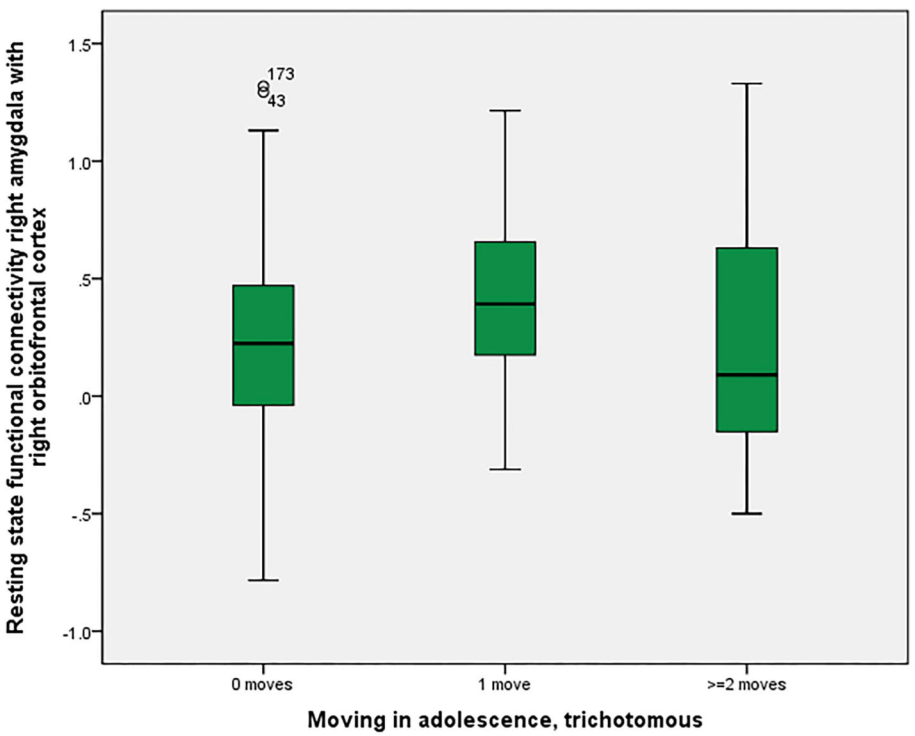


**FIGURE 2 |** Residential mobility in adolescence and functional connectivity right amygdala—right orbitofrontal cortex. Boxplot for the group comparison in functional connectivity between right amygdala and right orbitofrontal cortex (qualitatively similar for other amygdala-orbitofrontal connectivities, e.g., left amygdala-left orbitofrontal cortex; beta-values corrected for scan-to-scan motion and activations in the white matter/CSF segments) between subjects who did not move during adolescence (M = 0.21, SEM = 0.03, $n = 161$) with subjects who moved one time (M = 0.42, SEM = 0.06, $n = 41$) and twice or more than twice (M = 0.21, SEM = 0.11, $n = 20$). The ANOVA for simultaneous 3-group comparison is significant ($p$ uncorrected = 0.008, with Bonferroni-Holm correction $p = 0.016$). Uncorrected *post-hoc* Tukey tests showed a significant result for zero moves vs. one move ($p = 0.006$), but not for the other comparisons (zero with two or more: $p = 0.999$; one with two or more: $p = 0.140$).

a significant association between moving and serum BDNF concentrations ($p = 0.021$ with Bonferroni-Holm correction), with highest BDNF concentrations in non-movers, followed by single-movers and multi-movers. While anxiety/fear indices were all very strongly correlated, functional connectivity between right amygdala and right orbitofrontal cortex, and right amygdala activation and serum BDNF concentration were not correlated with each other, and not correlated with LSAS (see **Table 3**).

When controlling for the social status and income variables as linear covariates in ANCOVA, only self-rated social status substantially reduced the effect of the moving variable (e.g., on LSAS anxiety, reducing the eta-square effect size from 0.134 to 0.080; on BAI, reducing the eta-square effect from 0.046 to 0.023),

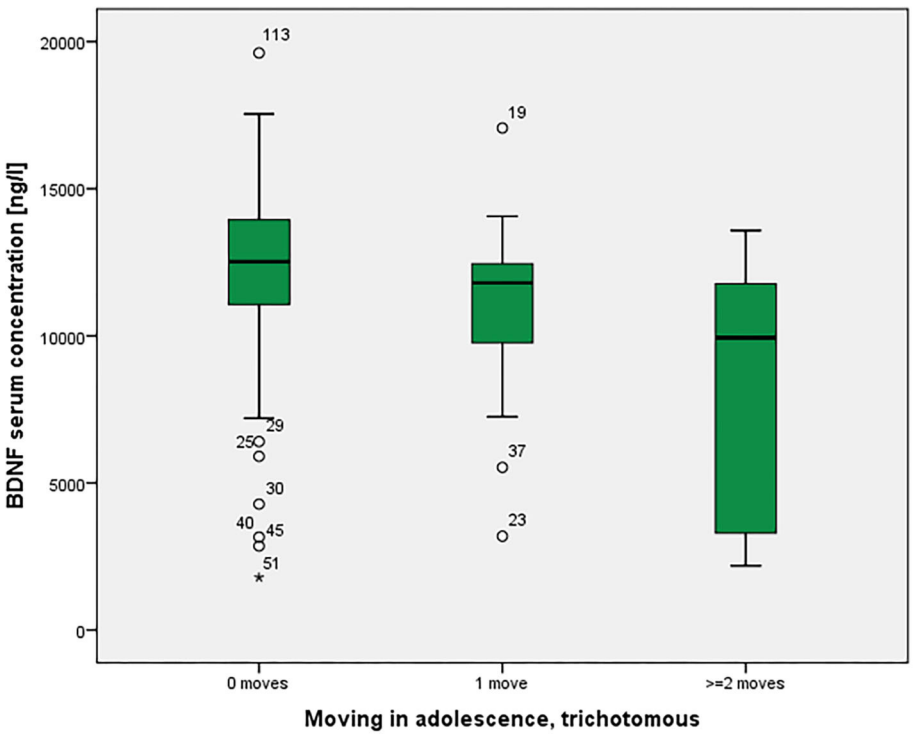


**FIGURE 3 |** Residential mobility in adolescence and Brain-Derived Neurotrophic Factor (BDNF) in the serum. Boxplot for the group comparison in serum BDNF concentration (ng/l) between subjects who did not move during adolescence (M = 12.0, SEM = 0.4, $n = 74$) with subjects who moved one time (M = 11.0, SEM = 0.7, $n = 21$) and twice or more than twice (M = 8.3, SEM = 1.3, $n = 11$). The ANOVA for simultaneous 3-group comparison is significant ($p$ uncorrected = 0.007, with Bonferroni-Holm correction $p = 0.021$). Uncorrected *post-hoc* Tukey tests showed a significant result for zero moves vs. two or more moves ($p = 0.002$), but not for the other comparisons (zero with one: $p = 0.481$; one with two or more: $p = 0.072$).

**TABLE 3 |** Correlations between psychiatric indicators and physiological variables.

| | LSAS avoidance | Neuroticism | BAI | OCIR | Functional connectivity rAMY-rOFC | BDNF |
|---|---|---|---|---|---|---|
| LSAS anxiety | **0.870** | **0.632** | **0.643** | **0.577** | (0.139) | (0.104) |
| LSAS avoidance | | **0.606** | **0.554** | **0.622** | (0.056) | (0.012) |
| neuroticism | | | **0.581** | **0.510** | (−0.041) | (−0.019) |
| BAI | | | | **0.490** | (−0.021) | (−0.112) |
| OCIR | | | | | (−0.035) | (−0.036) |
| Functional connectivity rAMY-rOFC | | | | | | (0.121) |

*Non-significant correlations in brackets; bold means $p < 0.010$.*

income of the parents reduced the effect size of right amygdala activation (eta-square from 0.020 to 0.004) whereas years of education, own income, income of the parents or social status of the parents did not significantly affect any of the results. As shown in **Table 1**, drug and alcohol consumption were not associated with residential mobility.

## DISCUSSION

In this study of young adults with an average education duration of 14 years, we found a positive relationship between moving during adolescence and social anxiety, anxiety symptoms as assessed with the BAI and low subjective status in adulthood. The examination of resilience-related biological measures pointed in the same direction: moving in adolescence was associated with low serum BDNF concentration and abnormal amygdala-orbitofrontal functional connectivity in adulthood.

There is increasing evidence from epidemiological and sociological research that compared with children, adolescents are more social, form more complex peer relations, and are more sensitive to acceptance and rejection by their peers. Social interactions have an important influence on mentalizing competences, such as perspective taking, that are still under development during adolescence (24). In this period, important

neuronal reorganizations make the brain vulnerable to change. Adolescence is the peak age of stress-related disorders (7). Specifically, the plasticity of the connection between the amygdala and the prefrontal cortex is of crucial importance since it is substantially involved in affect regulation after puberty (10). As a result, impairments of social integration and brain development may have lasting consequences on mental health.

Twin studies estimate that around 70% of risk factors of social anxiety are non-genetic in nature (25), and that both familial and non-familial environmental factors play an important role in the development of social anxiety disorders. So far, there is a lack of knowledge of concrete, modifiable environmental risk factors in psychiatry. Residential mobility can be considered a modifiable risk factor that has both familial and non-familial aspects. Based on animal and human research, theoretical models assume that inadequate development of the perception of control is strongly implicated in the pathogenesis of excessive anxiety (26). It is plausible that not only parenting style, but also moving in adolescence can impair the sense of control.

Our finding of an association of moving with social status and social avoidance fits well into previous research. Families that frequently move may have a general lack of connections to their neighbors and communities and may have more difficulty building these connections (5). Movers have fewer friends and are socially more isolated (1). Our study adds to these findings, demonstrating that moving during adolescence can lead to social avoidance well into adulthood.

In our study, adolescent income and parental income were not associated with moving. This suggests that economic factors may not be the main driver of the association between residential mobility and mental health, confirming previous results that "upward" moves into higher quality neighborhoods have a comparable negative impact on adolescents as "downward" moves into poorer neighborhoods (6).

Educational attainment has been found to be a strong protective factor against stress-related disorders such as depression. A meta-analysis of 37 studies demonstrated a 3% decrease in the risk of depression for each additional year of education (27). This effect seems to be largely independent of the genetic risk of mood and anxiety disorders (16). Given that most studies on the health consequences of residential mobility have been conducted in subjects with low educational attainment, the observation from our study that moving may have a significant negative health impact even in individuals with higher education adds to the existing literature. Previous studies have reported an association between high residential mobility and the development of alcohol and other drug-related problems among adolescents and young adults (28). We did not find such an association, possibly because high educational attainment and economic security in our study subjects provided protective factors against substance abuse (29).

The amygdala has been found to act as a central structure in the association between peripubertal stress, adolescent brain development and later behavioral problems including social avoidance (30, 31). The amygdala is under the influence of top-down pathways from cognitive control regions in the orbitofrontal cortex (32). These pathways develop fully during adolescence, and are plastic and stress-sensitive. Thus, abnormal amygdala-orbitofrontal functional connectivity is a plausible mediator of the association between adolescent stress and later anxiety traits and disorders. Our finding of increased right amygdala-orbitofrontal connectivity in single-movers suggests a compensated state, in which increased connectivity reflects an increased effort of the prefrontal cortex to control right amygdala overactivity. One might speculate that in subjects with exposure to several moves during adolescence, compensation is insufficient, leading to more social anxiety. However, the frequent mover sample was small and interpretation of this finding remains highly speculative.

There is increasing evidence from preclinical studies that serum BDNF concentration mediates the negative consequences of social stress including social isolation on the pathways from the prefrontal cortex to the amygdala that regulate fear and other negative emotions. In rats, social isolation is consistently associated with decreased expression of BDNF (33). In humans, downregulation of BDNF has been related to mood and anxiety disorders, while high BDNF concentration has appeared to be a resiliency factor (34). BDNF may be particularly important in the fear circuit maturation during adolescence (13, 35). In our study, we found a negative dose-response-type relationship between moving during adolescence and serum BDNF concentrations in adulthood. This may reflect a consequence of the stress symptoms experienced by the participants who were exposed to moving during adolescence. Alternatively, low serum BDNF may reflect long-term consequences of moving, possibly mediated by stress-related epigenetic modifications (36). Interestingly, the perceived social status of the mother reduced the effect of moving on BDNF and social avoidance. This is in line with previous literature on social capital that emphasizes the important role of parents in mitigating losses of community social capital resulting from a family's moves (37).

The following limitations merit comment. This was a cross-sectional study where moving in adolescence was assessed retrospectively. Since the participants were young adults, moving in adolescence involved a change in school and was a relatively recent event (or events) that can be easily and reliably recognized. Since we did not assess a full moving history, we cannot analyze our data regarding critical phases of the psychobiological effects of moving. Social factors contributing to moving may have confounded the relationship between mobility and psychopathology. We included mainly highly educated people, which may reduce generalizability of the results to populations with low socioeconomic status. We assessed BDNF in blood. Because the relationship between brain and serum BDNF has not yet fully been elucidated, the interpretation of serum BDNF should be undertaken with caution.

In conclusion, this study demonstrated associations between moving during adolescence and increased social stress-sensitivity in adulthood, illustrated by increased social avoidance, abnormal amygdala-orbitofrontal functional connectivity and low serum BDNF concentration. The results of this study are clinically and socially relevant since moving during adolescence is a potentially modifiable risk factor of stress sensitivity. The exploratory finding that the perceived social status

of the mother mitigated the effects of moving on BDNF encourages future research into protective factors on moving during adolescence.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Kantonale Ethikkommission Zürich. The patients/participants provided their written informed consent to participate in this study.

## AUTHOR CONTRIBUTIONS

GH: designed study and wrote first draft of the manuscript. MH: collected data and helped setting up the study. SM: collected data. RT: provided imaging methods and designed the study. CR: collected data and wrote parts of the manuscript. AB: collected data, conceptualized and performed data and statistical analyses, and wrote first draft. All authors revised and approved the final version of the submitted manuscript.

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# Neuropsychological Subgroups of Emotion Processing in Youths With Conduct Disorder

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**Background:** At the group level, youths with conduct disorder (CD) show deficient emotion processing across various tasks compared to typically developing controls (TDC). But little is known about neuropsychological subgroups within the CD population, the clinical correlates of emotion processing deficits [for instance, with regard to the presence or absence of the DSM-5 Limited Prosocial Emotions (LPE) specifier], and associated risk factors.

**Methods:** 542 children and adolescents with CD (317 girls) and 710 TDCs (479 girls), aged 9–18 years, were included from the FemNAT-CD multisite study. All participants completed three neuropsychological tasks assessing emotion recognition, emotion learning, and emotion regulation. We used a self-report measure of callous-unemotional traits to create a proxy for the LPE specifier.

**Results:** Relative to TDCs, youths with CD as a group performed worse in all three emotion domains. But using clinically based cut-off scores, we found poor emotion recognition skills in only 23% of the participants with CD, followed by emotion regulation deficits in 18%, and emotion learning deficits in 13% of the CD group. Critically, the majority of youths with CD (∼56%) did not demonstrate any meaningful neuropsychological deficit, and only a very small proportion showed pervasive deficits across all three domains (∼1%). Further analyses indicate that established DSM-5

subtypes of CD are not tightly linked to neurocognitive deficits in one particular emotion domain over another (i.e., emotion recognition deficits in CD+LPE vs. emotion regulation deficits in CD–LPE).

**Conclusions:** Findings from this large-scale data set suggest substantial neuropsychological diversity in emotion processing in the CD population and, consequently, only a subgroup of youths with CD are likely to benefit from additional behavioral interventions specifically targeting emotion processing mechanisms.

**Keywords: conduct disorder (CD), callous-unemotional (CU) traits, limited prosocial emotions specifier, emotion recognition, emotion learning, emotion regulation, neuropsychology, heterogeneity**

## INTRODUCTION

Conduct disorder (CD) is one of the most prevalent externalizing disorders in childhood and adolescence (1). It is a leading cause of referral to mental health and youth welfare services and incurs enormous healthcare and societal costs (2). Paradoxically, though, CD is one of the least studied, funded, and understood psychiatric disorders in youth (3). Children and adolescents with CD are characterized by severe antisocial and aggressive behaviors that violate age-appropriate societal norms and the rights of others (1). Empirical data emphasize that CD is a highly heterogeneous condition in terms of clinical phenotype (including different subtypes and psychiatric comorbidities), clinical course (i.e., persistent vs. desisting symptomatology), psychosocial outcomes throughout the lifespan, and contributing environmental and dispositional risk factors [see (3) for a comprehensive overview]. Regarding the latter, accumulating evidence suggests that deficits in different emotion processing domains, such as emotion recognition (e.g., difficulties in identifying facial expressions), emotion learning (e.g., difficulties in learning from punishment), and emotion regulation (e.g., difficulties in inhibiting impulsive responses to emotional cues), may offer a particularly powerful basis for explaining potentially different presentations and trajectories of CD behaviors, including aggression (4–8). For instance, deficits in the recognition of distress cues, such as emotional expressions of fear, sadness or pain, but also of other facial expressions, such as happiness, appear to be most pronounced in individuals with CD who have high levels of callous-unemotional (CU) traits (i.e., reduced guilt and empathy, callousness, and uncaring attitudes) (9). Individuals with CD who present with at least two of these CU traits fulfill criteria for the Limited Prosocial Emotions (LPE) specifier in DSM-5 (1). This subtype of CD is considered particularly severe as affected individuals typically present with an earlier age-of-onset and a more serious and stable set of symptoms, including proactive aggression, placing them at increased risk for poor treatment outcomes (10) [but see also (11, 12)] and for developing mental health problems in adulthood, such as antisocial personality disorder (ASPD) (6, 13, 14). In contrast, individuals with CD but without the LPE specifier (i.e., those showing subclinical levels of CU traits) are thought to show emotion regulation deficits, such as an inability to maintain behavioral control when confronted with acute emotional stimuli (e.g., visual threats), which may contribute to impulsive acts of reactive aggression and an increased risk for anxiety and depression (6). Finally, emotional learning deficits, such as a failure to learn how to avoid choices that lead to punishment rather than reward, occur more broadly in youths with CD irrespective of their LPE status (15).

However, most prior work on emotion functioning in CD, and its clinically defined subtypes, has been limited by relying on relatively small samples with varying selection criteria and neurocognitive tasks (16), including mixed samples of youths with CD or oppositional defiant disorder (ODD), or focusing on a single subdomain of emotion dysfunction instead of all three domains linked to CD, including emotion recognition, learning, and regulation (4, 5, 7). Thus, studies to date have largely been unsuited or underpowered for testing within-CD, individual variability of the underlying neurocognitive disease mechanism(s), including emotion dysfunction. To address the above-mentioned research gaps, we initiated the largest study to date to comprehensively investigate emotion recognition, emotion learning, and emotion regulation using a broad neuropsychological test battery within a single sample of youths with CD ($n = 542$) compared to typical controls ($n = 710$) (17). As traditionally done in this line of research, we first compared the group of youths diagnosed with CD with the typical controls, and based on statistically significant group differences or the lack thereof, we determined whether a CD-related neurocognitive deficit was present or not. As expected, we found that emotion deficits in the CD group spanned across the three neurocognitive domains. However, we also noted that the significant group differences between CD and controls in task performance had effect sizes in the small to very small range (i.e., Cohen's $ds < 0.29$). As this is in line with previous meta-analytic findings (18, 19), these results indeed suggest: (i) substantial distributional overlap *between* the CD and non-CD samples in terms of performance on emotion processing tasks; and (ii) substantial variation in emotion processing abilities *within* the CD population. Hence, it is reasonable to assume that the significant CD-vs.-control effects for emotion processing tasks—or any other neuropsychological measure reported in the literature [e.g., (20)], may either be truly small effects driven by the entire CD sample or, which appears more likely, they are driven by only a subset of youths with CD who have emotion processing deficits (21).

In fact, this notion of diversity in emotion processing is emphasized by current neurocognitive models of CD etiology [e.g., (6, 7)]. These models suggest that dysfunction in distinct emotion processing domains are associated with different subtypes of CD and related symptom sets (22). For instance, given the assumption that youths with CD with the LPE specifier show difficulties in perceiving other people's emotions, particularly distress and happiness, one might predict that performance in this neurocognitive domain would be disproportionately deficient in this subgroup, whereas the subgroup of youths with CD but without the LPE specifier would show specific difficulties with emotion regulation (4, 6).

In addition, emotion dysfunction might serve as an "intermediate phenotype"—i.e., developmental neurocognitive mechanism (23)—linking risk for psychopathology with the emergence of clinical symptomatology, including clinical subtypes of CD (24). There are multiple dispositional and contextual risk factors that have repeatedly been implicated in CD, such as birth complications, maladaptive parenting, or low socioeconomic status [reviewed in (3)]. Data from epidemiological and at-risk samples suggests that particular risk factors appear to have closer associations with a specific domain of emotion dysfunction (25). For instance, children exposed to physical violence or abuse exhibit altered emotion recognition processes (26), including an altered ability to identify and discriminate specific emotions (i.e., anger) contributing to 'hostile attribution biases' (i.e., misinterpreting neutral or ambiguous facial expressions as threatening), which, in turn, predict the emergence of CD behaviors, such as aggression (27, 28). In slight contrast, exposure to numerous adversities, such as poverty (incl. low socioeconomic status), deprivation (incl. institutional rearing), maltreatment, or pre- and perinatal influences (incl. maternal smoking during pregnancy, or birth complications), appears to be related to emotion regulation and learning difficulties predicting the onset of both externalizing and internalizing problems (29). Although the literature is far from being conclusive in linking adversity factors with specific neurocognitive processes as intermediate phenotypes of conduct problems, studying neuropsychologically defined subtypes of emotion dysfunction in CD may provide novel insights into mechanisms that presumably underlie the complex developmental pathways from risk for psychopathology to different clinical expressions of the disorder (30).

Thus, the primary aim of the current study was to adopt a clinically motivated, person-centered (rather than variable-centered) bottom-up analytic approach to explore the neurocognitive diversity of emotion functioning in CD. We accomplished this by re-analyzing the neuropsychological task performance data from our large sample of girls and boys with CD who were comprehensively clinically assessed and reliably diagnosed using standardized, semi-structured interviews (17, 31). For each of the three emotion processing tasks that assessed emotion recognition, emotion learning, and emotion regulation, respectively, we defined deficit as task performance within the bottom 10% of an age-matched control group (equivalent to approximately 1.3 standard deviations below the mean), following the common-metric approach usually applied in pediatric neuropsychology and as previously used in neurocognitive studies in ADHD (21, 32–35).

To our knowledge, this study is the first to investigate neuropsychological subgroups within the CD population by exploring the proportion of youths with CD who do vs. those who do not have deficits in emotion processing, including emotion recognition, emotion learning, and emotion regulation (but see (36, 37) for similar approaches focusing on other neurocognitive domains, such as verbal skills, mental flexibility, or memory, in smaller-scale studies). Our sample is particularly suited to investigate neurocognitive diversity within CD as it is one of the largest, most representative and clinically well-characterized cohorts of girls and boys with CD (vs. typical controls) recruited from a variety of sources, including the community, specialist schools, mental health clinics, welfare institutions, and youth offending services in different European countries (31). Given the magnitude of the effect sizes observed in our previous study (17), we expected to find subgroups of youths with CD without deficit in any domain vs. those who have deficits in only one domain, two domains, or across all three domains. Most importantly, we tested the extent to which neuropsychologically defined subgroups would map clinically onto the CD subtypes described in the DSM-5, including CD with vs. without the LPE specifier, and as a secondary aim, we explored whether the neuropsychological subgroups would be associated with specific CD-related risk factors.

# MATERIALS AND METHODS

## Participants

As part of the European multi-site project entitled "Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotion Processing" (FemNAT-CD; https://cordis.europa.eu/project/id/602407/reporting), we reanalyzed the neuropsychological data obtained from our large sample of youths with CD ($n = 542$, 317 girls) and TDCs ($n = 710$, 479 girls), aged 9–18 years (see (17) for details on recruitment, clinical assessments, and sample characteristics). In brief, we used data from participants who provided a complete neuropsychological dataset which included facial emotion recognition (*Emotion Hexagon task*), emotion learning (*Passive Avoidance Learning task*), and emotion regulation skills (*Emotional Go/Nogo task*). Participants were recruited through community outreach (e.g., mainstream schools) as well as from mental health clinics, welfare institutions, and youth offending services at 10 sites across Europe (**Supplementary Table 1**) (31). Overall exclusion criteria were IQ < 70, autism spectrum disorders, schizophrenia, bipolar disorder or mania, neurological disorders, and genetic syndromes. Individuals with CD were diagnosed according to DSM-IV-TR criteria (38). Youths with "only" ODD who did not fulfill the diagnostic criteria for CD were excluded from the current analysis. TDCs were free of current psychiatric diagnoses and lifetime diagnoses of CD, ODD, and ADHD. We excluded TDCs with lifetime histories of and/or current disruptive behavior disorders, such as ADHD, ODD, and CD, in order to rule out the influence of any subclinical or precursor symptoms that are potentially linked to CD. Written informed consent

**TABLE 1 |** Demographic and clinical characteristics.

| | CD *n*=542 | TDC *n*=710 | Group effect *p-values*[a] |
|---|---|---|---|
| **Age (years) *M* (SD)** | 14.4 (2.3) | 14.0 (2.5) | 0.001 |
| **Females (%)** | 58.5 | 67.5 | 0.001 |
| **Estimated IQ *M* (SD)** | 94.9 (12.4) | 103.5 (12.2) | <0.001 |
| **SES *M* (SD)** | −0.29 (0.93) | 0.28 (1.03) | <0.001 |
| **CD total symptoms *M* (SD)** | 5.45 (2.34) | 0.05 (0.23) | <0.001 |
| **Average age-of-onset of CD (years) *M* (SD)** | 10.3 (3.8) | N/A | |
| **CD age-of-onset subtype (%)** | | | |
| Childhood | 43.0 | N/A | |
| Adolescence | 53.3 | N/A | |
| Unspecified | 3.7 | N/A | |
| **CD severity (%)** | | | |
| Mild | 24.3 | N/A | |
| Moderate | 52.8 | N/A | |
| Severe | 20.5 | N/A | |
| Unknown | 2.4 | N/A | |
| **Impairment caused by current CD (%)** | | | |
| With peers | 63.7 | N/A | |
| With family | 85.9 | N/A | |
| With school | 78.9 | N/A | |
| Unknown | 1.2 | N/A | |
| **LPE specifier (%)** | 43.7 | 18.3 | <0.001 |
| **Current comorbidities *n* (%)** | | | |
| ODD | 78.2 | N/A | |
| ADHD | 38.4 | N/A | |
| SUD | 17.4 | N/A | |
| MDD | 14.8 | N/A | |
| PTSD | 6.7 | N/A | |
| GAD | 3.0 | N/A | |
| **Psychotropic meds (%)** | 30.2 | N/A | |

*Diagnoses and CD symptoms were based on the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version (K-SADS-PL). For TDC, any current psychiatric diagnosis as well as a history of ADHD, ODD, or CD was exclusionary. ADHD, attention deficit hyperactivity disorder; CD, conduct disorder; GAD, generalized anxiety disorder; IQ, estimated intelligence quotient; LPE, limited prosocial emotions specifier [see (39)]; MDD, major depressive disorder; Meds, on psychotropic medications; ODD, oppositional defiant disorder; PTSD, post-traumatic stress disorder; SES, socioeconomic status (SES was based on parental income, education level, and occupation (40)); SUD, substance use disorder (including substance abuse and dependence); TDC, typically developing controls.*

[a]*p-values are based on two-sample t-tests or* $\chi^2$ *tests.*

was obtained for all participants, and local ethics committees approved the study protocol. **Table 1** summarizes the sample's main demographic and clinical characteristics.

All individuals were clinically assessed with the Kiddie-Schedule for Affective Disorders and Schizophrenia–Present and Lifetime version [K-SADS-PL (41)]. The K-SADS-PL is a semi-structured clinical interview that is administered separately to caregivers and participants by trained staff members to assess current and lifetime psychiatric diagnoses, disorder severity, and age-of-onset and duration of a disorder. Additionally, where available, information from medical or case files was used. Summary ratings were derived from the clinical judgment using all sources. The items of the K-SADS-PL are scored on a scale from 0 to 3. A rating of 0 indicates no (insufficient) information, a score of 1 indicates a given symptom is not present, 2 indicates a subclinical expression, while a score of 3 is given when a symptom is present and clinically significant. Scores were recoded, so that a clinical rating of "not present" is represented by 0, a subclinical rating by a score of 1, and a clinically significant rating by a score of 2. Inter-rater reliability (IRR; $N = 75$, i.e., $n = 5$–8 per site) of CD was high (Cohen's $\kappa = 0.91$), with an agreement rate of 94.7%. IRR of other disorders, including ADHD, ODD, major depressive disorder (MDD), and generalized anxiety disorder (GAD), was also high (Cohen's $\kappa$s $\geq 0.84$, agreement rates $\geq$92%), which is in line with the reliability data reported by Kaufman et al. (41). These authors also report data which support the concurrent validity of the diagnoses generated with this instrument. Youths who met criteria for a specific disorder (e.g., behavior disorder) scored significantly higher than undiagnosed youths on rating scales assessing related symptom sets. Using the K-SADS-PL, we also determined the CD-onset type [i.e., childhood-onset (CO-CD): presence of at least one CD symptom and impairment prior to age 10; adolescent-onset (AO-CD): CD symptoms only emerge after age 10] (1).

Full-scale IQs were estimated using the vocabulary and matrix reasoning subtests of the Wechsler Intelligence Scale for Children-Fourth Edition (42), the Wechsler Adult Intelligence Scale-Fourth Edition (43), or the Wechsler Abbreviated Scale of Intelligence (44). The vocabulary subtest consists of 31 items, and youths are required to verbally define and/or describe a word or concept that is orally presented to them. Each item is scored on a 0-, 1-, or 2-point basis according to the manual. In the matrix reasoning subtest 30 visually-depicted incomplete matrices are presented, and youths are required choose one item from a selection of five options that correctly completes the matrix. Each correct item receives 1 point. The *T* and standard scores for each subtest were transformed into *z*-scores and then combined to yield estimates of full-scale IQ. For the two-subtest short form (FSIQ-2) internal consistency and test-retest reliability were reported to be excellent (>0.90). Estimated full-scale IQ scores were highly correlated with scores on tests purported to measure similar constructs. Correlations between the short form and the original tests were reported to be acceptable (0.71) to excellent (0.92) (45).

CU traits scores were derived from the Youth Psychopathic traits Inventory (YPI) (46). The YPI is a 50-item self-report measure of psychopathic traits. Each item is answered on a 4-point Likert scale ranging from "does not apply at all" (1) to "applies very well" (4). Higher scores indicate higher levels of psychopathy. CU traits scores were calculated using the total score for the subscales 'remorselessness' (e.g., "*To feel guilt and regret when you have done something wrong is a waste of time*"), 'unemotionality' (e.g., "*I usually feel calm when other people are*

*scared*"), and 'callousness' (e.g., *"I think that crying is a sign of weakness, even if no one sees you"*). The CU traits dimension showed good internal consistency (Cronbach's $\alpha = 0.81$). Test-retest reliability of the YPI over a 6-month period was reported to be adequate ($ICC = 0.76$) (47). Convergent and divergent validity was supported in a sample of 360 youths from the general population (e.g., CU traits scores correlated positively with narcissism, but negatively with empathy measures). We also used the three CU traits subscales of the YPI to create a proxy for the LPE specifier, following the procedure developed by Colins and Vermeiren (39). A participant was considered to meet criteria for one of the CU traits when she/he reported that at least one item on the corresponding subscale applied "very well" to her/him [i.e., a score of 4 on a 4-point Likert scale, ranging from "Does not apply at all" (1) to "Applies very well" (4)]. Participants were considered to meet criteria for the LPE specifier if two or more CU traits were endorsed to threshold.

Participants reported on their own aggressive behaviors using the Reactive-Proactive aggression Questionnaire (RPQ) (48), which includes 11 items related to 'reactive aggression' (e.g., *"I have damaged things because I felt mad"*), and 12 items related to 'proactive aggression' (e.g., *"I have had fights to show that I was on top"*). Each item is rated on a 3-point Likert scale ranging from 0 ("never") to 2 ("often"). The proactive and reactive aggression scales are sum scores of the respective items. Internal consistency for the two subscales was good (Cronbach's $\alpha = 0.75$ and 0.88, respectively). Raine et al. (48) also report data which support the validity of the two subscales.

In addition to gender/sex (i.e., male) and general cognitive abilities (i.e., low IQ), numerous longitudinal studies (e.g., (49, 50)) have identified several risk factors linked to CD (reviewed in (3)) of which the following were assessed in the present study: maternal smoking during pregnancy, parental maladaptive behavior (i.e., repeated delinquency of mother/father), and socioeconomic status [i.e., SES (40)]. These three variables were extracted from the Medical History Questionnaire which is a semi-structured interview for parents/caregivers specifically designed for this study with items included based on evidence about CD-related risk factors derived from epidemiological studies (31). Additionally, childhood exposure to parental violence/abuse/neglect, and deviant peer affiliations were evaluated with the Childhood Experience of Care and Abuse Questionnaire (CECA-Q, i.e., total sum of the subscale scores for "antipathy mother/father," "neglect mother/father," and "physical abuse mother/father", Cronbach's $\alpha = 0.78$) (51), and the Social and Health Assessment (SAHA, i.e., "affiliation with delinquent peers" subscale) (52), respectively. The CECA-Q is a self-report questionnaire to assess lack of parental care (neglect and antipathy), parental physical abuse, and sexual abuse from any adult (not used in this study) before age 17. Satisfactory reliability and validity have been reported by Bifulco et al. (51). The SAHA subscale consists of nine items, and youths are asked about how many of their close friends are involved in different types of risk-taking and delinquent behavior ("None"; "A few"; "Some"; or "Most or all"): e.g., dropping out of school, smoking cigarettes, drinking alcohol, or using marijuana. The summed score could range from 9 to 36 where higher scores indicate greater association with delinquent peers. The internal consistency was high (Cronbach's $\alpha = 0.91$), and published data support the validity of this subscale (53).

## Neuropsychological Test Battery

We used the *Emotion Hexagon task* to assess the accuracy of facial emotion recognition (54). Participants were asked to label morphed facial expressions as either happy, sad, angry, fearful, disgusted, or surprised (i.e., the six "basic" emotions). Morphs were created from six expression pairings: happy-surprised, surprised-fearful, fearful-sad, sad-disgusted, disgusted-angry, and angry-happy. Each pair included two prototype expressions in proportions 90:10, 70:30, 50:50, 30:70, and 10:90 (i.e., 10% happy and 90% surprised for the happy-surprised continuum). Morphed expressions were presented individually and randomly on a computer monitor for a maximum of 3 s, and participants were asked to select by mouse-click one of the six emotion labels that best described the expression shown. Participants were given as long as necessary to make their selection and were not given feedback about their performance accuracy. Participants completed one practice block, followed by five blocks that each displayed all 30 morphed expressions once (6 pairs x 5 morphs). The total score for incorrect recognition per expression ranged from 20 (100% error rate) to 0 (0% error rate), with 50:50 morphs not being scored or analyzed.

We administered a modified *Passive Avoidance Learning task* to assess the accuracy of emotional learning (55). The task involves assigning reward and punishment values to novel stimuli ("ziggerins" (56)). Novel stimuli were chosen to tap into pure learning effects without the bias of stimulus familiarity. Participants were instructed to learn by trial-and-error to respond through button press to four different reward stimuli (gaining 1, 700, 1,400, or 2,000 points, respectively; non-responses were counted as omission errors in %) and to avoid responding to four different punishment stimuli (losing 1, 700, 1,400, or 2,000 points, respectively; responses to these stimuli were counted as avoidance errors in %). Each stimulus was shown once within a block of 8 trials, with 10 blocks overall (including one practice block). Stimuli were displayed on a computer monitor for a maximum of 3 s, followed by performance feedback (i.e., amount of points won, or lost, as well as the running total points). Participants started the task with 10,000 points.

We administered the *Emotional Go/Nogo task* to assess the accuracy of emotion regulation defined as the ability to maintain cognitive control when confronted with interfering emotional information, including positive and negative facial expressions (57, 58). Participants were instructed to press a response button as quickly and accurately as possible whenever a named facial expression appeared on the screen (go trials) and not to press for any other expression (nogo trials). The task included six randomly presented blocks of go-nogo pairings: neutral-happy, neutral-fearful, happy-neutral, fearful-neutral, happy-fearful, and fearful-happy. Each block included 35 go (73%) and 13 nogo (27%) stimuli. The go trials occurred more frequently in order to create a pre-potent tendency for the participant to respond. Stimuli consisted of gray-scaled fearful, happy, and

neutral expressions from six male and six female adults, with four African-American, Asian, and Caucasian individuals for each expression type, respectively (NimStim set numbers: 6, 8, 11, 14, 15, 16, 27, 36, 39, 43, 44, and 45). Stimulus duration was 500 ms with 1 s interstimulus intervals. False alarm error rates in % for nogo trials indexed emotion regulation, with higher rates reflecting worse performance (59).

Order of tasks was pseudorandomized separately across group (CD, TDC), sex (female, male), and age brackets (9–12, 13–15, and 16–18 years). The extracted performance variables of the three tasks (see **Table 1**) had acceptable to good reliabilities (Cronbach's $\alpha \geq 0.70$). Details on the test battery and procedures are provided in **Figure 1** [for more details, see also (17)]. We chose this particular test battery based on influential models of emotion dysfunction in CD (see (17) for details), and because the three tasks have widely been used in neuropsychological research of emotion functioning in developmental psychopathology, including CD, ADHD, and internalizing disorders. Thus, the validity of the test battery comes from its proven usefulness to distinguish between clinical groups and controls in previous research (4). Available psychometric data further support both reliability and validity of all three neuropsychological measures (59–61). Standard operating procedures (SOP) ensured consistency of data collection, handling, and analysis across all data collecting sites.

## Statistical Analyses

First, all raw scores for the performance variables of interest from our neuropsychological battery (see above, and **Table 2** below) were age-, IQ-, and sex-adjusted using standard regression procedures, resulting in *z*-scores as the dependent variables in the following factor analysis (conducted in SPSS v25, IBM Corp., Armonk, NY). We ran a confirmatory principal component (PCA) "factor" analysis, using varimax rotation with Kaiser normalization, as we had *a priori* expectations about the number of factors that would be associated with the measured dependent variables (62), i.e., separate factors for emotion recognition, emotion learning, and emotion regulation, respectively. All participants were included in the PCA in order to maximize statistical power as well as to create a common metric of performance scores by which youths with CD and TDCs could be compared. Per component, factor scores were extracted for each participant using the Anderson-Rubin method (M = 0, SD = 1) to avoid multicollinearity. We then explored case-control differences for the three emotion domains within a repeated-measures analysis of variance model using the factor scores as the dependent variables. Effect sizes were calculated using partial eta squared ($\eta^2_p$), where 0.01, 0.06, and 0.14 represent small, medium and large effects, respectively (63). We additionally report 95% confidence intervals (CIs) for all effect size measures. Finally, and most importantly, in keeping with the clinically motivated subgrouping approach that has been very informative in the ADHD field (21, 32–35), we subdivided the individuals with CD into subgroups on the basis of their neuropsychological task performance. For each emotion processing domain identified in the factor analysis, participants were classified as "deficient" or "intact," with deficit being defined as performance (i.e., factor scores) within the bottom 10% of an age-matched control group using the following age brackets to recognize that test performance typically improves with age (64): 9–12, 13–15, and 16–18 years. We then investigated the proportion of youths with CD who had one or multiple deficits vs. no deficit at all. We had three reasons for choosing the 10th percentile criterion as a reasonable cutoff for deficit: First, we wanted to use a clinically useful definition of performance deficit that is established in the field of clinically oriented neuropsychological assessments as this is the core interest of person-centered approaches; second, to apply a threshold which is easily reproducible and comparable between studies within and across disorders (in contrast, for instance, to more elaborate analytic approaches based on machine learning algorithms which usually require specialized expertise that is not available in all research labs or clinics (65)); and third, any other reasonable cutoff (e.g., 5th percentile) would still classify many youths with CD as "intact" or conversely classify a substantial number of typically developing controls (TDC) as "deficient" (i.e., the positive predictive value increases, but the negative predictive value decreases with more stringent cutoffs) (21). Regression analyses, chi-square tests, and *t*-tests were then used to explore differences in clinical correlates and risk factors between the neuropsychologically defined CD subgroups.

# RESULTS

## Correlational and Principal Component Analyses

As expected, correlations between the dependent variables (i.e., age-, IQ-, and sex-adjusted performance scores) were larger within each of the three emotion domains (mean $r_{\text{Olkin \& Pratt}} = 0.37$, 95% CI: 0.34, 0.44) than between the domains (mean $r_{\text{Olkin\&Pratt}} = 0.12$, 95% CI: 0.07, 0.17; Fisher's $z = 7.28$, $p < 0.001$), indicating that our test battery did indeed capture emotion processing as a multifaceted construct rather than a unitary one. For the PCA, the Kaiser-Meyer-Olkin (*KMO*) measure confirmed that the sample size was adequate for the analysis [$KMO = 0.86$, which is a sufficiently high value (66)], and the *KMO* values for all dependent variables were substantially higher than 0.5 (i.e., *KMO*s $\geq 0.68$). Bartlett's Test of Sphericity indicated that correlations between variables were large enough for PCA [$\chi^2$ (190) = 7514.62, $p < 0.001$]. The dependent variables from the three tasks loaded onto the predicted three components, accounting for 48.1% of the total explained variance in performance scores. Components 1, 2, and 3 represented emotion regulation (17.4% variance), emotion learning (17.2% variance), and emotion recognition (13.5% variance), respectively (**Table 1**). Note: Using other factor analytic procedures, such as the Maximum Likelihood method or Principal Axis Factoring, yielded similar results which is in line with prior work (67) (data available on request).

## Comparing Dimensionally the CD and TDC Groups in Factor Scores

We analyzed the factor scores for the three emotion processing domains using a three (domain: emotion regulation vs. emotion learning vs. emotion recognition) by two (group: CD vs. TDC)

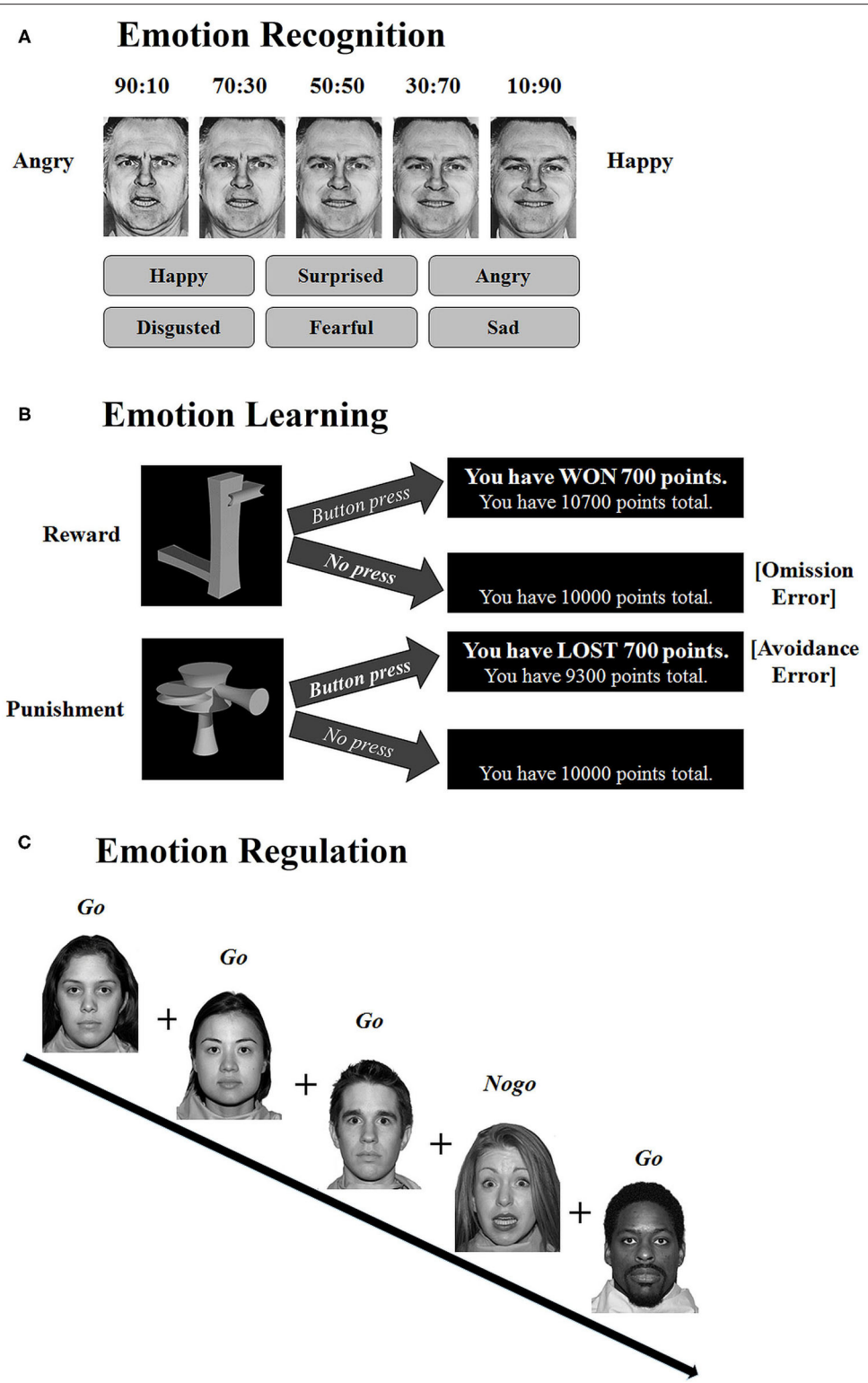


**FIGURE 1 |** Illustration of the model based neuropsychological test battery used to assess **(A)** emotion recognition, **(B)** emotion learning, and **(C)** emotion regulation, respectively. **(A)** As an example, the angry-happy facial expression continuum from the *Emotion Hexagon task* is depicted, including the five different morphs from this continuum as well as the six emotion labels used in the task. Only one facial expression is displayed in each trial. **(B)** Examples from the *Passive Avoidance Learning task*, depicting one stimulus associated with reward (e.g., gaining 700 points by button press), and one stimulus associated with punishment (e.g., losing 700 points by button press). **(C)** Example layout of the emotion regulation condition from the *Emotional Go/Nogo task*, including neutral expressions as the "Go" targets and fearful expressions as the "Nogo" non-targets. This Figure was republished from Kohls et al. (17) with permission from ELSEVIER.

**TABLE 2 |** Results from the confirmatory principal component analysis.

| Variables | Rotated "factor" loadings | | |
|---|---|---|---|
| | Emotion regulation | Emotion learning | Emotion recognition |
| **False alarm error rate in % (Go/Gogo pairings)** | | | |
| Neutral/Happy | 0.783 | | |
| Neutral/Fearful | 0.764 | | |
| Fearful/Happy | 0.746 | | |
| Happy/Neutral | 0.744 | | |
| Fearful/Neutral | 0.726 | | |
| Happy/Fearful | 0.723 | | |
| **Error rate in % (Punishment, and Reward conditions)** | | | |
| Losing 1,400 points | | 0.724 | |
| Losing 700 points | | 0.712 | |
| Losing 1 point | | 0.703 | |
| Losing 2,000 points | | 0.670 | |
| Gaining 1 point | | −0.686 | |
| Gaining 1,400 points | | −0.659 | |
| Gaining 700 points | | −0.535 | |
| Gaining 2,000 points | | −0.476 | |
| **Error rate in % (Emotion expression)** | | | |
| Happiness | | | 0.718 |
| Surprise | | | 0.704 |
| Fear | | | 0.667 |
| Sadness | | | 0.632 |
| Disgust | | | 0.605 |
| Anger | | | 0.590 |
| **Eigenvalues** | **3.48** | **3.44** | **2.71** |

repeated-measures analysis of variance model, followed by *post-hoc* pairwise comparisons in cases where significant main or interaction effects emerged (Bonferroni-corrected for multiple comparisons). This analysis revealed a small but significant group by domain interaction effect [$F_{(2,500)} = 3.34$, $p = 0.036$, $\eta^2_p = 0.003$, 95% CI: 0.0001, 0.008], and a significant main effect of group with a medium effect size [$F_{(1,250)} = 72.98$, $p < 0.001$, $\eta^2_p = 0.055$, 95% CI: 0.033, 0.081]. Compared to TDCs, youths with CD as a group performed worse in all emotion domains (in line with our prior analyses examining task performance separately for each neuropsychological task (17)), but the largest case-control differences were found for the emotion recognition domain ($\eta^2_p = 0.035$, 95% CI: 0.018, 0.058), followed by the emotion regulation domain ($\eta^2_p = 0.018$, 95% CI: 0.006, 0.035), with the smallest difference observed for the emotion learning domain ($\eta^2_p = 0.007$, 95% CI: 0.0009, 0.019) (**Figure 2**). We also explored the extent to which group membership (i.e., CD or TDC) was predicted by the three emotion domain scores using a logistic regression analysis. This analysis revealed significant effects of all three emotion domains (*Wald* $\chi^2$s > 9.43, *p*s $\leq$ 0.002). However, the final model [$\chi^2$ (3) = 77.78, $p < 0.001$; Hosmer-Lemeshow-Test: *ns*] successfully predicted group membership of 83% (95% CI: 79.8, 85.5%) of the TDCs, i.e., relatively high specificity, but only 36% (95% CI: 31.8, 40.0%) of the CD cases, i.e., relatively low sensitivity, again pointing to substantial variability in emotion processing skills within the CD group.

## Neuropsychologically Based Subgroup Analysis

### Proportion of Deficit

**Figure 3** presents a Venn diagram showing the proportion of CD cases who exceeded the threshold for one or multiple deficits in the emotion recognition, emotion learning, and/or emotion regulation domains, with deficit being defined as performance (i.e., factor scores) within the bottom 10% of their respective age-matched control group (which equals ≤-1.3 standard deviations from the mean of performance data by TDCs). In the CD group, 43.7% of the participants were deficient in at least one domain of emotion processing. Deficits in emotion recognition were the most common deficit, followed by emotion regulation, and emotion learning was the least common deficit. Overlap between the different deficits was rare, with only ∼1% of the youths with CD displaying a pervasive deficit across all three domains. Compared to TDCs, "deficit" was significantly more frequent among the youths with CD for the emotion recognition and emotion regulation domains (*p*s < 0.001), but not for the emotion learning domain ($p = 0.13$). Notably, a substantial subgroup of CD youths (56.3%) showed no deficit in their emotion processing abilities across the three domains. Among the TDCs, ∼27% showed at least one emotion deficit (i.e., 24.6% qualified for only one, 2.4% for two, and 0.1% for three deficits), leaving ∼73% of the TDCs who performed normally across the three emotion domains (Note: If the three neuropsychological tasks were completely independent, one would expect to find ≥30% of TDCs to be deficient in at least one emotion domain given the 10th percentile criterion as our cutoff for deficit per task).

### Clinical Correlates

Introducing the three emotion deficit domains (i.e., deficit: yes = "1," or no = "0") as predictors into multiple linear or logistic regression models—i.e., running one model with the three predictors for each dependent variable separately—did not reveal any significant associations with the main clinical variables of interest among the youths with CD [i.e., CD symptom severity, CD age-of-onset subtype, CU traits/LPE specifier, or the presence of major comorbidities, including ADHD, ODD, major depressive disorder (MDD), generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD), and substance use disorder (SUD)]. More specifically, the subgroup of youths with CD with an emotion recognition deficit did not differ significantly from those without such deficit regarding: (i) the presence of the LPE specifier (44.1% vs. 43.6%, $p = 0.92$), (ii) CD age-of-onset subtype (CO-CD/AO-CD: 43.3%/52.8% vs. 42.9%/53.5%, $p = 0.98$), (iii) number of CD symptoms (K-SADS-PL CD symptom count: 5.6 ± 2.4 vs. 5.4 ± 2.3, $p = 0.57$); or (iv) proactive aggression (RPQ proactive aggression

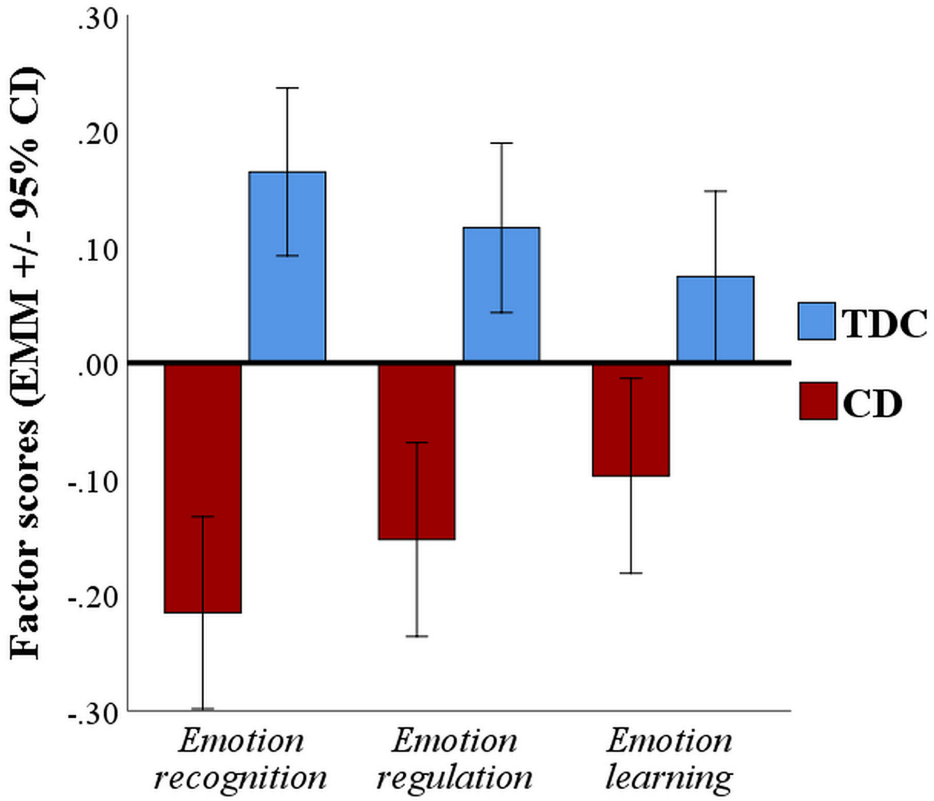


**FIGURE 2 |** Factor scores for youths with CD vs. TDCs for the three emotion processing domains investigated in this study. Relative to TDCs, youths with CD showed the expected deficits in all three domains, with the greatest deficits in the emotion recognition domain, followed by the emotion regulation and emotion learning domains (EMM, Estimated Marginal Means; 95% CI = error bars represent 95% Confidence Intervals).

subscale score: 5.0 ± 5.2 vs. 4.7 ± 4.6, $p = 0.56$). Moreover, the subgroup of youths with CD with an emotion regulation deficit did not differ significantly from those without such deficit in terms of: (i) the LPE specifier (38.8% vs. 44.8%, $p = 0.31$), (ii) the presence of comorbid anxiety disorders (16.2% vs. 11.7%, $p = 0.24$), or (iii) scores on the RPQ reactive aggression subscale (12.0 ± 4.7 vs. 12.1 ± 5.0, $p = 0.86$). Taken together, these findings suggest that deficits in emotion processing related to CD (4) do not map neatly onto established DSM-5 subtypes, such as CD+LPE or childhood-onset CD.

### Associated Risk Factors

As a secondary aim, we explored associations between the three emotion processing domains and established risk factors for CD within three logistic regression models, i.e., one for each neurocognitive domain (deficit: yes = "1," or no = "0") using the following predictors: gender/sex, general cognitive abilities (i.e., low IQ), maternal smoking during pregnancy, socioeconomic status (i.e., low SES), parental maladaptive behavior (i.e., delinquency), childhood exposure to parental violence/abuse/neglect, and deviant peer affiliations. For emotion recognition, boys with CD were 2.1 times more likely to have a deficit than girls with CD ($Wald\ \chi^2 = 4.19$, $p = 0.04$), and a lower IQ among the youths with CD was also significantly associated with an increased likelihood of exhibiting a deficit in this domain ($Wald\ \chi^2 = 6.10$, $p = 0.013$). For emotional learning, youths with CD whose mothers smoked during pregnancy were 3.2 times more likely to have a deficit in this domain than youths with CD whose mothers did not smoke during pregnancy ($Wald\ \chi^2 = 5.37$, $p = 0.021$). None of the assessed risk factors predicted an emotion regulation deficit. Please note that none of the risk factors were associated with task performance in the TDCs.

## DISCUSSION

The primary aim of this study was to investigate neuropsychological subgroups across three emotion processing domains linked to CD and test whether specific subgroups would map onto existing DSM-5 defined CD subtypes, including CD with vs. without the LPE specifier (4). Our dimensional analysis showed that, relative to TDCs, the CD group performed worse in all three emotion domains, but the largest case-control difference was found for the emotion recognition domain, followed by the emotion regulation domain, with the smallest difference observed for the emotion learning domain; this supports the

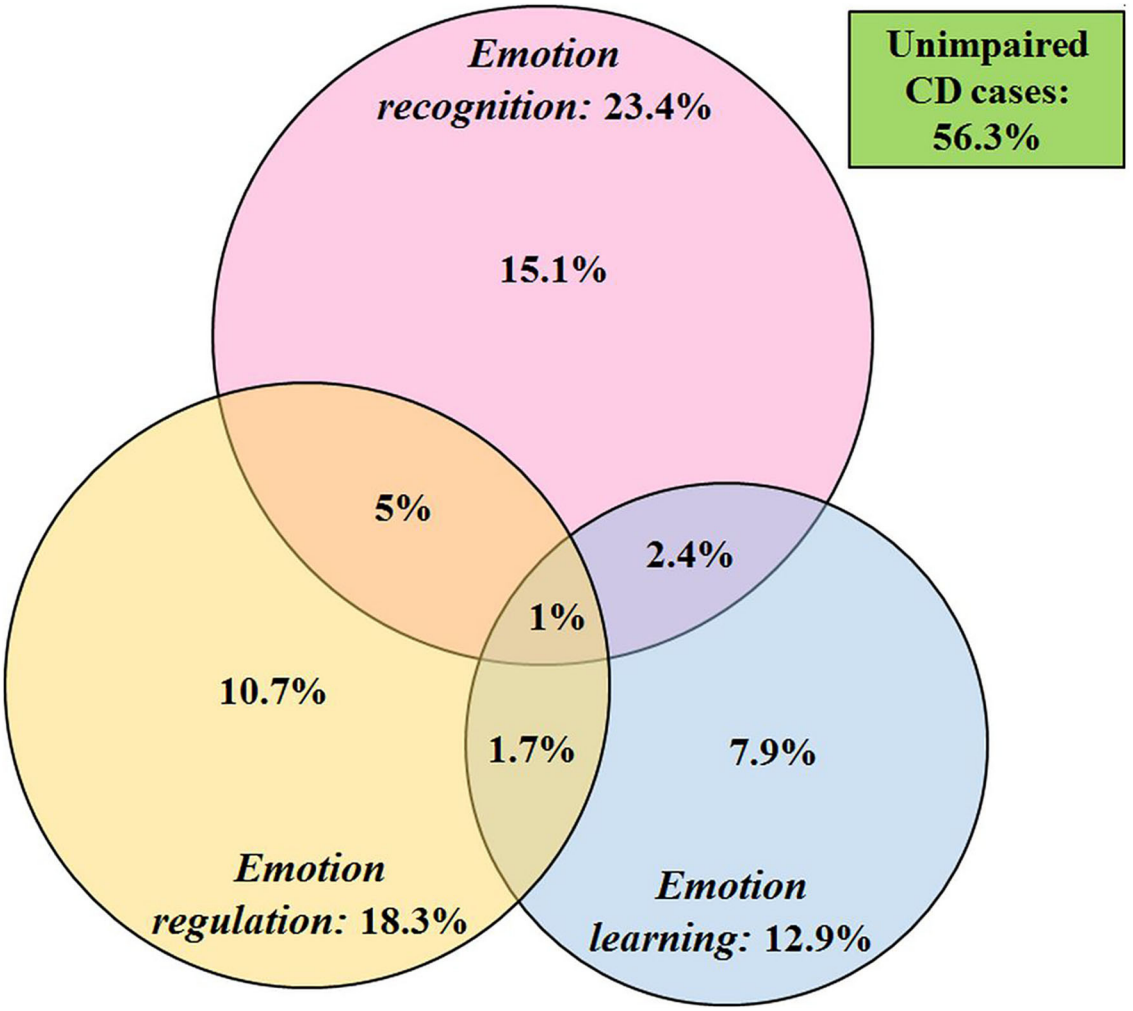


**FIGURE 3 |** Proportion of CD cases ($n = 542$) with deficits in emotion recognition, regulation, and learning, and their degree of overlap. The numbers reported next to the domain labels reflect the sum of those with a deficit in that particular domain, including those with single, or multiple deficit(s).

findings of our previous report (17). Our categorical subgroup analysis substantiated this finding by revealing that deficient emotion recognition skills were the most common deficit in CD (∼23%), followed by emotion regulation (∼18%), with emotion learning the least common deficit (∼13%). Critically, though, we also found that the majority of youths with CD (∼56%) did not demonstrate meaningful deficits in any of the three emotion domains, and only a very small proportion of the CD sample showed pervasive deficits across all domains (i.e., deficits in all three emotion functions: ∼1%). Overall, emotion processing deficits, if existent in youths with CD, appear to be unrelated to main phenotypic characteristics, such as age-of-onset of CD, symptom severity, or co-occurring psychiatric disorders. Moreover, contrary to our assumptions, the present data do not support notions that established clinical subtypes of CD, most importantly CD with vs. without the LPE specifier (1), are tightly linked to neurocognitive deficits in one particular emotion domain over another (i.e., emotion recognition deficits in CD+LPE vs. emotion regulation deficits in CD–LPE) (4, 6). Notably, being male and having a lower IQ increased the likelihood for showing a deficit in the emotion recognition domain, whereas maternal smoking during pregnancy increased the likelihood for having an emotion learning deficit. Please note, though, that our analytic approach to subdivide the CD sample into subgroups based on their neurocognitive performance (i.e., emotion domain deficit: "yes" or "no") likely attenuated statistical power to detect associations with clinical correlates and associated risk factors.

Although the present findings support recent theoretical models emphasizing that CD is a remarkably heterogeneous condition, with different individuals being affected to different degrees in different domains of emotion functioning (4, 6, 7), our data also suggest that these influential neurocognitive models need to be modified to account for the substantial proportion of youths with CD who performed normally across all emotion processing domains studied here. Thus, future

studies will need to (i) assess a broader range of emotion and non-emotion processes implicated in CD, such as executive function, decision-making, social cognition, and language skills (68, 69); (ii) investigate their performance profiles regarding neuropsychological heterogeneity; and then (iii) test their respective role in distinguishing between different developmental pathways of established and potentially novel clinical subtypes of CD, including testing the ability of each of these domains to predict the emergence or desistance of CD in high-risk groups as part of longitudinal studies (70).

It is, however, also conceivable that in fact emotion processing deficits only account for a proportion of youths with CD and that other biopsychosocial factors contribute to CD in those without such deficits (71). This idea is comparable to Moffitt's developmental taxonomy theory of CD suggesting that the adolescence-limited subtype does not suffer from neuropsychological deficits, whereas the early-onset and life-course-persistent subtype does (72) (see also (73) for a recent review). We note, however, that our data do not support this theory as age-of-onset of CD (although defined only retrospectively according to information from the K-SADS-PL interviews) was unrelated to the presence or absence of emotion processing deficits in this sample of youths with CD. This is consistent with previous smaller-scale studies showing no differences in emotion processing between CO-CD and AO-CD subtypes, including facial emotion recognition (74) and emotional learning (75), whereas both groups were deficient across these neuropsychological domains compared to TDCs. It should be stressed, though, that the empirical foundation of Moffitt's theory is not directly concerned with emotion functioning, but focuses instead on neurocognitive domains, such as reading, memory, vocabulary, and IQ (76). Therefore, more work is needed to determine the extent to which emotion functioning, in parallel to other neurocognitive mechanisms, contributes to different clinical manifestations and pathways within the CD population (including those with and without the LPE specifier) (77).

Both our dimensional and categorical data suggest that emotion recognition is the most consistently deficient neurocognitive domain in this sample of youths with CD. We can only speculate whether deficits in emotion recognition are more pivotal in the etiology of CD compared to both emotion learning and emotion regulation, or whether the specific task used to assess emotion recognition was simply more sensitive in detecting case-control differences than the two tasks that assessed the remaining emotion domains. Future studies might try to address this point, for instance, by creating tasks that are of comparable complexity and difficulty across various neurocognitive functions [e.g., emotion learning task (78), or emotion regulation task (79)].

Notably, our results neither confirm that youths with CD with the LPE specifier were disproportionately deficient in emotion recognition nor show that those without the LPE specifier displayed difficulties specifically in emotion regulation (4, 6). We did, however, find that being male and having a lower IQ—both well-documented risk factors for CD (50)—were associated with deficient emotion recognition skills [see for related findings (80, 81)], whereas maternal smoking during pregnancy—another well-known CD risk factor—increased the odds for deficient emotional learning; none of the risk factors tested here predicted an emotion regulation deficit. Although we are cautious in interpreting these results since we measured most of the risk factors retrospectively, the findings suggest that some biopsychosocial dispositions may increase the probability of developing specific types of emotion dysfunction, while others do not (or might do so only in interaction with other risk variables) (82). This idea is worth pursuing in future prospective longitudinal studies that examine a wider range of CD-related risk factors, including genetic and epigenetic processes (83–85), their complex interactions as well as their unique contribution to emotion dysfunctions as potential intermediate phenotypes at both the behavioral and brain level in CD.

This study had some additional limitations (see (17) for strengths and limitations regarding the sample composition): First, each emotion domain was assessed using only one experimental task which makes our neurocognitive battery less representative, thereby limiting the generalizability of the results. Follow-up studies should preferably apply more comprehensive test batteries including several tasks measuring overlapping emotion domains so as to replicate and extend our findings and, thus, obtain a richer understanding of emotion functioning in CD. Second, we stratified youths with CD as "deficient" or "intact" in terms of task performance, following a clinically motivated, person-centered subgrouping approach that is typical for neuropsychological assessments, highly relevant for clinical decision-making, and easily applicable by practitioners (86). However, the present procedure—and other "traditional" statistical data clustering methods aiming to fractionate clinical groups on the basis of neuropsychological scores—have been criticized for several reasons which go beyond the current study and cannot be discussed in depth here [but see (65)]. Notably, the most serious issue is that these clustering methods divide the data arbitrarily into a pre-specified number of severity classes regardless of the underlying data distribution (i.e., two classes here: "deficient" vs. "intact" individuals), and they always produce a result. This sometimes leads to even unmanageably small subgroups, such as the 1% of youths with CD who were found to show deficits across all three emotion domains in the present study. Thus, alternatively, more elaborate machine-learning approaches, such as "normative modeling" (87), have been proposed to map neuropsychological variation with the advantage of not making strong *a priori* assumptions about the existence or number of subgroups with abnormal task performance (i.e., defined as extreme value, or "outlier," from the normative range). It will be interesting to see how these novel subgrouping algorithms complement traditional clustering methods in identifying distinct neurocognitive subtypes of CD with potentially unique clinical profiles and underlying biology.

In conclusion, the current findings provide first evidence that youths with CD display strikingly diverse profiles in neuropsychological performance across three domains of emotion processing that have previously been linked to CD etiology, including emotion recognition, emotion learning, and emotion regulation (4). Similar to findings in ADHD (88), we

were able to reveal different neurocognitive subgroups in which emotion functioning was deficient to varying degrees, with a sizable subgroup of CD cases showing no meaningful emotion processing deficits at all. Clearly, deficits within a specific emotion processing domain may be clinically important for only a subgroup of patients, but not for the entire CD population. Consequently, treatments targeting emotion processing may be beneficial for some, but not all, individuals with CD (12, 89, 90). Whether, and if so which, neuropsychological interventions in non-emotion domains may be required to help patients with CD who have intact emotion processing skills needs to be evaluated in future studies. Importantly, while the current study should be regarded as exploratory and illustrative since we used, for the first time, a common-metric analytic approach from pediatric neuropsychology in order to subgroup youths with CD based on their emotion processing performance, novel classification algorithms based on machine learning are warranted to assist in identifying and validating distinct and meaningful neurocognitive phenotypes of CD, ideally replicating and thus substantiating the findings of this study.

## DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on reasonable request in line with the data sharing policy of the FemNAT-CD consortium.

## ETHICS STATEMENT

Written informed consent was obtained for all participants after they were informed about the experimental procedures and the aims of the study. Local ethics committees at all sites of the FemNAT-CD consortium reviewed and approved the study protocol. The study was carried out in accordance with the recommendations of good clinical practice and in accordance with the Declaration of Helsinki and national legislation.

## AUTHOR CONTRIBUTIONS

GK, GF, and KK conceived the current study. AB, AM, AS, KG-M, AW, JR, RP, HO, LJ, AR, LK, JA, and SB recruited participants and carried out assessments and data collection. GF, BH-D, AV, HL, AH, AF-R, AP, CS, SD, CF, and KK supervised the study. GK performed the statistical analyses and drafted the manuscript. GF, CS, SD, CF, and KK contributed to writing parts of the manuscript. CF coordinated the project which this study was part of. All authors read, commented on drafts of the paper, and approved the final manuscript and its submission.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2020.585052/full#supplementary-material

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# From Emotional Intelligence to Self-Injuries: A Path Analysis in Adolescents With Conduct Disorder

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**Objective:** Self-harm acts are highly prevalent among adolescents with conduct disorder. It has been shown that low level of emotional intelligence (EI) might be related to a higher risk of self-injuries. However, the exact mechanisms underlying this association are still unclear. The purpose of this study was to explore whether psychopathological symptoms and selected psychological processes mediate the association between EI and self-harm risk in adolescents with conduct disorders.

**Method:** Out of 162 adolescents with conduct disorder approached for participation, 136 individuals (aged 14.8 ± 1.2 years, 56.6% females) were enrolled and completed the questionnaires evaluating the level of EI, depression, anxiety, impulsiveness, empathy, venturesomeness, self-esteem, and disgust.

**Results:** Individuals with a lifetime history of self-injuries had significantly higher levels of depression, anxiety and impulsivity as well as significantly lower levels of EI and self-esteem. Higher levels of EI were associated with significantly higher levels of self-esteem, venturesomeness and empathy as well as significantly lower levels of depression, anxiety and impulsivity. Further analysis revealed that trait and state anxiety as well as self-esteem were complete mediators of the association between EI and self-harm risk.

**Conclusions:** Our findings indicate that anxiety and self-esteem might mediate the association between EI and a risk of self-injuries in adolescents with conduct disorder. However, a cross-sectional design of this study limits conclusions on the direction of causality. Longitudinal studies are needed to test validity of our model.

**Keywords: emotional intelligence, self-harm, self-injuries, conduct disorder, adolescent**

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## INTRODUCTION

Non-suicidal self-injuries (NSSI) are increasingly being recognized as a highly prevalent aspect of psychopathology in young people. Recent epidemiological studies have shown that self-harm occurs in 17–18% of adolescents in the general population (1) and 40–80% of psychiatric patients (2). It has been estimated that even 92% of people consulted at the general hospital due to self-injuries might have one or more mental disorders (3, 4). Self-injuries are listed among the diagnostic criteria for borderline personality disorder [DSM-5; (5)]; however, they can appear in patients with other mental disorders. The Diagnostic and

Statistical Manual Version 5 (DSM-5) (5) has pointed out "non-suicidal self-injury disorder" (NSSID) as a problem to further study that extends current diagnostic boundaries (1). According to the International Society for the Study of Self-Injury, NSSI can be defined as the deliberate, self-inflicted damage to body tissue without suicidal intent and for purposes not sanctioned by society or culture (6). It has been reported that self-injuries might be associated with a number of negative outcomes that include repetitive self- injuries (7) and suicide (8).

It is now widely accepted that self-harm may occur in the context of various mental disorders and psychopathological symptoms. To date, several mental disorders that might develop in adolescence have been associated with self-harm risk, including attention deficit hyperactivity disorder, anxiety and depressive disorders, and conduct disorder (9). It has been noted that depression is a risk factor for self-harm, with affective disorders, such as bipolar disorder and depression being the most common primary diagnoses of patients who engage in self-harm acts (72%) and commit suicide (45%) (3, 10). Based on a meta-analysis, Fox et al. (11) found that the possibility of externalizing disorder symptoms is higher than the one of internalizing disorder symptoms among individuals who engage in non-suicidal self-injuries. The study by Nock et al. (12) estimated the prevalence of any externalizing disorder at 62.9%, and the presence of any internalizing disorder at 51.7% in adolescents who engage in self-harm the prevalence. In turn, prevalence rates of self-harm acts in adolescents with conduct disorder have been estimated at 15.5–62.5% (13). For instance, our group has recently reported that almost 53% of adolescent girls with conduct disorder have a history of self-injuries (14).

It has been shown that emotional intelligence (EI) can be associated with a risk of self-harm. Indeed, EI provides effective ways of balancing negative affect in adolescence and protecting from the aftermaths of self-harm. According to Goleman (15), it is a set of social skills that refer to the capacity to understand own emotions, manage and control them as well as the ability to empathize. EI may be perceived as a tool to encompass a personality dimension and also as the means to comprehend, process, and use affect-laden information gained by monitoring other's and one's own emotions. EI relies upon the ability to take suitable action to overcome the problem (16).

It has been reported that lower EI is associated with higher risk of internalizing disorders, including depression and anxiety, as well as substance use and less efficient coping (17). Petrides and Furnham (18) reported that in people with a higher level of EI, it serves as a protective factor for suicidal attempts and ideation (17). However, emerging evidence indicates that EI is not directly associated with suicide risk. The recent study by Quintana-Orts et al. (19) showed that depressive symptoms mediate the association between low level of EI and suicide risk among people who were bullied. This mediation appeared to be stronger among girls. At least theoretically, other processes might also mediate the association between EI and self-harm risk.

Individuals engaging in self-harm experience a variety of negative emotions. The most common categories of unpleasant emotional states declared by these individuals include feelings of guilt, anger, frustration, fear, sadness, shame, tension, anxiety and contempt (20). Apart from these emotions, there is evidence that disgust often occurs in this group of individuals, and in contrast to most other emotions, it does not tend to decrease after self-harming. It can be recognized as one of trait-dependent aspects of those who are prone to engage in self-harm acts (21). Another important aspect connected to self-harm is "impulsivity." It refers to actions that are risky, unduly hasty, and damaging (22). Higher levels of impulsivity have been reported in subjects with a history of self-harm (23). Moreover, higher levels of impulsivity and aggression have been associated with lower levels of EI (24). Finally, there is evidence that lower self-esteem might be related to higher risk of self-harm. In this regard, self-dislike in adolescents can be perceived as the way of punishing oneself and developing self-injurious behaviors (25). On the other hand, a significant positive relationship between the levels of EI and self-esteem has been demonstrated (26).

A majority of previous studies have investigated single correlates of psychological constructs associated with EI and self-harm. In light of findings mentioned above, we aimed to investigate as to whether psychopathology and selected psychological processes mediate the association between EI and self-harm risk in adolescents with conduct disorder. More specifically, we tested the hypothesis that depressive and anxiety symptoms, aggression, impulsivity, self-esteem as well as disgust mediate this association in adolescents with conduct disorder.

We decided to focus on adolescent patients due to the highest prevalence of NSSI among people at this age. A broad spectrum of negative emotions leading to aggressive behavior is typical for conduct disorder. One of the key functions of NSSI is to relieve negative feelings. Thus, we decided to assess this specific group of patients because of co-occurrence of NSSI and emotional dysregulation which play important roles as triggers of NSSI.

# METHOD

## Participants

Participants were enrolled among the students of the Youth Sociotherapy Centre (YSTC) No. 2 in Wroclaw, Poland. YSTCs in Poland have been designed by the Ministry of National Education to provide comprehensive pedagogical, educational and psychological support for children and adolescents with different problems or disorders (developmental, learning or social) who are at risk of social maladjustment. Adolescents, being admitted to the YSTC No 2 in Wrocław (Poland), mainly present with conduct disorder (mild or moderate severity of symptoms). Residents of YSTCs receive accommodation and attend school at these facilities. Students are recruited to YSTCs based on the opinion stating special education needs issued by professionals from the psychological and pedagogical counseling centers. According to the DSM-V criterion F of non-suicidal self-injury disorder (NSSID), participants were excluded if they had presented with intellectual disability, delirium, intoxication or withdrawal symptoms, psychotic disorder or autism spectrum disorders. Out of 162 individuals approached for participation (all individuals residing in the YSTC at the time of the study), 144 adolescents were enrolled (3 individuals and/or their legal guardians refused to participate and 15 individuals were

transferred to another institution). Due to a lack of necessary data to perform analyses, eight participants were excluded. The final sample included 136 adolescents (77 females and 59 males).

## Procedures

The data were collected from September 2016 to August 2019 by a psychologist and a psychiatrist. Taking care of the comfort of the subjects, the study was divided into three parts, each lasting about an hour. During the first part, data on self-inflicted injuries were collected. A semi-structured questionnaire was administered to confirm a history of self-harm. This questionnaire recorded the information regarding the frequency of self-injuries and suicidal behaviors (suicidal thoughts and attempts) that had occurred at different time periods (lifetime as well as the preceding year, month, and week).

During the second part, all participants underwent psychiatric examination using the MINI-Kid interview. The MINI-Kid is a structured diagnostic tool, developed together by European and American psychiatrists and clinicians, for the DSM-IV and the ICD-10 criteria (27). This measure was used to establish a diagnosis of conduct disorder and comorbid mental disorders. Apart from the MINI-Kid, a diagnosis of CD was confirmed based on participants' psychiatric examination, medical records and psychological opinion. Furthermore, a diagnosis of potential comorbid mental disorders listed as exclusionary diagnoses of NSSID in the DSM-5 (criterion F), except for intellectual disability, was carried out. All students were assessed regarding intellectual functions before admission to YSTC by psychologists from the psychological and pedagogical counseling centers. After psychiatric examination, participants were divided into two groups – adolescents with a positive lifetime history of self-injuries and those who had never engaged in self-harm acts. We decided to focus our analyses on this categorization due to controversies around operationalization of the severity of self-injuries. For instance, although the NSSID has been developed in the DSM-5 as a new diagnostic category for further studies, there are studies showing insufficient validity of the NSSID frequency criterion (1, 14).

During the third part, emotional intelligence and concomitant psychopathology were assessed. Questionnaire data regarding self-esteem, impulsivity, depressive symptoms, anxiety and aggression levels and disgust sensitivity were collected using standardized self-reports. Self-reports were administered in the following order: (1) The Popular Emotional Intelligence Questionnaire (PEIQ); (2) The Buss-Perry Aggression Questionnaire (BPAQ); (3) The Children's Depression Inventory 2 (CDI2); (4) The State-Trait Anxiety Inventory (STAI); (5) The Rosenberg Self-Esteem Scale (SES); (6) The Eysenck's Impulsivity Inventory (IVE) and (7) The Questionnaire for the Assessment of Disgust Sensitivity (QADS).

The study was approved by the Bioethics Committee of Wroclaw Medical University, Poland. All participants and their statutory representatives gave written consent to all procedures carried out as the part of this study.

## Self-Report Measures

### The Popular Emotional Intelligence Questionnaire (PEIQ)

It measures EI and consists of 94 items of self-descriptive nature, using a five-point Likert scale. The PEIQ consists of the following subscales: acceptance (expressing and using own emotions), empathy (understanding and recognizing emotions of other people), control (control over one's emotions), and understanding (understanding and awareness of own emotions) (28). The Cronbach's alpha for the PEIQ was estimated at 0.89 in our sample.

### The Buss-Perry Aggression Questionnaire (BPAQ)

The BPAQ is a self-report measure of aggression in adolescents and adults. The BPAQ has 29 items, subdivided into four factors: physical aggression, verbal aggression, anger, and hostility (29). The Cronbach's alpha for the BPAQ total score in our sample was 0.80, for physical aggression 0.77, for verbal aggression 0.73, for anger 0.62 and for hostility 0.77.

### The Children's Depression Inventory 2 (CDI2)

This measure includes 28 items. It is a measure which allows for a comprehensive assessment of depressive symptoms in children and adolescents. The questionnaire also includes scales measuring emotional problems and problems related to everyday functioning. In addition, the self-rating version includes subscales measuring negative mood/somatic symptoms, low self-esteem, lack of behavior efficacy, interpersonal problems, emotional problems and problems in functioning (30). The Cronbach's alpha for the CDI2 was 0.94 in our sample.

### The State-Trait Anxiety Inventory (STAI)

This measure consists of two subscales measuring anxiety as a relatively stable personality component (state anxiety subscale) and the level of transient anxiety attributable to specific situations (trait anxiety subscale). Each subscale consists of 20 items which the subject answers by selecting one of four pre-categorized answers (31). The Cronbach's alpha for our sample was 0.94 for state anxiety and 0.99 for trait anxiety.

### The Rosenberg Self-Esteem Scale (SES)

This tool consists of 10 diagnostic questions. Each question is based on a four-point Likert scale illustrating the level of agreement with the statements. The SES is a one-dimension tool which measures the level of overall self-esteem—approximately consistent disposition understood as conscious attitude—positive or negative toward the self (32). The Cronbach's alpha for the SES total score in our sample was 0.89.

### The Eysenck's Impulsivity Inventory (IVE)

This measure consists of 63 diagnostic questions, using a two-point scale. The IVE consists of the following subscales: impulsivity, venturesomeness, and empathy (33). The Cronbach's alpha for each subscale was as follows: 0.75 (for impulsivity), 0.66 (for venturesomeness), and 0.65 (for empathy).

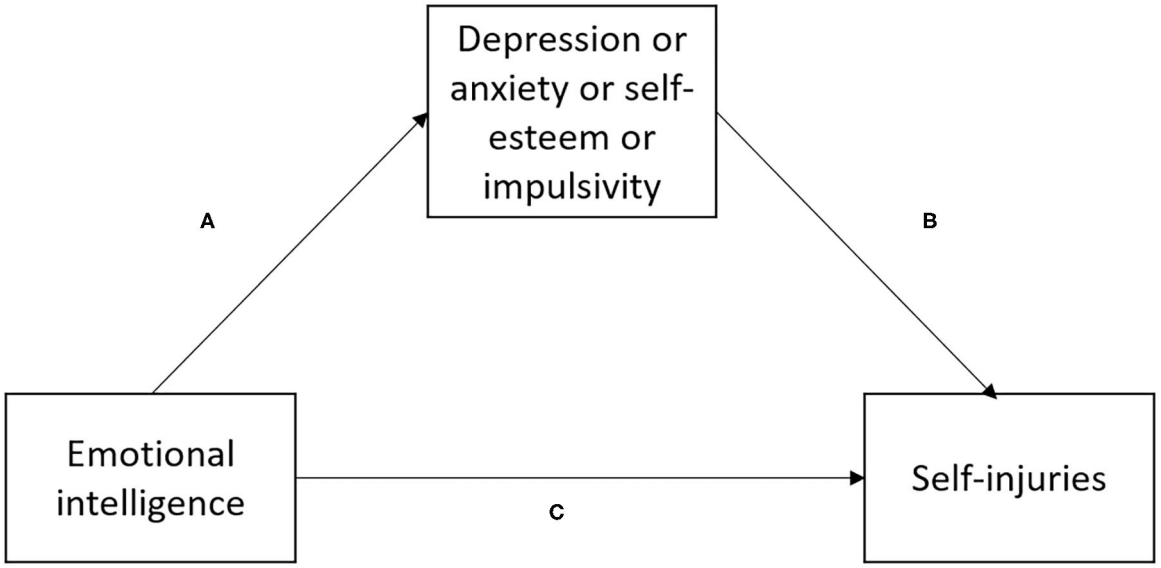


**FIGURE 1 |** A simple mediation model tested in this study. **(A)** effect of emotional intelligence on mediator, **(B)** effect of mediator on self-injuries, **(C)** direct effect of emotional intelligence on self-injuries.

### The Questionnaire for the Assessment of Disgust Sensitivity (QADS)

This measure consists of 37 statements, in which the severity of disgust is assessed on a Likert five-point scale. Disgust sensitivity refers to individual personality traits and describes a predisposition to react to specific situations and materials with disgust. There are three subscales in the questionnaire: Core Disgust, Animal-Reminder, and Contamination-Interpersonal (34). Animal – Reminder disgust sensitivity addresses these aspects of human functioning which are shared with animals i.e., death, sex, a lack of hygiene, and damage to the body surface. The Cronbach's alpha for the QADS total score in our sample was 0.94.

## Statistical analysis

The chi$^2$ test was applied to evaluate sex differences as well as differences in the rates of comorbid mood and anxiety disorders between participants with lifetime history of self-ham and those who did not engage in self-harm acts. Due to non-normal distribution, the Spearman rank correlation coefficients and the Mann-Whitney U test were used to analyze continuous variables. Results of bivariate tests were considered statistically significant if their $p$-value was $<0.05$. Simple mediation was analyzed using the PROCESS Macro Model 4 (35). Separate models for specific mediators were analyzed to avoid potential multicollinearity (**Figure 1**). The PEIQ score was inputted as an independent variable while a history of self-injuries was an outcome variable. One of main assumptions underlying mediation analysis is that the mediator must be associated with the independent variable and the outcome variable. Therefore, potential mediators were selected from the measures that were significantly associated with the PEIQ score and lifetime history of self-injuries. Age and sex were added as co-variates. The bootstrap calculation with 5,000 samples was applied to check direct and indirect effects. Mediation was considered significant if the 95% CI of indirect effect did not include zero. All analyses were conducted using the Statistical Package for Social Sciences, version 20 (SPSS Inc., Chicago, Illinois, USA).

# RESULTS

The comparison of adolescents with a positive history of self-harm and those who had never engaged in self-injuries was provided in **Table 1**. Females were overrepresented in the subgroup of adolescents who reported engaging in self-injuries. Individuals with a positive history of self-harming presented with significantly lower levels of EI (PEIQ – total score and scores of acceptance, control and understanding) and self-esteem as well as significantly higher levels of depression, state and trait anxiety and impulsivity.

**Table 2** shows bivariate correlations between EI and other measures tested in this study. There were significant negative associations between the level of EI (PEIQ – total score and scores of acceptance and control) and the scores of depressive symptoms and anxiety. Lower level of the PEIQ control subscale was related to significantly higher levels of core disgust. In turn, higher levels of the PEIQ acceptance subscale were associated with significantly higher levels of physical and verbal aggression, anger, hostility, venturesomeness as well as empathy. There were also significant negative correlations between the levels of impulsivity and the total PEIQ score as well as scores of two PEIQ subscales (control and understanding). Finally, higher levels of empathy (IVE) were significantly associated with the PEIQ total score and the scores of three PEIQ subscales (acceptance, control and empathy).

**TABLE 1 |** General characteristics of the sample.

| | **Self-harm (+) $n = 78$** | **Self-harm (–), $n = 58$** | **Statistics** |
|---|---|---|---|
| Age, years | 14.6 ± 1.1 | 15.1 ± 1.3 | $U = 1{,}814.5$, $r = -0.16$, $p = 0.055$ |
| Sex, F/M (%) | 57/21 (73.1/26.9) | 20/38 (34.5/65.5) | **$\chi^2 = 20.2$, $p < 0.001$** |
| Age of self-harm onset, years | 10.7 ± 4.4 | – | – |
| Lifetime number of self-harm acts | 179.3 ± 362.5 | – | – |
| The number of self-injuries in the preceding year | 35.8 ± 77.6 | – | – |
| Comorbid mood and/or anxiety disorder, *n* (%) | 28 (35.9%) | 12 (20.7) | $\chi^2 = 3.71$, $p = 0.054$ |
| CDI2 – depression | 20.4 ± 13.4 | 12.9 ± 11.0 | **$U = 601.5$, $r = 0.29$, $p = 0.024$** |
| STAI – trait anxiety | 47.0 ± 13.2 | 36.8 ± 9.5 | **$U = 3{,}120.5$, $r = 0.46$, $p < 0.001$** |
| STAI – state anxiety | 50.3 ± 12.7 | 37.7 ± 8.9 | **$U = 3{,}328.5$, $r = 0.55$, $p < 0.001$** |
| PEIQ – EI (total score) | 297.0 ± 29.2 | 309.8 ± 33.2 | **$U = 1{,}585.0$, $r = -0.21$, $p = 0.022$** |
| PEIQ – acceptance | 46.0 ± 9.0 | 50.1 ± 10.7 | **$U = 1{,}563.0$, $r = -0.21$, $p = 0.017$** |
| PEIQ – empathy | 65.1 ± 12.1 | 61.9 ± 10.4 | $U = 2{,}400.0$, $r = 0.14$, $p = 0.123$ |
| PEIQ – control | 30.0 ± 6.8 | 33.8 ± 5.6 | **$U = 1{,}301.5$, $r = -0.32$, $p < 0.001$** |
| PEIQ – understanding | 27.3 ± 6.9 | 29.9 ± 4.8 | **$U = 1{,}535.0$, $r = -0.22$, $p = 0.011$** |
| SES – self-esteem | 23.8 ± 6.4 | 28.6 ± 5.4 | **$U = 1{,}188.0$, $r = -0.35$, $p < 0.001$** |
| QADS - disgust (total score) | 123.1 ± 31.5 | 118.4 ± 32.6 | $U = 2{,}209.5$, $r = 0.06$, $p = 0.457$ |
| QADS – core disgust | 54.5 ± 15.2 | 54.3 ± 13.6 | $U = 2{,}070.5$, $r = 0.02$, $p = 0.787$ |
| QADS – animal reminder | 25.6 ± 10.1 | 28.8 ± 9.6 | $U = 1{,}634.0$, $r = -0.16$, $p = 0.069$ |
| QADS – contamination-intepersonal | 42.0 ± 12.8 | 39.7 ± 10.3 | $U = 2{,}278.5$, $r = 0.11$, $p = 0.205$ |
| BPAQ – physical agression | 19.4 ± 7.1 | 20.9 ± 7.3 | $U = 1{,}622.0$, r = −0.09, p = 0.295 |
| BPAQ – verbal agression | 13.8 ± 5.3 | 12.4 ± 4.7 | $U = 2{,}082.0$, r = 0.12, p = 0.185 |
| BPAQ – anger | 18.4 ± 6.3 | 19.5 ± 6.1 | $U = 1{,}648.5$, r = −0.09, p = 0.363 |
| BPAQ – hostility | 19.0 ± 8.1 | 17.8 ± 7.7 | $U = 1{,}985.0$, r = 0.07, p = 0.410 |
| IVE – adventuresomeness | 8.9 ± 3.4 | 8.9 ± 3.2 | $U = 1{,}931.0$, r = −0.01, p = 0.886 |
| IVE – empathy | 12.3 ± 3.3 | 11.4 ± 3.5 | $U = 2{,}232.5$, r = 0.12, p = 0.179 |
| IVE – impulsivity | 10.7 ± 4.2 | 8.5 ± 3.8 | **$U = 2612.5$, $r = 0.29$, p < 0.001** |

*Data expressed as mean ± SD or n (%).*

*Significant differences ($p < 0.05$) were marked with bold characters.*

*BPAQ, the Buss-Perry Aggression Questionnaire; CDI2, the Children's Depression Inventory 2; EI, emotional intelligence; IVE, the Eysenck's Impulsivity Inventory; PEIQ, the Popular Emotional Intelligence Questionnaire; QADS, the Questionnaire for the Assessment of Disgust Sensitivity; Self-harm (+), adolescents with a positive lifetime history of self-harm; Self-harm (–), adolescents with a negative lifetime history of self-harm; SES, the Rosenberg; Self-Esteem Scale; STAI, the State-Trait Anxiety Inventory.*

Results of mediation analysis were presented in **Table 3**. There were significant direct effects of EI on the level of depression (PEIQ – total score, PEIQ – acceptance score and PEIQ - control score), state and trait anxiety (PEIQ – total score, PEIQ – acceptance score and PEIQ - control score), impulsivity (PEIQ – total score, PEIQ – understanding score and PEIQ - control score) as well self-esteem (PEIQ – total score, PEIQ – acceptance score and PEIQ - control score). Similarly, direct effects of self-esteem, state and trait anxiety on a history of self-injuries were also significant in these models. No significant effects of depressive symptoms as mediators were found. Self-esteem, state and trait anxiety mediated the association between EI and a history of self-injuries in the models with the PEIW total scores as well as the scores of two subscales, including control and acceptance (significant indirect effects). Direct effects of EI on a history of self-injuries were non-significant in these models. Therefore, these results indicate that self-esteem, trait and state were complete mediators.

## DISCUSSION

Results of this study imply that individuals with conduct disorder and positive lifetime history of self-injuries present with significantly lower levels of EI and self-esteem together with higher levels of depressive and anxiety symptoms as well as impulsivity. Previous studies have also shown that on the one hand depression is associated with a higher risk of self-harm (36) as well as with lower level of EI on the other hand. A negative correlation between the level of EI or its components and depressive symptoms score has been replicated in early, middle and late adolescence (37–39). Regarding anxiety, similar results have been shown. In a cross-sectional study conducted in over 12,000 adolescents from 11 European countries, it was demonstrated that not only depression but also anxiety symptoms are significantly associated with self-harm risk (40). Furthermore, self-reported EI was negatively correlated with anxiety severity, social anxiety and the level of stress in adolescent samples (41, 42). Moreover, consistent findings have been

**TABLE 2 |** Correlations between the level of emotional intelligence and other measures recorded in this study.

| | PEIQ – total score | PEIQ - acceptance | PEIQ – control | PEIQ – empathy | PEIQ - understanding |
|---|---|---|---|---|---|
| CDI2 - depression | $r = -0.350^{b}$ | $r = -0.519^{c}$ | $r = -0.369^{b}$ | $r = 0.156$ | $r = -0.130$ |
| STAI - trait anxiety | $r = -0.248^{b}$ | $r = -0.350^{c}$ | $r = -0.297^{b}$ | $r = 0.086$ | $r = -0.077$ |
| STAI - state anxiety | $r = -0.423^{c}$ | $r = -0.477^{c}$ | $r = -0.400^{c}$ | $r = 0.103$ | $r = -0.205$ |
| SES - self-esteem | $r = 0.345^{c}$ | $r = 0.382^{c}$ | $r = 0.300^{b}$ | $r = -0.068$ | $r = 0.128$ |
| QADS - disgust (total score) | $r = 0.071$ | $r = 0.124$ | $r = -0.142$ | $r = 0.038$ | $r = -0.076$ |
| QADS – core disgust | $r = -0.048$ | $r = -0.002$ | $r = -0.268^{b}$ | $r = 0.103$ | $r = -0.160$ |
| QADS – animal reminder | $r = 0.018$ | $r = 0.021$ | $r = -0.167$ | $r = 0.014$ | $r = -0.119$ |
| QADS – contamination/interpersonal | $r = -0.023$ | $r = 0.056$ | $r = -0.126$ | $r = 0.100$ | $r = -0.172$ |
| BPAQ - physical agression | $r = 0.162$ | $r = 0.282^{b}$ | $r = -0.077$ | $r = 0.095$ | $r = -0.143$ |
| BPAQ - verbal agression | $r = 0.122$ | $r = 0.191^{a}$ | $r = -0.082$ | $r = 0.171$ | $r = -0.052$ |
| BPAQ - anger | $r = 0.102$ | $r = 0.230^{a}$ | $r = 0.009$ | $r = 0.081$ | $r = 0.013$ |
| BPAQ - hostility | $r = 0.077$ | $r = 0.219^{a}$ | $r = -0.062$ | $r = 0.121$ | $r = -0.075$ |
| IVE - venturesomeness | $r = 0.177^{a}$ | $r = 0.204^{a}$ | $r = -0.034$ | $r = 0.171$ | $r = 0.051$ |
| IVE - empathy | $r = 0.266^{b}$ | $r = 0.192^{a}$ | $r = -0.182^{a}$ | $r = 0.518^{c}$ | $r = -0.168$ |
| IVE - impulsivity | $r = -0.184^{a}$ | $r = -0.073$ | $r = -0.437^{c}$ | $r = 0.111$ | $r = -0.328^{c}$ |

*Spearman rank correlation coefficients were shown.*
*[a]$p < 0.05$.*
*[b]$p < 0.01$.*
*[c]$p < 0.001$.*
*BPAQ, the Buss-Perry Aggression Questionnaire; CDI2, the Children's Depression Inventory 2; EI, emotional intelligence; IVE, the Eysenck's Impulsivity Inventory; PEIQ, the Popular Emotional Intelligence Questionnaire; QADS, the Questionnaire for the Assessment of Disgust Sensitivity; SES, the Rosenberg Self-Esteem Scale; STAI, the State-Trait Anxiety Inventory.*

reported with respect to impulsivity. Chamberlain et al. (4) found that self-harm dimensions are associated with impulse control disorders. A higher level of impulsiveness has previously been found in subjects with a history of self-injuring (12, 23). Finally, people with higher levels of EI are characterized by less frequent engagement in self-harm acts (20, 40), less frequent suicide attempts (43) and better overall social functioning (40). These observations appear to be consistent and independent of age (40), cultural context (12), nationality (44) or self-harm method (2). Therefore, high EI level might be perceived as a protective factor for self-harm.

One of the most important variables associated with self-harm risk is self-esteem. Greydanus and Shek (45) found that adolescents with low levels of self-esteem are at higher risk of engaging in self-injuries. A large number of previous reviews have consistently shown links between self-harm behaviors and low levels of self-respect among adolescents (7, 9). Hodgson (46) demonstrated that those who reported self-harm have also more problems with self-criticism and self-denigration. Moreover, they tend to present lower levels of self-esteem in contrast to adolescents who never engaged in self-harm acts. Increased self-dislike also advocates for the concept of self-harm as a way of punishing oneself and growing self-hatred of one's own body (25).

We also found that higher levels of EI are related to higher levels of self-esteem, venturesomeness and empathy, and at the same time with lower levels of depressive symptoms, anxiety and impulsivity in adolescents with conduct disorder. High levels of EI have been reported in correlation with a lower severity of symptoms related to mood and anxiety disorders (17, 27). High level of EI has been related to a subjective perception of well-being and satisfaction with life as well as higher levels of self-esteem (47). In some studies, lower self-esteem has been associated with a higher frequency of self-injuries (46). Importantly, self-esteem has also been found to mediate the association between childhood maltreatment and self-injuries in adolescents (47).

Similar results have been reported with respect to impulsiveness. It has been found that higher levels of impulsiveness are linked with a risk of self-harm. Moreover, there is evidence that self-injuries are driven by a wish to lessen emotional distress, and increased negative affect may precede episodes of self-harm (48). Higher level of impulsivity has been identified in individuals with self-harm history, because they worry less about the long-term consequences (e.g., discomfort, scarring, stigmatization). They can also be encouraged to self-injurious behavior by the promise of the immediate benefits (e.g., relief) (49, 50). Notably, we did not find any significant association between self-injuries and disgust sensitivity. Higher levels of core disgust were weakly associated with lower levels of control over one's emotions. It was previously demonstrated in college students that another type of disgust referred to as self-disgust plays a role as a mediator between depressive symptoms and NSSI (51). However, this category of disgust was not included in our study.

Our path analysis demonstrated that trait and state anxiety as well as impulsivity completely mediate the association between EI and a lifetime history of self-injuries in this group of adolescents (non-significant direct effects on a history of self-injuries with significant indirect effects). Previous studies have also shown that EI is not directly related to a risk of self-injuries or suicide. For instance, a recent study by Quintana-Orts

**TABLE 3 |** Results of mediation analysis.

| Mediator | Effect | Predictor | | | |
|---|---|---|---|---|---|
| | | **PEIQ – total score** | **PEIQ - acceptance** | **PEIQ - control** | **PEIQ – understanding** |
| CDI2 - depression | Effect of EI on mediator (a) | B = −0.104[a], SE = 0.047, 95% CI = −0.189 to −0.007 | B = −0.523[c], SE = 0.137, 95% CI = −0.750 to −0.253 | B = −0.582[a], SE = 0.202, 95% CI = −0.928 to −0.122 | – |
| | Effect of mediator on self-injuries (b) | B = 0.001, SE = 0.002, 95% CI = −0.004 to 0.003 | B = 0.004, SE = 0.007, 95% CI = −0.011 to 0.018 | B = 0.006, SE = 0.006, 95% CI = −0.005 to 0.017 | – |
| | Direct effect of EI on self-injuries (c) | B = −0.001, SE = 0.009, 95% CI = −0.018 to 0.016 | B = 0.019, SE = 0.037, 95% CI = −0.047 to 0.085 | B = −0.018, SE = 0.047, 95% CI = −0.110 to 0.075 | – |
| | Indirect effect (ab) | B = −0.002, SE = 0.001, 95% CI = −0.005 to 0.001 | B = −0.006, SE = 0.004, 95% CI = −0.014 to 0.002 | B = −0.016, SE = 0.006, 95% CI = −0.029 to 0.004 | – |
| STAI - state anxiety | Effect of EI on mediator (a) | B = −0.145[c], SE = 0.032, 95% CI = −0.208 to −0.082 | B = −0.480[c], SE = 0.095, 95%CI = −0.659 to −0.288 | B = −0.579[c], SE = 0.170, 95% CI = −0.919 to −0.259 | – |
| | Effect of mediator on self-injuries (b) | B = 0.015[b], SE = 0.005, 95% CI = 0.006 to 0.025 | B = 0.016[b], SE = 0.005, 95% CI = 0.007 to 0.026 | B = 0.014[b], SE = 0.005, 95% CI = 0.005 to 0.024 | – |
| | Direct effect of EI on self-injuries (c) | B = 0.001, SE = 0.001, 95% CI = −0.003 to 0.003 | B = 0.001, SE = 0.005, 95% CI = −0.008 to 0.010 | B = −0.049, SE = 0.034, 95% CI = −0.111 to 0.023 | – |
| | Indirect effect (ab) | **B = −0.013, SE = 0.007, 95% CI = −0.032 to −0.004** | **B = −0.045, SE = 0.023, 95% CI = −0.104 to −0.015** | **B = −0.049, SE = 0.027, 95% CI = −0.118 to −0.012** | – |
| STAI - trait anxiety | Effect of EI on mediator (a) | B = −0.093[b], SE = 0.030, 95% CI = −0.149 to −0.031 | B = −0.332[b], SE = 0.003, 95% CI = −0.531 to −0.118 | B = −0.444[b], SE = 0.009, 95% CI = −0.780 to −0.130 | – |
| | Effect of mediator on self-injuries (b) | B = 0.010[a], SE = 0.004, 95% CI = 0.002 to 0.019 | B = 0.010[a], SE = 0.004, 95% CI = 0.002 to 0.019 | B = 0.009[a], SE = 0.004, 95% CI = 0.002 to 0.018 | – |
| | Direct effect of EI on self-injuries (c) | B = −0.002, SE = 0.001, 95% CI = −0.004 to 0.001 | B = −0.003, SE = 0.004, 95% CI = −0.011 to 0.006 | B = −0.012, SE = 0.006, 95% CI = −0.024 to 0.001 | – |
| | Indirect effect (ab) | **B = −0.006, SE = 0.004, 95% CI = −0.016 to −0.001** | **B = −0.021, SE = 0.014, 95%CI = −0.057 to −0.003** | **B = −0.026, SE = 0.019, 95% CI = −0.076 to −0.002** | – |
| IVE - impulsivity | Effect of EI on mediator (a) | B = −0.025[a], SE = 0.011, 95% CI = −0.046 to −0.004 | – | B = −0.218[b], SE = 0.001, 95% CI = −0.328 to −0.111 | B = −0.219[c], SE = 0.058, 95% CI = −0.328 to −0.101 |
| | Effect of mediator on self-injuries (b) | B = 0.019, SE = 0.011, 95% CI = −0.002 to 0.040 | – | B = 0.012, SE = 0.012, 95% CI = −0.011 to 0.035 | B = 0.016, SE = 0.011, 95% CI = −0.006 to 0.039 |
| | Direct effect of EI on self-injuries (c) | B = −0.002, SE = 0.001, 95% CI = −0.004 to 0.001 | – | B = −0.014, SE = 0.007, 95% CI = −0.029 to 0.001 | B = −0.010, SE = 0.007, 95% CI = −0.023 to 0.003 |
| | Indirect effect (ab) | B = −0.002, SE = 0.002, 95% CI = −0.007 to 0.001 | – | B = −0.014, SE = 0.014, 95% CI = −0.044 – 0.016 | B = −0.017, SE = 0.014, 95% CI = −0.050 to 0.007 |
| SES - self-esteem | Effect of EI on mediator (a) | B = 0.058[a], SE = 0.022, 95% CI = 0.013 to 0.101 | B = 0.206[b], SE = 0.064, 95% CI = 0.078 to 0.329 | B = 0.231[a], SE = 0.099, 95% CI = 0.033 to 0.423 | – |
| | Effect of mediator on self-injuries (b) | B = −0.018[b], SE = 0.007 95% CI = −0.031 to −0.004 | B = −0.019[b], SE = 0.006, 95% CI = −0.032 to −0.005 | B = −0.017[a], SE = 0.007, 95% CI = −0.030 to −0.003 | – |
| | Direct effect of EI on self-injuries (c) | B = −0.001, SE = 0.001, 95% CI = −0.004 to 0.001 | B = −0.002, SE = 0.005, 95% CI = −0.011 to 0.008 | B = −0.011, SE = 0.007, 95% CI = −0.025 to 0.001 | – |
| | Indirect effect (ab) | **B = −0.005, SE = 0.003, 95% CI = −0.013 to −0.001** | **B = −0.017, SE = 0.011, 95% CI = −0.046 to −0.003** | **B = −0.019, SE = 0.013, 95% CI = −0.049 to −0.003** | – |

[a] $p < 0.05$.
[b] $p < 0.01$.
[c] $p < 0.001$.
*CDI2, the Children's Depression Inventory 2; EI, emotional intelligence; IVE, the Eysenck's Impulsivity Inventory; SES, the Rosenberg Self-Esteem Scale; STAI, the State-Trait Anxiety Inventory. Significant indirect effects were marked with bold characters.*

et al. (19) demonstrated that depressive symptoms mediate the association between suicide risk and EI among victims of bullying. This effect was moderated by sex, and appeared to be stronger in girls compared to boys. It is important to note that we did not find that depressive symptoms mediate the association between EI and a risk of self-injuries. However, to the best of our knowledge, our study is the first which was performed in adolescents with conduct disorder and we focused on a risk of self-injuries. Similarly, another study demonstrated that the level of psychological distress mediates the relationship between EI and suicide risk in adults (52). In turn, (53, 54) revealed that recognition and expression of emotions mediate the association between mindfulness and distress. The same study provided evidence that emotional recognition and expression as well as emotional management and control mediate the association between mindfulness and depression in adolescents.

There are some limitations of this research that need to be addressed. Our sample was rather small and a type II error cannot be ignored. Similarly, type I error should be taken into consideration due to a large number of estimated effects and a lack of correction for multiple testing. Therefore, our findings should be perceived as exploratory and requiring independent verification. Moreover, a cross-sectional study design does not support causal associations. Indeed, it has been demonstrated that the cross-sectional approaches can generate biased estimates of associations that are hypothesized to have a temporal ordering (55). Moreover, our findings cannot be generalized to other clinical populations with high prevalence of self-injuries. Although previous studies indicate that various psychological processes and low emotional abilities precede depressive symptoms, anxiety and self-harm behaviors, longitudinal studies are needed to investigate validity of the model tested in our study. Another limitation is that two subscales of the IVE (venturesomeness and empathy) had questionable internal consistency. Finally, investigating our hypotheses in a specific group of adolescents with conduct disorder limits generalization of findings to other populations.

In conclusion, main findings of our studies indicate that EI is not directly associated with a risk of self-injuries in adolescents with conduct disorder. Anxiety and self-esteem might serve as complete mediators of this association. However, longitudinal studies are required to confirm direction of causality. Results of our study hold a great promise for developing specific interventions that aim to target or prevent self-injurious behaviors. In light of our findings, one of potential approaches would be to target emotional competences of vulnerable individuals (43–50). Moreover, focusing on the development of self-esteem and reducing the level of anxiety seems to have an important role.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of Wroclaw Medical University, Poland. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

JH-M collected data and wrote the first draft of the manuscript. MS-B participated in data analysis and manuscript writing. JR participated in manuscript writing. AA participated in data collection and manuscript writing. BM performed data analysis and participated in manuscript writing. All authors contributed to the article and approved the submitted version.

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# Feasibility and Effectiveness of a New Short-Term Psychotherapy Concept for Adolescents With Emotional Dysregulation

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**Background:** The 'Stress-Trauma-Symptoms-Regulation-Treatment' (START) is an innovative manualized short-term treatment program for stabilization and stress resilience in emotionally dysregulated adolescents, based on an approach of stress and management and emotional regulation. The current pilot trial aims to assess the feasibility and effectiveness of the START intervention program for improvement of emotion regulation.

**Methods:** Sixty-six adolescents between the age of 13–18 years admitted to a psychiatric unit for acute emotional or behavioral dysregulation took part in the START program for 5 weeks in an open group setting with two sessions per week (70 min/session). Before treatment, we assessed a history of adverse experience with the Child and Adolescent Trauma Screen (CATS) and the Child Posttraumatic Cognitions Inventory (CPTCI). Before and after treatment, the participants completed the FEEL-KJ, a self-report screening instrument of emotional regulation and coping strategies.

**Results:** A large proportion of this sample had experienced traumatic events based on the CATS (75%) and the CPTCI (82%). The mean FEEL-KJ score significantly decreased after the intervention ($d = -0.248$, $p = 0.037$), while no difference was observed with regard to mean level of adaptive emotion regulation strategies ($d = 0.202$, $p = 0.207$). A positive effect of the intervention was observed on three components of the adaptive FEEL-KJ scale: accepting ($d = 0.289$, $p = 0.08$), forgetting ($d = 0.271$, $p = 0.049$) and dealing with anger ($d = 0.309$, $p = 0.034$).

**Conclusion:** START demonstrates preliminary evidence for improvement in emotional dysregulation after a 5-weeks course of treatment. Therefore, this short-term intervention can possibly be regarded as a tool to improve emotional stability in children with a high load of trauma-related psychopathology. The results are promising and warrant future studies, specifically randomized controlled trials on the effectiveness of START for strengthening resilience at-risk-populations.

**Keywords: emotion regulation, stress, trauma, resilience, psychotherapy**

## INTRODUCTION

The ability to regulate emotional responses to events, situations, and experiences is central to mental health (1). Mood Regulation successfully contributes to higher self-effectiveness, a central element for identity development in adolescents (2). Emotional regulation (ER) strategies as well as a sense of self-worth are fundamental elements of resilience (3–6). Dysfunctional strategies for ER such as self-harming behavior, impulsive behavior, or substance abuse are often used for managing internal tension and negative emotions (7–12).

Incidence of mental disorders, specifically emotional disorders (13) in children is continuously increasing (14). Emotional dysregulation (ED) is associated with diverse forms of childhood psychiatric disorders and symptoms like post-traumatic stress disorder (PTSD), oppositional defiant- and conduct disorders (ODD and CD), borderline personality disorders (BPD), self-injurious behavior and suicidality and attention deficit hyperactivity disorder (ADHD).

ED represents a major health risk reported in about 5% of children and adolescents (15, 16). In clinical settings, dysregulation problems are especially prominent (17), occurring in 26–31% of children admitted to child and adolescent psychiatric clinics or mental health facilities. The occurrence of typical phenomena associated with ED has estimates of about 45 % in child psychiatric patients between 6 and 18 years (12).

Some data indicate a potential influence of early life stress on ED (18, 19). Adolescents without support, such as unaccompanied refugee minors without the protection of their parents or important caregivers are particularly affected and exposed to a greater risk of developing psychiatric disorders related to ED (20–23). A significant proportion of dysregulated adolescents are reported to have been exposed to successive periods of severe stress or trauma (24). Sequential traumatization in this regard is as a succession of traumatizing events maintaining severity of the psychological and physical consequences (25–27). Typical symptoms after experiencing maltreatment include hypervigilance and hyperarousal potentially accompanied by impulsive behavioral problems, and a reduced ability to verbally express emotional experience (28–30). Also it is known that children and adolescents suffering from persistent stress have a high risk of developing mental health problems (18, 24, 31–38).

Emotional stress has been shown do put the body under "permanent alarm" (32, 39, 40). Children and adolescents are at high risk of developing acute stress disorders, adjustment disorders, and also PTSD, grief, and mood disorders (34, 41–45).

Felitti et al. (24) described the relationship of health risk in adulthood of exposure to childhood emotional, physical, or sexual abuse and household dysfunction in a large sample during childhood.

Many afflicted adolescents have been reported to avoid problematic and trauma-associated emotions by use of escape strategies such as dysfunctional behaviors (7, 39, 46–48). Maladaptive ED strategies are thought to be risk factors and connected with the development of mental disorders including self-injurious behavior, substance use, pre-suicidal acts, and impulsive acts (32, 48–52).

Summing up, ED and the experience of traumatic events have repeatedly been described to play a central role in the development of mental disorders and in the development and maintenance of trauma-specific symptoms (49, 53–56). Twenty to 50% of people who have had traumatic experiences show PTSD, but also other child psychiatric conditions can be observed (57). Interventions strengthening stress resilience and emotion regulation seem to be of crucial importance in adolescents at risk.

Stress management has proven to be of importance for young children helping them cope with stressful situations (31, 58, 59). Specifically, low threshold interventions can be used effectively by children and adolescents to reduce stress and regulate emotions also by promoting self-efficacy (60, 61).

Furthermore, early interventions have been described to prevent the increase of trauma symptoms and psychopathology (4, 62, 63). For adaptive emotional regulation, skills such as those used in dialectic behavioral therapy (8, 64, 65, 73) are recommended.

However, the intellectual and motivational requirements of dialectic behavioral therapy exclude a patient population with shorter attention span and/or more unstable therapy commitment, as frequently presenting in acute child psychiatric clinics (66). Therefore, a low threshold program was designed to meet the acute treatment needs of emotionally highly unstable adolescents.

START (Stress-Traumasymptoms-Arousal-Regulation Treatment) is a manualized short-term (5 weeks) treatment concept of stabilization and emotional regulation for extremely stressed adolescents and also for minor refugees. The intervention was constructed to offer adolescents, who are unmotivated or too unstable for Dialectical Behavior Therapy (DBT), reprocessing treatment, or long-term psychotherapy conditions, a first aid for crisis management and emotional stabilization (67). The program can be used for adolescents with diverse cultural backgrounds and repeatedly severe emotional distress, as a low-threshold training program to manage emotional dysregulation including skills to reduce self-harming and impulsive aggressive behavior. The shortness of the treatment program was deliberately planned, as the motivation to seek treatment, adherence, and compliance is often fragile in adolescents (68). Especially adolescents with traumatic experiences as a very vulnerable group are presumed mistrustful and not particularly eager to be kept in therapy for

**Abbreviations:** ADHD, Attention Deficit Hyperactivity Disorder; BDP, Borderline Personality Disorder; CATS, Child and Adolescent Trauma Screen; CPT, Continuous Performance Test; CPTCI, Child Post-Traumatic Cognitions Inventory; DBT, Dialectical Behavior Therapy; DISYPS III, Diagnostik-System für psychische Störungen; ED, Emotional Dysregulation; EMDR, Eye Movement Desensitization and Reprocessing; ER, Emotional Regulation; FEEL-KJ, Fragebogen zur Erhebung der Emotionsregulation bei Kindern und Jugendlichen; ODD, Oppositional Defiant Disorder; PTSD, Post-traumatic Stress Disorder; START, Stress-Trauma symptoms-Arousal-Regulation-Treatment; Tf-CBT, Trauma-focused – Cognitive Behavioral Therapy.

longer periods of time. Therefore, a program not requiring a commitment for longer than 5 weeks seemed to be necessary for acute clinical purposes.

The intervention designed and evaluated in this study places special emphasis on the use of adaptive regulation strategies for acute crisis management and ED (69). In the first step, the short therapeutic program START was developed by Dixius and Möhler (70, 71) and originally conceived for the work with refugee minors only. Minor refugees appear to be a particularly vulnerable group for the development of mental disorders with a range from 20 to 82% (23, 72). In the second step, the intervention was clinically applied in the general population of an acute child and adolescent ward. The contents of the short-term therapy concept integrate and adapt elements and skills for mindfulness, stress regulation, emotion regulation, and self-care from Dialectic Behavioral Therapy (DBT) (11, 64, 65, 73, 74). Easy—to—apply and stimulus rich skills are postulated to improve motivation and emotion regulation capacities. Furthermore, the therapy concept integrates and adapts elements and skills for relaxation and stabilization techniques from psycho-trauma therapy, especially from the Trauma focused-Cognitive Behavioral Therapy (Tf-CBT) (9). As part of mindfulness exercises, the therapy concept includes implicitly bilateral stimulation from Eye Movement Desensitization and Reprocessing (EMDR) (75). Stress disturbs the cooperation of the brain hemispheres—under this aspect these exercises are designed to support the processing of stress (76).

This project examines the hypothesis that the 5-week treatment course of START is able to improve emotional regulation in adolescents referred to acute treatment for suicidal or highly aggressive behavior of mixed cultural backgrounds.

# METHODS

A total sample of 66 patients participated in the 5-week START study at an inpatient psychiatric unit.

## Sample

The sample consisted of 17 male and 49 female patients aged between 13 and 18 years (mean value 14,85; $SD = 1.57$) referred to acute inpatient treatment for suicidal or aggressive behavior.

Adolescents with the origin in the following countries were included: Germany (79 %), Afghanistan (9 %), Syria (8%), Poland (2%,) Pakistan (2 %), Gambia (2%).

The study inclusion procedure consists of a consultation with a child and adolescent psychiatrist regarding indication and motivation for treatment and to deliver information about the intervention as well as informed consent. After informed consent, adolescents are assessed for trauma with the Child and Adolescent Trauma Screen (CATS) and the Child Posttraumatic Cognitions Inventory (CPTCI) before treatment. Emotional regulation was measured with the FEEL-KJ scale before and after treatment.

Inclusion criteria were:

- Age 13–18
- Acute referral for suicidal or highly aggressive behavior
- Voluntary participation

Exclusion criteria were:

- Diagnosis of schizophrenic or affective psychosis
- Acute intoxication

The inclusion criteria in this study were not based on diagnoses but on symptoms of ED, such as suicidal behavior or aggressive behavior. Criteria for exclusion were psychoses and acute substance intoxication. Inclusion criteria were based on admission in acute crises for dysregulated emotions, not a diagnosis, nevertheless, the majority of the diagnoses consisted of a complex combination of response to severe stress and PTSD, adjustment disorder, depressive episodes, or borderline disorder. Confirmation of these ICD-10-diagnoses follows a clinical routine work flow with standardized diagnostic procedures specific for the disorder in question, such as e.g., DISYPS III, Conners Scales 3 for ADHD etc.

Drop-out occurred in one case, due to lack of motivation of the participant. The participants with missing information in a questionnaire were excluded from the analysis of this questionnaire.

# INSTRUMENTS

## CATS: Child and Adolescent Trauma Screening

Sachser et al. (77) assesses the occurrence and impact of traumatic events with a 15-item event scale. In case of the existence of a potentially traumatic event, the traumatic impact is assessed on a 20-item scale. A cut-off of 21 is a presumed indicator of post-traumatic stress. Reliability has been reported to range between 0.88 and 0.94 The convergent-discriminant validity pattern showed medium to strong correlations with measures of depression ($r = 0.62$–82) and anxiety ($r = 0.40$ −0.77) and low to medium correlations with externalizing symptoms ($r = -0.15$–0.43) for participants within informants in all language versions.

## CPTCI-25: Child Post-traumatic Cognitions Inventory – 25

The CPTCI is a self-report questionnaire. This Inventory assesses post-tramatic cognition on a 25-item scale (78).

Clinically relevant trauma is postulated at a score between 46 and 48. Posttraumatic psychopathology of clinical relevance is given at a score above 49. Each item is rated on a four-point Likert scale: "do not agree at all" (1 point), "do not agree a bit" (2 points), "agree a bit" (3 points), and "agree a lot" (4 points). Internal consistency of the scale was Cronbach's Alpha: 0.86–0.93 and Retest-Reliability 0.72–0.78.

## FEEL-KJ: Questionnaire for the Assessment of Emotional Regulation in Children and Adolescents

The questionnaire (79) quantifies 15 strategies for emotional regulation and regulation of the specific emotions (all of which are multi-dimensional and specific to a certain emotion):

anxiety, sadness, and anger. In two secondary scales, this instrument identifies seven adaptive and five maladaptive emotional regulation strategies. Adaptive strategies include the following sub-scales: problem-oriented acting, distraction, mood improvement, acceptance, forgetting, cognitive problem solving, dealing with fear, anger, and grief. Maladaptive strategies include the sub-scales: giving up, aggressive behavior, self-devaluation, withdrawal, perseveration, and also dealing with anxiety, anger, and grief. The additional scales are composed of social support, expression, and emotional control.

Internal consistency of the 15 scales ranges between $\alpha$ =0.69 and $\alpha = 0.91$. Secondary scales show a consistency of $\alpha = 0.93$ (adaptive strategies) and $\alpha = 0.82$ (maladaptive strategies). Retest-Reliability (6-week-stability) ranges between $r_{tt} = 0.62$ and $r_{tt} = 0.81$, and for the secondary scales between $r_{tt} = 0.81$ (adaptive strategies) and $r_{tt} = 0.73$ (maladaptive strategies). The secondary scale, called "adaptive scales" for specific emotions shows a very good internal consistency $\alpha = 0.88$ for sadness, $\alpha = 0.83$ for anxiety, and $\alpha = 0.83$ for anger. The maladaptive scale shows internal consistency for anxiety $\alpha = 0.59$, for sadness $\alpha = 0.59$ and for anger $\alpha = 0.58$. Furthermore, "additional scales" provide additional data on the strategies, "expression," "social support," and "emotion control," which are not covered in the two secondary scales. In addition, psycho-social skills and resources are included in this instrument (78).

Experimental Intervention

START (Stress-Arousal-Regulation-Treatment) is a manualized 5-week group-training, based on previous research. It comprises modules within 10 sessions of each 60 min. Each module is highly structured and follows a standard sequence of activities and tasks, including tools for improving mood, reducing maladaptive behavior, and regulation of stress, negative emotions, and tension. START was delivered by one therapist and one nurse twice a week in groups of five to six adolescents with severe dysregulation. The basic concept is derived from DBT, EMDR, and Tf-CBT. All participants obtained the worksheets for each step/module of the treatment program, as well as colorful and playful illustrations.

The manual contains multilingual therapy materials, numerous pictures, and additionally, all information/worksheets as audio files. START favors a play-like and multimedia atmosphere for skills training. The program encourages adolescents to try new skills, all modules are designed interactively and still follow a recurring, clearly understandable structure. A central element of the treatment is the hands on and easy to perform manual construction of an individual skills list as well as encouragement strategies for children and adolescents to discover their own tools for self-regulation with emphasis on individual strengths and resources.

The manual contains worksheets in English, Italian, Arabic, Dari, and German for each step/module of the treatment program. Central characteristic are many colorful illustrations—therefore, the language and attention span requirements are very low. The program has been described in more detail in the START-manual and articles of the authors Dixius and Möhler (66, 70). The treatment does explicitly not contain a narrative approach or exposition-based therapy as this would not be appropriate as a first step for adolescents in highly unstable emotional or psychosocial situations.

## Data Analysis and Statistics

All of the analyses were performed with IBM Statistics SPSS, version 21.0. A dependent *t*-test was applied for comparison of pre- vs. post-treatment raw scores and *t*-values. The mean value comparison of the FEEL-KJ was performed based on normalized *t*-values, taking into account the prerequisites by means of a *t*-test for dependent samples. The hypothesis postulates that the 5-week START- treatment course will show an effect on emotional regulation as indicated by a significant difference in the mean *t*-values pre- and post-treatment. The mean values of the FEEL-KJ were compared with a dependent *t*-test for paired samples. For this pilot trial in order to assess feasibility alpha level was not adjusted.

For the FEEL-KJ, the *t*-values of the major scales, as well as all sub-scales, were used.

While in almost all procedures a higher value is associated with a higher symptom score, the FEEL-KJ must be interpreted on the basis of the *t*-distribution. A value between 25 and 50 is considered as an average for all scales. For *adaptive strategies*, a lower value is considered to be worse while for *maladaptive strategies*, a higher value is considered less desirable.

A per-protocol analysis was conducted in the analysis if they answered all questions of the screenings or finished the post-screening. Furthermore, they were excluded from single questionnaires if items were missing in the respective questionnaire. Therefore, the participants can vary in numbers, depending on the different instruments.

# RESULTS

The frequency of the psychiatric diagnoses of the participants in the START intervention are shown in **Table 1**.

## Child and Adolescent Trauma Scale

The PTSD symptoms in our sample range from 6 to 50 with a mean of 31.97 ($SD = 12.59$).

Forty-five out of 60 patients (75%) scored above the cut off of 21 for clinical relevance of trauma.

**TABLE 1** | Diagnoses of participants.

| Diagnoses | Frequency | Percent |
|---|---|---|
| Mental and behavioral disorders due to psychoactive substance use | 1 | 2 |
| Depressive disorders | 9 | 14 |
| Anxiety disorders, mixed anxiety and depressive disorders, predominantly obsessional thoughts | 3 | 2 |
| Acute stress reaction, post-traumatic stress disorders, adjustment disorders | 40 | 61 |
| Eating disorders | 1 | 2 |
| Emotionally unstable personality disorders | 6 | 9 |
| Behavioral and emotional disorders with onset usually occurring in childhood and adolescence | 6 | 9 |

## CPTCI—Child and Adolescent Post-traumatic Cognitions Inventory CPTCI

The sample showed results ranging from 26 to 95 in the CPTCI, with a mean of 63.19 (SD = 17.39), based on the cut off between 46 and 48. Clinically relevant symptoms of PTSD can be found in 53 out of 64 participants (83%).

## FEEL-KJ

A significant increase was observed for the adaptive strategies "forgetting," changing from 39.39 ($SD = 11.88$) to 42.59 ($SD = 11.88$, $t = -2.01$ $n = 55$, $d = 0.271$, $p = 0.049$), "problem solving" changing from 39.59 to 43.86 ($SD = 12.55$, $t = -2{,}44$, $n = 55$, $d = 0.325$, $p = 0.018$) and "dealing with anger" from 38.54 to 41.84 ($SD = 12.55$, $t = -2{,}17$, $n = 55$, $d = 0.309$, $p = 0.034$).

A positive trend can be described in all other scales just missing significance (see **Table 2**).

As illustrated by **Figure 1** the change in the total maladaptive strategies before and after the intervention was statistically significant, changing from 65.13 to 61.5 ($SD = 12.68$, $t = 2.14$ $n = 55$, $d = -0.248$, $p = 0.037$). However, the differences between the mean scores for the subscales at baseline and after the intervention were not statistically significant (see **Table 3**).

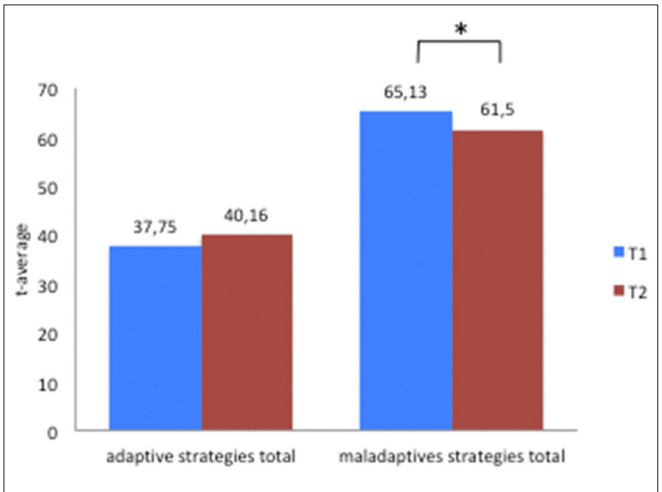


**FIGURE 1 |** FEEL-KJ-Adaptive and maladaptive scales-total. * symbol of significance.

The mean score for adaptive strategies is not statistically significant (see **Figure 1**), changing from 37.75 to 40.16 ($SD = 14.13$, $t = -1.28$, $n = 55$, $d = 0.202$, $p = 0.202$).

The results of the additional scales FEEL-KJ "social support" and "emotional control" pre- and post-treatment are presented in **Table 4** and **Figure 2**. Concerning the *additional strategies*, a statistical significant improvement was noticed on *social support* ($SD = 10.57$, $t = -1.14$ $n = 55$, $d = 4.415$, $p = 0.002$) and a reduction for *control of emotions* ($SD = 10.98$, $t = 2.47$, $d = -0.305$, $p = 0.017$) was identified.

## DISCUSSION

The present study aimed at investigating whether the 5-week structured START-intervention has a positive impact on emotional regulation in adolescents in acute emotional crises. A first result of the study is a history of clinically relevant trauma in about 75% of adolescents referred for acute treatment of symptoms of ED. As these referrals were due to suicidal or highly aggressive behavior our findings underline the general necessity of trauma-informed diagnostic and therapeutic approaches in child and adolescent psychiatry. Specifically, medical guidelines for assessment of child and adolescent psychiatric disorders should all include a through investigation of traumatic or adverse life experiences of the young patient, requiring trauma sensitive care in everyday interaction as well as therapy of the young patient.

Furthermore, this evaluation indicates the feasibility and potential usefulness of START for highly stressed children and adolescents of different nationalities in acute crisis. The largest proportion of the sample showed symptoms of PTSD (75–83%). Almost all adolescents completed the whole therapy program, thereby showing that the program is capable of keeping even highly dysregulated and easily frustrated adolescents with a short attention span and low frustration tolerance motivated and with a good to satisfactory compliance for the program. The results,

**TABLE 2 |** FEEL-KJ adaptive scales.

| FEEL-KJ | Mean T1 | Mean T2 | M_Diff | M.Diff_SD | *t* | df | Sign. | Cohens d |
|---|---|---|---|---|---|---|---|---|
| Adaptive strategies total | 37.75 | 40.16 | −2.41 | 14.13 | −1.28 | 55 | 0.207 | 0.202 |
| Problem orientated action | 36.66 | 38.77 | −2.11 | 14.04 | −1.12 | 55 | 0.266 | 0.176 |
| Distraction | 38.45 | 40.61 | −2.16 | 10.79 | −1.5 | 55 | 0.14 | 0.2 |
| Mood improvement | 39.11 | 31.96 | −2.86 | 12.8 | −1.67 | 55 | 0.101 | 0.269 |
| Accepting | 38.79 | 42.18 | −3.39 | 14.21 | −1.79 | 55 | 0.08 | 0.289 |
| Forgetting | 39.39 | 42.59 | −3.2 | 11.88 | −2.01 | 55 | 0.049 | 0.271 |
| Proplem solving | 39.59 | 43.68 | −4.09 | 12.55 | −2.44 | 55 | 0.018 | 0.325 |
| Reframing | 44.66 | 47.18 | −2.52 | 14.59 | −1.3 | 55 | 0.202 | 0.271 |
| Dealing with anger | 38.54 | 41.84 | −3.3 | 11.4 | −2.17 | 55 | 0.034 | 0.309 |
| Dealing with anxiety | 38.32 | 40.59 | −2.27 | 13.6 | −1.25 | 55 | 0.217 | 0.196 |
| Dealing with grief | 38.23 | 40.95 | −2.71 | 13.56 | −1.5 | 55 | 0.14 | 0.187 |

however, are clearly limited by the size of the sample and the lack of treatment as usual control group.

These preliminary data give first indications of the feasibility and effectiveness of the short-term treatment program START in ED by reducing maladaptive strategies and a trend for increasing the use of adaptive strategies after 5 weeks of treatment. This might indicate a potentially suitable approach to fill a gap in the treatment of adolescents with low treatment motivation and limited frustration tolerance and attention span or severe stress and adverse experiences. Highly unstable adolescents tend to not benefit sufficiently from routine clinical care. Furthermore, some adolescents seem not stable enough to participate in treatment programs with higher thresholds regarding intellect or motivation, i.e., programs such as Dialectic Behavior Therapy (DBT) or Tf-CBT. The low threshold treatment program START presented here might easily be implemented in routine clinical practice and combined with other treatments like DBT or exposure oriented therapies, once a first emotional stabilization has been achieved.

Prominent results are an increase in some adaptive strategies of ER and a decrease of maladaptive strategies for emotional regulation as expected for these variables, constituting the primary target of the 5-week program. Adaptive strategies for ER could contribute to the self-validation of one's own emotions. ER is important for a healthy development (32) and plays a central role in the development of mental disorders. Gross and Thomson (80) postulate, that first of all, it is important to develop ER strategies for then being able to use them contextually.

Regarding the fact that START is a short-term group program in a playful and low threshold manner without narrative elements or trauma exposition, it might be assumed that for a strong, significant, and lasting improvement in general mental health a more profound and individualized therapeutic setting could be necessary. However, more complex and structured approaches such as DBT (11) and Tf-CBT require more behavioral stability than adolescents in acute crises or transition situations are able to display or willing to develop.

Tf-CBT was started after completing START in 21 cases out of our sample as the patients were now found to display enough behavioral stability and therapeutic motivation for a narrative approach after achieving fast success with emotional regulation and self-control. The capability for self-regulation seems to be of utmost importance for successful longterm psychotherapeutic treatments. The capability of handling emotional frustration without the additional necessity for hospitalization, or involuntary constraint, involving potential re-traumatization, is regarded as a major goal of this novel treatment program. However, as emotion regulation is also considered a resilience factor START might be in a second step applied for preventive purposes, e.g., by professionals within the youth welfare system or even in schools.

Limitations of the study exist in the small sample size and the absence of a treatment as usual—control group. Another limitation is that all information was obtained using self-report measures only. A randomized control study including clinician and caregiver report measures is warranted and underway.

These future studies should therefore (a) include a treatment as usual control group (b) use other than self-report instruments also and (c) focus on other settings and include broader assessment tools. Some authors (10) postulate that the challenge for clinicians is to incorporate clinical interventions into non-clinical settings for preventive purposes.

## Clinical Relevance

The capability to handle extreme stress without the additional necessity for hospitalization, or involuntary constraint, involving potential re-traumatization is regarded as a major target of START and a major potential patient benefit. The novel

**TABLE 3 |** FEEL-KJ maladaptive scales.

| FEEL-KJ | Mean T1 | Mean T2 | M_Diff | M.Diff_SD | *t* | df | Sign. | Cohens d |
|---|---|---|---|---|---|---|---|---|
| Maladaptives strategies **total** | 65.13 | 61.5 | 3.63 | 12.68 | 2.14 | 55 | 0.037 | −0.248 |
| Aggressive behavior | 55.88 | 55.18 | 0.7 | 13.07 | 0.4 | 55 | 0.692 | −0.046 |
| Giving up | 60.95 | 59.88 | 1.07 | 15.09 | 0.53 | 55 | 0.597 | −0.073 |
| Withdrawal | 62.59 | 60.73 | 2.21 | 9.34 | 1.78 | 55 | 0.081 | −0.181 |
| Self-deprecating | 59.02 | 59 | 0.02 | 13.21 | 0.01 | 55 | 0.922 | −0.001 |
| Perseveration | 52.98 | 51.14 | 1.84 | 13.44 | 1.02 | 55 | 0.31 | −0.141 |
| Dealing with anger | 62.36 | 60.16 | 2.2 | 13.48 | 1.22 | 55 | 0.228 | −0.157 |
| Dealing with anxiety | 61.68 | 59.82 | 1.86 | 12.15 | 1.14 | 55 | 0.258 | −0.12 |
| Dealing with grief | 62 | 59.63 | 3.38 | 12.41 | 1.43 | 55 | 0.158 | −0.172 |

**TABLE 4 |** FEEL-KJ additional scales.

| FEEL-KJ | Mean T1 | Mean T2 | M-Diff | M-Diff_SD | *t* | N | Sign. | Cohens d |
|---|---|---|---|---|---|---|---|---|
| Expression | 48.05 | 49.32 | −1.27 | 8.34 | −1.14 | 55 | 0.260 | 0.108 |
| Social support | 42.21 | 46.70 | −4.48 | 10.57 | −3.17 | 55 | 0.002 | 4.415 |
| Emotion control | 57.30 | 53.68 | 3.63 | 10.98 | 2.47 | 55 | 0.017 | −0.305 |

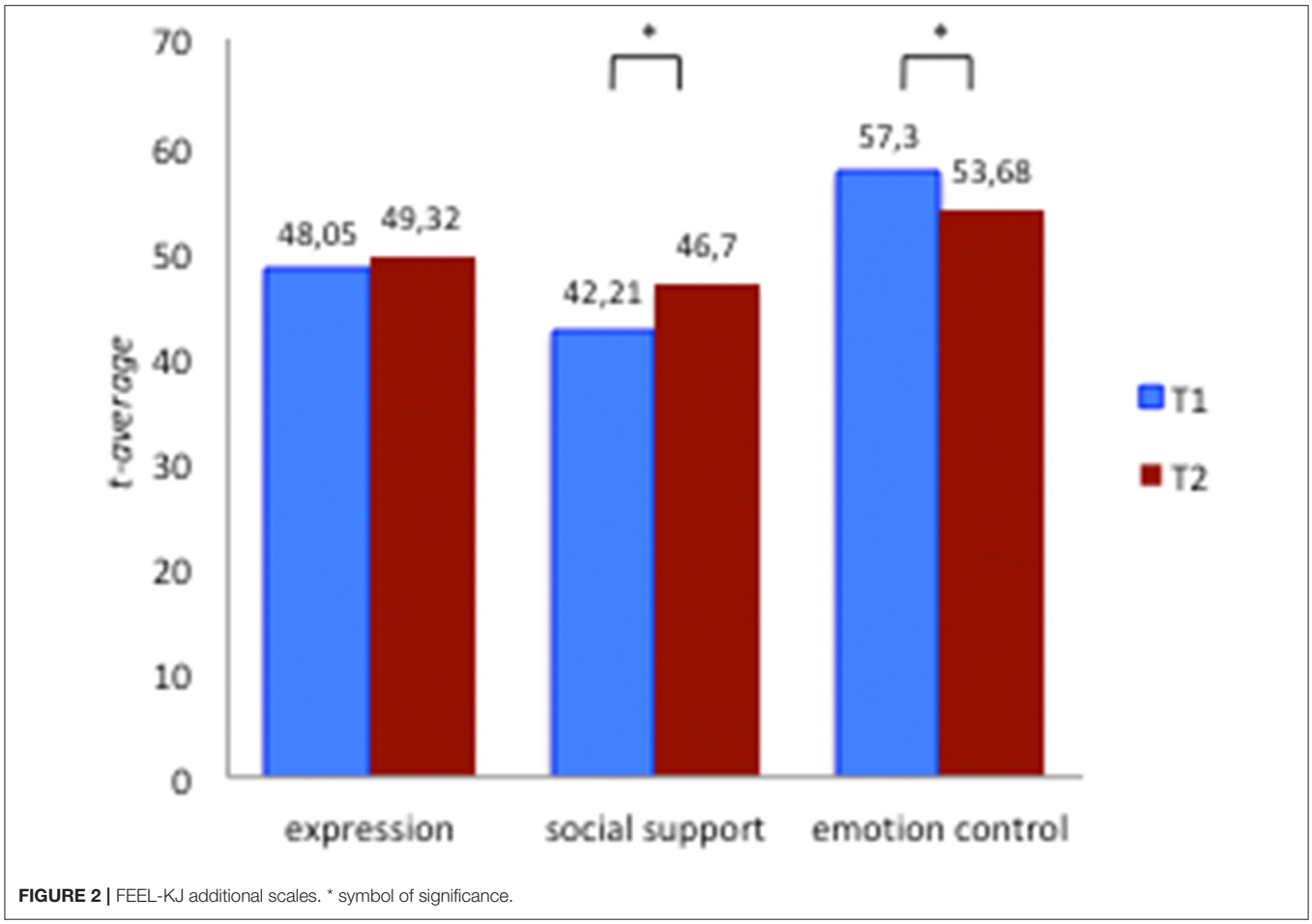


**FIGURE 2 |** FEEL-KJ additional scales. * symbol of significance.

intervention offers emotionally dysregulated adolescents a first aid for crises management and emotional stabilization including skills to reduce self- and other harming behaviors as well as impulsive behavior. START might potentially become a highly useful and cost-saving tool for patients with acute ED because (1) length of inpatient acute treatment might be decreased and (2) hospital re-admissions might be avoided, thus saving mental health or juvenile care costs. Short, simple, intercultural programs like START appears to become more and more necessary.

Due to the simple but structured system of the manual, including worksheets in different languages for each step, it could in a second step also be applied by childcare professionals without intense psychotherapeutic background.

In addition to this, self- esteem might potentially be promoted by START, since ER can be regarded as a central aspect of resilience. Several studies have highlighted the significance of ED for the development of psychopathology. Moreover, comorbid severe dysregulation can (1) be the primary cause for admission to psychiatric wards, and (2) pose a significant hurdle for the successful intervention for core symptoms of the primary disorder, such as PTSD. As a consequence, the length of stay on emergency/closed wards is increased, and acute interventions "by force" might lead to re-traumatizations, posing a significant burden on patients and their families, but also on the health care system.

In the long run, early ED in children and adolescents predicts a range of psychiatric, general medical, and social problems in adolescence and young adulthood emphasizing its public health significance. Adolescents with ED experience significant social impairments (e.g., relationship difficulties with parents, siblings, and teachers, school suspension, service use (mental health and general medical), and poverty. An improvement in ED can improve the social and emotional as well as academic development in children and adolescents. The results might support the applicability and efficacy of START with an additional advantage of integration and strengthening of resilience in several populations at risk. This study shows that the 5 weeks low threshold START intervention is being very well-accepted by acutely de-stabilized adolescents and shows a trend to positively influence ED, and therefore potentially stress resilience in adolescents. Future studies in different settings, different age groups and with larger sample sizes are underway.

Our preliminary findings also suggest that the targeted effects warrant further investigation in randomized control trials as well as different settings and populations.

## DATA AVAILABILITY STATEMENT

The datasets are available on request (a.dixius@sb.shg-kliniken.de).

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the studies involving human participants were reviewed and approved by the Regional Ethics Board of Medical Association Saarland, Germany (No: 189/1). The study was performed in accordance with ethical standards laid down in the Declaration of Helsinki 1964 and its later amendments. All legal guardians gave their informed consent, and children and adolescents provided their informed assent prior to their inclusion in the study. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

AD conducted the statistical analysis. EM and AD drafted the first version of the text and EM reviewed and revised the manuscript. All authors contributed to the article and approved the submitted version.

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# Examining Associations Between Child Abuse and Neglect Experiences With Emotion Regulation Difficulties Indicative of Adolescent Suicidal Ideation Risk

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**Objective:** Preliminary work indicates one specific aspect of emotion dysregulation (i.e., limited access to emotion regulation strategies) uniquely associates with adolescent suicide ideation. An optimal score cut point on a measure of this emotion dysregulation impairment has been identified to indicate risk for past-year suicidal ideation. Examining types of child abuse and neglect associated with being above cut-off on this measure may point to interactive environmental effects associated with subsequent risk for suicidal ideation. The primary aim of this study was to investigate the relations between multiple types of child abuse and neglect with being above cutoff on a measure of limited access to emotion regulation strategies in a psychiatrically severe adolescent sample.

**Method:** The full sample included 203 psychiatric adolescents (Mean age = 15.31 years; 66.5% female; 74.4% White), assigned to two groups: (1) those at or above cutoff on the access to emotion regulation strategies subscale ($n = 139$); and (2) those below cutoff ($n = 64$).

**Results:** Significant differences were only evidenced between the emotion regulation cutoff groups on emotional abuse, after covarying for other types of abuse and neglect; significant group differences were not evidenced on any other type of abuse or neglect (sexual or physical abuse, emotional or physical neglect).

**Conclusion:** Relative to other types of abuse and neglect, emotional abuse may be differentially related to experiencing limited access to emotion regulation strategies, at the level indicative of suicide ideation risk. Clinical implications are discussed.

**Keywords: emotion regulation, child trauma, abuse, neglect, adolescents, emotional abuse, suicide ideation**

## INTRODUCTION

Emotion dysregulation, or "difficulties in emotion regulation," is identified as a central, transdiagnostic risk factor for psychopathology in adolescence. Conceptualized as multifaceted difficulties in one's ability to identify, be aware of, accept, and modulate one's emotion appropriately and flexibly to a situation (1), emotion dysregulation has been indicated as an affective

risk factor underlying many forms of psychopathology in adolescence [e.g., anxiety, eating pathology, aggressive behavior, post-traumatic stress disorder; (2, 3)]. One of the most concerning psychopathology outcomes that emotion dysregulation has been linked to is suicidal ideation, or thoughts about suicide (4). A substantial base of theoretical (5–7) and empirical research (8–10) implicates both broadband emotion regulation difficulties, as well as specific difficulties in emotion dysregulation, with increased risk for suicidal ideation, and this has been shown in adolescents specifically (11). Given the alarming prevalence of adolescent suicidal ideation [i.e., 18.8% considering a suicide attempt in the past-year; (12)], and rising rates of adolescents' hospitalization and emergency care visits for suicidal ideation (13), further investigation of affective risk factors (e.g., emotion dysregulation) for adolescent suicidal ideation, and especially factors which are malleable to intervention, is important.

One notable finding to emerge from this research indicates a unique association between suicidal ideation and one specific difficulty in emotion regulation, having limited access to emotion regulation strategies (i.e., referred to as "limited ERS" in the current paper). To illustrate, recent studies found that limited ERS, as captured with the Difficulties in Emotion Regulation Scale (DERS) "strategies" subscale (1), significantly predicted suicidal ideation, while covarying for all other emotion regulation difficulties and psychiatric diagnoses in both adolescents (11) and young adults (14). In other words, limited ERS differentially associates with suicidal ideation, when accounting for other types of emotion dysregulation (e.g., emotion non-acceptance, lack of clarity) and psychiatric disorder. Further, using receiver operating characteristic curve analysis, Hatkevich et al. (11) identified a score of 22.5 on a measure of limited ERS, the DERS strategies subscale, as the optimal cut-point for determining past-year suicidal ideation in a psychiatric adolescent sample. Taken together, research shows emotion dysregulation, and specifically having limited ERS at/or above the score of 22.5 on the DERS strategies subscale, confers risk for suicidal ideation.

Research is needed to better understand early-life risk factors associated with limited ERS and experiencing limited ERS at the level associated with suicidal ideation risk. Examining childhood-specific risk factors for limited ERS is vital, as emotional development and self-regulation in childhood provide the foundation upon which later adolescent emotion regulation is formed (15). Thus, examining emotion-relevant risk factors in childhood provides a key way that researchers can better understand the factors that place youth at-risk for limited ERS in adolescence, and better inform both prevention and intervention efforts.

One risk factor that has been extensively researched and linked to disruptions in emotional development and later emotion dysregulation is child maltreatment. Although definitions vary [see (15–17)], child maltreatment is generally conceptualized as the experience of any one of the following types of abuse and/or neglect in childhood (all definitions as proposed by 18, p. 175): (a) sexual abuse (i.e., sexual contact or conduct between a child and adult; 2003); (b) physical abuse (i.e., physical assault to a child with potential for injury; 2003); (c) physical neglect (i.e., caregiver failure to provide physical necessities, like housing or healthcare; 2003); (d) emotional abuse (i.e., any verbal acts that denigrate, humiliate, threaten, or otherwise devalue a child; 2003); or (e) emotional neglect (i.e., caregiver failure to provide emotional necessities, like love and support; 2003). Theory [e.g., (18, 19)] has long posited about the profound and deleterious impacts of child maltreatment on socioemotional, behavioral, and mental health development. In a developmental psychopathology model (15), child maltreatment is seen as a chronic "pathogenic environment" that impedes children in attaining fundamental developmental tasks (e.g., self-regulation, emotional development), and these disruptions carry forward and cascade through development, creating risk for later emotion dysregulation, maladaptive functioning, and psychopathology in adolescence (p. 414–415).

Consistent with theory, substantial research establishes child maltreatment as a salient risk factor for emotion dysregulation. Broadly, child abuse and neglect are linked with difficulties in emotion identification [e.g., alexithymia; (20)], lability (21), non-acceptance (22), and in use of adaptive emotion regulation strategies (23, 24). In line with developmental theory (15), this link has been demonstrated longitudinally, with early child maltreatment predicting greater emotion dysregulation in adolescence (25, 26). The robust nature of this relation was typified by a recent meta-analysis (27) finding that, across studies, maltreatment was significantly associated with both broadband emotion dysregulation, as well as specific difficulties in emotion regulation.

Emerging research in this area indicates that distinct child maltreatment experiences (i.e., different types of abuse and neglect) associate with different difficulties in emotion regulation. This was first demonstrated in longitudinal research by Egeland et al. (28), who found differences in developmental outcomes and emotion processes between different maltreatment groups (e.g., physical abuse; neglect).

Since this seminal work, trauma research has begun to further investigate how different types of child abuse/neglect associate with specific difficulties in emotion regulation. Although many forms of child trauma co-occur [i.e., "polyvictimization" "multi-type maltreatment"; (29, 30)], multiple findings have emerged about emotion regulation difficulties associated with specific forms of abuse/neglect. First, converging research indicates child physical abuse is linked to impairment in accurately identifying emotion/anger [e.g., inaccurately interpret hostile intent; (31)], and using more maladaptive emotion regulation strategies [e.g., aggressive and disruptive behavior; (31, 32). This is consistent with the experience of physical violence, and that emotion regulation develops in part through social learning and observing how parents/family members regulate emotion (33, 34).

Another notable finding to emerge is that emotional abuse and neglect appear to be associated with particularly severe and distinct patterns of emotion regulation deficits. Broadly, work (15, 35) links emotional neglect to greater impairment in emotion identification, including difficulty in identifying one's own emotions [i.e., alexithymia; (36)] and others' [e.g., reduced accuracy in identifying facial expressions and anger specifically; (37, 38)]. Further highlighting these

emotion awareness deficits, Berzenski (35) found child emotion neglect was differentially associated with a factor comprised of difficulties in emotion clarity and awareness, but not with a factor comprised of other emotion regulation difficulties (e.g., in impulse control, goal-directed behavior, limited ERS). Making sense of these findings, Berzenski (35) and Cicchetti et al. (15) suggest emotion neglect, unlike abuse, presents an impoverished environment, where children lack the emotional "input" and modeling to learn to identify emotion [see (35)].

In contrast, emotional abuse has been more often linked to difficulties with using appropriate and adaptive emotion regulation strategies [i.e., "response-focused difficulties"; (39)]. Converging research (35, 40–42) suggests emotional abuse is more closely related to using maladaptive strategies to modulate affect, such as brooding/rumination (43), experiential avoidance (44), and with deficits engaging in goal-directed emotion-regulation behavior (45). In the first study to complexly account for the co-occurrence of other child trauma types in examining specific emotion regulation difficulties, Berzenski (35) found child emotional abuse was significantly associated with a factor represented by difficulties in limited ERS, using goal-directed behavior, and impulse control, but not with the factor (emotional awareness/clarity) linked to emotional neglect. Berzenski (35) and others (15, 41, 42) explain that emotional abuse environments likely provide youth with adequate opportunities to observe emotion, but are simultaneously characterized by modeling maladaptive emotion regulation strategies and reinforce youth in using maladaptive strategies themselves [e.g., emotion invalidation; (40)]. Taken together, emerging research indicates multiple forms of child abuse (physical, emotional) may be more closely related to deficits in implementing appropriate emotion regulation strategies/limited ERS, especially relative to emotional neglect, which appears to be more closely linked to deficits in emotion identification.

To our knowledge, no studies have bridged this research with newly emergent findings (11) that limited ERS uniquely associates with adolescent suicide ideation risk. Specific gaps exist in prior research and studies have not yet: (a) examined the differential relations of all child abuse/neglect types to limited ERS, accounting for other forms of child/abuse neglect; (b) investigated the association between different forms of child abuse/neglect and experiencing limited ERS above or below the level indicative of suicide ideation risk [22.5 DERS strategies score; (11)]; and (c) examined the aforementioned in a sample of clinically severe psychiatric adolescents with heterogeneous trauma presentations. Indeed, this is a critical priority addressed by prior studies (46). A comprehensive study which addresses these limitations has the potential to elucidate the unique associations of each child abuse/neglect type with limited ERS, and indicate which child abuse/neglect types may contribute to youth experiencing limited ERS at the level associated with adolescent suicide ideation risk. Empirical research identifying child abuse/neglect experiences associated with clear markers for suicide risk is important and has potential to inform early prevention and clinical intervention programs [e.g., in indicating the potential utility of trauma-focused interventions, like Trauma-Focused Cognitive Behavioral Therapy (TF-CBT) (47), to address affective suicide risk factors].

To this end, the current study will address these specific research gaps and study the differential relations between child abuse/neglect types and being above and below cutoff on a measure of limited ERS associated with suicide ideation risk, in a psychiatric adolescent sample. Specifically, the current study will investigate the differential relations of each trauma type to being above/below cutoff on limited ERS as captured with the DERS Strategies scale, while accounting for other trauma types concurrently. We will address these questions in a sample of psychiatric adolescents presenting to an inpatient treatment program. Based on prior aforementioned research, we expect that emotional and physical abuse will be significantly related to being above cutoff on limited ERS indicative of suicide ideation risk, while adjusting for other child trauma types. Given past work demonstrating emotional neglect is more closely related to emotion identification/awareness deficits [e.g., (35, 36)], we do not expect emotional neglect to be significantly related to being above/below cutoff on limited ERS, adjusting for other trauma types.

# METHODS

## Participants and Procedures

### Participants

Adolescents admitted to an inpatient treatment program serving youth with severe and treatment-refractory psychiatric disorders (i.e., those unremitted by prior treatments) were approached for consent. This treatment program specifically serves youth with a spectrum of co-occurring psychiatric diagnoses, though mood and anxiety-related disorders are amongst the most prevalent presenting diagnoses (see section Results for further details). Participants are a subset of participants who have completed the primary study measures from a larger study on assessment and treatment outcomes [see (48) for a description]. As the study battery was modified over time, there are subsets of adolescents who completed certain measures which were not administered to the full sample; 331 adolescents were administered the specific measures included in this study. Inclusion criteria for study participation were: (a) participants were aged between 12 and 17 years; (b) fluent in English; and (c) did not present with a psychotic-spectrum disorder or intellectual disability. Of the 331 adolescents approached for consent and participation, 58 were excluded from participation: 26 declined to participate, 15 did not meet eligibility criteria at admission, 8 were discharged before participation, 7 displayed signs of psychosis during assessment, 1 revoked consent, and 1 was excluded due to prior completion of a study battery including some of the same instruments. Of the remaining 273 adolescents, 203 fully completed the assessment battery and measures used in the current analyses, and were included in the final sample. The final sample consisted of $N = 203$ adolescents.

### Procedures

This study was approved by the appropriate institutional review board. All assessments were conducted in private on the unit by trained clinical psychology doctoral students and clinical research assistants. Both parental consent and adolescent assent were obtained prior to assessment battery administration.

## Measures

### Sociodemographic Information

Sociodemographic information (e.g., age, biological sex, race; household income) was obtained via a standard sociodemographic questionnaire and administrative intake.

### Trauma History

Child abuse and neglect was assessed using the Childhood Trauma Questionnaire short form [CTQ-SF; (49)]. The CTQ-SF is a 28-item self-report based measure that asks participants to retrospectively recall how often they encountered or experienced various types of abuse and neglect; CTQ-SF items comprise five subscales of abuse and neglect, including: (a) sexual abuse (e.g., "Someone tried to touch me in a sexual way, or tried to make me touch them"); (b) physical abuse (e.g., "I got hit so hard by someone in my family that I had to see a doctor or go to the hospital"); (c) physical neglect (e.g., "I had to wear dirty clothes"); (d) emotional abuse (e.g., "People in my family said hurtful or insulting things to me"); and (e) emotional neglect (e.g., "My family was a source of strength and support," reverse coded). Items are rated on a 5-point Likert scale (range: 1 "Never True," to 5 "Very Often True"). Psychometric properties have been established for the CTQ-SF (49), and the CTQ-SF has been used with adolescent inpatients specifically [e.g., (50)]. Cronbach's alpha were as follows for CTQ-SF subscales in the current study: emotional abuse ($\alpha = 0.86$), sexual abuse ($\alpha = 0.96$), physical abuse ($\alpha = 0.63$), emotional neglect ($\alpha = 0.90$), and physical neglect ($\alpha = 0.54$).

### Difficulties in Emotion Regulation

Difficulties in emotion regulation, including limited ERS specifically, were measured with the Difficulties in Emotion Regulation Scale [DERS; (1)]. The DERS is a 36-item self-report based measure that assesses six facets of emotion dysregulation, consistent with the multidimensional conceptualization proposed by Gratz and Roemer (1): (a) lack of emotional awareness (awareness); (b) lack of emotional clarity (clarity); (c) non-acceptance of emotional states (non-acceptance); (d) difficulties engaging in goal-directed behaviors (goals); (e) impulse control difficulties (impulse); and (f) limited ERS (DERS "strategies" subscale). Participants respond to all items on a 5-point Likert scale, and indicate how much each item pertains to them (1 = "almost never," to 5 = "almost always"), and items are summed onto each of the six aforementioned subscales; higher scores on DERS subscales indicate greater emotion regulation impairment. For the current study, all subscales were included for descriptive purposes, though the strategies subscale capturing limited ERS was the focus of primary analyses. As aforementioned, prior work (11) conducted receiving operating characteristics and identified a score of 22.5 on the DERS strategies scale as the optimal cut-point (i.e., having maximal sensitivity and specificity) for determining past-year suicidal ideation; for the cut point of 22.5, sensitivity was 74.3% and specificity was 64.1%. The cut-point of 22.5 on DERS strategies was used to divide the sample into the following groups: (1) those at or above cutoff for limited ERS, indicative of risk for suicidal ideation; and (2) those below cutoff. Psychometric properties of the DERS are well-established in adolescent populations [e.g., (10, 51)], with its factor structure validated in adolescent inpatients specifically (52). Reliability was $\alpha = 0.905$ for the DERS strategies subscale in the current study.

### Psychiatric Diagnoses

Psychiatric diagnoses were assessed with the Computerized Diagnostic Interview Schedule for Children [CDISC; (53)], a structured diagnostic interview with well-established psychometric properties (53, 54), which has been used in a number of psychiatric adolescent samples [e.g., (55, 56)]. The CDISC assesses for the presence of psychiatric diagnoses consistent with DSM-IV, and is administrated by a trained clinician and/or assessor. In the current study, presence of any Mood Disorder, Externalizing Disorder, and Anxiety Disorder diagnoses were included in descriptive, bivariate and *post-hoc* analyses, given the high rates of psychiatric disorder and comorbidity of youth presenting to this psychiatric care setting. Any Mood Disorder diagnosis was defined as meeting criteria for Major Depressive Disorder, Dysthymia, Hypomania, and/or Mania. Any Anxiety Disorder diagnosis was defined as meeting criteria for Generalized Anxiety Disorder, Specific Phobia, Social Phobia, Separation Anxiety Disorder, Obsessive-Compulsive Disorder, Post-traumatic Stress Disorder, Panic Disorder, and/or Agoraphobia. Any Externalizing Disorder was defined as meeting criteria for Oppositional Defiant Disorder, Conduct Disorder, and/or Attention-Deficit/Hyperactivity Disorder. Psychometric properties have been well-established for this measure, with interrater reliability calculated between 0.91 and 1.00 for all disorders (57), and excellent test-retest reliability (58).

### Data Analytic Strategy

All analyses were conducted in SPSS statistical software. Descriptive statistics were used to examine characteristics of main study variables (CTQ-SF abuse/neglect scales, DERS subscales), sociodemographics (age, sex, race, household income), and clinical characteristics (psychiatric diagnoses) of the full sample. As described in the methods, participants in the full sample were classified into two groups based on their score on the DERS strategies subscale: (1) Participants at or above cutoff for limited ERS, indicative of risk for suicidal ideation (referred to as the limited ERS above cutoff group); and (2) Participants below cutoff (referred to as the limited ERS below cutoff group). These two groups were then used in subsequent and primary analyses. Bivariate analyses (i.e., bivariate correlations, independent sample *t*-tests, chi-square analyses) were conducted to examine relations amongst main study variables, sociodemographic, and clinical characteristics. For our primary analyses, we conducted a series of analyses of covariance (ANCOVA) to examine group differences between

the limited ERS groups on each CTQ-SF abuse/neglect scales (emotional abuse, emotional neglect, physical abuse, physical neglect, sexual abuse), while covarying for each of the remaining CTQ-SF abuse/neglect scales. In each respective model with CTQ-SF abuse/neglect scale as the dependent variable, we included the other four remaining CTQ-SF abuse/neglect scales as covariates (see below for rationale). Given sample size and power considerations, we originally did not include additional clinical or sociodemographic variables as covariates in our primary ANCOVA models, with exception of the model examining CTQ-SF sexual abuse as the outcome, in which we included biological sex as an additional covariate to the remaining CTQ-SF abuse/neglect scales. For ANCOVA models, adjusted means with Bonferroni corrections, standard error, and pairwise comparisons were calculated.

# RESULTS

## Full Sample Demographic and Clinical Characteristics

The full sample consisted of 203 adolescent inpatients completing all primary study measures and meeting inclusion criteria. Demographic and clinical characteristics are fully depicted in **Table 1**. Demographically, the full sample was 66.5% female, 74.4% White/Caucasian, with a mean age of 15.31 years, and the majority of participants' household incomes were above $100,000. Clinically, as determined on the CDISC interview, 70.9% of the sample met diagnostic criteria for any Mood Disorder diagnosis, 69% met for any Anxiety Disorder diagnosis, and 42.9% met for any Externalizing Disorder diagnosis.

## Descriptive Statistics for Main Study Variables

Means, standard deviations and ranges for CTQ-SF abuse/neglect scales and DERS subscales are depicted in **Table 2**. For the CTQ-SF scales, highest mean scores were reported for emotional neglect ($M = 11.11$; SD = 5.04) and emotional abuse ($M = 10.26$; SD = 5.23), with all other scale means between 6.49 (physical abuse) and 7.16 (physical neglect). For the full sample, 76.8% of the sample endorsed some experience of emotional abuse, 83.7% of some emotional neglect, 42.4% of some physical abuse, 66% of some physical neglect, and 16.7% of some experience of sexual abuse; these percentages specifically depict the portion of participants who endorsed any non-zero response on each of the aforementioned CTQ-SF scales. For the DERS subscales, the highest overall mean was indicated for the primary variable of interest, limited ERS (Strategies subscale $M = 26.62$), followed by lack of emotional awareness, difficulties engaging in goal-directed behavior, and non-acceptance of emotional responses.

As described in the section Methods, participants in the full sample ($N = 203$) were assigned to the following groups, based on their DERS strategies score: (1) limited ERS above cutoff group ($n = 139$; 68.5% of full sample); and (2) limited ERS below cutoff group ($n = 64$; 31.5% of full sample).

## Bivariate Relations

Bivariate correlations were conducted to examine associations between all CTQ-SF abuse/neglect scales, DERS strategies, age in years, and any CDISC mood, anxiety, and externalizing diagnoses. Correlational analyses are depicted in **Table 3**. In summary, age was not significantly correlated with any CTQ-SF abuse/neglect scale, nor with DERS strategies or any CDISC diagnoses. DERS strategies was significantly positively correlated with CTQ-SF scales of emotional abuse ($r = 0.28$; $p < 0.001$), emotional neglect ($r = 0.23$; $p = 0.001$), and physical neglect ($r = 0.15$; $p = 0.032$), and with CDISC mood and anxiety diagnoses, such that greater limited ERS was associated with these diagnoses and forms of child abuse/neglect. With regards to CDISC diagnoses, mood and anxiety diagnoses shared no significant relations with any CTQ-SF abuse/neglect subscale; in contrast, CDISC externalizing diagnosis was significantly related to all forms of CTQ-SF abuse/neglect, except sexual abuse. In examining correlations between the CTQ-SF abuse/neglect scales, significant positive correlations exist between all CTQ-SF abuse and neglect scales (physical abuse, physical neglect, emotional abuse, emotional neglect, sexual abuse), with effect sizes ranging between 0.22 and 0.71, with most values between 0.2 and 0.5 (see **Table 3**).

Further bivariate analyses were conducted to examine the relations between biological sex, limited ERS cutoff groups, and CTQ-SF abuse/neglect scales. Chi square analyses indicated there was no significant association between biological sex and limited ERS cutoff group assignment, $\chi^2(1) = 0.672$, $p = 0.412$. Independent sample *t*-tests were conducted to examine the relation between biological sex and CTQ-SF abuse/neglect scales. Results indicated no significant sex differences existed for all CTQ-SF abuse/neglect subscales, with exception of sexual abuse [$t(191.570) = 3.388$, $p = .001$], such that females reported significantly greater sexual abuse experiences ($M = 7.15$, SD = 5.362), than males ($M = 5.37$, SD = 2.073). Due to extremely small cell sizes for groups identifying racial identities other than White/Caucasian racial identity (e.g., 1 individual identitying as American Indian/Alaskan Native, 6 identifying as Asian), we were not sufficiently powered to conduct group analyses examining the link between racial identity and main study variables (e.g., CTQ-SF abuse/neglect scales, limited ERS cutoff groups).

Overall, bivariate analyses indicated that CTQ-SF abuse and neglect scales (i.e., physical abuse, physical neglect, emotional abuse, emotional neglect, sexual abuse) are significantly correlated with one another, consistent with research indicating individuals experiencing child abuse and neglect are likely to experience multiple forms of abuse and neglect, or "multi-type maltreatment" [e.g., (30)]. In order to account for this overlap in subsequent analyses, and thus examine the unique relation of each abuse/neglect type to limited ERS cutoff group in sequence, remaining types of abuse/neglect were included as covariates in our primary analyses; this is consistent with the analytic approach of other child maltreatment research [e.g., (59)]. In regards to sociodemographics, age was not significantly related to limited ERS as captured by DERS strategies, or any CTQ-SF

**TABLE 1 |** Full sample demographic and clinical characteristics.

| | Full sample ($n = 203$) |
|---|---|
| Patient age | 15.31 (1.43) |
| **Race** | |
| White/Caucasian | 151 (74.4%) |
| American Indian or Alaskan Native | 1 (.5%) |
| Asian | 6 (3%) |
| Black or African American | 2 (1%) |
| Multiracial or other-identified | 13 (6.4%) |
| Missing data | 30 (14.8%) |
| **Biological sex** | |
| Female | 135 (66.5%) |
| Male | 68 (33.5%) |
| **CDISC psychiatric diagnoses** | |
| Any mood disorder | 144 (70.9%) |
| Any anxiety disorder | 140 (69%) |
| Any externalizing disorder | 87 (42.9%) |
| **Household income** | |
| Below $100,000 | 11.5% |
| Above $100,000 | 66.3% |
| Missing data/decline to answer | 22.2% |

*Age data is depicted in years, with the mean age followed by standard deviation in parentheses. Race and Biological Sex data depicted is the number of youth reporting each identity, followed by the percent of the full sample with this identity depicted in parentheses. CDISC Psychiatric Diagnoses data depicts first the number of youth meeting criteria for each diagnosis, followed by the percent of the full sample meeting criteria for the diagnosis. Household income data depicts percentage of the full sample identifying in the following income brackets, and lastly those with missing income data or declining to answer.*

**TABLE 2 |** Descriptive statistics for CTQ-SF abuse and neglect scales and DERS subscales.

| Study variable | Mean | Standard deviation | Range |
|---|---|---|---|
| CTQ-SF emotional abuse | 10.26 | 5.23 | 5–25 |
| CTQ-SF physical abuse | 6.49 | 2.58 | 5–17 |
| CTQ-SF sexual abuse | 6.55 | 4.61 | 5–25 |
| CTQ-SF emotional neglect | 11.11 | 5.04 | 5–24 |
| CTQ-SF physical neglect | 7.16 | 2.59 | 5–21 |
| DERS non-acceptance | 17.15 | 7.18 | 6–30 |
| DERS goals | 18.97 | 5.09 | 5–25 |
| DERS impulse | 16.51 | 6.65 | 6–30 |
| DERS awareness | 18.97 | 5.96 | 6–30 |
| DERS strategies | 26.62 | 8.30 | 8–40 |
| DERS clarity | 15.89 | 5.19 | 5–25 |

*CTQ-SF, Childhood Trauma Questionnaire short form; DERS, Difficulties in Emotion Regulation Scale, each DERS subscale is listed above and is described in the Methods section..*

abuse/neglect type, and biological sex was not significantly associated with limited ERS cutoff group, nor any form of abuse/neglect, with exception of sexual abuse. As a result of sex differences evident for sexual abuse, we additionally elected to include biological sex as a covariate in our ANCOVA with sexual abuse as outcome.

Importantly, in bivariate relations, CDISC psychiatric diagnoses shared multiple significant relations with main study variables (e.g., any mood and anxiety diagnosis were significantly related to limited ERS, and any externalizing diagnosis was significantly related to most types of child abuse and neglect). Due to sample size and power considerations, we elected to follow our original analytic plan, and first test the aforementioned ANCOVA models examining limited ERS group differences for each CTQ-SF abuse/neglect type, without any additional psychiatric diagnosis covariates. In order to further consider potential links between CDISC psychiatric diagnoses, limited ERS group status, and CTQ-SF abuse/neglect, we then conducted additional exploratory *post-hoc* analyses (see below for further detail).

## Primary Analyses—ANCOVA Models

We conducted a series of five analysis of covariance (ANCOVA) models to examine group differences between the groups above and below cutoff on limited ERS, on each respective CTQ-SF abuse and neglect scale. In each model, we included the other CTQ-SF abuse/neglect scales as covariates, and additionally included biological sex as a covariate in the ANCOVA model with sexual abuse as outcome.

Results of the ANCOVA models are depicted in **Table 4**. In the model examining CTQ-SF emotional abuse as outcome, a significant difference was evidenced between groups [$F_{(1,197)} = 4.452$, $p = 0.036$, partial $\eta^2 = 0.022$], after covarying for other CTQ-SF abuse/neglect scales, such that the limited ERS above cutoff group reported significantly greater emotional abuse (adjusted $M = 10.599$), than the limited ERS below cutoff group (adjusted $M = 9.528$). In the model examining CTQ-SF emotional neglect as outcome, no significant differences were evidenced between limited ERS above and below cutoff groups on emotional neglect [$F_{(1,197)} = 0.426$, $p = 0.515$, partial $\eta^2 = 0.002$], after adjusting for other CTQ-SF abuse/neglect scale covariates. In the model examining CTQ-SF physical abuse as outcome, no significant differences were evidenced between limited ERS above and below cutoff groups on physical abuse [$F_{(1,197)} = 2.223$, $p = 0.138$, partial $\eta^2 = 0.011$], after adjusting for other CTQ-SF abuse/neglect scale covariates. In the model examining CTQ-SF physical neglect as outcome, no significant differences were evidenced between limited ERS above and below cutoff groups on physical neglect [$F_{(1,197)} = 0.000$, $p = 0.991$, partial $\eta^2 = 0.000$], after adjusting for other CTQ-SF abuse/neglect scale covariates. Lastly, in the model examining CTQ-SF sexual abuse as outcome, no significant differences were evidenced between limited ERS above and below cutoff groups on sexual abuse [$F_{(1,196)} = 0.273$, $p = 0.602$, partial $\eta^2 = 0.001$], after adjusting for other CTQ-SF abuse/neglect scales and biological sex. In summary, significant differences were only evidenced between the limited ERS above vs. below cutoff groups on the CTQ-SF trauma scale of emotional abuse, after covarying for other types of CTQ-SF abuse and neglect; significant group differences were not evidenced on any other form of CTQ-SF trauma [emotional neglect, physical abuse,

**TABLE 3 |** Bivariate correlation matrix.

| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Emotional abuse | - | | | | | | | | | |
| 2 | Physical abuse | 0.51** | - | | | | | | | | |
| 3 | Sexual abuse | 0.40** | 0.41** | - | | | | | | | |
| 4 | Emotional neglect | 0.71** | 0.34** | 0.22** | - | | | | | | |
| 5 | Physical neglect | 0.45** | 0.32** | 0.26** | 0.55** | - | | | | | |
| 6 | DERS strategies | 0.28** | −0.01 | 0.06 | 0.23** | 0.15* | - | | | | |
| 7 | Age | 0.02 | 0.01 | −0.00 | −0.04 | −0.07 | −0.10 | - | | | |
| 8 | Mood Dx. | 0.06 | −0.02 | 0.06 | 0.05 | −0.03 | 0.42** | 0.04 | - | | |
| 9 | External. Dx. | 0.26** | 0.19** | −0.01 | 0.19** | 0.18** | 0.09 | 0.05 | −0.02 | - | |
| 10 | Anxiety Dx. | 0.10 | 0.06 | 0.12 | 0.02 | 0.03 | 0.20** | 0.05 | 0.25** | 0.09 | - |

*Data are bivariate Pearson correlations. 1–5 are from the CTQ-SF measure. 8–10 are from the CDISC interview, with Mood Dx., CDISC any mood diagnosis; External. Dx., CDISC any externalizing diagnosis; and Anxiety Dx., CDISC any anxiety diagnosis.*

***Correlation is significant at the 0.01 level (2-tailed).*

**Correlation is significant at the 0.05 level (2-tailed).*

**TABLE 4 |** ANCOVA results showing CTQ-SF abuse/neglect scale outcomes for the limited ERS above and below cutoff groups.

| CTQ-SF abuse/neglect scale | Limited ERS above cutoff group ($n = 139$) | Limited ERS below cutoff group ($n = 64$) | *F* | *p* | Partial eta squared ($\eta^2$) |
|---|---|---|---|---|---|
| | *M* (SD) | *M* (SD) | | | |
| Emotional abuse | 10.599 (0.280) | 9.528 (0.417) | 4.452 | 0.036 | 0.022 |
| Emotional neglect | 11.215 (0.283) | 10.878 (0.423) | 0.426 | 0.515 | 0.002 |
| Physical abuse | 6.331 (0.183) | 6.828 (0.273) | 2.223 | 0.138 | 0.011 |
| Physical neglect | 7.159 (0.185) | 7.155 (0.276) | 0.000 | 0.991 | 0.000 |
| Sexual abuse | 6.655 (0.344) | 6.327 (0.514) | 0.273 | 0.602 | 0.001 |

*N = 203 youth were included in ANCOVAs. All ANCOVAs included all other CTQ-SF Abuse/Neglect scales as covariates (see section Methods for further description), and the ANCOVA with CTQ-SF Sexual Abuse additionally included sex as a covariate. Data shown for the CTQ-SF Abuse/Neglect scales are adjusted means. CTQ-SF, Childhood Trauma Questionnaire short form.*

physical neglect, sexual abuse], after adjusting for all other types of abuse/neglect.

Across all ANCOVA models, other CTQ-SF abuse/neglect scale covariates emerged as significant predictors of the examined CTQ-SF abuse/neglect outcome (e.g., in the emotional neglect outcome model, the covariates of emotional abuse and physical neglect were significant predictors, with greater emotional abuse and physical neglect significantly predicting greater emotional neglect).

## Post-hoc Analyses

Additional exploratory *post-hoc* analyses were conducted based on our bivariate and primary ANCOVA model findings. Given that bivariate analyses revealed multiple significant relations between CDISC psychiatric diagnoses (mood, anxiety, externalizing) and primary study variables (limited ERS, CTQ-SF abuse/neglect scales), we elected to conduct additional analyses to examine CDISC psychiatric diagnoses as additional covariates in models examining the link between limited ERS group status and CTQ-SF abuse/neglect. Given our primary ANCOVA results that significant group differences were only evidenced for the CTQ-SF emotional abuse scale, but not other types of abuse/neglect, we conducted two additional *post-hoc* ANCOVA models examining limited ERS group differences on emotional abuse specifically: (a) in the first, we included all original covariates (i.e., other CTQ-SF abuse/neglect types: emotional neglect, physical abuse, physical neglect, sexual abuse) and CDISC any mood diagnosis as an additional covariate; and (b) in the second model, we included all the aforementioned CTQ-SF abuse/neglect scales, and three psychiatric diagnoses (CDISC any mood, anxiety, and externalizing) as covariates.

In the first *post-hoc* ANCOVA model with CDISC any mood diagnosis and all other CTQ-SF abuse/neglect scales (physical abuse, physical neglect, emotional neglect, sexual abuse) as covariates, significant group differences were found for limited ERS status groups on emotional abuse [$F_{(1,196)} = 4.125$, $\eta^2 = 0.021$, $p = 0.044$], even while covarying for any mood disorder diagnosis and all other types of CTQ-SF abuse/neglect. Notably, the effect size of this significant finding remained almost the same as compared to the original ANCOVA model without CDISC any mood diagnosis included as a covariate.

In the second *post-hoc* ANCOVA model with the covariates of three psychiatric diagnoses (CDISC any mood, anxiety, and externalizing diagnoses) and all remaining CTQ-SF

abuse/neglect scales (physical abuse, physical neglect, emotional neglect, sexual abuse), no significant differences were evidenced between limited ERS groups on emotional abuse [$F_{(1,194)} = 2.831$, $\eta^2 = 0.014$, $p = 0.094$]. Of the CDISC psychiatric diagnoses included as covariates, only CDISC any externalizing disorder diagnosis was significant [$F_{(1,194)} = 4.906$, $\eta^2 = 0.025$, $p = 0.044$] in predicting the outcome, CTQ-SF emotional abuse. Observed power was calculated, given our addition of three covariates to the original model and initial power concerns. Importantly, the observed power for examining limited ERS group differences on emotional abuse was 0.388, which is below the accepted value of 0.80 for adequate power. Thus, there was inadequate power to detect a true effect of limited ERS group differences on emotional abuse, in this model with three additional psychiatric diagnosis covariates.

## DISCUSSION

The current study examined the differential relations between child abuse/neglect types and being above and below cutoff on a measure of limited ERS associated with suicide ideation risk, in a psychiatric adolescent sample. For primary analyses, we conducted a series of ANCOVAs to examine differences between the limited ERS groups (above, below cutoff) on each CTQ-SF abuse/neglect scales (emotional abuse, emotional neglect, physical abuse, physical neglect, sexual abuse), while covarying for all other CTQ-SF abuse/neglect scales. Results revealed significant differences for limited ERS groups on only the CTQ-SF emotional abuse scale, when covarying for other types of abuse and neglect, and significant group differences were not evidenced for any other type of abuse or neglect (sexual or physical abuse, emotional or physical neglect). Addressing critical gaps in prior research, this study represents a novel first-look at the differential associations of various forms of child abuse and neglect to a clear affective risk marker (i.e., a cut-point on limited ERS) for adolescent suicide ideation; further, it extends prior work conducted in undergraduate samples (35, 41) to a high-risk sample of psychiatric youth with diverse clinical and trauma presentations.

Our primary finding that emotional abuse is the only trauma type significantly related to being above cutoff on limited ERS converges with prior theoretical and empirical research. This finding, which persisted even after accounting for other types of child abuse and neglect, closely mirrors results of one key study informing this work, Berzenski (35). Akin to our findings, Berzenski (35) showed that emotional abuse was most closely linked to an emotion regulation difficulties factor comprised of limited ERS and other behavior-regulation difficulty subscales of the DERS; importantly, other trauma types (i.e., emotional neglect) were not related to this overarching factor. Our pattern of results parallel these findings, and indicate emotion abuse is differentially related to limited ERS, relative to other types of abuse and neglect.

The fact that emotional abuse was uniquely linked to experiencing limited ERS at the level indicative of suicide risk falls in line with literature documenting the severe and deleterious impacts of emotional abuse on both mental health broadly and emotion regulation specifically. Although all forms of child maltreatment have adverse impacts on child development (60), emerging studies (59, 61–63) show that emotional abuse has especially deleterious and long-lasting effects on mental health, emotion functioning, and suicide outcomes. Substantial literature (15, 35, 40–42)] documents the profound impact emotion abuse has on emotion regulation specifically. Prior work establishes that emotional abuse impairs emotion regulation in a multitude of ways, through its chronicity (64), ruptures and betrayal in the primary attachment relationship (45, 65), and early disruptions in emotion regulation and the development of internal working models (15, 42), which crystallize through development and form the basis for later emotion dysregulation (15). In whole, our finding that emotional abuse uniquely associates with limited ERS at the level associated with suicide ideation risk converges with this large body of work demonstrating the profound impacts of emotional abuse on developing emotion regulation. It also converges with specific work (34, 35, 66) suggesting that environments characterized by emotional abuse likely include modeling of maladaptive emotion regulation strategies, punishment/invalidation of appropriate emotional expression, which subsequently leave youth with limited ERS.

In contrast, all other forms of abuse/neglect (i.e., emotional neglect, physical abuse, physical neglect, and sexual abuse) did not significantly differ by limited ERS cutoff groups, when accounting for other trauma types in each respective model. An interesting and complicated pattern of findings emerged for emotional neglect specifically: at the bivariate level, emotional neglect was significantly associated with limited ERS, such that greater emotional neglect was related to more impairment in limited ERS; however, when covarying for other trauma types, ANCOVA results indicated no significant limited ERS group differences by emotional neglect. Taken together, this pair of findings may suggest that emotional neglect *is* linked to limited ERS, but it does not appear to be associated with limited ERS at the level indicative of suicide ideation risk, or when other trauma types are accounted for. Given work [e.g., (35, 36, 38)] suggesting emotion neglect is more closely linked to emotional identification difficulties, it is surprising and counter to our initial hypotheses that emotional neglect related with limited ERS in correlational results. One potential explanation is that emotionally-absent caregiving experiences may also leave youth to develop their own emotion regulation strategies, without instruction in how to "match" appropriate strategies to context, or with strategies that are maladaptive/socially-unacceptable, but insufficient caregiver correction is provided over time.

No significant differences were evidenced for limited ERS cutoff groups on physical abuse, physical neglect, or sexual abuse, when other trauma types were accounted for. One tentative explanation for these findings is that perhaps these forms of trauma are not unrelated to limited ERS, but that these relations may be only be evident when studied in specific diagnostic subsamples. To illustrate, Jennissen et al. (67) found significant relations between all CTQ-SF subscales and emotion regulation difficulties on the DERS in adults with diverse psychopathology,

whereas a more nuanced pattern of relations between forms of abuse/neglect and emotion regulation difficulties emerged in samples with particular diagnoses. For example, in adults with substance use disorders, physical abuse was significantly related to emotion regulation difficulties in goal-directed behavior and impulse control, and sexual abuse to no emotion regulation difficulties (68). Taken together, these results may suggest that for certain forms of child trauma, like physical and sexual abuse, relations with emotion regulation deficits may be most evident in diagnostic-specific subsamples; for example, the relations of sexual abuse and emotion regulation deficits may differ when examined in youth with trauma and stressor-related disorders specifically. Alternatively, it may also be the case that physical abuse, physical neglect, and sexual abuse are better typified by other patterns of adolescent emotion regulation deficits, and not limited ERS, as examined in the current study. Elucidating these questions and the nature of our findings will be a key next step for future research.

In a highly preliminary attempt to address the potential role of psychiatric diagnoses in our primary study findings, exploratory *post-hoc* analyses were conducted to sequentially account for various psychiatric diagnoses (mood, anxiety, externalizing) as covariates in ANCOVA models examining limited ERS group differences on emotional abuse. *Post-hoc* analyses indicated that group differences remained when mood disorder alone was included alongside CTQ-SF abuse/neglect types, but not in the model including all forms of psychiatric diagnoses concurrently (i.e., mood, anxiety, and externalizing diagnoses together). Unfortunately, due to being significantly under-powered to detect a true effect in our latter model, our study is ultimately unable to definitively speak to whether significant limited ERS group differences persist for emotional abuse, when covarying for mood, anxiety, and externalizing psychopathology concurrently. Given the potential role of psychopathology in the relation between limited ERS and child trauma experiences, this will be a key direction for future research in a larger psychiatric adolescent sample.

## Limitations

The current study has multiple limitations and related implications for future research. First, our study elected to investigate the links between specific child trauma types and a limited ERS risk indicator for suicide ideation, but did not examine suicide ideation specifically. This study was designed to primarily investigate the potential early child maltreatment experiences associated with this affective risk factor, while accounting for other forms of child trauma. Thus, while suicide ideation is relevant as the ultimate risk outcome for this emotion regulation impairment, examining ideation directly moved beyond the scope of the current study. A critical next step will be to longitudinally examine the links between childhood emotional abuse, adolescent limited ERS, and either concurrent or subsequent suicidal ideation. Second, demographically, our study was predominantly white (74.4%), which limits the generalizability of our findings. Prior research (69) highlights the differences in emotion socialization for European American, African American, Asian American, and Latin American families, and indicates that emotion-related parenting practices may differentially impact outcomes in youth of varying backgrounds. Thus, it will be important for future research to replicate these findings in an ethnoracially diverse youth sample. Lastly, adolescents were recruited from a psychiatric treatment unit designed to address treatment-refractory mental illness; thus, although this sample is psychiatrically complex, the majority of participants have previously received treatment, and likely differ from youth with equally complex clinical and trauma histories who have not previously obtained mental health services.

## Clinical Implications

Notwithstanding these limitations, the current study has important strengths and implications for prevention and intervention efforts. Notably, the current study is the first known investigation to investigate which child abuse/neglect types associate with youth experiencing limited ERS at the level conferring risk for suicide ideation. Our study identified preliminary evidence that emotional abuse may be a unique child trauma associated with specific emotion regulation impairments indicative of suicide ideation risk. Although this preliminary finding is first in need of further empirical study and replication, implications may be indicated for both prevention and intervention efforts. In particular, this finding may indicate that children identified as experiencing emotional abuse are an important target population for early suicide prevention efforts. Specifically, prevention efforts aimed at addressing early emotion regulation skills and adaptive/effective strategy use may be of critical to mitigating the development of limited ERS in adolescence. Dually, current findings point to the importance of early evidence-based, trauma-focused intervention for youth identified as experiencing emotional abuse, and their caregivers. Evidence-based treatments, such as TF-CBT (47) and Child-Parent Psychotherapy [CPP; Ghosh (70)] that flexibly and sensitively address trauma psychoeducation, affect regulation, parenting practices, and increase safety and security in the child-caregiver attachment relationship are clinically indicated.

# DATA AVAILABILITY STATEMENT

The data analyzed in this study is subject to the following licenses/restrictions: Data was collected as part of a larger IRB-approved study and data is maintained in accordance with the IRB-approved protocol. Requests to access these datasets should be directed to csharp2@central.uh.edu.

# ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Boards at University of Houston and Baylor College of Medicine. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

CH and ES conceived the presented empirical research questions, focus of the current manuscript, and wrote the manuscript with support from CS. CS conceived and principally investigated the overarching study, including supervising the study and its implementation. CH and ES conducted the analyses. All authors provided critical input to the manuscript writing and final manuscript.

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# An Exploratory Study of Emotional Dysregulation Dimensions in Youth With Attention Deficit Hyperactivity Disorder and/or Bipolar Spectrum Disorders

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Emotional dysregulation (ED) is currently the most frequently used term to describe children with an impaired regulation of emotional states. Recent research studies speculate whether ED may be a neurodevelopmental disorder itself, a shared risk factor, or a common key feature of several psychiatric disorders, including, among others, attention deficit hyperactivity disorder (ADHD), and bipolar spectrum disorders (BSD). The association between ADHD and ED is one of the main reasons of misconceptions in the definition of boundaries between ADHD and BSD, leading to the frequent misdiagnosis of ADHD as BSD. Since ED is a multidimensional concept, a novel instrument—the Reactivity, Intensity, Polarity and Stability (RIPoSt) scale—was recently developed to assess the different dimensions of ED, which could help in detecting specific ED profiles in clinical youths. Our study included 154 patients, aged 13.8 ± 2.3 years, diagnosed with either ADHD, BSD, or comorbid condition, and a school-based sample of 40 healthy control (HC) adolescents, aged 12.5 ± 1.2 years. The RIPoSt scale and the Child Behavior Checklist were administered to both groups. Our results indicate that affective instability and negative emotionality subscales, as well as negative emotional dysregulation, are higher in BSD, both pure and comorbid with ADHD, while emotional impulsivity is higher in the comorbid condition and similar in the ADHD and BSD alone group; all clinical groups scored higher than HC. Conversely, positive emotionality is similar among clinical groups and within them and HC. Our findings also support the validity of the RIPoSt questionnaire, since the instrument proved to have good-to-excellent internal consistency, and strongly significant positive correlations were found with the CBCL-Dysregulation Profile, which is a commonly used, indirect measure of

ED. Hence, the five subscales of the RIPoSt can be reliably used as an effective tool to study the emotional dysregulation in different clinical conditions, to help disentangle the complex relationship between ADHD and juvenile BSD and to provide clinicians with crucial evidence for better diagnostic characterization and therapeutic indications.

**Keywords: emotional dysregulation, ADHD, bipolar disorder, children, adolescents**

## INTRODUCTION

Children with an impaired regulation of emotional states, including mood lability and instability, severe irritability, low tolerance to frustration, temper outburst, and hyperarousal, have become a diagnostic challenge in the last two decades (1, 2). The core features of emotional impairment, with possible different combinations, are low threshold, excessive intensity, inappropriate expression, and slow normalization (1). This clinical picture does not completely fit any of the current nosological categories, including attention deficit hyperactivity disorder (ADHD), mood disorders (MD) such as bipolar spectrum disorders (BSD) or disruptive mood dysregulation disorder, and impulse control disorders such as oppositional defiant disorder (ODD)/conduct disorder (CD), although they may share features of all these domains. Different definitions of this condition have been proposed (3), but the term emotional dysregulation (ED) is currently the most frequently used.

More recent advances tend to interpret ED as a neurodevelopmental, early-onset disorder of the regulation of emotions, often associated to other psychiatric disorders, strongly related with comorbidity between internalizing and externalizing disorders, suggesting that it could be a shared risk factor for both kinds of disorder (4), or a common key factor in the development of later psychopathology (5–8).

Most if not all descriptions in children are focused on the association with ADHD (1, 9). At least 40% of subjects with ADHD present an associated ED (9–14), particularly in the combined presentation (15, 16), with strong continuity in adults with ADHD (17–19). Symptoms of ED significantly and negatively impact quality of life (11), social functioning (20), acceptability by peers (21), need for interventions (11), and higher rates of persistence of irritability and impulsivity up to adulthood (10). Moreover, ED has been shown to predict risky behaviors in adolescents with ADHD, such as, for instance, substance use and abuse, especially amphetamine and cannabinoids, other addictive behaviors, self-harm, and suicidality (22, 23). Finally, ED is a negative predictor of short-term response to methylphenidate monotherapy in drug-naïve youth with ADHD, especially of changes in hyperactive–impulsive symptoms, and thus should be systematically assessed in ADHD at baseline (24).

The association between ADHD and ED is one of the main reasons of misconceptions in the definition of boundaries between ADHD and BSD, leading to the frequent misdiagnosis of ADHD as BSD, or to an overinflated rate of comorbidity between ADHD and BSD. The issue of the boundaries between ADHD and BSD is still difficult to solve, given the partial overlap of symptoms, namely when ED is a prominent feature. Whether ED is an associated feature or a specifier of ADHD—which defines a specific subtype of the disorder—or even a core feature of the disorder—additional to hyperactivity/impulsivity and inattention—or, finally, a comorbidity, is still a matter of discussion (9). Recent advances in ED research revealed that it can also be a specific feature of youths with BSD (25), and unaffected relatives of BSD youth can still present subthreshold deficits in emotion regulation and processing (26).

One of the most troublesome issues in the assessment of dysregulated children is the availability of cost-effective and reliable diagnostic measures. To date, the Child Behavior Checklist (CBCL), one of the most used instruments for the assessment of developmental psychopathology (27), has been considered a possible diagnostic tool for identifying children with these features. The CBCL-Dysregulation Profile (CBCL-DP) is an indirect index of ED, characterized by simultaneously high values [above two standard deviations (SD)] in three syndrome scales (anxious/depressed, attention problems, and aggressive behavior). Interestingly, this index was initially thought to be more closely related to the pediatric BSD, and thus, it was named CBCL-Pediatric Bipolar Disorder profile (CBCL-PBD) (28). Further research has questioned this relationship (5, 29–31), supporting the notion that it may be of a measure of a wider dysregulation profile (DP), rather than a proxy for a single disorder (32). Consequently, longitudinal studies have highlighted that higher CBCL-DP scores in at-risk subjects predict the risk for substance use, suicidality, and poorer overall functioning (5). Similarly, higher scores of DP in ODD patients predict a greater risk for ADHD and mood disorder in adolescence (33), while higher scores in ADHD patients predict impaired psychosocial functioning, psychiatric hospitalizations, and subsequent diagnoses of CD and BSD at the follow-up (34). In other words, research clearly suggests that ED, as indirectly assessed with an empirically derived measure (CBCL-DP), has high clinical relevance in different kinds of samples.

Although ED is a multidimensional concept, including emotional reactivity and impulsivity, affective intensity and polarity—both positive or elated and negative or irritable—and behavioral self-control, CBCL does not allow clinicians to disentangle these different components, which may be different in different subjects. Assessing all these components may need different measures, which are currently unavailable in youth (35, 36). However, a recently developed instrument to assess these different dimensions is the Reactivity, Intensity, Polarity, and Stability (RIPoSt) scale (37).

Starting from 60 items concerning reactivity, intensity, polarity of emotional responses, and affective stability, a first

validation in both clinical and non-clinical adult subjects led to a 40-item version with four scales (38). The four scales are the following: affective instability (AI), with 12 items exploring the presence of a cyclic pattern of sudden mood shifts between positive and negative polarity; emotional impulsivity (EI), with 8 items on the over-reactivity to negative or frustrating stimuli and the inability to inhibit impulsive behavioral responses; negative emotionality (NE), with 10 items evaluating the propensity for experiencing more often and more easily strong negative feelings, such as sadness, worry, anxiety and dissatisfaction; and positive emotionality (PE), with 10 items exploring the tendency to experience more often and more easily strong positive feelings, such as euphoria, joy, enthusiasm, and exuberance. The first three subscales also sum up to a negative ED (NED) scale, totally including 30 items. Measures of reliability (test–retest $r = 0.71$–$0.84$) and internal consistency (Cronbach's $\alpha = 0.72$–$0.95$) were high, and concurrent validity was also supported by correlations with the brief TEMPS-M subscales (39). Discriminant validity was finally significant ($p < 0.001$) since cyclothymic and ADHD patients exhibited higher scores than non-clinical controls for each subscale, except for PE.

In the present exploratory study, we employed, for the first time, the 40-item version of the RIPoSt questionnaire in a clinical and non-clinical sample of youths, providing initial psychometric assessment and thoroughly examining ED profiles in a sample of ADHD and/or BSD patients, in order to detect possible specificities. Our main hypotheses are that emotional regulation is more impaired in the comorbid condition (ADHD + BSD) than in ADHD or BSD alone patients and that all clinical groups score higher than a control group of healthy adolescents in all subscales of the questionnaire. We lack specific *a priori* hypotheses on each single dimension of the construct, since no previous clinical study applied the RIPoSt questionnaire in youths. Nonetheless, according to the theoretical model proposed by Banaschewski et al. (40) and Petrovic and Castellanos (41), we may only hypothesize a selective increase in EI scores in ADHD patients, both pure and comorbid with BSD, unless this specific subscale reflects the high sensitivity to emotionally salient stimuli with reduced self-control and behavioral inhibition described by the model.

# MATERIALS AND METHODS

## Recruitment and Diagnostic Procedures

Our study included 154 participants (104 males and 50 females, age range 9–18 years, mean age 13.8 ± 2.3 years) recruited in our third-level Department of Child and Adolescent Psychiatry and Psychopharmacology from 2017 to 2020 (clinical group; CG). Inclusion criteria were diagnoses of ADHD, BSD, or both, made according to the Diagnostic and Statistical Manual of Mental Disorders—fifth edition (DSM-5) (42), based on medical history, clinical observations, and a semistructured interview, the Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime version (K-SADS-PL) (43), administered by trained child psychiatrists to both patients and parents.

Exclusion criteria for the CG were as follows: older than 18 years old or younger than 9 years old; presence of comorbid intellectual disability, as detected through formal psychometric assessment (either the Full-Scale Intelligence Quotient or the General Ability Index below 85 at the WISC-IV); and presence of comorbid autism spectrum disorders, schizophrenia spectrum, and other psychotic disorders.

Three clinical subgroups were identified in the CG: the ADHD group (namely, without comorbid BSD), consisting of 72 subjects (62 males and 10 females, mean age 12.9 ± 2.2 years); the BSD group (namely, without comorbid ADHD), consisting of 53 subjects (18 males and 35 females, mean age 14.9 ± 1.8 years); and the comorbid ADHD + BSD group, consisting of 29 subjects (24 boys and 5 females, mean age 13.8 ± 2.4 years).

A school sample of 40 healthy control adolescents (HC group) (8 boys and 32 females, age range 9–18 years old, mean age 12.5 ± 1.2 years) was recruited on a voluntary basis upon engagement of a nearby junior high school in Pisa. Exclusion criteria for the HC group were as follows: older than 18 years old or younger than 9 years old, presence of intellectual disability, and presence of any psychiatric disorder.

All participants and parents were informed about assessment instruments, and there was voluntary participation in the study after written informed consent was obtained for assessment procedures from the parents of all children. The institutional review board of our hospital approved the study.

## Measures

A clinical questionnaire, the Child Behavior Checklist, was used in the both CG and HC samples to support clinical assessment and diagnostic procedures. The Child Behavior Checklist for ages 6–18 years (CBCL-6/18) (27, 44) is a 118-item scale, completed by parents or caregivers, with eight different syndromes scales, a total problem score, and two broad-band scores designated as internalizing problems and externalizing problems. In the current study, emotional dysregulation was assessed based on the CBCL-DP, using the sum of *t* scores of the following subscales, anxious/depression, attention problems, and aggressive behaviors. The reliability coefficients (Cronbach's $\alpha$) were 0.82, 0.81, and 0.82, respectively.

CG and HC were also assessed by means of the Italian 40-item version of the Reactivity, Intensity, Polarity and Stability (RIPoSt-40) questionnaire (37, 38), a self-rated measure of emotional dysregulation. The RIPoSt-40 has been recently validated in an adult Italian sample of 174 cyclothymic and/or ADHD patients and 396 non-clinical subjects. The 40 items are unequally distributed across four subscales, respectively identified as measures of AI, EI, NE, and PE; the first three subscales also sum up to a NED score which includes 30 items. The instrument showed generally high test–retest reliability ($r = 0.71$–$0.84$) and good-to-excellent internal consistency (Cronbach's $\alpha = 0.72$–$0.95$). Concurrent and discriminant validity were also demonstrated to be significant. Thus, the RIPoSt-40 questionnaire proved to be a valid, reliable, and useful tool to assess emotional dysregulation, both in clinical and non-clinical contexts.

## Statistics

Statistical analyses were performed by means of MATLAB® and RStudio® software. For each clinical variable with continuous distribution, outliers were defined as observations lying outside

the range between (first quartile − 2 * interquartile range) and (third quartile + 2 * interquartile range) and removed. Cronbach's alphas were computed as measures of internal consistency of each subscale of the RIPoSt-40 questionnaire. The $\chi^2$ test was used to detect significant differences ($p < 0.05$) between the three clinical groups and the HC group in the distributions of demographic and clinical nominal categorical variables, such as gender and clinical comorbidities. When more than 20% of observations had expected frequencies <5, Fisher's exact test was performed. Analyses of covariance (ANCOVA) were conducted to assess significant differences ($p < 0.05$) between group means in the demographic and clinical variables with continuous distribution, such as subscale scores of the RIPoSt-40 questionnaire while controlling for gender as covariate. A Tukey *post hoc* test was used whenever ANCOVA led to a statistically significant result in order to identify significant comparisons between couples of groups.

Pearson's linear correlation coefficients were estimated to detect significant relationships of the RIPoSt-40 questionnaire subscales with each other and between these and the CBCL-6/18 subscales in the CG and HC group. The Bonferroni correction method for multiple comparisons was applied after assessing significant differences at a traditional significance level of 5%. Finally, linear multivariate regression models were applied to identify statistically significant associations between the RIPoSt-40 questionnaire subscales and the presence of psychiatric comorbidities, notably anxiety disorders and disruptive behavior disorders, while controlling for the principal diagnoses (ADHD and BSD) as covariates.

## RESULTS

Our sample included 194 participants, of which 154 were in the CG (72 ADHD, 53 BSD, and 29 ADHD + BSD) and 40 in the HC group. Demographic and clinical characteristics of the four groups are reported in **Table 1**. As shown, gender and age were significantly different among the groups; *post hoc* comparisons are detailed in the table legend. Clinical comorbidities also significantly differed, with the BSD group exhibiting the greatest mean number of comorbid psychiatric conditions, followed by the ADHD + BSD, and then by the ADHD. Specific comorbidities, according to DSM-5, are listed in **Table 1**.

Internal consistency of the RIPoSt-40 questionnaire was initially assessed by computing Cronbach's $\alpha$ coefficients for each subscale. Cronbach's coefficients were generally high for most subscales (AI: $\alpha = 0.896$; EI: $\alpha = 0.870$; NE: $\alpha = 0.864$; AI: $\alpha = 0.896$), except for PE, whose internal consistency was still good (PE: $\alpha = 0.814$). An excellent reliability value was identified for the NED subscale (NED: $\alpha = 0.946$).

We then compared the RIPoSt-40 subscale scores between the three CG and the HC through ANCOVAs, while correcting for gender distributions as covariate. Age was also initially assessed through a linear multivariate model, though displaying no significant effects on any of the questionnaire subscales and not altering the effect of the other variables of the model; thus, we decided to remove it from the analyses. As shown in **Table 2** and **Figure 1**, the AI, EI, NE, and NED subscales demonstrated highly significant differences among the groups, while the analysis revealed no significant effect of diagnosis or gender on the PE subscale. *Post hoc* comparisons are detailed in the table legend. Notably, the BSD and ADHD + BSD groups scored the highest in the AI, NE, and NED subscales, without significant differences between the groups, and the ADHD group presented significantly lower scores in the three scales, but higher than the HC group. As for the EI subscale, the ADHD + BSD group scored the highest, followed by the BSD and the ADHD groups, which did not differ significantly between them, and finally the HC group, with significantly lower scores. *Post hoc* comparisons between males and females in the RIPoSt-40 questionnaire subscales revealed highly significant gender-related differences for the AI, NE, and NED subscales, with females scoring higher than males (data not shown).

As shown in **Table 3**, the AI, EI, and NE subscales were all highly significantly positively correlated in the whole sample, with coefficients *r* ranging between 0.660 for the correlation between AI and EI and 0.829 for the correlation between AI and NE. The PE subscale was also positively correlated, though less significantly, with the AI, EI, and NE subscales, with coefficients *r* between 0.184 for the correlation with NE and 0.227 for the correlation with EI. Significantly positive correlations were finally identified between the NED and other subscales of the questionnaire.

We also estimated linear correlation coefficients to detect significant relationships between the RIPoSt-40 and the

**TABLE 1** | Demographic and clinical characteristics of the sample.

| Total = 194 | Group 1 ADHD | Group 2 BSD | Group 3 ADHD + BSD | Group 4 HC | *p* |
|---|---|---|---|---|---|
| *N* | 72 | 53 | 29 | 40 | – |
| Males, *N* (%) | 62 (86.1) | 18 (34.0) | 24 (82.8) | 8 (20) | <0.001*** |
| Age, *M* (SD) | 12.9 (2.2) | 14.9 (1.8) | 13.8 (2.4) | 12.5 (1.2) | <0.001*** |
| Comorbidities, *M* (SD) | 0.8 (1.0) | 2.7 (1.0) | 1.8 (1.5) | 0 (0) | <0.001*** |
| Single AD, *N* (%) | 9 (12.5) | 13 (24.5) | 6 (20.7) | 0 (0) | <0.001*** |
| Multiple AD, *N* (%) | 7 (9.7) | 20 (37.7) | 7 (24.1) | 0 (0) | |
| OCD, *N* (%) | 2 (2.8) | 6 (11.3) | 2 (6.9) | 0 (0) | 0.017* |
| Tics, *N* (%) | 5 (6.9) | 1 (1.9) | 3 (10.3) | 0 (0) | 0.134 |
| ODD, *N* (%) | 21 (29.2) | 18 (34.0) | 16 (55.2) | 0 (0) | <0.001*** |
| CD, *N* (%) | 3 (4.2) | 11 (20.8) | 4 (13.8) | 0 (0) | <0.001*** |
| Eating disorders, *N* (%) | 1 (1.4) | 6 (11.3) | 0 (0) | 0 (0) | 0.003** |

*Post hoc comparisons: age: group 1–group 2: p < 0.001 < 0.001***; group 1–group 3: p = 0.208; group 1–group 4: p = 0.703; group 2–group 3: p = 0.061; group 2–group 4: p < 0.001 < 0.001***; group 3–group 4: p = 0.044*. Comorbidities: group 1–group 2: p < 0.001 < 0.001***; group 1–group 3: p < 0.001 < 0.001***; group 1–group 4: p < 0.001 < 0.001**; group 2–group 3: p = 0.005**; group 2–group 4: p < 0.001 < 0.001***; group 3–group 4: p < 0.001 < 0.001***. AD, anxiety disorder; ADHD, attention deficit hyperactivity disorder; BSD, bipolar spectrum disorder; CD, conduct disorder; HC, healthy controls; M, mean; N, number; OCD, obsessive–compulsive disorder; ODD, oppositional defiant disorder; SD, standard deviation. *p < 0.05; **p < 0.01; ***p < 0.001.*

**TABLE 2 |** RIPoSt-40 subscales: comparisons among the PAT and HC groups.

| Total = 194 | Group 1 ADHD | Group 2 BSD | Group 3 ADHD + BSD | Group 4 HC | *p* |
|---|---|---|---|---|---|
| *N* | 72 | 49 | 28 | 38 | – |
| RIPoSt-40 AI, *M* (SD) | 30.7 (9.8) | 41.4 (14.3) | 37.6 (12.2) | 23.4 (9.1) | <0.001*** |
| RIPoSt-40 EI, *M* (SD) | 25.3 (7.5) | 28.0 (9.6) | 30.5 (9.1) | 16.8 (5.9) | <0.001*** |
| RIPoSt-40 NE, *M* (SD) | 27.4 (7.9) | 37.6 (12.7) | 32.7 (10.5) | 23.8 (7.3) | <0.001*** |
| RIPoSt-40 PE, *M* (SD) | 37.8 (9.4) | 36.8 (9.7) | 38.8 (10.9) | 39.1 (9.2) | 0.702 |
| RIPoSt-40 NED, *M* (SD) | 83.4 (21.5) | 107.1 (33.0) | 100.8 (28.3) | 64.0 (20.4) | <0.001*** |

*Post hoc comparisons: AI: group 1–group 2: $p < 0.001 < 0.001$***; group 1–group 3: $p = 0.027$*; group 1–group 4: $p = 0.007$**; group 2–group 3: $p = 0.464$; group 2–group 4: $p < 0.001 < 0.001$***; group 3–group 4: $p < 0.001 < 0.001$***; males < females: $p = 0.001$**. EI: group 1–group 2: $p = 0.279$; group 1–group 3: $p = 0.022$*; group 1–group 4: $p < 0.001 < 0.001$**; group 2–group 3: $p = 0.555$; group 2–group 4: $p < 0.001 < 0.001$***; group 3–group 4: $p < 0.001 < 0.001$***; males < females: $p = 0.087$. NE: group 1–group 2: $p < 0.001 < 0.001$***; group 1–group 3: $p = 0.056$; group 1–group 4: $p = 0.244$; group 2–group 3: $p = 0.119$; group 2–group 4: $p < 0.001 < 0.001$***; group 3–group 4: $p = 0.001$**; males < females: $p < 0.001 < 0.001$***. PE: group 1–group 2: $p = 0.952$; group 1–group 3: $p = 0.968$; group 1–group 4: $p = 0.903$; group 2–group 3: $p = 0.834$; group 2–group 4: $p = 0.698$; group 3–group 4: $p = 0.999$; males < females: $p = 0.409$. NED: group 1–group 2: $p < 0.001 < 0.001$***; group 1–group 3: $p = 0.011$*; group 1–group 4: $p < 0.001 < 0.001$***; group 2–group 3: $p = 0.719$; group 2–group 4: $p < 0.001 < 0.001$***; group 3–group 4: $p < 0.001 < 0.001$***; males < females: $p = 0.001$**. AI, affective instability; ADHD, attention deficit hyperactivity disorder; BSD, bipolar spectrum disorder; EI, emotional impulsivity; HC, healthy controls; M, mean; N, number; NE, negative emotionality; NED, negative emotional dysregulation; PE, positive emotionality; RIPoSt-40, 40-item Reactivity, Intensity, Polarity and Stability questionnaire; SD, standard deviation. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.*

CBCL-6/18 subscales. The AI, EI, NE, and NED subscales of the RIPoSt-40 questionnaire were highly significantly positively correlated with all syndromes and problems subscales and most DSM-oriented diagnostic category subscales, while the only significant negative relationships of the PE subscale were identified with the anxious/depressed, the withdrawn/depressed, and the affective problems subscales. Notably, the dysregulation profile index of the CBCL-6/18 was highly positively associated with the AI, EI, NE, and NED subscales, while no significant correlation was detected with the PE subscale. Correlation coefficients and statistics are detailed in **Tables 4A,B**.

Five linear multivariate regression models were finally applied to identify statistical associations between the subscales of the RIPoSt-40 questionnaire, as dependent variables, and the presence of psychiatric comorbidities [i.e., single and/or multiple anxiety disorder (AD) and ODD and/or CD], as independent variables, while controlling for the principal diagnoses (ADHD and BSD). As displayed in **Tables 5A–E**, significant positive associations were found between the AI, NE, and NED subscales and both BSD and multiple AD. Moreover, EI was significantly positively associated with both ADHD and BSD, while PE displayed no significant associations. Neither the presence of a single AD nor that of ODD/CD was significantly associated with any of the RIPoSt-40 subscales.

## DISCUSSION

This is the first study aimed to explore ED in a clinical sample of children and adolescents using a specific measure, the RIPoSt questionnaire, which includes four dimensions of dysregulation, that is affective instability, emotional impulsivity, negative emotionality, positive emotionality, and the negative emotional dysregulation derived from the sum of the first three dimensions. The first aim of our study was to explore the different dimensions of ED in youth with ADHD, BSD, and the two comorbid conditions. The secondary aims of the study were to preliminarily explore the psychometric characteristics of the RIPoSt questionnaire and to compare this measure with a well-established dimensional measure of psychopathology in youth, the CBCL-6/18, and more specifically with the CBCL-Dysregulation Profile, derived from the three symptom scales of the instrument.

The boundaries between ADHD and BSD raised a controversy in the literature, given the partial overlap of symptoms, such as hyperactivity, impulsivity/aggressiveness, and distractibility, particularly when ED is associated. Indeed, when this latter is prominent, inflated rates of comorbidity between the two disorders have been reported in the literature (45). The greater awareness of ED in ADHD individuals (1, 14) has contributed to a better comprehension of the relationship between ADHD and BSD, but the lack of reliable and sensitive measures of ED significantly limited this exploration. Thus, the RIPoSt questionnaire may represent a possible new tool for exploring different dimensions of ED in ADHD, BSD, and the comorbid condition, compared with heathy controls, which helps to better understand the relationship between the two disorders and to finely disentangle the disorders, highlighting possible targets for a well-adjusted intervention.

Our findings indicate that AI and NE, as well as the combined NED scale, are mostly related to the BSD, both pure and with ADHD, and can reliably differentiate these conditions from pure ADHD. Similarly, these three dimensions are able to discriminate the dysregulated profile of ADHD youth compared with the heathy controls. A more nuanced difference was shown with emotional impulsivity, which was found to be similar in ADHD and BSD alone and higher in the comorbid condition, and notably, all clinical groups exhibited higher scores than the healthy controls.

On the other hand, PE is unable to differentiate clinical and healthy groups and seems a sort of temperamental dimension, which can be found in both patients and healthy individuals, without a significant impairing effect. Moreover, it seems more difficult to be detected, at least compared with NE, and would thus require larger sample size to achieve statistical significance (38). Also, differences among groups in PE may be more qualitative than quantitative, but even more reactive and transitory in clinical samples, and/or with different behavioral correlates. Further studies are hence needed to support the clinical utility of the PE subscale.

A comparison between these results and those reported in a parallel study, conducted on adult patients explored with the same diagnostic tool (38), is highly informative, given the strong

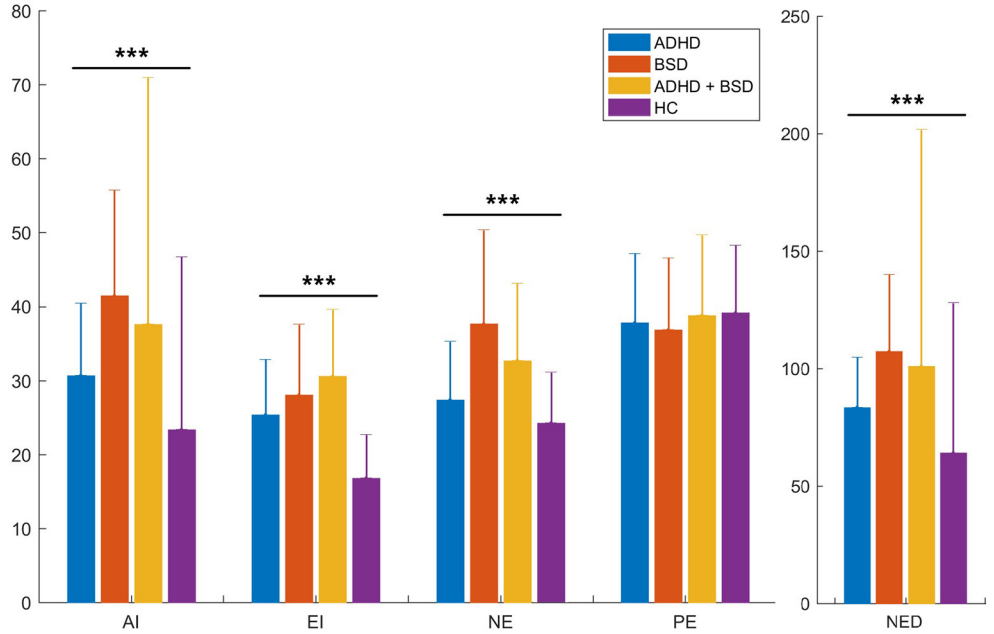


**FIGURE 1 |** RIPoSt-40 subscales: comparisons between clinical and non-clinical groups. Scores obtained by the four groups in our sample, namely the three clinical groups and the control group, in the five RIPoSt-40 questionnaire subscales—AI, EI, NE, PE, and NED—are here illustrated. Scores are compared between ADHD patients (blue bars), BSD patients (red bars), comorbid ADHD + BSD patients (yellow bars), and HC individuals (purple bars). Graphs represent means with standard deviation bars. ADHD, attention deficit hyperactivity disorder; AI, affective instability; BSD, bipolar spectrum disorder; EI, emotional impulsivity; HC, healthy controls; NE, negative emotionality; NED, negative emotional dysregulation; PE, positive emotionality; RIPoSt-40, Reactivity, Intensity, Polarity and Stability questionnaire. ***$p < 0.001$.

**TABLE 3 |** RIPoSt-40 subscale internal correlations.

| | RIPoSt-40 AI | RIPoSt-40 EI | RIPoSt-40 NE | RIPoSt-40 PE | RIPoSt-40 NED |
|---|---|---|---|---|---|
| RIPoSt-40 AI | $r = 1$ | $r = 0.660$ | $r = 0.829$ | $r = 0.184$ | $r = 0.938$ |
| | $p = 1$ | $p < 0.001 < 0.001$*** | $p < 0.001 < 0.001$*** | $p = 0.012$* | $p < 0.001 < 0.001$*** |
| RIPoSt-40 EI | $r = 0.660$ | $r = 1$ | $r = 0.667$ | $r = 0.227$ | $r = 0.835$ |
| | $p < 0.001 < 0.001$*** | $p = 1$ | $p < 0.001 < 0.001$*** | $p = 0.002$** | $p < 0.001 < 0.001$*** |
| RIPoSt-40 NE | $r = 0.829$ | $r = 0.667$ | $r = 1$ | $r = 0.158$ | $r = 0.928$ |
| | $p < 0.001 < 0.001$*** | $p < 0.001 < 0.001$*** | $p = 1$ | $p = 0.031$* | $p < 0.001 < 0.001$*** |
| RIPoSt-40 PE | $r = 0.184$ | $r = 0.227$ | $r = 0.158$ | $r = 1$ | $r = 0.207$ |
| | $p = 0.012$* | $p = 0.002$** | $p = 0.031$* | $p = 1$ | $p = 0.005$* |
| RIPoSt-40 | $r = 0.938$ | $r = 0.835$ | $r = 0.928$ | $r = 0.207$ | $r = 1$ |
| NED | $p < 0.001 < 0.001$*** | $p < 0.001 < 0.001$*** | $p < 0.001 < 0.001$*** | $p = 0.005$* | $p = 1$ |

*AI, affective instability; EI, emotional impulsivity; NE, negative emotionality; NED, negative emotional dysregulation; PE, positive emotionality; RIPoSt-40, 40-item Reactivity Intensity Polarity Stability questionnaire. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.*

consistencies in the findings, with remarkable implications in a developmental perspective. In Brancati et al. (38), the RIPoSt questionnaire was administered to two clinical samples, namely cyclothymic and ADHD patients, along with a community-based sample of healthy controls. Consistent with our data, AI, NE, and NED lead to overlapping scores in cyclothymic and ADHD patients, and both groups scored higher than healthy controls, while PE failed to discriminate clinical patients and healthy individuals. Noteworthy, adult ADHD scored higher than both cyclothymic and healthy individuals in the EI subscale, suggesting that this dimension would be more likely related to the hyperactive–impulsive trait of ADHD rather than to the affective instability of BSD. On the contrary, in our youth, ADHD and BSD exhibited similar scores in EI, and only the comorbid condition was associated with higher scores. A possible explanation of this phenomenon may be related to the developmental divergences between juvenile and adult BSD, since among youth, impulsivity, both emotional and behavioral, is considered as a marker of earlier-onset juvenile BSD, which makes this condition more similar to

**TABLE 4 |** RIPoSt-40 and CBCL-6/18 subscale correlations.

| | RIPoSt-40 AI | RIPoSt-40 EI | RIPoSt-40 NE | RIPoSt-40 PE | RIPoSt-40 NED |
|---|---|---|---|---|---|
| **(A) Coefficients *r*** | | | | | |
| CBCL AD | 0.440 | 0.457 | 0.492 | −0.171 | 0.502 |
| CBCL WD | 0.431 | 0.341 | 0.441 | −0.240 | 0.445 |
| CBCL SomP | 0.382 | 0.249 | 0.427 | −0.014 | 0.391 |
| CBCL SocP | 0.448 | 0.473 | 0.462 | 0.012 | 0.499 |
| CBCL TP | 0.381 | 0.439 | 0.386 | −0.061 | 0.433 |
| CBCL AP | 0.322 | 0.430 | 0.279 | −0.030 | 0.367 |
| CBCL RBB | 0.368 | 0.474 | 0.314 | 0.045 | 0.412 |
| CBCL AB | 0.331 | 0.482 | 0.322 | 0.042 | 0.402 |
| CBCL DPI | 0.428 | 0.530 | 0.426 | −0.066 | 0.495 |
| CBCL Int | 0.463 | 0.480 | 0.495 | −0.122 | 0.520 |
| CBCL Ext | 0.397 | 0.546 | 0.367 | 0.028 | 0.466 |
| CBCL Tot | 0.437 | 0.544 | 0.436 | −0.049 | 0.507 |
| CBCL Aff | 0.310 | 0.298 | 0.323 | −0.213 | 0.343 |
| CBCL Anx | 0.167 | 0.250 | 0.276 | −0.180 | 0.250 |
| CBCL Som | 0.189 | 0.078 | 0.302 | 0.0172 | 0.219 |
| CBCL ADHD | −0.048 | 0.208 | −0.058 | 0.020 | 0.018 |
| CBCL ODP | 0.061 | 0.286 | 0.107 | 0.025 | 0.150 |
| CBCL CP | 0.098 | 0.338 | 0.054 | 0.040 | 0.161 |
| **(B) *p* values** | | | | | |
| CBCL AD | <0.001*** | <0.001*** | <0.001*** | 0.045* | <0.001*** |
| CBCL WD | <0.001*** | <0.001*** | <0.001*** | 0.004** | <0.001*** |
| CBCL SC | <0.001*** | 0.003** | <0.001*** | 0.862 | <0.001*** |
| CBCL SP | <0.001*** | <0.001*** | <0.001*** | 0.881 | <0.001*** |
| CBCL TP | <0.001*** | <0.001*** | <0.001*** | 0.477 | <0.001*** |
| CBCL AP | <0.001*** | <0.001*** | <0.001*** | 0.726 | <0.001*** |
| CBCL RBB | <0.001*** | <0.001*** | <0.001*** | 0.600 | <0.001*** |
| CBCL AB | <0.001*** | <0.001*** | <0.001*** | 0.619 | <0.001*** |
| CBCL DPI | <0.001*** | <0.001*** | <0.001*** | 0.445 | <0.001*** |
| CBCL Int | <0.001*** | <0.001*** | <0.001*** | 0.156 | <0.001*** |
| CBCL Ext | <0.001*** | <0.001*** | <0.001*** | 0.745 | <0.001*** |
| CBCL Tot | <0.001*** | <0.001*** | <0.001*** | 0.569 | <0.001*** |
| CBCL Aff | 0.001** | 0.002** | 0.001** | 0.034* | <0.001*** |
| CBCL Anx | 0.096 | 0.012* | 0.005** | 0.074 | 0.012* |
| CBCL Som | 0.061 | 0.441 | 0.002** | 0.865 | 0.029* |
| CBCL ADHD | 0.633 | 0.038* | 0.566 | 0.840 | 0.858 |
| CBCL ODP | 0.547 | 0.004** | 0.290 | 0.803 | 0.135 |
| CBCL CP | 0.331 | <0.001*** | 0.590 | 0.688 | 0.109 |

*ADHD, attention deficit hyperactivity disorder; AB, aggressive behavior; AD, anxious/depressed; Aff, affective problems; AI, affective instability; Anx, anxiety problems; AT, attention problems; CBCL, Child Behavior Checklist; CP, conduct problems; DPI, dysregulation profile index; EI, emotional impulsivity; Ext, externalizing problems; Int, internalizing problems; NE, negative emotionality; NED, negative emotional dysregulation; ODP, oppositional defiant problems; PE, positive emotionality; RBB, rule-breaking behavior; RIPoSt-40, 40-item Reactivity, Intensity, Polarity and Stability questionnaire; SC, somatic complaints; Som, somatic problems; SP, social problems; Tot, total problems; TP, thought problems; WD, withdrawn/depressed. *p < 0.05; **p < 0.01; ***p < 0.001.*

**TABLE 5 |** Linear regression models with clinical comorbidities.

| | *β* | SE | *t* value | *p* |
|---|---|---|---|---|
| **(A) RIPoSt-40 AI** | | | | |
| Intercept | 26.099 | 1.626 | 16.051 | <0.001*** |
| ADHD | 1.527 | 1.863 | 0.820 | 0.414 |
| BSD | 10.001 | 2.348 | 4.259 | <0.001*** |
| Single AD | 4.147 | 2.653 | 1.563 | 0.120 |
| Multiple AD | 6.756 | 2.620 | 2.578 | 0.011* |
| ODD/CD | 1.724 | 2.094 | 0.823 | 0.412 |
| **(B) RIPoSt-40 EI** | | | | |
| Intercept | 18.105 | 1.134 | 15.969 | <0.001*** |
| ADHD | 5.720 | 1.299 | 4.404 | <0.001*** |
| BSD | 7.088 | 1.637 | 4.329 | <0.001*** |
| Single AD | 2.265 | 1.850 | 1.224 | 0.223 |
| Multiple AD | 2.598 | 1.827 | 1.422 | 0.157 |
| ODD/CD | 0.426 | 1.460 | 0.292 | 0.771 |
| **(C) RIPoSt-40 NE** | | | | |
| Intercept | 26.081 | 1.342 | 19.436 | <0.001*** |
| ADHD | −0.232 | 1.537 | −0.151 | 0.880 |
| BSD | 9.137 | 1.938 | 4.714 | <0.001*** |
| Single AD | 3.178 | 2.190 | 1.450 | 0.149 |
| Multiple AD | 5.672 | 2.163 | 2.623 | 0.006** |
| ODD/CD | −2.127 | 1.729 | −1.231 | 0.220 |
| **(D) RIPoSt-40 PE** | | | | |
| Intercept | 38.513 | 1.373 | 28.044 | <0.001*** |
| ADHD | −0.463 | 1.573 | −0.294 | 0.769 |
| BSD | −0.340 | 1.984 | −0.172 | 0.864 |
| Single AD | 3.419 | 2.241 | 1.526 | 0.129 |
| Multiple AD | −0.380 | 2.213 | −0.172 | 0.864 |
| ODD/CD | −0.624 | 1.769 | −0.353 | 0.725 |
| **(E) RIPoSt-40 NED** | | | | |
| Intercept | 70.285 | 3.629 | 19.369 | <0.001*** |
| ADHD | 7.015 | 4.157 | 1.687 | 0.093 |
| BSD | 26.226 | 5.241 | 5.004 | <0.001*** |
| Single AD | 9.587 | 5.921 | 1.619 | 0.107 |
| Multiple AD | 15.026 | 5.848 | 2.569 | 0.011* |
| ODD/CD | 0.023 | 4.674 | 0.005 | 0.996 |

*ADHD, attention deficit hyperactivity disorder; AD, anxiety disorders; AI, affective instability; BSD, bipolar spectrum disorders; CD, conduct disorder; EI, emotional impulsivity; NE, negative emotionality; NED, negative emotional dysregulation; ODD, oppositional defiant disorder; PE, positive emotionality; RIPoSt-40, 40-item Reactivity, Intensity, Polarity and Stability questionnaire; SE, standard error. *p < 0.05; **p < 0.01; ***p < 0.001.*

ADHD (46). Conversely, adult BSD is less impulsive and more affective, while impulsivity of ADHD adult patients is much more prominent.

Our findings also provide a preliminary support to the construct and concurrent validity of the 40-item version of the RIPoSt questionnaire to assess ED. Indeed, the instrument proved to have good-to-excellent internal consistency in both clinical and non-clinical samples. Cronbach's coefficients were high for all subscales and for their combination in the NED subscale, while they were lesser, though still good, for the PE subscale. Furthermore, consistent with clinical findings, the AI, NE, and NED subscales were strongly and positively correlated with each other, while PE was more feebly correlated with the other three dimensions.

Construct validity was also assessed in terms of gender-related differences. Indeed, males and females significantly differed in both clinical and non-clinical samples. As expected, girls scored higher in most ED dimensions, namely the AI, NE, and NED subscales, while EI was similar across gender. Moreover, gender differences were also detected in the relative distribution among groups, with ADHD exhibiting strong male prevalence and BSD with an even gender distribution. On the contrary, no age effect was found for any of the dimensions of dysregulation.

Correlations between RIPoSt and CBCL subscales further supported the concurrent validity of the new instrument. Indeed, the significant positive correlation between the AI, EI, NE, and NED subscales of the RIPoSt-40 and all syndromes and problems subscales and most DSM-oriented diagnostic category subscales of the CBCL-6/18, but especially their strongest and most significant correlations with the CBCL-DP, indicates that the four subscales and their combination can be used as an effective tool for studying ED in different clinical conditions. On the contrary, PE was limitedly correlated with the anxious/depressed, withdrawal/depressed, and affective problems subscales; thus, it seems to be only related with the affective dimensions of the CBCL, and notably, it did not exhibit a significant correlation with CBCL-DP.

Finally, when comorbidities were also taken into account, the AI, NE, and NED subscales presented a positive significant association with multiple anxiety disorder, which has been repeatedly found as a possible precursor of and frequently associated with BSD (47–49). Unexpectedly, disruptive behavior disorders did not show such an association, not even with the EI subscale. This result is in apparent contrast with previous findings from the available literature on the topic (22, 33) and would need further research. Indeed, disruptive behavior disorders are heterogeneous conditions, according to associated emotional features, in which ED, present in a strong minority of disruptive patients, may be specifically characterized by a deficit in emotional and behavioral self-control, with a greater risk of externalizing and aggressive behaviors (41).

This study should be considered preliminary, given some significant limitations: first of all, the lack of a formal standardization of the RIPoSt questionnaire in young people. Indeed, psychometric validation of multiple-item scales is considered to be an integral part, if not a crucial step, of data analysis in most substantive research studies (50). We largely based our study on the recent validation of the instrument in an adult sample of both clinical and non-clinical individuals (38), but future studies aimed at robustly validating and psychometrically assessing the RIPoSt in youth will be definitely required. Moreover, despite replicating common male-to-female ratio distributions in clinical samples of ADHD and BSD as ordinarily reported in literature (51) and correcting for gender whenever required in statistical comparisons, our samples significantly differed in terms of gender distribution. Future studies with more homogeneous distributions, or rather with larger proportions of the lacking sex, are warranted. Other limitations also include that we recruited modestly sized clinical samples and compared them with a school-based control group; nonetheless, we supposed this latter to be representative of the general population and applied strict exclusion criteria to prevent non-healthy controls to be recruited. Finally, we could not control for medication use and current interventions as potential confounding factors, which may affect our results, since full data were not available.

Despite these limitations, our study paved the way for future directions of research in clinical practice. Indeed, a thorough validation of the RIPoSt questionnaire along with an assessment of its psychometric properties is warranted. Our results also need to be further corroborated in larger samples. As pointed out before, the RIPoSt represents a potential clinical tool that may help in disentangling the complex relationship between ADHD and juvenile BSD for better diagnostic characterization and therapeutic indications. Future studies may further explore the longitudinal course of emotional dysregulation in these two partially overlapping disorders and assess the changes in their ED profile after psychopharmacological interventions. Moreover, the questionnaire may be used in the frame of evidence-based psychotherapeutic settings for psychopathological conditions characterized by ED to monitor the clinical course of its different dimensions and provide further evidence of effectiveness. Finally, the assessment of ED dimensions may be also useful in adolescents with conduct disorders, especially comorbid with ADHD, to further characterize the complex relationship between emotional regulation and executive functioning.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by IRCCS Stella Maris Scientific Institute of Child Neurology and Psychiatry, Pisa, Italy. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

GM and AMi: conceptualization. GM, AMi, GS, and SP: methodology. CP, EV, AMo, FP, SB, NL, FD, and ARM: data collection and discussion on the first draft and conclusions. GS and SP: statistical analyses. GM, GS, AMi, and SP: writing first draft. All authors have read and agreed to the published version of the manuscript.

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# Modular Psychotherapy Outcomes for Youth With Different Latent Profiles of Irritability and Emotion Dysregulation

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**Background:** Severe irritability is a common, impairing problem among youth referred for mental health services, but evidence to guide care is limited. Treatment research can be advanced by adopting a transdiagnostic perspective, leveraging existing evidence-based treatment (EBT) techniques, and situating irritability within the context of emotion dysregulation. Accordingly, this study examined treatment outcomes for youth with different levels of irritability and dysregulation who received cognitive-behavioral therapy (CBT) or behavioral parent training (BPT) in a modular EBT framework.

**Method:** We analyzed data from a community-based implementation trial of a transdiagnostic youth psychotherapy. Two-hundred treatment-referred youths (7-15 years; 47% female; 33% White, 28% Black, 24% Latinx, 14% multiracial, 2% other) and their caregivers completed measures of clinical problems and emotion dysregulation at baseline, with repeated outcomes assessments over 18 months. First, latent profile analysis was applied to baseline irritability and emotion dysregulation data; then, latent growth curve models were used to examine outcome trajectories, controlling for covariates.

**Results:** A two-class solution fit well, differentiating youth with high ($n$ = 54) vs. low ($n$ = 146) levels of dysregulation and irritability at baseline. Nearly all high-dysregulation youth received either BPT ($n$ = 26) or CBT-Depression ($n$ = 23). Across measures, both groups showed statistically and clinically significant improvements over time. High-dysregulation youth had greater baseline severity than low-dysregulation youth, but otherwise their longitudinal trajectories were mostly similar, with few between-group slope differences. There was virtually no evidence of differential effects for BPT vs. CBT on clinical outcomes.

**Conclusions:** Youth with severe irritability and dysregulation, treated with a transdiagnostic, modular, EBT approach, showed significant within-person improvements over time. Their outcome trajectories did not differ according to

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whether they received BPT or CBT. Findings extend the literature on modular, transdiagnostic, and EBT approaches for irritability and dysregulation, suggesting comparable benefits associated with BPT and CBT when treatment selection is guided by comprehensive assessment.

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## INTRODUCTION

Severe irritability is a common treatment concern among children and adolescents (herein "youth") referred for mental health services (1). Although some degree of irritability is normative across development, severe irritability is defined as a problem of emotion dysregulation characterized by a heightened proneness toward anger (2–4). A transdiagnostic symptom, irritability is an essential or associated feature of many different diagnostic categories (e.g., disruptive, depressive, anxiety, personality, and stress-related disorders). Despite recent advances in the developmental psychopathology of irritability (5–7), research to guide assessment and treatment remains limited. The best available evidence points to behavioral parent training (BPT) and cognitive-behavioral techniques (CBT) as being effective for irritability (2, 3, 8), and some research suggests these approaches may be *more effective* in a personalized, transdiagnostic format (9). However, CBT and BPT are seldom investigated together in the same study, making it hard to draw conclusions about relative effects. Further, it is challenging to interpret the evidence on treatment of irritability and related constructs [e.g., chronic irritability; severe mood dysregulation; Disruptive Mood Dysregulation Disorder (DMDD); symptoms of Oppositional Defiant Disorder (ODD)] because they have been inconsistently defined and measured in the literature (6), and available studies and treatments have most often focused on related problems like ADHD (10, 11). Responding to these challenges, researchers have emphasized the need to examine irritability from more established conceptual frameworks, including emotion regulation theory (4, 7, 12–14). The current study advances this literature by investigating clinical outcomes among youth with elevated irritability and emotion dysregulation, treated primarily with BPT or CBT in a transdiagnostic, personalized framework.

Broadly, emotion dysregulation refers to a maladaptive pattern of emotional management and expression (15, 16). Theorists have come to view emotion dysregulation as a common feature across many, if not most, forms of psychopathology (16, 17). It has been proposed that emotion dysregulation arises from dysfunctions in the processes that *generate* emotion and occurs due to problematic emotional arousal and reactivity—i.e., when the type, intensity, frequency, and duration of experienced emotions interfere with appropriate goal-directed behavior (18–20). Others have focused on emotion dysregulation that arises from dysfunctions in the processes that *regulate* emotions—i.e., from dysfunctions in individuals' emotional awareness and understanding, emotion regulation goals, and ability to implement different emotion regulation strategies (21–23). These views are not mutually exclusive, and various attempts at synthesis have been made [e.g., (24)]. In the context of youth psychopathology, emotion dysregulation has been characterized (17) by the occurrence emotions that (a) *endure*, despite attempts at regulation; (b) *interfere* with appropriate behavior; (c) are *context-inappropriate*; and (d) *change atypically*, that is, too abruptly or too slowly. These parameters align with current thinking about youth irritability, defined as an "increased proneness to anger compared with peers at same development level," situated beneath the supraordinate construct of emotion dysregulation (p. 722) (2). Diagnostically, these terms algin with DMDD in DSM-5 (25) and with ODD with Chronic Irritability/Anger in ICD-11 (6), as well as across internalizing and externalizing psychopathology more broadly.

Indeed, the two components of emotion dysregulation—generation and regulation—are involved in the development and maintenance of youth internalizing and externalizing problems. Among youth with anxiety disorders/symptoms, researchers have documented greater intensity and frequency of negative emotional experiences (26); difficulties using cognitive reappraisal effectively (26, 27); and deficits in understanding and managing emotions (28). Youth with internalizing symptoms are also more likely to use emotion regulation strategies that increase negative emotion and functional impairment. Adolescents with anxiety and depressive symptoms show less frequent use of more adaptive strategies like cognitive reappraisal, problem-solving, and acceptance, and more frequent use of maladaptive strategies like avoidance, suppression, and rumination (29). Patterns of emotion regulation strategy use have also been implicated in youth externalizing problems and disorders, with anger rumination predicting aggressive behavior (30–32). High emotional reactivity, deficits in emotional understanding, and difficulty in managing negative emotions have been linked to aggressive behavior among youth both concurrently (33–35) and prospectively (36). And youth with ADHD are more likely to experience intense negative and positive emotions and show deficits in emotion regulation (37, 38). Importantly, emotion regulation strategies are not only a feature or correlate of psychopathology; they also predict increasing psychopathology over time (e.g., rumination and internalizing problems) (39, 40). Given these findings, it seems reasonable that research might be advanced through transdiagnostic approaches that collectively considers these multiple dimensions of emotion (dys)regulation and broad and narrow forms of psychopathology.

Severe irritability represents one form of emotion dysregulation that is implicated across the spectrum of psychopathology (2, 4). Like emotion dysregulation more broadly, youth irritability shows robust associations with anxiety, depressive, and externalizing disorders (41). Nosologically, the chronic form of severe irritability (i.e., not limited to mood episodes) has been situated as a disorder of depressive mood and disruptive behavior (6). Emotion dysregulation and irritability are both viewed as transdiagnostic phenomena (2). Many of the emotion-regulatory deficits that are maladaptive in other areas of psychopathology also play a role in irritability (4, 13). Indeed, the very term "dysregulation" is often used to name dimensions and categories of youth irritability, such as DMDD and SMD (3). The overlap among relevant diagnostic categories and absence of nosological consensus around irritability and dysregulation underscores the need for researchers to use empirical methods—and to evaluate these methods—for identifying severely irritable, dysregulated youth in clinical research. Accordingly, the present study seeks to advance the literature by considering multi-informant indicators of irritability and emotion dysregulation in forming subgroups, empirically derived through latent profile analysis.

One critical gap in the literature concerns the psychosocial treatment of youth irritability and dysregulation. The last half-century of psychotherapy research has seen considerable growth in the number of treatment protocols for psychopathology, most of which target rather specific problems or diagnostic categories (e.g., depression, ADHD) (42). Among existing evidence-based therapies, two have been highlighted as first-line interventions for youth irritability: CBT and BPT. A broad intervention framework, CBT has substantial empirical support for improving symptoms across a variety of youth mental health concerns including anxiety, depression, and aggression—all of which can include irritability. Youth CBT is primarily child-directed and often considered a first-line treatment for youth with emotional disorders. Treatment focuses on teaching youth specific skills for regulating and expressing their emotions. Targeting a different set of mechanisms related to youth psychopathology, BPT is considered the first-line and most effective treatment for children presenting with aggressive or disruptive behavior. Focusing mainly on the youth's caregiver(s) and social environment, BPT seeks to alter parenting practices and reverse the negative parent-youth interactions that reinforce youth disruptive behavior. Core BPT components include labeled praise for appropriate behavior, giving effective directives, ignoring attention-seeking behaviors, and consistent implementation of consequences.

Recent developments in intervention science have increasingly moved away from problem- or disorder-specific protocols and in a more *transdiagnostic* direction (43, 44). This has partly reflected the growing recognition that patient presentations do not usually fit cleanly within a single category like the ones around which manualized therapies have been designed. Presentations of severe irritability and emotion dysregulation have therefore been identified as strong candidates for transdiagnostic youth psychotherapies (45, 46). One approach, the *Modular Approach to Therapy for Children with Anxiety, Depression, Traumatic Stress, or Conduct Problems* (MATCH), is a modular, transdiagnostic intervention targeting multiple forms of psychopathology by bringing together common therapeutic procedures shown to be effective (47). Specifically, MATCH includes behavioral/cognitive-behavioral strategies organized within protocols targeting specific psychological problems, including CBT for anxiety, depression, and trauma, and BPT for conduct problems.

We recently re-analyzed data from a randomized effectiveness trial (48) of MATCH to investigate its effectiveness for youth with severe irritability. Overall, results showed that youth with severe irritability who had been randomly assigned to received MATCH tended to show greater improvements compared to those who had received treatment with standard manualized therapies or usual care (9). Yet, this study was primarily a trial of intervention *format* (i.e., modular/transdiagnostic vs. standard/diagnostic vs. usual care), rendering it challenging to draw conclusions about important questions of intervention *content*—i.e., what techniques work best for irritable, dysregulated youth? The modular transdiagnostic guidance and clinical judgment provides some insight into how MATCH could be used clinically (45), but such guidance must be interpreted with caution in the absence of empirical evidence. More generally, there is a paucity of interventions targeting severe irritability directly (2, 8). More research is needed to understand which approaches and content (parent-focused BPT, youth-focused CBT) might be most effective for this subset of youth.

The present study seeks to help fill these gaps regarding the treatment of severe irritability and emotion dysregulation. Specifically, we use data from a community-based implementation trial of MATCH among 200 youth referred for various emotional and behavioral problems (49). In this sample, the number of youth who received MATCH was more than 3× larger than that analyzed in our previous study (9), allowing for a closer and more sophisticated analysis of outcomes. Thus, in this paper we (a) investigate treatment outcomes for empirically derived classes of youth based on their transdiagnostic profiles of irritability and dysregulation, and (b) test whether clinical outcomes differed according to whether they had received BPT for disruptive behavior or CBT for depressed mood.

# MATERIALS AND METHODS

## Participants and Procedures

This study was part of a randomized effectiveness trial of MATCH (47), a transdiagnostic, modular, cognitive-behavioral psychotherapy protocol for youth with anxiety, depression, traumatic stress, and/or disruptive behavior [see Weisz et al. (49) for primary study details]. All participating youth received community-based empirically supported psychotherapy via MATCH. Youth and therapists were randomly allocated to either the *Low-Cost* condition (consisting of therapist training in MATCH, plus inexpensive elements like access to online therapist resources) or the *Consultation + Low-Cost* Condition (consisting of everything in the Low-Cost Condition plus weekly consultation with MATCH clinical experts). Because there were essentially no differences in clinical outcomes between the two

conditions (49), we analyzed the full sample together while accounting for condition as a covariate.

Two-hundred children and adolescents (46% female; $M_{age}$ = 10.73 years, $SD$ = 2.42, range = 7-15) representing diverse racial/ethnic backgrounds (33% White, 28% Black, 24% Hispanic/Latinx, 14% multiracial, 2% other) and their caregivers were referred for youth therapy at four community outpatient mental health clinics in the Northeastern United States. Study inclusion criteria included ages 6-15 on the day of the initial study telephone screen and scoring in the borderline or clinical range on at least one relevant scale (e.g., Withdrawn/Depressed, Aggressive Behavior, Anxiety Problems, Conduct Problems, Internalizing, and Externalizing) of the Youth Self Report (YSR) or Child Behavior Checklist (CBCL). Youth were excluded if they had a recent (past-year) history of suicide attempts or hospitalization for psychiatric concerns, or if they had been diagnosed with schizophrenia, autism spectrum disorder, or an eating disorder. Families were contacted at 0, 3, 6, 9, 12, and 18 months post-baseline to participate in caregiver-report and youth-report outcomes assessments administered by masked research staff. Informed consent and assent were collected from caregivers and youths, respectively. All study procedures were approved by review boards of Harvard University and the Department of Children and Families for the State of Connecticut.

## Measures

### Internalizing and Externalizing Problems

Youth internalizing and externalizing problems were assessed using the CBCL and YSR (50). These are widely used, comprehensive rating scales with parallel caregiver-report (CBCL) and youth-report (YSR) forms. Items are rated on a 3-point scale: 0 (*not true*), 1 (*somewhat or sometimes true*), and 2 (*very true or often true*). The CBCL and YSR both generate a Total Problems scale, two broadband syndrome scales (Internalizing Problems and Externalizing Problems), and eight narrowband syndrome scales (e.g., Aggressive Behavior, Anxious/Depressed). These scales have shown strong evidence for internal consistency, reliability, validity, and utility across multiple samples (50). Both measures were administered approximately quarterly from 0 to 18 months. To promote clinical relevance in interpreting our findings, *t*-scores were used for outcomes analyses models using Internalizing, Externalizing, and Total Problem scale data.

### CBCL/YSR Irritability

Brief parent- and youth-report irritability scales were derived from three items on the CBCL and YSR. These items tap problems with temper loss, mood lability, and stubbornness, rated on the same 0-1-2 scale as described above. The CBCL/YSR irritability scales have been used in several prior studies (51–54). Between the two informants, CBCL irritability has been used more extensively and shows better psychometric properties than YSR irritability, although both were acceptably valid and reliable in a large sample of clinically referred youth (55). In the present investigation, we use these scales as multi-informant dimensional measures of irritability (range: 0-6), administered at all occasions. Baseline irritability data showed that Cronbach's alpha was 0.64 for caregiver-report and 0.63 for youth-report.

### Top Problems

The Top Problems (TP) scale (56) is an idiographic measure designed for youth and caregivers to separately identify up to three "top problems" of greatest concern to be addressed in treatment. Once youth and caregivers identified their top problems in a pre-treatment interview, they completed weekly and quarterly assessments of the current severity of each problem on a 5-point scale from 0 (*not a problem*) to 4 (*a very big problem*). Given that this is an idiographic measure where top problem content varies across participants, Cronbach's alpha is not an appropriate indicator of reliability. Prior research has shown that the TP has shown strong test-retest reliability, convergent and discriminant validity, and sensitivity to change during treatment (48, 56–58).

### Irritability Top Problems

One benefit of the TP measure is that the responses given by caregivers and youth can be reliably recoded into their nearest-matching item on the CBCL/YSR using a well-established coding protocol (59, 60). Applying this protocol, we coded which TPs represented at least one of the CBCL/YSR irritability items—that is, whether or not they identified irritability was one of their TPs for treatment at baseline. Youth and caregivers who reported a TP related to temper loss, mood lability, and so on, were identified by this variable as having an irritability TP (1 = present, 0 = absent). This approach has previously demonstrated evidence of validity and reliability (1). Based on double-coding of a randomly selected 49 cases, reliability was excellent for identifying irritability TPs identified by caregiver-report ($\kappa = 0.95$) and youth-report ($\kappa = 0.98$).

### Emotion Regulation and Dysregulation

The ***Emotion Regulation Checklist*** (ERC) (61) is a 24-item parent-report questionnaire used to assess youth's ability to manage emotions. Caregivers were asked to rate items on a 4-point Likert scale from 1 (*never*) to 4 (*always*) across two scales: *Emotion Regulation* (e.g., happiness, recovering from negative mood, positive responses to adults and peers) and *Lability/Negativity* (e.g., outbursts of anger, intrusive enthusiasm, frustration, mood swings). Evidence supports the reliability and validity of the ERC (61). In this sample, reliabilities were 0.83 for negative lability and 0.55 for regulation.

The ***Children's Emotion Management Scale*** (CEMS) (62–64) was used to examine how youth managed their *sadness* (12 items), *anger* (11 items), and *worry* (13 items). The CEMS subscales assess youths' *inhibition*, *dysregulation*, and *coping* patterns with respect to each particular emotion (i.e., 3 subscales, 3-5 items each, within each emotion). Dysregulation measures inappropriate emotional expression (e.g., "I do things like slam doors when I'm mad," "I cry and carry on when I'm sad.") and coping measures adaptive methods of emotion regulation (e.g., "When I am mad, I can control my temper," "I keep myself from losing control of my worried feelings"). Youth and their caregivers were asked to rate items on a 3-point Likert scale from

1 (*hardly ever*) to 3 (*often*). The present analyses used composite scores for *emotion coping* (calculated as the mean of sadness coping, anger coping, and worry coping scores) and *emotion dysregulation* (calculated as the mean of sadness dysregulation, anger dysregulation, and worry dysregulation scores). The CEMS has shown good reliability and validity (2–6), with alpha of 0.71 for coping and 0.64 for dysregulation.

## Analytic Approach

Analyses were conducted within a latent multivariate framework, in two phases.

### Phase 1: Latent Profile Analysis (LPA)

First, we used latent profile analysis (LPA) to differentiate high- vs. low-dysregulation classes of youth based on 10 indicators: (a) *irritability levels*, as rated on the CBCL and YSR three-item scales; (b) caregiver and youth identification of *irritability as a treatment concern* on the TP measure; (c) *emotion regulation*, as indicated by the CEMS Coping scale and ERC Regulation scale; (d) *emotion dysregulation*, as indicated by the CEMS Dysregulation scale and the ERC Lability/Negativity scale; and (e) *overall psychopathology* on the CBCL and YSR Total Problem raw scores, minus the three irritability items. Irritability TPs were binary variables, treated as probability estimates. Continuous variables were standardized. The emotion regulation variables (CEMS Coping and ERC Regulation) were the only measures where higher scores are considered more favorable; the other measures follow the reverse pattern, where higher scores are considered more severe. As shown in the results, LPA can accommodate these different types and directionality in the data. These 10 variables were selected to collectively capture the key facets of the relevant phenomena—including severe irritability specifically as well as the generation, regulation, and dysregulation of negative emotions broadly—per two informants, multiple methods, and in multiple directions.

Considering the overall complexity of our analytic plan and our *a priori* goal of investigating treatment outcomes for youth with high vs. low levels of multivariate dysregulation/ irritability, we decided to simply estimate a two-class LPA solution and then evaluate its fit overall and relative to a one-class solution. This focused two-class strategy follows in the tradition of some of the earliest applications of latent class/profile modeling (65). More recently, it has been used by Young (66) and Youngstrom (67) to delineate impulsive/reactive aggression constructs in clinical samples. In other LCA/LPA applications, investigators may enumerate many more classes to identify the best-fitting solution—e.g., going up to 6, 7, or more classes, or until convergence problems or fit decrements are encountered. We have adopted this type of thorough k-class enumeration approach in our own work, as appropriate to the research question and the data (68). But this practice requires very large samples and some rather subjective-decision-making on the part of the analyst, leading quantitative experts to recommend that it is almost always advisable to specify a focused *a priori* hypothesis, especially in smaller samples (66). It is possible that our data would reveal that a 3- or 4- or 5-class solution might also fit these baseline data, but such a solution would be inconsistent with the literature and our research question, adding greater complexity to our models while also limiting the utility and generalizability of our findings. Indeed, to continue with class enumeration risks the possibility of spuriously over-extracting classes that do not really exist (69), with the size classes getting smaller, chipping away at the major classes, and threatening the generalizability of the findings. Thus, for this analysis, the two-class solution of high and low dysregulation was well-justified and offered the greatest power for exploring treatment outcomes.

After estimating and evaluating our LPA, all 200 youths were assigned to their most likely class membership: high dysregulation and irritability (hereafter "HIDYS") or low dysregulation and irritability ("LODYS"). These class assignments and their uncertainty (i.e., posterior probability of class assignment) were exported for subsequent analysis. Characteristics of youth within each latent profile were explored to assess the groups' validity and clinical, demographic, and study characteristics.

### Phase 2: Latent Growth Curve (LGC) Models

Next, the two LPA-derived classes were specified as predictors of clinical outcome trajectories via latent growth curve (LGC) models. Our overall approach to these analyses draws from the log-transformed modeling strategy used in several prior randomized trial studies (9, 48, 57), including the primary outcomes of the present study (49). That is, we estimated outcome trajectories as longitudinal models wherein our metric of time was the natural logarithm of the number of days since baseline +1. This approach produces a single log-linear slope coefficient useful for interpretation of clinical outcomes. It is also more parsimonious than alternative approaches such as polynomial strategies to achieve a similar result with more terms (linear + quadratic) or estimating different outcome occasions separately (3-month, 6-month, etc., producing 5× more outcomes to interpret). Results confirmed that log-linear slopes fit the data well.

Substantively, our first question in these models was whether HIDYS and LODYS youth differed in their trajectories of improvement over time. It was expected that youth in the HIDYS group would show greater severity *at baseline*, but it was not clear whether they would improve faster or slower than the LODYS group over time. If the HIDYS group improved faster, this might suggest they are showing a greater response to intervention and/or a pattern of regression to the mean (i.e., higher scores have more room to decline simply as a function of chance and time). If the HIDYS group improved more slowly (or showed no change, or even deteriorated), this would indicate that highly dysregulated and irritable youth are not responding as well to MATCH in the same way that the majority of the sample is. And if the two groups showed parallel trajectories of improvement over time, this would suggest MATCH was similarly beneficial for all youth in this sample, irrespective of whether they are HIDYS or LODYS.

Our second question in these LGC models was about the relative effects of MATCH primary problem/protocol area, DEP or CON. That is, based on results of the baseline clinical assessment, youths were classified into their most appropriate treatment track, including (a) those who were viewed as having a primary depression problem and treated with the MATCH *Depression* CBT protocol ("DEP"); and (b) those who were

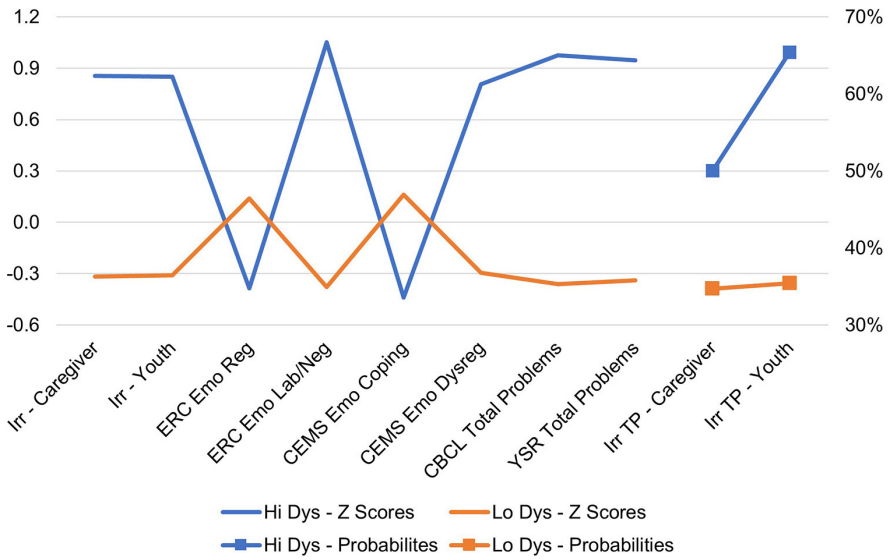


**FIGURE 1 |** Two latent profiles: high dysregulation ($n = 54$) and low dysregulation ($n = 146$). Irr, irritability; ERC, Emotion Regulation Checklist; CEMS, Children's Emotion Management Scales; CBCL, Child Behavior Checklist; YSR, Youth Self-Report; TP, top problems.

viewed as having a primary disruptive behavior problem, and treated with the MATCH *Conduct Problems* BPT protocol ("CON"). If assignment to DEP vs. CON showed significantly different effects on slopes, this would indicate a differential treatment response favoring either CON or DEP. If they were not different, this would suggest that CON and DEP are similarly effective in for treating youth with HIDYS and LODYS profiles.

These questions were investigated in a series of multigroup LGC models for each outcome variable. Within each model, results were simultaneously estimated separately for two groups (HIDYS, LODYS) with major protocols—the MATCH Depression and Conduct protocols (DEP, CON)—modeled as fixed effect predictors of intercepts and slopes within group. The parameters of interest were the coefficients for latent intercepts and slopes within the HIDYS and LODYS groups, as well as the coefficients for the effects of CON and DEP on those slopes. Study questions were examined through individual model $\chi^2$ Wald tests of the equality of these coefficients. A statistically significant $\chi^2$ contrast for the latent intercepts of HIDYS and LODYS would mean one group had higher baseline problem levels than the other group; and a slope difference would mean that one group showed faster problem reduction than the other. Regarding treatment type, if the effect of DEP on slope was different from the effect for CON on slope, this would indicate differential effectiveness such that membership in one protocol/problem group (DEP vs. CON) predicted faster improvement than the other. Significant differences were investigated by examining other model terms to help contextualize the differential effect on slopes, and by probing the differences within each group.

LGC models controlled for covariates representing demographics (age, gender, race), study and treatment variables (clinic, RCT condition, medications, number of sessions), and uncertainty of class assignment. Covariates were specified as predictors of latent slopes and intercepts and were constrained to be equal across groups. Therapist nesting was not included in group-specific models due to the complex patterns of cross-nesting of therapists often treating patients in both LPA groups. Models were estimated in Mplus Version 8 with robust maximum likelihood estimation. Variables were mean-centered within dysregulation groups, such that the latent intercept and slope terms can be interpreted as representing the trajectories for hypothetical average HIDYS and LODYS youth. Baseline indicators of LGC slopes and intercepts were held to variance at 0 for model convergence.

# RESULTS

## Class Differentiation

The two-class solution converged successfully and fit the data well. Entropy was 0.839, indicating a high degree of "cleanness" in the separation between the two classes. Average latent class probabilities for most likely class membership was 0.931 for Class 1 (HIDYS) and 0.966 for Class 2 (LODYS). The Lo-Mendell-Rubin (LMR; $p = 0.0137$), Vuong-LMR (VLMR; $p = 0.0128$), and bootstrapped ($p < 0.0001$) likelihood ratio tests all showed that the two-class solution fit the data better than a one-class solution, and the pattern of AIC/BIC results between the one- and two-class models supported this conclusion as well. **Figure 1** presents the two profiles that characterized youth with high ($n = 54$; 27%) and low ($n = 146$; 73%) levels of dysregulation and irritability. As shown, the highly dysregulated group was nearly 1 *SD* above the sample mean on measures of irritability, dysregulation, and total problems. They also had below-average levels of coping/regulation skills and were considerably more likely to have a TP defined by irritability, especially by youth report.

**TABLE 1 |** Characteristics of the high and low dysregulation groups.

| | Hi dysregulation ($n = 54$) | Lo dysregulation ($n = 146$) | $t$ or $\chi^2$ | $p$ |
|---|---|---|---|---|
| **Proportions, *n* (%), $\chi^2$** | | | | |
| CLC condition, *n* (%) | 21 (38.9) | 78 (53.4) | 3.33 | 0.068 |
| MATCH-depression | 23 (42.6) | 57 (39.0) | 0.21 | 0.649 |
| MATCH-conduct | 26 (48.1) | 49 (33.6) | 3.58 | 0.059 |
| MATCH-anxiety/trauma | 5 (9.3) | 40 (27.4) | 7.44 | 0.006 |
| Receiving medication | 24 (44.4) | 41 (28.1) | 4.81 | 0.028 |
| Female | 24 (44.4) | 68 (46.6) | 0.07 | 0.788 |
| White | 13 (24.1) | 52 (35.6) | 2.39 | 0.122 |
| Black | 16 (29.6) | 39 (26.7) | 0.17 | 0.682 |
| Hispanic/Latinx | 13 (24.1) | 35 (24.0) | 0.00 | 0.988 |
| Multiracial | 9 (16.7) | 18 (12.3) | 0.64 | 0.425 |
| **Levels, *M* (*SD*), *t*** | | | | |
| Age | 10.31 (2.25) | 10.88 (2.48) | −1.48 | 0.141 |
| Sessions attended | 10.43 (10.33) | 10.90 (8.90) | −0.32 | 0.747 |
| **Caregiver report** | | | | |
| TP mean score [a] | 3.72 (0.39) | 3.52 (0.51) | 2.56 | 0.011 |
| Internalizing t-score | 68.44 (7.51) | 63.58 (9.11) | 3.51 | 0.001 |
| Externalizing t-score | 72.61 (5.34) | 61.07 (8.83) | 9.01 | < 0.001 |
| Total t-score [a] | 72.81 (4.23) | 63.90 (6.41) | 9.48 | < 0.001 |
| Irritability sum score [a] | 5.02 (1.07) | 2.95 (1.64) | 8.61 | < 0.001 |
| Defiance sum score | 4.52 (1.30) | 2.47 (1.68) | 8.11 | < 0.001 |
| Aggressive t-score | 76.85 (8.36) | 62.15 (8.31) | 11.09 | < 0.001 |
| Rule-breaking t-score | 67.17 (7.01) | 60.05 (6.95) | 6.41 | < 0.001 |
| Attention t-score | 71.04 (10.03) | 60.95 (8.11) | 7.31 | < 0.001 |
| Withdrawn/Dep t-score | 68.52 (10.69) | 64.53 (9.96) | 2.47 | 0.015 |
| Anxious/Dep t-score | 67.85 (9.30) | 62.72 (8.88) | 3.58 | < 0.001 |
| Conduct t-score | 70.87 (7.41) | 61.41 (7.96) | 7.60 | < 0.001 |
| ODD t-score | 72.80 (6.30) | 60.91 (8.34) | 9.51 | < 0.001 |
| ADHD t-score | 70.22 (7.90) | 60.42 (7.71) | 7.93 | < 0.001 |
| Anxiety t-score | 65.67 (8.31) | 61.64 (8.37) | 3.03 | 0.003 |
| Affective t-score | 70.30 (7.41) | 63.38 (8.77) | 5.15 | < 0.001 |
| **Youth report** | | | | |
| TP mean score [a] | 3.39 (0.72) | 3.15 (0.72) | 2.12 | 0.035 |
| Internalizing t-score | 65.34 (9.84) | 54.77 (10.62) | 6.32 | < 0.001 |
| Externalizing t-score | 64.09 (9.07) | 50.44 (8.47) | 9.85 | < 0.001 |
| Total t-score [a] | 67.34 (8.28) | 54.19 (9.33) | 9.04 | < 0.001 |
| Irritability sum score [a] | 3.94 (1.55) | 1.91 (1.50) | 8.31 | < 0.001 |
| Defiance sum score | 3.30 (1.31) | 1.75 (1.16) | 8.08 | < 0.001 |
| Aggressive t-score | 69.25 (10.71) | 54.93 (5.79) | 12.02 | < 0.001 |
| Rule-breaking t-score | 57.66 (6.41) | 52.88 (3.79) | 6.43 | < 0.001 |
| Attention t-score | 69.09 (10.85) | 57.12 (7.47) | 8.77 | < 0.001 |
| Withdrawn/Dep t-score | 64.70 (10.94) | 57.23 (7.38) | 5.49 | < 0.001 |
| Anxious/Dep t-score | 65.04 (11.11) | 57.23 (7.58) | 5.62 | < 0.001 |
| Conduct t-score | 64.58 (9.82) | 54.48 (5.51) | 9.10 | < 0.001 |
| ODD t-score | 64.45 (7.60) | 54.54 (5.26) | 10.35 | < 0.001 |
| ADHD t-score | 65.83 (7.67) | 56.94 (6.64) | 8.00 | < 0.001 |
| Anxiety t-score | 61.06 (8.73) | 57.78 (7.53) | 2.60 | 0.010 |
| Affective t-score | 65.91 (9.99) | 57.32 (7.34) | 6.58 | < 0.001 |

[a] *Denotes a variable that was included in the LPA model that differentiated the two classes.*

**Table 1** presents further results showing the clinical and demographic characteristics of the two groups. The HIDYS group showed significantly greater severity on the TP and all CBCL/YSR symptom scales and were significantly more likely to be receiving medication and less likely to be receiving the anxiety protocol. However, there were no differences in terms of study condition, gender, race/ethnicity, age, or number of sessions attended. **Table 1** also reveals that youth in the HIDYS class tended to be most often assigned to Conduct (48%) and Depression (43%) MATCH protocols, with only five (9%) falling into the Anxiety or Trauma protocols. Youth in the LODYS Class were somewhat evenly distributed across the protocols for Conduct (34%), Depression (39%), and Anxiety/Trauma (27%). In other words, proportions were sufficient to allow us to compare the effects of Conduct (CON) vs. Depression (DEP) protocols within both the LODYS group ($n = 49$ vs. $n = 57$, respectively) and within the HIDYS group ($n = 26$ vs. $n = 23$, respectively). Given the smaller size of those in the Anxiety/Trauma group, an examination of treatment outcomes for this group was not possible. Instead, analyses focused on the effects of CON group membership and DEP group membership as binary predictor variables, with specific implications for results interpretation noted below where applicable.

## Clinical Outcomes for Youth With High and Low Dysregulation

Outcome trajectories for these the HIDYS and LODYS groups were examined in a series of ten LGC models—five for youth-report variables and five for caregiver-report variables. For brevity and clarity, these results are presented in **Tables 2**, **3** and **Figures 2A,B** organized by coefficient and model number. That is, across all table sections and figure panels, results labeled with the same model number (#1-10) were generated from the same LGC model. The model-implied and observed outcome trajectories followed by youths in the HIDYS and LODYS groups are presented in **Figures 2A,B**, with the corresponding intercept and log-linear growth coefficients reported in **Table 2**. Generally, the degree to which group intercepts (i.e., baseline levels) and log-linear slopes (i.e., change over time) appear visually similar in these charts is a reasonable indicator of whether they are statistically different, with the exact $\chi^2$ ($df = 1$) difference tests reported in the far right column of **Table 2**.

On all outcome measures, the HIDYS group showed significantly higher problem scores at baseline compared to the LODYS group (top portion of **Table 2**). This is as expected given how the classes were formed, but the consistency of this result across internalizing and externalizing problems is notable because classes were not formed based on those scales. In terms of outcomes, caregiver- and youth-rated internalizing, externalizing, total problems, and irritability all showed statistically significant log-linear declines over time, and this effect was largely similar between the high and low dysregulation groups (bottom portion of **Table 2**). On caregiver-rated internalizing problems, for example (see **Table 2**), youth in the HIDYS group started at 68.44 and improved over time at a rate of −1.28 points per log-day, whereas the LODYS

**TABLE 2 |** Latent intercept and log-linear slope growth terms for high and low dysregulation groups.

| LGC model term | Hi dysregulation | Lo dysregulation | Hi vs. Lo |
|---|---|---|---|
| **LGC models (#1-10)** | **Est (SE)** | **Est (SE)** | **$\chi^2$ (*df* = 1)** |
| **Intercept coefficient** | | | |
| Caregiver internalizing | 68.44(0.80)*** | 63.58(0.58)*** | 24.00*** |
| Caregiver externalizing | 72.61(0.57)*** | 61.07(0.56)*** | 209.91*** |
| Caregiver total | 72.82(0.46)*** | 63.90(0.47)*** | 183.60*** |
| Caregiver irritability | 5.02(0.13)*** | 2.95(0.12)*** | 133.44*** |
| Caregiver top problems | 3.72(0.05)*** | 3.52(0.04)*** | 9.18** |
| Youth internalizing | 65.34(1.26)*** | 54.77(0.83)*** | 49.12*** |
| Youth externalizing | 64.09(0.99)*** | 50.44(0.63)*** | 136.09*** |
| Youth total | 67.34(1.06)*** | 54.19(0.75)*** | 103.43*** |
| Youth irritability | 3.94(0.18)*** | 1.91(0.11)*** | 89.97*** |
| Youth top problems | 3.39(0.09)*** | 3.15(0.06)*** | 5.38* |
| **Log-linear slope coefficient** | | | |
| Caregiver internalizing | −1.28(0.21)*** | −1.67(0.12)*** | 2.63 |
| Caregiver externalizing | −1.04(0.18)*** | −1.10(0.10)*** | 0.09 |
| Caregiver total | −1.18(0.19)*** | −1.51(0.12)*** | 2.29 |
| Caregiver irritability | −0.27(0.04)*** | −0.19(0.02)*** | 3.05$^+$ |
| Caregiver top problems | −0.19(0.02)*** | −0.28(0.01)*** | 12.18*** |
| Youth internalizing | −2.32(0.31)*** | −1.75(0.15)*** | 2.64 |
| Youth externalizing | −1.87(0.25)*** | −1.05(0.12)*** | 9.06** |
| Youth total | −2.37(0.29)*** | −1.65(0.14)*** | 5.32* |
| Youth irritability | −0.26(0.05)*** | −0.08(0.02)*** | 11.58*** |
| Youth top problems | −0.30(0.03)*** | −0.31(0.02)*** | 0.01 |

*Models control for the following covariates, mean-centered: clinic (3 dummy codes for 4 clinics), study condition, medication status, age, gender, ethnicity (White, Black, Latinx), number of sessions, problem focus (dummy codes for CON and DEP, not ANX), and probability of latent profile class membership. Thus, these model terms can be interpreted as characterizing the clinical trajectories followed by the average youths in the Hi Dys and Lo Dys groups. LGC, latent growth curve.* $^+p < 0.10$,*$p < 0.05$,**$p < 0.01$,***$p < 0.001$.

group started at 63.58 and improved at a rate of −1.67 points per log-day. These trajectories differed in their baseline scores ($\chi^2 = 24.00$, $p < 0.001$) but not in their rates of change over time ($\chi^2 = 2.63$, $p = 0.105$).

This same pattern for HIDYS vs. LODYS results held across 6 of the 10 outcome variables. That is, the two groups differed at baseline but showed statistically similar slopes of improvement over time on CBCL irritability, internalizing, externalizing, total problems, and on youth-reported top problems and internalizing problems. The other 4 outcome measures, where slopes differed, can be interpreted as follows. On youth-rated irritability, externalizing, and total problems, the HIDYS group was more severe at baseline and improved faster over time than the LODYS group. The values on the scale metrics suggest that, despite these statically significant slope differences, trajectories of improvement were clinically significant for both groups. For example, in both groups youth-reported Total Problems dropped several points below the cutoffs for the "Borderline" (*t*-score $\geq$ 60) and "Clinical" (*t*-score $\geq$ 63) ranges, per Achenbach and Rescorla's interpretive guidelines (50). In fact, this was the case for the outcome trajectories for both groups, per both informants,

**TABLE 3 |** Effects of DEP and CON problem/protocol area on LGC interprets and slopes.

| Regression effect | Hi Dys | Lo Dys | Hi vs. Lo | Dep. vs Con. |
|---|---|---|---|---|
| **LGC Models (#1-10)** | **Est (SE)** | **Est (SE)** | **$\chi^2$ (*df* = 1)** | **$\chi^2$ (*df* = 2)** |
| **LGC intercept regressed on DEP** | | | | |
| Caregiver internalizing | 1.23(2.05) | 3.28(1.36)* | 0.42 | 62.64*** |
| Caregiver externalizing | 1.32(2.91) | 4.13(1.71)* | 0.76 | 32.24*** |
| Caregiver total | 1.02(1.40) | 2.76(1.32)* | 0.90 | 1.09 |
| Caregiver irritability | −0.23(0.46) | 0.73(0.31)* | 3.14$^+$ | 3.58 |
| Caregiver top problems | 0.34(0.22) | −0.09(0.11) | 3.33$^+$ | 2.13 |
| Youth internalizing | 5.53(4.19) | 1.83(2.18) | 0.65 | 11.19** |
| Youth externalizing | 3.06(3.22) | 3.54(1.66)* | 0.02 | 9.66** |
| Youth total | 4.35(4.10) | 2.57(1.95) | 0.16 | 1.98 |
| Youth irritability | 1.35(0.57)* | 0.25(0.30) | 3.08$^+$ | 2.03 |
| Youth top problems | 0.67(0.39)$^+$ | 0.15(0.16) | 1.57 | 2.15 |
| **LGC intercept regressed on CON** | | | | |
| Caregiver internalizing | −5.86(2.22)** | −7.88(1.62)*** | 6.29 | |
| Caregiver externalizing | 3.87(2.62) | 10.58(1.55)*** | 5.10* | |
| Caregiver total | 0.09(1.16) | 2.00(1.28) | 1.24 | |
| Caregiver irritability | −0.72(0.46) | 0.94(0.35)** | 8.74** | |
| Caregiver top problems | 0.19(0.22) | −0.17(0.11) | 2.20 | |
| Youth internalizing | 0.79(4.11) | −4.70(2.10)* | 1.45 | |
| Youth externalizing | 9.21(2.68)** | 6.45(1.90)** | 0.67 | |
| Youth total | 5.41(4.01) | 0.04(1.99) | 1.45 | |
| Youth irritability | 1.06(0.45)* | −0.16(0.31) | 5.02* | |
| Youth top problems | 0.45(0.37) | 0.27(0.17) | 0.19 | |
| **LGC slope regressed on DEP** | | | | |
| Caregiver internalizing | −0.09(0.50) | −0.44(0.34) | 0.37 | 8.06* |
| Caregiver externalizing | −0.18(0.38) | −0.56(0.30)$^+$ | 0.69 | 0.10 |
| Caregiver total | 0.27(0.43) | −0.36(0.33) | 1.45 | 4.05 |
| Caregiver irritability | −0.02(0.08) | −0.12(0.05)* | 1.06 | 2.15 |
| Caregiver top problems | −0.06(0.08) | 0.03(0.04) | 0.98 | 2.64 |
| Youth internalizing | −1.35(0.99) | 0.04(0.40) | 1.66 | 3.03 |
| Youth externalizing | −0.70(0.83) | −0.17(0.30) | 0.35 | 0.29 |
| Youth total | −0.52(1.01) | 0.02(0.36) | 0.24 | 1.54 |
| Youth irritability | −0.25(0.15) | 0.06(0.04) | 3.90* | 4.00 |
| Youth top problems | −0.18(0.10)$^+$ | −0.03(0.04) | 1.93 | 0.45 |
| **LGC slope regressed on CON** | | | | |
| Caregiver internalizing | 0.43(0.42) | 0.40(0.31) | 0.00 | |
| Caregiver externalizing | −0.10(0.30) | −0.50(0.28)$^+$ | 1.02 | |
| Caregiver total | 0.58(0.33)$^+$ | 0.18(0.29) | 0.87 | |
| Caregiver irritability | 0.10(0.07) | −0.09(0.06) | 4.48* | |
| Caregiver top problems | 0.00(0.07) | 0.07(0.04)$^+$ | 0.64 | |
| Youth internalizing | −0.35(0.95) | 0.44(0.41) | 0.58 | |
| Youth externalizing | −0.44(0.75) | −0.09(0.34) | 0.17 | |
| Youth total | 0.07(0.94) | 0.33(0.40) | 0.07 | |
| Youth irritability | −0.06(0.15) | 0.10(0.05)* | 0.98 | |
| Youth top problems | −0.13(0.09) | −0.04(0.05) | 0.82 | |

*Models control for the covariates noted previously* ***(Table 2)****. LGC, latent growth curve; DEP, Depression problem focus, treated with CBT; CON, Conduct problems focus, treated with BPT.* $^+p < 0.10$, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

on all normed outcome measures. Lastly, on caregiver-rated TP severity, the groups showed somewhat more similar ratings at baseline (though still statistically different), and over time the LODYS group improved faster than the HIDYS group. These diverging trajectories are potentially meaningful, result in a ∼1-point score gap at 18-months, with the HIDYS falling closer to the 4 (*very big problem)* end of the severity scale and the LODYS group winding up closer to 0 (*not a problem*).

## Effects of BPT-Conduct and CBT-Depression Protocols on Outcome Trajectories

The effects of LGC intercepts and slopes regressed on DEP and CON are presented in **Table 3**. Again, these DEP and CON variables represent binary dummy codes for 2 of the 3 possible MATCH primary problem/protocol areas; thus, the values presented in **Table 3** can be interpreted as regression coefficients summarizing the effects that membership in the DEP or CON group had on "nudging" the LGC intercepts and slopes, relative to an ANX reference group (for which estimates are not presented). The benefit of this approach is that it yields results for the *absolute* effects that DEP and CON have on LGC slopes and intercepts (i.e., whether the effect is different from zero, reported in the HIDYS and LODYS columns) as well as a method for comparing the *relative* size of those effects in the rightmost two columns. Specifically, the model Wald $\chi^2$-tests in this table show whether the coefficients for those effects (a) differ from one another ("Dep vs. Con" column) and (b) whether they differ between the dysregulation groups ("Hi vs. Lo" column).

Of highest interest are the effects of DEP and CON on latent slopes (see **Table 3**, far right), where significant slope contrast values served as a gateway for further inspection of the other terms in the table. Here, there was only one outcome out of 10—caregiver-rated internalizing problems—that showed a significant differential effect for DEP vs. CON, $\chi^2$ (2) = 8.06, $p = 0.018$. When probed, the DEP vs. CON effect on slope was evident in the LODYS group ($\chi^2$ (1) = 7.37, $p = 0.007$) but not the HIDYS group ($\chi^2$ (1) = 1.18, $p = 0.278$), and was also accompanied by a differential effect on intercept ($\chi^2$ (1) = 17.40, $p < 0.001$). These results (see **Figure 3**) suggest that these effects within the LODYS group might be accounted for by regression to the mean, where those treated with DEP had much higher internalizing *t*-scores at baseline compared to those treated with CON in that same group. It makes sense that youth with higher internalizing scores should be treated with DEP, and that they would decline faster, for reasons of treatment appropriateness and perhaps regression to the mean. Further, the LODYS-CON youth had little room to improve, as they were already below the threshold for clinical significance ($t < 60$) on caregiver-rated internalizing problems at baseline.

# DISCUSSION

We investigated multi-informant clinical outcome trajectories for two latent classes of treatment-referred youth—those characterized by high vs. low profiles of irritability and emotion dysregulation—and we tested whether these trajectories differed for those treated with BPT for conduct problems vs. CBT for depression. Overall, two findings emerged. First, high- vs. low-dysregulation youth were mostly similar in their trajectories, showing statistically and clinically significant improvement over time. Although a few significant differences in slopes emerged (caregiver top problems and some YSR scales), the overall pattern (**Table 2**, **Figures 2A,B**) was one in which both groups showed clear improvements across all measures. Second, we found virtually no evidence of different treatment outcomes based on one's primary problem/protocol area. That is, in treating clinically referred youth with (or without) severe dysregulation, a modular transdiagnostic approach involving BPT for externalizing problems and/or CBT for depression appears to be helpful. Importantly, the highly dysregulated youths (27% of the sample) showed significant and comparable improvements in all outcomes regardless of whether they received BPT ($n = 26$) or CBT ($n = 23$) as a primary approach.

One important caveat should be highlighted here to inform further interpretation of our findings: There was not random assignment to problem/protocol (CBT-Depression vs. BPT-Conduct), so causal explanations cannot be drawn as if this were a randomized trial comparing these two approaches. But while random treatment allocation is appropriate for causal inference regarding effectiveness, the world of routine youth mental health care is one of non-randomized allocation. That is, community clinicians do not randomly select one of two protocols to administer to patients referred to them who meet eligibility criteria. Instead, best practices involve conducting a comprehensive baseline assessment and developing a treatment plan involving EBTs based on the best available evidence, clinician judgment, and family preference. In this regard, our non-randomized comparison of CBT vs. BPT for youths with high and low dysregulation represents more of a real-world comparison and a useful contribution to the literature, highlighting the potential value of prospective randomized trials in the future.

In regard to the four variables where the groups' slopes differed, the pattern of this difference varied by informant and appeared to be largely related to baseline differences. For instance, on youth-rated externalizing, total, and irritability, the HIDYS group improved faster than the LODYS group. This pattern may suggest greater clinical benefits for the HIDYS group; however, it is a small difference with unclear practical significance and likely related to regression to the mean (i.e., youth in the HIDYS group started treatment with higher scores, and therefore had more room to improve even if only due to random chance with the passage of time). More importantly, both groups improved to such an extent that they fell well below the borderline and clinical cutoffs on these measures, consistent with the overall pattern described above. However, a unique pattern was observed for caregiver-rated TP severity, where the groups were equivalent at baseline and the LODYS group improved faster than the HIDYS group. Importantly, this suggests that greater levels of dysregulation/irritability predicted slowed improvement and greater treatment needs in these personalized domains of functional problems, at least per

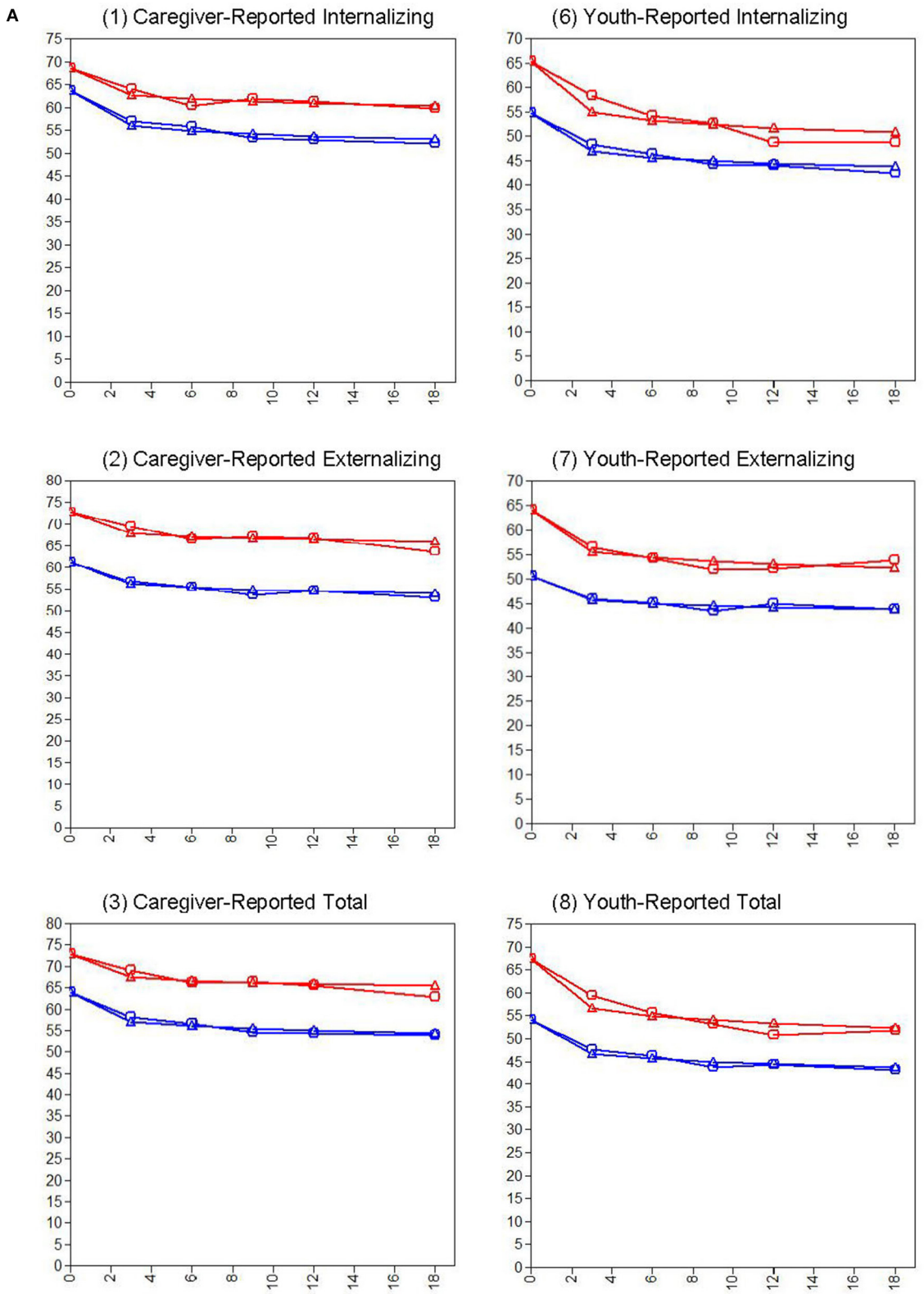


**FIGURE 2 |** Continued

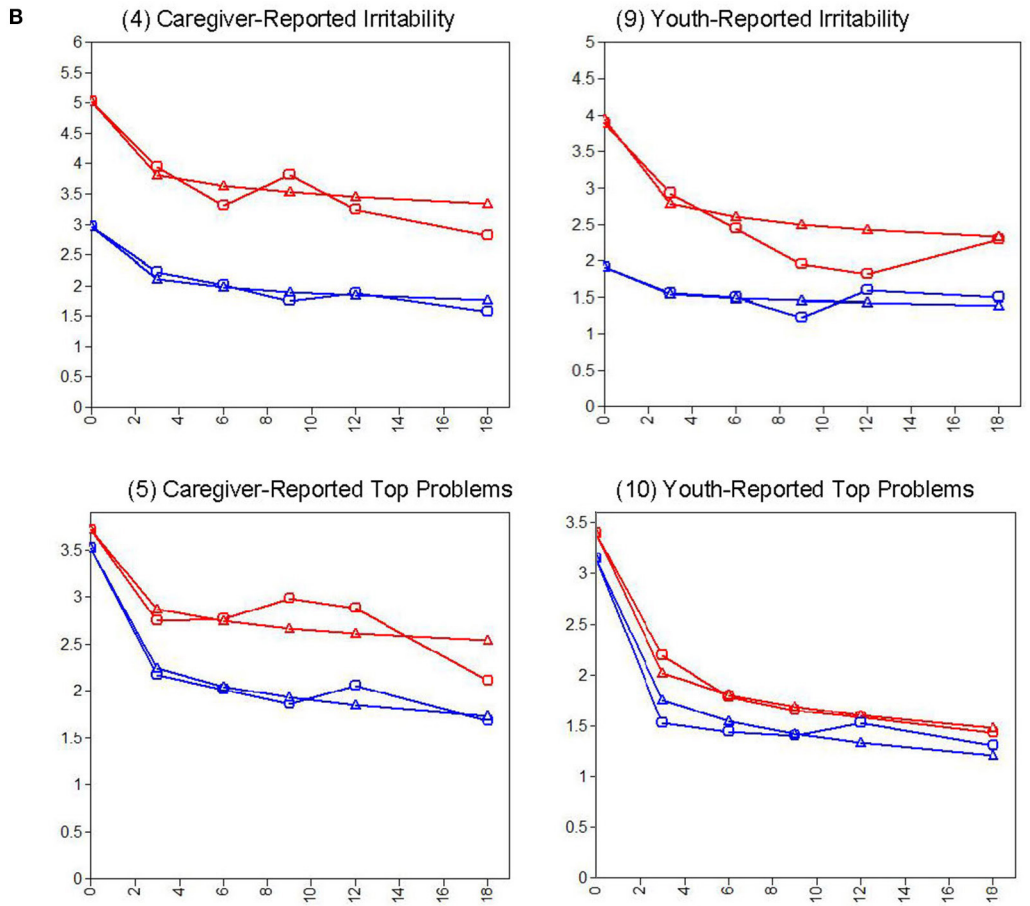


**FIGURE 2 | (A)** CBCL and YSR problem trajectories for youth in the high dysregulation (Red) and low dysregulation (Blue) groups over time (0 to 18 months). Models control for the covariates noted previously **(Table 2)**. **(B)** Irritability and top problem trajectories for youth in the high dysregulation (Red) and low dysregulation (Blue) groups over time (0 to 18 Months). Models control for the covariates noted previously **(Table 2)**.

caregiver report. Alternatively, this pattern might be explained by the unique properties of the TP measure, which is designed to pull for high scores from *all* participants at baseline, regardless of clinical severity. That is, although the HIDYS and LODYS groups appeared similarly severe on TPs in a *subjective, idiographic sense* (see intercepts in **Figure 2A**, Panel 5), we know that the HIDYS group was more severe at baseline in an *objective, nomothetic sense* (see **Figure 1**, **Table 2**). Thus, caregiver TP scores for the LODYS group should be interpreted in light of these properties—i.e., there might be some degree of inflation in the LODYS baseline TP scores, and one might expect their scores to drop faster simply as a function of the group's lower overall severity (as seen across all other measures and informants).

## Implications and Limitations

One important aspect of this study's design was that a thorough clinical assessment was conducted at baseline in order to guide treatment according to how each case was conceptualized. Youth whose assessment data indicated a primary mood problem received CBT, whereas those whose primary problem was disruptive behavior received BPT (2, 45). Although assessment is sometimes given limited attention in intervention research, accurate identification of the problem is an essential precondition for effective treatment. Perhaps especially in youth mental health, careful measurement is important and challenging, requiring multi-informant, evidence-based assessment approaches (60, 70, 71). Challenges with assessment and diagnosis of severe irritability are what prompted a groundswell of controversy and research in this area to begin with, and which continue presently (3, 6). Differential diagnosis for youth irritability can involve over a dozen different diagnostic categories—cutting across internalizing, externalizing, neurodevelopmental, and other domains—of which irritability is a core symptom or associated feature. Interventions such as MATCH rely heavily on assessment data for (a) the initial routing of the treatment plan to target a core problem area, and (b) ongoing progress-monitoring for treatment personalization and outcomes evaluation (48, 49). Thus, effective intervention for severe irritability begins with an effective assessment to clarify the presentation and focus of treatment (9, 45).

Treatments like MATCH might be considered part of a "first-generation" of transdiagnostic protocols—what some have begun

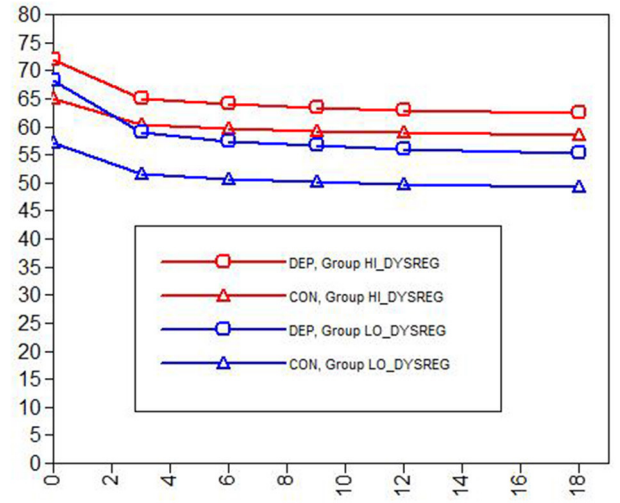


**FIGURE 3 |** Caregiver-rated internalizing problems by dysregulation group (HI vs. LO) and problem/protocol (CON vs. DEP). DEP, Depression problem focus, treated with CBT; CON, Conduct problems focus, treated with BPT.

calling "multi-diagnostic" rather than truly transdiagnostic. Research is emerging on promising new transdiagnostic approaches. One example is FIRST (72–74), which includes cross-cutting evidence-based principles that have been shown to be effective for disruptive behavior, mood, and anxiety problems; thus, a therapist could employ one or more principles tailored to address irritability and dysregulation as it manifests across these different dimensions of psychopathology. Another example is the Unified Protocol for Children and Adolescents (UP) (75), which was originally developed for emotional disorders (i.e., anxiety, depression) and has recently been adapted for irritability/anger as well (46, 76). Rather than compiling a large, complicated menu of treatment elements as MATCH does, these newer interventions focus more on transdiagnostic *principles* that have evidence supporting their effectives across major swaths of youth psychopathology (e.g., emotional disorders, or internalizing and externalizing disorders). It is possible that interventions like FIRST and UP, which do not require the clinician to classify each patient into this or that category, would be more efficient and effective. These are important questions for future research.

Some limitations and strengths should be noted. Limitations include the lack of certain instrumentation that could have shed further light on study questions. Namely, diagnostic data were not collected; nor were there multi-informant or multi-modal assessments of irritability, mood, or emotion dysregulation beyond the caregiver and self-report versions included here. More objective interviewer, behavioral, and physiological data could be helpful in future studies, especially to appropriately measure the emotion generation vs. regulation components of emotion regulation phenomena. However, the present study did help overcome these challenges by using carefully selected indicators in line with an irritability and emotion dysregulation framework, to tease apart empirically derived profiles of high vs. low dysregulation. This represents a methodological improvement over prior secondary analyses of trial data, which have employed observed variables with greater measurement error (9, 10). One additional strength of the present study is the diversity reflected in the participant sample, and the implementation of procedures in routine care settings with community clinicians. By nature, LGC models are exploratory, so generalizability and replicability may be limited. Alternative "manual" approaches to sample splitting are sometimes used, such as using a median split or applying cutoffs on one or more measures. This approach has been used in previous analyses attempting to simulate an randomized trial comparing different therapies among a subsample with irritability and impairment (9). However, these approaches are only as strong as the chosen instruments, informants, and cutoffs, which all have their own limitations. In the present study, such concerns were mitigated by our multivariate two-class LPA, our four community outpatient clinics, and the diverse clinical and demographic characteristics of our sample—all of which help promote generalizability and replicability. Lastly, our data cannot speak to specific treatment elements that might be responsible for the observed clinical gains, or the mechanisms of change underlying those gains. It is likely that well-established therapeutic principles in these EBTs (e.g., behavioral activation, changing environmental contingencies, increasing positive attention, restructuring negative cognitions, exposure, and rehearsal of adaptive behaviors) are likely to play important roles [for a practitioner-oriented discussion, see (45)]. It is important for future research to disentangle therapeutic components and mechanisms, to support the development of more personalized and effective approaches.

## Conclusions

The present findings lend support to the notion of applying "old" treatments (CBT, BPT) to "new" problems (irritability/dysregulation), at least when doing so is guided by assessment data and clinician judgment. Well-established cognitive-behavioral treatments and principles provide large toolbox of potentially effective tools. These tools seem to remain effective for practitioners who continue to treat common presentations of emotional and behavioral disturbance in youth, even as researchers work to shed light on new questions about irritability and dysregulation within the context of those presentations. Indeed, evidence-based practice requires using strategies that are known to be effective in general, applying them with a particular youth, a particular clinician, and a feedback loop involving treatment guided by assessment guided by treatment—and so on (77). In this regard, the present study advances the literature while also highlighting important directions for future research. Specifically, there is a need to learn how to make new and old interventions *even more effective* for a variety of clinically referred youth populations—including the most irritable and dysregulated among them.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Committee on the Use of Human Subjects at Harvard University; and the State of Connecticut, Department of Children and Families' Institutional Review Board (IRB). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

SE was responsible for the initial conceptualization, data curation, analysis, writing, and editing of this paper. MW and SH contributed to the literature review and initial drafting. JW was principal investigator on the study and made contributions including data, resources, and editing/revising. All authors contributed to conceptualization, reviewing, approved, and agreed to the submission of this manuscript in its current form.

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**Conflict of Interest:** JW is a co-author of the treatment protocol (MATCH; Chorpita & Weisz, 2009) used in this study and receives some income from its sales.

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# Deficits in Emotion Regulation Partly Mediate the Relation Between Sleep Problems and Depressive Symptoms in Adolescent Inpatients With Depression

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Sleep problems are a risk factor for the development of depressive disorders and influence the severity and treatment of depressive symptoms negatively. To enhance treatment for depression in young people, it is important to advance the understanding of the relationship between sleep problems and depressive symptoms. Since deficits in emotion regulation are discussed as possible underlying mechanisms, the present study investigated the mediating effect of maladaptive and adaptive strategies for emotion regulation on the association between sleep problems and depressive symptoms. Emotion regulation strategies, depression and sleep quality were assessed via self-report in a large clinical sample of 602 adolescents (age 13–18 years) who reported clinically relevant symptoms of depression. The questionnaires were assessed at admission for inpatient psychiatric treatment. Correlation and mediation analyses were performed. There was a significant partial mediation effect ($\beta = 0.554$, $p < 0.001$, $R^2 = 0.527$), indicating that sleep problems influenced depressive symptoms via the decreased use of adaptive strategies and the increased use of maladaptive strategies. Additionally, a direct effect of sleep problems on depressive symptoms emerged ($\beta = 0.251$, $p < 0.001$, $R^2 = 0.364$). This cross-sectional study provides first indications that additional treatment modules focusing on sleep and ER skills in prevention and treatment programs for adolescents would be important steps. Longitudinal studies are needed to substantiate these results.

**Keywords: sleep problems, depressive symptoms, deficits in emotion regulation, adaptive and maladaptive strategies, adolescents**

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## INTRODUCTION

Depression in youth is a prevalent disease associated with a high risk of chronicity and functional impairment (1). Sleep problems are common and may aggravate the course of the disease (2, 3). Recent evidence outlines the importance of emotion regulation (ER) as a possible underlying mechanism of the association between sleep problems and depression (4, 5). Mood disorders were indirectly related to sleep problems through lower problem solving and greater rumination in a nationally representative adolescent US sample (5). Also longitudinal evidence emphasized the role

of maladaptive ER as mediator between poor sleep quality and depression in adults with current and remitted depression as well as in healthy controls (4).

However, in adolescents with clinically relevant levels of depression empirical evidence is missing. Furthermore, the described studies miss to include adaptive strategies in contrast to maladaptive strategies when looking at the indirect association of depression with sleep problems through dysfunctional ER (6). The present study aims to fill these gaps. It seems to be relevant to examine the associations between sleep problems, dysfunctions in ER and depressive symptoms in clinical adolescents with depression to strengthen prior findings. The results may help to provide insights to inform treatment and prevention efforts in adolescent depression.

## Sleep and Depression

Around 75% of children and adolescents with depression report sleep problems, mainly in the form of insufficient sleep, non-restorative sleep and increased daytime sleepiness (7, 8). The natural circadian phase shift toward eveningness during adolescence (9) contrasts with social duties encouraging early waking (e.g., school/working timing). This social jetlag may lead to sleep loss and insomnia in many adolescents with consecutive mental health problems such as clinical depression (10). Sleep problems are not just a diagnostic criterion for depression according to the International Classification of Diseases (ICD-10), but are also a relevant risk factor for the development and maintenance of depressive disorders. In adolescents, a recent meta-analysis showed that shorter sleep duration increased the risk of mood deficits (OR = 1.55) (11). Another meta-analytic study revealed that people with sleep problems have a twofold higher risk of developing depressive disorders compared to people without sleep problems (2). In addition, sleep problems in adolescence are associated with more severe symptoms of depression, longer depressive episodes and suicidal thinking, and have a negative influence on the course of treatment (3, 12–14).

Two studies examined differences in sleep problems between healthy girls and boys (between 9 and 16 years) at low and high familial risk for depressive disorders (one parent with recurrent depression) (15, 16). They found significant differences between subjective reports of sleep disturbances (e.g., daytime sleepiness, difficulties falling/staying asleep) between both groups, especially in girls (16). The authors hypothesized that the high-risk adolescents had an increased risk to develop psychopathology such as depression due to cognitive and affective impairments which were caused by disturbed sleep (16). There are several studies that support these assumptions by (1) showing that sleep problems impair executive functioning skills such as acquisition, consolidation and recall of information (17) and (2) indicating that sleep problems increase negative affective states and decrease positive ones as well as impair emotion regulation processes (18).

Although the association between sleep problems and depressive symptoms is complex and seems to be bidirectional (19), a systematic review emphasizes that the impact of sleep problems on depression is much stronger and persistent than the other way around (20).

## Deficits in ER and Depression

ER refers to the ability to influence emotions in terms of their intensity, duration, timing and expression (21). In general, ER strategies are classified as adaptive and maladaptive according to their functionality (22). Adaptive strategies (e.g., cognitive reappraisal, acceptance) aim to reduce unpleasant emotional experiences and to maintain a person's well-being with regard to his/her goals and needs in the long term. Maladaptive strategies (e.g., rumination, suppression) are also able to reduce unpleasant emotions, but only in the short term. Thus, maladaptive strategies are often unable to maintain this inhibiting effect on unpleasant emotional experiences, and in the long term, such strategies counteract a person's well-being (23). The usefulness of ER strategies is context-dependent and cannot be generalized for every situation (24). Nonetheless, evidence suggests that the frequent use of maladaptive strategies such as avoidance and suppression is associated with impairing psychopathology such as depressive symptoms in adolescents (6).

Adolescence appears to be a critical time period for difficulties in ER due to endocrinological, cognitive and socio-emotional changes and challenges, e.g., emotional separation from the parents, first sexual encounters and higher social stressors due to a greater importance of the peer group (6). This leads to a higher frequency and intensity of emotions in adolescence compared to childhood, and an increased demand to regulate emotions (25). Given that cognitive skills, especially executive functions, are not fully developed in adolescents, cognitive strategies (such as reappraisal and problem solving) may be less accessible for children and adolescents (6). In addition, as mentioned above sleep problems impair executive functions (17) which in turn might reduce the ability to regulate emotions. As a consequence, an increased use of maladaptive strategies may enhance the development of depressive symptoms, whereas the use of adaptive strategies may be protective against the development of psychopathology. The increased demand to regulate emotions in adolescence on the one hand, and difficulties in ER on the other hand, may contribute to the emergence of depressive disorders during adolescence (26, 27). ER deficits may pose a risk factor for adolescent psychopathology. For example, a meta-analysis showed that rumination as one maladaptive strategy was a significant predictor of depressive symptoms (28).

Furthermore, a meta-analytic review of studies encompassing school samples revealed an association between the habitual use of adaptive or maladaptive strategies and depressive symptoms (i.e., fewer symptoms for adaptive strategies; $r = -0.35$, more symptoms for maladaptive strategies; $r = 0.42$) (6). Also in adult samples, the relation between maladaptive ER and depressive symptoms emerged in a sample of diagnosed depressive patients (22). In particular, the use of maladaptive strategies was more important for psychopathology than the non-use of adaptive strategies. However, evidence among youth with clinical relevant levels of depression is scarce.

## Relationship Between Sleep and ER

Studies exploring the relationship between sleep and ER found that experimentally induced poor sleep led to deficits in ER in adolescents and adults (29, 30). After sleep deprivation,

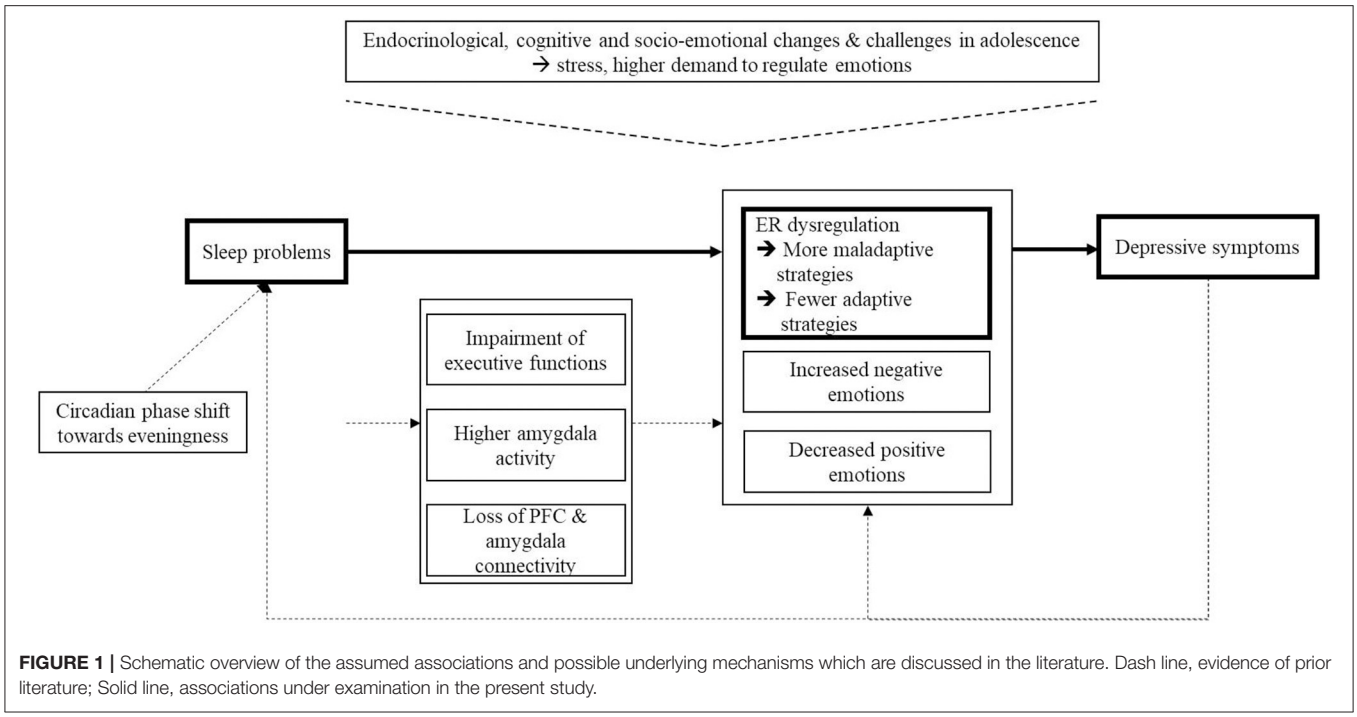


**FIGURE 1 |** Schematic overview of the assumed associations and possible underlying mechanisms which are discussed in the literature. Dash line, evidence of prior literature; Solid line, associations under examination in the present study.

participants reported a greater intensity of negative emotions, such as being more anxious, angry and irritable, and more difficulties in ER. Neuroimaging studies indicate that brain regions involved in ER are influenced by poor sleep (31, 32). Yoo et al. (32) investigated the effect of sleep deprivation on an emotional stimulus viewing task by using functional magnetic resonance image (fMRI) in young adults. The authors examined the activation of and the connectivity between the amygdala and the medial-prefrontal cortex (MPFC), both of which play an important role in the processing of emotional information (33). The results revealed higher amygdala activation and a loss of connectivity between the amygdala and the MPFC in a sleep-deprivation group compared to a sleep-control group (32), suggesting a higher amygdala response to negative emotional stimuli and a failure of top-down control after sleep deprivation. **Figure 1** illustrates the assumed associations and summarized possible underlying mechanisms which were discussed in the literature (as described above).

The present study aims to replicate the reported mediation of ER dysfunction on the association of sleep problems and depressive symptoms in a clinical sample of adolescents with diagnosed depression (4). Dysfunctional ER is defined as increased use of maladaptive strategies to regulate emotions and a decreased use of adaptive strategies. Thus, we expect high correlations between poor sleep, depressive symptoms and an increased use of maladaptive strategies and a decreased use of adaptive strategies. To investigate differences between age and gender, these variables are examined as continuous covariates in the analyses. In addition, we compare two age groups—early adolescence (age 13–15) and late adolescence (age 16–18)—regarding the extent of sleep problems, depressive symptoms and ER strategies. Due to an increased circadian phase shift and higher emotional challenges in adolescence, we assume more severe symptoms in older adolescents. According to prior literature, we hypothesize that girls will show greater sleep problems, depressive symptoms and dysfunctional ER.

# MATERIALS AND METHODS

## Sample

Routine data, including questionnaires assessing sleep problems, depressive symptoms and ER were collected from all patients (aged 13–18 years) who were admitted to the LWL-University Hospital Hamm, Germany from 01/2016 to 06/2018. The hospital provides child and adolescent psychiatric care in an area with a population of 1.5 million inhabitants covering both urban and rural areas. It is the sole provider of inpatient child and adolescent psychiatric care for the study area. The final sample comprised 602 inpatients, of whom 421 (69.9%) were female. The mean age of the sample was 15.16 years (SD = 1.32). All included inpatients were diagnosed by clinicians with a depressive disorder or a depressive conduct disorder (inclusion criteria), which was the main diagnosis for 542 (90%) of the participants (F32.0; F32.1; F32.2; F32.3; F33.0; F33.1; F33.2; F33.3; F92.0; ICD-10). 78 of the 602 inpatients were diagnosed by clinicians with an anxiety disorder. 238 (39.5%) of the inpatients were diagnosed with one comorbid diagnosis, 90 (15%) with two comorbid diagnoses and 48 (8%) with more than two diagnoses. 226 (37.5%) were diagnosed with one diagnosis. The scientific use of the routine data was approved by the ethical review board of the Ruhr-University Bochum (registration number: 4359-12). All participants completed questionnaires on a laptop and were supported by a psychologist to provide the opportunity to ask

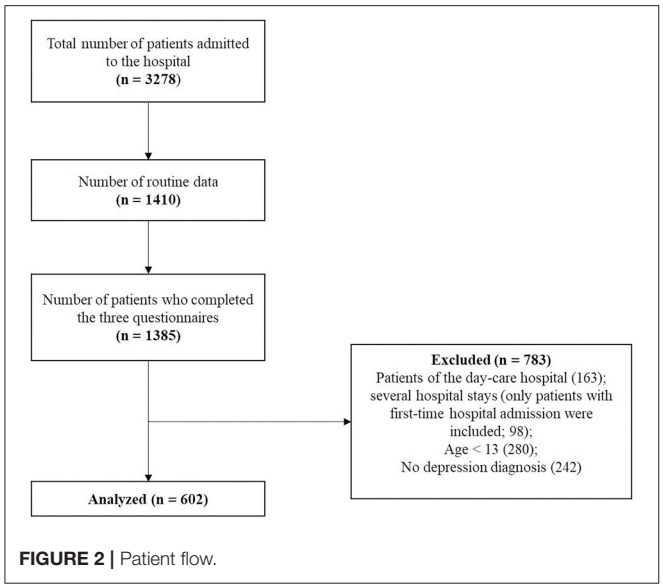


**FIGURE 2 |** Patient flow.

questions if necessary. Details of the flow of participants are provided in **Figure 2**.

## Measures

### ER

ER was assessed using the German-language Questionnaire on ER Strategies in Children and Adolescents (Fragebogen zur Erhebung der Emotionsregulation bei Kindern und Jugendlichen; FEEL-KJ) (34). The FEEL-KJ is a self-report questionnaire assessing different ER strategies in response to the emotions anger, sadness and anxiety. It consists of 90 items and was developed for children and adolescents aged from 10 to 20 years. For each of the three emotions, both adaptive and maladaptive strategies are assessed with two items each. Adaptive strategies are Problem Solving (e.g., "I try to change what makes me sad."), Distraction (e.g., "I do something fun."), Lightening the mood (e.g., "I think about cheerful things."), Acceptance (e.g., "I accept what makes me sad."), Forgetting (e.g., "I try to forget what makes me sad."), Reappraisal (e.g., "I tell myself it is nothing important.") and Cognitive Problem Solving (e.g., "I think about how I can solve the problem."). Maladaptive strategies are Giving up (e.g., "I do not want to do anything."), Aggressive Action (e.g., "I start a quarrel with someone."), Withdrawal (e.g., "I do not want to see anyone."), Self-Devaluation (e.g., "I blame myself.") and Perseveration (e.g., "I keep thinking about why I am sad."). These strategies are subsumed into two subscales, "adaptive strategies" and "maladaptive strategies." Each item is rated on a 5-point scale from almost never (1) to almost always (5). Sum scores range from 42 to 210 for adaptive strategies and from 30 to 150 for maladaptive strategies. Norm values are indicated with $T$-values. For adaptive strategies $T$-values $< 40$ are conspicuous (less use of adaptive strategies) and for maladaptive strategies $T$-values $> 60$ are conspicuous (often use of maladaptive strategies). The FEEL-KJ has shown good internal consistencies, with Cronbach's $\alpha = 0.93$ and a test-retest reliability of $r_{tt}$ =0.81 for adaptive strategies and Cronbach's $\alpha = 0.82$ and a test-retest reliability of $r_{tt}$ =0.73 for maladaptive strategies (34). Construct validity between CERQ (Cognitive Emotion Regulation Questionnaire for Children) (35) and the FEEL-KJ was investigated in a large sample of Dutch-speaking Belgian children and adolescents ($N = 1102$) (36). The correlations revealed a strong positive relation between the adaptive emotion regulation scales of these questionnaires ($r = 0.67$, $p < 0.001$) and a positive relation between the maladaptive scale of the FEEL-KJ and the Non-Adaptive-Emotion-Regulation scale of the CERQ ($r = 0.36$, $p < 0.001$).

### Sleep Habits

The German-language Sleep Inventory for Children and Adolescents (Schlafinventar für Kinder und Jugendliche; SI-KJ) (37) is a 28-item questionnaire to assess the sleep habits of children and adolescents aged 5–18 years over the past 3 months. To assess sleep problems, the two subscales "difficulties in initiating and maintaining sleep" (e.g., "In the evening I have a hard time falling asleep.") and "daily well-being" (e.g., "During the day, I am tired at school or when I am playing.") were used in the present study. The items are measured on a 3-point Likert-scale ranging from 0 (not applicable) to 2 (exactly or frequently applicable). Sum scores range from 0 to 12. The sum score divided by the number of items $\geq 1$ is defined as a cut-off for sleep problems. The internal consistency of these items in the current sample was Cronbach's $\alpha = 0.76$. As norms are only available for children aged 8–11 years, sum scores were used for the statistical analyses.

### Depressive Symptoms

Depressive symptoms were assessed with the German-language Depression Inventory for Children and Adolescents (Depressions-Inventar für Kinder und Jugendliche; DIKJ) (38). The DIKJ is a 26-item self-report questionnaire assessing the severity of depressive symptoms. It covers all relevant DSM-5 criteria for a depressive episode in a manner suitable for children and adolescents from the age of 8 years (39). Sum scores range from 0 to 50. The presence of clinically relevant depressive symptoms is indicated by a $T$-value $> 60$. The DIKJ has shown good psychometric properties, with Cronbach's $\alpha = 0.92$ in a clinical sample (38). The internal consistency in the current sample was Cronbach's $\alpha = 0.86$. To minimize item content overlap between the SI-KJ and the DIKJ, the sleep item was removed from the depression scale; therefore, sum scores were also used for the statistical analyses.

## Statistical Methods

All analyses were performed using SPSS 26.0 for Windows. The two-sided level of significance was set at $\alpha$ =0.05. To investigate direct and indirect effects between sleep problems and depressive symptoms, and the use of adaptive and maladaptive ER strategies as possible mediators, a regression analysis using PROCESS (40) was conducted. The regression model with depressive symptoms as dependent variable included the z-transformed sum score

of the SI-KJ as independent variable and z-standardized FEEL-KJ total scores of adaptive and maladaptive ER strategies as mediators. Based on sample size calculations for mediation analyses using bootstrapping of Fritz and Mac Kinnon (41), for assumed weak pathways of the mediation model a sample size of 558 participants is needed. Age and gender were entered as covariates. Bootstrapping was performed with 10,000 samples. Independent *t*-tests were performed for the variables age (age $< 16$ and age $\geq 16$) and gender (girls and boys). Correlation analyses were conducted between the three variables ER (adaptive and maladaptive strategies; measured with the FEEL-KJ, total score) and sleep problems (two subscales measured with the SI-KJ) as well as depressive symptoms (measured with the DIKJ; total score without the sleep item). Furthermore, these variables were correlated to age (Pearson correlation) and gender (Spearman's rank order correlation).

# RESULTS

## Sample Description

**Table 1** presents means and standard deviations (SD) for sleep problems, depressive symptoms, and maladaptive and adaptive strategies for the total sample, for boys and girls and the two age groups separately. Independent *t*-tests revealed significant differences between girls and boys, with girls showing more sleep problems and depressive symptoms as well as a greater use of maladaptive strategies and a reduced use of adaptive strategies compared to boys. There was no significant effect of age. Clinically relevant depressive symptoms were reported by 74.8% of the sample. 78% of the sample showed conspicuous values for adaptive strategies and 61.1% for maladaptive strategies. 74.5% of the sample reported clinically relevant sleep problems.

## Correlations Between Adaptive and Maladaptive Strategies, Sleep Problems and Depressive Symptoms

Depressive symptoms and sleep problems were significantly correlated ($r = 0.592$, $p < 0.001$). The use of adaptive ER strategies was significantly associated with depressive symptoms ($r = -0.489$, $p < 0.001$) and with sleep problems ($r = -0.373$, $p < 0.001$). The use of maladaptive ER strategies was also significantly associated with depressive symptoms ($r = 0.655$, $p < 0.001$) and with sleep problems ($r = 0.623$, $p < 0.001$).

## Mediation by Adaptive and Maladaptive ER Strategies

The mediation analysis revealed a significant partial mediation model, with a positive standardized indirect effect on the relationship between sleep problems and depressive symptoms via the use of maladaptive strategies ($\beta = 0.226$, *CI* [0.177, 0.280]) and a negative standardized indirect effect via the use of adaptive strategies ($\beta = 0.079$, *CI* [0.051, 0.109]). The direct effect of sleep problems on depressive symptoms was weaker but still significant ($\beta = 0.251$, $t = 6.765$, $p < 0.001$, *CI* [0.178, 0.323], $R^2 = 0.364$) compared to the total effect ($\beta = 0.554$, $t = 16.012$, $p < 0.001$, *CI* [0.486, 622], $R^2 = 0.527$). Gender (*coefficient* $= 0.256$, $p < 0.001$, *CI* [0.112, 0.401]) and age (*coefficient* $= 0.067$, $p = 0.0057$, *CI* [0.020, 0.114]) were significant covariates for maladaptive strategies. For depressive symptoms, age was a significant covariate in the total effect model (*coefficient* $= -0.052$, $p = 0.017$, *CI* [−0.094, −0.009]) and gender in the direct effect model (*coefficient* $= 0.239$, $p = 0.002$, *CI* [0.089, 0.388]). The mediation model is illustrated in **Figure 3**.

# DISCUSSION

In line with our assumptions and prior literature in adults (4), there was a significant partial mediation effect, insofar as sleep problems influenced depressive symptoms via dysfunctional ER. In contrast to adults, not just the increased use of maladaptive strategies but also the decreased use of adaptive strategies partly mediated the association between sleep problems and depressive symptoms. Additionally, a direct effect of sleep problems on depressive symptoms emerged. In this clinical sample, sleep problems were positively correlated with depressive symptoms as well as maladaptive ER strategies and negatively correlated with adaptive ER strategies. Furthermore, depressive symptoms were associated with an increased use of maladaptive strategies and with a decreased use of adaptive strategies. In addition, gender was a significant covariate in the present study, whereas age was not.

## The Mediating Effects of Maladaptive and Adaptive Strategies on the Association Between Sleep and Depression

The present findings confirm previous suggestions that ER acts as a possible mechanism underlying the association between sleep and depression (4, 19). Sleep problems seem to influence ER negatively insofar as more maladaptive strategies and fewer adaptive strategies are used to regulate emotions, which in turn might facilitate the development of depressive symptoms. Interestingly, in the present study, the decreased use of adaptive ER strategies was also associated with psychopathology, and mediated the association between sleep problems and depressive symptoms. This is in line with the findings of Schäfer et al. (6), who reported negative associations between the habitual use of adaptive strategies and depressive symptoms in a meta-analysis of non-clinical school samples. In contrast, a meta-analytic-study in adults by Aldao and Nolen-Hoeksema (22) only revealed associations between maladaptive ER strategies and depressive symptoms. As a consequence, the authors concluded that the use of adaptive strategies seems less important for psychopathology than the use of maladaptive strategies. These conflicting findings may be explained by the different age groups of the respective samples (children and adolescents vs. adults). In sum, in contrast to adults, both adaptive and maladaptive strategies might be important for psychopathology in adolescents.

In accordance with our assumptions, poor sleep was associated with more depressive symptoms, and both poor sleep and depressive symptoms were correlated with an increased use of maladaptive strategies and a decreased use of adaptive strategies. Different underlying mechanisms for these associations have been discussed before. E.g., neuroimaging studies indicated that brain regions involved

**TABLE 1 |** Sample characteristics (sum scores, *T*-values in brackets) regarding sleep, emotion regulation and depressive symptoms.

| | Group | | | Test statistics | | Group | | Test statistics | |
|---|---|---|---|---|---|---|---|---|---|
| | **Total sample** ***N* = 602** | **Boys** ***N* = 181** | **Girls** ***N* = 421** | | | **Age < 16** ***N* = 346** | **Age ≥ 16** ***N* = 256** | | |
| | | | | ***t*** | ***p*** | | | ***t*** | ***p*** |
| DIKJ | | | | | | | | | |
| M | 23.85 | 20.00 | 25.51 | $t_{(600)} = -7.694$ | <0.001 | 24.17 | 23.42 | $t_{(589)} = 1.113$ | 0.266 |
| (*T*-value) | (68.01) | (62.49) | (70.38) | | | (67.95) | (68.08) | | |
| SD | 8.44 | 7.90 | 8.12 | | | 8.99 | 7.63 | | |
| (*T*-value) | (11.12) | (11.06) | (10.28) | | | (11.49) | (10.62) | | |
| SI-KJ | | | | | | | | | |
| M | 7.40 | 5.86 | 8.06 | $t_{(594)} = -8.484$ | <0.001 | 7.34 | 7.49 | $t_{(594)} = -0.590$ | 0.555 |
| SD | 3.07 | 3.03 | 2.85 | | | 3.16 | 2.94 | | |
| FEEL-adaptive | | | | | | | | | |
| M | 106.53 | 113.32 | 103.61 | $t_{(600)} = 3.936$ | <0.001 | 106.4 | 106.7 | $t_{(600)} = -0.128$ | 0.898 |
| (*T*-value) | (36.65) | (38.83) | (35.72) | | | (36.62) | (36.70) | | |
| SD | 28.09 | 29.02 | 27.21 | | | 28.63 | 27.40 | | |
| (*T*-value) | (12.41) | (13.34) | (11.88) | | | (12.74) | (11.93) | | |
| FEEL-maladaptive | | | | | | | | | |
| M | 96.68 | 87.84 | 100.48 | $t_{(600)} = -7.725$ | <0.001 | 95.4 | 98.41 | $t_{(589)} = -1.947$ | 0.052 |
| (*T*-value) | (62.26) | (55.71) | (65.08) | | | (61.24) | (63.64) | | |
| SD | 19.29 | 19.23 | 10.40 | | | 20.49 | 17.41 | | |
| (*T*-value) | (16.47) | (16.89) | (15.48) | | | (17.22) | (15.32) | | |

*DIKJ, Depression Inventory for Children and Adolescents; SI-KJ, Sleep Inventory for Children and Adolescents; FEEL-adaptive, German Questionnaire on Emotion Regulation Strategies in Children and Adolescents – subscale "adaptive strategies"; FEEL-maladaptive, German Questionnaire on Emotion Regulation Strategies in Children and Adolescents – subscale "maladaptive strategies".*

in ER, predominantly in the limbic system, were influenced by sleep deprivation and worse sleep (42). Sleep deprivation and worse sleep seem to interrupt the connection between the MPFC and amygdala, leading to difficulties in inhibiting negative emotions (32). A negative memory bias due to sleep problems has also been discussed as an underlying mechanism (19). Evidence suggests that insufficient sleep leads to difficulties in encoding positive and neutral emotional memories, whereas negative experiences can be remembered (19). Recently, evidence emerged that supports these assumptions: whereas differences between subjective reports of sleep disturbances between low and high familial risk for depressive disorders emerged, objective measurements, namely actigraphy and sleep diary-based measures of sleep duration and midpoint of sleep, revealed no significant differences between high and low risk adolescents. These differences in subjective and objective measures of sleep disturbances may reflect a potential cognitive bias (to negative information) in parents with depression and in adolescents with high risk for depression (16).

## Gender and Age as Covariates

As many studies showed that girls are two to three times more afflicted by depressive symptoms at the age of 13 or 14 than boys [e.g., (43)], it is not surprising that gender was a significant covariate in the present study. Furthermore, the results revealed that girls are more affected by depressive symptoms, sleep problems and emotion dysregulation. These findings are also in line with previous research [e.g., (16, 44)]. For example, Hankin (44) investigated cognitive vulnerabilities and stressful life events as mediators for sex differences in depressive symptoms during adolescence in a prospective, multiwave study. Therein higher levels of depressive symptoms in girls were mediated by a negative cognitive style x stressors interaction as well as rumination x stressors interaction. Girls reported higher levels of depressive symptoms, negative cognitive style, rumination and greater exposure to stressors than did boys. In sum, girls seem to be more afflicted than boys due to higher levels of stress in adolescence and a greater use of maladaptive strategies, which in turn leads to higher levels of depressive symptoms. The associations between sleep problems, the use of ER strategies and depressive symptoms seem to be more important for girls than for boys.

Age did not moderate these associations in this clinical adolescent sample, although older adolescents were more afflicted due to their greater use of maladaptive strategies. As the use of maladaptive strategies seems to be more important for psychopathology than the non-use of adaptive strategies in adulthood (22), it might be assumed that the positive association

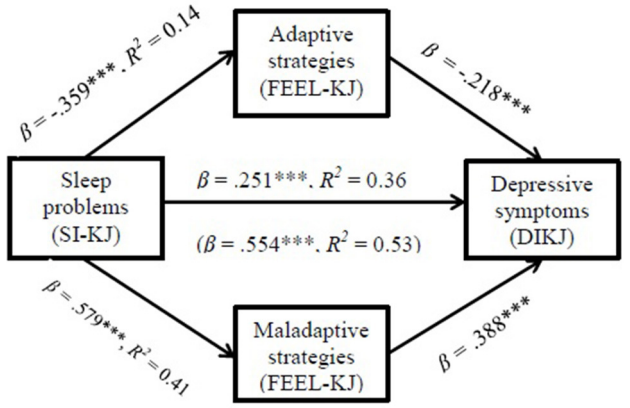


**FIGURE 3 |** Indirect effects of adaptive and maladaptive strategies on the relationship between sleep problems and depressive symptoms. SI-KJ Sleep Inventory for Children and Adolescents; FEEL-KJ German Questionnaire on Emotion Regulation Strategies in Children and Adolescents; DIKJ Depression Inventory for Children and Adolescents; date in brackets refer to the total effect of the model; ***$p < 0.001$.

between age and maladaptive strategies correlates with the duration and chronicity of depression insofar as longer duration of depression (in adults and older adolescents) leads to a higher use of maladaptive strategies. However, as we have no information about the duration and chronicity of depression, we were unable to verify this hypothesis in the current sample.

## Limitations

The present study overcomes some of the limitations of previous studies by investigating the associations between sleep, depression and ER in a large clinical sample of adolescents with clinical levels of depression. However, limitations of this study are the cross-sectional design and the use of self-report assessment tools to reflect habitual use of ER strategies and sleep habits over time and across different contexts (22), which might have impacted the results and thus reduced the generalizability of the findings. Also the use of a clinical sample limits the generalizability of the results to population samples. Thus, the associations should be investigated in population-based samples. Further studies should also provide data on treatment course. As two-thirds of the inpatients were diagnosed with a comorbid psychiatric disorder, another limitation is that we did not controlled for the confounding bias of comorbid disorders, especially the influence of anxiety might be consider in further studies. Differences in the relevance of the non-use of adaptive strategies for psychopathology between adults and youth might be caused by longer depressive illness duration, thus a further limitation is that we were unable to control for the age of onset and duration of depression in the present analyses. Another limitation is that the study sample also included the heterogenous category F92.0 and not just depressive diagnoses. But the naturalistic design of the study and the clinical experience of the authors that especially younger adolescents which were diagnosed with F92.0 show high depressive symptoms led to the decision to include this diagnosis group. Due to the cross-sectional study design, the results should be interpreted with caution and should be seen as preliminary. Longitudinal and experimental studies are needed to replicate the results and to provide a more thorough understanding of the influence of sleep problems and ER deficits on depressive symptoms. In addition, further studies are needed to investigate the impact of further variables such as experiences of stress and a cognitive bias to negative information processing and to strengthen the findings of possible underlying mechanisms and their associations (see **Figure 1**).

## Implications and Contribution

Taken together, the present results indicate deficits in ER as a mechanism partly explaining the established relation between sleep problems and depressive symptoms. If longitudinal studies in adolescents with clinical levels of depression substantiate these findings the application of additional treatment modules focusing on sleep and ER skills in prevention and treatment programs for children and adolescents would be important steps. To reduce the risk of developing depressive symptoms, children and adolescents should acquire strategies to manage their emotions. There is already preliminary evidence that the application of ER prevention programs has positive effects on depressive symptoms. For example, adolescents with non-clinical depressive symptoms or clinically anxious youth were trained to use strategies of cognitive reappraisal, which led to a reduction in the frequency of negative emotions and improved self-reported ER (28, 45).

Due to the influence of sleep problems on depressive symptoms, the improvement of sleep could represent another treatment opportunity in the prevention and treatment of depression. In adults, evidence suggests that cognitive behavioral therapy for insomnia (CBT-I) reduces insomnia and depressive disorders to a greater extent than relaxation training (46). In addition, first evidence suggests that morning bright light therapy may be efficient as an add-on treatment option to reduce sleep problems in adolescent depression (47, 48).

# DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

# ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethical review board of the Ruhr-University Bochum (registration number: 4359-12). Written informed consent for participation was not provided by the participants' legal guardians/next of kin because: Ethical approval for the routine data has been giving without written consent from all patients and their legal guardian. Participants consented to the study by completing the questionnaires. This procedure is regulated by law regarding using routine data in hospitals (Art. 9, Paragraph 2, Letter j DSGVO (data protection declaration of Germany) in relation to §5 Paragraph 5 DSG NRW(data

protection declaration of Nordrhein-Westfalen) and §17 DSG NRW in relation to §6 Paragraph 2 GDSG (data protection law for health care) NRW. This procedure of the scientific data use of the routine data was approved by the ethical review board of the Ruhr-University Bochum (registration number: 4359-12).

## AUTHOR CONTRIBUTIONS

IK-L, MH, and TL designed the study. IK-L managed the literature searches and analyses, undertook the statistical analyses, and wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

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# Digital Phenotyping of Emotion Dysregulation Across Lifespan Transitions to Better Understand Psychopathology Risk

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Ethical and consensual digital phenotyping through smartphone activity (i. e., passive behavior monitoring) permits measurement of temporal risk trajectories unlike ever before. This data collection modality may be particularly well-suited for capturing emotion dysregulation, a transdiagnostic risk factor for psychopathology, across lifespan transitions. Adolescence, emerging adulthood, and perinatal transitions are particularly sensitive developmental periods, often marked by increased distress. These participant groups are typically assessed with laboratory-based methods that can be costly and burdensome. Passive monitoring presents a relatively cost-effective and unobtrusive way to gather rich and objective information about emotion dysregulation and risk behaviors. We first discuss key theoretically-driven concepts pertaining to emotion dysregulation and passive monitoring. We then identify variables that can be measured passively and hold promise for better understanding emotion dysregulation. For example, two strong markers of emotion dysregulation are sleep disturbance and problematic use of Internet/social media (i.e., use that prompts negative emotions/outcomes). Variables related to mobility are also potentially useful markers, though these variables should be tailored to fit unique features of each developmental stage. Finally, we offer our perspective on candidate digital variables that may prove useful for each developmental transition. Smartphone-based passive monitoring is a rigorous method that can elucidate psychopathology risk across human development. Nonetheless, its use requires researchers to weigh unique ethical considerations, examine relevant theory, and consider developmentally-specific lifespan features that may affect implementation.

**Keywords: digital phenotyping, emotion dysregulation, perinatal, emerging adulthood, adolescence, psychopathology risk, lifespan transitions, passive monitoring**

## INTRODUCTION

In our increasingly digital society, a person's unique technological interactions can provide meaningful information about their mental health symptoms (1). One device with great potential for revealing individual-level behavior is the smartphone. Digital phenotyping, limited here to smartphone-based passive monitoring, is defined as using smartphone data to better understand human traits, behaviors, and functioning. Smartphone-based assessment of daily activity provides a novel window into multifaceted aspects of behavior, which may in turn help mental health researchers better understand risk trajectories (2–5).

Passive monitoring thus allows for highly objective and dynamic assessment of psychopathology-related behavior that extends beyond the confines of diagnostic syndromes. Emotion dysregulation underlies risk for diverse forms of psychopathology across the lifespan (6), and may be assessed well with passive monitoring approaches. We argue that passive monitoring holds particular benefit for the assessment of emotion dysregulation across major lifespan transitions. The primary goal of this paper is to identify passive measures that may prove fruitful for understanding daily life emotion dysregulation. We also discuss future directions, limitations, and highlight persistent challenges in this area, including navigating participant privacy and data security.

## KEY TERMS: PASSIVE MONITORING, EMOTION DYSREGULATION, AND LIFESPAN TRANSITIONS

In this paper, we restrict our discussion of digital phenotyping to consensual and ethical passive monitoring of behavior *in situ* (1, 3). Passive monitoring refers to collection of raw smartphone-based data streams, requiring little participant effort. Smartphones are regularly improved and modified, so it is important to situate this discussion in the context of existing technology. In this manuscript, we do not discuss digital data collection that occurs without participant awareness, such as web scraping or anonymized social media analysis. Smartphone-based passive monitoring is a structured, consented process, in which participants are aware that researchers will gather various forms of smartphone data to understand their behavior. Current examples of smartphone-based raw data streams include screen activation time, location via GPS, Bluetooth activity, and texting speed, among others. Through passive monitoring, raw data streams are manipulated into more meaningful variables. For instance, by gathering ambient light and accelerometry data, researchers can currently estimate sleep time, and with GPS, one can calculate various features of mobility ((7, 8); **Figure 1**). When paired with self-reported symptom measures, passive monitoring can provide more comprehensive mental health data, such as onset of psychotic and manic episodes (9–13). Given its multifaceted capabilities, passive monitoring can help reveal discrete mental health states. Passive monitoring methods may also lead to improved understanding and prediction of risk factors for psychopathology that cut across a number of disorders, such as emotion dysregulation.

Emotion dysregulation refers to emotional experiences and expressions that are over- and/or under-controlled in a manner that interferes with goal-related behavior (14). Emotion dysregulation is a complex multilevel construct, with trait- and state-level components, associated with numerous psychiatric disorders (15, 16). This construct also predisposes individuals across the lifespan to risk for maladaptive coping responses to distress (e.g., self-harm, substance use; (17–19)). For example, children, adolescents, and young adults with emotion regulation difficulties are at heightened risk for internalizing and externalizing syndromes as they develop (14, 20, 21). Dysregulated emotion is a function of both trait-level individual differences in impulsivity and anxiety, as well as state-level fluctuations in affect (15). Passive monitoring methods are particularly well-positioned to tap into state dynamics but their ability to do so is no doubt a function of person- and observation-level sampling. With a large number of participants, individual differences will emerge more readily, and observations will be a function of between-person effects. Passive methods lend themselves well to the gathering of numerous within-person observations, leading to a stronger understanding of within-person dynamics (1, 4). Regardless, the multifaceted and broad nature of emotion dysregulation make it an ideal construct for digital methods, particularly for individuals navigating major lifespan transitions, who must manage significant daily stress and adjustment.

Lifespan transitions often confer risk. For instance, rates of internalizing and externalizing psychopathology increase in adolescence in part due to hormonal shifts and changes in social groups (22, 23). Emerging adults also have relative increases in risk due to continued neurological development, shifts in autonomy, and identity formation (24, 25). Additionally, the perinatal period is a critical transition, leading to increased psychiatric sensitivity and profound changes in identity (e.g., labeling oneself as a "parent"), the effects of which can confer risk for longstanding neurodevelopmental outcomes in infants (26, 27). Transitions also involve a great deal of adjustment. Adolescents navigate high school, young adults often move out and seek independent careers, and perinatal women and their partners manage newfound health challenges and parenting stress—all of which make it difficult to gather rich psychopathology data in the laboratory. Smartphone-based monitoring of behavior represents an innovative way to understand dynamic, daily life, and transdiagnostic risk trajectories.

## LIFESPAN TRANSITIONS AND PASSIVE MONITORING OF EMOTION DYSREGULATION

In this manuscript, we explore three lifespan transitions marked by both smartphone use and increased psychopathology risk: adolescence, emerging adulthood, and the perinatal period. We discuss key features of each transition with respect to

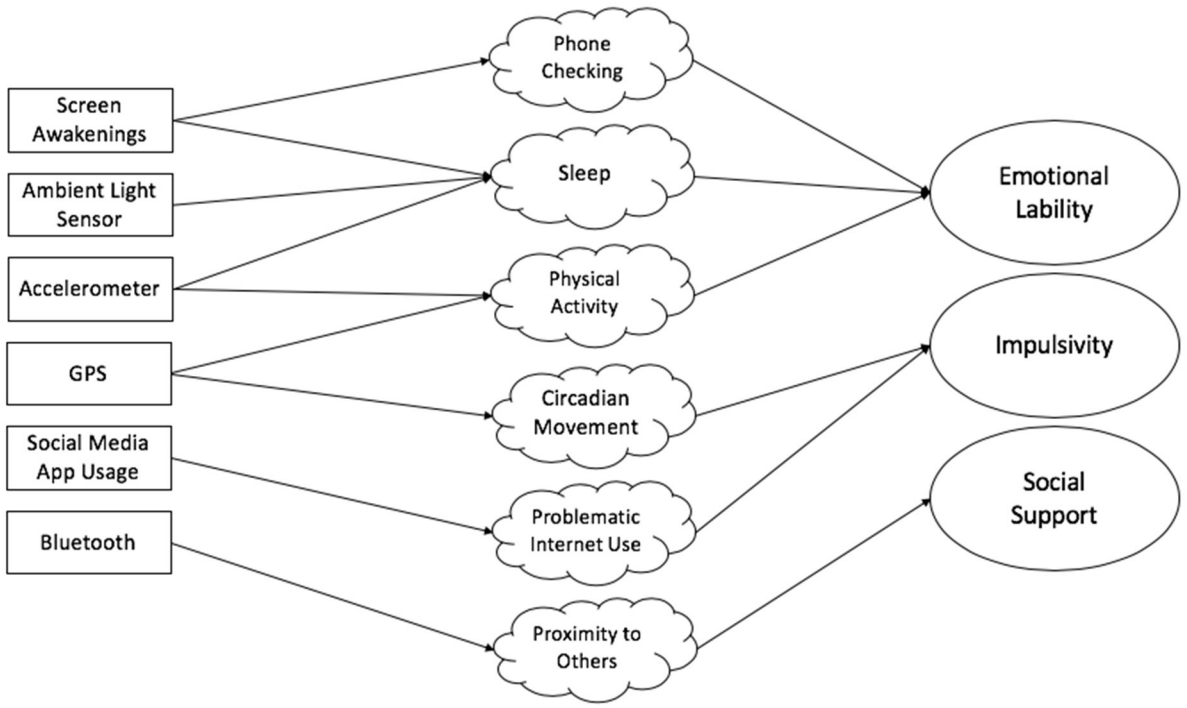


**FIGURE 1 |** Conceptual illustration of current smartphone-based passive monitoring methods. Raw data streams are collected directly from smartphones and then converted into more useful variables/measures through cloud-based interfaces. These measures convey meaning about relevant constructs—in this case, emotion dysregulation. Note that, for simplicity, this figure conveys merely a small sample of current possible data streams and variables, and many others exist.

emotion dysregulation as well as how passive monitoring might be applied. We chose to limit our discussion to these three transitions due to space constraints, and because smartphone ownership is limited in childhood. In addition, we outline potential passive measures of emotion dysregulation by strength of support in the literature (moderate-strong, tenuous, or conceptual/author perspective). We also note the extent to which each highlighted measure has been associated with emotion dysregulation directly (e.g., with a "gold standard" measure) or indirectly (e.g., associated with an emotion regulation disorder, such as depression), and if the measure has been gathered via smartphone-based passive means in that population (see **Figure 2**).

## Adolescence Transition

Adolescence comprises the time between late childhood and emerging adulthood (28). Specific age range definitions vary but we restrict our definition to the 12–17 age range, avoiding overlap with childhood and emerging adulthood and capturing pubertal onset for most people. Though there is much literature on media exposure in childhood (especially violent media) in relation to psychopathology risk (29), this research is beyond the scope of the current paper. Very little smartphone-based passive monitoring research has been conducted among children (as few children under 12 currently own smartphones). Moreover, a discussion of ethics with respect to smartphone monitoring in childhood warrants a more in-depth analysis than can be done here.

Post-pubertal adolescent brains undergo extraordinary changes in structure and function, including gray matter pruning and increased connectivity in the prefrontal cortex (30). By the end of puberty, adolescents have experienced significant maturation of the hypothalamic-pituitary-adrenal (HPA) axis and respective sexual organs (31), as well as overall decreases in serotonin and increases in dopamine (32, 33). Complex interactions between hormones, brain maturation and functioning, and genomic (de)activation increase adolescent risk for mental health problems (28, 33, 34). Given the risk and stress of this transition, it follows that an approach that minimizes research participation burden, such as daily life smartphone monitoring, could be fruitful.

Two variables that can be passively monitored appear to have at least moderately strong support as emotion dysregulation indices in this stage: sleep disturbance and problematic Internet usage. Countless studies have demonstrated that poor sleep, often measured via self-report or actigraphy, is a viable index of mood disorder risk across the lifespan (34–38). Smartphone monitoring (i.e., raw data from ambient light sensor and

| | | | |
|---|---|---|---|
| **Moderate to strong support** | • Sleep (e.g., duration, efficiency)[1,b]<br>• Problematic Internet/social media use (e.g., to manage negative emotions)[1,b] | • Sleep (e.g., duration, efficiency)[1,b]<br>• Problematic Internet/social media use (e.g., to manage negative emotions)[1,b] | • Sleep (e.g., duration, efficiency)[2,b] |
| **Tenuous support** | • Mobility (e.g., exercise time)[2,b]<br>• Weekend time spent near liquor stores[2,a]<br>• Overall phone activity[2,b]<br>• Social network (e.g., number of in-person or virtual interactions)[2,b] | • Mobility (e.g., exercise time)[2,a]<br>• Social network (e.g., number of in-person or virtual interactions)[2,b]<br>• Overall phone usage[1,a]<br>• Phone checking (i.e., quick screen unlocks)[2,a]<br>• Keystroke dynamics (e.g., typing speed, autocorrect frequency)[2,a] | • Radius of gyration (i.e., average daily distance traveled from home)[2,a]<br>• Time spent near partner/close friends/sources of social support[2,b] |
| **Conceptual/ theoretical support only** | • Keystroke dynamics (e.g., typing speed, autocorrect frequency)<br>• Phone checking (i.e., quick screen unlocks)<br>• Circadian movement (e.g., weekly to monthly activity patterns) | • Circadian movement (e.g., weekly to monthly activity patterns)<br>• Time spent near partner/close friends/sources of social support | • Keystroke dynamics (e.g., typing speed, autocorrect frequency)<br>• Phone checking (i.e., quick screen unlocks)<br>• Social network (e.g., number of in-person or virtual interactions)<br>• Problematic Internet/social media use (e.g., to manage negative emotions)<br>• Circadian movement (e.g., weekly to monthly activity patterns) |

**FIGURE 2 |** Use of digital phenotyping summary measures as markers of emotion dysregulation across major lifespan transitions. Moderate to strong empirical support: >2 peer-reviewed studies. Tenuous empirical support: 1–2 peer-reviewed studies. Conceptual/theoretical support only: author perspective, important measures for future study. [1]Use of this variable has been supported by at least one study demonstrating its association with a "gold standard" emotion regulation measure (e.g., affective lability, difficulty controlling emotions). [2]Use of this variable is supported by evidence of its association with indirect markers of emotion dysregulation (e.g., depression, anxiety, well-being). [a]Cited study (or studies) gathered evidence through smartphone-based passive monitoring. [b]Evidence acquired without passive monitoring. Note: no notation used for the last row because these items are not currently backed by evidence, representing the authors' perspective only.

accelerometer) has been used to assess sleep across populations, often validated by actigraphy (39–43). In one study, researchers demonstrated a clear link between emotion regulation problems and poor adolescent sleep (36). Additionally, problematic Internet/social media use, or technology use as a means of regulating distress (e.g., using a smartphone to distract oneself from anxiousness), has also been linked to psychopathology, and may be explained by emotion dysregulation across diverse samples (20, 44–48), though in none of these studies was passive monitoring used. Nevertheless, adolescence is a time of increased emotional responsivity (due to increases in limbic volume) with incomplete prefrontal cortex development, which may explain adolescents' propensity to unhealthy emotion regulation strategies (28). Although empirical support has been acquired without passive monitoring, abundant evidence suggests a link between problematic Internet use, sleep, and emotion dysregulation, indicating at least moderate support for these indices.

There are several passive measures with weak or tenuous support. Many of these measures still require rigorous validation in the adolescent context. Physical activity is related to general well-being in adolescents [though untested with passive monitoring methods; (49, 50)]. Robust social networks and close relationships also associate with less adolescent emotion dysregulation (51, 52). Network analyses have revealed interesting contagion effects across adolescent peer groups (53), which could potentially be captured through passive monitoring methods. Contagion-like effects could be assessed through social media app activity and through the use of phone-phone closeness via Bluetooth. Finally, passive monitoring studies have shown that adolescent weekend proximity to liquor stores (54) and daily smartphone use (44) may index behavior problems and suicidality, respectively—both proxies for dysregulated emotion.

We have identified several untested candidate measures that may prove useful for detecting emotion dysregulation. Keystroke dynamics (i.e., texting speed, autocorrect frequency) and frequent, brief phone checks can detect emotion regulation problems and may be worth examining with adolescents (13, 44). Both may be useful because individuals who are highly dysregulated struggle to allocate attention effectively

(14, 15), similar to problematic Internet/social media use. Finally, circadian movement, a measure of variability in GPS locations over a day or week, may also index dysregulation. Individuals with more irregular daily patterns may have more financial or social insecurity and could be more dysregulated, making this a fascinating candidate marker for future research.

## Emerging Adulthood Transition

We define emerging adulthood broadly as between age 18 and the late 20s, as this period captures the time between adolescence and the tapering of neurological development (55). Like adolescence, emerging adulthood is a time of increases in psychopathology risk, relative to childhood and adulthood. This change in risk for mental illness may occur because many emerging adults experience exponential growth in autonomy and identity formation, often pursuing higher education, careers, and intimate relationships (56). Yet there is also more lifestyle and day-to-day heterogeneity in this period relative to adolescence. Adolescents typically attend school, making it relatively simple for researchers to apply digital methods uniformly. However, much of what is known about emerging adults is limited to college students. Thus, passive monitoring may provide an effective way to better understand heterogeneous mental health risk trajectories in this population.

Similar to adolescence, effective passive markers for emotion dysregulation include both sleep and problematic Internet/social media use, the latter of which is often defined as Internet/social media use that leads to social, emotional, or behavioral problems or negative outcomes (56). For example, using the Internet as a primary means for managing distress or avoidance might be considered problematic, especially because prefrontal cortices only finish developing by the end of young adulthood (57). Many non-digital studies have demonstrated links between self-reported sleep and emotion dysregulation in college student samples (58, 59). Note that there are several studies on passively-monitored sleep in adults, not young adults (35). Likewise, self-report studies of college students link problematic Internet/social media use and dysregulated emotion (60, 61). There is a need for more smartphone-based assessment of these measures, though the large number of significant self-report studies suggests they are at least moderately supported indices.

There are also several passive measures that have at least weak support as emotion dysregulation indices. Some have been examined in only adult populations, and others have been examined via self-report in a limited fashion. Similar to adolescents, there is good reason to suspect that daily mobility and interpersonal interaction patterns, measured, for instance, via GPS and Bluetooth, might index emotion dysregulation. As adolescents transition into young adulthood, frontal lobes tend to become increasingly active, leading to increased desire for social engagement and interpersonal risk taking (28, 55). Among adults in general, smartphone-derived mobility indices, including number of locations visited, normalized entropy (i.e., variability in time spent at significant locations), and time spent at home predicted depression and anxiety, though associations with emotion dysregulation itself are untested (62–64). Additionally, young adults who engage in effective interpersonal emotion regulation tend to have greater popularity and social network size, indexed via peer report and Twitter following [though not passive monitoring; (65)]. This aligns with numerous emotion regulation theories, such that affect is regulated through both intrapersonal and interpersonal means (66, 67).

Additionally, there is evidence that total daily phone usage may predict depression in adults (62, 68). However, a more nuanced usage measure is phone checking, a common behavior among young adults (69). Frequent checking, defined here as brief lapses between screen lock-unlock, may index ineffective regulation of distress and reassurance seeking, making it a potential measure of utility (45, 70, 71). Finally, keystroke dynamics (e.g., typing more quickly during a manic episode) have been examined in adult clinical populations and are worth examining in emerging adults, given that this measure predicts mood states (13).

Two additional measures that may warrant investigation are circadian movement (see "Adolescence") and time spent near a close partner. This latter marker could be approximated through Bluetooth. When activated, smartphones can use Bluetooth to detect proximity to other smartphones. Although the identity of non-participant smartphones would be withheld, researchers could determine if the same smartphone is in proximity repeatedly, as one would expect with a close friend or partner (8). Oftentimes, healthy relationships with close friends and romantic partners associate with better regulated emotion (72), so it stands to reason that this could be true when examined via passive monitoring.

## Perinatal Transition

The perinatal period is a time of significant change for women and families. In less than a year, pregnant women experience numerous profound neurobiological changes, matched only by fetal and pubertal development, likely to facilitate child bearing and parent-infant bonding (27). Preparing for and raising a new child can cause significant financial and social stress, as pregnant women must navigate newfound daily routines, finances, health concerns, and identity shifts (73). Thus, this lifespan transition confers increased mental health risk, yet much perinatal psychopathology is under- or misdiagnosed (74). Perinatal mental health problems can manifest in highly idiosyncratic ways, unique from other parts of the lifespan (e.g., perinatal depression is more likely to have anxious and obsessive-compulsive features), and symptoms are also quite variable from day to day (75, 76). Moreover, perinatal mental health affects not only a pregnant woman's long-term health, but that of her newborn. Significant stress, depression, and emotion dysregulation during pregnancy may predispose newborns to maladaptive development (27, 77, 78). These intergenerational implications underscore the need to better understand risk during this stage.

To our knowledge, little passive monitoring research has been done with perinatal women and none with their partners. Likely, the most supported emotion dysregulation measure that can be assessed with passive monitoring is sleep disturbance. Though mild to moderate sleep disturbance is quite common throughout this transition, not all perinatal women develop sleep

disorders (79). Though empirical work is lacking, non-digital studies have shown that prenatal and postnatal sleep disturbances are associated with postpartum depression and other indirect markers of emotion regulation problems, suggesting this could be a useful index (80–82).

One passive measure with at least tenuous promise is "radius of gyration," or the average daily distance traveled from home (8). In one of the only published studies that used passive monitoring during pregnancy, researchers found that a lower radius of gyration associated with day-to-day change scores in self-reported mood, though not daily mood itself (83). In this same study, smartphone-detected mobility (i.e., daily distance traveled on foot) did *not* predict self-reported emotion. This finding may speak to the unique features of this transition. Pregnant women tend to move less over the course of gestation, meaning that mobility may not be as consistently linked to emotion as it is for adolescents and emerging adults. Also, because smartphones can be used to detect proximity to other individuals, the presence of supportive attachment figures during the perinatal period seems to help reduce distress and, indirectly, lead to more effective emotion regulation (84). Indeed, prenatal maternal brains experience a remarkable amount of "rewiring" in the prefrontal cortex, likely to facilitate attachment bonds with partners and with their new child (27). Assessing time spent in proximity with others via Bluetooth could help researchers understand regulatory problems in pregnancy.

Due to a lack of research in this area, there are many additional passive measures that, from our perspective, may enrich our understanding of perinatal emotion dysregulation. These proposed measures have already been discussed in detail throughout this paper. For instance, keystroke dynamics may prove a useful measure of mood dysregulation during the perinatal period; individuals who are dysregulated may have high variability in texting speed, autocorrect frequency, etc. across temporal shifts in negative affect (13). We also propose phone checking, social network assessment (both in-person and virtual), and problematic Internet/social media use as candidate emotion dysregulation indices, as they appear effective at other points across the lifespan. Last, given the theoretical justification described previously, researchers may also consider validating circadian movement as an emotion dysregulation index during the perinatal transition.

## DISCUSSION

Emotion dysregulation is a heterogeneous, transdiagnostic risk factor with health implications across the lifespan. Smartphone-based passive monitoring presents researchers and clinicians with a relatively inexpensive way to monitor psychopathology-related behavior. However, much passive monitoring research has relied on exploratory and atheoretical methods, ultimately inhibiting advancement (43). We presented key concepts and articulated a framework that will be helpful for understanding how passive monitoring might be used for daily life emotion dysregulation assessment across three major lifespan transitions: adolescence, emerging adulthood, and the perinatal transition. The most robust indices are likely smartphone-based assessment of sleep disturbance and problematic Internet/social media use, followed by derivations of mobility, sociality, and phone activity. Given that most research cited consists of self-report and other types of measurement, there is a critical need to validate all of these indices with passive, digital methods. As recommended (85), we encourage digital researchers to simultaneously gather daily life self-reports (i.e., ecological assessment).

There are several limitations and caveats to note as well. The passive monitoring markers outlined likely have complex, bidirectional relations with emotion dysregulation. For instance, numerous researchers have debated the extent to which sleep issues predispose one to regulatory problems or if sleep problems are a consequence of emotion dysregulation (86). For the purposes of this paper, underlying mechanisms are not crucial; our focus was on the utility of a potential marker. To estimate causality, researchers must use intensive longitudinal approaches with well-validated, multilevel measurement (87, 88). We expect these designs will be even easier with passive monitoring. Additionally, as described earlier, it is difficult to disentangle the extent to which these measures index state- or trait-level emotion dysregulation. Specific study designs will be helpful in doing so.

Additionally, the indices we discussed are not exhaustive. We have scratched the surface on how passive monitoring can inform psychopathology. Emerging research is highlighting how diverse technological interactions can help create comprehensive digital phenotypes of an individual's mental health. Cutting-edge studies show how to integrate multiple aspects of smartphone monitoring, wearable physiological technology, and built-in machine learning algorithms (2, 89). This type of work has incredible potential for increasing scalability and translation of mental health findings. For instance, one potential intervention involves using smart home features to lock gun safes and alert clinicians when individuals are detected to be in high distress [e.g., through voice sampling and texting; (90)].

However, exciting this type of work could be, researchers must remain attentive to ethical issues at play. Passive monitoring scientists balance participant privacy and data security with a need for rich data. Researchers should follow recommended data protection strategies from passive monitoring experts; for instance, it is important for scientists to store their data in encrypted servers, used hashed phone/Wifi identifiers (to avoid leaving identifying cellphone information in a dataset), and only publicly share de-identified data (1, 6). For instance, one passive monitoring platform known as Beiwe uses front-end and back-end interfaces, and identifiable participant data remain in the front-end server (8).

Ethics becomes especially complicated when working with adolescents, as navigating parent-child dynamics and dyads in the laboratory already has its own challenges (91), let alone outside of the laboratory. Researchers should take several additional steps to protect human rights. Due to the ongoing nature of smartphone-based data collection, it is

important for researchers to provide not only detailed informed consent at study onset but opportunities for participants to re-consent and opt out if desired. Additionally, as mentioned, due to the sheer volume of highly sensitive data, researchers should take advantage of encrypted cloud-based servers that de-identify participant information prior to storage. Researchers should also consider explaining, in detail, how passive monitoring works during the informed consent process, and ensuring understanding when working with minors. It may be important to emphasize that only consented data are gathered, meaning data beyond what a smartphone can currently collect automatically are unobtainable (typically specific app usage, texting content, etc.). Researchers should do as much as they can to reassure participants that they will not be "watched" in real time; passive monitoring data go through numerous cloud-based data checks prior to becoming visible to researchers (8; **Figure 1**). Although a detailed discussion of these issues is beyond the scope of this manuscript, several excellent resources exist already (2, 87, 92, 93).

To advance the science of psychiatry, researchers have called for targeted application of digital methods to understand specific daily life behaviors underlying psychopathology risk and maintenance (9). Passive monitoring of emotion dysregulation is a complex and emerging area of interest (94). By understanding transdiagnostic risk factors across the lifespan through cutting-edge digital methods, we will enrich our understanding of psychopathology mechanisms and treatment directions. There is still much to be learned about how to advance this research area, and just as much critical knowledge to be gained.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

## AUTHOR CONTRIBUTIONS

RV-H conceptualized the structure and perspectives articulated in this manuscript and wrote the majority of the paper. MG, LT, PK, and EC provided editing, feedback, and comments on the writing and figures to strengthen the paper. SC provided detailed feedback and edits on the writing and contributed significantly to the conceptualization of the paper's themes. All authors are accountable for the accuracy and integrity of this work.

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# Disruption of Neural Activity and Functional Connectivity in Adolescents With Major Depressive Disorder Who Engage in Non-suicidal Self-Injury: A Resting-State fMRI Study

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**Background:** Non-suicidal self-injury (NSSI), which commonly occurs during adolescence, often co-occurs with major depressive disorder (MDD). However, the underlying neurobiological mechanisms in adolescents with MDD who engage in NSSI remain unclear. The current study examined the aberrant local neural activity in certain areas of the visual regions and the default mode network (DMN) and the resting-state functional connectivity (rs-FC) in changed brain regions in adolescents with MDD who engage in NSSI and adolescents with MDD only.

**Methods:** A total of 67 adolescents with MDD were divided into two groups based on their NSSI behavior: the NSSI group ($n = 31$) and an age-, gender-, and education-matched MDD group ($n = 36$). The Hamilton Depression Rating Scale (HAMD) was used to assess the severity of MDD. Amplitude of low-frequency fluctuation (ALFF) analysis was used to detect alterations in local neural activity. Brain regions with aberrant neural activity were considered regions of interest (ROI). ALFF-based rs-FC analysis was used to further explore the underlying changes in connectivity between ROI and other areas in the NSSI group. Correlation analyses were performed to examine the relationship between neural changes and clinical characteristics.

**Results:** There was no significant difference in HAMD scores between the two groups. ALFF analysis revealed that, compared to adolescents with MDD only, adolescents with MDD who engaged in NSSI displayed significantly enhanced neural activity in the right fusiform gyrus (FFG. R) and the right median cingulate and paracingulate gyri (DCG. R). Significantly reduced rs-FC of the FFG. R-bilateral medial orbital of the superior frontal gyrus (ORBsupmed. L/R)/bilateral medial superior frontal gyrus (SFGmed. L/R), FFG. R-bilateral posterior cingulate gyrus (PCG. L/R), DCG. R-left pallidum (PAL. L), DCG. R-right superior temporal gyrus (STG. R), and DCG. R-right postcentral gyrus (PoCG. R)/right inferior parietal lobule (IPL. R) was found in adolescents with MDD who were

engaged in NSSI. Additionally, no significant correlations were observed between ALFF or rs-FC values and the HAMD scores between the two groups.

**Limitations:** Owing to the cross-sectional design, the alterations in ALFF and rs-FC values in the FFG. R and DCG. R could not demonstrate that it was a state or feature in adolescents with MDD who engaged in NSSI. Additionally, the sample size was relatively small.

**Conclusions:** This study highlights changes in regional brain activity and remote connectivity in the FFG. R and DCG. R in adolescents with MDD who engage in NSSI. This could provide a new perspective for further studies on the neurobiological mechanism of NSSI behavior in adolescents with MDD.

**Keywords: major depressive disorder, non-suicidal self-injury, amplitude of low-frequency fluctuation, resting-state functional connectivity, visual regions, default mode network**

## INTRODUCTION

Major depressive disorder (MDD) is the most prevalent mental disorder and is mainly characterized by aberrant emotion (lack of pleasure) and cognitive function (dysfunctional attention and memory) (1). MDD is a widely accepted risk factor for suicide attempts. Up to 50–70% of suicide victims may be affected by MDD (2). Adolescence is a pivotal period during which considerable changes occur in physiological, psychological, and social relationships (3). Adolescent individuals are highly vulnerable to mental disorders and maladaptive behaviors, including MDD and non-suicidal self-injury (NSSI). NSSI, which refers to directly and deliberately damaging one's own body tissue without intending to end one's life (4), often occurs in the context of a diagnosis such as borderline personality disorder [BPD; (5)], MDD (6) or other psychiatric disorders. In addition, it can also occur independently of a psychiatric diagnosis. NSSI, as a common method of regulating stress, is generally used by adolescents to improve interpersonal difficulties and regulate negative emotions (7). The prevalence of adolescents who engage in NSSI has been estimated to be 17% in community samples (8) and more than 40% in clinical samples (9). Prior research has demonstrated that NSSI is a crucial precursor for future suicidal behavior (10, 11). Therefore, adolescents with MDD who engage in NSSI may have a higher risk of suicidal behavior. Although NSSI has gradually attracted attention from scholars owing to its high incidence rate and high risk of suicide in adolescence, its neurobiological mechanism remains unclear.

Facial expressions are one of the best methods for mapping an individual's emotional status. Visual regions play an important role in facial expression recognition and visual information processing when processing emotional facial stimuli (12). Functional magnetic resonance imaging (fMRI) studies have shown that functional changes in the visual regions are significantly associated with MDD (13–15). Alterations in the visual pathway involving the middle occipital gyrus and downstream regions (e.g., the fusiform gyrus [FFG]) have been reported in MDD during visual categorization (16, 17), attention (14), and working memory tasks (13). Significantly enhanced activity in the occipital gyrus has been reported in patients with MDD in a task-based fMRI study (18). In addition, neural pattern aberrations in the occipital gyrus were also found in individuals with NSSI while watching emotional and NSSI images (19). The FFG, a vital region of the high-level visual cortex, has been thoroughly researched in recent years because of its abnormal structure and function in patients with mental disorders. A previous study showed that the FFG may be associated with cognitive processing in patients with MDD (20). Increased amplitude of low-frequency fluctuation (ALFF) in the FFG and decreased resting-state functional connectivity (rs-FC) and resting-state global functional connectivity density between the FFG and other regions were observed in patients with MDD (21, 22). Moreover, research also reported that, compared to patients with MDD without NSSI, MDD youth with a history of NSSI had an enhanced response in the FFG after completing an interpersonal self-processing task from their mother's perspective using fMRI, which indicated that FFG activation may be associated with the intense socioemotional processing of NSSI youth (23). Although this evidence has provided crucial clues to the potential neurobiological underpinning of MDD or NSSI, to the best of our knowledge, there are few neuroimaging studies on patients with MDD with NSSI, despite the high prevalence rate and high risk of suicide, let alone in adolescents. Furthermore, there are no rs-fMRI studies on the neural function of visual regions in adolescents with MDD who engage in NSSI. Hence, the neural function of the visual regions is one of the focuses of the current study.

Brain networks that are effectively used for the segregation and integration of information processing have been extensively explored in the past decade. Many disrupted neural networks in MDD have been reported; however, the pervasively concerned networks are the default mode network (DMN), salience network, and central executive network (24–26). These networks are obviously connected with emotional regulation and cognitive processing in patients with MDD; therefore, changes in neural networks that contribute to emotional disorders in patients with MDD might also negatively influence cognitive function. The DMN, which is linked to rumination, has received the most

attention (27). The DMN is divided into two components. The key regions of the anterior DMN are the medial prefrontal cortex (MPFC) and ventral anterior cingulate cortex, and the key regions of the posterior DMN are the precuneus/posterior cingulate cortex (PCC) and bilateral angular gyrus (28, 29). Berman et al. demonstrated that rumination in patients with MDD correlates with increased rs-FC between the PCC and the subgenual cingulate cortex (30). A meta-analysis of rumination in patients with MDD demonstrated that rumination has a positive relationship with the rs-FC between the DMN (especially the PCC) and the subgenual prefrontal cortex (27). Rumination, as one of the core symptoms of MDD, not only is related to vulnerability to the onset and relapse of MDD, but also facilitates the maintenance of negative mood (31). It is also an effective predictor of NSSI because it regulates emotions in NSSI (32). Prior evidence suggests that it may be an effective emotion regulation method to mediate the relationship between NSSI behavior and depressive symptoms (33, 34). Several neuroimaging studies on patients with NSSI have found that self-processing, a feature of NSSI, is correlated with abnormal brain regions in the DMN, including the PCC, precuneus, and MPFC (35, 36). Although imaging studies on NSSI are limited, existing studies have shown that adults with deliberate self-injury have stronger activity in the PCC than depressed patients without a history of self-injury when performing emotional processing tasks (37). In addition, patients with NSSI have also presented higher neural activity in the MPFC than healthy controls during emotional picture processing (19). Hence, illustrating the underlying relationship between neural function in certain areas of the DMN and NSSI in patients with MDD is important for understanding the neurobiological mechanisms of NSSI behavior.

Guo et al. reported decreased voxel-mirrored homotopic connectivity in certain areas of the visual regions and DMN in patients with first-episode, drug-naive MDD relative to healthy controls (38), which demonstrated that neural alterations in these regions may be connected to the neurobiological mechanisms of MDD. Based on these studies, it is worth further exploring whether there are differences in ALFF and rs-FC in these regions between adolescents with MDD who engage in NSSI and adolescents with MDD only. The ALFF and rs-FC analyses are extensively used and effective rs-fMRI analysis methods, which are generally accepted by the academic field. The ALFF (the specific frequency range is 0.01–0.08 Hz) analysis is used to investigate neural activity by detecting the regional spontaneous fluctuations in brain blood oxygenation level dependent (BOLD) signals (39). The rs-FC analysis was proposed to discover the relevant fluctuations in BOLD signals among distant regions (40). Based on previous studies, we performed ALFF analysis and ALFF-based whole-brain rs-FC analysis to investigate the following hypotheses: (1) the differences in neural activity between adolescents with MDD who engage in NSSI and adolescents with MDD only may be located in certain areas of the visual regions and DMN and (2) the remote rs-FC in the changed regions may be obviously different in adolescents with MDD with and without a history of NSSI.

# METHODS

## Subjects

A total of 76 right-handed Han Chinese adolescents (age range: 13–19 years) with a first episode of MDD were recruited from the Department of Psychiatry at the First Affiliated Hospital of Chongqing Medical University. None of the patients took any antidepressants for at least 4 weeks before participating in the study. Subjects with a neurological disorder, history of head trauma with loss of consciousness, history of electroconvulsive therapy, any history of Diagnostic and Statistical Manual IV (DSM-IV) Axis I diagnosis, history of substance or drug addiction/abuse, or contraindications for MRI were excluded. Nine patients who did not meet the criteria for NSSI behavior in the present study were excluded based on clinical interviews. The last NSSI behavior of two of the excluded patients had occurred 6 months previously and seven patients had attempted suicide.

This study was approved by the Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. All subjects, accompanied by their parents or legal guardians, were informed about the study in detail, and written informed consent was obtained (signed by a parent or legal guardian for subjects younger than 18 years of age).

## Clinical Assessment

MDD was diagnosed by two senior psychiatrists using the DSM-IV Structured Clinical Interview (SCID) (41) for subjects aged 18 years or older and the Kiddie Schedule for Affective Disorder and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (42) for subjects younger than 18 years. The 17-item Hamilton Depression Rating Scale (HAMD) was used to assess the severity of MDD owing to its relatively high reliability and validity. In addition, clinical interviews related to NSSI behavior were conducted with all patients with MDD, regardless of whether they had a parent- or self-reported NSSI. Adolescents with MDD who were engaged in NSSI were screened out. The frequency and methods of NSSI in the past 6 months, including skin cutting, scratching, and hair pulling were also obtained. Patients with MDD were divided into the NSSI group (patients with MDD who engaged in NSSI) and MDD group (patients with MDD only) based on their NSSI behavior.

## Acquisition of rs-fMRI Data

MRI images were obtained using a 3T GE Signa HDxt MRI scanner (General Electric Healthcare, Chicago, IL, USA) with an 8-channel head coil. The subjects were instructed to relax with their eyes closed, stay awake, and avoid thinking as much as possible. None of the patients reported falling asleep during scanning. Suitable and comfortable foam pads and earplugs were used to fix their heads to minimize head motion and reduce machine noise, respectively. The EPI pulse sequence parameters were as follows: repetition time (TR), 2,000 ms; echo time (TE), 40 ms; field of view (FOV), 240 × 240 $mm^2$; matrix, 64 × 64; flip angle, 90°; slice number, 33; slice thickness/gap, 4.0/0 mm; scanner time, 8 min; and 240 volumes. Three-dimensional T1-weighted MRI images were used for rs-fMRI co-registration. The parameters were also recorded: TR, 24 ms; TE, 9 ms; FOV,

240 × 240 $mm^2$; matrix, 256 × 256; flip angle, 90°; and slice thickness/gap, 1.0/0 mm.

## Preprocessing of rs-fMRI Data

The rs-fMRI images were preprocessed using the SPM12-based DPABI software (43) (http://www.restfmri.net) running in MATLAB (MathWorks, Natick, MA, USA). To allow the subjects to adapt to the scanning environment and the magnetization signal to become relatively stable, the first 10 volumes were discarded. The images underwent the following preprocessing steps: (1) slice timing correction, (2) realignment to correct head motion, (3) normalization to the standard Montreal Neurological Institute (MNI) space using the Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) tool (44) and resampling to a 3 × 3 × 3 mm resolution. To reduce the effect of physiological noise, a series of nuisance covariates were regressed using the Friston-24 model (45), including the white matter signal, cerebrospinal fluid signal, and head motion parameters. A linear detrend was conducted to reduce the effect of drift in the BOLD signal. Subjects with head translation >3 mm and rotation >3° were removed.

## ALFF Analysis

After preprocessing the data, DPABI software was used to conduct the ALFF analysis. A band-pass filter (0.01–0.08 Hz) was then applied to reduce the influence of lower-frequency drift and high-frequency noise. Each voxel's time series was transformed into the frequency domain using the fast Fourier transform algorithm. After obtaining the power spectrum, the average square root of the power spectrum, namely, the ALFF value, was calculated. The ALFF values were then converted to z-ALFF values using the Fisher's z transformation. The z-ALFF values were spatially smoothed with an isotropic Gaussian kernel with a 4-mm full-width at half-maximum (FWHM). These data were used as the final ALFF values for the statistical analysis.

## Seed Region selection

After the ALFF analysis, the regions with statistical differences in brain activity were regarded as regions of interest (ROI). The seed regions were set in the ROI to further study the integration of the brain function network. The sphere was plotted with the peak voxel of each positive cluster as the center, with a radius of 6 mm, which was considered as the seed region of the rs-FC analysis.

## ALFF-Based Whole-Brain rs-FC Analysis

The DPABI software was used again to study the integration of the brain function network by ALFF-based whole-brain rs-FC analysis. First, after preprocessing, the data were processed using a band-pass filter (0.01–0.08 Hz) and spatially smoothed with a 4-mm FWHM Gaussian kernel. Second, an FC map was generated by calculating the linear correlations between the average time series within each ROI and the rest of the brain voxels. Third, Fisher's r-to-z transformation was conducted to create subject-specific maps, and further statistical analysis was performed.

## Statistical Analysis

To investigate the differences in the demographics and clinical characteristics of the NSSI and MDD groups, the two-sample *t*-test and chi-square test were used to analyze the continuous variables and categorical variables using IBM-SPSS for Windows version 21.0 (IBM Corp., Armonk, NY, USA), respectively. The statistical analysis of ALFF and FC was completed using DPABI software. We used a two-sample *t*-test with age, gender, educational level, and whole-brain gray matter volume as covariates to identify the difference in ALFF between the two groups. The significance level was set at $p < 0.05$. The threshold-free cluster enhancement (TFCE) (46) correction with 1,000 permutations (47) was used to correct for multiple comparisons. For the FC analysis, a one-sample *t*-test was conducted to identify FC abnormalities in each group. The difference in FC between the NSSI and MDD groups was evaluated using a mask created by a one-sample *t*-test statistical map of the two groups. A two-sample *t*-test with age, gender, educational level, and whole-brain gray matter volume as covariates was used to evaluate the significantly distinct FC values in the two groups. During the two-sample *t*-test of FC, the significance level was set at $p < 0.05$. The TFCE (46) correction with 1,000 permutations (47) was used to correct for multiple comparisons. In addition, after extracting the averaged eigenvalues of ALFF and FC with significant inter-group differences, a two-tailed Pearson's correlation analysis with a statistical significance threshold set to $p < 0.05$, was used to investigate the relationship between the abnormal regions and HAMD scores.

# RESULTS

## Demographic Data and Clinical Characteristics

Nine subjects who did not meet the criteria for NSSI behavior in the present study were excluded. The demographics and clinical characteristics of the remaining 67 patients with MDD are shown in **Table 1**. The age range was 13–19 years. A total of 31 adolescents (8 male and 23 female subjects) with MDD who engage in NSSI with a mean age of 16.13 ± 1.69 years were assessed as the NSSI group. A total of 36 adolescents (9 male and 27 female subjects) with MDD only with a mean age of 16.78 ± 1.48 years were assessed as the MDD group. There were no significant differences in age, gender, and education level between the NSSI and MDD groups (all $p > 0.05$). No obvious differences in HAMD scores were observed between the NSSI and MDD groups ($t = 0.697$, $p > 0.05$). Cutting was the main method of NSSI, and a few individuals used multiple NSSI methods.

## ALFF Results

The brain regions with statistical differences in ALFF values between the NSSI and MDD groups are displayed in **Table 2**, **Figure 1A**. Compared to the MDD group, the NSSI group showed significantly increased ALFF in the right FFG (FFG. R) (MNI peak voxel coordinates: 27, −36, −15), and the right median cingulate and paracingulate gyri (DCG. R) (MNI peak voxel coordinates: 12, −24, 39) ($P < 0.05$). There was no evidence of brain regions with decreased ALFF in the NSSI group. The clusters that presented significantly increased ALFF in the NSSI group relative to the MDD group were used as ROI for further rs-FC analysis. We defined a sphere with a radius of 6 mm centered

**TABLE 1 |** Demographics and clinical characteristics of adolescents with MDD who engage in NSSI and adolescents with MDD only.

| Characteristics | | NSSI ($n = 31$) | | MDD ($n = 36$) | | Statistical test | *P*-value |
|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | | |
| Age (years) | | 16.13 | ±1.69 | 16.78 | ± 1.48 | $t = -1.679$ | 0.098 |
| Gender (Male: Female) | | 8:23 | | 9:27 | | $\chi^2 = 0.006$ | 0.940 |
| Education level (years) | | 9.98 | ± 1.91 | 10.47 | ± 1.59 | $t = -1.180$ | 0.242 |
| HAMD score | | 21.19 | ± 3.27 | 20.61 | ± 3.52 | $t = 0.697$ | 0.488 |
| **NSSI** | | | | | | | |
| Frequency | | | | | | | |
| | 1–5 acts | 13 (41.94%) | | | | | |
| | 6–10 acts | 11 (35.48%) | | | | | |
| | 11–20 acts | 5 (16.13%) | | | | | |
| | $21^+$ | 2 (6.45%) | | | | | |
| Ways | Cutting | 25 | | | | | |
| | Interfere with wound | 3 | | | | | |
| | Sever scratching | 3 | | | | | |
| | Hair pulling | 1 | | | | | |
| | Banging/hitting self | 5 | | | | | |

*MDD, major depressive disorder; NSSI, non-suicidal self-injury; HAMD, Hamilton Depression Rating Scale. The chi-square test was used for gender comparisons. The two-sample t-test was used to compare age, education level, and HAMD score.*

**TABLE 2 |** Brain regions showing significantly decreased ALFF values in the adolescents with MDD who engage in NSSI compared with the adolescents with MDD only.

| Cluster | Region | Side | Cluster size (voxels) | MNI coordinate | | | Peak intensity |
|---|---|---|---|---|---|---|---|
| | | | | x | y | z | |
| NSSI > MDD | | | | | | | |
| Cluster 1 (ROI1) | FFG | R | 52 | 27 | −36 | −15 | 4.9059 |
| Cluster 2 (ROI2) | DCG | R | 29 | 12 | −24 | 39 | 3.9877 |

*ALFF, amplitude of low-frequency fluctuation; MDD, major depressive disorder; NSSI, non-suicidal self-injury; MNI, Montreal Neurological Institute; R, right; FFG, fusiform gyrus; DCG, median cingulate and paracingulate gyri.*

on the peak voxel coordinates of the ROI as the seed region for further analysis, as shown in **Figure 1B**.

## ALFF-Based rs-FC Analysis

Based on the ALFF analysis, spherical ROI with a radius of 6 mm centered on the peak voxel coordinates in the FFG. R and DCG. R as seed regions (ROI1 and ROI2, respectively) were obtained to conduct the subsequent ALFF-based rs-FC analysis (see **Table 2**, **Figure 1B**). Compared with the MDD group, the rs-FC of the FFG. R-bilateral medial orbital of the superior frontal gyrus (ORBsupmed. L/R)/bilateral medial superior frontal gyrus (SFGmed. L/R) and FFG. R-bilateral posterior cingulate gyrus (PCG. L/R) was decreased in the NSSI group (**Table 3**, **Figure 1C**). In addition, the rs-FC of the DCG. R-left pallidum (PAL. L), DCG. R-right superior temporal gyrus (STG. R), and DCG. R-right postcentral gyrus (PoCG. R)/right inferior parietal lobule (IPL. R) was significantly reduced in the NSSI group compared to the MDD group (**Table 3**, **Figure 1D**). There was no evidence of brain regions with increased rs-FC in the NSSI group.

## Correlation of ALFF/FC With HAMD Scores

Average eigenvalues of ALFF in the FFG. R and DCG. R and FC from these two ROI to the other regions (see **Table 3**) were extracted to further evaluate their association with HAMD scores. There was no significant association between HAMD scores and ALFF or FC values in the NSSI and MDD groups ($p > 0.05$).

# DISCUSSION

Rs-fMRI, a non-invasive imaging method, is widely used to study anomalous neural function in individuals with psychiatric disorders. In the current study, 67 adolescents with MDD were registered, and 31 patients had NSSI behavior according to clinical interviews. Abnormal neural function in certain areas of the visual regions and DMN in the NSSI group relative to the MDD group was detected using ALFF analysis. Our results showed that, compared to the MDD group, the brain regions with increased ALFF in the NSSI group were located in the FFG. R and DCG. R, but there was no evidence of brain regions with decreased ALFF in the NSSI group. After ALFF analysis,

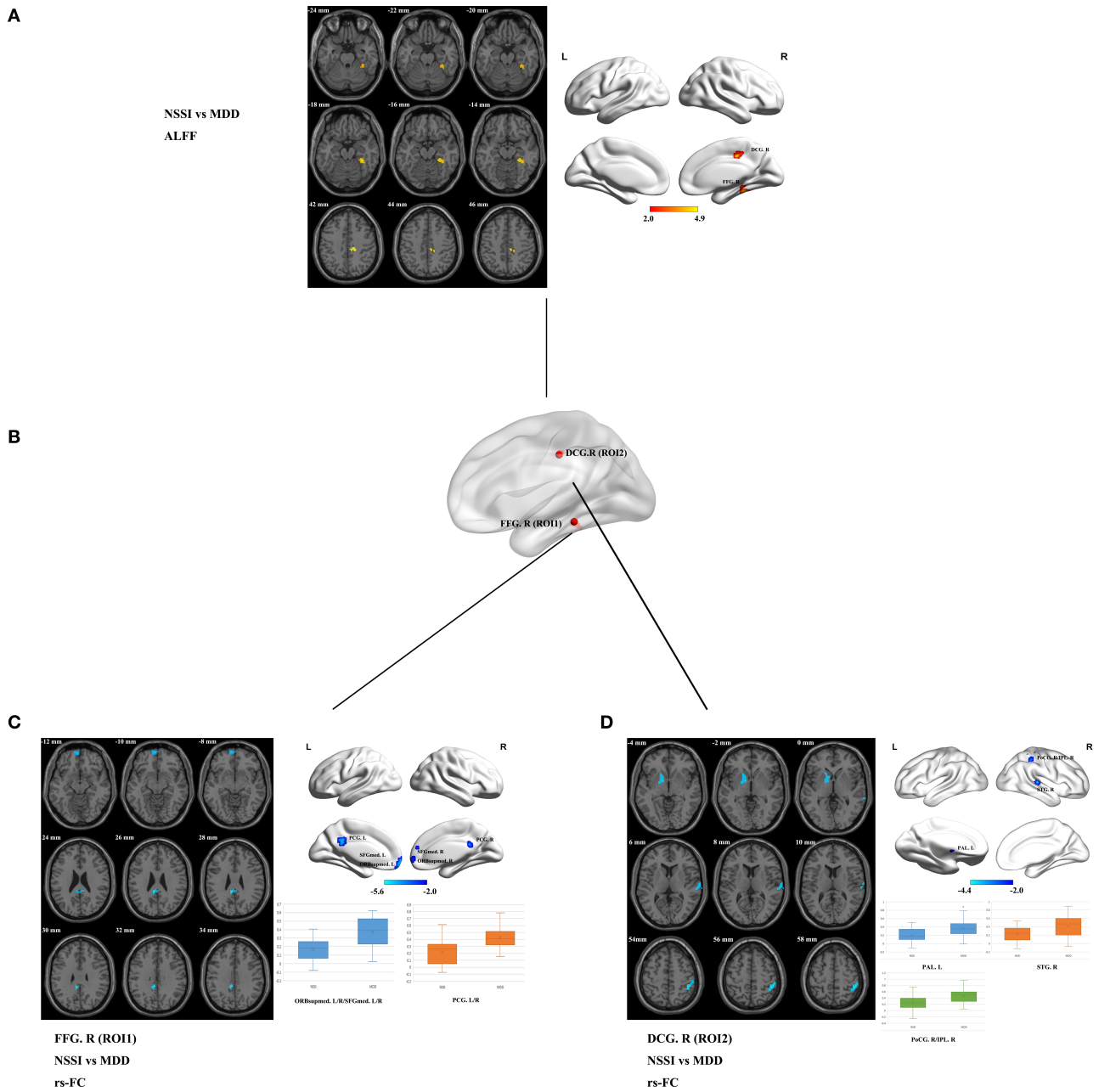


**FIGURE 1 | (A)** Brain regions showing significant differences in ALFF values in the NSSI group compared with the MDD group ($p < 0.05$, 1,000 permutations, TFCE corrected). Regions where the ALFF values have increased are shown in red. The color bar indicates the *T*-value. **(B)** The locations of the seed regions are based on the ROI (ROI1 and ROI2). **(C)** Brain regions showing significant differences in ROI1 (FFG. R)-based rs-FC in the NSSI group compared with the MDD group. Regions where the rs-FC has decreased are shown in blue ($p < 0.05$, 1,000 permutations, TFCE corrected). Box plot showing the comparisons of ROI1 (FFG. R)-based rs-FC values between the NSSI and MDD groups. The center line, the lower bound of the box, and the upper bound of the box represent the median value, the 25th percentile, and the 75th percentile, respectively, and the whiskers represent the maximum and minimum values. **(D)** Brain regions showing significant differences in ROI2 (DCG. R)-based rs-FC in the NSSI group compared with the MDD group. Regions where the rs-FC has decreased are shown in blue ($p < 0.05$, 1,000 permutations, TFCE corrected). Box plot showing the comparisons of ROI2 (DCG. R)-based rs-FC values between the NSSI and MDD groups. The center line, the lower bound of the box, and the upper bound of the box represent the median value, the 25th percentile, and the 75th percentile, respectively, and the whiskers represent the maximum and minimum values. ALFF, amplitude of low-frequency fluctuation; MDD, major depressive disorder; NSSI, non-suicidal self-injury; rs-FC, resting-state functional connectivity; ROI, region of interest; TFCE, threshold-free cluster enhancement. FFG. R, right fusiform gyrus; DCG. R, right median cingulate and paracingulate gyri; ORBsupmed. L/R, bilateral medial orbital of the superior frontal gyrus; SFGmed. L/R, bilateral medial superior frontal gyrus; PCG. L/R, bilateral posterior cingulate gyrus; PAL. L, left pallidum; STG. R, right superior temporal gyrus; PoCG. R, right postcentral gyrus; IPL. R, right inferior parietal lobule.

**TABLE 3 |** Brain regions showing significantly decreased ROI1-based rs-FC and ROI2-based rs-FC in adolescents with MDD who engage in NSSI compared with the adolescents with MDD only.

| Cluster | Region | Side | Cluster size (voxels) | MNI coordinate | | | Peak intensity |
|---|---|---|---|---|---|---|---|
| | | | | x | y | z | |
| **ROI1** | | | | | | | |
| NSSI < MDD | | | | | | | |
| Cluster 1 | ORBsupmed/SFGmed | L/R | 130 | 0 | 63 | 18 | −5.5762 |
| Cluster 2 | PCG | L/R | 40 | −9 | −39 | 27 | −5.4528 |
| **ROI2** | | | | | | | |
| NSSI < MDD | | | | | | | |
| Cluster 1 | PAL | L | 61 | −12 | 3 | −3 | −3.8052 |
| Cluster 2 | STG | R | 51 | 63 | −33 | 3 | −4.0349 |
| Cluster 3 | PoCG/IPL | R | 85 | 45 | −39 | 57 | −4.4425 |

*MDD, major depressive disorder; NSSI, non-suicidal self-injury; rs-FC, resting-state functional connectivity; MNI, Montreal Neurological Institute; ROI, region of interest; L, left; R, right; ORBsupmed, medial orbital of the superior frontal gyrus; SFGmed, medial superior frontal gyrus; PCG, posterior cingulate gyrus; PAL, pallidum; STG, superior temporal gyrus; PoCG, postcentral gyrus; IPL, inferior parietal lobule.*

significantly decreased connectivity of the FFG. R-ORBsupmed. L/R/SFGmed. L/R, FFG. R-PCG. L/R, DCG. R-PAL. L, DCG. R-STG. R, and DCG. R-PoCG. R/IPL. R in the NSSI group relative to the MDD group was also detected using whole-brain ALFF-based rs-FC analysis. These main findings are consistent with our hypotheses, suggesting that the abnormal patterns within certain areas of the visual regions and DMN in adolescents with MDD who engage in NSSI and adolescents with MDD only may be correlated with NSSI behavior.

In the present study, the brain areas with increased ALFF in adolescents with MDD who engaged in NSSI were located in the FFG. R and DCG. R. The FFG. R is involved in the composition of visual regions that play a vital role in the perception of emotion during facial stimuli tasks (48). Enhanced neural activity in response to sad facial expression in the FFG. R was observed in patients with MDD compared to healthy controls, while a decreased response was also exhibited in the bilateral FFG in response to happy facial stimuli, which was inversely correlated with depression severity (49). In addition, Chan et al. demonstrated that increased activity in the FFG. R is associated with a high risk of depression (50). These studies suggest abnormal neural activity in the FFG. R may be associated with the severity of depression or susceptibility to depression. The alteration of the FFG. R between the NSSI and MDD groups suggested that NSSI behavior may be a potential measure of the severity of the MDD. However, there was no significant correlation between the HAMD scores and ALFF alterations in the FFG. R in our study. Therefore, it is necessary to expand the sample size for further studies. Contrary to the above results, another rs-fMRI study found significantly decreased ALFF in the FFG. R among patients with MDD compared to healthy controls (51). Skokauskas et al. reported similar results after analyzing abnormal neural activity in patients with MDD only, patients with MDD and sexual abuse, and healthy controls using task-based fMRI (52). The inconsistent results of the aforementioned studies may have been due to differences in sample size, imaging parameters, task modes, and effect of MDD symptoms. Our work focused on rs-fMRI in adolescents with MDD who engage in NSSI, especially in certain areas of the visual regions and DMN. Individuals with NSSI behavior usually have an aberrant ability to recognize, understand, process, and express emotion (53). NSSI is a common strategy among adolescents to regulate negative emotions (54). Emerging studies have demonstrated that greater difficulty with emotional awareness (55) and regulation (56) in individuals who engage in NSSI may be connected to NSSI behavior. Adolescent inpatients who engage in NSSI showed greater deficits in emotional face recognition than healthy controls (57), which suggests that deficits in emotional face recognition may be correlated with dysfunctional visual regions, including the FFG. R. We found increased ALFF values in the FFG. R in adolescents with MDD who engaged in NSSI relative to adolescents with MDD only. This result is in line with a report that, compared to healthy controls and subjects with depression only, NSSI youth exhibited enhanced neural activity in the FFG (23). The differences in neural activity of the visual areas such as the FFG between the two groups imply that it may potentially be involved in the neurobiological process of NSSI in adolescents with MDD. However, further research is required in the future. The NSSI group also showed an increased ALFF in the DCG. R. The DCG is involved in the composition of the cingulate gyrus, which is the key node in the DMN and plays an important role in information transmission and cognitive processing. The DMN is significantly associated with episodic memory and rumination processing of depressive symptoms (27, 58). However, there was no prior rs-fMRI study on DCG and MDD or NSSI. Previous studies have focused more on PCC, one of the major subdivisions of the DMN. Aberrant neural activity in the PCC and PCC-based FC in patients with MDD has been widely reported (59, 60). FC in the PCC has been shown to be correlated with rumination in MDD (30). In the present study, the rs-FC between the FFG. R and PCG. L/R in the NSSI group compared to the MDD group was also decreased, which is similar to previous evidence showing that, compared to healthy controls, patients with MDD had significantly reduced rs-FC between the PCC and FFG (61). Taken together, these results indicate that differences in brain activity between the NSSI and MDD

groups might exist at multiple levels including visual information processing, the perception of emotions, and the integration of affective and cognitive information, and to some extent, it could provide an explanation for the occurrence of NSSI behavior in adolescents with MDD.

Based on the changes in the ALFF in the FFG. R, rs-FC from the FFG. R to the whole brain was analyzed in the present study. To the best of our knowledge, the connectivity patterns of the FFG. R with other brain areas in adolescents with MDD who engage in NSSI has not been previously reported. Our findings showed that, compared to patients with MDD only, significantly decreased connectivity of the FFG. R-ORBsupmed. L/R/SFGmed. L/R and FFG. R-PCG. L/R was detected in adolescents with MDD who were engaged in NSSI. There was no evidence of brain regions with increased rs-FC in the NSSI group. These findings support our hypotheses that the differences in neural activity between adolescents with MDD who engage in NSSI and adolescents with MDD only might be located in certain areas of the visual regions and DMN, and the remote rs-FC in the changed brain regions might be significantly different. The frontal cortex is a pivotal part of the fronto-striatal circuit, which involves the superior frontal gyrus (ORBsupmed and SFGmed) and PAL. Previous studies have demonstrated that the superior frontal gyrus is associated with cognitive processing involved in executive function and memory retrieval in patients with MDD (62). Moreover, a limited number of studies have shown that individuals with NSSI behavior show hyperactivation in frontal areas, including the ORBsupmed and SFGmed, striatum, and STG (63, 64); however, no research on FC in these regions in patients with NSSI has been reported. An fMRI study suggested that, compared to healthy controls, patients with MDD showed decreased FC in the superior frontal gyrus, which is similar to our results (65). Given the association between the frontal cortex and emotional regulation and impulsive control (66), the decreased FC in the superior frontal gyrus in adolescents with MDD who engage in NSSI prompted us to carefully consider the effect of the superior frontal gyrus on NSSI behavior.

Decreased FC from the DCG. R to the PAL. L, STG. R, and PoCG. R/IPL. R was also examined in adolescents with MDD who were engaged in NSSI. The PAL, which is not only a component of the striatum but also a transmission node connecting the PFC and amygdala, participates in the mediation of reward processing and anhedonia in MDD (67). Reward processing is related to the feeling of "relief" in patients with NSSI. The association between striatum activity and relief was greater in NSSI youth than that in non-NSSI youth, indicating that the striatum might be involved in the neurobiological process of NSSI behavior (63). Interestingly, a previous study suggested that adolescents with NSSI thoughts also showed enhanced striatal activity during the monetary reward task relative to those without any NSSI thoughts (68), which could be another evidence of a link between the striatum and NSSI. However, there has been no research on FC in the striatum of individuals with NSSI. In accordance with prior research, the present study further confirmed that the abnormal connection in the PAL may participate in the NSSI behavior of adolescents with MDD. Furthermore, accumulating evidence has demonstrated that the temporal lobe is linked to human emotional and mental activities. In addition to auditory processing, the STG is also implicated in emotional processing and social cognition in patients with MDD (69, 70). Guo et al. found that, compared to healthy controls, drug-naive patients with MDD had significantly decreased FC in the STG (71). In addition, an enhanced BOLD response in the STG was also demonstrated in individuals with NSSI behavior (63). The rs-FC was also reduced in the PoCG, which participates in somatosensory processing, in youth with MDD relative to healthy controls (72). However, to our knowledge, there are no reports on the changes in FC in the STG and PoCG in NSSI individuals. In the present study, compared to the adolescents with MDD only, the adolescents with MDD who engaged in NSSI demonstrated significantly reduced connectivity of the DCG. R-STG. R and DCG. R-PoCG. R. Taken together, these differences have the potential to be used as specific brain regions to help differentiate patients with MDD who engage in NSSI from all patients with MDD and contribute to further studies on the neurobiological mechanism of NSSI in the future. In addition, these results also imply that NSSI behavior may be a potential measure of the severity of MDD. However, further studies are required.

## Limitations

This study has limitations that merit mention. First, the history of NSSI behavior in adolescents with MDD came from a parent or self-report and further clinical interviews, so it is probable that subjects may engage in self-injury behavior with the intention of ending their life but deny it owing to a sense of shame. However, to date, we have not been able to determine their purpose. Second, owing to the cross-sectional design, the changes in ALFF in the FFG. R and DCG. R or in rs-FC from the FFG. R and DCG. R to other related regions did not demonstrate that it was a state or trait effect in adolescents with MDD who engage in NSSI; therefore, it is necessary to conduct a longitudinal study in future research. Third, to explore the neurobiological changes in adolescents with MDD who engage in NSSI, we used adolescents with MDD only as a control, but, healthy controls may be needed to determine whether there are differences between patients with MDD and healthy people in the same brain region. Fourth, the present study lacks an objective assessment of the IQ of all subjects, although IQ scores are more likely to be correlated with the frontoparietal network (73). Finally, the sample size was relatively small. It is necessary to increase the sample size for further rs-fMRI studies on adolescents with MDD who engage in NSSI.

# CONCLUSION

In conclusion, the current study has demonstrated that, in comparison with adolescents with MDD only, significantly enhanced local brain activity in the FFG. R and DCG. R and the significantly reduced rs-FC of the FFG. R-ORBsupmed. L/R/SFGmed. L/R, FFG. R-PCG. L/R, DCG. R-PAL. L, DCG. R-STG. R, and DCG. R-PoCG. R/IPL. R was detected in adolescents with MDD who engage in NSSI. These results are in line with our hypotheses that the differences in local neural activity between

adolescents with MDD who engage in NSSI and adolescents with MDD only may be located in certain areas of the visual regions and DMN, and the remote rs-FC based in the changed regions in adolescents with MDD with and without a history of NSSI may be obviously different. These differences may be helpful in understanding the neural alterations of adolescents with MDD who engage in NSSI and could provide a new perspective for further study on the neurobiological mechanism of NSSI behavior in adolescents with MDD.

## DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

QH designed the research, collected samples, analyzed data, and wrote the original of manuscript. MX collected samples, supervised, and analyzed data. MA, WW, and JCh supervised data and conducted quality control. LH collected samples and gave some advice. JCa supervised the research, gave some advice, and revised the manuscript. MW collected samples. LK supervised the research, provided funding, and gave some advice. All authors contributed to the article and approved the submitted version.

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# Emotional Reactivity and Family-Related Factors Associated With Self-Injurious Behavior in Adolescents Presenting to a Child and Adolescent Psychiatric Emergency Service

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**Background:** Adolescents presenting in a child and adolescent psychiatric emergency service show various psychiatric disturbances, most commonly suicidal ideation, suicide attempts, and non-suicidal self-injury (NSSI). It was postulated that especially disturbed emotion regulation contributes to self-injurious behavior of young people. This study aims to investigate the relevance of emotional reactivity (ER), as part of emotion regulation, during an acute crisis, how it relates to self-injurious behavior reinforcement and how a family as well as peers' history of self-injurious behavior are associated with self-injurious behavior of presenting adolescents. Additionally, crisis-triggering background factors were evaluated from the perspective of patients and their caregivers.

**Methods:** A consecutive sample of 86 adolescents aged 11–18 years presenting to the emergency outpatient department due to self-injurious thoughts and behavior received a pretreatment psychiatric evaluation. Among other psychometric measures and structured clinical interviews, ER was measured via the Emotion Reactivity Scale (ERS). Family-related aspects were collected both through evaluation of history and through questionnaires filled in by custodians or parents.

**Results:** Data analysis revealed that suicidal ideation was significantly related to family history with self-injurious behavior in comparison with a family background without such a history. A significant positive correlation was apparent between the ERS sensitivity score and occurrence of NSSI within the past year. A relationship between the ERS and distinct types of reinforcement as a motivation factor for NSSI was found. *Post-hoc* tests revealed a significant difference between boys and girls when no positive peers' history is present with boys having lower ERS scores than girls, but no difference when both groups had friends engaging in self-injurious behavior. There was only moderate agreement between parents and their children in naming reasons for the current crisis involving NSSI.

**Conclusion:** Emotional regulation, especially ER, has an influence on patients' acute psychiatric symptomatology and when experiencing an acute crisis should be brought into focus early at psychiatric assessment. A history of self-injurious behavior taken from patient's family members and close circle of friends and agreement on reasons for the crisis should be routinely included in the exploration of a patient presenting with self-injurious behavior.

**Keywords: emotional reactivity, suicidal behavior, self-injurious behavior, non-suicidal self-injury, emergency, adolescents, family related factors**

## INTRODUCTION

A psychiatric emergency is defined as an acute disturbance of a patient's mood, thought or behavior, by which the individual may cause harm to either himself or others (1). Initial support for those patients, in many cases, is psychiatric emergency care (2, 3), where circumstances for urgent presentations by young people range from small events to life-threatening situations (4, 5). Multiple reasons are presented for emergency appearances, the main symptoms are self-injurious thoughts and self-injurious behaviors (6). Self-injurious thoughts and behaviors (SITB) range from non-suicidal self-injury (NSSI), which is carried out with no intention to die, to suicidal behavior, in which the individual has at least some intention to die (7). Although NSSI and suicidal behavior must be distinguished in terms of motivation/intention and medical severity, there is a high and not negligible overlap between the two behaviors (8), which supports a combined examination in an emergency setting.

While the prevalence of SITB up to puberty is low (9), these symptoms develop into a very common pattern of behavior during adolescence. In a large sample of adolescents from European countries, an overall lifetime prevalence of direct self-injurious behavior (regardless of suicidal intent) of about 27.6% could be found (8). In child and adolescent psychiatric hospitals, the prevalence rate of NSSI is as high as 60% of admitted patients (10). NSSI is understood as self-inflicted, voluntary, direct injury, or damage to body tissue without conscious suicidal intention, which is not socially accepted (11). Although NSSI can manifest itself without mental illness, it is often associated with emotional abnormalities and behavioral problems (12). Those affected show a high degree of suffering and in addition NSSI is linked to affective (8) and personality disorders, particularly borderline personality disorder (BPD) (13). Self-injurious behavior among young people applies as an important risk factor for the prediction of a borderline personality disorder (14). Unfortunately, many parents have no knowledge of NSSI and its treatment and thus suffer from great emotional stress because of it (15). An additional risk factor is the strong association between NSSI and suicidal behavior (16). In some cases, NSSI is a potent predictor of suicide attempts, which underlines the importance in preventing these behaviors (17–19).

Teenagers who reported frequent suicidal ideation showed an 18-fold increased risk of NSSI (20). It was revealed that stopping self-injurious behavior reduces the risk of suicidal ideation and behavior in adolescents and therefore contributes to reducing further suicidal behavior (16), which can be defined as suicidal ideation, suicide plans, suicide attempts, and completed suicides (21). Suicidal behavior tends to be recurrent and can be a harbinger of the completion of suicide (22). The transition between different self-injurious thoughts and behaviors is quite fast and an important time-frame for prevention and intervention is between 6 and 12 months after the occurrence of suicidal ideation (23). Thus, emergency care is crucial for the prevention and therapy of recurrent suicidal ideation. In addition, NSSI and suicidal behavior have been inserted into section Results of the new DSM-5 (24, 25), which supports the relevance of a combined approach.

Research on the origin of suicidal behavior suggests for it to be familial and liability for suicidal behavior in families is apparently transferred independently of the psychiatric disorder itself (26, 27). In addition, a suicide attempt and suicide completion of friends is considered a risk factor for one's own suicidal behavior (28). A recently attempted suicide of a friend is a significant predictor for a future suicide attempt (29). Furthermore, exposure to self-injurious behavior of family members and friends is associated with adolescents' own self-injurious behavior (30, 31). NSSI of teenagers has been reported to be associated with an increasing perception of their friends' involvement in depressive/self-injuring thoughts and behaviors (32). This result has also been replicated in young adults (33).

Apart from NSSI and suicidal behavior within the familial and social network, also other aspects have been identified as determinants for NSSI during youths' development. Numerous studies have demonstrated the importance of emotional dysregulation for development and the clinical course of mental disorders (34). The results of In-Albon et al. (35) illustrate that adolescents with NSSI compared to a healthy control group have difficulties with their emotion regulation in certain areas. In addition, compared to a similarly psychiatrically affected clinical control group, adolescents with NSSI had significantly more difficulties in the regulation of their emotions, particularly impulse control, clarity about one's own feelings, goal-oriented behavior and difficulties in accessing emotion regulation strategies (35). It is therefore surprising that the assessment of emotion regulation strategies has so far been poorly integrated into the diagnosis of mental disorders (34). A study by Glenn and Klonsky (36) also showed that the NSSI disorder explains a unique proportion of variance in almost all aspects of emotion dysregulation (36).

Emotional reactivity (ER) is part of the emotional-response-process; an individual considers a situation, rates it as relevant and feels the activation of an emotion that can be described in terms of experience, behavior and physiology (37). Nock et al. (38) specified ER as "the extent to which an individual experiences emotions (a) in response to a wide array of stimuli (i.e., emotion sensitivity), (b) strongly or intensely (i.e., emotion intensity), and (c) for a prolonged period of time before returning to baseline level of arousal (i.e., emotion persistence)." According to this concept increased ER results in emotion regulation difficulties (38). In line with these results, individuals who engage in NSSI report higher ER compared to a healthy control group (39). To the best of our knowledge, previous studies in clinical (40) and non-clinical samples (39, 40) have not examined the importance of ER in the aftermath of an acute crisis. Thus, conclusions cannot be drawn as to whether increased ER is a key factor in maladaptive emotion regulation after crisis situations.

Patients with NSSI often engage in this behavior when confronted with overwhelming negative emotions (41). In accordance with the model outlined by Nock (7), apart from automatic negative reinforcement (intrapersonal), i.e., NSSI is followed by an immediate reduction or a cessation of aversive feelings, there are three other important functions by which NSSI can be perpetuated (42). The second intrapersonal aspect is automatic positive reinforcement (i.e., behavior is followed by occurrence or increase in desired feelings) (7, 42). NSSI can also be maintained by interpersonal factors, namely social positive reinforcement (i.e., occurrence or increase of a desired social event), but also by social negative reinforcement (i.e., decrease or termination of a social event) (7, 42). In a group of child psychiatric inpatients aged 12–19 years, most adolescents reported that they engaged in NSSI to get away from bad feelings (43). NSSI is often reported as a coping strategy to handle negative emotional states better (44). Thus, the current research question is specifically about NSSI and whether higher ER is associated with the assumed four significant functions just described above.

Not only ER plays a crucial role, but also the social environment. In a school-based survey, friends were significantly more likely than family to be asked for support when engaged in NSSI (45). In general, seeking official services or medical professionals was even more difficult for youths and many young people felt that they should be able to cope on their own and were concerned that seeking help would cause them more problems and hurt people they cared about (45). For this reason, we were interested in whether caregivers' and patients' explanatory models agree or not. We assumed that if there is a high degree of agreement, adolescents are more likely to open up to the caregivers (46) and, in the best case, to be motivated by the caregivers to allow expert support. However, our daily routine work with adolescent patients leads us to believe that the reasons given differ between caregivers and patients which leads to a significant impediment to a successful therapeutic intervention.

Adolescents who are admitted to an emergency service at clinics of child and adolescent psychiatry show a broad range of psychopathological disorders, but above all primarily suicidal behavior and NSSI. The present study aims at investigating the extent of young people's psychiatric burden and the extent to which ER is conspicuous even in the case of an acute crisis. Given the state of current knowledge, we proposed the following hypothesis that youths with NSSI have increased ER measured via the Emotion Reactivity Scale (ERS). Furthermore, we expected a significant relationship between ERS scores and both positive and negative automatic reinforcement, as it is most commonly reported as a motivation for NSSI. In addition, we also focused on psychiatric family history with regards to psychological/psychiatric illnesses (including suicide, attempted suicide, NSSI) and the occurrence of suicide attempts or NSSI among close friends (peers' history). Here we assumed an association between a positive family or peers' history on the occurrence of thoughts and actions of NSSI as well as suicidal ideation and suicide attempts. Lastly, it seems important for the management of crisis situations to know which explanatory models for the emergence of the acute crisis the adolescents themselves and their caregivers claim and whether these models agree or contradict each other. It was hypothesized that the reasons for the crisis given by guardians and patients differ significantly.

# MATERIALS AND METHODS

## Participants and Recruitment

Eighty-six patients [75.6% female, age M = 15;8 (years; months)] were recruited via the emergency outpatient department of the Clinic of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy of the University Regensburg, Germany. This clinic is a typical child and adolescent psychiatric hospital of maximum care. Patients between 11 and 19 years, who are presented for emergencies during the day and at night because of SITB, are offered a standardized emergency management with specified diagnostic assessments and short-term intervention by means of two further time points (time point 2 and time point 3). The existing standardized emergency management is characterized by rapid time point allocation [time interval between emergency appointment and time point 2: M = 6.59 days (SD = 4.67 days), time interval between emergency appointment and time point 3: M = 17.12 days (SD = 9.43 days)] and including an initial early intervention for adolescents with NSSI and suicidal behavior with the aim of preventing an aggravation of SITB or bringing it to remission. Patients with acute psychotic disorder or other acute psychiatric conditions that could affect the patient's ability to consent, intellectual impairment (IQ lower than 80) according to clinical assessment or acute suicidal tendencies requiring prolonged inpatient treatment (more than 12 nights) on one of the hospital units were not included. The specified diagnostic assessment and short-term intervention by means of two further time points were also not offered to those patients who already receive regular outpatient treatment from established child and adolescent psychiatric services and who did not require a specified treatment offer. Thus, our sample represents a typical child and adolescent psychiatry outpatient clinic, as

patients with a longer acute need for inpatient treatment were not included.

Outliers were defined as more than 3 standard deviations from the mean and were removed a priori for lifetime prevalence ($n = 2$ for suicidal ideation, $n = 1$ for suicidal attempts, $n = 3$ for NSSI thoughts, $n = 5$ for NSSI behavior) and the past year's prevalence ($n = 2$ for suicidal ideation, $n = 1$ for suicidal attempts, $n = 1$ for NSSI thoughts, $n = 4$ for NSSI behavior) for the dependent variables.

The specified standardized psychiatric assessment included a problem hierarchy to enable further recommendations to be made. In addition, a detailed safety plan was developed with the patient for prevention or support in future crisis situations. At time point 3, caregivers and patients were asked whether they agree to participate in two follow-up examinations (4 and 8 weeks after the third time point to evaluate the effectiveness of the standardized procedure). The first emergency presentation time point as well as the standardized specified assessments (time point 2) and the short-term intervention and notification of further recommendations (time point 3) were clinical procedures. The two follow-up time points represent the longitudinal part of the study design and will be reported after completion of the follow-up investigations.

The present study was approved (No.: 19-1426-101) by the ethics committee of the University of Regensburg. Participants and their caregivers gave their informed and written consent to take part in the study. If a crisis-like worsening of symptoms became apparent in one of the clinical time points or in one of the two follow-up examinations, an inpatient crisis admission was provided as an option, if necessary. The purpose of this paper is to describe the baseline sample that participated in the specified psychiatric assessments (time point 2) as well as in the short-term intervention (time point 3) and address the relationship between ER and NSSI and suicidal behaviors.

## Measures

The sociodemographic information as well as the clinical characterization with regard to NSSI and suicidal behavior, a possible concomitant borderline personality disorder and psychiatric comorbidities were performed in all patients by means of a semi-structured clinical interview with the following variables: Age/date of birth, type of school, treatment setting, relationship status of parents, type of residence, psychiatric family history. Teenagers were also asked about any close friends who showed NSSI or attempted suicide (positive peers' history). The time points 2 and 3 were handled by 4 experienced clinicians in the field of child and adolescent psychiatry. These clinicians were instructed and trained in conducting the structured clinical interviews.

Several clinical interviews were conducted on categorical and dimensional psychiatric dimensions. The psychiatric diagnoses were determined as follows: The German Version of the Mini-International Neuropsychiatric Interview for Children and Adolescents (M.I.N.I. KID 6.0), which is a short structured interview for diagnosing according to DSM-IV and ICD-10 (47), was administered by experienced clinicians. The final diagnoses were made on the basis of those results of the M.I.N.I. KID and an interactive discussion between at least two clinical experts including at least one child psychiatrists based on the clinical interviews. Also the German version of the Structured Clinical Interview for DSM-IV, Axis II (SCID-II), subsection borderline personality disorder (BPD), was conducted with patients to assess the diagnostic criteria of BPD (48). This subsection contains 9 questions according to the DSM-IV diagnostic criteria, and fulfilled criteria on at least 5 items confirm the diagnosis of BPD. The Self-Injurious Thoughts and Behaviors Interview (SITBI) (49) is a structured interview that is divided into 6 modules (including suicidal ideation, suicide plans, suicide gestures, suicide attempts, thoughts of NSSI, and NSSI itself) measuring the presence, frequency and characteristics of six types of self-injurious thoughts or behaviors. The SITBI is a well-suited diagnostic tool for clinic and research with good psychometric properties, which has also been reported for the German version of the SITBI (43). The four functions of NSSI measured in the SITBI reflect the general characteristics of reinforcement as described by Nock and Prinstein (42): Automatic negative reinforcement is queried by "getting rid of bad feelings," automatic positive reinforcement is queried by "to feel something," social positive reinforcement is queried by "to get attention" and social negative reinforcement is queried by "to get out of doing something"(42). Two self-questionnaires were included in the study: The German version of the Symptom Checklist-90 Revised (SCL-90-R) (50, 51) is a multidimensional self-report symptom inventory that comprises 90 items scored on a 5-point-Likert-scale from 0 to 4, which can be averaged over 9 subscales and the Global Severity Index (GSI), an indicator for general mental distress. The internal consistency, especially for the GSI is very good ($\alpha = 0.97$), also for the German version ($\alpha = 0.94, -0.98$) and sufficient evidence of validity has been shown (50). Additionally, the ERS was used to measure emotional sensitivity, arousal/intensity, persistence and a total ER score (38). The ERS contains 21 items (10 items for sensitivity, 7 items for arousal/intensity, 4 items for persistence) for self-report on a 5-point-Likert-scale, with preliminary evidence regarding reliability and validity by the original authors (38). Further evidence of psychometric properties was presented within a community screening assessment, highlighting the mediating, and/or reinforcing effect of ER for SITB in adults (52).

We also administered several self-developed questionnaires to the accompanying guardians. If the patients did not live at home with their parents, the questionnaires were filled in by the caregiver who could provide the most detailed information about the respective patient [e.g., legal guardian, (foster) parent or caregiver of the residential group]. We also interviewed the custodians of our patients about suffering from neurological diseases or mental illness and specifically whether attempted suicide/completed suicide and NSSI in family members had occurred. If one of these descriptors was affirmed, we defined this as positive family history. Additionally, we specifically added the pertinent parts from the SITBI (49) that query possible causes for the current crisis to the accompanying guardians in order to explore their point of view.

Furthermore, the general functional level as well as the severity of the mental illness were assessed. The psychological, professional, and social capacities were evaluated using the Global Assessment of Functioning Scale (GAF) (53). The GAF scale is divided into 10 levels of function with 10 points each. It ranges from 1 (lowest performance level) to 100 (highest performance level). The Clinical Global Impressions Scale (CGI-S) was used to assess clinical severity (54). The severity of the patient's disease was evaluated with a 7-point-Likert scale, ranging from 1 (normal) to 7 (among the most extremely ill).

## Statistical Analyses

First, as the outcome variables (suicidal ideation, suicidal attempts, NSSI thoughts, NSSI behavior) were not normally distributed and the sample size reduced due to group splits, the effect of grouping variables (sex, presence of positive family history, presence of positive peers' history) was examined through Mann-Whitney-*U*-tests. Mann-Whitney-*U*-tests have the advantage of being robust against unequal sample sizes and do not require the assumption that the dependent variable is approximately normally distributed (55). As ERS scores were normally distributed, the relationship between positive family or positive peers' history and ER was determined through an analysis of variance (ANOVA). In the subsequent procedure, the relationship between patients' ERS scores, age, and outcome variables was analyzed through bivariate correlations (Kendall's $\tau$). Subscales of the ERS that correlated significantly while controlling for age were added as predictors into a linear regression model in order to determine the proportion of variance that could be explained by ER. In order to examine the relationship between ER and NSSI further, bivariate correlations (Kendall's $\tau$) were computed between the ERS scores and the four items measuring the types of reinforcement that may serve as motivators for NSSI behavior. Finally, Cohen's $\kappa$ was run to compare patients' reasons NSSI behavior to their guardian's reasons for the emergency presentation. According to Dunn (56) also $\kappa_{max}$ was reported to demonstrate the extent to which raters' ability to agree might be constrained by pre-existing factors. To correct for multiple comparisons where appropriate, the false discovery rate (FDR) (57) was used. Reported *p*-values already correspond to the correction. All major statistical analyses were conducted using SPSS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). The statistical significance level was set to $\alpha = 0.05$.

# RESULTS

## Sample Characteristics

Detailed sociodemographic characteristics are found in **Table 1**. Overall, a total of 86 children and adolescents between the ages of 11 and 19 with SITB participated in time point 2. An additional number ($n = 7$) were recruited but could not be included in the sample as they either showed none of the critical variables ($n = 1$), failed to come to the time points ($n = 2$), had language difficulties ($n = 3$), or eventually decided not to take part in the study ($n = 1$). The presented data were collected from July 2019 to November 2020. As mentioned above, the mean age was $M = 15;8$ (years; months) ($SD = 1;8$, range = 11;3–18;3) and 75.6% were female. Girls and boys did not differ in age ($t_{(86)} = 0.12$, $p = 0.322$).

**TABLE 1 |** Sociodemographic characteristics of participants at time point 2.

| | | | Total *N* |
|---|---|---|---|
| **Sex** | ***N*** | **%** | 86 |
| Female | 65 | 75.6 | |
| Male | 21 | 24.4 | |
| **Age** | ***M*** | ***SD*** | 86 |
| | 15;8 | 1;8 | |
| **School type** | ***N*** | **%** | 86 |
| Gymnasium | 16 | 18.6 | |
| Realschule | 24 | 27.9 | |
| Mittelschule | 19 | 22.1 | |
| Förderschule | 3 | 3.5 | |
| Berufsschule | 10 | 11.6 | |
| Other/No school | 7 | 8.1 | |
| Unknown | 7 | 8.1 | |
| **Parental relationship status** | ***N*** | **%** | 76 |
| Live together | 32 | 37.2 | |
| Separated/divorce | 36 | 41.9 | |
| Separated by death | 1 | 1.2 | |
| Never lived together | 7 | 8.1 | |
| **Household composition** | ***N*** | **%** | |
| With biological mother | 58 | 87.8 | 66 |
| With other mother figure | 3 | 4.5 | |
| With no mother/mother figure | 5 | 7.7 | |
| With biological father | 37 | 63.8 | 58 |
| With other father figure | 13 | 22.4 | |
| With no father/father figure | 8 | 13.8 | |
| With mother/father | 68 | 93.1 | 73 |
| At institutional care | 4 | 5.5 | |
| Lives with partner | 1 | 1.4 | |

*Gymnasium (higher level education, usually 8–9 years of school after 4 years of elementary school, terminating with the general university entrance qualification), Realschule (intermediate secondary school, 6 years of school after 4 years of elementary school), Mittelschule (9 years of elementary school), Berufsschule (2 to 3 years vocational training school most commonly after Mittelschule or Realschule, but also possible after Gymnasium) and Förderschule (special needs school).*

The distribution of psychiatric diagnoses according to ICD-10 (sorted by its frequency) is as follows: F3 (Mood [affective] disorders), $n = 74$; F4 (Neurotic, stress-related and somatoform disorders), $n = 49$; F9 (Behavioral and emotional disorders with onset usually occurring in childhood and adolescence), $n = 26$; F1 (Psychological and behavioral disorders caused by psychotropic substances), $n = 12$; F6 (Disorders of adult personality and behavior), $n = 5$; F5 (Behavioral syndromes associated with physiological disturbances and physical factors), $n = 3$ and F8 (Disorders of psychological development), $n = 3$. It should be taken into account that several diagnoses were possible per patient (mean number of diagnoses: 2.3).

The SCID was used to determine the presence or absence of a borderline personality disorder among the investigated

**TABLE 2 |** Clinical characteristics of participants at time point 2.

| | | | | Total *N* |
|---|---|---|---|---|
| **SCID (Borderline-Personality Disorder section)** | ***N*** | **%** | **Range** | 80 |
| 3 fulfilled criteria | 12 | 15.0 | | |
| 4 fulfilled criteria | 15 | 18.8 | | |
| >5 fulfilled criteria | 2 | 2.6 | | |
| **SCL-90-R: GSI** | ***M*** | ***SD*** | | 82 |
| | 1.23 | 0.66 | 0.02–3.03 | |
| **GAF** | ***M*** | ***SD*** | | 86 |
| | 48.0 | 8.13 | 35–72 | |
| **CGI-S** | ***M*** | ***SD*** | | 86 |
| | 3.64 | 0.57 | 3–5 | |
| **ERS** | ***M*** | ***SD*** | | 84 |
| Sensitivity | 21.33 | 9.73 | 0–3.9 | |
| Arousal/Intensity | 14.55 | 7.10 | 0–3.86 | |
| Persistence | 7.75 | 3.92 | 0–4 | |
| Total | 43.64 | 19.59 | 0.43–11.01 | |
| **Types of NSSI reinforcement** | ***M*** | ***SD*** | | 68 |
| Automatic positive reinforcement | 3.04 | 1.07 | 0–4 | |
| Automatic negative reinforcement | 2.29 | 1.55 | 0–4 | |
| Social positive reinforcement | 0.35 | 0.84 | 0–4 | |
| Social negative reinforcement | 1.22 | 1.35 | 0–4 | |
| **Suicidal thoughts** | ***N*** | **%** | | 85 |
| Prevalence | 79 | 92.9 | | |
| | ***M*** | ***SD*** | | 79 |
| Lifetime (number of episodes) | 13.39 | 21.01 | 0–100 | |
| Last year (number of episodes) | 6.0 | 8.50 | 0–40 | |
| **Suicide attempts** | ***N*** | **%** | | 83 |
| Prevalence | 27 | 32.5 | | |
| | ***M*** | ***SD*** | | 82 |
| Lifetime (number of episodes) | 0.65 | 1.22 | 0–5 | |
| Last year (number of episodes) | 0.43 | 0.92 | 0–3 | |
| **NSSI thoughts** | ***N*** | **%** | | 84 |
| Prevalence | 72 | 85.7 | | |
| | ***M*** | ***SD*** | | |
| Lifetime (number of episodes) | 44.26 | 105.40 | 0–500 | 76 |
| Last year (number of episodes) | 30.47 | 76.53 | 0–398 | 79 |
| **NSSI behavior** | ***N*** | **%** | | 84 |
| Prevalence | 69 | 82.1 | | |
| | ***M*** | ***SD*** | | |
| Lifetime (number of episodes) | 38.03 | 88.71 | 0–600 | 73 |
| Last year (number of episodes) | 19.86 | 34.35 | 0–200 | 73 |

*The ERS (Emotion Reactivity Scale) scores reported are the projected ERS scores for compatibility. Mean scores were used for the analysis. The four reported types of NSSI reinforcement are items from the Self-Injurious Thoughts and Behaviors Interview (SITBI) with a maximum score of 4 which represents agreement. SCID, Structured Clinical Interview for DSM-IV; Axis II; SCL-90-R, Symptom Checklist-90 Revised; GSI, Global Severity Index; GAF, Global Assessment of Functioning Scale; CGI-S, Clinical Global Impressions Scale.*

group of patients and $n = 2$ patients qualified for a borderline personality disorder.

Overall, details on clinical variables including the dependent variables can be found in **Table 2**.

**TABLE 3 |** Results of Mann-Whitney-*U*-tests for dependent variables through lifetime.

| Dependent variables | Group variable | *N* | Mean rank | *U* | *P*-value |
|---|---|---|---|---|---|
| Suicidal ideation | Sex | 79 | Male = 41.42<br>Female = 39.55 | 543.00 | 0.756 |
| | Family history | 69 | Neg = 28.26<br>Pos = 41.18 | 816.50 | 0.021 |
| | Peers' history | 77 | Neg = 40.63<br>Pos = 37.71 | 675.50 | 0.756 |
| Suicidal attempts | Sex | 82 | Male = 34.80<br>Female = 43.66 | 754.00 | 0.224 |
| | Family history | 72 | Neg = 36.36<br>Pos = 36.64 | 653.00 | 0.942 |
| | Peers' history | 80 | Neg = 37.68<br>Pos = 42.81 | 893.500 | 0.337 |
| NSSI thoughts | Sex | 76 | Male = 34.80<br>Female = 39.82 | 634.00 | 0.381 |
| | Family history | 67 | Neg = 27.82<br>Pos = 39.01 | 740.50 | 0.057 |
| | Peers' history | 75 | Neg = 33.23<br>Pos = 41.75 | 850.50 | 0.381 |
| NSSI behavior | Sex | 73 | Male = 30.02<br>Female = 39.63 | 669.50 | 0.249 |
| | Family history | 65 | Neg = 31.12<br>Pos = 34.82 | 588.00 | 0.429 |
| | Peers' history | 72 | Neg = 32.66<br>Pos = 39.58 | 763.00 | 0.241 |

*p-values have been corrected according to the false discovery rate (FDR). Positive (Pos) Family History, suffering from neurological diseases or mental illness and specifically attempted suicide/completed suicide and NSSI in family members. Negative (Neg) Family History, no suffering from neurological diseases or mental illness and specifically attempted suicide/completed suicide and NSSI in family members. Positive (Pos) Peers' History, occurrence of suicide attempts or NSSI among close friends. Negative (Neg) Peers' History, no occurrence of suicide attempts or NSSI among close friends.*

## Family History and Peers' History of NSSI

In order to determine the effects of sex, positive family history, and positive peers' history, Mann-Whitney-*U*-tests were computed for the four dependent variables (suicidal ideation, suicide attempts, NSSI thoughts, NSSI behavior). This was done for the patient's lifetime prevalence since sex and family history are factors to be present early on. There was no effect of sex or positive peers' history, however, there was a significant effect of family history on suicidal ideation, indicating that suicidal ideation was significantly greater for positive family history ($Mdn = 10$) than for a negative family history ($Mdn = 2$). See **Table 3** for the detailed $U$ and $p$-values for the whole set of variables. The effect of age was determined through bivariate correlations between age calculated in days at time point 2 and the suicidal ideation/attempts and NSSI thoughts/behavior. As patients' age ranged from 11 to 18 and thus older patients had more time to experience suicidal ideation and NSSI, the outcome variables for the past year were chosen. There was no significant correlation between age and any of the outcome variables ($\tau = -0.12, -0.01, p > 0.1$).

The effect of sex, family and peers' history and the covariate age on the ERS score was examined separately through a Three-Way ANOVA. The main effect of the covariate age on the ERS score was statistically significant, $F_{(1, 64)} = 10.95$, $p = 0.002$, $\eta^2 = 0.146$ (large), but no other main effects. There was a significant interaction effect between sex and peers' history, $F_{(1, 64)} = 4.74$, $p = 0.033$, $\eta^2 = 0.07$ (medium). *Post-hoc* tests revealed a significant difference between boys and girls when no peers' history is present ($t_{(34)} = 2.07$, $p = 0.049$) with boys having lower ERS scores ($M = 4.69$, $SD = 2.68$) than girls ($M = 6.71$, $SD = 2.86$), but no difference when both groups had positive peers' history [$t_{(44)} = 0.12$, $p = 0.907$]. See **Figure 1** for a graphical overview of the interaction effect.

## Emotional Reactivity and NSSI

As there was a significant positive correlation between age and the ERS score ($\tau = 0.25$, $p = 0.019$), the relationship between ERS and the outcome variables was examined through partial correlations while controlling for age. As above, only the relationship for outcome variables over the period of 1 year were examined since older patients had more opportunities to experience suicidal ideation and NSSI throughout lifetime. There were no significant correlations between ERS scores and suicidal ideation, suicide attempts, and NSSI thoughts. However, there was a significant correlation between the ERS scores and NSSI behavior within the past year (see **Table 4** for an overview of correlations). Only the correlation with the ERS sensitivity score remained significant in a partial correlation when controlling for age ($r = 0.28$, $p = 0.029$). Thus, the ERS sensitivity score was considered relevant for the prediction of NSSI behavior. A simple linear regression was calculated to predict NSSI behavior as dependent variable in the past year based on the ERS sensitivity score as independent variable. A significant regression equation was found [$F_{(1, 70)} = 4.77$, $p = 0.032$)] with an $R^2$ of 0.06. Number of NSSI behaviors increased 8.95 for each score point of ERS sensitivity. Since the relationship remained significant when controlling for age in a partial correlation, age was not added as an independent variable into the regression. However, also when adding age as an independent variable, only ERS sensitivity remained as a significant predictor.

To examine the relationship between ER and the outcome variable NSSI behavior in the past year in more detail, additional correlations with automatic positive reinforcement, automatic negative reinforcement, social positive reinforcement, and social negative reinforcement were computed. After correcting for multiple comparisons, only automatic positive reinforcement ($\tau = 0.22$, $p = 0.034$) and social negative reinforcement ($\tau = 0.27$, $p = 0.016$) significantly correlated with the ERS score. Only the correlation with social negative reinforcement remained significant when controlling for age in a partial correlation ($r = 0.35$, $p = 0.005$). When considering the subscales, automatic positive reinforcement was only related to the ERS sensitivity score and the ERS persistence score, whereas social negative reinforcement was related to the ERS sensitivity scale and the ERS arousal/intensity scale (see **Table 4**). When controlling for age in partial correlations, the correlation between the automatic positive reinforcement and the ERS sensitivity score ($r = 0.65$, $p = 0.042$) and the ERS persistence score ($r = 0.35$, $p = 0.004$) remained significant and increased in strength. For social negative reinforcement partial correlations revealed significant correlations with both ERS subscales when controlling for age (ERS sensitivity: $r = 0.33$, $p = 0.008$; ERS arousal/intensity:

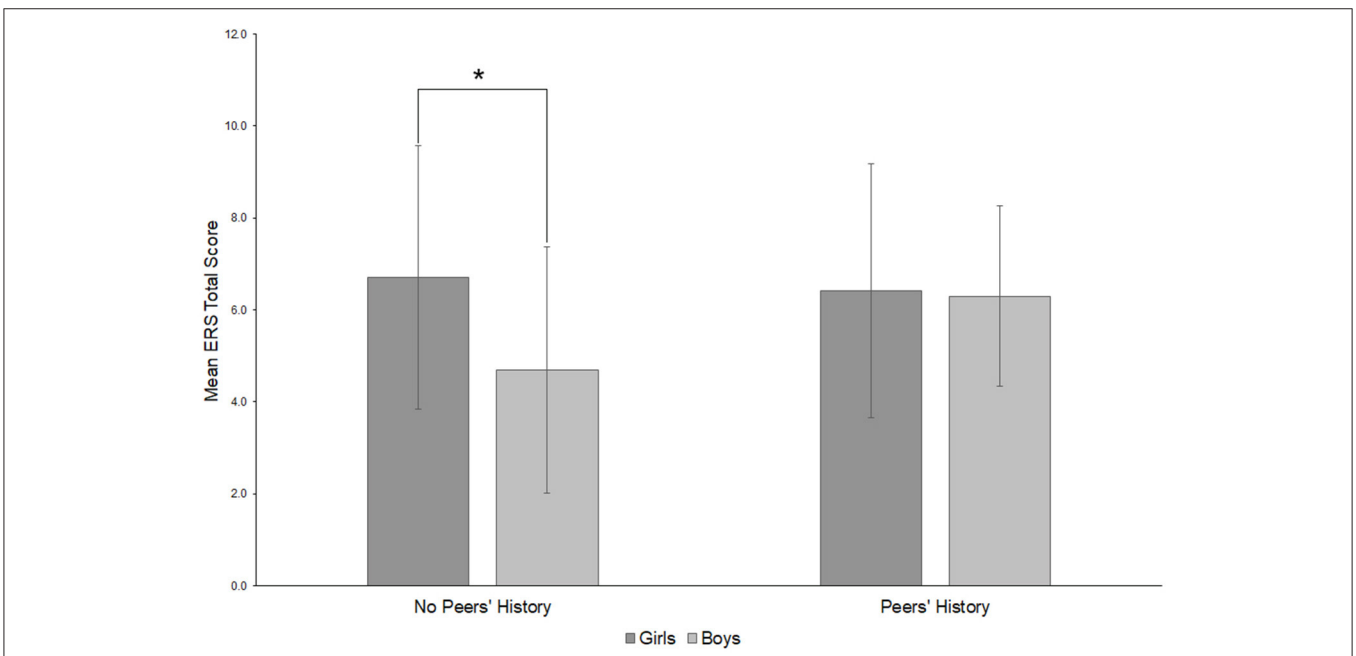


**FIGURE 1 |** *Post-hoc* overview of the interaction between sex and having close friends with a history of suicide attempts or NSSI (peers' history) (on ERS mean scores). *$p < 0.05$. Emotional Reactivity Scale (ERS).

**TABLE 4 |** Correlation matrix for study variables.

| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Suicidal thoughts past year | – | | | | | | | | | | | |
| 2. Suicide attempts past year | 0.24* | – | | | | | | | | | | |
| 3. NSSI thoughts past year | 0.18* | 0.05 | – | | | | | | | | | |
| 4. NSSI behavior past year | 0.14 | 0.10 | 0.38* | – | | | | | | | | |
| 5. ERS total score | 0.01 | −0.12 | 0.14 | 0.25** | – | | | | | | | |
| 6. ERS sensitivity | 0.03 | −0.14 | 0.16* | 0.25** | 0.82** | – | | | | | | |
| 7. ERS arousal/intensity | −0.01 | −0.13 | 0.14 | 0.22* | 0.81** | 0.74** | – | | | | | |
| 8. ERS persistence | −0.00 | −0.09 | 0.10 | 0.24** | 0.76** | 0.63** | 0.59** | – | | | | |
| 9. Automatic negative reinforcement | −0.06 | −0.08 | −0.06 | 0.12 | 0.15 | 0.15 | 0.08 | 0.19 | – | | | |
| 10. Automatic positive reinforcement | 0.02 | 0.85 | −0.05 | 0.22* | 0.22* | 0.19* | 0.17 | 0.25* | 0.39*** | – | | |
| 11. Social positive reinforcement | 0.09 | −0.14 | 0.17 | −0.03 | 0.19 | 0.18 | 0.20 | 0.18 | −0.05 | 0.06 | – | |
| 12. Social negative reinforcement | 0.07 | 0.09 | 0.04 | 0.23* | 0.27* | 0.27* | 0.30* | 0.20 | 0.05 | 0.22* | 0.14 | – |

*Correlation coefficients correspond to Kendall's τ. An FDR correction has been applied. *p < 0.05, **p < 0.01, ***p < 0.001.*

$r = 0.34$, $p = 0.005$). All partial correlations increased in effect size upon controlling for age. Interestingly, even though all four items specifically address reasons for NSSI, only the two items that were correlated with the ERS were also significantly correlated with the outcome variable NSSI in the past year.

## Reasons Triggering the Crisis

In order to determine the degree of agreement between guardians and patients on reasons for the emergency presentation (guardians) and for NSSI behavior (patients), Cohen's κ was computed. Agreement was determined for the surveyed reasons. See **Table 5** for level of agreement for the different reasons. Overall, agreement was significant on about 60% of the reasons. However, significance was tested against 0, thus, mean agreement was only at 0.38, which constitutes only fair agreement (58). Reasons on which no significant agreement was present were problems with friends, problems with physical health and problems with mental health. For these reasons also $\kappa_{max}$ was reduced which indicates a portion of agreement that cannot be achieved due to pre-existing factors which produce unequal marginal totals.

**TABLE 5 |** Cohen's κ and proportion of agreement between guardians and patients on reasons for emergency presentations in respect to NSSI behavior.

| Reasons | Cohen's κ | *P*-value | $\kappa_{max}$ |
|---|---|---|---|
| School | 0.33 | 0.009 | 0.97 |
| Family | 0.34 | 0.005 | 0.72 |
| Friends | 0.18 | 0.140 | 0.75 |
| Romantic partner | 0.30 | 0.015 | 0.88 |
| Finances | 0.89[a] | | 0.98 |
| Bullying | 0.25 | 0.040 | 0.80 |
| Physical health | 0.06 | 0.609 | 0.74 |
| Death of a person | 0.68 | <0.001 | 0.68 |
| Mental health | 0.03 | 0.790 | 0.71 |
| Humiliating experience | 0.39 | 0.002 | 0.93 |

*Correlation coefficients correspond to Kendall's τ. An FDR correction has been applied.* [a]*observed concordance was smaller than mean-chance concordance, therefore proportion of agreement was calculated instead of κ.*

# DISCUSSION

The major purpose of the present study was to report a cross-sectional analysis of the phenomenology and family-related factors of adolescents with SITB presenting to a specialized emergency out-patient setting within a clinic for child and adolescent psychiatry.

Whereas, in our sample 75.6% of the patients were female and the mean age was 15;8 (years; months), Porter et al. (5) showed no observable sex difference (51% male) with a mean age of 14.5. We included the emergency clientele from the age of 11 onward, which explains the higher average age. The above-mentioned study (5) deals with patients under 18 years who visited the emergency pediatric department who needed psychiatric evaluation, while in our case a distinct selection was made of NSSI and suicidal behavior in a child and adolescent psychiatric setting. The higher proportion of girls has also been confirmed in other studies on NSSI and suicide attempts in adolescents (20, 59, 60).

We also interviewed the custodians of our adolescent patients about the psychiatric history of family members. We identified a significant effect of family history on suicidal ideation, indicating that suicidal ideation was significantly greater for positive family history. Regarding suicidal ideation and acts of suicide, previous research (26) has shown corresponding results. It has been found that the rate of attempted suicide was higher among first-degree relatives of adolescent suicide participants compared to the relatives of controls (61). First-degree relatives of suicide completers had twice as much suicidal ideation as the relatives of control persons (61). It has been shown that there is an association between familial transmission of suicidal ideation and transmission of psychiatric disorders. But the essential liability to respond to suicidal ideation was discussed as a significant mechanism for suicidal behavior transmitted within the family

(26). The reason that our sample only shows an effect on suicidal ideation could be due to recent and newly emerging symptoms. As Glenn et al. (23) showed that the earliest age of entry was at NSSI and suicidal ideation, followed by NSSI behavior, suicide plans and attempted suicides (23), it is possible that the transition from suicidal ideation to suicidal behavior could not yet have reached its full extent in our sample. In addition, our sample has been selected in such a way that we have not included any patients who are especially burdened and require a longer inpatient stay due to their symptoms, nor have we included any patients who already had adequate child and adolescent psychiatric care.

*Post hoc* tests revealed a significant difference between boys and girls when no peers' history is given with boys having lower ERS scores than girls, but no difference when both groups had a positive peers' history (i.e., the teenagers report that close friends show NSSI and/or attempted suicide). Adolescents with a history of NSSI most often named their peers as source for the idea of hurting themselves (62). Our results may indicate that for boys close friends who did not report suicide attempts and/or NSSI function as a protective factor and consequently they show lower ER. For girls, this assumed protective factor could not be found in our sample. Consequently, it would be important and useful to focus on a possible sex difference in further research.

We identified a significant correlation between the ERS sensitivity score and NSSI behavior within the last year, independent of age. This indicates that responding to many stimuli is what is demanding, not the intensity or duration of the emotions. According to Nock et al. (38), ER refers to the extent to which an individual experiences emotions. Our results show that an emotional reaction to a wide range of stimuli (e.g., emotion sensitivity) is the only explanatory factor among the ERS scale for NSSI behavior during the last year. Previous research showed that young adults who engage in NSSI showed significantly higher emotional sensitivity, arousal/intensity, and persistence than a control group (39). Overall, ER appears to be only one variable that affects NSSI in this present study (40). Numerous anamnestic, but also psychopathological variables can influence it (38). Nock et al. (38) showed significantly higher ER in adolescents with a mood, anxiety, or eating disorders compared to people without such disorders. There are latent subgroups of individuals who engage in NSSI (adults) with different difficulties in emotion regulation (63). It is questionable whether this differentiation is already present in adolescent patients, or whether the psychopathology only develops in this way throughout puberty. This statement is supported by the fact that our results show that the older the patients are, the higher the ERS scores. According to analyses by Lannoy et al. (64) there was no significant relationship between ER and age; there, however, an adult sample (participants from the community) were examined. In addition, the results of a study that investigated the course of emotion regulation strategies in different age ranges indicate a general trend toward increasing adaptive emotion regulation (65). Specifically, middle-aged adolescents showed the smallest repertoire of emotion regulation strategies. In our study, the average age is also located in middle adolescence. The above-mentioned study sample included healthy subjects from young adolescent to middle-aged adults. It could be assumed the described temporal sequence occurs with a delay in people with NSSI and/or suicidal behavior.

A relationship between the ERS and distinct types of reinforcement (automatic positive reinforcement, social negative reinforcement) as a motivation factor for NSSI was found. This suggests that for automatic positive reinforcement it is especially the sensitivity to various kinds of stimuli and the persistence of these feelings that plays a crucial role, whereas for social negative reinforcement it is the sensitivity to various kinds of stimuli and the intensity of these feelings. The most strongly affirmed function for each form of SITB was according to the results of Nock et al. (49) automatic negative reinforcement, that was followed by automatic positive reinforcement, emphasizing the relevance of these functions and suggesting that different forms of SITB may serve somewhat similar functions (49). The only aberration from this pattern was with regard to suicidal gestures, which adolescents reported using for social reinforcement (49). Up to this point, research has been less focused on examining the intrapersonal positive or interpersonal negative reinforcement functions of self-injury, and these continue to be pivotal directions for future research (7). The two intrapersonal functions can be particularly relevant in the case of individuals with emotional dysregulation and it was shown that the two intrapersonal functions can be merged into an affect regulation function. In addition, we found the correlation between ER, negative social reinforcement and NSSI of special interest. In our experience, this aspect also plays a subordinate role in everyday clinical practice and should be investigated more closely in the context of future therapy research on NSSI.

We were able to confirm the hypothesis that the reasons given by caregivers for the current crisis might be different from the reasons given by patients for NSSI behavior. Especially if the trigger for the crisis is for example a dispute with the family/parents, differences in agreement are of great relevance for further therapy planning. Therefore, the parents' point of view should not be overestimated, but also the patients' opinion should be investigated. Otherwise, it could happen that the influence of the family situation, but possibly also other factors (i.e., problems with friends, problems with physical health, and problems with mental health) which might be responsible for triggering the crisis, are underestimated. The results of Fu et al. (15) demonstrated that parents lack knowledge about NSSI and its treatment and suffer from great emotional stress (66). In addition to this lack of knowledge, an aggravating factor is that according to our results, parents partly assume other causes for the crisis compared to their children. This could either result from the fact that patients are more reserved toward their caregivers and parents cannot know any better. Or perhaps the caregivers tend to externalize reasons for the crisis. Especially the reasons problems with friends, problems with physical health and problems with mental health are topics that can probably also be better judged by the patients themselves than the guardians, since these are topics that concern the young people themselves and are rather difficult to assess by the caregivers. When parents and their children appraise the child's emotional and behavioral health problems, their valuations are often divergent (67), especially for internalizing problems (68). For example, relying only on parents

to identify depression in children may lead to young people with depression being overlooked and therefore going undetected as well as untreated (69, 70). Our findings show that it is particularly important to consider family dynamics and other contextual factors when choosing the appropriate therapy for youths with self-injurious behavior (71).

Although our study addresses a patient clientele that increasingly requires emergency care in child and adolescent psychiatric clinics and outpatient services, there are some limitations regarding this study. The psychiatric assessments were performed by four experienced and trained clinicians and final decision on categorical diagnoses has been made including certified child psychiatrists. A limitation to be mentioned here is that no interrater reliability was calculated. However, these colleagues were carefully instructed and trained in conducting the interviews. An additional aspect that can be considered a limitation is that the number of SITB episodes shows a large range. This is due to patients providing numerical values to the questions. Measures that rely on patients' self-report may suffer from a bias and especially in clinical contexts there are not many objective ways to acquire frequency estimates of NSSI behavior. Still, in cases with unrealistic replies clinicians ensured to acquire the most realistic response possible. For a comprehensive standardized diagnostic procedure within the context of an acute psychiatric setting, the number of subjects has reached a respectable size. However, the current sample was drawn from a single psychiatric clinic and regional differences across countries may be possible. Future studies with a similar sample might be able to extend the current findings to international contexts. Finally, in our sample, patients with long-term inpatient child and adolescent psychiatric treatment needs and patients who already had adequate outpatient care were excluded. Therefore, our results do not reflect a complete utilization sample of an emergency department for SITB. This in turn has an impact on the results since including these subgroups might have led to more abnormalities/pathologies in our sample of emergency outpatient patients. Still, the current sample can be considered representative for outpatients of a psychiatric clinic for children and adolescents that do not require long-term inpatient care but nevertheless have a strong need for interventions.

However, a major strength of our study is that our examination of the outpatients in the emergency department and evaluation of their reasons/motivation for SITB took place without delay. In addition, we have used a clinical gold standard for specified psychiatric assessments, especially with the structured clinical interviews M.I.N.I. KID and SITBI, conducted by experienced clinicians. In addition to symptoms regarding NSSI and suicidal ideation and behavior, we have also addressed questions which are relevant for patient care and future treatments. We identified ER as a relevant aspect of NSSI and extended these findings by relating them to distinct types of reinforcement in respect to NSSI. Especially social negative reinforcement has rarely been emphasized and its relation to ER has not been examined previously. Furthermore, we investigated the influence of positive family and peers' history on self-injurious behavior of patients and compared patients' statements with those of their caregivers regarding the causes of the crisis. The results of the present study may facilitate future research on risk and influencing factors in adolescents with SITB as determined in this sample.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by ethic commission of the University of Regensburg. Written informed consent to participate in this study was provided by the patients and the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

SK and RB had the idea for the study and developed the study design. IJ contributed to hypotheses, sample size calculation, and statistical analyses. First manuscript has been written by SK and IJ. AE, DS, and AO participated in the design and coordination of the study. As a clinical collaborator, JM plays a major role in patient coordination and has conducted a significant proportion of time points with patients. All authors read and approved the final manuscript.

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# Emotional Dysregulation in Preschool Age Predicts Later Media Use and Gaming Disorder Symptoms in Childhood

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**Background:** The aim of this study was to evaluate the role of early Emotional Dysregulation (ED) at preschool age as a risk factor or predictor of later media use behavior and Gaming Disorder (GD) in school age.

**Methods:** 80 patients (63.7% male; mean age = 4.2, SD = 1.23) who had attended a special outpatient program for preschoolers at measuring point time t1 were contacted at measuring point time t2 (mean age = 9.2, SD = 2.03). At t1, the comprehensive clinical assessment comprised Child Behavior Checklist—Dysregulation Profile (CBCL-DP). At t2, parents completed a questionnaire on their children's media availability, usage times, and GD.

**Results:** ED predicts a more intense use of digital media in the future. The daily average screen-use time at t2 varies significantly between the groups (148 min for children with ED at t1 and 85 min for children without ED at t1). The intensity of media use can be considered a significant predictor for the presence of a GD in dimensional assessment. When GD is classified categorically, according to the DSM-5 criteria, there is no significant correlation between ED and later GD diagnosis, neither between screen-use time and GD diagnosis. However, at dimensional level, preschool children with ED show significantly higher GD symptom scores at 9 years of age.

**Conclusion:** ED at preschool age is strongly associated with time spent video gaming and GD symptoms 5 years later. Our results strongly indicate that emotion dysregulation in preschool children is a risk factor for later problematic video game playing behavior. This strengthens the concept of ED in the etiology of media use and provides potential targets for early GD prevention.

**Keywords: Emotional Dysregulation, Gaming Disorder, media use, preschool age, school age**

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## INTRODUCTION

Emotional Dysregulation (ED) is characterized by difficulties in understanding, accepting, and dealing with emotions [i.e., emotion regulation; (1)]. Due to these deficits, children and adolescents with ED symptoms often show little flexibility and spontaneity, with a lack of control and disruptive behavior (2). Findings suggest that ED may influence the development and course of various disorders, including different substance use disorders [e.g., alcohol, cocaine, or nicotine dependencies; (3–8)] as well as behavioral addictions [e.g., pathological gambling; (9)].

These named deficits in emotion regulation also lead to assume that some individuals try to mitigate, facilitate, or avoid (especially unpleasant, negative) emotional experiences by engaging in video games as distraction (10, 11). More specifically, it is believed that children and adolescents with ED use video game playing as a maladaptive coping strategy to deal with negative emotions (10). In addition, the disruptive and often poorly controllable behavior of children with ED can also make them less likely to socialize in preschool and school, which may lead to uncertainty in face-to-face interactions. In this respect, the lack of direct interaction with others in video games can reduce social insecurity in such situations. This probably leads to a tendency for children with low social skills and especially children with ED to prefer the internet in general but also video games in particular as a place for social interactions rather than real-life interactions (12).

With regard to early media use, some studies indicate that use of digital media might positively influence attitudes to learning and reading skills (13–18). At the same time, digital media and especially computer games are entertainment products *with clinical relevance*.

Various studies suggest that the use of digital media can also affect children negatively in their physical, social, and psychological development [(19–29); for current reviews, see (30–32)].

Especially video gaming has increased enormously in recent years (33). Gentile et al. (34) showed in a longitudinal design that more time spent gaming is a significant predictor of a later Gaming Disorder (GD). The Internet Gaming Disorder (IGD) was first recorded in the DSM-5 and is characterized by nine diagnostic criteria: excessive involvement in Internet gaming, withdrawal symptoms, tolerance development, loss of interest in previous activities, loss of control, continued gaming despite knowledge of negative consequences, deceiving significant caregivers about the gaming's extent, use of Internet gaming to end or reduce negative feelings, and endangerment or loss of an important relationship (35). Furthermore, GD has now been included in the ICD-11 (36) which includes the main diagnostic criteria listed in the DSM-5. Whereas, population-based studies estimate the representative prevalence of IGD at 2% [a mean value of representative studies from different countries: Germany, the Netherlands, Norway, Spain, UK, the USA, and one Europe-wide study; for a systematic review, see (32)], some studies conclude that the prevalence in schoolchildren is about 8–9% or more (34, 37, 38) and likewise in healthcare utilization groups.

High prevalence rates, increased usage times, dynamic development of digital technology, and the physical, social, and psychological consequences of GD pose an increasingly important public health problem in the understanding of the development and etiology of GD, including risk factors and precursors to GD. Although playing video games seems to be more and more integrated in everyday life, there is little research on the risks of the GD development in schoolchildren.

Studies have found indications that ED seems to have a significant impact on media usage and GD (12, 39–41). Hollett and Harris (40) investigated the relationship between ED and problematic video gaming using a sample of 928 adult subjects. They identified two dimensions of ED, i.e., difficulties with impulse control and limited access to emotion-regulation strategies, as significant predictors of problematic video gaming. Hormes et al. (42) assumed in undergraduate students (20 years of age) that disordered online social networking ("craving Facebook") endorsed more ED, including non-acceptance of emotional responses, reduced emotion regulation strategies, and poor impulse control. In addition, Wichstrøm et al. (12) also found indications that symptoms of GD in 10-year-olds could be predicted by social skills and emotion regulation deficits in children at age 8, a rare research result in childhood.

Despite the increased research interest in the correlation of ED symptoms in children and the development of GD in adolescents, to our knowledge, no study has investigated whether ED symptoms in preschool age can predict GD or GD symptoms in school age. Our basic assumption is that the relation between ED and GD starts even earlier in development.

More specifically, we investigated the following hypotheses:

1. Preschool-aged children with ED meet the criteria of GD or show higher GD symptom scores in school age compared with children without ED in pre-school age.
2. Children with ED in preschool age will use media in school age longer than children without ED at preschool age. The duration of media use is a significant predictor for the presence of a GD in school age.

# MATERIALS AND METHODS

## Participants

Participation in the study was voluntary and there was no financial compensation. All children and their parents gave informed consent. The local ethics committee approved the study.

In the present study, we used a quasi-experimental design with two measurement points. The study group included all young children who had attended the preschool special outpatient clinic of a Clinic for Child and Adolescent Psychiatry between 2011 and 2017, regardless of the diagnosis made (measuring point time t1). These families were contacted again at measurement time t2 (at the end of 2019) with a cover letter and a questionnaire. Of the original 148 children, 25 families could not be reached at t2. Of the remaining 123 children, 10 families expressed no interest, 113 families confirmed their participation by telephone, of which 33 did not return the documents despite repeated reminders and inquiries (for a schematic overview of the methodical approach, see **Figure 1**). The study was finally conducted with $N = 80$ (70% of the original children) subjects (63.7% male; mean age (t1) = 4.2, SD = 1.23, min = 1.4, max = 6.9). These 80 patients were contacted again at the end of 2018 (mean age = 9.2, SD = 2.03, min = 4.6, max = 13); there was no further personal patient presentation at measuring time t2. The average time difference t1 – t2 is therefore M = 4.9 years (SD = 1.64).

Because all the children had previously attended child and adolescent psychiatry, most participants ($N = 76$) in the study

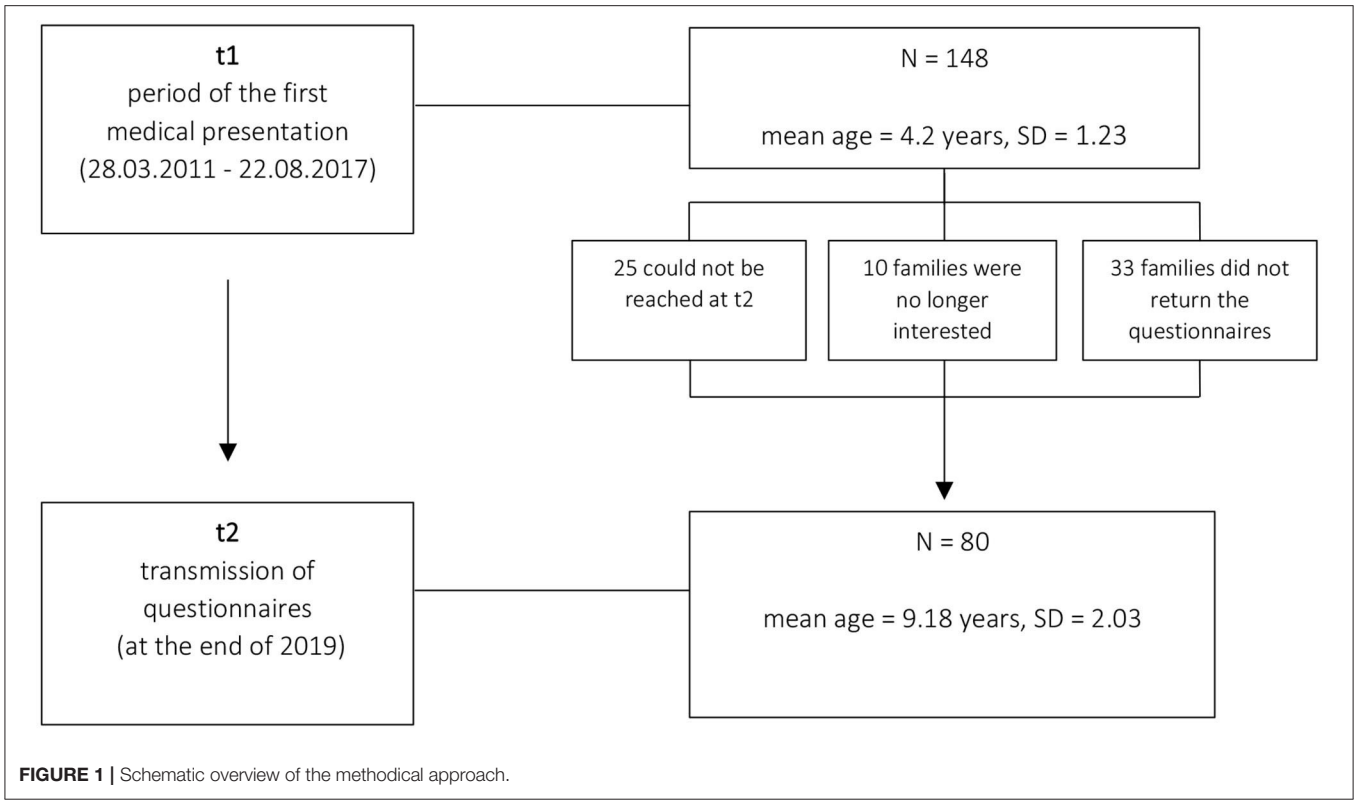


**FIGURE 1 |** Schematic overview of the methodical approach.

at t1 had a diagnosis with at least one disorder defined by ICD-10. The most frequent diagnosis was that of the Oppositional Defiant Disorder with $N = 31$ (ICD-10: F91.3), followed by Attention Deficit Hyperactivity Disorder with $N = 21$ (ICD-10: F90). In addition, $N = 19$ children suffer from non-organic insomnia (ICD-10: F51), $N = 15$ children suffer from specific developmental disorder of motor function (ICD-10: F82), and $N = 13$ children had a diagnosis of specific speech articulation disorder (ICD-10: F80.0). Other diagnoses that were given multiple times include the expressive language disorder with $N = 10$ (ICD-10: F80.1), the receptive language disorder with $N = 4$ (ICD-10: F80.2), feeding disorder of infancy and childhood with $N = 6$ (ICD-10: F98.2), and social anxiety disorder of childhood with $N = 4$ (ICD-10: F93.2).

In addition, IQ data were available for 71 of 80 subjects in t1 (mean IQ (t1) = 100.61, SD = 17.16). Due to the large variability in age, different test procedures were used to measure IQ [WIPPSI-III (56.3%), K-ABC-II (13.8%), SON-R 2,5–7 (8.8%), and other tests (21.2%)].

At t2, most children were attending elementary school (51%), followed by high school (19%), community schools (13%), day care (10%), special schools (6%), and Waldorf schools (1%). The majority of the children (68%) are living with both their biological parents; 24% of them are living with only their mother (and her partner) and one child is living with only its father (and his partner). Also, 5% of the children are living in foster care and 3% are living in a different living situation. $N = 11$ (13.8%) of the participants were taking medication, including Methylphenidate (3.8%), Atomoxetine (1.3%), or other medication (11.3%), including Asthma spray (1.3%), Guanfacine (1.3%), Opipramol (1.3%), Melatonin (1.3%), MTX (1.3%), Naproxen (1.3%), Dekristol (1.3%), Sulgen (1.3%), Vomex, and Salbutamol (1.3%).

## Instruments and Procedure

### Assessment of Emotional Dysregulation

We used the Child Behavior Checklist [CBCL 1½−5; (43)] to assess ED in pre-school children at t1. CBCL 1½−5 is one of the most commonly used tools for assessing developmental psychopathology in children and adolescents (43–47). From the 99 items of CBCL 1½−5, seven scales (Emotional Reactivity; Anxiety/Depressive; Physical Complaints; Social Withdrawal; Sleep Problems; Attention Problems and Aggressive Behavior) and three superordinate scales are formed, which represent External, Internal, and Total Problem Score. Good reliability and validity have been reported for the CBCL/1.5–5; Cronbach's alpha of the superordinate scales is above 0.86 (43). We assessed deficits in emotional regulation with the Deficient Emotional Self-Regulation Profile (DESR), which is characterized by simultaneous increases (between 1 and 2 SDs) on the three syndrome scales anxiety/depression, aggression, and attention (48, 49). Furthermore, we used the Child Behavior Checklist—Dysregulation Profile (CBCL-DP) as a more severe form of the ED profile. CBCL-DP is described by simultaneous extreme values (more than 2 SD) on the three syndrome scales [(49–51), S. 192]. For categorization, the respective $T$-values were used, $T$-value >60 and <71 for DESR profile and $T$-value >70 for Dysregulation profile. In general, the DESR profile, as well as the

CBCL-DP, are established diagnostic procedures for identifying ED (50–55).

## Assessment of Media Usage Behavior

At t2, parents were sent a questionnaire assessing media use and GD. The questionnaire included items referring to media use (i.e., time spent with TV and computer or video games during the week and on weekends, availability of computer access, child's ownership of a video game console or a handheld video game) and items measuring GD. To assess media usage time, parents were asked how long their child used electronic devices such as computers, laptops, smartphones, tablets, or game consoles on average every day—separately for working days and the weekend (with the following response categories: 0, 1–30, and 30–60 min; 1–2, 2–3, 3–5 h, 5–7 h, and more than 7 h). The calculation of the media usage time in minutes was done by determining the respective category mean (0 min, 15 min, 45 min, 90 min, 150 min, 240 min, 360 min) and 450 min for "more than 7 h" at the presumption, that the mid point of each interval is used as the best and most robust estimate of the answer category.

For GD, parents should answer nine questions (e.g., "Does your child become restless, irritable, moody, angry, anxious or sad when he or she has no opportunity to play?") on a four-level Likert scale from "never" to "always." The questions were formulated according to the criteria proposed by Petry et al. (56), with each question comprising one of the DSM-5 criteria relating to IGD. A total score was calculated by adding up the nine items, and mean values by dividing the sum value by nine; missing items were replaced by mean values. To assess the performance of nine GD-items and the GD total score, an item analysis was performed and the reliability was determined. Reliability was high with Cronbach's $\alpha = 0.883$. As confirmed by a reliability analysis, total reliability did not increase significantly by eliminating any of the nine items. In addition, discriminatory power analyses ensured a value of $r > 0.5$ for every item. Thus, all nine items remained in the scale for the calculations. Since each item of the questionnaire includes one of the DSM-5 criteria regarding IGD, the DSM-5 classification criteria were applied, according to which at least five of the nine items must be fulfilled to comply with GD. An item was considered fulfilled if either "often" or "always" was selected on the four-level Likert scale (categorical value: GD yes or not). Besides this categorical assessment (GD: yes or no), a dimensional conceptualization

**TABLE 2 |** Listing of ICD-10 diagnoses per subject with ED.

| Subjects with ED | ICD-10 diagnoses | Type of ED |
|---|---|---|
| 1 | F90.1, F93.0 | DESR |
| 2 | F91.3, F51.0 | CBCL-DP |
| 3 | F91.3 | DESR |
| 4 | F51.0, F80.0, F45.8, F93.2 | CBCL-DP |
| 5 | F91.3, F90.0V, F80.0V | DESR |
| 6 | F82, F80.0, F51.0, F52.0, F91.3 | DESR |
| 7 | F91.3, F90.0V | CBCL-DP |
| 8 | F93.8, F34.1V | DESR |
| 9 | F91.3, F90.0V | DESR |
| 10 | F34.1, F91.3, F90.0, F51.5, F80.0 | CBCL-DP |
| 11 | F90.0, F91.3 | DESR |

*2 children had a total of 5 disorders, 1 child had a total of 4 disorders, 1 child had a total of 3 disorders, 6 children had a total of 2 disorders, and 1 child had 1 disorder in t1.*

**TABLE 1 |** Item characteristics of the nine GD criteria ($N = 80$).

| DSM-5 criteria: Gaming disorder (GD) | M (SD) | Item difficulty | Discriminatory power | Cronbach's alpha* |
|---|---|---|---|---|
| 1 Preoccupation: The child thinks about gaming when it is not playing | 1.50 (0.827) | 0.17 | 0.716 | 0.875 |
| 2 Withdrawal symptoms: The child is irritable, anxious, sad when devices are taken away | 1.41 (0.706) | 0.14 | 0.737 | 0.869 |
| 3 Tolerance: Impression of intensified media usage | 1.90 (0.963) | 0.30 | 0.627 | 0.895 |
| 4 Addictiveness: Child wants to play less, but does not manage | 1.21 (0.520) | 0.07 | 0.777 | 0.866 |
| 5 Loss of other interests: Child quits other activities | 0.136 (0.767) | 0.12 | 0.872 | 0.852 |
| 6 Psychosocial problems: occurrence of sleep deprivation, unpunctuality, disputes, neglect of chores | 1.24 (0.621) | 0.08 | 0.777 | 0.864 |
| 7 attempt to deceive: Child hides gaming from family members | 1.28 (0.477) | 0.09 | 0.630 | 0.877 |
| 8 Escapism: Child uses gaming to escape or relief negative mood | 1.14 (0.470) | 0.05 | 0.638 | 0.877 |
| 9 Impairment: Child has jeopardized or lost school performance or social relationships | 1.24 (0.641) | 0.08 | 0.864 | 0.855 |

**The value of Cronbach's alpha of each item indicates the value of Cronbach's alpha when that particular item is taken out of the equation. Cronbach's alpha for all nine items equals $\alpha = 0.883$.*

of GD was calculated by adding up the nine items for a GD symptom score (never = 1; sometimes = 2; often = 3; always = 4 with individual values between 9 and 36). For more details on psychometrics properties of the used nine GD-items, see **Table 1**.

## Statistical Analysis

Data were analyzed by IBM SPSS Statistics Version 26. Categorical variables were analyzed by Fisher–Yates test (ED and media devices) and binary logistic regression (ED as predictor of a future GD diagnosis). *T*-tests were performed for group analyses of continuous variables. If the requirements for a *t*-test for independent samples were not met, a Mann–Whitney *U*-test was calculated (ED and ordinally scaled daily average media usage). For modeling the relationships within the data, univariate linear regression was conducted (ED as predictor of media usage times, media usage times as predictor of GD). A significance level of 0.05 was used for all statistical tests.

# RESULTS

## Emotional Dysregulation

$N = 11$ children (14%) had deficits in the regulation of emotions (mean age = 8.91 years, SD = 1.49, min = 7.08, max = 11.25). Of these, $N = 7$ (9% of all participants) showed increased values of between 1 and 2 SDs on the three syndrome scales anxiety/depression, aggression, and attention of CBCL, thus fulfilling the criteria of the Deficient Emotional Self-Regulation Profile (DESR). $N = 4$ children (5%) showed simultaneous extreme values (more than 2 SD) on the three syndrome scales and thus corresponded to the CBCL-DP. The gender comparison showed that $N = 9$ boys (18%) and $N = 2$ girls (7%) had deficits in the regulation of emotions. However, this descriptively discernible difference of ED between boys and girls did not reach statistical significance (Fisher's exact test: $p = 0.31$). With regard to medication, only one child with ED was taking medication (i.e., Opipramol). All children with ED ($N = 11$) had at least one disorder defined by ICD-10. The most common diagnosis was the conduct disorder with oppositional defiant behavior (ICD-10: F91.3; $N = 8$), followed by attention deficit hyperactivity disorder (ICD-10: F90.0; $N = 5$). For more details on comorbidities of children with ED, see **Tables 2**, **3**.

**TABLE 3 |** Frequency of individual ICD-10 diagnosis in children with ED.

| Disorders in children with ED in t1 (diagnosed with ICD-10) | Frequency |
|---|---|
| F91.3 | 8 |
| F90.0 | 5 |
| F80.0 | 4 |
| F51.0 | 3 |
| F34.1 | 2 |
| F90.1 | 1 |
| F93.0 | 1 |
| F45.8 | 1 |
| F93.2 | 1 |
| F82.0 | 1 |
| F52.0 | 1 |
| F93.8 | 1 |
| F51.5 | 1 |

## Access to Media Devices and Usage Time

In terms of access to a computer/laptop ($p = 0.974$), smartphone ($p = 0.933$), Smartwatch ($p = 0.362$), tablet ($p = 0.751$), stationary game console ($p = 0.169$), portable game console ($p = 0.726$), and television ($p = 0.100$), there were no significant differences between children with and without ED (for more details, see **Table 4**). As shown in **Figures 2**, **3**, children with deficient emotional regulation used media significantly longer on weekdays ($U = 211.5$, $Z = -2{,}413$, $p < 0.05$) as well as on weekends ($U = 214.5$, $Z = -2.36$, $p < 0.05$) than children without ED, confirming the second hypothesis. The calculation of media usage time at t2 presented children with at t1 diagnosed ED to have elevated usage times compared with those cases, when an ED was not determined. On weekdays, children with ED used media for averagely 124 min per day (vs. 68 min for children without ED, $p = 0.003$). On the weekend, media was used more frequently by children with ED, averaging 209 min per day (vs. 129 min for children without ED, $p = 0.019$). For details, see **Table 5**.

Based on the finding that longer usage times (34) as well as ED (39, 40) are significant predictors of GD, we investigated exploratively whether ED at t1 is also predictive for longer media usage times at t2. A linear regression with dimensional conceptualization of ED as predictor and the metric scaled variable of the subjects' duration of media use during the daily average as criterion showed that preschool ED at t1 significantly

**TABLE 4 |** Access to different media devices in children with ED and children without ED.

| Media devices | Children with ED ($n = 11$) | Children without ED ($n = 69$) | Statistics (*Fisher's exact test*) |
|---|---|---|---|
| Computer/laptop | $n = 5$ (45.45%) | $n = 31$ (44.93%) | $p = 0.974$ |
| Smartphone | $n = 7$ (63.64%) | $n = 43$ (62.32%) | $p = 0.933$ |
| Smartwatch | $n = 1$ (9.09%) | $n = 2$ (2.90%) | $p = 0.362$ |
| Tablet | $n = 7$ (63.64%) | $n = 39$ (56.52%) | $p = 0.751$ |
| Stationary game console | $n = 6$ (54.55%) | $n = 21$ (30.43%) | $p = 0.169$ |
| Portable game console | $n = 4$ (36.36%) | $n = 20$ (28.99%) | $p = 0.726$ |
| Television | $n = 11$ (100%) | $n = 64$ (92.75%) | $p = 0.100$ |

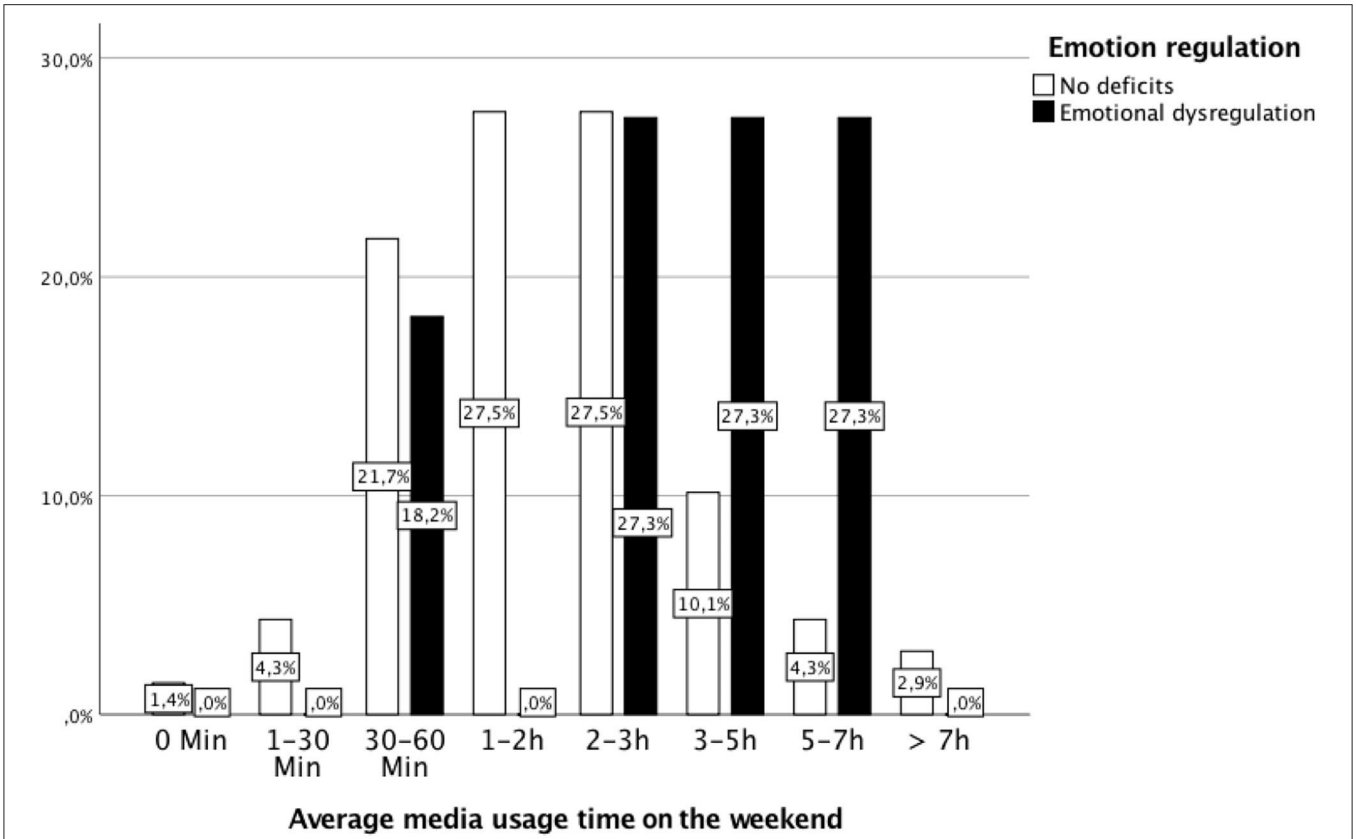


**FIGURE 2 |** Daily average media usage time at the weekend by children with ED and without ED. Children with ED used media significantly longer at weekends than children without ED (Mann–Whitney *U*-test: $M_{rank}$ with ED = 55.50, $M_{rank}$ without ED = 38.11; U = 214.5, Z = −2.36, $p < 0.018$).

predicts usage times of digital media use per week ($F_{(1)} = 8.698$, $p = 0.004$, $R^2 = 0.100$, $R^2_{adjusted} = 0.089$) 5 years later at t2. To test our second hypothesis, that duration of media use is a predictor of a GD, further linear regression analyses were carried out, which showed that the time criterion of media usage behavior is a significant predictor for the presence of a GD dimensionally ($F_{(1,78)} = 22.863$, $p = 0.000$, $R^2 = 0.227$, $R^2_{adjusted} = 0.217$). Categorically, it did not explain a significant amount of the variance in GD ($F_{(1,78)} = 2.679$, $p = 0.106$, $R^2 = 0.033$, $R^2_{adjusted} = 0.021$).

## Media Use Behavior

If gaming behavior is assessed dimensionally and the mean values of the two groups are compared, a descriptive difference between children with ED (M = 15.82, SD = 4.08) and children without ED (M = 11.71, SD = 5.05) is already apparent. This difference is also statistically significant ($t = -3{,}0$; $p = 0.004$; $d = 0.895$). However, if gaming behavior is categorically classified according to the DSM-5 criteria for GD (diagnosis when >4 criteria from 9), only one of the 11 children with ED (9.09%) and three of the 69 children without ED (4.35%) met the criteria for a diagnosis of GD. A binary logistic regression showed no significant correlation between ED and future GD diagnosis (Wald(1) = 31.989, $p = 0.51$; n.s.). The differences between children with ED and children without ED on dimensional and categorical assessment of gaming disorder are listed in **Table 6**.

# DISCUSSION

In recent years, the everyday use of digital media and especially the increase in playing video games seems to have a huge, and potentially negative, impact on child and adolescent development, to the point of a manifest GD (35, 36). A potential factor, which probably affects the development of GD, is ED (12, 40). All studies carried out on this subject so far investigated the influence of ED in schoolchildren, adolescents, or young adults on the development of GD. To the best of our knowledge, this is the first study to examine the impact of preschool ED on media use and GD in later childhood. To potentially find early prevention possibilities, we conducted the study with the aim of examining the predictive value of ED in preschool age for the development of GD in school age.

In summary, the results show higher GD symptom scores (dimensionally) in school age for children with preschool ED compared with children without ED in preschool age. ED does not predict a diagnosis of GD (categorically) (hypothesis 1). Children with ED at preschool age have significantly longer media use times 5 years later, than preschool children without

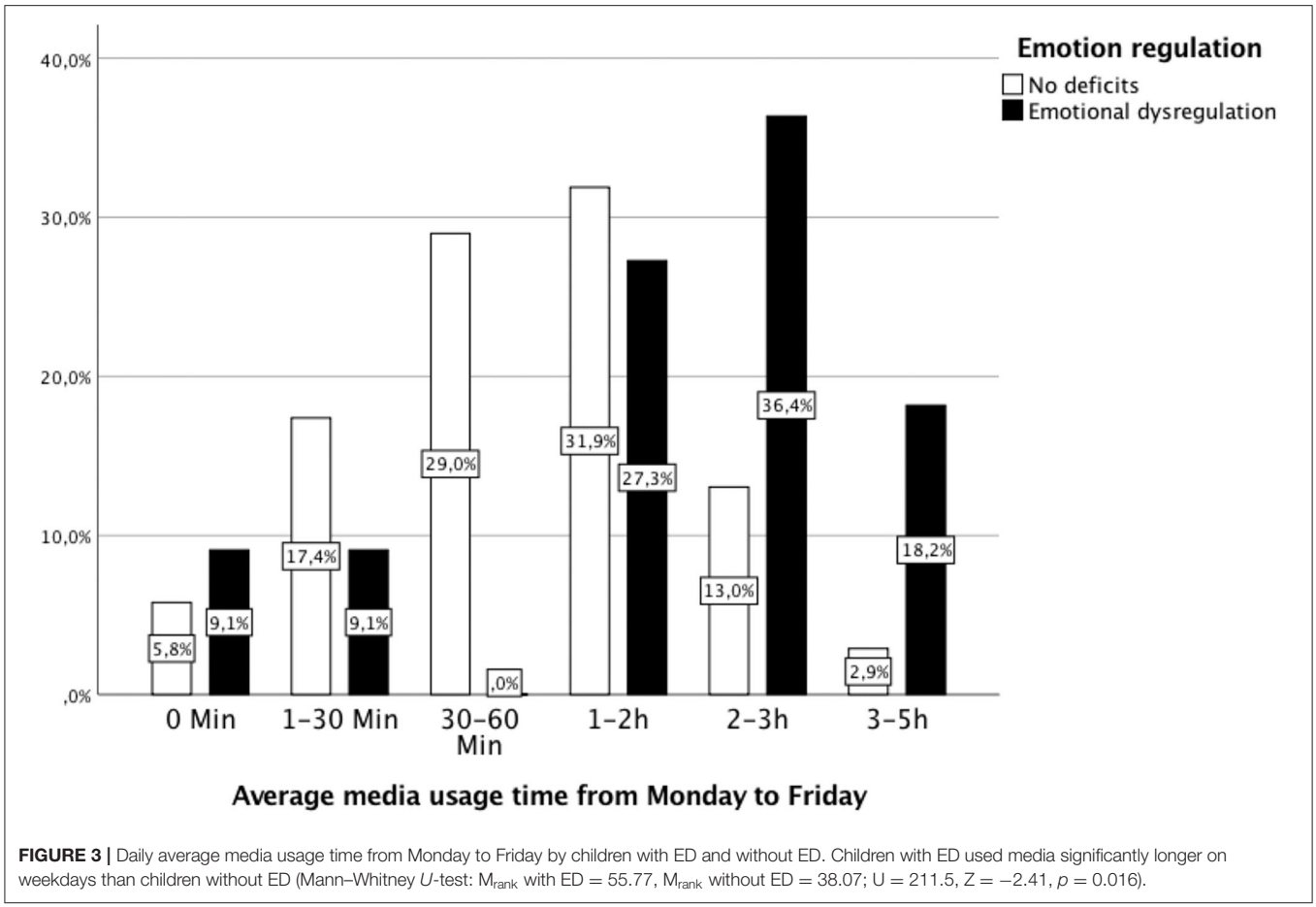


**FIGURE 3 |** Daily average media usage time from Monday to Friday by children with ED and without ED. Children with ED used media significantly longer on weekdays than children without ED (Mann–Whitney *U*-test: $M_{rank}$ with ED = 55.77, $M_{rank}$ without ED = 38.07; U = 211.5, Z = −2.41, $p = 0.016$).

**TABLE 5 |** Differences in media usage time in minutes in children with ED and without ED.

| Period of usage time | Children with ED ($n = 11$) | Children without ED ($n = 69$) | Statistics (*t*-test) |
|---|---|---|---|
| Weekdays (Monday–Friday) | M = 124 min (SD = 77.68) | M = 68 min (SD = 52.76) | t(78) = −3.075; $p = 0.003$; d = 0.851 |
| Weekends (Saturday and Sunday) | M = 209 min (SD = 122.91) | M = 129 min (SD = 98.27) | t(78) = −2.421; $p = 0.018$; d = 0.719 |
| Daily average* | M = 148 min (SD = 88.31) | M = 85 min (SD = 62.06) | t(78) = −2.949; $p = 0.004$; d = 0.828 |

**Daily average usage time was calculated by adding up five times the usage time on weekdays and two times the usage times on weekends divided by seven.*

emotion regulation difficulties. Temporal excessive video game playing behavior at school age is correlated with higher GD symptom scores (dimensionally), but not with the presence or absence of a GD diagnosis (categorically) (hypothesis 2).

It amounts to a difference between a dimensional and a categorical approach to GD. ED in preschool age, as well as screen time use predict higher GD symptom scores on a dimensional scale, but do not predict a GD diagnosis on a categorical scale. Possible explanations for these differences could lie in (a) larger required samples to yield sufficient statistical power. (b) It may be speculated that the GD criteria of the DSM-5 do not apply as well to the according age group (9 years) compared with adolescents or young adults (developmental adequacy). The item analysis of the nine GD criteria supports this speculation: the means lie in the lower range (see **Table 1**). The item difficulties are all with one exception under 0.20. (c) A reflection of the differences between the dimensional and the categorical approach of diagnostic and psychopathology is fundamental. A dimensional approach allows the clinician more latitude in assessing the severity of a condition and does not imply a concrete threshold between "normality" and the disorder, such as GD (57–59).

The reported increase of usage time in children with ED can be attributed to the ED profile because in general, children with psychiatric disorders use digital media significantly longer (60). Children with ED may use video game playing as a maladaptive coping strategy to deal with negative emotions. Because ED

**TABLE 6 |** Differences between children with emotional dysregulation and children without emotional dysregulation on dimensional and categorical assessment of gaming disorder.

| Assessment of GD | Children with ED ($n$ = 11) | Children without ED ($n$ = 69) | Statistics ($t$-test) |
|---|---|---|---|
| Dimensional GD | M = 15.82 (SD = 4.08) | M = 11.71 (SD = 5.05) | t(68) = −3,0; $p$ =0.004; $d$ = 0.895 |
| Categorical GD | Children with GD $n$ = 1 (9.09%) | Children with GD $n$ = 3 (4.35%) | Wald(1) = 31.989 $p$ = 0.51; n.s. |
| | Children without GD $n$ = 10 (90.90%) | Children without GD $n$ = 66 (95.65%) | |

*Dimensional GD was calculated by adding up the response characteristics of 9 GD symptoms to the GD symptom score (1 = never, 2 = sometimes, 3 = often, 4 always). A categorical GD was diagnosed only if at least 5 out of 9 items were answered with "often" or "always."*

is characterized by difficulties in understanding and accepting unpleasant emotions, it is assumed that children with ED often try to avoid such emotional experiences, e.g., by using excessive video gaming to escape psychological difficulties (10, 11, 40, 42). Therefore, young children with ED should be seen as being at risk of developing a GD. This risk may be further increased by the game-associated induction of positive feelings. During the game, children and adolescents feel particularly free and heroic, which in turn leads to a stabilization of their self-esteem. They have a direct sense of achievement and self-efficacy, make social contacts more easily than in real life, and are able to escape the emotional difficulties of the real world, whereas the latter may be a maladaptive coping strategy leading to more excessive gaming (10). Considering all these aspects, in regard to future prevention, it could be a promising approach to limit the time spent on video games. More specifically, children prone to difficulties in dealing with negative emotions should be restricted or monitored more closely in their video game playing behavior. This falls in line with the proposition of Donald et al. (61) to reduce video gaming by restricting access to devices (despite them having considered ED as a result of GD instead of ED predicting GD, as we have found). At the same time, more adequate coping and action alternatives should be offered that both act as an adaptive strategy for dealing with negative emotions and can contribute to experiencing positive feelings.

Furthermore, in the context of the assessment of our second hypothesis, the analyses show that the time criterion of media usage behavior in school age is associated with the existence of a GD, in dimensional GD conceptualization. Therefore, our second hypothesis and the findings from Gentile et al. (34) could be confirmed, whereby the time criterion could be assumed as a manifest risk factor for the development of a GD. We conclude that the time aspect of video game playing behavior should be considered as playing a more prominent role in the development of GD. The tolerance development in DSM-5 is time associated (e.g., feeling the need to play for increasing amounts of time, augmentation of play time). This assumption is strengthened by various findings of other authors, which show a significant association between the usage time of video games and GD (62–66). Again, the time limitation of video game usage behavior, as well as the usage of alternative and adaptive activities, could be useful for the prevention of GD. To our knowledge, there are no efficient studies of possible prevention measures for GD in the context of ED. Therefore, it would be of great interest to undertake further research on prevention measures, e.g., time limitation. Studies indicate that daily use of digital media is not limited to school age and adolescence but also widespread in pre-school age, e.g., Vandewater et al. (67) reported 16% of 5–6-year-old pre-school children playing video games daily. Mendoza et al. (68) reported that already 2–5-year-old children used a computer daily. Thus, effectiveness studies on prevention programs for GD in the context of ED would also be highly relevant for children of younger age. To explore the relation between ED and GD (hypothesis 1), we used a dimensional (i.e., symptom score of GD), as well as a categorical (i.e., diagnosis of a GD), assessment of this construct. In the dimensional assessment of video game playing behavior, children with ED in preschool age show a higher GD symptom score at school age than those without ED. These findings largely confirm our hypothesis 1, as do the findings of Hollett and Harris (40) and Wichstrøm et al. (12). These findings suggests that early detection and treatment of ED could have a preventive effect on the development of GD. Especially in young age, increasing social support with a family- and parent-based approach could reduce Internet addiction (41). Nevertheless, to make more detailed statements in this regard, further research is needed.

## LIMITATIONS

One restriction of the present study is the limitation to parental reports. Parents may report their children spending less time using media, either because of underestimation or because of omitting time spent on media outside home, e.g., with friends. They may also react biased toward social desirability, being aware that their children should not spend that much time online. Furthermore, for future research it would be interesting to consider parents' media use as a mediator variable.

Another limitation of this study is that we only assessed the total usage time of modern electronic media, without differentiating for computer/laptop, smartphone, smartwatch, tablet, gaming consoles, and television. It was also not differentiated between pedagogically valuable content and problematic content. For the calculation of the media usage time in minutes based on the assessed answer categories, we performed a transformation of each category in an average value in minutes with the presumption, that the mid point of the interval serves as the best estimate of the answer category.

Our study does not provide any data on socioeconomic status (SES) and psychiatric family history; therefore, an influence of SES and psychiatric family history can neither be demonstrated nor excluded. Patients of our preschool program are living in the surrounding regions which are characterized by a quite homogenous socioeconomic status. Future studies considering

SES and psychiatric family history as an important variable are underway.

In addition, the group of children actually meeting criteria for ED was small. Retention rate from the original sample was 70% only; however, a time span of 5 years was covered. Also limiting this study in its generalizability is the fact that we investigated a clinical sample. Finally, our study uses a quasi-experimental design. It would be of great value to conduct an a priori defined experimental long-term study with a larger sample, in which the course of possible development of GD in the context of ED would be recorded. In addition, the gender comparison in children with ED did not reach statistical significance and medication use was also unevenly distributed across the sample, which is probably due to the small size of the sample. Therefore, a larger sample would possibly also allow the examination of these variables as covariates in statistical analyses, which would allow the results of the present study to be illuminated against the background of further potential influencing variables.

## CONCLUSION

Our results suggest that preschool ED symptoms and duration of media use predict a higher score of GD symptoms in schoolchildren. Therefore, identifying ED could be the first step for parents to reduce the likelihood for the emergence of GD in schoolchildren. For example, parents should strive to convey the value of self-control and offer training in self-reflection with the aim of promoting self-regulated behavior. Therefore, one noteworthy strength of the present study is that it explores the rarely investigated and relevant area of risk factors of children's video gaming behavior. Excessive computer use and GD becomes a dysfunctional solution or an inadequate coping for pre-existing ED. Therefore, preventing ED contributes to the prevention of GD.

Regardless of the significant associations between ED in preschool and later media use and GD in childhood, the question of the relationship between ED and ICD-10 nosology arises, which has not been clarified as yet. Would ED be the "Grand Unifying Theory" of psychological symptoms and disorders?

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethikkommission der Ärztekammer des Saarlandes Ha 147/19. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

FP: conceptualization, implementation, data collection, statistical analysis, text creation, and discussion. KH: data collection, data entry, and ethics application. FM: statistical analyses and text creation. EM: discussion and correction. All authors contributed to the article and approved the submitted version.

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# The Association Between Resting State Functional Connectivity and the Trait of Impulsivity and Suicidal Ideation in Young Depressed Patients With Suicide Attempts

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Suicide is a leading cause of death among youth and is strongly associated with major depressive disorder (MDD). However, the neurobiological underpinnings of suicidal behaviour and the identification of risk for suicide in young depressed patients are not yet well-understood. In this study, we used a seed-based correlation analysis to investigate the differences in resting-state functional connectivity (RSFC) in depressed youth with or without a history of suicide attempts and healthy controls (HCs). Suicidal attempters (ATT group, $n = 35$), non-suicide attempters (NAT group, $n = 18$), and HCs exhibited significantly different RSFC patterns with the left superior prefrontal gyrus (L-SFG) and left middle prefrontal gyrus (L-MFG) serving as the regions of interest (ROIs). The ATT group showed decreased RSFC of the left middle frontal gyrus with the left superior parietal gyrus compared to the NAT and HC groups. Decreased RSFC between the left superior frontal gyrus and the right anterior cingulate cortex (rACC) was found in the ATT group compared to the NAT and HC groups. Furthermore, the left prefrontal-parietal connectivity was associated with suicidal ideation and levels of impulsivity, but RSFC of the left prefrontal cortex with the rACC was correlated exclusively with impulsivity levels and was not related to suicidal ideation in the ATT group. Our results demonstrated that altered RSFC of the prefrontal-parietal and prefrontal-rACC regions was associated with suicide attempts in depressed youth, and state-related deficits in their interconnectivity may contribute to traits, such as cognitive impairments and impulsivity to facilitate suicidal acts. Our findings suggest that the neural correlates of suicidal behaviours might be dissociable from those related to the severity of current suicidal ideation. Neural circuits underlying suicide attempts differ from those that underlie suicidal ideation.

**Keywords: youth suicide, depression, functional magnetic resonance imaging, impulsivity, resting-state functional connectivity**

## INTRODUCTION

Suicide is an important public health problem worldwide (1) and a leading cause of death among youth aged 15–24 years in China (2). Youth suicide has elicited great concern from the public, policy-makers, and health care providers. In addition, suicide attempts occur 10–20 times more frequently than completed suicide and are known to be the most powerful predictor of future completed suicide (3). Thus, youth who survive a suicide attempt continue to be at risk for completed suicide (4). The majority of suicide victims or suicide attempters suffer from a mood disorder, the most frequent of which is major depressive disorder (MDD) (5). Improving our ability to predict and subsequently prevent suicidal behaviour in depressed patients has become an important priority. To date, the assessment of suicidal risk is based on sociodemographic and clinical factors, often yielding a high sensitivity but a low specificity (6). Evidence of a neurobiological basis of vulnerability to suicidal behaviour is increasing (7). Thus, a better understanding of the mechanisms underlying risk for a suicide attempt from a neuroscience perspective will provide a framework for conceptualising potential interventions. However, we have limited understanding of the neurobiological roots of suicidal behaviour, especially in adolescents. Because adolescence and early adulthood is a time of high risk for suicide as well as a period that is marked by significant neural development (8), investigating the neurobiological underpinnings of suicidality within this population is critical to better understand the psychopathology in its early stages and aid in developing intervention and prevention strategies that promote healthy neurodevelopmental trajectories.

Functional magnetic resonance imaging (fMRI) studies provide a promising strategy for learning about neurobiology that may confer risk for suicidal behaviour and potentially provide an objective neurobiological marker of suicidal risk in depressed youth (9). fMRI can help identify neurobiological underpinnings of pathophysiologic mechanisms that are not observable at the behavioural level and can also provide targets for future neurobiological interventions (9). Resting-state fMRI (RS-fMRI) has recently emerged as a useful tool for investigating brain functional connections without using externally controlled task paradigms. Resting-state functional connectivity (RSFC) analysis has been suggested as an established, powerful technique for an unbiased analysis that reveals correlations in the activity of discrete brain regions during rest (10), and it has been successfully employed to detect abnormal functional integration in several brain disorders and provide some important information for the understanding of these diseases, such as in Alzheimer's disease (11–13), heroin addiction (14), schizophrenia (15), and depression (16, 17). An increasing number of RSFC studies have investigated the associations between abnormal FC of particular brain regions and the pathophysiology of brain diseases (16, 18). The investigation of RSFC could provide important insights into the intrinsic FC in depressed youth with suicide attempts, and these studies will make important contributions to a better understanding of the neural circuitry underlying suicide in depression. However, the number of RSFC studies examining suicide in youth is small.

Previous neuroimaging studies have demonstrated the involvement of the prefrontal cortex (PFC) in suicidal behaviour in young adults and adolescents (9, 19–23). A model-based structural neuroimaging study with a translational perspective confirmed structural prefrontal alterations in adults with histories of suicide attempts (9). A near-infrared spectroscopy (NIRS) study revealed that MDD patients with suicidal ideation displayed reduced haemodynamic activation in prefrontal regions, and haemodynamic changes in the prefrontal cortex were negatively correlated with the severity of suicidal ideation in patients with MDD, suggesting that the PFC is a brain substrate of suicidal ideation in depressive states in adult patients with MDD (24). A previous study (25) found a relative hypometabolism in the middle frontal gyrus and superior parietal lobule in depressed adults with suicide plans when compared to depressed patients without suicidal ideation or suicide plans. Reduced left ventrolateral prefrontal cortex (VLPFC) volumes were found in attempters vs. non-suicide attempters and healthy controls aged between 18 and 60 (9, 22). Task-based fMRI studies have revealed that the activity of the right superior frontal gyrus is decreased in depressed adolescents with a history of suicide attempt in response to exposure to angry faces (26, 27), and adult males with a history of suicide attempt showed decreased activity in the right superior frontal gyrus in response to 100% intensity angry vs. neutral faces relative to healthy and depressed non-attempter controls (28). Another study found decreased bilateral perfusion in the superior/medial PFC in a cohort of depressed individuals who would later complete suicide (29). In adolescents, one study found that the dorsolateral PFC and temporoparietal junction was less activated with suicidal ideation than in same-age control subjects during passive viewing of negative stimuli (30). Our previous neuroimaging study on suicide in adolescents, we found decreased activity in the left superior prefrontal gyrus (L-SFG) and left middle prefrontal gyrus (L-MFG) in depressed patients with suicidal behaviour and decreased activity in the L-SFG and L-MFG was associated with increased impulsivity. Dysfunction of the L-SFG and L-MFG may underlie the behavioural disinhibition associated with impulsivity and increase the risk for suicide in depressed youth. In sum, these two brain areas seem to play an important role in the neurobiological mechanisms of suicidal behaviour and represent a potential neurobiological diathesis or predisposition to suicidal behaviour in depressed patients. These two brain areas might be suitable for functional neuroimaging studies on suicide.

In the current study, we selected the L-SFG and L-MFG as regions of interest (ROIs), and to investigate the association between RSFC and suicide attempts, we used a seed-based correlation analysis to explore and characterise abnormal resting-state FC patterns *in vivo* in depressed youth with a history of a suicide attempt relative to other depressed patients without a history of suicide attempt and healthy controls (HCs). We hypothesised that depressed youth who had a history of suicide attempt would show abnormal RSFC patterns of the L-SFG and L-MFG with other cortical regions, and there would be significant

associations between aberrant RSFC and the traits of suicide-related behaviour.

# METHOD

## Participants

The Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University approved this study, and informed consent of all participants was obtained after the nature of the procedures had been fully explained. We would tell participants the purpose and specific content of this study, all participants would sign an informed consent before the study. We recruited 53 right-handed depressed youth from the Department of Psychiatry, the First Affiliated Hospital of Chongqing Medical University. The Structured Clinical Interview for Diagnostic and Statistical Manual IV (DSM-IV) Axis I disorders (SCID-I) (31) was administered to each patient by two qualified psychiatrists for the diagnosis of depressive disorder. The inclusion criteria were as follows: (a) unipolar subtype, (b) refrained from antidepressants for at least 1 month at the time of study and (c) total score of 17-item Hamilton Depression rating scale (HAMD) more than 17 and Beck Depression Inventory (BDI) 14 on the day of their scan. The exclusion criteria included any other psychotic disorders or comorbid DSM-IV axis I major psychiatric disorders, any history of significant head trauma with loss of consciousness, and other clinically relevant abnormalities in their medical history or laboratory examinations, and/or any contraindications for MRI scan. The patients were categorised into two groups: suicide attempters (ATT group, $n = 35$) with a history of at least one suicide attempt within the 6 months prior to magnetic resonance scanning and non-suicide attempters (NAT group, $n = 18$) without such a history. A suicide attempt was defined as self-destructive behaviour committed with some degree of intent to die and was assessed using the Columbia Suicide History Form, and the history of suicide attempts for a patient was confirmed based on the documentation of suicide attempts in their medical records or a history of visits to the hospital emergency department after attempting suicide. The severity of depression was assessed by using the HAMD and BDI, and the Scale for Suicide Ideation (SSI) was used to evaluate suicidal ideation severity. Additional assessments used were the Beck Hopelessness Scale (BHS) and the Barratt Impulsivity Scale, Version 11 (BIS-11).

Additionally, 47 right-handed HCs with no history of neurologic or psychiatric diseases were recruited from among the friends and spouses of the patients and were matched with the patients for age, gender, and education.

## MRI Acquisition

MRI scans were performed on a 3T GE Signa HDxt MRI system (General Electric Healthcare, Chicago, Illinois, USA) using a standard eight-channel head coil. RS-fMRI data were acquired using an echo-planar image (EPI) pulse sequence at 2-s intervals for a total of 8 min, employing the following imaging parameters: 33 axial slices, repetition time (TR) = 2000 ms, echo time (TE) = 40 ms, slice thickness = 4.0 mm, flip angle = 90°, field of view (FOV) = 240 × 240 $mm^2$, and in-plane resolution = 64 × 64. A total number of 240 time points were axially recorded. Foam pads were used to minimise head motion, and the participants were instructed to relax in a comfortable position with their eyes closed, to remain still and awake. In addition, a high-resolution 3D T1-weighted MRI image to which the RS-fMRI data were to be coregistered was obtained using a fast gradient echo (FGRE) sequence, TR/TE = 24 ms/9 ms, flip angle = 90°, thickness/gap = 1.0/0 mm, FOV = 24 × 24cm, and matrix = 256 × 256. No obvious brain abnormalities on conventional MRI were observed, and none of the subjects felt discomfort during or after the procedure.

## Pre-processing of fMRI Data

The RS-fMRI data were pre-processed using Data Processing and Analysis for (Resting-State) Brain Imaging (DPABI) software (32) (http://www.restfmri.net) running in MATLAB (Mathworks, Natick, MA, USA). The pre-processing steps included slice timing correction, realignment for head motion, spatial normalisation in Montreal Neurological Institute (MNI) space, spatial smoothing, linear trend removal and filtering (0.01–0.08 Hz), and nuisance signal regression. The first 10 EPI time points were removed to ensure steady state, slice timing correction, realignment for head motion across the time series incorporating nuisance covariate regression using the Friston 24-parameter model (33) and use of signals from segmentations of the white matter (WM) and cerebrospinal fluid (CSF) compartments in the 3D T1-weighted image as regressors to reduce respiratory and cardiac effects. Additionally, linear trend removal and filtering (0.01–0.08 Hz) was included as a regressor to account for potential drifts in the BOLD signal. The resulting aligned image time series for each subject were each co-registered with the corresponding 3D T1-weighted image and the Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) tool (34) was used to normalise the data for all subjects to Montreal Neurological Institute (MNI) space (resampling with 3 × 3 × 3 $mm^3$ resolution), and spatially smoothed with a Gaussian kernel of 4 mm full-width half-maximum (FWHM).

Six parameters associated with head motion signals were regressed out (three for shift and three for rotation), and the overall head motion was calculated as the average magnitude of the head motion. No significant differences were found in the root mean square (RMS) head movement among the three groups ($p = 0.35$). All participants had <1 mm maximum displacement head movement in any direction (x, y, and z) and <1° maximum displacement in any angular dimension.

## Functional Connectivity Analysis

Based on previous literature and our prior study results, we selected the L-SFG and L-MFG as seed ROIs (9, 19–23), and the centred MNI coordinates of the seed regions were x, y, z = −33, 63, −6 (L-SFG) and x, y, z = −27, 30, 30 (L-MFG). The seed regions were defined by generating a 6-mm radius in the ROIs. A voxel-wise FC analysis was performed by computing the temporal correlation between the mean time series of each seed ROI and the time series of each voxel in the brain. The correlation

coefficients (r) were then normalised to Z-scores with the Fisher r-to-z transformation using the following equation:

$$z = 0.5 \log \left[ \frac{1+r}{1-r} \right] \quad (1)$$

The Z-score maps of each ROI for all subjects were created, and they were defined as RSFC maps.

## Statistical Analysis

Demographic and clinical characteristics were analysed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, New York). For the FC analysis, one-sample *t*-tests were first conducted with the individual Z-maps for within-group comparisons (within the grey matter mask) in each group ($p < 0.05$), and a mask was created by combining the statistical maps of one-sample *t*-test results. Then, one-way analysis of variance (ANOVA) was used to compare the differences in RSFC among the three groups (ATT vs. NAT vs. HC) in the combined mask as above. Age, gender, education level, and mean framewise displacement (FD) were used as covariates. Statistical significance was set at corrected $p < 0.05$ (uncorrected $p < 0.01$) using Gaussian random field correction, which was performed using DPABI software. We further extracted Z values from the grey matter mask showing significant differences among the three groups, and *post hoc* two-sample *t*-tests of the Z values between each pair of groups (ATT vs. NAT, ATT vs. HC, NAT vs. HC) were applied to correct for multiple comparisons ($p < 0.05$, Bonferroni-corrected). Finally, two-tailed Pearson correlation analyses were separately performed to assess the relationships between RSFC and the HAMD, BDI, BIS-11, BHS, and SSI scores within the ATT group in SPSS 22.0. Statistical significance was determined following family-wise error (FWE) correction at $p < 0.05$.

# RESULTS

## Demographics and Clinical Characteristics

Demographics and clinical characteristics are shown in **Table 1**. The patient groups (ATT and NAT group) had higher HAMD ($20.03 \pm 5.61$ vs. $23.50 \pm 8.92$ vs. $3.85 \pm 2.32$, $p < 0.001$), BDI ($23.91 \pm 7.94$ vs. $24.94 \pm 7.14$ vs. $3.94 \pm 3.33$, $p < 0.001$) and SSI scores ($11.06 \pm 4.71$ vs. $10.22 \pm 2.98$ vs. $2.87 \pm 2.31$, $p < 0.001$) than the HC group. In addition, there were significant differences in impulsivity (BIS-11 total score) ($73.86 \pm 10.68$ vs. $68.39 \pm 8.81$ vs. $61.79 \pm 8.19$, $p < 0.001$) and hopelessness (BHS total score) ($12.14 \pm 3.97$ vs. $7.50 \pm 2.41$ vs. $3.79 \pm 2.40$, $p < 0.001$) among the three groups. By definition, the BIS-11 and BHS scores of the ATT patients were significantly higher than those of the NAT patients ($p < 0.001$). The number of suicide attempts in the ATT patients is displayed in **Figure 1**.

## Group Differences in RSFC Analysis

The ATT group demonstrated decreased RSFC between the L-MFG and L-SPG (FWE corrected, $p < 0.05$) compared to the NAT group. And decreased RSFC of the L-SFG with rACC (FWE corrected, $p < 0.05$) was found in the ATT group relative to both the NAT and HC groups. In addition, the NAT group showed decreased RSFC of the L-MFG with the left insular cortex, as well as with the L-SPG relative to the HC group (**Table 2** and **Figures 2**, **3**).

## Correlations Between RSFC and Clinical Characteristics

The correlation analysis indicated that decreased RSFC between the L-MFG and L-SPG was negatively associated with SSI scores ($r = -0.4056$, $p = 0.0156$) and BIS scores ($r = -0.3498$, $p = 0.0394$) in the ATT group. Additionally, the RSFC of the L-SFG with the rACC was negatively correlated with BIS-11 scores ($r = -0.3472$, $p = 0.0410$) within the ATT group, but no significant negative correlation of the SSI total scores with the RSFC between the L-SFG and rACC was observed in this group ($r = -0.2602$, $p = 0.1312$) (**Figure 4**).

# DISCUSSION

In the current study, we investigated the differences in RSFC in depressed youth who had (suicide attempters; ATT group) or did not have a history of suicide attempts (NAT group) and healthy controls (HC). Decreased RSFC of the left middle frontal gyrus with the left superior parietal gyrus and decreased RSFC between the left superior frontal gyrus and the right anterior cingulate cortex (rACC) was found in the ATT group compared to the NAT and HC groups. Furthermore, the left prefrontal-parietal connectivity was associated with suicidal ideation and levels of impulsivity, but RSFC of the left prefrontal cortex with the rACC was correlated only with impulsivity levels and was not related to suicidal ideation in the ATT group. These results indicated that the decreased RSFC of the left PFC with the left parietal cortical areas and with the rACC may be implicated in the neurobiology of suicidal behaviour in young depressed patients. The findings suggest that impaired neural circuit connections may be vulnerability factors and the manifestations of suicide. This study would contribute to the detection of suicide risk and provide insight in a neurobiological target for suicide interventions in youth depression at the clinical level.

## Prefrontal-Parietal RSFC

Abnormal RSFC of the left PFC with left parietal cortical areas was observed in young depressed patients with suicide attempts in this study. The left hemisphere exhibited particular features with regards to not only general emotion processing but also specific depression pathophysiology (35), and a greater left hemispheric response to positive stimuli was noted during general emotion processing (36).

Elsewhere, in our study, we found the RSFC of the fronto-parietal circuit was correlated with the SSI and BIS-11 scores in the ATT group. The results of our study provide preliminary evidence that an abnormal left fronto-parietal circuit may be the underlying neural circuit related to suicidal behaviour associated with depression. The reduced resting-state metabolic activity in frontopolar and parietal brain regions that are involved in decision-making and choice, more particularly in exploratory behaviour, was associated with suicide plans in depressed

**TABLE 1 |** Demographic and clinical characteristics of patients and healthy.

| Characteristic | ATT (*N* = 35) | NAT (*N* = 18) | HC (*N* = 47) | *P*-value | *post-hoc* test |
|---|---|---|---|---|---|
| Age (years) | 20.63 ± 3.65 | 21.26 ± 3.02 | 20.48 ± 1.86 | 0.584 | - |
| Gender (male/female) | 10/25 | 8/10 | 16/31 | 0.602 | - |
| Education (years) | 12.97 ± 1.90 | 13.22 ± 1.44 | 13.55 ± 1.52 | 0.289 | - |
| BIS-11 | 73.86 ± 10.68 | 68.39 ± 8.81 | 61.79 ± 8.19 | <0.001 | ATT > NAT > HC |
| HAMD | 20.03 ± 5.61 | 23.50 ± 8.92 | 3.85 ± 2.32 | <0.001 | ATT, NAT > HC |
| BDI | 23.91 ± 7.94 | 24.94 ± 7.14 | 3.94 ± 3.33 | <0.001 | ATT, NAT > HC |
| BHS | 12.14 ± 3.97 | 7.50 ± 2.41 | 3.79 ± 2.40 | <0.001 | ATT > NAT > HC |
| SSI | 11.06 ± 4.71 | 10.22 ± 2.98 | 2.87 ± 2.31 | <0.001 | ATT, NAT > HC |

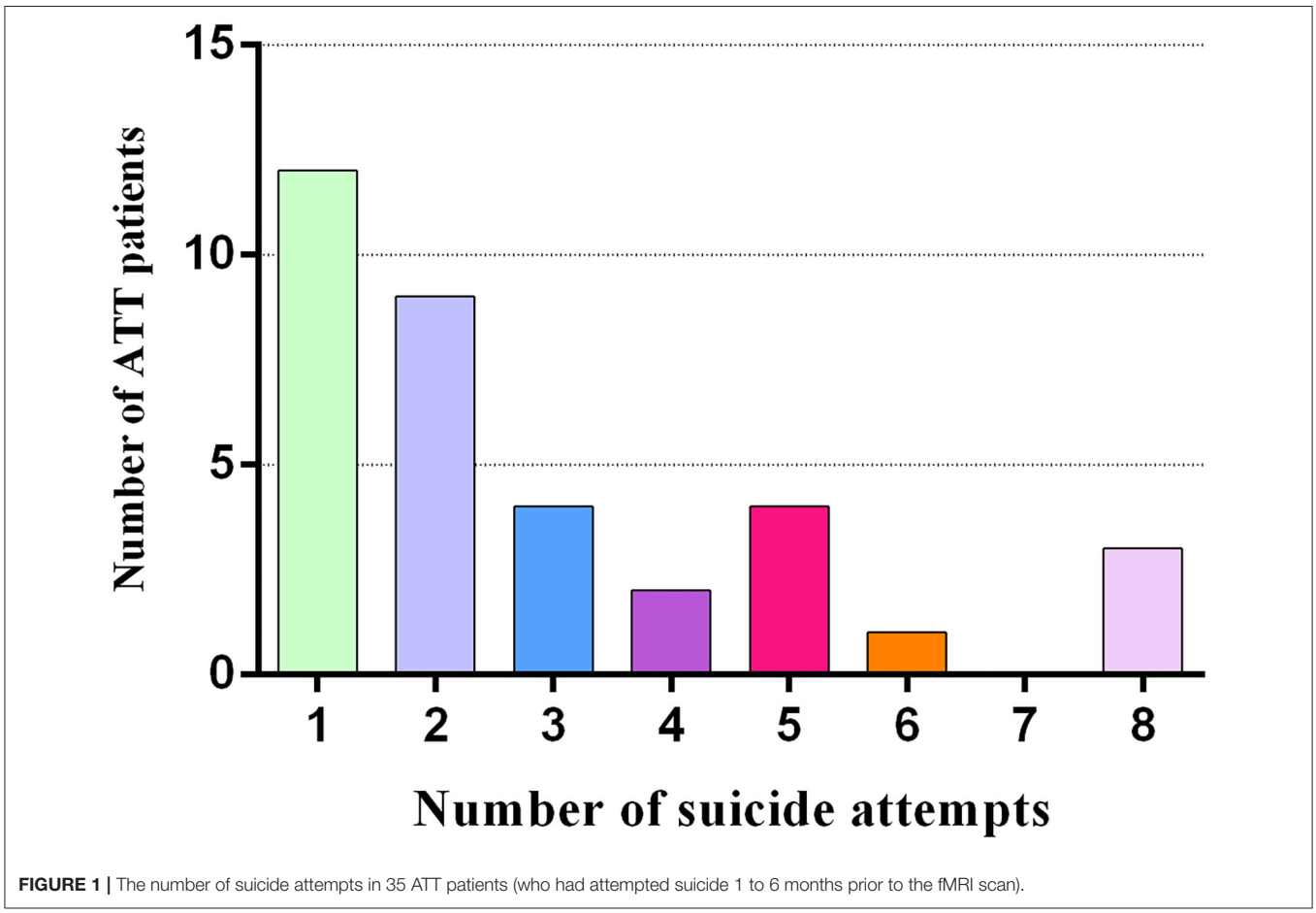


**FIGURE 1 |** The number of suicide attempts in 35 ATT patients (who had attempted suicide 1 to 6 months prior to the fMRI scan).

individuals. Furthermore, another RSFC study found that MDD patients with suicidal ideation (SI group) exhibited decreased intrinsic functional connectivity (iFC) between the orbitomedial prefrontal cortex (OMPFC) and the rACC (37).

Elevated trait impulsivity in suicidal depressed patients was observed in our study, which was reported in a previous study. A preponderance of evidence has suggested that impulsivity (as measured by the BIS-11) likely predisposes individuals to suicide. The middle frontal gyrus is considered to play a role in reorienting attention, where both ventral and dorsal attention networks converge. Abnormal functioning and connectivity within the middle frontal gyrus have been documented in a meta-analysis as well as in a more recent study of adults with MDD (38). Furthermore, reduced cortical thickness of the middle frontal gyrus has been related to impulsivity in adolescents (39) and has been associated with motor impulsivity in particular (40). The neural substrate underlying impulsivity in suicidal depressed patients has also been illustrated in our previous research, which demonstrated that decreased activity in the L-MFG was associated with increased impulsivity in young suicidal depressed patients. In the present study, we found that decreased prefrontal-parietal RSFC was negatively correlated

**TABLE 2 |** Differences in left MFG and SFG seed functional connectivity among the ATT group, NAT group, and HC group.

| Brain area | MNI coordinates | | | *T*-value | Voxels size |
|---|---|---|---|---|---|
| | x | Y | z | | |
| **Seed 1: left middle frontal gyrus (L-MFG, Peak MNI: −27 30 30)** | | | | | |
| **ATT < NAT** | | | | | |
| Parietal-Sup-L | −17 | −52 | 71 | −1.22 | 4 |
| **NAT > HC** | | | | | |
| Frontal-inf-Orbit-R | 48 | 48 | −9 | 2.95 | 33 |
| Frontal-Mid-R | 27 | 15 | 33 | 3.46 | 35 |
| **NAT < HC** | | | | | |
| Insula-L | −32 | −13 | 18 | −3.70 | 28 |
| Parietal-Sup-L | −24 | −54 | 66 | −3.12 | 18 |
| **ATT > HC** | | | | | |
| Frontal-Mid-R | 30 | 15 | 36 | 3.05 | 30 |
| **ATT < HC** | | | | | |
| Insula-L | −18 | −18 | 18 | −3.12 | 23 |
| Parietal-Sup-L | −21 | −54 | 66 | −3.64 | 33 |
| **Seed 2: left superior frontal gyrus (L-SFG, Peak MNI: −33 63 −6)** | | | | | |
| **ATT > NAT** | | | | | |
| Frontal-Sup-R | 15 | 12 | 57 | 3.96 | 24 |
| **ATT < NAT** | | | | | |
| Anterior Cingulate-R | 24 | 30 | −6 | −2.46 | 32 |
| **NAT > HC** | | | | | |
| Frontal-Mid-Orbit-L | −30 | 57 | −15 | 4.34 | 22 |
| **ATT < HC** | | | | | |
| Anterior Cingulate-R | 9 | 27 | −3 | −4.31 | 32 |

with elevated BIS-11 impulsivity scores in the ATT group. The correlation with BIS-11 scores demonstrated that impulsivity and prefrontal-parietal connectivity is highly relevant to our preliminary finding, further supporting the role of the PFC in suicide. In addition, adolescents with MDD and high suicidality showed lower activation in the medial PFC and anterior cingulate cortex (ACC) compared to MDD adolescents with low suicidality and HCs (41). Some research (41, 42) proposed that vulnerability to suicidal behaviour can be attributed to increased self-focus and hopelessness derived from emotional dysregulation in combination with abnormalities in the fronto-limbic or fronto-parietal-cerebellar pathways. These findings suggest that the altered fronto-parietal connectivity implicated in affective and cognitive processing procedures might contribute to the pathogenesis of suicidal behaviour in MDD.

The fronto-parietal circuit is also involved in goal-directed top-down processing, attention and executive function, decision-making and conflict resolution and is engaged in cognitive control (43). The aberrant FC of the prefrontal region with the parietal cortex may impair decision-making and cognitive control, which increases suicidal vulnerability and suicidal risk. Thus, the disruption of the fronto-parietal circuit may be involved in the pathogenesis of suicidal behaviour in depressed youth, and it may be implied as underlying neural substrate. However, it would necessitate further research to replicate and verify this finding.

## Prefrontal-rACC RSFC

In addition to the decreased connectivity in prefrontal-parietal circuits, reduced connectivity between L-SFG and rACC was also observed in the suicidal depressed patients compared to non-suicidal depressed patients. Our results are in agreement with several results from previous studies in depressed patients with and without suicide behaviour (25, 30, 44). A comparative study of regional cerebral glucose metabolism (rCMRglu) using 18-FDG-PET demonstrated that compared to depressed patients without suicidal ideation or suicide plans, depressed patients with suicidal ideation and suicide plans showed hypometabolism in the L-SFG, and comparing depressed patients with suicidal ideation to those without suicidal ideation revealed an association between suicidal ideation and decreased metabolism in the right cingulate gyrus (25, 30). One study (44) found that youths with suicide attempts exhibited increased activation in the right anterior cingulate gyrus and left dorsolateral PFC (dlPFC) while viewing negative facial expressions during an emotion perception task. Compared to those without suicidal ideation and HCs, depressed patients with suicidal ideation showed decreased RSFC between the rostral ACC and the middle temporal pole (37). Schreiner et al. (45) reported that higher suicidality was associated with lower RSFC between the posterior cingulate cortex (PCC) and a cluster encompassing the left superior and middle frontal gyri and superior parietal lobule. In addition, one study showed adolescents with MDD

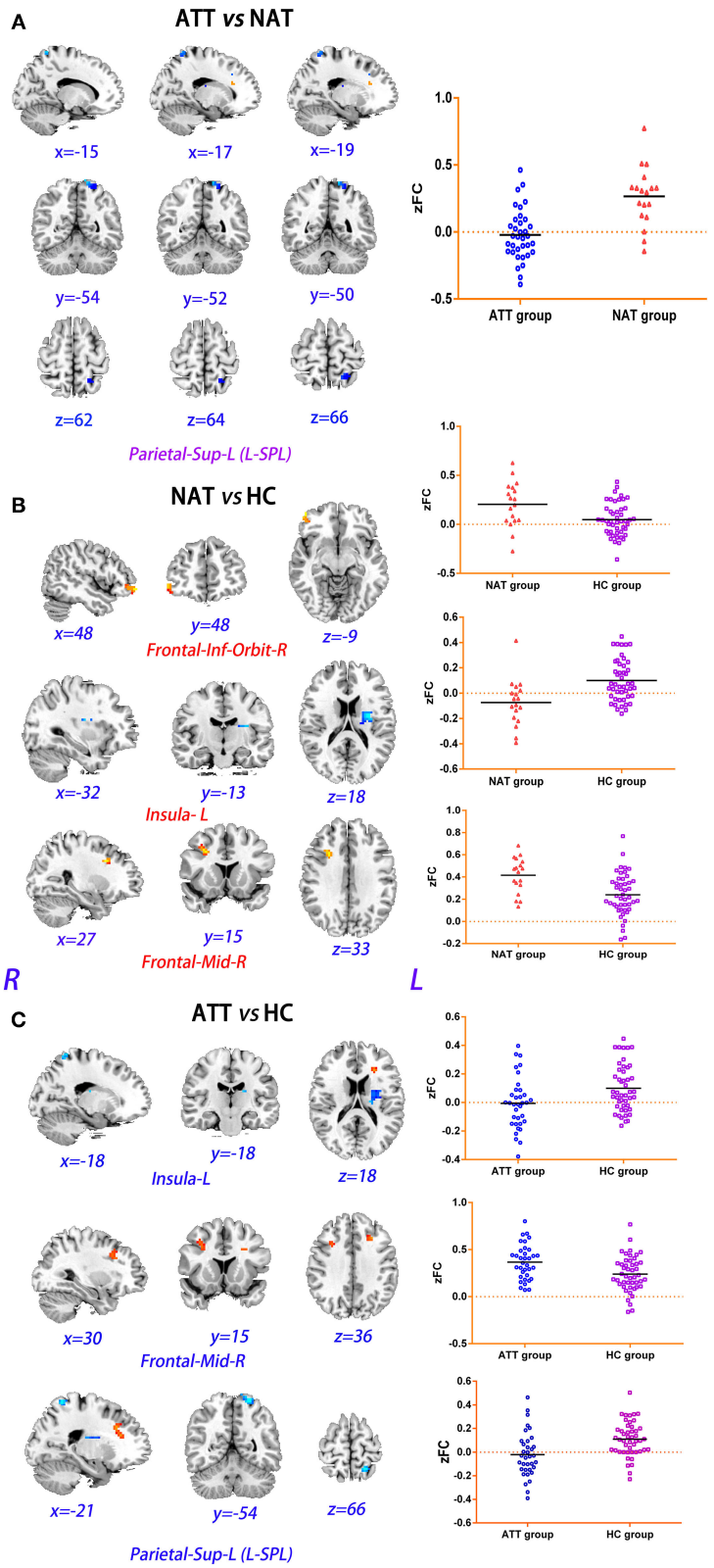


**FIGURE 2 |** Group differences in RSFC analysis using L-MFG as seed of ROIs. **(A)** *post hoc t*-tests revealed that the ATT group demonstrated decreased RSFC between the L-MFG and L-SPG compared to the NAT group (FWE corrected, $p < 0.05$). **(B)** Compared to HC group, NAT group showed decreased RSFC of the L-MFG with the left insular cortex, as well as with the right inferior frontal grus and R-MFG (FWE corrected, $p < 0.05$). **(C)** Compared to the HC group, the ATT group showed decreased RSFC of the L-MFG with the left insular cortex and L-SPG, and increased RSFC between the L-MFG and R-MFG (FWE corrected, $p < 0.05$).

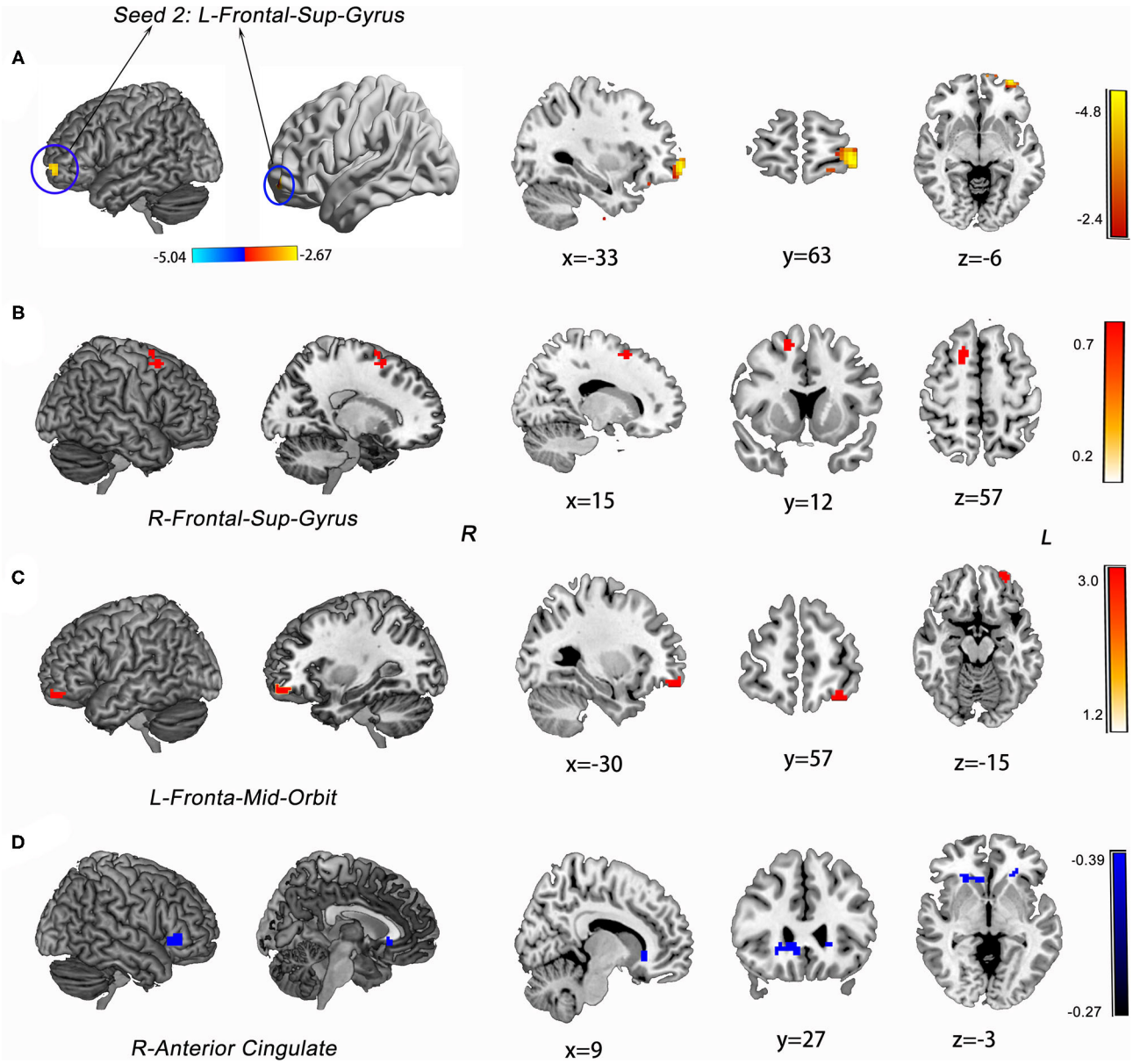


**FIGURE 3 |** Group differences in RSFC analysis using L-SFG as seed of ROIs and the statistical maps showing *post hoc t-test* results of RSFC analysis among the three groups. **(A)** The map of seed region of interest (ROI): left superior frontal gyrus (L-SFG, Peak MNI: −33 63 −6). **(B)** ATT group vs. NAT group; **(C)** NAT group vs. HC group; **(D)** ATT group vs. HC group; Red and blue denote increased and decreased RSFC, respectively, and the colour bars indicate the *t*-value from *post-hoc* analysis between each pair of groups.

and suicide attempts had reduced FC between the ACC and bilateral insula when viewing angry faces (44), suggesting further aberrations in affective experience. Taken together, these findings indicate that functional abnormalities in the associations between the PFC and ACC are related to a vulnerability to suicide attempts.

As has been highlighted in the literature, reduced connectivity of the dorsal anterior cingulate cortex (dACC) with the medial thalamus and left pallidostriatum was found in patients suffering from depression, and there was a trend for decreased connectivity between the ACC and the amygdala (46). The orbito-frontal cortex (OFC), which receives connections from the amygdala and thalamus, has a significant role in the interpretation of stimuli in the environment, notably in attributing value to stimuli (stimuli–outcome association), which may be important for the triggering of the suicidal crisis in the face of environmental stressors. The lateral PFC receives motivational inputs from ACC and represents cognitive information from memory, which is deficient in suicide attempters. Dysfunction of this interconnected prefrontal

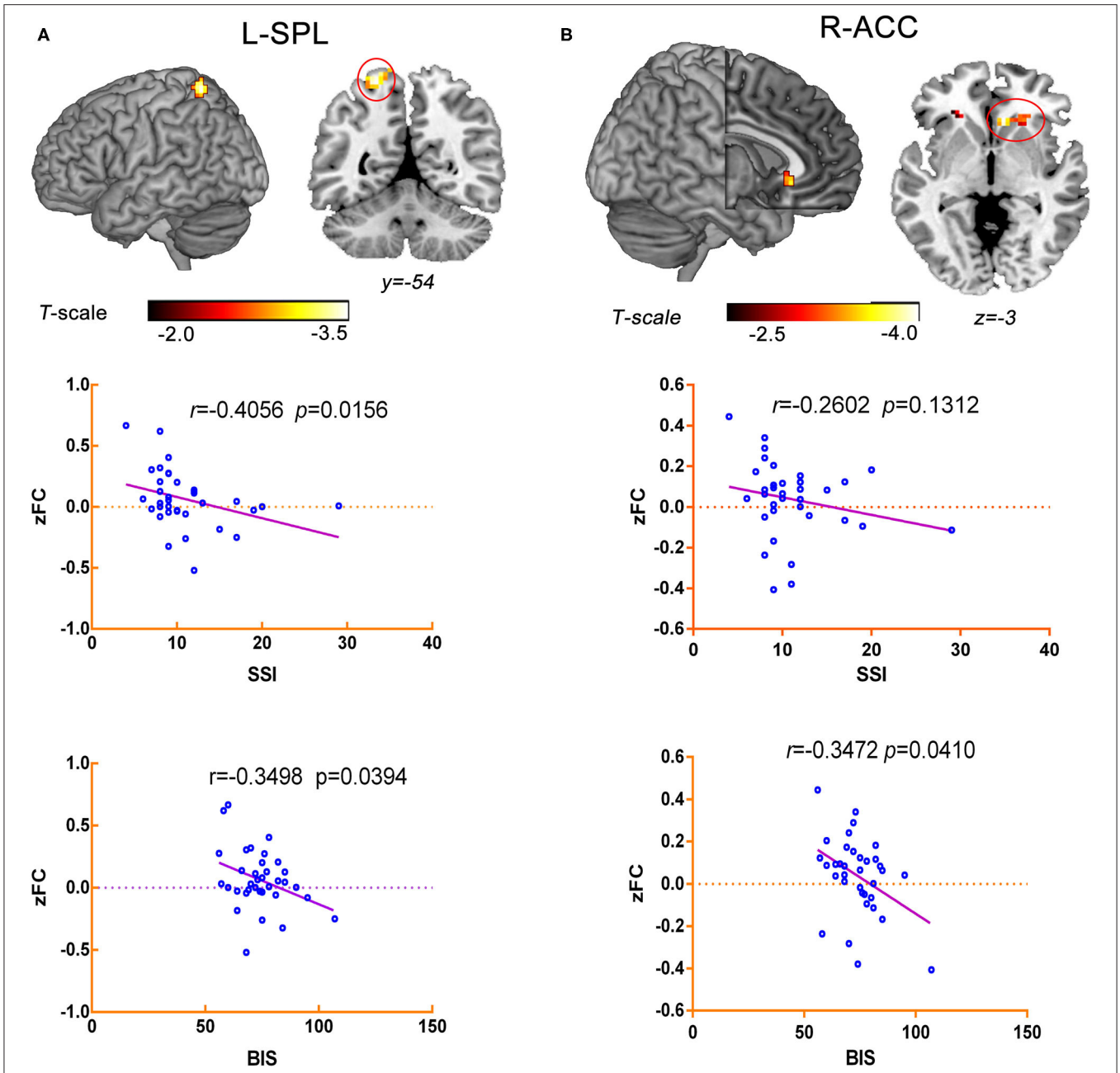


**FIGURE 4 |** Correlation analysis between aberrant RSFC and the traits of suicide-related behaviour in ATT group. **(A)** The RSFC between the L-MFG and L-SPG was negatively associated with SSI scores ($r = -0.4056$, $p = 0.0156$) and BIS scores ($r = -0.3498$, $p = 0.0394$). **(B)** The RSFC of the L-SFG with the rACC was negatively correlated with BIS-11 scores ($r = -0.3472$, $p = 0.0410$), but it was not associated with the SSI total scores ($r = -0.2602$, $p = 0.1312$).

network may, therefore, be instrumental in the suicidal process by corrupting information acquisition and processing, resulting in impaired decision-making. It would be reflected by negative assessments of life events and the automatic triggering of intense emotional responses, and the inability to control the evoked emotional responses and particular negative thoughts (including hopelessness, ruminations, and suicidal ideas), and to prevent choosing to commit a suicidal act over alternative options.

In the present study, the BIS-11 score was significantly associated with RSFC values between the L-SFG and rACC in the suicide attempt group, but there was no significant association between L-SFG-rACC connectivity and SSI scores. It is possible that the neural circuits that underlie suicidal behaviour are different from those that underlie suicidal ideation. Furthermore, our findings suggested that abnormal RSFC between the L-SFG and rACC may not be associated with the severity of current

levels of suicidal ideation but might be related to a trait of suicidal behaviour. This study also provided evidence that the neural correlates of suicidal behaviours might be dissociable from those related to the severity of current suicidal ideation (47, 48). Therefore, we speculated that it will be necessary to identify traits and biological neuroimaging markers which are related to suicidal behaviour rather than suicidal ideation in early prevention and intervention of suicide.

The superior frontal gyrus and ACC play a key role in affect regulation, self-referential processing and inhibition of responding, and impulsivity has been more specifically associated with the inability to inhibit responding (49). A previous study revealed that reduced cortical thickness of the middle and superior frontal gyrus was associated with impulsivity in adolescents (39) and was linked to motor impulsivity in particular (40). The literature to date has suggested that suicidal patients have more difficulty inhibiting responses, resulting in more commission errors than non-suicidal patients. Therefore, abnormal prefrontal-rACC RSFC might prompt aberrant affect regulation and response inhibition, which results in high levels of impulsivity that facilitate suicidal acts.

### Limitations

Several limitations of our study should be acknowledged. First, this was a case–control design study, and suicidal behaviour was retrospectively assessed by psychiatrists and medical records. Longitudinal prospective studies are needed to follow young depressed patients to compare alterations in RSFC before and after a suicide attempt and track the changes in FC. Second, we did not evaluate the effects of antidepressant medications taken by the young depressed patients on the findings. The effects of medications or other treatments on functional connectivity were not evaluated and therefore, represent a confounding factor. Thus, pre-enrolment medications should be controlled in future studies investigating the altered physiology of the brain in patients with suicidal depression. Future research we will recruit first-episode drug-naive depressed patients to exclude the influence of pre-enrollment medications or other treatments on the results. Finally, we did not perform multiple comparison corrections when exploring the relationships between RSFC values and clinical scales, and therefore replication of these findings is required. In addition to the above limitations, the relatively modest group size may have influenced the statistical power, and future studies are needed to validate the findings in a larger sample size.

### Conclusion

In summary, we found hypoconnectivity of the L-MFG with the L-SPG and the L-SFG with the rACC in the ATT group compared with NAT group. In addition, the left prefrontal-parietal connectivity was associated with SSI and BIS-11 scores. In contrast, the RSFC of the left PFC with the rACC was correlated only with BIS-11 scores and was not related to SSI scores. Our findings may suggest that the neural correlates of suicidal behaviours might be dissociable from those related to the severity of current suicidal ideation. There may be different neural circuits underlying suicide attempts from those that underlie suicidal ideation. The state-related deficits in the RSFC of prefrontal areas with the parietal cortex and rACC may contribute to traits such as cognitive impairments or impulsivity to facilitate suicidal acts. These results may contribute to the development of neurobiologically informed interventions that are targeted towards normalising aberrant connectivity related to suicidality in young depressed patients in the future.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

## AUTHOR CONTRIBUTIONS

JC and XC designed the trial and analysed the data. YG and JH recruited and scheduled participants and collected the fMRI data. JC and MA tested the participants. JC wrote the report. LK designed the study and revised the manuscript. All authors have read and approved the submission of this manuscript.

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# The Relationship Between Sugar-Sweetened Beverages, Takeaway Dietary Pattern, and Psychological and Behavioral Problems Among Children and Adolescents in China

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**Background and Aim:** The association of sugar-sweetened beverage (SSB) consumption and takeaway dietary pattern with psychological problems in Chinese children and adolescents has not been concretely reported. Our study aimed to investigate the association between SSB consumption, takeaway dietary pattern, and psychological and behavioral problems (PBPs).

**Methods:** Cluster sampling method has been adopted from April to May 2019 to conduct a questionnaire survey among 30,188 children and adolescents in grades 1 to 12 from 14 schools in six streets in Bao'an District of Shenzhen. This cross-sectional study investigated the association of consumption of SSBs and takeaway patterns with PBPs, and PBPs were measured by the Strengths and Difficulties Questionnaire (SDQ) in primary, junior, and senior high school students.

**Results:** A total of 33,801 primary, junior, and senior high school students (mean age = 12.44, SD = 3.47) ranging from 6 to 18 years old were recruited in this study using a health survey of children and adolescents in junior and senior high schools (grades 1–12), and 30,188 students with no missing data were finally analyzed (questionnaires with missing value >5% were excluded). The top three SSBs in the intake frequency were milk beverage drinks (not milk), vegetable protein drinks, and fruit and vegetable juice drinks. Adjusted for demographic factors, the higher the frequency of students consuming SSBs who have significantly higher PBPs, the higher the frequency of students with takeaway dietary patterns who also have significantly higher PBPs. More frequent intake of SSBs [odds ratio (OR) = 2.23, 95%CI = 2.0–2.47, $p < 0.01$] and higher takeaway dietary patterns (OR = 2.34, 95%CI = 1.81–3.03, $p < 0.01$) were associated with higher SDQ total difficulties scores. When low and medium consumption of SSB was compared, children and adolescents who have high SSB intake were more associated

with total difficulties score (OR = 3.10, 95%CI = 2.67–3.59, $p < 0.01$), and when low and medium takeaway dietary patterns were compared, children and adolescents who have high takeaway dietary patterns were more associated with total difficulties score. The joint associations of SSBs and takeaway pattern with SDQ were stronger than the associations individually.

**Conclusions:** Students consuming higher SSBs and having takeaway dietary pattern are associated with increased levels of PBPs individually and interactively. These results may have implications for mental health prevention in adolescents.

**Keywords: sugar-sweetened beverages, take-away dietary patterns, strengths and difficulties questionnaire, children, adolescents, psychological and behavioral problems**

## INTRODUCTION

Throughout the past few decades, sugar-sweetened beverages (SSBs) account for most of the growth in global sugar consumption (1–3). In a previous study, we found that SSBs and foods with high sugar contents may cause obesity and carious disease, may stimulate chronic diseases, may also activate hyperactivity disorders (4) and obesity-related type 2 diabetes mellitus, cancers, metabolic syndrome, and cardiovascular disease (5, 6). Additionally, SSBs also contain other additives that could cause children's behavioral problems and obesity (7–10). As we have known, common daily SSBs include carbonated and fizzy drinks, sweetened milk and milky tea drinks, sparkling water, energy drinks, sweetened orange fruit drinks, sports and energy drinks, vitamin-water drinks, and vegetable protein drink (10–13). The 2015 Dietary Guidelines for Americans recommends limiting total added sugar intake to <10% of daily calories (14). Therefore, a series of problems caused by SSBs should also be noted.

It is worth noting that the impacts of SSBs on mental health have attracted widespread interest from researchers. Previous evidence suggests that the increase in sugar drinks consumption is thought to be a predictor and a result of mental health problems (15). A cross-sectional study explored the association between soft drinks, and hyperactivity and behavioral problems in adolescents (16). And we also have found in Australia that there is a correlation between the consumption of sugar drink and passively acquired mental health problems among adolescents (17). Some others also indicated similar results such as sugar consumption have being linked to an increased risk of attention deficit/hyperactivity disorder (ADHD), depression, and anxiety symptoms (13, 16–18). These results almost suggest that SSBs may have adverse effects on the mental health susceptibility of adolescents (19). These beverages should be consumed with caution, not only because excessive sugar intake can lead to an imbalance in caloric intake that affects a balanced diet but also because it may be associated with mental health problems (20–22), especially among school-aged children.

Previous studies have also shown that the proportion of food spending on eating out of home in Chinese cities rose from 7.9% in 1992 to 21.2% in 2010 (23), which is consistent with a longitudinal study with data collected from the China Health and Nutrition Survey, which found that eating away from home became more common (24). The tempo of life is becoming faster, more and more people also will chose convenient lifestyles, and one of the most obvious characteristics of fast foods and takeaway foods is comfort, which means they save extra time greatly (25, 26). However, in one longitudinal study, researches have found the associations between fast food and physical health (27, 28). Even so, with the rapid development of the economy, more and more electrical products appear in front of us. Many people are ordering fast food takeout online via electronic products (e.g., automobile phone) and ordering food at home (takeaway, takeout, and fast food), which has become more and more popular in the recent decades. These all belonged to unhealthy diet patterns (UDPs). Fast-food consumption is significantly and positively associated with total energy, total fat, saturated fat, total carbohydrate, added sugars, SSBs, and non-beverage energy density. The consumption of fast food and takeaway food represents a public health problem and has been found to be associated with overweight and poor diet quality, as these fast-food and takeaway food menus often contain foods high in energy and fat/sugar (29, 30). More than that, some studies have found significant independent associations between the takeaway dietary patterns and sweet and fast foods and the prevalence of mental health (31–35). For adolescents, a review of nine cohort and three cross-sectional studies confirmed the association between unhealthy diets (including fast food and takeaways) and an increased risk of mental illness (36).

Previous researches exactly reported the relationships between SSBs and takeaway dietary patterns (25, 37, 38). Relative fast-food and takeaway environment exposure was positively associated with SSB intake (39, 40). Given the growing data on children with mental health problems, there is an urgent need to fully identify underlying dietary intake problems, which may not only exacerbate these problems but may also contribute to physical health problems later in life for these growing children. Despite this evidence, the effects of other common diet components, such as fats and sugar, on mental health are still unclear. Furthermore, to our knowledge, few previous studies have analyzed the association between takeaway patterns, SSBs, and psychological behavioral problems among children and adolescents, and few have been about the interactive effect of this association. Based on the results of the reviews mentioned above that fast-food

consumption and carbonated soft drink consumption in children and adolescents tend to co-occur, we hypothesized that there might be interactive effects of takeaway patterns and SSBs in the psychological behavioral problems among children and adolescents. In addition, our study explored multiple types of sugary drinks. In this study, we used data of cross-sectional investigation from China to analyze the interactive model. Therefore, our study aimed to investigate the individual and interactive relationships between SSBs, takeaway dietary pattern, and psychological and behavioral problems (PBPs) among Chinese children and adolescents.

# METHODS

## Study Designs

We took into account both the sampling method and the partnership. We first contacted the Centers for Disease Control and Prevention (CDC) in Bao'an District of Shenzhen, and the local CDC finally selected six streets according to the geographical distribution and the degree of school cooperation. Fourteen schools were selected randomly. A total of 33,801 primary, junior, and senior high school students (mean age = 12.44, SD = 3.47) ranging from 6 to 18 years old were recruited in this study using a health survey of children and adolescents in junior and senior high schools (grades 1–12). In each school, a cluster sampling method was used to extract three classes from each grade. The participants were then asked to complete a questionnaire. Written informed consent and questionnaires were obtained from the students (grades 5–12) or their parents (grades 1–4) (one for parents (grades 1–4) and one for self-reporting (grades 5–12), so the grade 1–4 children obtained their consent from their parents, and consent from grade 5–12 students was obtained directly from them). There were two types of questionnaires: one for parents (grades 1–4) and one for self-reporting (grades 5–12). The survey was conducted from April to May 2019. Due to an unwillingness to respond to the questionnaire, absence from school, high levels of missing data (a questionnaire with missing value >5%), or obviously fictitious responses, 3,613 (10.7%) participants were excluded from the study. Thus, the data from 30,188 participants (response rate: 89.3%) were analyzed. This sample is well-represented in the general population of China, as it also involves almost all children's and adolescents' age groups, including primary, junior, and senior high school samples. This study was approved by the Ethics Committee of Anhui Medical University.

## Measures

We conducted a comprehensive questionnaire to measure some variables, including SSB intake, fast-food/takeaway consumption assessment of psychological behavioral problems, and demographic variables. Participants filled out questionnaires in separate classrooms where privacy was guaranteed. During the investigation, two or three investigators in each room provided technical support. The assessment of psychological behavioral problems was perfumed through the Strengths and Difficulties Questionnaire (SDQ) content on the questionnaire. SDQ includes 25 items, including hyperactivity problems, emotional symptoms, conduct problems, peer problems, and prosocial problems (41). The SDQ is a short screening instrument that addresses the positive and negative behavioral attributes of children and adolescents; the SDQ is widely used to evaluate child developmental disabilities, and psychological and psychiatric conditions or disorders (42); and SDQ scales have been used as a tool in various studies for child mental health and validated for internal consistency (43). Children's responses can be categorized as normal, borderline, or abnormal for each of the subscales. Total difficulties of SDQ scores above the 90th percentile were classified as abnormal; the 80th to 90th percentiles were classified as "borderline," and those below the 80th percentile were classified as "normal" (44). The internal consistency of the SDQ total score was good (Cronbach's alpha 0.762) in our manuscript.

The frequency of carbonated, soda, tea and milk beverage, fruit and vegetable juice drinks, coffee drinks and energy drinks, and vegetable protein drink consumption has used in the questionnaire to figure out the total scores (45). Low SSB intake was defined as the lowest quintile (≤20th percentile) of the total score of SSBs serving equivalents per week; medium SSB intake was defined as the second to fourth quintiles (>20th to <80th percentile); and high SSB intake was defined as the highest quintile (≥80th percentile) (46). In our study, takeaway dietary pattern mainly refers to the takeaway behavior. Students were asked by one question: "How many times do you eat takeaways each week? (37)". The frequency answers were never, one to two times, three to four times, and more than five times. The frequency was categorized as never, low frequency, medium frequency, and high frequency.

## Statistical Analysis

The database was created by EpiData 3.0. Statistical analyses were performed with SPSS 23.0 and GraphPad Prism. Descriptive analyses were used to show demographic information of the sample. Pearson's chi-squared tests were performed to test the prevalence of PBPs. Additionally, the dose–response trend test was conducted in the one-way analysis of variance. Multivariable logistic regression was used to explore the independent and interactive associations of takeaways, SSBs, and PBPs. GraphPad Prism was used to draw the correlation graphs. Models controlled for age, gender, grade, residential areas, family economic level, and parents' educational level. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. The significance level was set at $p < 0.05$.

# RESULTS

## Participants

We first arranged staff to input the questionnaires, and then data were imported into SPSS. Questionnaires with missing values >5% were deleted. Then we use multiple imputation to fill in data with missing values <5%. In total, 33,801 students consented to participate and have completed the questionnaire. Excluding participants whose data were incomplete and did not meet the criteria (excluding questionnaires with a missing value of >5%), the final study had 30,188 participants. The sample's mean age

**TABLE 1 |** General characteristics of the samples, *n* (%).

| Variables | Total | Male | Female | $\chi^2$ |
|---|---|---|---|---|
| **Age (years)** | | | | |
| ≤12 | 14,484 (48.0) | 8,127 (48.1) | 6,357 (47.8) | 0.21 |
| >12 | 15,704 (52.0) | 8,770 (51.9) | 6,934 (52.2) | |
| **Grade** | | | | |
| Primary | 13,420 (44.5) | 7,544 (44.6) | 5,876 (44.2) | 0.58 |
| Junior high | 8,232 (27.3) | 4,590 (27.2) | 3,642 (27.4) | |
| Senior high | 8,536 (28.3) | 4,763 (28.2) | 3,773 (28.4) | |
| **Academic record** | | | | |
| Good | 7,580 (25.1) | 4,246 (25.1) | 3,334 (25.1) | 73.65** |
| Medium | 17,573 (58.2) | 9,567 (56.6) | 8,006 (60.2) | |
| Bad | 5,035 (16.7) | 3,084 (18.3) | 1,951 (14.7) | |
| **Residential areas** | | | | |
| Country | 5,585 (18.5) | 3,254 (19.3) | 2,331 (17.6) | 16.88** |
| Town | 2,754 (9.1) | 1,490 (8.8) | 1,264 (9.5) | |
| City | 21,849 (72.4) | 12,153 (71.9) | 9,696 (72.9) | |
| **Father's education** | | | | |
| Junior high or lower | 9,461 (31.9) | 5,574 (33.0) | 4,067 (30.6) | 22.79** |
| Senior high | 11,387 (37.7) | 6,339 (37.5) | 5,048 (38.0) | |
| Junior college or above | 9,160 (30.3) | 4,984 (29.5) | 4,176 (31.4) | |
| **Mother's education** | | | | |
| Junior high or lower | 12,203 (40.5) | 6,992 (41.4) | 5,211 (39.2) | 14.70** |
| Senior high | 11,184 (37.0) | 6,170 (36.5) | 5,014 (37.7) | |
| Junior college or above | 6,801 (22.5) | 3,735 (22.1) | 3,066 (23.1) | |
| **Family economic level** | | | | |
| Under moderate | 4,113 (13.6) | 2,596 (15.4) | 1,517 (11.4) | 100.22** |
| Moderate | 20,395 (67.6) | 11,144 (66.0) | 9,251 (69.6) | |
| Over moderate | 5,680 (18.8) | 3,157 (18.7) | 2,523 (19.0) | |
| **SSB frequency** | | | | |
| High intake | 6,482 (21.5) | 4,290 (25.4) | 2,192 (16.5) | 358.88** |
| Medium intake | 15,623 (51.8) | 8,421 (49.8) | 7,202 (54.2) | |
| Low intake | 8,083 (26.8) | 4,186 (24.8) | 3,897 (29.3) | |
| **Takeaway frequency** | | | | |
| Never | 17,183 (56.9) | 9,788 (57.9) | 7,395 (55.6) | 26.86** |
| Low frequency | 11,426 (37.8) | 6,216 (36.8) | 5,210 (39.2) | |
| Medium frequency | 1,126 (3.7) | 611 (3.6) | 515 (3.9) | |
| High frequency | 453 (1.5) | 282 (1.7) | 171 (1.3) | |

*SSB, sugar-sweetened beverage.*
*$p < 0.05$; **$p < 0.01$.

was 12.44 years (SD = 3.47). There were 13,291 (44.0%) girls and 16,897 (56.0%) boys. The primary participants were 44.5%. There were no association between gender, age, and grade. Females were more likely to have SSBs and takeaway consumption. The characteristics of the participants' demographics are shown in **Table 1**.

## Sugar-Sweetened Beverages, Takeaway, and Psychological and Behavioral Problem Symptoms (Strengths and Difficulties Questionnaire Scores)

The top three SSBs in the intake frequency were milk beverages drinks (not milk), vegetable protein drinks, and fruit and vegetable juice drinks. Intake of milk beverages drinks accounted for the largest proportion, while the intake frequency of vegetable protein drinks was more than twice as much as fruit and vegetable juice drinks across the overall intake frequency groups; soda drinks and energy drinks were the least frequent. In our results, 56.9, 37.8, 3.7, and 1.5% of adolescents' takeaway dietary pattern was never, high frequency, medium frequency, and low frequency. And females were more likely to report emotional symptoms. In addition, high SSBs and takeaway consumption were associated with hyperactivity problems, emotional symptoms, conduct problems, peer problems, prosocial problems, and total difficulties. Other findings are shown in **Tables 2**, **3**.

**TABLE 2 |** The gender difference of SDQ scores among the samples, *n* (%).

| Variables | Total | Male | Female | $\chi^2$ |
|---|---|---|---|---|
| **Hyperactivity problems** | | | | |
| Normal | 23,139 (76.6) | 12,621 (74.7) | 10,518 (79.1) | 89.34** |
| Borderline | 3,109 (10.3) | 1,830 (10.8) | 1,279 (9.6) | |
| Abnormal | 3,940 (13.1) | 2,446 (14.5) | 1,494 (11.2) | |
| **Emotional symptoms** | | | | |
| Normal | 21,499 (71.2) | 12,698 (75.1) | 8,801 (66.2) | 325.21** |
| Borderline | 3,103 (10.3) | 1,632 (9.7) | 1,471 (11.1) | |
| Abnormal | 5,586 (18.5) | 2,567 (15.2) | 3,019 (22.7) | |
| **Conduct problems** | | | | |
| Normal | 25,663 (85.0) | 14,026 (83.0) | 11,637 (87.6) | 130.25** |
| Borderline | 2,439 (8.1) | 1,496 (8.9) | 943 (7.1) | |
| Abnormal | 2,086 (6.9) | 1,375 (8.1) | 711 (5.3) | |
| **Peer problems** | | | | |
| Normal | 25,431 (84.2) | 13,934 (82.5) | 11,497 (86.5) | |
| Borderline | 2,822 (9.3) | 1,754 (10.4) | 1,068 (8.0) | 91.42** |
| Abnormal | 1,935 (6.4) | 1,209 (7.2) | 726 (5.5) | |
| **Prosocial problems** | | | | |
| Normal | 22,030 (73.0) | 11,836 (70.0) | 10,194 (76.7) | |
| Borderline | 4,929 (16.3) | 2,936 (17.4) | 1,993 (15.0) | 197.71** |
| Abnormal | 3,229 (10.7) | 2,125 (12.6) | 1,104 (8.3) | |
| **Total difficulties** | | | | |
| Normal | 24,216 (80.2) | 13,599 (80.5) | 10,617 (79.9) | |
| Borderline | 3,327 (11.0) | 1,869 (11.1) | 1,458 (11.0) | 4.46 |
| Abnormal | 2,645 (8.8) | 1,429 (8.5) | 1,216 (9.1) | |

*SDQ, Strengths and Difficulties Questionnaire.*
*$p < 0.05$; **$p < 0.01$.

## The Relationship Between Sugar-Sweetened Beverages, Takeaway, and Psychological and Behavioral Problems

In **Table 4**, after gender, grade, residential area, academic record, parents' educational level, and self-reported family economic level were adjusted for, more frequent intake of SSBs (OR = 2.23, 95%CI = 2.0–2.47, $p < 0.01$) and higher takeaway consumption (OR = 1.81, 95%CI = 1.66–1.97, $p < 0.01$) were associated with higher SDQ total difficulties scales. The same results about SSB consumption were also found in emotional symptoms (OR

**TABLE 3 |** Scores on SDQ total difficulties and subscales, among sugar-sweetened beverages and takeaway.

| | Total difficulties | Emotional symptoms | Conduct problems | Hyperactivity problems | Peer problems | Prosocial problems |
|---|---|---|---|---|---|---|
| **SSBs** | | | | | | |
| High intake | 19.40 ± 5.29 | 2.91 ± 2.33 | 2.38 ± 1.63 | 4.02 ± 2.11 | 3.15 ± 1.60 | 6.94 ± 2.11 |
| Medium intake | 18.30 ± 4.86 | 2.52 ± 2.18 | 1.99 ± 1.44 | 3.97 ± 2.19 | 2.88 ± 1.59 | 6.94 ± 2.06 |
| Low intake | 17.63 ± 4.89 | 2.16 ± 2.09 | 1.81 ± 1.42 | 3.98 ± 2.28 | 2.75 ± 1.64 | 6.93 ± 2.09 |
| *p*-value | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | 0.038 |
| **Takeaway** | | | | | | |
| Never | 18.06 ± 4.94 | 2.34 ± 2.14 | 1.94 ± 1.47 | 3.91 ± 2.23 | 2.89 ± 1.63 | 6.98 ± 2.08 |
| Low frequency | 18.57 ± 4.97 | 2.64 ± 2.23 | 2.07 ± 1.46 | 4.05 ± 2.14 | 2.90 ± 1.56 | 6.91 ± 2.04 |
| Medium frequency | 19.93 ± 5.34 | 3.24 ± 2.43 | 2.50 ± 1.65 | 4.33 ± 2.14 | 3.09 ± 1.65 | 6.76 ± 2.11 |
| High frequency | 20.48 ± 5.78 | 3.40 ± 2.59 | 2.80 ± 1.88 | 4.44 ± 2.18 | 3.36 ± 1.86 | 6.49 ± 2.49 |
| *p*-value | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |

*SDQ, Strengths and Difficulties Questionnaire; SSB, sugar-sweetened beverage.*
*$^{*}p < 0.05$; $^{**}p < 0.01$.*

**TABLE 4 |** Individual effects of sugar-sweetened beverages (SSBs) and takeaway patterns on psychological and behavioral problems.

| | SSBs (reference group: low SSB intake) | | Takeaway pattern (reference group: never) | | |
|---|---|---|---|---|---|
| | Medium | High | High | Medium | Low |
| **Hyperactivity problems (reference group: normal)** | | | | | |
| Borderline | 1.03 (0.94–1.12) | 1.02 (0.94–1.10) | 1.70 (1.30–2.23)** | 1.35 (1.11–1.64)* | 1.16 (1.07–1.25)* |
| Abnormal | 1.27 (1.14–1.41)** | 1.03 (0.93–1.14) | 1.40 (1.07–1.83)* | 1.51 (1.27–1.79)** | 1.07 (0.99–1.15) |
| **Emotional symptoms (reference group: normal)** | | | | | |
| Borderline | 1.20 (1.10–1.31)** | 1.30 (1.21–1.42)** | 1.69 (1.26–2.27)** | 1.61 (1.33–1.95)** | 1.23 (1.14–1.33)** |
| Abnormal | 1.39 (1.25–1.54)** | 1.73 (1.60–1.87)** | 2.51 (2.03–3.10)** | 2.26 (1.96–2.60)** | 1.27 (1.19–1.35)** |
| **Conduct problems (reference group: normal)** | | | | | |
| Borderline | 1.28 (1.15–1.42)** | 1.73 (1.53–1.96)** | 2.17 (1.64–2.86)** | 1.86 (1.54–2.25)** | 1.14 (1.04–1.24)** |
| Abnormal | 1.25 (1.10–1.41)** | 2.31 (2.02–2.64)** | 2.82 (2.17–3.66)** | 2.14 (1.77–2.58) | 1.04 (0.94–1.14) |
| **Peer problems (reference group: normal)** | | | | | |
| Borderline | 1.02 (0.92–1.12)** | 1.15 (1.09–1.22)** | 1.65 (1.25–2.17)** | 1.34 (1.11–1.62)** | 1.01 (0.93–1.09) |
| Abnormal | 0.98 (0.87–1.09) | 1.27 (1.14–1.43)** | 1.84 (1.37–2.47)** | 1.04 (0.83–1.32) | 0.80 (0.72–0.88)** |
| **Prosocial problems (reference group: normal)** | | | | | |
| Borderline | 0.92 (0.84–1.0) | 1.12 (1.04–1.20)** | 1.31 (1.02–1.68)* | 1.31 (1.53–2.14)** | 1.05 (0.97–1.13) |
| Abnormal | 1.02 (0.92–1.14) | 1.11 (1.01–1.21)* | 2.34 (1.81–3.03)** | 1.88 (1.56–2.26)** | 1.16 (1.06–1.26)** |
| **Total difficulties (reference group: normal)** | | | | | |
| Borderline | 1.15 (1.06–1.26)** | 1.59 (1.44–1.75)** | 1.53 (1.17–2.01)** | 1.80 (1.53–2.14)** | 1.05 (0.97–1.13) |
| Abnormal | 1.38 (1.26–1.52)** | 2.23 (2.00–2.47)** | 2.34 (1.81–3.03)** | 1.88 (1.56–2.26)** | 1.16 (1.06–1.26)** |

*The model was controlled for age, gender, grade, residential areas, academic record, family economic level, and parents' education level.*
*$^{*}p < 0.05$; $^{**}p < 0.01$.*

= 1.73, 95%CI = 1.60–1.87, $p < 0.01$), conduct problems (OR = 2.24, 95%CI = 2.05–2.44, $p < 0.01$), peer problems (OR = 1.67, 95%CI = 1.55–1.80, $p < 0.01$), and prosocial problems (OR = 1.11, 95%CI = 1.01–1.21, $p < 0.01$), except for hyperactivity problems (OR = 1.03, 95%CI = 0.93–1.14). In addition, higher takeaway consumption was also associated with higher SDQ scales. These results are shown in **Table 4**. Results from multivariate logistic regression analysis indicated that both takeaway dietary pattern and SSBs are independently associated with SDQ scores. Besides, they had a multiplied interaction impact between SSBs and takeaway dietary pattern on SDQ scores. Higher SSBs were more associated with total difficulties (OR = 3.10, 95%CI = 2.67–3.59, $p < 0.01$), emotional symptoms (OR = 2.10, 95%CI = 1.86–2.36, $p < 0.01$), conduct problems (OR = 3.24, 95%CI = 2.86–3.65, $p < 0.01$), peer problems (OR = 1.89, 95%CI = 1.69–2.12, $p < 0.01$), prosocial problems (OR = 1.26, 95%CI = 1.07–1.47, $p < 0.01$), hyperactivity problems (OR = 1.33, 95%CI = 1.15–1.55, $p < 0.01$), and higher takeaway

dietary pattern than low and medium SSB consumption. These results are shown in **Figure 1**.

## DISCUSSION

Our study demonstrated the correlations between SSBs, takeaway dietary pattern, and PBPs in Chinese children and adolescents. After gender, age, family economic level, parents' education level and academic record, and residential area were adjusted for, SSBs and takeaway eating patterns were found to have individual and interactive effects on PBPs. In consideration of the discrepancies in unhealthy eating patterns for emotional and behavioral problems between Asians and other ethnicities, the results of this study may help us explore the influence of SSBs and takeaways on psychological behavioral problems in eastern dietary patterns.

Demographic characteristics and conditions known or considered to be correlates of psychological behavioral problems were measured; the consumption of SSBs, takeaways consumption, and psychological behavioral problems both associated with a variety of sociodemographic characteristics, which may confound the essential association between SSBs, takeaway consumption, and psychological behavioral problems (45). Children and adolescents with lower economic levels were at risk for poor diet status, for example, lower intake of fruits and vegetables, and higher intake of unhealthy snacks, fast food, and SSBs. A possible explanation was that the relative low prices on SSBs could explain why lower economic levels were associated with higher SSB intake, and lower economic levels were not enough for healthy dietary. Others include gender, parents' educational levels, age, and grade. This might imply that adolescents' personal economic levels should be included in the studies of health-related behaviors. So we determined the selection of covariates by referring to previous studies and literatures, as well as the preliminary experimental results of the research group (37). In addition, gender and age effects differ in behavioral and emotional problems. Gender differences were found in the distribution of PBPs. Compared with girls, boys were more likely to score higher conduct problems, peer problems, hyperactivity problems, prosocial problems, and total difficulties. These results were similar to previous studies (47–49). In terms of emotional problems, girls are more likely to have higher score than boys (47, 48). Similarly, children and adolescents with low family income, compared with high family income, were more likely to report PBPs; and those with low parental education were also more likely to have PBPs than those with high parental education. Our study revealed that SSB consumption and takeaway dietary pattern brought an individual and interactive relationship risk of PBPs after adjustments for confounders.

SSBs have been found to be associated with a higher prevalence of mental health problems (15, 19, 32). The most consumed non-alcoholic beverages were SSBs, coffee, and tea and may have important health consequences; others such as energy drinks also have same results (50). Schwartz et al. conducted a survey of 1,649 U.S. children about the Health Behavior Survey and Hyperactivity Disorder questionnaire and found that higher SSB intake was associated with an increased risk of ADHD (22). This is similar to Alsamghan's result: a significance association was found with risk of hyperactivity/inattention who consumed energy drinks (51). More important, some of the bad behaviors established in childhood, such as the SSB eating pattern, may persist into adulthood (52, 53). Considering that students spend most of their time in school, the type of food sold or served in schools is an important environmental factor affecting children's eating patterns, and governments should restrict SSB provision in schools to promote healthy eating behavior among young people (54), so it is important for school leaders to take action to prevent adolescents' SSBs and takeaway dietary consumption. The results should catch the attention from not only parents and policymakers but also the producers and sellers of SSBs. In our study, we have not found a relationship between SSB consumption and hyperactivity problems. One possible reason was that our SSB scores included numerous varieties; some of these beverages were positively correlated with hyperactivity and prosocial problems, while others were negatively correlated, so there might be an offsetting effect.

The PBP consequences of SSBs can be summarized as follows: a) sugar intolerance (physical discomfort after eating or drinking sugary foods); b) body's reactive hypoglycemia after ingestion; and c) decrease in intake of essential micronutrients. We extracted some of the more important results: if psychological problems are not paid attention to, these can easily lead to depression and mental disorders. So how are sugary drinks related to depression and mental disorders? Some researches have verified their correlated mechanisms. Continual consumption of SSBs, especially diet SSBs, may increase the risk of depression, while coffee consumption may reduce the risk. We hypothesized that there are several possible mechanisms linking sugar intake and anxiety/depression, including oxidative stress response (55) and serotonin (5-HT) mechanisms (56). Other researches have discussed the connection between high sugary behavior and mental health, including high-sensitivity C-reactive protein (hsCRP) (57, 58). Other studies demonstrated that the consumption of sodium benzoate (found in beverages) impairing memory and motor coordination, reducing glutathione, increasing the malondialdehyde level in the brain, and inducing ADHD in children is emphasized (59). In Yu's study, compared with those who did not consume SSBs, children who consumed SSBs at moderate levels and high levels were associated with having ADHD (60); and another study conducted by Howard revealed that an "unhealthy," western-style preference diet (i.e., more meat and sweets and fewer vegetables and fruits) was associated with ADHD (61).

The theory of planned behavior (TPB) states that SSB intake causes not only PBPs but also a range of behaviors (62) and that they influence one other (31, 63). Experimental results showed that more frequent intake of SSBs was associated with higher prevalence of middle and lower annual household income, lower frequency of physical activity, more takeaway dietary behavior, more fast-food behavior, and more frequency of screen time. And the results from the human sample show the same result of sensitivity to reward and adolescents' unhealthy

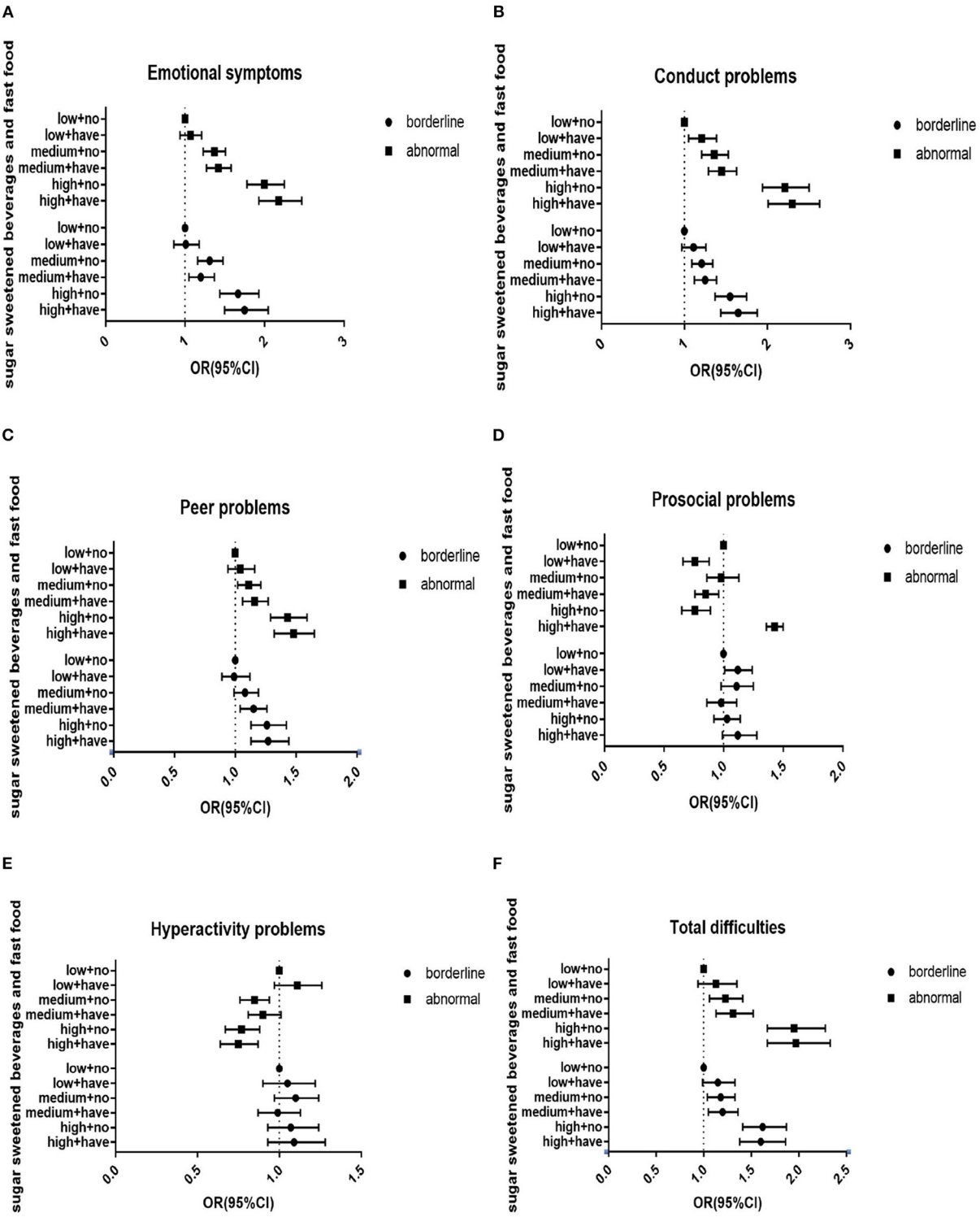


**FIGURE 1 |** Interactive effects of sugar-sweetened beverages and takeaway pattern on psychological and behavioral problems among Chinese children and adolescents. **(A)** Interactive effects of sugar-sweetened beverages and takeaway pattern on emotional symptoms. **(B)** Interactive effects of sugar-sweetened beverages and takeaway pattern on conduct problems. **(C)** Interactive effects of sugar-sweetened beverages and takeaway pattern on peer problems. **(D)** Interactive effects of sugar-sweetened beverages and takeaway pattern on prosocial problems. **(E)** Interactive effects of sugar-sweetened beverages and takeaway pattern on hyperactivity problems. **(F)** Interactive effects of sugar-sweetened beverages and takeaway pattern on total difficulties. Low, low SSB intake; Medium, medium SSB intake; High, high SSB intake; Have, have takeaway consumption; No, no takeaway consumption. The model was controlled for age, gender, grade, residential areas, academic record, family economic level, and parents' education level. *$p < 0.05$; **$p < 0.01$.

snacking and drinking behaviors (64). So we also proposed the takeaway dietary pattern and found that takeaway dietary pattern was correlated with PBPs. Our results further suggest that psycho-pathological symptoms, including emotional, conduct and prosocial problems, were significantly associated with SSB consumption and takeaway dietary pattern in a dose-dependent manner. Specifically, after variables were controlled for, takeaway and SSB eating patterns are associated with increased risk of psycho-pathological symptoms; these results were consistent with previous cross-sectional studies (29, 65). One possible reason is that people find healthier foods to be tastier and more popular than unhealthy foods (66).

We found an obvious interaction between high SSBs and takeaway dietary pattern on PBPs. High SSB intake causes an increase in the risk of PBPs in students with high takeaway dietary pattern compared with students with low takeaway dietary pattern. The possible underlying mechanisms for this interaction are complex. One possible reason was de Bruijn's research: TPB also means that health behaviors in youth tend to cluster and that interventions that succeed in inducing positive changes in cognition and intention in a behavior may lead to positive changes in an aggregation behavior (62). Another possible reason was a positive correlation between SSBs and takeaway diet pattern (67). Higher takeaway dietary pattern was associated with higher SSB consumption (63). The unhealthy association is thought to be caused by high exposure to food and drink advertisements during screen time. Unhealthy home food availability increased takeaway diet pattern, further influencing the consumption of SSBs (68). Because when some take the takeaway diet pattern, they do not notice what they were eating, which could eventually lead to overconsumption (69). So we could think of the interactive correlation between SSBs and UDP on PBPs (37).

Our study has several limitations. First, this study is cross-sectional research; it cannot detect a causal relationship and could not judge causality or direction, and a future longitudinal study is suggested. Second, SSBs and takeaway consumption were acquired through self-reporting, which may have caused recall bias. Third, there were many factors influencing PBPs, and we only have explored two of them, so further researches will pay attention to other factors. Despite these limitations, our research has some strengths. First, most importantly, this is a survey of Chinese children and adolescents, and the results of our study can be applied to public health and clinical practice in other populations. The limitations of other reports were the small sample sizes. Our research aims to explore the mental health behavioral problems of children and adolescents through a large sample and multi-age perspectives. In addition, 30,188 adolescents were sampled from 14 schools in Shenzhen, China, with a wide sampling range and a large sample size. The cluster stratified random sampling method was used to identify the sample, and primary schools, as well as middle schools, were included in this multilevel survey. These data were somewhat representative. We also analyzed several potential confounders. In this study, we analyzed the interactive effect to explore the correlation between SSBs, takeaway consumption, and PBPs, further demonstrating that we should pay close attention to the factors influencing children's and adolescents' mental health. Our study can also provide a good theoretical basis for the follow-up large sample of children and adolescents regarding SSBs, takeaway food, and mental health issues.

In summary, this study offers discernment into the association between SSB consumption, takeaway consumption, and PBPs among Chinese children and adolescents. Our results suggested that higher SSB consumption and higher takeaway consumption were all positively associated with PBPs. Also, the interactive relationship between SSBs and takeaway consumption was stronger than SSB consumption and takeaway consumption individually. This is a public health issue that cannot be ignored, given China's large population base and the growing trend of SSB consumption and takeaway consumption.

## DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Anhui Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

FT designed the study. YZ, XW, ST, QW, RW, TL, and QZ performed the survey research. YZ, XW, ST, and QW analyzed the data. YZ drafted the manuscript. All authors read and approval the final manuscript.

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# A "Proof of Concept" Randomized Controlled Trial of a Video Game Requiring Emotional Regulation to Augment Anger Control Training

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Emotional dysregulation leading to clinically significant anger and aggression is a common and substantial concern for youth and their families. While psychotropic medications and cognitive behavioral therapies can be effective, these modalities suffer from drawbacks such as significant side effects, high rates of attrition, and lack of real-world skill translation. **R**egulate **a**nd **G**ain **E**motional Control (RAGE-Control) is a video game designed as an engaging augment to existing treatments. The game facilitates emotional regulation skill building through practice modulating physiological arousal while completing a challenging inhibitory task. We compared reduction in anger, aggression, oppositionality, and global severity between two treatment conditions: Anger Control Training (ACT) augmented with RAGE-Control and ACT with a sham version of the game, in a pilot double-blind randomized controlled trial. To begin to understand mechanisms of change, we examined heart rate during game play over the course of the study and explored associations between symptom changes and heart rate changes.

**Materials and Methods:** Forty youth with clinically significant anger dyscontrol (age 10–17) were randomly assigned to 10 sessions of ACT with RAGE-Control or ACT with sham video game.

**Results:** Both treatments similarly reduced self-reported anger. However, ACT with RAGE-Control led to larger improvements in aggression (CI: −17 to −1.0, ES: 0.55, $p = 0.015$); oppositionality (CI: −9.0 to −7e-6, ES: 0.48, $p = 0.032$); and global severity (CI: −1.0 to −5e-6, ES: 0.51, $p = 0.023$) relative to sham. Participants in the RAGE-Control group saw a decrease in median heart rate during game play ($\beta = 1.2$, $p < 0.001$). Larger pre to post decreases in heart rate were significantly associated with larger pre to post decreases in aggression and oppositional behaviors.

**Discussion:** Augmenting ACT with RAGE-Control reduced behavioral expression of anger, but not the experience of angry feelings, as compared to ACT with a sham

version of the game. Increased heart rate control, demonstrated by reduction in median heart rate during gameplay, was associated with decreased aggression and oppositional behavior. Together these findings support that augmenting traditional treatment with technology facilitating heart rate control through skill practice translates to enhancements in real-life behavioral change. Therefore, further exploration into engaging skill-focused games such as RAGE-Control is warranted.

**Clinical Trial Registration:** ClinicalTrials.gov, identifier: NCT01551732.

**Keywords: anger control, biofeedback, video game, cognitive behavior therapy, emotional control, self-regulation**

# INTRODUCTION

## Why Build a Video Game Targeting Emotional Dysregulation?

Emotional dysregulation, defined as a limited ability to initiate and regulate one's emotional reaction and response in a manner consistent with the situation (1), is a major challenge for children and adolescents who struggle with anger and aggression (2–4). Emotional dysregulation is also a common feature of behavioral health and neurodevelopmental disorders including ADHD, Autism Spectrum Disorders, oppositional defiant disorder, and others (5–7). Irritability, an increase studied facet of emotional dysregulation, is becoming transdiagnostic hallmark of child and adolescent psychopathology (8). Several evidence-based treatments including medication, cognitive behavioral therapies (CBT), and parent management training have been developed to address emotional dysregulation, anger, and aggression in youth (2, 9, 10). However, each modality suffers from downsides. Medication, despite moderate to large effect sizes in second-generation antipsychotics, is often considered a last resort due to significant side effects (11, 12). CBT and family/parent-based interventions have relatively moderate effect and suffer from high rates of attrition (2, 9, 10). Some potential pitfalls of psychotherapy for youth with emotional dysregulation include the lack of focus on problem-solving skills or experiential practice *outside* of therapy (13, 14), and the heavy focus on parental monitoring, which might elicit negative side-effects among adolescents in particular (15, 16). These challenges are particularly relevant to emotional regulation, as autonomy in practicing problem solving and reducing physiological arousal may promote youth's emotional development (17). The aim of building a video game for developing emotional regulation was to create an engaging, challenging augment to CBT to address the lack of outside practice and translatable application of emotional regulation skills.

Interest and development of video games, mobile applications, and other technology-based interventions, often called serious games, has grown over the past decade. In part, these interventions are attractive because they are easily accessible and provide an extension of clinical settings (18). Serious games also benefit from having high intensity, immediate reinforcement of learning objectives (19). Serious games have diverse applications, ranging from physical (20) to cognitive and social emotional domains (21–33) with both educational (34) and remedial (35) purpose. Games targeting regulation are examples of remedial social emotional interventions.

Studies on many emotional regulation-focused games have shown promising results, including games dedicated to development of emotion regulation skills (e.g., GameTeen) (23, 24), practicing intrapersonal or interpersonal responses to facilitate emotional intelligence (e.g., Spock) (25), enhancing rational thinking (e.g., REThink) (26), and reducing stress/anxiety [e.g., Dojo; (27) Mindlight; (28) Breathify (29)]. While much of this work has targeted adult populations (30–33), the positive impact of serious games for emotional regulation extends to adolescent populations as well (23–28). Perhaps one of the most well-studied serious games is PlayMancer, a bioresponsive game where a player's emotional state is measured using galvanic skin response, oxygen saturation, heart rate, and heart rate variability (30). Using PlayMancer has been associated with increases in self-report and physiological indicators of emotional regulation in individuals with eating disorders (31, 32) and severe gambling disorder (33).

## Why Focus on Heart Rate?

RAGE-Control (**R**egulate **a**nd **G**ain **E**motional Control) is a space-themed, non-violent video game that uses a player's heart rate to help them practice modulating physiological arousal while completing a challenging inhibitory task. In the game, the player is asked to "shoot" asteroids while allowing friendly craft to pass. Should the player's heart rate increase, they become unable to "shoot" the asteroids. Thus, players are rewarded for down-regulating physiological arousal (36, 37). As mentioned above, RAGE-Control was created to facilitate experiential learning and practice of emotional regulation. In order to successfully translate to emotional regulation, RAGE-Control operates under two overarching hypotheses. First, that children and adolescents are motivated and challenged enough by gameplay to practice skills learned in therapy to regulate their heat rate. Second, that greater control over one's physiological arousal, measured here by heart rate, can lead to greater emotional regulation.

While heart rate is a crude signal of regulation, a robust set of existing literature demonstrates a link between parasympathetic control over heart rate and self-regulatory capacity; (38–40) and parasympathetic control over heart rate and emotional regulation

(41, 42). This work extends to behaviors and diagnostic categories associated with poor emotional regulation in children and adolescents, as high heart rate reactivity in response to stressors is associated with externalizing behaviors (43–45) and aggression (46). Furthermore, children with conduct disorder have greater heart rate reactivity to frustration as compared to those without (47). This study, and the creation of RAGE-Control, proposes that heart rate regulation in the moment of difficult or demanding situations is a clinically useful translation of existing theory.

## "Proof of Concept" Randomized Controlled Trial

The objective of this double-blind randomized controlled trial (RCT) is to provide an initial assessment of clinical benefits from incorporating RAGE-Control into Anger Control Therapy (ACT), an empirically supported, manualized CBT for anger control (48, 49). A large body of evidence suggests that interventions in the form of video games are a well-accepted and clinically impactful area of study (21–33), however, most widely available digital interventions do not have evidence from rigorous participant and clinician blinded RCTs (50, 51). In this study, children and adolescents with clinically significant anger problems were randomized to either ACT augmented with RAGE-Control at the end of each session, or ACT with a sham version of RAGE-Control. We hypothesized that participants assigned to the ACT with active RAGE-Control group would have greater decreases in anger, oppositionality, overt aggression, and clinician rated global severity as compared to those assigned to the ACT with sham group.

# MATERIALS AND METHODS

## Patients

Patients between 10 and 17 years of age were recruited from the outpatient psychiatry clinic at Boston Children's Hospital (BCH) between July 2011 and February 2013. Patients were referred to the study if they experienced symptoms consistent with clinically impairing anger or aggression.

Inclusion criteria were age, clinician referral, and elevated self-reported anger confirmed by a score of $\geq$15 on the Trait Anger subscale of the State Trait Anger Expression Inventory-Child and Adolescent version (STAXI-CA) (52). Exclusion criteria were change in psychotropic medication dose within the 4 weeks prior to enrollment, anticipated change in psychotropic medication dose throughout the study period, or DSM-IV-TR diagnosis of intellectual disability.

Prior to enrollment, patients attended a screening visit where a licensed clinical social worker performed a mental health evaluation, reviewed available past records, and assigned a best estimate primary DSM-IV-TR diagnosis using a DSM-IV-TR symptom checklist (53). Parents provided information necessary to complete the Modified Overt Aggression Scale (MOAS) and Disruptive Behavior Rating Scale (DBDRS) for the patient based on the month before entering the study (54–56).

Fifty-four children and adolescents were screened and 40 were enrolled/randomized ($n$ = 20 in each group; **Figure 1**). Sample size was determined by power analysis, targeting 80% power to detect effect sizes (ES = 0.63–1.68) from a prior, preliminary, open-label study (57). All procedures contributing to this work comply with international ethical standards on human experimentation including the Helsinki Declaration of 1975, as revised in 2008 and were approved by the BCH institutional review board (IRB-P00000440). Written informed consent was obtained from a parent or legal guardian of all participating patients. Verbal assent was also obtained from patients and formally recorded. Families received $125 and complimentary parking for participation.

## Study Design

Immediately following screening and enrollment, patients were randomized into two groups: ACT augmented with RAGE-Control (ACT-R) or ACT augmented with a sham version of RAGE-Control (ACT-S; see below for details). Research staff generated the randomization sequence, enrolled patients, and assigned patients to treatment groups. Clinicians, families, and patients were blinded to group assignments throughout the study. Patients completed 10 weeks of ACT-R or ACT-S followed by a final study visit occurring 2 weeks post-treatment. To minimize data loss and bias associated with early termination, parents or guardians agreed to return for the post-treatment visit even if the intervention was terminated early.

The primary outcome measure for this study was the STAXI-CA. Patients completed this self-report measure at the screening visit, every other week at ACT sessions, and at the post-treatment visit. Secondary measures included standard assessments of aggression (Modified Overt Aggression Scale; MOAS), oppositionality (Disruptive Behavior Rating Disorder Scale; DBDRS), and global severity/improvement (Clinical Global Impressions Severity/Improvement; CGI-S and CGI-I, respectively). These measures were completed by parents (MOAS and DBDRS) or blinded clinicians (CGI) at screening and post-treatment visits only. Each time the patient played their assigned version of RAGE-Control, the device recorded their heart rate, allowing us to calculate median heart rate during gameplay.

## Interventions

### RAGE-Control Video game

RAGE-Control is loosely based on the arcade game *Space Invaders*, requiring players to maneuver a spaceship at the bottom of the screen to fire at enemy spaceships while inhibiting fire as friendly spaceships fly past. During gameplay, players must control their heart rate, measured by pulse oximeter, to allow their spaceship to fire. That is, if a player's heart rate exceeds baseline by 7 bpm, their spaceship will fire blanks. These blanks do not destroy the asteroids and are accompanied by a different sound, indicating that the player needs to regulate their heart rate. Baseline heart rate was measured at the beginning of each play session while players sat quietly for 30 s.

Each round of RAGE-Control is 3 min long and patients played several rounds at the end of each session, followed by discussion about what worked well to lower their heart rate.

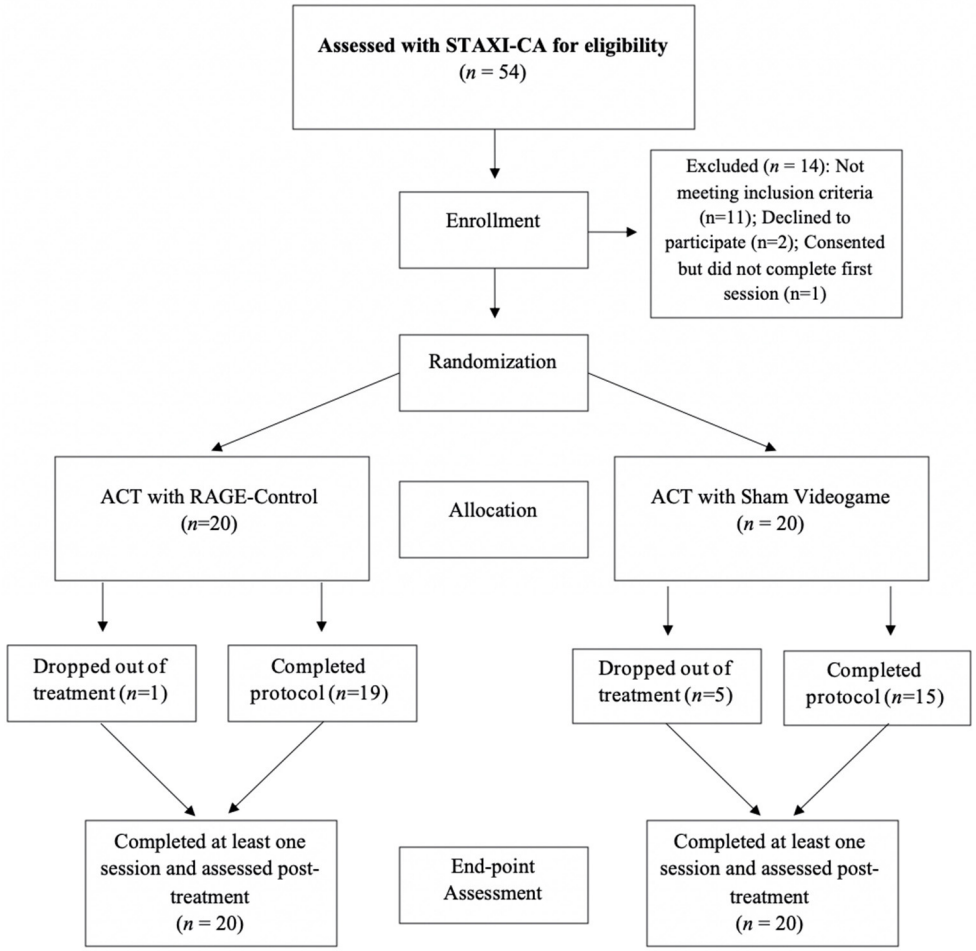


**FIGURE 1 |** Participant recruitment and study flow.

### *Active vs. Sham Game Condition*

The active (ACT-R) and sham (ACT-S) versions of the RAGE-Control game were identical, including wearing a heart rate monitor collecting heart rate data, except in the sham condition the player's heart rate was not an input into the game. As a result, patients in the ACT-S condition did not need to control their heart rate for their spaceship to function.

## Anger Control Therapy

Each patient was assigned to one of two research therapists (licensed clinical social workers) based on scheduling convenience. The lead therapist (first author) trained the second study therapist in a 2-h initial training and then met for weekly supervision during the study. Both the ACT-R and the ACT-S groups engaged in 10 h-long ACT sessions once a week.

During the first five sessions of ACT, patients learned a specified coping skill to regulate their mood and behavior; they subsequently spent 15 min playing either the real or sham version of RAGE-Control, during which they were instructed to use the coping skills learned. A parent check-in took place at the end of each session that ranged from 5 to 15 min to discuss how the child was doing from the parent's perspective.

Sessions 6–10 involved structured problem solving on applying coping skills to real-life current problems and continued practice with the assigned version of RAGE-Control. A parent check-in also took place at the end of the sessions 6–10 that ranged from 5 to 15 min to review problems and have patients teach their parents the coping/relaxation skills they have learned by showing them how to play RAGE-Control and playing together as a team.

### *Treatment Fidelity*

Sessions were delivered using a detailed manual written by the first author, P.D., as an adaptation of Anger Control Training by Sukhodolsky et al. (49) This is the first study using this manual. We have made the manual available at the following web address: https://drive.google.com/open?id=0BwtznSVw1ibUSndUMV9YdnROZGc. Sessions were audio recorded and fidelity checklists were used to document implementation of the specific ACT goals for each session (58). Twenty percent of the recorded sessions were selected at random

and rated by an independent social work intern using the fidelity checklist. A high level of treatment fidelity was demonstrated (93% mean; range 81–100%).

## Outcome Measures

### State Trait Anger Expression Inventory—Children and Adolescents Trait Anger Subscale

This 35-item scale measures self-reported feelings of anger. The STAXI-CA has good construct validity and internal consistency with Cronbach's alpha coefficients range from 0.86 to 0.93 (52). It was administered at baseline and at the end of every other treatment session. Because it measures how often and intensely angry feelings are experienced over time, the STAXI-CA-Trait Anger (TA) subscale was chosen to measure levels of self-reported anger symptoms.

### Modified Overt Aggression Scale

This 5-point scale rates the severity of four types of aggression: verbal, against property, against self (auto-aggression), and physical toward others (54). Each of these four subscores contains five different levels that contribute to the score. These individual levels are differentially weighted to discriminate behavior in increasing severity (e.g., for verbal aggression, "Shouts angrily" is weighted as 1 and "Threatens violence toward others" is weighted as 4). Each subscore is calculated by adding up the weights for each level present. In total, each of these subscores has a range of 0–10. The subscores are further weighted in the calculation of total score by multiplying each by a number representing its relative severity (e.g., one for verbal aggression and increasing to a multiplier of 4 for aggression against others). The weighted subscores are then added to get the total score. A copy of the scale can be found at https://depts.washington.edu/dbpeds/Screening%20Tools/Modified-Overt-Aggression-Scale-MOAS.pdf.

The assessor read each item of the MOAS to the parent, including the examples of behaviors anchoring each potential scoring statement, asked whether each statement describes the child's behavior over the previous week, and noted the parent's response.

### Disruptive Behavior Disorders Rating Scale

This 8-item scale evaluates symptoms of Oppositional Defiant Disorder (ODD). It rates the parent's perspective of their child's oppositional behavior in four domains (1) degree of symptom presence, (2) level of concern/interference with daily activities, (3) level of monitoring required, and (4) level of attention required. Each item is rated on a 4-point Likert scale ranging from 0 = never or rarely to 3 = very often and derives a total score by summing all items together. Internal consistency ranges from 0.86 to 0.93 (55, 56).

The assessor read the parent each question of the DBDRS and asked the parent to indicate the degree to which each statement describes the child's behavior in the past week ("not at all," "just a little," "pretty much," and "very much"). The MOAS and DBDRS thus assessed the parent's perspective of their child's level of aggression and oppositionality in the previous week.

### Clinical Global Impression-Severity and Improvement Scale

The CGI-S scale requires a clinician to rate the overall severity of psychopathology on a 7-point Likert scale, ranging from 1 (normal, not ill) to 7 (extremely ill). The CGI-I requires the clinician to rate total improvement whether or not, in the raters judgment, it is due to treatment. The clinician compared the patient's condition at baseline to 2 weeks after the study treatment ended on a scale ranging from 1 (very much improved) to 7 (very much worse) (59).

Clinician-parent interviews were audiotaped and an independent assessor re-rated a randomly selected 20% of parent interviews to establish inter-rater reliability for the MOAS, DBDRS, CGI-S, and CGI-I measures. A weighted Cohen's *K* documented acceptable inter-rater reliability in the study for the MOAS (0.92 at baseline; 0.88 at post treatment), DBDRS (0.91 at baseline; 0.83 at post treatment), CGI-S (0.77 at baseline, 0.82 post treatment) and CGI-I (0.83 at post treatment).

### Median Heart Rate

Heart rate was captured at 1 Hz intervals using a pulse oximeter during gameplay in both ACT-S and ACT-R conditions. The median heart rate during gameplay for each patient at each session was calculated.

## Statistical Methods

To reduce bias resulting from drop-out, statistical analyses were conducted using an intent to treat methodology. Therefore, data from patients who completed at least one treatment session were included in the analysis. Per protocol, all parents of participants who entered the study provided data at the post-intervention timepoint. *T*-tests and Fisher's exact tests were used to compare demographic characteristics and retention/early dropout rates. Pre-post treatment changes in outcome measures were compared between the groups using Wilcoxon rank-sum tests.

For the STAXI-CA-TA subscale, a mixed linear regression model with fixed effects of session, group, and their interaction, and random effects for participants was used to estimate change over time. The treatment group by time interaction term in this model was examined as an indicator of whether one treatment was more efficacious in decreasing frequency of angry feelings than the other. To account for multiple comparisons, we used a false discovery rate method (FDR) (60) as recommended for health studies when the study endpoints are interdependent with each other and not independent as assumed in a Bonferonni correction (61). The procedure employed a tail-based false discovery rate that takes as its input the two-tailed *p*-values obtained from the multiple hypotheses tests (62, 63). We report an adjusted *p*-value for each comparison.

Changes in median heart rate during game play were explored with a linear mixed effects model with fixed effects of session, group, and their interaction, and random effects for participants. Exploratory relationships between change in symptoms and change in median heart rate were examined by calculating post-pre change scores for all variables and employing bivariate Spearman's correlations.

**TABLE 1 |** Demographic and clinical characteristics of treatment groups.

| | ACT-R ($n = 20$) | ACT-S ($n = 20$) | $t$ | $p$ $t$-test |
|---|---|---|---|---|
| Age mean (std) min, max | 13.1 (2.4) 10.0, 17.0 | 12.4 (2.1) 10.0, 17.0 | 0.98 | 0.31 |
| School grade mean (std) min, max | 7.8 (2.6) 4.0, 11.0 | 6.7 (2.3) 4.0,12.0 | 1.42 | 0.16 |
| | | | | **Fisher's exact** |
| Male | 14 (70%) | 15 (75%) | | 1.0 |
| Black | 3 (15%) | 6 (30%) | | 0.45 |
| White Non-Hispanic | 13 (65%) | 8 (40%) | | 0.20 |
| Hispanic | 4 (20%) | 6 (30%) | | 0.72 |
| Father at home | 3 (15%) | 6 (30%) | | 0.45 |
| Medication* | 4(20%) | 5 (25%) | | 1.0 |
| | **Baseline ratings** | | | |
| **Rating scale** | **Median (interquartile range)** | | **W** | **Wilcoxon rank-sum test** |
| MOAS | 18 (18.75) | 5 (19.5) | 173.5 | 0.48 |
| DBDRS | 17 (7.75) | 17 (9.25) | 187.5 | 0.74 |
| CGI-S | 5 (1) | 4 (1) | 165.5 | 0.32 |
| STAXI-CA-TA | 21 (8) | 21 (5) | 198 | 0.97 |
| | **Clinician Assigned Best Estimate Primary DSM-IV TR Diagnoses** | | | |
| **Participant DSM-IV diagnosis** | **ACT-R** | | | **ACT-S** |
| Opposition defiant disorder (ODD) | 13 | | | 10 |
| Attention deficit hyperactivity disorder (ADHD) | 3 | | | 5 |
| Major depressive disorder (MDD) | 2 | | | 2 |
| Generalized anxiety disorder (GAD) | 1 | | | 1 |
| Post traumatic stress disorder (PTSD) | 1 | | | |
| Depressive disorder NOS | | | | 1 |
| Anxiety disorder (NOS) | | | | 1 |

**Five (25%) patients on the ACT-R arm were on medications (n = 2 stimulant, n = 1 SSRI, n = 2 antipsychotic). Four (20%) patients on the ACT-S arm were taking medications (n = 1 stimulant; n = 1 antipsychotic; n = 1 stimulant, mood stabilizer and antipsychotic; n = 1 SSRI and mood stabilizer).*

All hypotheses were accepted at a two tailed significance level of $\alpha = 0.05$.

# RESULTS

## Patient Characteristics

**Table 1** demonstrates that the groups were comparable in baseline demographic and clinical characteristics and describes the diagnoses assigned at the screening visit to each patient.

## Outcomes

**Table 2** shows pre-post changes in outcome measures for the two groups and results of statistical tests.

### Retention/Early Dropout Rate

One patient in the ACT-R group dropped out after the fifth session; five in the ACT-S group dropped out after the third to fifth session. All patients dropped out because they did not want to continue. This difference in dropout between ACT-R and ACT-S groups was not statistically significant ($p = 0.18$).

### Patient Self-Ratings of Anger

The analysis reported in **Table 3** indicates that patients in both groups had decreased feelings of anger on the STAXI-CA over the treatment period with no between-group differences.

### Parent Reported Aggression and Oppositional Behavior

Pre to post changes in parent reported aggression and behavior were significantly greater in the ACT-R group than the ACT-S group (**Table 2**).

### Blinded Clinician Ratings

As shown in **Table 2**, patients in the ACT-R group showed significantly greater decreases in overt aggression (MOAS), disruptive behaviors (DBDRS), and global severity (CGI-S).

### Median Heart Rate

Median heart rate for each group at each session is displayed in **Figure 2**. Because keeping heart rate from becoming elevated during game play was an object of the active RAGE-Control game

**TABLE 2 |** Pre-post treatment changes in outcomes.

| | ACT-R ($n = 20$) Median change pre to post (interquartile range) | ACT-S ($n = 20$) Median change pre to post (interquartile range) | Statistic | 95% CI | ES | *p* |
|---|---|---|---|---|---|---|
| MOAS | −8 (18.25) | 0 (6.5) | W = 110 | −17.0 to −1.0 | 0.55 | **0.015*** |
| DBDRS | −7 (9) | 0 (9.25) | W = 121 | −9.0 to −7e-6 | 0.48 | **0.032*** |
| CGI-severity | −1 (2) | 0 (1) | W = 119 | −1.0 to −5e-6 | 0.51 | **0.023*** |
| | Median (interquartile range) | Median (interquartile range) | | | | |
| CGI-I | 2 (1) | 3 (2) | W = 190 | −3e-5 to 2.0 | 0.37 | 0.10 |
| Early drop out rate | 1/20 | 5/20 | | 0.0–1.7 | 0.07 | 0.18 |

**Statistically significant at $p < 0.05$; Bolded p-values indicates that the comparison remained statistically significant after accounting for multiple comparisons with FDR (62, 63).*

**TABLE 3 |** Change in STAXI-CA-TA.

| **(A) FIXED EFFECTS** | | | | | |
|---|---|---|---|---|---|
| | **Estimate** | **df** | ***t*** | ***p*** | **5–95% CI** |
| Intercept (ACT-R group) | 21.3 (±0.9) | 63.2 | 23.2 | <0.001 | 19.5–23.1 |
| Session number | −0.6 (±0.08) | 153.2 | −7.5 | <0.001 | −0.8 to −0.5 |
| ACT-S group (control) | −0.6 (±1.3) | 63.2 | −0.5 | 0.630 | −3.2 to 1.9 |
| Session number x ACT-S group | 0.11 (±0.12) | 154.7 | 1.0 | 0.340 | −0.1 to 0.4 |
| **(B) RANDOM EFFECTS BY PARTICIPANT** | | | | | |
| | **Parameters** | **AIC** | | **df** | ***p* (>chi square)** |
| No random effect | 5 | 1,109 | | | |
| Random effect by participant | 6 | 1,042 | | 1 | <0.001 |

*A mixed model for change in STAXI-CA-TA ratings with **(A)** fixed effects for group, session, and for the interaction of group and session; and **(B)** random effects for participant. Analysis shows no interaction between group and session number such that group did not have an impact self-reported anger frequency over the course of the study.*

but not of the sham RAGE-Control game, a linear mixed effects model was used to test if there were group differences in the median heart rate during game play as the number of sessions increased. The analysis of the random effect of participant and fixed effects of session, group, and their interaction is displayed in **Table 4**. Median heart rate decreased each session for the ACT-R group, while it remained approximately constant across sessions for the ACT-S group ($\beta = 1.2$, $p < 0.001$).

Consistent with previous analyses, exploratory bivariate Spearman's correlations between STAXI-CA, MOAS, and DBDRS change scores revealed significant relationships between behavior change and heart rate, but not self-reported anger. Specifically, larger pre to post decreases in heart rate were significantly associated with larger pre to post decreases in aggression (MOAS; $r_s = 0.43$, $p = 0.009$) and oppositional behaviors (DBDRS; $r_s = 0.38$, $p = 0.024$), but not pre to post changes in self-reported anger (STAXI-CA; $r_s = -0.28$, $p = 0.1$).

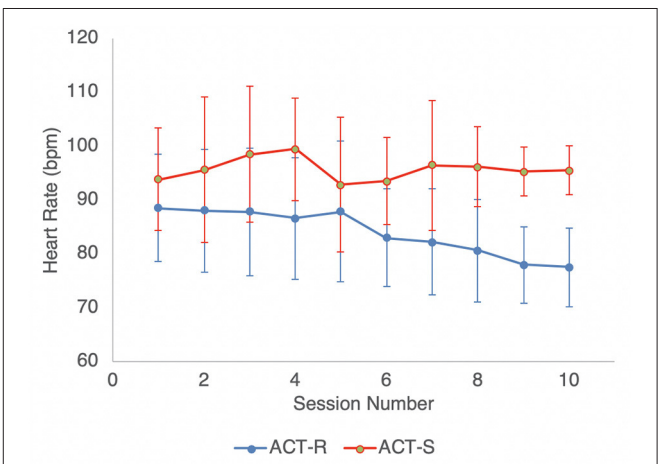


**FIGURE 2 |** Median heart rate during gameplay by Session.

## DISCUSSION

This "proof-of-concept" pilot study demonstrates that ACT augmented with RAGE-Control yielded greater improvements in oppositional behavior, overt aggression, and clinician rated global severity as compared to ACT supplemented with a sham version of the game. However, the group receiving ACT augmented with RAGE-Control did not show greater decreases in self-reported

**TABLE 4 |** Change in heart rate.

| **(A) FIXED EFFECTS** | | | | | |
|---|---|---|---|---|---|
| | **Estimate** | **df** | ***t*** | ***p*** | **5–95% CI** |
| Intercept | 90.9 (±2.2) | 46.1 | 41.6 | <0.001 | 87.3–94.6 |
| Session number | −1.1 (±0.2) | 264.8 | −7.4 | <0.001 | −1.4 to −0.9 |
| ACT-S Group (Control) | 4.9 (±3.3) | 47.8 | 1.5 | 0.143 | −0.6–10.4 |
| Session number x ACT-S Group | 1.2 (±0.3) | 269.4 | 4.3 | <0.001 | 0.7–1.6 |
| **(B) RANDOM EFFECTS BY PARTICIPANT** | | | | | |
| | **Parameters** | **AIC** | | **df** | ***p* (>chi square)** |
| No random effect | 6 | 2,028.2 | | | |
| Random effect by participant | 5 | 2,254.5 | | 1 | <0.001 |

*A mixed model for change in median heart rate during game play with **(A)** fixed effects for group, session, and for the interaction of group and session; and **(B)** random effects for participant. Analysis shows an interaction between group and session number such that the ACT-R but not the ACT-S patients have a decrease in median heart rate during game play as session number increases.*

levels of anger. This argues that augmenting ACT with RAGE-Control enhanced children's control of the expression of their anger rather than decreasing the frequency or intensity of their angry feelings.

## Implications for Treatment of Anger

While strongly related, the experience of anger and expression of anger are conceptualized as distinct (64). Anger is an affective state that includes increased physiological arousal and predisposition toward aggressive behavior whereas anger expression references the tendency to show anger outwardly, suppress it, or actively cope with the emotional experience (65). One explanation for the observed behavioral, rather than emotional, effect might be that skills introduced in ACT and reinforced in discussions about playing RAGE-Control were framed as skills to use when already experiencing strong emotions rather than to prevent experiencing the emotion itself. In fact, the initial studies examining the efficacy of ACT found a similar pattern of reduction in observed and self-reports of anger expression but not intensity of anger experiences (64, 66). In addition, RAGE-Control only indicates that a player's heart rate is high 1–2 s *after* it has happened. Therefore, the ACT-R group engaged in practice down-regulating their heart rate as a behavioral response, rather than preemptively working to maintain lower levels of arousal that might be interpreted as angry feelings.

## Relationship Between Heart Rate and Emotional Regulation

RAGE-Control was built on the premise that playing an engaging video game that rewards maintaining baseline heart rate would lead to increased heart rate control even in the face of in-game challenges. The present study supports that assertion, as the group playing the active version of RAGE-Control showed decreased median heart rate with gameplay, whereas median heart rate in the group who played the sham version remained approximately constant. Moreover, change in median heart rate was associated with change in reports of oppositional and aggressive behaviors, suggesting that ability to modulate heart rate is linked to maladaptive behavioral patterns in this population. While the sample size in this study prevents statistical analyses that would allow for more strong conclusions about causality or mechanisms of change, prior work demonstrating that parasympathetic heart rate control is *predicative* of self-regulatory capacity supports that interpretation (38–40).

Prior work utilizing HR biofeedback as a part of a gamified intervention called Playmancer failed to demonstrate reductions in HR across sessions, despite showing adaptive change in other physiological indicators of arousal (e.g., greater heart rate variability and lower respiration rate) (31). The inconsistency in these findings is likely a result of varied game goals. The focus of RAGE-Control is to explicitly down regulate HR, whereas goals for Playmancer were largely skill acquisition.

## Role of Context-Independence and Automaticity

One of the main criticisms of serious games is that such programs often do not have compelling evidence for generalizable, real world change (i.e., far-transfer effects) (21). Yet the current study suggests that playing RAGE-Control facilitated behavioral change noted by both blinded caregivers and blinded clinician raters outside of the game setting. A potential explanation for why RAGE-Control facilitates generalization is that RAGE-Control utilizes a different mechanism of learning than previous serious games. Rather than focus on application of skills in specific game contexts, RAGE-Control focuses on utilizing in game practice to establish an automatic response to internal stimuli (e.g., the player's heart rate). Not only does this mechanism allow for development of individualized skill, but it is also implicit, fast, and frequent during gameplay, facilitating automatic response learning. We propose that in combination, context-independence and repetition allow for far transfer effects (67). Future research would benefit the field by disentangling the relative contributions of context-independence and repetition.

## Potential Clinical Impact of RAGE-Control

One of the greatest advantages of incorporating games into youth therapy is the ability to engage individuals who might

otherwise be hesitant to participate in treatment, including those with significant emotional dysregulation (68). In the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), anger/irritability are core symptoms of Oppositional Defiant Disorder, Disruptive Mood Dysregulation Disorder, and aggression (anger expression) is the hallmark of Conduct Disorder. Furthermore, anger, irritability, and disruptive behaviors are commonly comorbid with other psychopathologies (69). In fact, 15 unique DSM-5 diagnoses identify some kind of emotional dysregulation as a symptom (70) and 7 DSM-4-TR diagnoses include irritable mood (53) (American Psychiatric Association, DSM4). The near ubiquity of emotional dysregulation in child psychopathology and high acceptability indicates that RAGE-Control could be a beneficial augment to cognitive-behavioral therapies with a wide range of patients.

Taken together these results are exciting because they demonstrate that (1) a video game can be used to practice heart rate regulation with skills taught in a therapeutic setting and (2) that such practice translates to behavioral and physiological change. This pilot study set a relatively high standard for proof-of-concept by way of a randomized design, equivalent therapist contact, exposure to the same CBT skills, and blinded raters. Additionally, the use of a sham computer game controlled for non-specific effects from the child playing a computer game at the end of each session. This pattern of results argues for further research to test the replicability of this study's findings, to understand if the results transfer to functional settings, and to clarify by what mechanism children randomized to the ACT-R condition are exerting better control of their angry behavior.

### Limitations

Despite rigorous design and promising findings, this proof-of-concept study has several limitations that warrant discussion. The first limitation is that the study includes a relatively small number of patients that restricts generalizability, inhibits exploration of age and sex differences, and necessitates replication of findings. The second limitation is a short follow up duration, as we did not assess patients further out than 2 weeks after completion of the intervention. Thus, these results do not provide information on how long observed behavioral improvements were sustained. Additionally, though the difference was not statistically significant, the ACT-S group had lower median MOAS score for the month prior to study entry than that ACT-R group (5 vs. 18, $W = 173.5$, $p = 0.48$), so that improvement in the ACT-S group may have been hampered by floor effects.

Early attrition from randomized control trials is a recognized problem that the study was designed to address. Specifically, all participants provided follow up data regardless of study completion. However, more patients in the ACT-S group discontinued treatment than in the ACT-R group. The decrease in early attrition for the ACT-R group did not reach statistical significance, however, the numerically greater early attrition from the ACT-S group raises the question of how much improvement in the ACT-R group was due to attending more ACT treatment sessions vs. practice of emotional regulation skills using RAGE-Control. Also, the median heart rate during the first game play session was lower for the ACT-R than for the ACT-S participants. This could have been because the ACT-R participants understood the game and were actively trying to control heart rate even during the first session; however, there could also have been failure of randomization and some unaccounted for physiologic difference between the groups may be responsible for the different trajectories of median heart rate over the 10 sessions. An additional limitation to this study is that it did not administer any adverse effect rating scale and thus did not systematically assess for adverse effects of the video games.

## FUTURE DIRECTIONS

Despite the failure of the groups to separate on the primary measure of frequency and intensity of angry feelings (STAXI-CA-TA), the consistent advantage of ACT-R over ACT-S on the secondary measures of oppositionality, overt aggression, and global severity in this proof of principle pilot study argue for further development of emotional regulation training games and further studies of their effects. Since the study reported here was completed, additional games requiring emotional control during game challenges have been developed and access to the games increased by porting them to mobile platforms such as smart phones and computer tablets (71). It will be important to determine if the greater variety and accessibility of these games improve their effectiveness in empowering parents to build their child's emotional regulation at home by providing more opportunity for practice. Additionally, providing an online forum where multiple people play together would also increase practice of emotional regulation skills and their generalization to social interactions. Given the difficulties parents experience in accessing child psychotherapists, enhancing these games with parent education modules should be studied to see if the games can be effective with little or no therapist contact. If successful, this would provide greater access for children and families in need of treatment for emotional regulation problems. Lastly, if the benefit of emotional regulation training video games is replicated in additional studies, more focused efforts to study the mechanisms of this benefit will be warranted. For example, ecological momentary assessment techniques could be employed at home along with heart monitoring to see if patient's actively controlling heart rate correlates with decreased aggressive and oppositional behavior in the home (72).

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Boston Children's Hospital Institutional Review Board. Written informed consent to participate in this

study was provided by the participants' legal guardian/next of kin. Participants also provided verbal assent that was formally documented.

## AUTHOR CONTRIBUTIONS

PD, JK, and JG-H were integral in the study design, data collection, data analysis, and writing of this manuscript. DW contributed to study design and data analysis. ARot contributed to study design. CV, ARos, ARob, and KK were responsible for data collection. MG and AP were responsible for manuscript writing and preparation. All authors contributed to the article and approved the submitted version.

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The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Emotional Dysregulation in Children and Adolescents With Psychiatric Disorders. A Narrative Review

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**Background:** Emotional dysregulation (ED) is a transdiagnostic construct defined as the inability to regulate the intensity and quality of emotions (such as, fear, anger, sadness), in order to generate an appropriate emotional response, to handle excitability, mood instability, and emotional overreactivity, and to come down to an emotional baseline. Because ED has not been defined as a clinical entity, and because ED plays a major role in child and adolescent psychopathology, we decided to summarize current knowledge on this topic based on a narrative review of the current literature.

**Methods:** This narrative review is based on a literature search of peer-reviewed journals. We searched the databases ERIC, PsycARTICLES, PsycINFO and PSYNDEX on June 2, 2020 for peer reviewed articles published between 2000 and 2020 in English language for the preschool, school, and adolescent age (2–17 years) using the following search terms: "emotional dysregulation" OR "affect dysregulation," retrieving 943 articles.

**Results:** The results of the literature search are presented in the following sections: the relationship between ED and psychiatric disorders (ADHD, Mood Disorders, Psychological Trauma, Posttraumatic Stress Disorder, Non-suicidal Self-Injury, Eating Disorders, Oppositional Defiant Disorder, Conduct Disorder, Disruptive Disruptive Mood Dysregulation Disorder, Personality Disorders, Substance Use Disorder, Developmental Disorders, Autism Spectrum Disorder, Psychosis and Schizophrenia, and Gaming Disorder), prevention, and treatment of ED.

**Conclusion:** Basic conditions of ED are genetic disposition, the experience of trauma, especially sexual or physical abuse, emotional neglect in childhood or adolescence, and personal stress. ED is a complex construct and a comprehensive concept, aggravating a number of various mental disorders. Differential treatment is mandatory for individual and social functioning.

**Keywords: emotional dysregulation, psychiatric disorders, treatment, psychopathology, children, adolescents, mental disorder**

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## INTRODUCTION

Emotions are strong and visible feelings that allow us to adapt to our environment. These feelings emerge in reaction to pleasant or unpleasant internal or external stimuli, helping us to react even before we rationally may analyze and deal with the stimulus.

Emotion regulation (ER) is the ability to recognize, evaluate, modify, and manage emotions in a personal and socially acceptable way, in order to maintain mental control over strong feelings, and arrive at adaptive functioning (1–4). This is achieved by applying various goal oriented, adaptive strategies, e.g., acceptance, problem solving, and reappraisal (5). One frequently cited definition (1, pp. 27–8) states that ER "consists of the extrinsic and intrinsic processes responsible for monitoring, evaluating and modifying emotional reactions, especially their intensive and temporal features, to accomplish one's goals." Another attempt to define ER (2) emphasizes awareness, understanding, accepting emotions, and the ability to implement strategies that modulate emotional responses in a flexible and appropriate way, while considering situational demands.

Social cognition comprises the mental operations that enable social interactions. Social cognition and interactions need well-functioning ER abilities and (later on) intact theory of mind (TOM) capacities. Newborn infants and toddlers learn ER through the interaction with their sensitive and reliable attachment persons. ER helps in initiating, inhibiting and modulating actions that are triggered by emotions. TOM, the ability to reason about one's own and others' mental states, develops later, and is necessary to understand and predict the actions of other persons. It is learned by experiencing and analyzing synchronuous and asynchronuous social interactions.

Neurobiologically, the basic emotions are represented subcortically with projections throughout the brain, reaching the cingulate cortex, hippocampus, amygdala, and the insular cortex (6), and are modulated by forebrain structures. Glutamatergic/GABA-ergic balance plays an important role in emotional control (7). The "limbic cerebellum" is also involved in ER, and congential malformations or later acquired lesions may lead to ED (8). ER neural circuits include rostral and subgenual regions of the anterior cingulate, the orbitofrontal and the dorsomedial prefrontal cortex (PFC), and regions involved in executive and attentional control, the dorsal anterior cingulate, ventrolateral PFC, and dorsolateral PFC (9, 10). Besides genetically determined malformations, genetic polymorphisms [e.g., (11)], and functional connectivity problems may cause structural damage. Acute and chronic stress may have long-term consequences. Especially longer lasting stressful life events alter the CNS structures and functionality, leading not only to persisting neurological, social and behavioral dysfunctions but also contribute to the development of pre-disorders later in life.

The ability to regulate emotions develops in early childhood within a process starting at birth (12). Babies learn from interacting with their caregivers 1. To differentiate their primary emotional states (neutral, pleasurable, and not pleasurable), and 2. That these states are variable in intensity, and can be modified, later on by using self-control, self-soothing or distracting. Learning to recognize and understanding emotions in the interaction with a sensitive caregiver is a prerequisite for later self-regulation (13–15). At the age of 3 years, children already understand their emotions (16). Various processes, such as the development of executive functions and language influence the development of ER (17–19). Next to the encoding of internal emotional cues, ER involves accessing of coping resources, using a broad range of regulation strategies (20). The development of these strategies is complex, involving genetics, epigenetics, cognition, social experiences, and learning (20, 21). Children acquire their primary regulation strategies that include help seeking, avoiding, redirecting attention, suppressing impulses, and problem solving, by the age of seven (20). Later on, ER becomes more and more self-controlled.

Internal and external factors determine the efficacy of ER: internal factors comprise neuroregulatory reactivity, temperament, cognitive abilities attachment and related positive internal working models; external factors are related to caregiving style, behavioral models, and experience (22).

Children express negative emotions in order to regulate their own emotions and to appropriately communicate with others. Under psychopathologic conditions, one or more negative emotions (such as sadness, panic, anger) are experienced either overly intense or exceedingly long, and fail to be adaptive (23). As such, healthy social–emotional functioning is contingent on being able to dynamically respond to contextual demands in a culturally appropriate way (19).

Emotion Dysregulation (ED), a trans-nosologic condition, manifests as maladaptive processing of external or internal stimuli when ER strategies and processes are impaired (24). Clinically, hyperarousal, mood instability, irritability, aggression, and temper tantrums are observed (25). Reactions appear excessive to social norms, and inappropriate or detrimental to a person's interests (26). They are often influenced by internalizing or externalizing problems or comorbid disorders, such as anxiety, autoaggression, borderline personality disorder (BPD), post traumatic stress disorder (PTSD), uni- or bipolar affective disorders (21, 25, 27–29). ED reflects a limited set of problematic strategies to understand or accept one's own emotional states, and disposing of a relatively limited set of strategies for dealing with one's own emotional states (2). ED has received considerable attention in the last decades because of its negative effects on emotional development, cognitive and behavioral adaptation, self-efficacy, social relationships and functioning, and quality of life (27, 30).

Attempting to provide an overview on the various aspects of ED in children and adolescents with psychiatric disorders, focusing on clinical characteristics, prevention, and therapy, we

**Abbreviations:** ACE, Adverse Childhood Experiences; ADHD, Attention Deficit/Hyperactivity Disorder; AN, Anorexia Nervosa; ASD, Autism Spectrum Disorder; BD, Bipolar Disorder; BN, Bulimia Nervosa; BPD, Borderline Personality Disorder; CBT, Cognitive Behavioral Therapy; CD, Conduct Disorder; CU, Callous-Unemotional (traits); DBD, Disruptive Behavioral Disorder; DMDD, Disruptive Mood Dysregulation Disorder; EatD, Eating Disorder(s); ED, Emotional Dysregulation; ER, Emotional Regulation; LGB, Lesbian, Gay and Bisexual; MPH, Methylphenidate; NSSI, Non-Suicidal Self-Injuring; OB, Obesity; ODD, Oppositional Defiant Disorder; PFC, Prefrontal Cortex; PTSD, Post Traumatic Stress Disorder; RSA, Respiratory Sinus Arrhythmia; SES, Socio Economic Status; SUD, Substance Use Disorder; TD, Typically Developing.

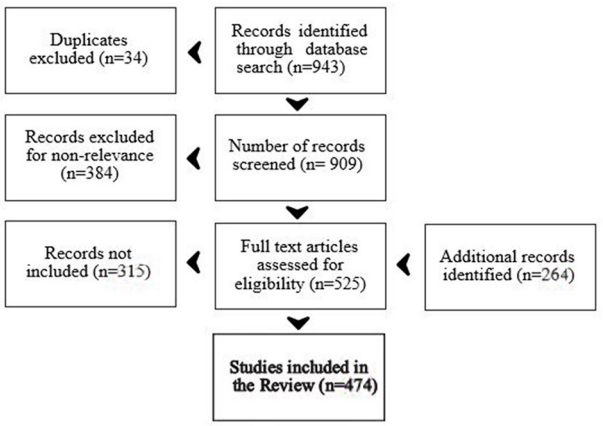


**FIGURE 1 |** Processing of records.

explored the scientific literature for relevant contributions in the last 20 years.

## METHODS

This narrative review is based on a thorough literature research in peer-reviewed journals. We searched the literature databases ERIC, PsycARTICLES, PsycINFO and PSYNDEX on June 29$^{th}$, 2020 for peer reviewed articles on ED in children and adolescents, published in English language between January, 2000 and June, 2020 related to children and adolescents (2–17 years). Using the search terms, "emotional dysregulation" OR "affect dysregulation," we retrieved 943 articles (cf **Figure 1**). After removing duplicates, 909 articles remained and were screened by title and abstract for the appropriateness of the contents. We thus excluded 384 articles: 1. dealing with subjects outside the target age range ($\geq$ 2 years $\leq$ 17), 2. related to ED or affect dysregulation of the parents and the resulting parent-child interaction, 3. anecdotical or single case reports, 4. articles without ED or affect dysregulation being the main focus, such as articles on Disruptive Mood Disorder Dysregulation (DMDD), emotions and regulation of emotions without reference to ED, dysregulation of other functions, and articles on ED as future research objective without current data, 6. articles mainly dealing with neurobiology of the emotions, neuro-pathophysiology, and stress. Thus, excluding 384 articles, we thoroughly screened 525 articles for their relevance in terms of content and subjective importance, and retained 210 articles of primary research (excluding another 315 articles), and retrieved 264 additional articles seen as "necessary," and retrieved during the course of the writing process. The additional, secondary references were retrieved in addition, related to 1. references on subtopics, 2. references cited in the initially retrieved references and estimated as important, 3. our own knowledge of the literature, 4. recommended by the two reviewers and the editor.

This sums up to a total of 474 articles cited in this narrative review (cf. **Figure 1** for a summary of article handling).

## RESULTS

In the following, we describe various neuropsychiatric disorders that are related to or influenced by ED. We **first** describe the clinical picture, then the neuropsychiatric background and various facettes of the disorder, and the impact of ED for the psychopathology of the disorder.

## Psychopathology and ED

### ADHD

ADHD is a common, mostly inherited neuropsychiatric disorder with various degrees of severity (31, 32) and three predominant presentations that may change ove time: inattentive, hyperactive – impulsive, and combined. Since 1995 (33), ED has been recognized as a key problem in children and later in adults with ADHD. Social, behavioral, and educational problems may already be present in early childhood (34), and continue into adulthood with severe clinical, personal, and vocational sequelae (35–37). A few studies have shown that ED occurs independent of the ADHD subtype (38, 39), whereas others (40, 41) found an increased incidence of ED in children with the combined type.

An underdeveloped working memory (18) and problems of impulse inhibition may contribute to ED. Thereby emotional impulsiveness and problems of impulse inhibition are associated with greater emotional and behavioral dysregulation (42, 43). Children with ADHD express more negative affect, a higher emotional instability, and difficulties in regulating and expressing their emotions (44–46). They also have difficulties in recognizing and understanding the emotions of others (44, 46). In addition, young children with ADHD have an attention bias toward positive emotions (47).

Children with ADHD perform worse in a go/no-go task when meaningful stimuli are provided in parallel (48). They also exhibit more parasympathetic dysregulation and less sympathetic reactivity, although López-Martín et al. (49) found no differences in autonomous activation during go/no-go task performance comparing children with and without ADHD. Children with ADHD need stronger activation of inhibition-related neural mechanisms in order to achieve a similar performance, especially in emotional contexts. This explains why children with ADHD have difficulties in controlling their behavior and emotions in an emotionally burdened situation. Furthermore, in boys, Seymour et al. found an association between ED unique subregion expansion in the right globus pallidus, putamen and amygdala (50).

ER mediates the association between ADHD and social skills in youth (51). Less distinct emotional and social competence could explain the higher degree of peer rejection in children with ADHD (52). In addition, the common sleep problems in children with ADHD will further aggravate their attentional and emotional dysregulation (53). Medication with methylphenidate reduces ED by reducing impulsivity in children with ADHD (39, 54, 55).

### Mood Disorders

The spectrum of affective mood disorders comprises unipolar, bipolar, schizo-affective, dysthymic, cyclothymic, and adjustment

disorder with depressive reaction and has been conceptualized a disorder of ER. Mood disorders run in families but may also be triggered by negative experiences. The severity of mood disorders may vary, and typical manifestations are named major disorders (31, 32). Dysregulation of positive and/or negative affect in affective disorders include under- or overreactivity to stimuli, abnormalities in the time flow of an emotional response, for example, in maintaining or enhancing positive affect or in limiting sadness (56). FMRI studies showed an exaggerated amygdala response to negative, and attenuated amygdala responses in reaction to positive stimuli (57).

### *Depression*

Depressive symptoms are linked to a disrupted regulation of negative emotions (58, 59). Some studies indicate that ER difficulties precede the onset of depressive symptoms (58, 60). Depressive symptoms have also been associated with overregulated negative affect (61). Children with depressive symptoms do not experience more difficulties than their peers in regulating positive affect but return more slowly to their emotional baseline following a depressive reaction to negative feedback (62).

Children and adolescents with depressive symptoms are more likely to engage in rumination than using active ER strategies, such as problem solving, distracting or cognitive reappraisal (63). Symptoms of depression might overstrain a child's ER capacities. Peer rejection and failing to down-regulate negative and up-regulate positive emotions may lead to diminished self-confidence and failing to perceive and control one's own feelings, thus aggravating depressive symptoms (21, 64).

### *Bipolar Disorder*

Children diagnosed with bipolar disorder (BD) fail to remit depressive symptoms and affective instability (65). Structural abnormalities in the orbito-frontal and subgenual white matter are consistent with neuro-biological models that implicate dysregulated affective systems and impulsiveness in BD (66). Mood dysregulation centered around limbic overactivity and relative prefrontal underactivity, indicate decreased prefrontal influence on limbic structures mediating mood regulation (67). Functional dysconnectivity of the Inferior Frontal gyrus is involved in ER and accounts for trait abnormalities in children with BD (68). Severe dysregulation of affect and behavior is associated with difficulties in falling asleep and sleeping through (69, 70). In addition, ED is associated with a greater impairment of episodic memory (71).

Kim et al. (72) found abnormal gaze patterns as a a potential endophenotype for difficulties of labeling emotions in patients with BD. Difficulties ascertaining the correct emotional tone of a spoken sentence may possibly contribute to ED in youth with BD (73). Non-verbal emotion labeling deficits such as misinterpreting facial expressions may reflect general abnormalities in emotion processing and contribute to poor emotion regulation skills (15, 74). Children with BD require higher levels of emotional intensity to accurately interpret emotional expressions and have difficulties in differentiating subtle variations in the intensity of facial expressions (75).

### *Cyclothymia*

Cyclothymia manifests as early-onset, enduring reactive mood fluctuations. ED is one of its core features, manifesting with extreme mood instability and reactivity (76). In children and adolescents, cyclothymic temperament is one of the strongest predictors of BD (77) that, as mentioned above, is also strongly connected to ED. Akiskal et al. (78) described the prototypical emotional symptoms of cyclothymia in adolescents as intermittently intense emotionality (sullen, irritable, restless, boastful) that shifts from one phase to another.

Compared to other manifestations of affective disorders, such as depressed, hyperthymic, or irritable mood, cyclothymia is associated with the most severe emotional and behavioral problems, such as sleep anxiety, separation sensitivity, eating disorders in girls, and antisocial-aggressive behavior in boys. The association of cyclothymia, sleep anxiety, and antisocial-aggressive behavior increases with age and is related to both, internalizing and externalizing disorders (79).

### *Suicidality*

Suicidality is strongly associated with psychiatric disorders and ED. Linehan's (80) biosocial theory suggests that ED is a key factor in maintaining suicidality: adolescents experiencing that their exaggerated emotional states are not well-accepted by their environment will experience feelings of guilt and shame. Suicidal ideation is then a strategy to reduce or avoid these overwhelming negative emotions (81). Interestingly, poor positive affect is a stronger predictor of suicidality than increased negative affect (82). Depression is the most common psychiatric condition leading to suicide (83). Difficulties in regulating emotions may contribute to increased reactivity toward interpersonal stressors in depressed and suicidal adolescents (84).

## Psychological Trauma

Early, recurrent, severe, chronic interpersonal, developmental, cumulative traumatic experiences (defined by number, duration and severity of trauma), and poly-victimization, are associated with ED [e.g., (85, 86)], often presenting with severe dysregulation of physical, affective, behavioral, cognitive, and interpersonal functioning [e.g., (87)]. These symptoms are merely related to dysfunctional coping strategies [e.g., (85, 88)].

Interpersonal trauma experience (sexual, physical and emotional abuse) and post-traumatic stress is associated with various psychiatric comorbidities and psychosocial, developmental, and physical impairment [e.g., (87, 89)], and a reduced ability to understand and regulate emotions [e.g., (87, 90)]. Difficulties in regulating emotions is a consequence of trauma, as well as a predictor of psychopathology (91).

In traumatized children and adolescents, ED

- increases the risk of psychopathology (89)
- is a feature of developmental trauma disorder (DTD) (85, 92, 93)
- is related to increased negative affect (90), and negative mental health outcomes (94)
- mediates the relationship between childhood trauma and the resulting internalizing/externalizing behavior problems

[e.g., (86, 95–97)], between severe trauma experience and the resulting symptomatology (90, 98), and between maltreatment of children and their aggression toward peers (99)
- is a core feature accounting for the increased risk of acute and life-time impairment [e.g., (87)], and an important target for therapeutic interventions (87)
- mediates or moderates treatment related changes (100)

The DSM-5 classification relates three disorders to childhood trauma and maltreatment: PTSD, Reactive Attachment Disorder, characterized by low social-emotional responsiveness and ED, and Disinhibited Social Engagement Disorder, characterized by active approaches to and interactions with unfamiliar adults (101). Abusing and neglectful parents mostly suffer themselves from severe harmful personal experiences (102).

### *Child Misuse, Maltreatment, Neglect*

Child misuse, maltreatment and neglect, later reported by about a third of adults (103), relate to significant harm, lead to impaired health or development, is responsible for about 45% of mental disorders in childhood (104), with effects persisting into adulthood (105). There is also a transgenerational risk of later abusive parenting (106). Warmingham et al. (107) described three often overlapping subgroups: 1. chronic multi-subtype maltreatment (57%), 2. only neglect in a single developmental period (31%), and 3. single subtype of maltreatment (emotional maltreatment, physical or sexual abuse) occurring in a single developmental period (12%).

According to the self-trauma theory (108, 109), a child's coping strategies with stressful experiences depend on intact ER skills. If a trauma occurs during the development of ER and interpersonal skills, it may interfere with the normal development, leading to an increased risk of becoming emotionally overwhelmed "by trauma reminders and future stressful events". According to the betrayal trauma theory (110), post-traumatic symptoms, including ED, may develop if a child is repeatedly maltreated, physically or sexually abused or neglected by an originally trusted close person. Then, the post-traumatic symptoms (e.g., dissociation) develop in order to protect the child's attachment to his/her significant person because during this developmental phase, significant persons are not allowed to fail.

### *Betrayal Trauma and ED*

Trauma negatively influences the ability to regulate anger and affect (111). Longitudinal studies demonstrated that higher levels of ED are associated with aggressive behavior over time [e.g., (112, 113)]. Symptoms of ED relate more to reactive (i.e., "hot," impulsive aggression in response to perceived provocation or threats), than to proactive aggression (i.e., "cold," instrumental, goal-oriented aggression) (114).

Adolescents exposed to betrayal trauma had severe difficulties with ER, reported more severe PTSD symptoms, and expressed a more aggressive communication style (115). ER difficulties mediated the relationship between betrayal trauma and negative interpersonal communication skills.

ED [undercontrolled/ ambivalent or overcontrolled/ unresponsive regulation (116)] resulting from adverse childhood experiences (ACE), and especially neglect (117), may manifest in response to stress (118) as biased perceptions of threat (119), increased responsivity to negative information with increased reactivity of the autonomous nervous system, based upon gene-environment interactions (117), and leading to increased irritability (120), poor problem solving skills (121), more negative emotionality (122), poor academic performance (123), and internalizing or externalizing reactions (89, 124, 125).

### *Internalizing and Externalizing Reactions*

Internalizing reactions and victimization are associated with depression, anxiety disorders, addictive behaviors, painful medical conditions (126), self-harm (127), and PTSD (89). Externalizing reactions are associated with pervasive anger, aggression, impulsiveness, risky sexual behavior, intimate partner violence, and conduct problems, accentuating victim-perpetrator dynamics, and precipitating culprid-victim thinking and juvenile delinquency (122, 124, 128). Internalizing and externalizing problems may also appear as comorbid conditions (129), are mediated by ED (97), and may trigger suicidality (130) and early death (131). Witnessing violence (132) and harsh discipline (133) may lead to externalizing and aggressive behavior. Irritability may also be related to antisocial, borderline and narcissistic personality disorders, most frequently represented among delinquent and incarcerated youth (134) (cf. chapter Personality Disorders). Resilience in maltreated children is, however, rare (123).

### *Maternal Influences*

Trent et al. (135), studying inpatient psychiatric patients with depressive symptoms and childhood exposure to maternal threatening behaviors, observed that maternal threatening behavior was related to the severity of depressive symptoms in those children who had more pronounced deficits in emotional clarity [which is defined by Gratz & Roemer as "the extent to which individuals are confused about the specific emotions they are experiencing" (2)]. Pat-Horenczyk et al. (28) confirmed maternal ER mediating the association between maternal PTSD and children's ED in a community sample of traumatized Israeli mothers and children.

### *Substance Misuse in Traumatized Patients*

Substance misusing and socially disadvantaged mothers showed less observed emotional availability for their 12–42 months old children than mothers without social disadvantage and substance abuse (136). The former were also more often traumatized in childhood and exhibited more often borderline personality traits, such as higher levels of emotional distress and poor ER. Mothers having experienced childhood adversities had difficulties in providing appropriate caregiving when exposed to highly stressful conditions (136). At the same time, childhood trauma increases the risk of later substance abuse because of a limited access to ER strategies [e.g., (137)]. Furthermore, traumatic experiences during childhood are indirectly associated with suicidal ideation through non-acceptance of emotional

responses, limited access to functional ER strategies, and lacking emotional awareness (138).

### *Sexual Abuse and Sex Trafficking*

Especially sexual abuse is associated with post traumatic symptoms, such as dissociation, significant impairment of psycho-social adjustment and self-regulatory abilities, and ED. Because disclosure of maltreatment would lead to serious consequences within the family, the child remains helpless, cannot stop maltreatment, even not express his/her emotions, and has to adapt to the dysfunctional environment (139). The consequences are impaired emotion recognition and management, the development of maladaptive coping strategies, such as dissociation, self-injurious behavior (140, 141), and internalizing or externalizing behavior, interrupting the emotional development and the developing of constructive peer relationships, causing peer rejection, with sequelae persisting into adulthood (95, 139, 141–143). 30% of sexually abused children are <7 years old (144), putting this most vulnerable group at extreme risk for later (transgenerational) malfunctioning, and severe health-related problems. Because especially small children need sensitive and functional caregivers, they may dissociate their experiences of abuse and blame themselves. This will lead to ED, sleep difficulties, and poor attachment behavior. Later on, females are at increased risk of developing sexual anxiety and re-victimization in romantic relationships (145). Sexual assaults on adolescent girls will lead to PTSD, complex PTSD, and life-impairing disturbances in self-organization, ED, negative self-concept, and interpersonal problems, leading in about 40% to continued traumatization (146).

Research on the impact of developmental trauma on juvenile victims of sex trafficking is limited. Greenbaum (147) summarized the (limited) knowledge about child sex trafficking. Using qualitative research methods, Hopper et al. (148), analyzed hospital charts of sex trafficking youth and found that already existing ED and behavioral problems increased the vulnerability for sex trafficking. Thus, a vicious cycle of ED in traumatized children may be detected: on one hand, ED can be seen as a consequence of trauma (91), on the other hand, children and adolescents with ED are at risk to be exposed to traumatizing situations.

### *Trauma and ED*

The neurological regions of interest for the regulation of emotions are the prefrontal cortex and the amygdala (149). If the maturation of the associated pathways is delayed until early adulthood, this asynchronous development may lead to problems of ER and decision-making. Neurobiologically, stressful situations in early life lead to early and persistent changes in the amygdala circuitry and function (150). According to Cohen and colleagues, these functional changes do not seem to recover even after the stressor is eliminated, and to persist despite developmental changes in the prefrontal regions for regulating emotions. In a study on 553 children aged 10–12 years, Fishbein et al. (151) found that exposure to personal stressors affected at least one neurocognitive function: community stressors were related to problems of recognizing emotions and problem-solving abilities, neglect was related to problems of recognizing emotions and deficits of intellectual abilities, and physical abuse was related to disturbed problem-solving abilities. Cicchetti et al. (152) found decreased afternoon cortisol levels in children experiencing early physical and sexual abuse in 168 school aged maltreated children, indicating persistent neuro-endocrine dysregulation of the HPA axis. Maltreated children present with neuro-endocrine dysregulation of the HPA axis only if they experienced physical or sexual abuse in the first 5 years of life, and if they suffered from depression or other internalizing problems (152).

Early experiences of maltreatment and neglect, leading to ED is extremely common (98%!) in adopted children (153, 154). There is also a high comorbidity of ADHD and conduct and attachment disorders, and in about 2/3 with continued, severe personal and social difficulties despite happy placements. 38% do not achieve a stable adoption. Studies of the hypothalamic-pituitary-adrenal (HPA) axis showed that 6 months after adoption, morning cortisol levels were improved but, also post adoption, dysregulation of the HPA axis was associated with more emotional and behavioral problems (129), possibly increasing the risk of negative developmental outcomes. Therefore, early interventions, even involving out of home care are justified to enable a sustainable development of vulnerable children if no change of the detrimental environment may be expected (155). The effect of such serious measures will not be paramount but will at least represent an opportunity (153), especially if appropriate care is established before the age of 6 months (156).

## Posttraumatic Stress Disorder

PTSD is a disorder of ED (94, 157), and represents an individual's attempt to achieve an emotional equilibrium following severe traumatic experience(s) (157). Intrusions emerge from emotional under-regulation, whereas emotional numbing, avoidance, and dissociation are indicative of emotional over-regulation (158). ED is a critical risk factor for developing [e.g., (89, 94, 159–162)] and maintaining PTSD [e.g., (89, 160–162)].

Examining neural underpinnings of ED in pediatric PTSD, Wolf & Herringa (163) found that adolescents with severe PTSD showed abnormal function and connectivity in prefrontal–amygdala circuits. These changes are related to threat processing and fear regulation. Adolescents with PTSD demonstrated an age-related decline of dorsomedial PFC activation, inversely related to the severity of PTSD, and an age-related decrease of the PFC - amygdala connectivity. The authors suggested abnormal developmental processes to influence key emotional pathways of pediatric PTSD.

### *Age Dependent Characteristics*

Infants and toddlers are especially vulnerable to traumatic experiences, and therefore at high risk of developing severe PTSD, ED, internalizing and/or externalizing symptoms, and long-term impairment (89, 164–166). PTSD in toddlers differs from PTSD in older children and adults in relation to the severity and number of symptoms, e.g., toddlers express less avoidance or numbing [e.g., (167, 168)].

Difficulties of ER, escpecially emotional clarity (2), play an essential role in trauma-related psychopathology. Viana et al. (169) showed that lower emotional clarity, a sub-dimension of ED, indirectly influences the severity of PTSD because of an increased sensitivity for anxiety. Viana et al. (170) also found lower emotional clarity in traumatized adolescents to be related to suicidal ideation at higher (and not lower) levels of distress tolerance.

Younger age at traumatization (below the age of 14 years) relates to increased psychopathology, including ED and PTSD (159, 171). ED, negative self-concept, interpersonal problems and core PTSD symptoms represent moderately correlated dimensions in traumatized adolescents (146). There is an ED related link between

- Violence exposure and PTSD (172),
- Depressive symptoms and PTSD (173),
- Traumatic exposure and reactive aggression (174).

Assessing the inter-generational impact of ED, Powers et al. (94) investigated 105 African American mother-child dyads and found PTSD significantly associated with childhood trauma experience, maternal depressive symptoms, ED, and maternal child abuse. The authors considered ED a trans-diagnostic treatment target across the life span, and recommended treating maternal ED in order to reduce traumatizing of the next generation. PTSD includes various heterogeneous symptom clusters - specific factors, such as type of trauma exposure or ED - influencing the severity of symptoms within these clusters and leading to distinct clinical phenotypes of PTSD (175). Empirically, there are various facets of ED, such as lack of emotional awareness, lack of clarity of emotions, difficulties of controlling behavior, achieving goal-directed behavior, non-acceptance of emotional responses, and limited access to problem-solving strategies. These facets act as indirect pathways through which trauma is associated with specific DSM−5 PTSD symptom clusters, such as intrusion, avoidance, negative alterations and arousal (175).

### *PTSD and Behavior*

PTSD predicts aggressive and delinquent behavior in youth, especially in those who are also experiencing high levels of ED (174). Miller and Marsee (176) compared two groups of incarcerated boys, a low reactivity group with symptoms of emotional numbing and callous-unemotional (CU) traits, and a high reactivity group with symptoms of hyper-arousal and ED. Frequent violent offending, CU traits, and proactive aggression correlated with emotional numbing and combined hyper-arousal symptoms. Delinquent adolescents experienced high levels of ED (141, 175), girls more than boys (141, 177). ED also predicted a higher risk for subsequent offending behavior (177). Especially interpersonal trauma exposure corresponds to negative effects on youth's psychological functioning, severe PTSD symptoms [e.g., (146, 175, 178, 179)], poor ER strategies [e.g., (95)], and diffiulties in self-organization [e.g., (146)]. Delinquent adolescents who experienced sexual abuse may show higher rates of PTSD (141).

### *Poly-Victimization*

Experiencing repeated traumatic events is an important predictor for developing PTSD [e.g., (94, 180)]: Lehmann et al. (101) found a strong association between the number of self–reported potentially traumatic events and the development of PTSD in a sample of adolescents raised in foster care. Youth living in foster care had an increased risk of developing PTSD (101, 181, 182). PTSD and ED were significant predictors of depressive symptom trajectories, more pronounced in females than in males (182). The risk of more severe ER difficulties, ED, and PTSD is higher in poly-victimized adolescents, having experienced multiple types of interpersonal and non-interpersonal childhood traumata (101, 175, 183–185), girls again being more severely affected than boys (101, 185).

Charak et al. (186) investigated a large sample of incarcerated adolescents, and studied associations between poly-victimization, ED, DSM-5 PTSD symptoms, and related behavioral health problems, including alcohol/drug misuse, anger, irritability, depression, anxiety, somatic complaints, and suicide ideation. The authors distinguished three distinct sub-groups:

1. violent environment (such as being exposed to natural disasters, accidents, war, physical abuse or assault, witnessing physical violence, unexpected death of a beloved person, facing a dead body (excluding at funerals), painful medical treatment, and acts of violence
2. poly-victimization (such as, serious injuries, psychological abuse, domestic violence, family members being badly injured or sick, parental drug use, unexpected death of someone close, removal from parental custody or parental threats of abandonment, neglect, and sexual abuse); psychopathology on all four DSM-5 PTSD symptoms clusters, as well as depression/anxiety, somatic complaints, and suicidality
3. mixed adversity (such as, a parent being incarcerated, or someone they knew had attempted suicide, or was severely injured or ill, experience of physical abuse). Youth in the "mixed adversity class" reported about exposure to traumatic events (such as severe accidents), and were less likely having been exposed to violent victimization.

There is a positive relationship between developing and maintaining PTSD, and avoiding trauma-related emotions, thoughts and activities (187). Woodward et al. (188) confirmed this theory for traumatized inpatient adolescents, showing positive associations of emotional non-acceptance and greater distraction- coping in relation to more severe PTSD.

### *Influence of Comorbid Disorders*

Various psychiatric disorders increase the risk of being exposed to traumatic events (189). For Dvir et al. (87), bipolar disorder is the best example of psychopathology involving ED. Biederman et al. (189) indicated that children with Bipolar-I disorder are at a 20-fold risk to develop full or subthreshold PTSD compared to healthy children. In patients with early non-affective psychosis, Liu et al. (190) found maladaptive ER strategies (catastrophizing, ruminating, and blaming others), global ED, and poor cognitive insight as psychological risk factors for PTSD.

### *Developmental Trauma Disorder*

The complexity of early childhood developmental trauma is not optimally covered by a PTSD diagnosis. Hence, Developmental Trauma Disorder (DTD) is a proposed diagnosis for children, who have experienced disrupted attachment and multiple or chronic exposure to developmentally disabling interpersonal traumata, such as emotional or sexual abuse, abandonment, threats to physical integrity. Seven levels of functioning are involved in DTD (88, 191):

1. Attachment (e.g., restricted attachment in the form of a distrustful behavior pattern toward attachment figures as well as toward protective social institutions).
2. Biology (e.g., stress hormones).
3. Cognition (e.g., depersonalization, derealization, confusion, sense of safety).
4. ER (impairments in the regulation of e.g., anger, fear, resignation, defeat).
5. Behavioral control (e.g., acting out, cutting, re-enacting).
6. Dissociation.
7. Self-concept (e.g., self-attribution, self-hate, self-blame). Most often, DTD involves complex traumatic experiences in childhood, usually corresponding to sexual, physical abuse or war experiences in early childhood (92).

## Non-suicidal Self-Injury and Suicidality

According to the biosocial theory of Marsha Linehan (80), individuals use deliberate self-harm and self-injurious behavior as maladaptive ER strategies against overwhelming intense negative emotions [e.g., (127, 192)]. Because of their increased emotional reactivity and lability, and their immature prefrontal control, adolescents have a higher risk for engaging in extreme dysfunctional ER strategies, such as Non-Suicidal Self-Injury (NSSI) [e.g., (193)]. NSSI therefore typically begins in adolescence (192). NSSI:

1. is defined as direct and deliberate damage of body tissue without conscious suicidal intent [e.g., (192, 194–196)], and for not culturally sanctioned purposes (31).
2. is triggered by ED (80), and predominantly goes along with high levels of emotional distress (197).
3. assists in the escape, management, or regulation of emotion (198), in particular in the escape of negative emotional states, such as anger, depression, loneliness and frustration, and unwanted thoughts (199).
4. is maintained by positive and negative reinforcement in intra- and interpersonal domains (192).
5. has a serious impact on health and well-being [e.g., (200)], and
6. increases the risk of later suicide (201), especially if low emotional clarity (2) is linked to high distress tolerance (169).

### *NSSI and Borderline Personality Disorder*

"The relationship between NSSI and BPD features in adolescence seems to be more controversial than in adulthood" (203, p. 24). Recurrent NSSI is a core feature of BPD (31) and often precedes suicidal behaviors in adolescents [e.g., (202)]. Specific aspects of ED, such as lack of emotional awareness, poor coping strategies, and non-acceptance of emotions, predict repeated NSSI [e.g., (2, 203)] and are highly prevalent among suicidal adolescents, regardless of their psychiatric diagnoses [e.g., (82)].

NSSI is included in the DSM-5 (31) as a condition requiring further study, and classified as an independent diagnostic entity since 2013. ED and NSSI are closely related [e.g., (193, 204–206)]. ED in NSSI is considered

- A risk factor [e.g., (141, 207)], and a core feature of NSSI [e.g., (208, 209)],
- The primary drive for NSSI in adolescents [e.g., (81)],
- A major factor for developing (200) and maintaining NSSI [e.g., (210)].

NSSI and BPD overlap in adolescents, 52% of adolescents practicing NSSI suffer from BPD (193). Underlying mechanisms for both disorders, although to a different degree, include affective instability (i.e., ED), and interpersonal instability (i.e., instability of attachment to significant others). Interpersonal instability in BPD is more generalized, extending beyond family functioning to peer relationships (205).

Sadeh et al. (211) investigated the relationship between BPD symptoms and NSSI: BPD affective dysregulation was associated with intra- (e.g., affect regulation, anti-dissociation and self-punishment) but not interpersonal functions (i.e., peer relations, autonomy) of NSSI. In contrast, BPD interpersonal dysfunction was associated with inter- rather than intrapersonal functions of NSSI. These data indicate that clusters of BPD symptoms show unique relationships with functions of NSSI in adolescents. Somma et al. (201) found a moderate association between self-reported features of BPD and NSSI in a sample of non-clinical adolescents, not fully explained by ED. The authors suggested that NSSI may represent just one of several dysfunctional ER strategies in adolescents at risk for BPD, and that NSSI in adolescence may not represent an exclusive ER strategy but may fulfill various other intra- and interpersonal needs.

Nakar et al. (212) found three distinct developmental trajectories for self-reported harmful behaviors in a community-based adolescent sample: self-injurious behavior, suicidal behavior, and substance misuse.

High-risk trajectories for the three behaviors greatly overlapped (80–90%), and this overlap was significantly associated with higher levels of BPD. The authors found a symptom shift, typically associated with BPD in adolescents: the high-risk trajectory of self-injurious behavior, and the high-risk trajectory of suicidal behavior had a high initial degree of engagement with decrease over time, while the high-risk trajectory of substance misuse had a medium initial degree of engagement with increase over time.

### *Influencing Factors*

NSSI is maintained more frequently because of intrapersonal functions, such as affect regulation, self- punishment, and because of interpersonal functions, such as peer bonding, autonomy, that are especially relevant in youth with interpersonal difficulties (211, 213, 214).

Neurobiologically, adolescents with NSSI are less able to interpret social cues and regulate their emotions (215): female

adolescents with NSSI but without BPD showed an increased activity in amygdala regions, the anterior cingulate cortex (ACC), and the inferior and middle orbitofrontal cortex, as well as a reduced sensitivity in the cuneus and right inferior frontal cortex during an emotional processing task.

ED moderates the longitudinal relationship between NSSI and disordered eating: Turner et al. (216) found a strong relationship between disorderd eating and later NSSI, together with high levels of ED but no significant moderating effect of ED for predicting concurrent NSSI and vice versa (217). Internalizing symptoms predicted NSSI in inpatient adolescent girls (218). Female adolescents with higher levels of depression had a higher risk of utilizing NSSI for regulating strong emotions (219). Both, ED and depressive symptoms, are related to the frequency of NSSI in adolescents [e.g., (127, 195)].

Environmental factors, such as stimuli that elicit emotional arousal, promote NSSI (209): there is a significant relationship between ED, interpersonal problems, and NSSI [e.g., (208, 220, 221)]. Interpersonal problems with the family and peers have independent negative effects on ED, with ED mediating the influence of interpersonal problems on the frequency and severity of NSSI. Higher levels of conflict and lacking support for ER in family and peer relationships went along with higher ED in adolescent girls hospitalized for psychiatric problems (208).

Children and adolescents with severe ED are at higher risk of NSSI when facing stressful life events (199). Especially child maltreatment increases the risk for NSSI (127, 222, 223). ED mediates the relationship between childhood maltreatment and the frequency of NSSI [e.g., (195, 223)]. Peh et al. (127) demonstrated ED to mediate the association between severity of child maltreatment and frequency of self-harm, while controlling for depressive symptoms in adolescent psychiatric outpatients. The authors considered exposure to childhood maltreatment as a distal, and ED as a more proximal associative factor, linking maltreatment exposure to self-harm.

A history of sexual abuse is strongly related to NSSI, particularly in girls. Chaplo et al. (141) investigated associations between sexual abuse and NSSI in traumatized delinquent youth on the basis of the dual mediating variables, ED and dissociation: higher levels of dissociation were associated with more frequent NSSI.

ER mediates the relationship between sexual orientation and NSSI in lesbian, gay and bisexual (LGB) adolescents. LGB youth are exposed to a greater risk of NSSI (224), probably related to bullying and peer harassment (225), and possibly parental rejection.

### *Suicidality*

Suicidality is based on mental suffering, lacking self-respect, respect by others or of the feeling of being not loved by others (226). Erwin Ringel (227) described a presuicidal syndrome with 3 principal components, constriction, inhibited aggression turned toward the self, and suicidal fantasies (nowadays suicidal ideation, "escaping from a predicament"). The transition to suicide is characterized by the idea of hopelessness, feelings of anhedonia and severe anxiety, and direct planning of committing suicide (228). Suicidality is linked to depression but not exclusively (228). The risk of completing suicide increases with the number of suicide attempts, mental narrowing, and the emergence of a stressor, such as separation, loss of support. 90% of completed suicides are associated with psychiatric disorders, namely major depression and alcohol or substance abuse. The prevalences of suicide ideation, plans, and attempts are 2%, 0.6%, and 0.3% (229). The lifetime prevalence of suicidal ideation is 9.2%, and of attempted suicide 2.7% (230).

### *NSSI and ED*

ER skills play a key role in the ability of adolescents to adequately identifying emotions, and helping them in selecting adequate coping strategies that may reduce suicidal ideation (231). Pan et al. (232) with the example of processing slightly angry faces, suggested that dysfunctions of the neural circuitry involved in processing emotions could smooth the path to suicidality in adolescents. Selby et al. (233) found ED to interfere with the ability to activate adequate emotional processing, and therefore would evoke suicidal thoughts. More specifically, ED is a well-established risk factor or even an underlying mechanism for suicidal ideation, suicide plans and suicide attempts in youth (130, 234, 235). The readiness for attempting suicide may be increased by impulsiveness and dysregulated behaviors (236). Comparing adolescents who attempted a number of suicides with those experiencing only one attempt, the former reported stronger deficits in ER and poorer impulse control (237).

## Eating Disorders

Eating disorders (EatD) comprise anorexia nervosa (AN), with the subtypes, restrictive and binge-purging, bulimia nervosa (BN), and obesity (OB) (31, 238).

According to the affect regulation model, EatD serve as maladaptive coping strategies for pervasive emotional and behavioral dysregulation (239–242). ED is a key trans-diagnostic characteristic, arising from emotional vulnerability, combined with an invalidating familial environment that commonly can be targeted (243–245).

### *ED in Eating Disorders*

Adolescents with EatD are significantly more impaired in their ability to regulate emotions compared to non-clinical samples [e.g., (244)]. In this study, patients with EatD scored higher in the Difficulties in Emotion Regulation Scale (DERS total score and subscale scores, "Non-Acceptance," "Awareness," "Strategies," and "Clarity"). Symptoms were most strongly associated with "Strategies." ED also plays a role in obesity, particularly among girls with self-reported loss-of-control (LOC) and binge eating (183). In contrast to individuals with adult-onset obesity, individuals with childhood-onset obesity showed a higher prevalence of EatD, particularly BN (246). The severity of an eating disorder relates to the severity of ED (241, 244, 247). High levels of parental ED are also associated with the severity of the children's EatD pathology (248). Maladaptive adolescent attentional bias toward anger and social threats predict a strong association between maladaptive parental responses to emotions and adolescent ED (249). There are specific emotional factors in developing and maintaining adolescent EatD:

- deficient ER strategies across a variety of domains (183, 241, 243, 250–257),
- "emotional" eating, defined as eating for emotional reasons in response to negative emotional states and in order to escape from negative affect (240, 251, 258, 259),
- poor emotional awareness (244, 250, 251, 257), and
- high and low approach on dysregulated positive emotions, such as avoiding positive affect and rewards (251).

Dysfunctional metacognitions represent another vulnerability factor for ED: Laghi et al. (257) found interaction effects between metacognitions and emotional functioning in binge eating adolescents. Metacognitions, the need to control thoughts, moderated the relationship between lack of emotional awareness and binge eating.

Jakovina et al. (256) found significantly higher levels of attachment related anxiety and avoiding strategies in adolescents with BN compared with controls, but only attachment related anxiety predicted BN symptoms, and was mediated by ER.

Monell et al. (244), comparing patients with various EatD subtypes, found only a few meaningful differences in relation to ED: patients with AN, binge-purging subtype showed more difficulties in controlling impulses than those with AN, restrictive subtype. Individuals with binge-eating disorders had higher impulsiveness scores than those with AN, restrictive or binge-purging subtypes, and EatD otherwise specified. The authors concluded that differences between EatD subtypes may depend on the study design, and possibly also on other factors than the eating disorder type. In contrast to Monell et al. (244), other authors [e.g., (255, 260)] found higher ER deficits in individuals with BN and binge-purging AN compared to individuals with restrictive AN. Across ages, Anderson et al. (255) found less self-reported acceptance of emotional responses, higher impulsiveness, fewer ER strategies and low emotional clarity (2) in patients with AN binge-purging type or BN, whereas patients with restrictive AN showed more goal-directed behaviors in stressful situations than those with BN, and a better awareness of emotions than in those with binge-purging AN.

### *Influence of Emotional Child Abuse*

Emotional child abuse may induce the development of severe ED and severe eating disorder (EatD), including AN. A number of studies support the strong psycho-pathological relationship and long-term comorbidity of the two disorders (252, 261). ED mediates the relationship between emotional child abuse and AN. Nature and magnitude of this influence do not differ regardless of the AN subtype (252). AN is also associated with higher levels of comorbid depressive or anxiety disorders, OCD, PTSD, and interpersonal problems. Individuals with binge-purging AN had experienced more severe maltreatment, neglect (261), and sexual abuse (252) than those with restrictive AN. McDonald et al. (262) found binge-purging AN to co-occur more frequently with BD than with restrictive AN. Patients with BD and EatD usually are more impulsive and have more severe EatD. They also suffer more from alcohol and substance abuse, suicidality and mood instability than patients with BD only. Slane et al. (263) investigated monocygotic twins with dysregulated BN and comorbid alcohol use disorders at ages 17 and 25 years. They found non-shared environmental effects (i.e., factors that create differences in monocygotic twins) that did not influence the association between BN and alcohol use disorder.

## Oppositional Defiant Disorder, Conduct Disorder, and Disruptive Mood Dysregulation Disorder

### *Oppositional Defiant Disorder*

Oppositional Defiant Disorder (ODD) is a disruptive behavior disorder (DBD) of childhood and adolescence that can be described as recurrent, persistent, developmentally inappropriate patterns of anger, irritability, negativity, defiance, disobedience and deliberate hostility toward others, resulting in functional and social impairment (31). Children with ODD commonly experience dysregulated emotions such as temper tantrums, intense fears, inconsolable despair, problems to feel and express emotions, and a low tolerance to frustration (264), co-occurring with externalizing behavior problems (265, 266).

For these children, emotions seem uncontrollable or absent. They tend to think simplisticly, rigidly, and reactively, and are led by defiance and aggression (264). Adolescents with ODD and higher scores on the Child Behavior Checklist, Dysregulation Profile (CBCL-DP) possess poor abilities to regulate affect, behavior and cognition, and are more likely to present with auto-aggression (267). ODD is associated with impairments of social, academic, occupational and family relationships over the lifespan (268). Most studies concentrate on the association between ED and externalizing behavioral problems (269, 270). Studies on the relationship between ODD and ED are lacking, except for a few studies suggesting a strong association between ED and ODD (270–273). It is unclear if ODD criteria are uni-dimensional, if ODD is better conceptualized as an ER disorder (271), or if ODD is a multidimensional construct and better conceptualized as a disorder of mood regulation (273, 274).

### *Conduct Disorder*

Conduct disorder (CD) is a behavioral and emotional disorder characterized by functional impairment that includes intentional violations of the rights of others, societal norms or rules (31). Children with CD typically show aggressive, antisocial behavior, and callous-unemotional (CU) traits including low prosocial emotions and behaviors, such as blunted affect, lack of guilt, physiological under-arousal, and lack of empathy (275). Antisocial behavior of children with ODD or CD have partly been explained by deficits of information processing and ER. The combination of misinterpreting social cues in a negatively biased and stereotypic way, limited strategies for coping with anger, and lack of behavioral control, especially difficulties in response inhibition, lead to inappropriate handling of distressing emotions and impulsive behavior (264, 273). Fehlbaum (275) investigated adolescents with CD in a controlled fMRI study.

Both groups were confronted with an emotional stimulus and a Stroop task with varying cognitive load. Adolescents with CD made significantly more errors, while reaction times were not significantly different compared to typically developing (TD) youths. In children with CD, left amygdala activity failed to be down-regulated in response to incongruent trials, and anterior

insular activity increased during the Stroop task. The authors concluded that children with CD could not adequately process distracting emotional information and suppress impulsive thoughts, leading to antisocial behavior. They also concluded that rather their neurological problems than ED was responsible for their inappropriate behavior.

Mitchison et al. (273) examined the relationship between ED, ODD symptoms and conduct problems in preschool children: problematic behavior occurred more often at home than in the kindergarten setting, and there was a strong relationship between ED, ODD symptoms and conduct problems especially regarding lability/negativity. Boys had more severe ED problems than girls. Furthermore, ED was found to be a strong, gender-independent predictor of ODD symptoms and conduct problems. This is also supported by the work of Schoorl et al. (276). Multimodal extensive treatment is recommended including socio-therapy, individual and family psychotherapy, and medication. Methodologically sound controlled trials are still lacking (265).

### *Influence of Comorbid Disorders*

ODD is very frequently (almost 50–60%) comorbid with ADHD (277). Children with ADHD and comorbid ODD showed significantly more negative emotional lability compared to children without ODD, involving impairment in the regulation of a variable, intense pattern of emotional responses (278).

There is an association between early traumatic experiences and later aggressive, impulsive and antisocial behavior [e.g., (279–281)].

Another study focused on CU traits, manifesting as a consequence of traumatic experience and resulting deficits in ER. Adolescents with high expression of CU traits showed impaired emotional responses and exhibited severe aggressive-dissocial behavior. Potentially traumatized adolescents with highly expressed CU traits showed significantly more external-dysfunctional ER strategies than traumatized adolescents with low CU expression (282).

Investigating incarcerated adolescents, Sevecke et al. (111) observed ED and psychopathic traits to occur only in boys. Hoskins et al. (283) found past trauma exposure in three quarters of first-time offending, court-involved, non-incarcerated Latino youth. Traumatized girls presented with more severe internalizing symptoms and affect dysregulation, traumatized boys with more externalizing symptoms.

ED and antisocial behavior are commonly observed in juvenile offenders, depending on the co-occurrence of emotional neglect. Physical abuse in incarcerated boys was related to ED only in those with co-occurring emotional neglect (117).

ED was associated with more severe aggressive behavior in urban adolescent boys and girls who witnessed community violence (284). Ford (264) developed a three-step model explaining the relationship between trauma and victimization in childhood:

1. "survival coping" characterized by dysregulation of emotions and deficient social information processing (77)
2. "oppositional-defiant" behavior, involving covert or overt aggression and PTSD
3. "victim coping" in a chronological sequence.

Plattner et al. (285), comparing delinquent adolescents and high-school students, observed that delinquents had higher levels of negative emotions (fear, sadness, and anger) as state and trait conditions, probably linked to childhood trauma experience. The duration of trauma exposure influenced trait emotions, and the severity of trauma (emotional abuse and witnessing violence) had an impact on state emotions. When stressed, delinquent adolescents showed more state emotions of sadness, anger, and a wider range of negative emotions.

There are also associations between deficient executive functions and ADHD: Landis et al. (286) reported that children with dysexecutive problems (operationalized by a questionnaire and a well-established survey tool) were classified as more inattentive and hyperactive. Both, hyperactivity and inattention, were associated with ED.

### *Disruptive Mood Dysregulation Disorder*

A new and controversial disorder of children similar to ODD is Disruptive Mood Dysregulation Disorder (DMDD) (31). The disorder is characterized by severe, chronic, non-episodic irritability, frequent temper tantrums, and verbally or behaviorally expressed outbursts that are disproportionate to the trigger and inappropriate to their developmental level. Children with DMDD generally present annoyed, touchy, and persistently angry, with mood swings and irritability (287–289). They have poor ER abilities and frequently lose behavioral control, contributing to rising frustration and distress (290). It remains controversial whether DMDD is a unique entity or if it is closely related to ODD (290, 291). According to Dougherty et al. (292), a DMDD diagnosis is associated with concurrent and predictive indicators of emotional and behavioral dysregulation, and poor social functioning. They also noted that temperamental surgency, a construct reflecting high levels of activity, reward seeking, low shyness and impulsiveness, of 3-year old children predicted DMDD at the age of 6. Zepf et al. (293) reported about diminished cognitive flexibility in children with DMDD, assessed by a reversal learning task (294), and poor motor inhibition (295).

## Personality Disorders

ED plays a substantial role in personality disorders (PD) with the majority of research focusing on borderline personality disorder (BPD). We only found a few recent studies, investigating ER problems in adolescents with PDs other than BPD. Compared with healthy controls, children with obsessive compulsive personality disorder exhibit more alexithymia (296), impulsivity, behavioral activation (297), and poorer effective ER strategies (296, 298).

### *Borderline Personality Disorder*

BPD is a serious mental illness that includes ED and interpersonal problems. Based on the bio-psycho-social developmental model of BPD (80) there is a predisposition toward increased emotional sensitivity and intensity of responses to emotional stimuli with a slow return to baseline following emotional responses, and

adverse social influences. ED mediates the relationship between BPD, emotional vulnerability (299), and over-mentalizing (excessive inaccurate mentalizing, i.e., excessive Theory of Mind, TOM) (300). In accordance with Linehan (80), Carpenter and Trull (301) conceptualized ED in BPD as consisting of four components: 1. emotional sensitivity, 2. heightened and labile negative affect, 3. deficits of appropriate regulation strategies, and 4. excessive maladaptive regulation strategies.

BPD and ADHD share a number of common features, such as impulsiveness, ED, deficits in attention and decision-making, comorbid major depression; brain volume reductions and impairments of connectivity in prefrontal, anterior cingulate and limbic areas (302, 303).

Results of studies assessing neural correlates of ED in adolescents with BPD are heterogeneous. Comparing female adolescents with BPD and healthy controls, Krauch et al. (304) found increased activation in the left posterior insula and left dorsal striatum as well as in the inferior frontal gyrus and parts of the mentalizing network. This suggests an enhanced emotional reactivity to interpersonal threat- or rejection-related situations early in the development of BPD.

Attachment, ED, and BPD are strongly interrelated [e.g., (80, 305, 306)]. Disordered attachment plays a significant role in the pathogenesis of BPD (307, 308). Maternal ED mediates the relationship between maternal BPD and child functioning (309). There is an interplay between disordered attachment and features of BPD mediated through ED (310). Secure attachment to the father functioned as a buffer against adolescent BPD via enhanced positive ER strategies, while negative ER strategies served as a pote correlate of clinically significant levels of BPD, weakening the protective effects of attachment and positive regulation strategies.

Genetic and environmental effects are likely to influence attachment patterns and personality disorders (311). In monocygotic twins, the associations between self-reported anxious attachment (i.e., fears of abandonment and difficulties in regulating worries about the availability of attachment persons) and PDs were mostly explained by genetic factors, while self-reported avoidant attachment (i.e., discomfort with close relationships and depending on others) was entirely influenced by non-shared environmental effects. Factor analyses revealed that anxious attachment loaded on ED, while avoidant attachment loaded on inhibitedness. Attachment anxiety correlated with affective lability and self-harm (characteristic for BPD), increased self-satisfaction (characteristic for narcissistic PD), oppositionality, submissiveness, and the lack of self-fulfillment (characteristic for identity problems). The authors suggested that probably different sets of genes contribute to the specific associations observed between these variables to explain why anxious attachment correlates with different psychopathologies. Neither avoidant nor anxious attachment showed any relationship with PD scales indexing dissocial behavior or compulsivity, suggesting that these dimensions of personality pathology are not related to attachment styles (311).

More severe features of BPD are significantly associated with increased hypermentalization, ED, and internalizing or externalizing symptoms (312). Hypermentalization and ED mediates the relationship between attachment coherence and features of BPD. Hypermentalization and ED are independently related to BPD. Kalpakci et al. (313) investigated relations between ER, hypermentalization (i.e., incorrect, over-inference of thoughts and feelings of self and others), and cognitive and affective empathy in inpatient adolescents with and without BPD. In both groups, ED was related to increased affective empathy.

There are differences between BPD and healthy controls in information processing (80, 314): patients with BPD showed alterations in early validation processes that determine the emotional response and trigger ED (315). Analyzing patterns of emotional responses to stimuli, patients with BPD showed significantly greater arousal and greater valence (more positive emotions) than healthy controls when looking at unpleasant and neutral images, but lower dominance (greater insecurity and discomfort) when looking at positive images. These results are similar to the pattern found in depressive patients (315).

Features of BPD were associated with significantly higher levels of experiential avoidance (i.e., the unwillingness to remain with uncomfortable thoughts, emotions, sensations, memories and urges by escaping or avoiding them), and difficulties in ER. Experiential avoidance partially mediated the relationship between difficulties in ER and features of BPD. The authors suggested a reciprocal relationship between ER and features of BPD - difficulties in ER being associated with both, experiential avoidance and features of BPD (316).

Trait impulsiveness and the three dimensions of ED (difficulties in controlling impulsive behaviors when distressed, limited access to effective ER strategies, and lack of emotional clarity) were significantly associated with BPD features in two independent non-clinical samples of Italian adolescents (317).

Aggressiveness most substantially differentiated between patients with and without BPD. Parents rating adolescents on BPD scales described them as presenting with more anger, hostility, and indirect aggression (318). ED and trait anger sequentially mediated the association between BPD and reactive aggression, generated by increased interpersonal threat sensitivity (319, 320). Banny et al. (321) observed features of BPD predicting increases in reactive (i.e., impulsive/dysregulated) relational aggression and proactive (i.e., premeditated/controlled) relational aggression, and decreases in proactive physical aggression in girls 1 year later. Measurements of systolic and diastolic blood pressure, and skin conductance reactivity supported the hypothesis that aggression is a strategy for girls with features of BPD to cope with overwhelming intense negative affect in the context of ED, more precisely in response to stressful peer interactions (threats or exclusion).

Yen et al. (318) compared suicidal adolescent inpatients with and without BPD. They found that suicidal patients with BPD had more Axis I co-morbidities, higher levels of aggression, and a greater likelihood of a history of serious suicide attempts. There were no significant differences in ED between the two groups. The authors suggested that affective dysregulation may be more trans-diagnostic and not specific for BPD, particularly in a high-risk sample of suicidal adolescents.

There is a close relationship between interpersonal trauma experience and PD (87). ED is a consequence of exposure to direct or indirect physical or sexual violence associated with posttraumatic stress symptoms [e.g., (184)] and BPD pathology [e.g., (322, 323)]. Ford and Courtois (324) provide an extensive summary of the role of trauma and ED in BPD. Buckholdt et al. (172) examined the mediating role of ED in the relation between exposure to violence and PTSD or BPD pathology in adolescents. They found that patients exposed to violence presented with more ED, which, in turn, was related to more PTSD and BPD pathology. ED mediated the association between exposure to violence and PTSD or BPD pathology.

For BPD and NSSI, please refer to the section on Eating Disorders. Frequently observed comorbidities of BPD are bipolar disorder (BD), ADHD, and disordered sleep. The number of BPD symptoms is correlated with the severity of BPD (325). The BPD factors, affective dysregulation, involving affective instability, fear of abandonment, and inappropriate anger, is associated with BPD chronicity and severity. In addition, threat sensitivity and impulsivity in the context of negative affect were related to a higher risk of BPD (65). Preliminary research indicates that patients with BPD and comorbid sleep disturbance have an increased risk of suicidality [e.g., (326)], suggesting impulsivity and ED as potential psychological mechanisms driving the insomnia – suicide link in BPD.

There is a strong negative relationship between personal life objectives, ED, and BPD. Patients with BPD have a lower feeling of meaning in life than mentally handicapped individuals without BPD. Marco et al. (327) designed a multiaxial model, consisting of the axes, "ED," "emotional suppression," "satisfaction and meaning in life" (subscale and overall score), and "personal life objectives." The model explained more of the variance in BPD symptoms than the ED scales alone.

### *Narcissistic Personality Disorder*

Narcissistic personality disorder with its various manifestations is associated with ED beyond personality characteristics and constitutes an important factor in the psychopathology of the disorder (328, 329). The latter authors studied 1,018 undergradutate students, based on the narcissitic admiration and rivalry concept model and the related questionnaire (330). They found that merely narcissitic rivalry was associated with problematic responses to and poor recognition of emotions, whereas persons with the admiration variant could regulate emotions more effectively.

### *Psychopaths*

Higher levels of psychopathic traits were assiociated with increased brain tissue volumes in the left putamen, left ansa peduncularis, right superiomedial prefrontal cortex, left inferior frontal cortex, right orbitofrontal cortex, and right medial temporal regions, and reduced brain tissue volumes in the right middle frontal cortex, left superior parietal lobule, and left inferior parietal lobule (331).

## Substance Use Disorder

Adolescents with ED are at high risk for substance use and misuse disorder (SUD) (332). Adolescents with ED start misuse earlier, and transition more rapidly into SUD. Longitudinal studies identified externalizing symptoms in early adolescence predicting SUD in late adolescence and early adulthood [e.g., (333)]. Differences in brain cortical thickness have been described in association with problems of ED, inhibition, and behavioral control in female adolescents with SUD (334). Disturbance of the endocannabinoid signaling in the amygdala-prefrontal cortical circuit may lead to abnormalities in the processing of emotionally salient information, learning, and memory (335). ADHD has been identified as a risk factor for early substance use [e.g., (336)]. Disturbances of the circadian rhythm and sleep are associated with affect dysregulation, increased drug and alcohol misuse, and other risky behaviors in adolescents (337). Poor emotional control is related to the frequency of alcohol, marijuana and cigarette use in adolescence, mediated by proximal influences like exposure to negative experiences and social motives for substance use (332). Consistent with these observations, affect dysregulation is associated with a history of misusing various substances, including marijuana, alcohol, cocaine and downers (338, 339). This may indicate a general tendency to engage early in risky behaviors, being more susceptible to peer influences, or attempting to control emotions by substance use (340).

Although negative sequelae have to be feared, adolescents engage in binge drinking because they are emotionally, behaviorally, or cognitively dysregulated (113). Cortical thickness - to be specific, thinner dorsolateral prefrontal cortex and inferior frontal cortex in early adolescence - is predictive of binge drinking and externalizing symptoms in late adolescence (341). Theory and research about emotionally labile youth suggests that lacking of internal regulation resources is frequently associated with exposure to external maladaptive coping strategies, such as alcohol misuse (342). This is consistent with self-medication theories where consuming alcohol serves as a coping strategy for overcoming negative emotions (343).

Marijuana use (occasional, heavily increasing, chronic) is associated with ED, nicotine and alcohol abuse and dependency (344). Adolescents with poor ER strategies may be prone to regular use of marijuana (345, 346) that may impair cognitive abilities and emotional reactivity. Marijuana and alcohol use are associated with white matter disorganization, which in turn predicts ED (347, 348).

Nicotine dependence among adolescents is a widespread health concern (349). ED predicts adolescent smoking behaviors (342, 350), and SUD (351). High levels of distress combined with ED may predict smoking-naive adolescents to develop positive expectations about social acceptance with smoking. This may promote the decision to start smoking [e.g., (352, 353)]. Longitudinal data suggest that low levels of ER predict initial adolescent attempts to start smoking, as well as the transition to regular smoking (350). The higher the ED the higher the risk of smoking (338). Following the self-medication model of Khantzian (343), poor regulation of negative affect (especially of anger) increases the vulnerability to smoking and SUD [e.g.,

(354, 355)]. Adolescents may engage in cigarette smoking or substance use, in order to cope with anger-related distress (355). Personal motives, such as reducing negative affect, are among the most common reasons for cigarette smoking [e.g., (356–358)], a process that - besides nicotine dependency - reinforces and maintains smoking behavior (359). Padovano et al. (360) found high positive or negative arousal related to smoking relapse, again highlighting the importance of affective dysregulation as a risk factor for adolescent smoking. Therefore, smoking prevention and intervention programs for high risk adolescents should include practicing cognitive and behavioral ER strategies [e.g., Contextual Emotion-Regulation Therapy; (361)].

Recent studies identified ED as a mediator between drug abuse and SUD (184, 362). As an example, the (weak) opioid agonist, tramadol, is misused in order to enhance positive mood and to perceive pleasant emotions (363). Ghorbani et al. (137) suggested that lacking ER strategies may be related to heroin craving in individuals with heroin dependence who experienced a history of CT.

Prenatal cocaine exposure is associated with long-term dysregulation of arousal (364). Neuroimaging data confirm these observations by findings that prenatal cocaine exposure has deleterious long-term effects on the arousal regulation system (365).

## Developmental Disorders Including Autism Spectrum Disorder

Autism spectrum disorder (ASD) is defined as a neurodevelopmental disorder, characterized by impaired social communication and interaction as well as repetitive behaviors or restricted interests (31). ASD also goes along with various emotional and behavioral difficulties, such as ED (366–368). Although ED is not considered a core feature of ASD, the prevalence of ED in the context of ASD is up to 50 or 60% (369, 370), significantly higher than in other clinical disorders or in children with normotypical development (291, 369–376). In general, ER problems manifest especially in a more frequent use of maladaptive ER strategies, such as avoiding (377), or a less frequent or ineffective utilization of adaptive strategies for regulating emotional states (98, 367, 368, 378, 379). ED often leads to increased problems of social adaptation, school related problems (380, 381), higher rates of social and general anxiety (382–384), and other difficulties (385–387). Moreover, ED is associated with higher rates of repetitive behavior, communication and social skills deficiencies (370, 371). Owing to the intensifying effect of ED on ASD specific symptoms, various studies aimed at identifying predictors of this co-occurrence (366, 370, 371, 375, 380, 388–390).

Gadow et al. (380) described a modulating effect of dopaminergic polymorphisms on ED in the context of ASD. Fenning et al. (388) suggested problems of internalizing and generalizing parental ER strategies to promote ED in ASD patients. This assumption is supported by observations that parental scaffolding helps children in overcoming frustrating situations and in improving ER. Children with ASD seem to benefit less of this support (372, 388). Samson et al. (98, 379) found that therapy programs focusing on teaching adaptive ER strategies improved both, ED and ASD-related symptoms. There are also observations that pharmacotherapy with the ß-blocking agent, propranolol, acting on the consolidation of anxiety memories, improves problem-solving skills and ED in children with ASD (274). Thus, approaching ED may improve the complex association of ASD and ED (390–392).

The diagnosis of ED may be facilitated by using specific inventories. Mazefsky et al. developed and evaluated the Emotion Dysregulation Inventory for assessing deficient ER in the context of ASD (391, 392). Future research should focus on this interesting topic because specific diagnostic and therapeutic instruments are still scarce (370).

## Psychosis and Schizophrenia

Schizophrenia is considered a "severe and persisting brain disorder" (393) with psychotic symptoms that may occur as a single episode or (in the majority of cases) as recurrent chronic disorder. The lifetime prevalence of schizophrenia is ∼1%, children and adolescents having a lower risk of 0.018% (393–395). Schizophrenia usually goes along with intrusive thoughts, impaired cognitive functions, marked changes of personality, and symptoms of ED (97, 393, 396).

The clinical characteristics of schizophrenia are manifold, symptoms may be non-specific. Usually positive (such as hallucinations, delusions) and negative symptoms (such as affective flattening, avolition, catatonia) are distinguished (397). Symptoms are not exclusively characteristic for schizophrenia but have been refined since the development of the DSM-IV. Symptoms may vary with age and also depend on comorbid problems, such as affective dysregulation. Jerrell et al. (393) described symptoms of ED, especially in older adolescents needing in-ward treatment. ED has a moderating effect on the severity of schizophrenia associated "positive" symptoms, such as acoustic and optic hallucinations in relation to the severity of ED (398–400). In addition, subclinical changes of personality seem to be associated with more accentuated manifestations of ED. For example, pronounced schizotypal personality may be considered a subclinical stage of schizophrenia and associated with a higher risk of developing schizophrenia (401–405). This close relationship between ED and schizophrenia or schizotypal disorder suggests a genetic link for this co-occurrence (405). This could help improving the specificity and sensitivity of diagnostics of ED in schizophrenia, and especially in adapting multimodal treatment approaches individual needs (402).

## Gaming Disorder

The use of electronic media (computers, internet, video and mobile phone use) has dramatically increased in the last two decades, especially in children and adolescents. Daily electronic media use has increased to a mean of 7.4 h in 8–18 year old adolescents (406). The gain in entertainment and knowledge acquisition is opposed to reductions of real social and physical activities, and has a negative impact on physical and mental health. ER abilities also become compromised (407). Available data are, however, limited, especially for children and adolescents.

Adolescents having difficulties in regulating their emotions, are especially prone to problematic technology use (408, 409). The association between ED and problematic internet use (more than 4 h/day) is partly mediated by meta-cognitions in young adults (410). Donald et al. (411) found ED to be correlated to the amount of problematic internet use. Playing internet games is used to regulate unpleasant emotions. In addition, escapism is another important motivator for excessive gaming (412). Problematic internet use promotes ED, such as difficulties in recognizing emotions and goal setting.

In addition to problematic internet use, the use of video and computer games is also increasing. The median prevalence of internet gaming disorder is about 2% for children and adolescents (413). Excessive use of computer or video games leads to impairments or distress depending on the amount of activity. As early as in the preschool age, the presence of ED has been shown to be a predictor of media use and GD symptoms 5 years later (at about age 9) (414). Difficulties in impulse control and a limited access to emotions is associated with problem video gaming (415, 416). Wichstrom et al. (417) showed that ER deficits in 8 year olds predicted symptoms of internet gaming disorder at 10 years.

## Prevention and Treatment

In the following, we will describe meaningful preventive and therapeutic strategies for improving ER or ameliorating ED. Because of the complex background of ED, prevention and therapy will primarily focus on recognizing risk factors such as personality, familial and social conditions, underlying disorders, such as ADHD, affective or trauma related disorders and and their comorbidities. Especially familial factors will be susceptible to parental training, youth welfare support, and in case of not sufficiently improvable conditions, early placement in suitable foster families may be necessary.

Therapies for treating underlying disorders, such as medication for ADHD or affective disorders, for decreasing internal tension or improving stability and reactivity may be necessary. In addition, building-up or improving sensitivity and appropriate coping strategies in social or self-regulatory skills training will be beneficial (see below, section Treatment). In the following, we will describe specific measures and strategies that have proved to be successful.

### Prevention

Prevention of ED includes identifying risks and learning or applying appropriate measures in order to prevent damage. This has been shown e.g., by treatment of postpartum depression (418), positive parenting programs (419), or early placement in care families or adoption of children from maltreating families (cf. chapter Psychological Trauma). The results of such preventive measures to date are disappointing (too late, too inefficient, too many children missed) (420). In fact, only a few studies reported about effective prevention methods.

Adolescents attending alternative schools because of behavioral and emotional problems, and youth at odds with the law have difficulties in managing strong emotions. This may also concern their sexual behavior. Effective Human immunodeficiency virus (HIV) prevention programs for adolescents should include the training of keeping a cool head dealing with strong emotions in sexual relationships. Affect management skills for reducing the risk of HIV infection are comparable to techniques used in dialectical behavioral therapy (DBT), and have successfully been applied (421, 422).

Teachers working in schools with socially and economically disadvantaged children have been trained for improving their children's social skills and emotional self-regulation, to reduce their conduct problems, and involve the parents in their supporting role. Results indicate that teachers in the intervention group used more positive classroom management strategies, their students were better in applying social skills and emotional self-regulation, and had less conduct problems compared to the non-intervention control group (423).

Transdiagnostic interventions for internalizing disorders target common underlying mechanisms and may attract a larger proportion of these youths than concepts developed for single disorders (424). As an example, the recently developed CBT-based transdiagnostic prevention program, EMOTION (425) for internalizing disorders, includes techniques for improving children's ER skills, psychoeducation, behavioral activation, cognitive restructuring, building of a problem hierarchy and exposure to feared or until now avoided situations. The 10 weeks lasting program has been shown to improve children's ER skills.

Deplus et al. (426) tested an intervention adapted from mindfulness-based cognitive therapy aiming at enhancing self-regulation skills in adolescents. The nine sessions' program was well-accepted and increased self-reported mindfulness. In addition, depressive symptoms, impulsivity (dealing with urges, and lack of perseverance), and dysfunctional strategies of ER improved.

Guendelman et al. (427) extensively reviewed mindfulness-based therapies from a neurobiological, psychological and clinical perspective. They reported changes in ER based on clinical and functional data (e.g., decreased activation changes in the amygdala, hippocampus, anterior insula, anterior cingulate cortex), following mindful meditation even in novices. We found only one randomized trial (428) comparing hypnotherapy and self-care in juvenile post cancer patients, showing evidence for the efficacy of hypnosis in improving ER. Targeted real-time fMRI-neurofeedback, downregulating amygdala activation, may induce longterm improvements of ED in patients with PTSD, BPD and schizophrenia (429).

### Treatment

ED symptoms occur in many psychiatric disorders, often as promoting or comorbid condition. Since ED may significantly influence the development of children and adolescents, effective and available treatment is of utmost importance. Psychotherapy may be divided into four groups: (i) Dialectic Behavioral Therapy [reviewed by Courtney-Seidler et al. (430)], (ii) Behavioral and Cognitive Behavioral Therapy (including Schema Therapy) [recently reviewed by López-Pinar et al. (431)] in adults, (iii) multimodal treatment (including, e.g., parental interventions, pharmacotherapy, and others), (iv) other therapies, such

as analytic group therapy, hypnotherapy, neurofeedback, and others.

Garrett et al. (432) studied pre-post effects of 4 months psychotherapy in youth with ED and a risk of BD in an fMRI setting, presenting a facial expression task. At baseline they found hypoactivation of the dorsolateral prefrontal (DLPFC) and posterior cingulate cortex compared to matched healthy controls.

Following treatment, activation of the DLPFC increased, and decreased in the amygdala, paralleling the improvement of symptoms.

Dixius and Möhler developed a low threshold program START showing positive impact on ER in traumatized teenagers (433). Thornback and Muller (91) investigated the relationship between improvement of ER and improvement of trauma related symptoms in children receiving trauma focused cognitive behavior therapy: improvement in ED was associated with improvement in the child's internalizing, externalizing, and PTSD symptoms. Mindfulness based group therapy can improve ER in children with ADHD (41, 434).

Because ED is very common, especially in children and adolescents (although only in the focus in the last decade), various treatment options primarily concentrate on this dimension (426, 435–444).

Mode Deactivation Therapy [MDT; (436, 438)], and Modular Approach to Therapy for Children with Anxiety, Depression, Trauma, or Conduct Problems [MATCH; (443)] were particularly effective. MATCH, a cognitive behavioral therapy, improves ED faster than other programs. Apsche et al. (436) and Bass & Apsche (438) described an extended version of cognitive behavioral therapy (MDT) superior to conventional cognitive behavioral therapy, especially in reducing anger and aggressive behavior in adolescents and juvenile offenders (435) (see **Tables 1**, **2**). Since up to 90% of children with ED meet criteria for a categorized disorder (441), a number of treatments are available for treating the primary disorder. Most therapies also help in improving ED (91, 100, 164, 210, 258, 430, 432, 445–448, 450–457). Only the Light Therapeutic Procedure (447), and the Emotion Regulation Training (ERT) for adolescents with BPD (455) showed no improvement (for details, see **Tables 1**, **2**).

**Tables 1**, **2** summarize evaluated therapies focusing on ED. The tables are organized depending on ED being the primary therapeutic target (**Table 1**) or, if the underlying disease was the primary, and treatment of ED the secondary target (**Table 2**). The order of the listed studies is alphabetical according to the name of the first author of the respective study.

### *Pharmacotherapy*

ED leads to psychopathology and a number of externalizing and internalizing symptoms, including anxiety, mood dysregulation, impulsiveness, behavioral issues, and serious debilitating social problems. Two forms of stress related sequelae have to be considered: (i) acute emotional cues triggering experiential, behavioral, central and peripheral physiological systems (458), and (ii) chronic mental stress resulting from continuous burdens, such as maltreatment or familial discord, leading to personality modification, ED, and related problems.

To date, there is no substance available for a causal treatment of ED. Among the available pharmaceuticals, the following classes of medication have been shown to alleviating symptoms of ED:

- Antipsychotics - sedating and distancing from mental tension (459, 460)
- Antidepressants and mood stabilizing medication - alleviating anxiety, improving mood, and decreasing maniac symptoms (458, 461)
- Sedatives/anxiolytics - sedating and alleviating anxiety
- ADHD Medication (55, 462)
- Combined medication (463)
- Experiential therapies, such as oxytocin (464)

### *Other Therapies*

fMRI neurofeedback produces promising lab results for improving ER by changing the bloodflow to the amygdala, and the interconnection between the amygdala and the prefrontal cortex in patients with BPD (429, 465), MDD (466), or PTSD (467). The disadvantages lie in the poor availability and the complexity of the technology. Relaxation and mindfulness based therapy have been shown to reduce chronic stress activation interacting with the impaired threat perception of ED (468). Biofeedback has been shown to produce relaxing, threat and stress reducing effects within a short training time, depending on the patients' hypnotic ability (469). There are, however, only a few uncontrolled observational studies and single case reports supporting this approach.

Early parenting programs are effective in preventing or changing unfavorable environmental conditions. These programs focus on sensitivity, acceptance, making aware and avoiding self-defeating strategies, such as harsh educational measures, and help in improving empathic understanding, clarity, fairness, decision making, and coming to a decision (22). There are, however, reports of failing parenting programs [e.g., (470)], possibly related to the timing of the intervention and the already established dysfunctions on both sides, the caregivers and the children.

## DISCUSSION

ED influences most child and adolescent psychiatric disorders by interfering with cognitive processes that interact with reactive processes. In some disorders, such as ADHD, psychosis, or affective disorders, ED is an essential but often neglected part of the related pschopathology.

Several mechanisms lead to the development of ED, with reference to anatomical, functional, family, social and relational bases. This causes severe stress, misunderstandings, relationship-difficulties, maladaptive ER strategies such as self-injurious behavior, externalizing and internalizing responses, endangerment of self, self-perception and social relationships.

The relationship between ED and nosology according to ICD or DSM has not been clarified as yet. The further development of this topic raises more questions than answers:

- Is ED the lowest common denominator of psychological disorders?

**TABLE 1 |** Clinical trials focusing on ED as primary target.

| References | A: primary target, B: secondary target | Treatment | Age groups participants (n) | Results |
|---|---|---|---|---|
| Apsche et al. (436) | A: ED, B: - | MDT vs. CBT | Male adolescents (14–18 years) $n = 84$ | MDT was more effective than CBT for the treatment of externalizing and internalizing disorders & ED. MDT especially reduced the dysregulation of anger and aggression in male adolescents to a greater extent |
| Bass et al. (438) | A: ED, B: - | MDT | Male adolescents (14–18 years) $n = 84$ | Replication of findings of Apsche et al. (436) |
| Deplus et al. (426) | A: ED, B: Depression; impulsive behavior | Mindfulness-based CT | Adolescents (11–19 years) $n = 21$ | Reduction of depressive symptoms, impulsive behavior and ED |
| Dixius and Möhler (433) | A: ED B. PTSD | START | Adolescents (13–17) $n = 66$ | Treatment significantly improved emotional regulation |
| Döpfner et al. (441) | A: ED, B: - | ADOPT | children (8–12 years) $n = 597$ | Versions of ADOPT (i.e., ADOPT online/institution etc.) were associated with an improvement of ED symptoms |
| Ducharme et al. (437) | A: ED, B: - | DBT, CBT | Children & adolescents (9–17 years) $n = 37$ | Reduction of anger scores caused by decrease of ED |
| Evans et al. (443) | A: ED, B: - | Match (BT) vs. other treatments | Children & adolescents (7–13 years) $n = 175$ | General improvement of ED symptoms. MATCH led to faster decrease of ED compared to other standard treatments; ES = 0.49 |
| Pardo et al. (444) | A: ED, B: impulse control disturbance | DBT | Adolescents (Ø = 15.4 years) $n = 20$ | General improvement of ED and symptoms of impulse control. Qualitative reports of adolescents: positive statement of adolescents who terminated the treatment program |
| Ravindran et al. (439) | A: ED of parents, B: - | MFWSB | Parents of children (4–8 years) $n = 84$ | Reduction of ED only in mothers of children |
| Simpson et al. (442) | A: ED, B: - | Mindfulness-Based Intervention | male incarcerated youth (18–21 years) $n = 48$ | Improvement of ED, sleeping quality, stress-level etc.; ES (impulsivity) = 0.72, ES(mental well-being) = 0.50, ES (inner resilience) = 0.35, ES (mindfulness) = 0.32 |
| Thoder and Cautili (435) | A: ED, B: - | MDT | Juvenile offenders (14–17 years) $n = 39$ | Decrease of internalizing and externalizing symptoms (i.e., ED). Reduction of aggressive and delinquent behavior. Positive effects on relapse risk |
| West et al. (440) | A: ED, B: - | Sensory room | Adolescents (12–18 years) $n = 112$ | Reduction of stress level, especially aggressive behavior, general improvement of ED symptoms |
| Winiarski et al. (445) | A: ED, B: - | MST | Adolescents (12–17 years) $n = 180$ | Decrease of physiological and behavioral indicators of ED, significant differences between male and female adolescents: females had higher responder-rates |

*ADOPT, Affective Dysregulation–Optimizing Prevention and Treatment; BT, Behavioral Treatment; CBT, Cognitive Behavioral Treatment; DBT, Dialectic Behavioral Treatment; ERIC, Emotion Regulation and Impulse Control Treatment; ERT, Emotion Regulation Training; ES, effect size; IGST, Individual / Group Supportive Therapy; MATCH, Modular Approach to Therapy for children with anxiety, Depression, Trauma or Conduct Problems; MDT, Mode Deactivation Therapy; MFWSB, More Fun with Sisters and Brothers; MIT-G, Metacognitive Interpersonal Therapy in Groups; MMT, Mindfulness Meditation Therapy; MST, Multisystemic therapy; START, Stress-Trauma-Symptoms-Regulation-Treatment; TAU, Treatment as Usual.*

- How specific is its predictive value for explaining psychological disorders? Or does it rather sum up to one single concept concerning all psychological disorders?
- Would it therefore be the "Grand Unifying Theory" of psychological disorders?

ED may possibly be a new concept, allowing psychological disorders to be defined by their essential nature instead of being defined by their phenotype and objectively measured symptoms. ER and emotion processing would be more meaningful than single well-defined symptoms. It would render the individual personality and the dynamics of social relationships and communication more understandable.

As part of the health care system, many hospitals and psychotherapists are required to provide ICD-10 or DSM-5 diagnoses. These symptom-based and descriptive nosologies are useful for improving the accuracy and consistency of clinical diagnostics and form the basis for effective treatments.

Other transdiagnostic approaches can be seen as a very good supplement to traditional categorical diagnoses using the DSM or ICD thesauri. The approach of systemic therapy, for example, sees psychological symptoms, disorders, and their change, embedded in interactive and narrative structures.

Another very significant transdiagnostic approach are the Research Domain Criteria (RDoC) (471). Fernandez et al. proposed conceptualizing ER as a new, sixth domain in the RDoC matrix (472).

It is argued that in order to understand causes and mechanisms of mental disorders, many clinical symptoms can be

**TABLE 2 |** Clinical trials focusing on ED as secondary target.

| References | A: primary target, B: secondary target | Treatment | Age groups participants (n) | Results |
|---|---|---|---|---|
| Adrian et al. (450) | A: NSSI & suicidality, B: ED | DBT vs. IGST vs. other treatments | Adolescents (Ø = 14.89 years) $n = 99$ | DBT appears to be more effective for the treatment of suicidal adolescents with higher levels of ED than IGST |
| Bjureberg et al. (210) | A: NSSI, B: ED | ERITA online (BT) | Adolescents (13–17 years) $n = 25$ | After treatment reduction of NSSI and ED in adolescents & improvement of parental adaptive behavior ES (past month NSSI frequency) = 0.88, ES (global functioning) = 1.01, ES (ED) = 0.75, ES (NSSI versatility)= 0.63 (number of different types of NSSI behaviors) |
| Blader et al. (447) | A: ADHD, B: DMDD | Family-based BT | Children (6–13 years) $n = 156$ | Reduction of DMDD symptoms. Decrease of aggressive behavior in 51% |
| Bogen et al. (448) | A: Depression, B: ED | Light therapy | Adolescents (12–17 years) $n = 57$ | No improvement of ED, but ED could eventually be enhanced by amelioration of sleep & circadian rhythm; partial $Eta^2$(sleep quality) = 0.02, partial $Eta^2$(restorative sleep) = 0.09, partial $Eta^2$(circadian preference) = 0.22 |
| Boutelle et al. (258) | A: Eating Disorder, B: ED | PEER (BT) | Adolescents (13–17 years) $n = 53$ | Significant reduction of emotional eating situations. Trend toward reduction of ED; ES = 0.32 |
| Ford et al. (449) | A: PTSD, B: ED | TARGET vs. ETAU | Female delinquent adolescents (13–17 years) $n = 59$ | Both therapies reduced anxiety, anger, depression, and posttraumatic cognitions (medium effect sizes). Interaction effect between TARGET and time with respect to PTSD, anxiety, posttraumatic cognitions, and emotion regulation |
| Ford et al. (473) | A: PTSD, B: ED | TARGET | Detained adolescents (11–16 years) $n = 394$ | TARGET was associated with fewer disciplinary incidents and seclusion |
| Garrett et al. (432) | A: Depression/Mania, B: ED | Multimodal therapy | Adolescents (13–17 years) $n = 24$ | Improvement of mood dysregulation was associated with increased activation in DLPFC, decreased activation in amygdala, and reduced maniac symptoms; ES(maniac symptoms) = 0.59, ES(CDRS) = 0.56 |
| Goldstein et al. (451) | A: Bipolar Disorders, B: ED | DBT | Adolescents (12–18 years) $n = 10$ | Significant improvement of all symptoms (NSSI, suicidality, depressive, maniac, and ED symptoms) ES(ED) = 0.3 |
| Heinrich et al. (452) | A: ADHD, B: ED | Neuro-feedback | Children (8–12 years) $n = 30$ | Improvement of ED symptoms & cognitive and behavioral dysregulation. Decrease of ADHD specific symptoms, |
| Kaufman et al. (453) | A: Self-injury, B: ED | DBT | Female adolescents (13–17 years) $n = 60$ | Reduction of self-injury and ED symptoms |
| Kiani et al. (434) | A: ADHD, B: ED & executive functions | MMT | Female adolescents (13–15 years) $n = 30$ | Improvement of ED symptoms and executive functions scores ES = "large" |
| Marco et al. (454) | A: ODD, B: ED | DBT | Female adolescents (12–18 years) $n = 2$ | Reduction of impulsive behaviors, maladaptive ER strategies |
| Marrow et al. (474) | A: PTSD, B: ED | TAU & trauma training for staff (CG) vs. TAU & environmental modifications (trauma training for staff, trauma affect regulation) (EG) | Detained adolescents (11–19 years) $n = 74$ | Significant reduction in depression, threatening of staff, use of physical restraints, seclusion rates in the intervention program |
| McCauley et al. (164) | A: suicidality & NSSI, B: ED | DBT | Adolescents (12–18 years) $n = 173$ | Improvement of all outcomes: Decrease of NSSI, risk of lifetime suicide attempt and ED; ES (end of active treatment) = 0.34, ES (end of follow up) = 0.11 |
| Popolo et al. (446) | A: Personality disorder, B: ED & Alexithymia | MIT-G | Adolescents & young adults (16–25 years) $n = 17$ | Improvement of specific symptoms of personality disorder and of functioning. Reduction of ED symptoms; ES(different symptoms) = 0.14–1.17 |
| Schuppert et al. (455) | A: BPD, B: ED | ERT vs. TAU | Adolescents (14–19 years) $n = 43$ | ERT had no additional effect on symptoms of BPD (including ED). Only TAU (medication, psychotherapy, systemic therapy …) improved BPD-symptoms (including ED) |

*(Continued)*

**TABLE 2** | Continued

| References | A: primary target, B: secondary target | Treatment | Age groups participants (n) | Results |
|---|---|---|---|---|
| Sharma-Patel et al. (100) | A: PTSD, B: ED | Tf-CBT | Children & adolescents (4–17 years) $n = 118$ | Decrease of PTSD symptoms (ED included) |
| Sloan et al. (456) | A: SAD, B: ED & Anxiety & Depression | ERIC | Adolescents & young adults (16–20 years) $n = 79$ | Significant reduction of ED in 60%, significant decrease of depression and anxiety ratings in 50–60%; ES= −0.53 |
| Suveg et al. (457) | A: Anxiety disorders, B: ED | CBT | Children & adolescents (7–15 years) $n = 37$ | Significant reduction of anxiety symptoms, improvement of ED and coping strategies for only one emotion ("worry"); ES = 0.82 |
| Thornback and Muller (91) | A: PTSD, B: ED | Tf-CBT | Children (7–12 years) $n = 107$, 44 at follow up | Significant reduction of PTSD symptoms, decrease of the use of maladaptive ER strategies. ED was the best predictor for improvements of PTSD symptoms; ES (pre treatment to 6 months follow up) = 0.36 |

*BT, Behavioral Treatment; CBT, Cognitive Behavioral Treatment; Tf-CBT, Trauma-focused Cognitive Behavioral Treatment; CDBT, Dialectic Behavioral Treatment; CDRS, Children's Depression Rating Scale Revised; ERIC, Emotion Regulation and Impulse Control Treatment; ERITA, Emotion Regulation Individual Therapy for Adolescents; ES, effect size; ERT, Emotion Regulation Training; ETAU, Enhanced Treatment as Usual; IGST, Individual/Group Supportive Therapy; MATCH, Modular Approach to Therapy for children with anxiety, Depression, Trauma or Conduct Problems; MDT, Mode Deactivation Therapy; MFWSB, More Fun with Sisters and Brothers; MIT-G, Metacognitive Interpersonal Therapy in Groups; MMT, Mindfulness Meditation Therapy; PEER, Preventing Emotional Eating Routines; TARGET, Trauma Affect Regulation, Guide for Education and Therapy; TAU, Treatment as Usual; Tf-CBT, Trauma-focused Cognitive Behavioral Treatment.*

viewed as being caused by emotionally dysregulated processes. In this way, the underlying structure of the mental disorder can be captured better (at least complementarily) than by a pure ICD or DSM approach. In the area of interventions, treatments that target common features of multiple disorders should be developed on this basis. ED is to be considered as such a common feature.

ER and ED concepts are relatively new on the agenda, therefore, specific treatments are still under development – including child and adolescent psychotherapies, positive parenting initiatives, sedating and mood stabilizing medication. To date no causal pharmacologic treatment is available. Research in patients with ASD suggests that oxytocin might be a candidate for future treatment options. Available treatment tools, such as CBT, DBT or mindfulness training need to be explored and evaluated more extensively.

Our narrative review, although carefully prepared and elaborated, bears the limitations of subjective selection of references and setting of priorities. The explained search strategy is not sufficient to conduct a systematic review because considerable heterogeneity in the definitions used by researchers and the possible variants of the label are not taken into account. Moreover, the review was apparently not conducted following PRISMA guidelines, as usually requested and expected, and the search was not preregistered on an international database of systematic reviews such as PROSPERO. Due to the complexity of the association of ED with numerous mental disorders, a systematic literature review as well as work based on the PRISMA criteria was not feasible. On the other hand, this review covers a very broad spectrum of major psychiatric disorders in general, rather than a specific one.

In addition, our review includes a limited age range of children and adolescents between 2 and 17 years. Therefore, ED in infancy has not been covered in this review.

Our review sheds light on a central topic of individual and social functioning that to date has been more regarded in its dysfunctional aspects of single psychiatric disorders. The concept of ED will probably help in discovering basic approaches to the understanding, diagnosis and treatment of psychiatric disorders especially in children and adolescents but will probably also prove a key issue in adult psychiatry.

## DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. We searched the literature databases ERIC, PsycARTICLES, PsycINFO and PSYNDEX on June 29th, 2020 for peer reviewed articles, published in English language in between January, 2000 and June, 2020, and related to children and adolescents (2–18 years).

## AUTHOR CONTRIBUTIONS

FP: idea, conceptualization, structure of the work, preparations, literature analysis, methods section, several chapters, tables, the figure, corrections, and discussion. SO: several chapters, tables, and corrections. EM and PP: corrections and discussion. CP: several chapters, structure of the work, tables, literature, corrections, and discussion. All authors contributed to the article and approved the submitted version.

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## SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2021.628252/full#supplementary-material

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# Development and Initial Validation of the Disruptive Mood Dysregulation Disorder Questionnaire Among Adolescents From Clinic Settings

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**Objectives:** Disruptive mood dysregulation disorder (DMDD) is a new DSM-5 diagnosis. It is observed in youths and is characterized by chronic irritability and temper outbursts. This study aimed (i) to develop a brief questionnaire administered during a semi-structured interview and (ii) to assess its psychometric properties with adolescents 12–15 years old by estimating its internal consistency and its concurrent association with measures of depressive symptoms and borderline personality traits.

**Methods:** A 10-item questionnaire was developed based on the DSM-5 criteria and input from mental health professionals. The questionnaire was administered to 192 adolescents from youth centres, inpatient units and specialized outpatient clinics in Montreal, as were the Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS-PL), the Abbreviated version of the Diagnostic Interview for Borderlines revised (Ab-DIB), and the Dominic Interactive for Adolescents-Revised (DIA-R).

**Results:** A DMDD Questionnaire among adolescents from clinic settings is obtained. The content of the instrument's items was initially developed based on DSM-5 criteria and expert judgment to ensure that this new instrument covered the theoretical concepts of DMDD in English and French. Twelve participants (6.3%) met nine or more criteria and 11 youths (5.7%) met the three main criteria of DMDD (A, C, and D), which suggested the likely presence of DMDD. The total Cronbach's alpha was 0.90. In addition, the DMDD Questionnaire was significantly associated with depressive symptoms and borderline personality traits.

**Conclusion:** The reliability and concurrent validity indices suggest that the questionnaire as a decision-support tool may be used with adolescents in clinical settings. It highlights that the DSM-5 DMDD criteria seem associated with depressive symptoms and borderline personality traits. Finally, future studies will be necessary to establish more robust calculations in relation to the validity and reliability of this questionnaire.

**Keywords: adolescents, psychometric, disruptive mood dysregulation disorder, depression symptoms, borderline traits**

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**TABLE 1 |** DSM-5 diagnostic criteria for DMDD and DMDD Questionnaire items.

| DSM-5 criteria | Item number | Description of diagnostic criterion and item |
|---|---|---|
| $A_1$ | 1 | Severe recurrent temper outbursts manifested verbally and/or behaviourally. |
| $A_2$ | 2 | These outbursts are grossly out of proportion in intensity or duration to the situation or provocation. |
| B | Not assessed | The temper outbursts are inconsistent with developmental level. |
| C | 3 | The temper outbursts occur, on average, three or more times per week. |
| $D_1$ | 4 | The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day. |
| $D_2$ | 5 | This mood is observable by others. |
| $E_1$ | 6 | Criteria A–D have been present for 12 or more months. |
| $E_2$ | 7 | There has not been a period lasting three or more consecutive months without all of the symptoms in Criteria A–D. |
| $F_1$ | 8 | Criteria A and D are present in at least two of three settings (at home, at school, with peers). |
| $F_2$ | 10 | These criteria are severe in at least one of these settings. |
| G | Assessed pre-administration | The diagnosis should not be made for the first time before age 6 years or after age 18 years (condition met by virtue of age of target client group) |
| H | 9 | The age of onset of Criteria A–E is before 10 years. |
| I | Not assessed | Exclusion criterion: presence of all the symptoms of a manic or hypomanic episode for more than 1 day. |
| J | Not assessed | Symptoms not better explained otherwise. |

*This diagnosis cannot co-exist with oppositional defiant disorder, intermittent explosive disorder, or bipolar disorder.*

## INTRODUCTION

Disruptive mood dysregulation disorder (DMDD) is a condition characterized by chronic irritability observed in youths 6–18 years of age. Temper outbursts and emotional dysregulation are common reasons for seeking child and adolescent psychiatric and psychological consultations. However, what sets DMDD apart is the frequency and severity of the outbursts (at least three times a week) and the persistence of negative affect practically all day and every day (1). The American Psychiatric Association (2) classified DMDD as a depressive disorder and has indicated that it affects 2–5% of children and adolescents in the general population. For a diagnosis to be made, all of the DSM-5 criteria listed in **Table 1** must be present.

A link has been observed between DMDD and unipolar depression. Young people with DMDD generally develop unipolar depressive disorders or anxiety disorders as they move through adolescence into adulthood (3–5). In this regard, Copeland et al. (6) noted a co-occurrence between DMDD and depression among young people 2–17 years old (odds ratios between 9.9 and 23.5). Besides, the relationship between DMDD and borderline personality traits as defined under the DSM-5 has yet to be investigated in adolescents. This link makes sense considering the central role of emotional dysregulation suggested by the biosocial model of the development of borderline personality (7). Although this model does not refer directly to the concept of DMDD, hypersensitivity and intense reactions to emotional stimuli are key components of this personality disorder. In this regard, Glenn and Klonsky (8) observed a significant association ($r = 0.54$) between a measure of emotional dysregulation and borderline personality traits among young adults. In short, it would be interesting to explore the relationship between DMDD and, respectively, depressive symptoms and borderline personality traits to reflect on the matter further.

Furthermore, Mürner-Lavanchy, Kaess (9) recently published a systematic review of existing measures of DMDD. They noted that there was no gold standard for assessing the disorder. However, the authors indicated that the DMDD module created in 2016 by Kaufman, Birmaher (10) included in the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS-PL) had been used in 25% of the studies of DMDD, making it the most popular measure to date. To our knowledge, however, only one study measured the module's validity. In fact, Unal, Oktem (11) examined the concurrent validity between a clinical psychiatric interview based on DSM-5 diagnostic criteria ($\kappa = 0.70$) and the Turkish version of the K-SADS-PL ($\kappa = 0.63$). Consequently, we cannot consider the DMDD module of the K-SADS-PL a validated measure solely on this basis. Moreover, the K-SADS-PL remains a time-consuming instrument used mainly for research purposes. Consequently, it would be useful to have a short clinical decision-support instrument, based on the DSM-5 criteria for DMDD, for use before or during a classic psychiatric evaluation.

It need be underscored, also, that DMDD studies to date have focused on psychometric instruments completed by parents (12–15). According to Achenbach, McConaughy (16), however, there exists a reporting bias associated with children's informants (parents, peers, teachers). Examining the answers given by mothers and their children 6–23 years old in the context of the latter's psychiatric evaluation, Weissman (17) found that the former tended to underestimate symptoms, compared with the latter. Other researchers have specified that such underestimation occurred primarily when children presented symptoms of internalizing disorders (18). This is why some authors have suggested that, with children 10 years and over, instruments based on child and adolescent report should be included as part of their psychological evaluation (16, 19, 20). Consequently, it would be useful to develop a questionnaire for assessing DMDD symptoms reported by adolescents themselves in addition to one completed by their legal guardians.

Against this background, we undertook a study aimed at further developing the DMDD Questionnaire and assessing its psychometric properties among adolescents 12–15 years old from clinical settings. From a psychometric point of view, this is the first step in the validation of a decision-support tool for screening adolescents for DMDD (21, 22). Two objectives were formulated:

(1) to develop a brief questionnaire administered during a semi-structured interview and (2) to assess its initial psychometric properties with adolescents 12–15 years old by estimating its internal consistency and its concurrent association with measures of depressive symptoms and borderline personality traits.

# MATERIALS AND METHODS

## Participants

The DMDD Questionnaire was administered to adolescents in Montreal from 2011 to 2014 as part of a cross-sectional study of the psychometric properties of the French and English versions of the Dominic Interactive for Adolescents–Revised (DIA-R). The initial sampling plan of this study aimed at recruiting a sufficiently large convenience sample, which included a school subsample and a clinic subsample, to obtain accurate estimates to determine the instrument's reliability by age, sex and language subgroups and its criterion-related validity (20). Adolescents had to meet two inclusion criteria to participate: be 12–15 years old and speak French or English. The respondent parent, too, had to understand and speak French or English to complete the ethical consent form. Sight- and hearing-impaired adolescents were excluded, as were those with severe intellectual or learning disabilities (20). The sample comprised 447 adolescents living in the Greater Montreal Area: 243 adolescents (130 French speaking, 113 English speaking) selected in regular classrooms at four high schools reflecting a wide array of socioeconomic levels and 204 adolescents (171 French speaking, 33 English speaking) from two youth centres and specialized psychiatric clinics, inpatient units, and day treatment centres at three hospitals. These clinical settings provided services for adolescents from families with different cultural and socioeconomic backgrounds. Because the DMDD Questionnaire was designed for clinical purposes, we ran statistical analyses only on the subsample of adolescents recruited in clinical settings. Participants with missing data ($n = 12$) were excluded. As a result, the convenience sample considered in the analyses consisted of 192 adolescents. The percentages of adolescents by age, sex and language subgroups remained quite similar after these 12 were excluded (see descriptive statistics).

## Primary Measure: DMDD Questionnaire

The *DMDD Questionnaire* (**Figure 1**) was developed at the Research Centre of the Rivière-des-Prairies Mental Health Hospital. As shown in **Table 1**, work regarding the questionnaire's content validity led to the creation of an algorithm to establish correspondence between the questionnaire's items and some of the DSM-5 criteria (A, C, D, E, F, G, and H). It should be noted that some criteria were split in two so that questions could be as simple as possible. It should be noted, also, that exclusion criteria were omitted, namely, criteria B, I, and J, for the sake of brevity. The DMDD Questionnaire is composed of 10 yes/no questions. If the answer to the first question is "yes," then the nine other questions are asked. However, if the answer to the first question is "no," the subsequent questions are not completed and "no" is indicated throughout (except at question 7, which is an inverted item). Thus, the DMDD Questionnaire, which covers seven DSM-5 criteria, yields a continuous score ranging from 0 to 10. Each yes (except for the inverted item 7) adds a point to the total. The higher the score, the higher the likelihood of DMDD.

## Reference Measures

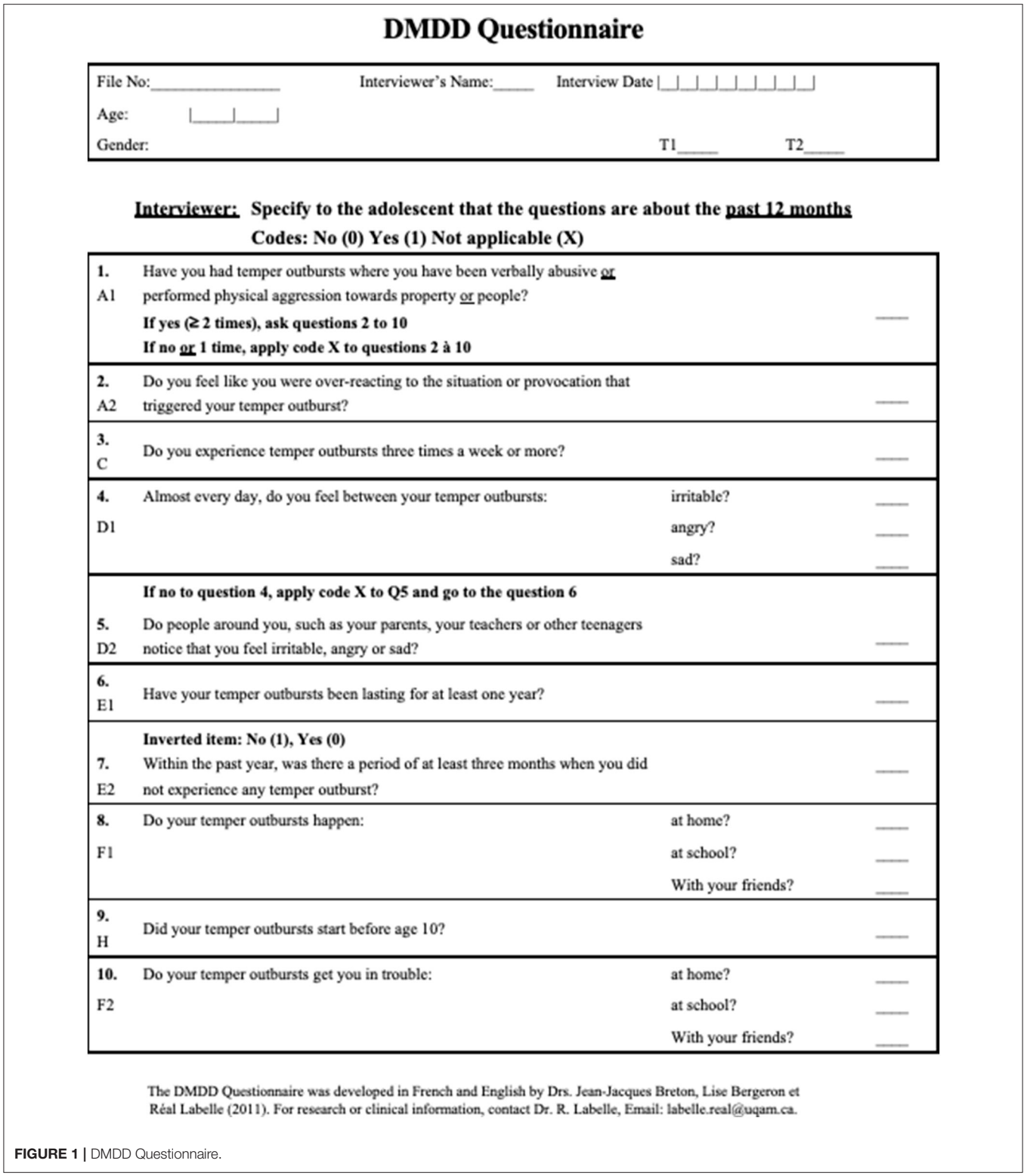
The Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS-PL) is a semi-structured interview widely used in psychiatry to assess the mental disorders most common among 7- to 17-year-olds. Given that the DSM-5 version of the instrument with the DMDD module was not yet available at the time of our study (10), the *Present and Lifetime* version (1997) of the child-report instrument was used (23). However, changes proposed by the DSM-5 were taken into account during interviews (20). The instrument possesses moderate-to-high test-retest reliability ($K = 0.63$–$0.90$) and almost perfect inter-rater reliability (93–100%) (23). In the psychometric study of the DIA-R, the English and French versions of the K-SADS-PL were used to assess the adolescents' perception of their symptoms for nine disorders in the past 6 months. In our study, we examined the relationship between the DMDD Questionnaire and depression based on the criteria score.

The Abbreviated version of the Diagnostic Interview for Borderlines revised (Ab-DIB) is a 26-item self-report questionnaire for examining borderline personality traits in the past year. Scores range from 0 to 52. Its reliability and criterion validity have been investigated among suicidal adolescents 14–17 years old (24). Reliability coefficients were $\geq$0.80. Compared with the Diagnostic Interview for Borderlines–Revised, the Ab-DIB demonstrated an AUC of 0.87 (24). Although the Ab-DIB was previously used with older adolescents, preliminary analyses in the main study of the DIA-R yielded alpha coefficients $\geq$0.80 for all age (12–13 years, 14–15 years), sex, and language subgroups (20).

The Dominic Interactive for Adolescents–Revised (DIA-R) is a 121-item pictorial computerized self-report questionnaire for adolescents based on DSM-5 diagnostic criteria (20). It allows clinicians to screen for major mental health problems, including depressive symptoms and borderline personality traits, based on symptom and criteria scores. The color pictures present Dominic as a function of the respondent's sex and ethnicity (Caucasian, Hispanic, African American, or Asian). Adolescents respond by clicking "Yes" or "No" on the screen. For the total sample, Cronbach alpha coefficients were $>$0.80 for the major depressive disorder scale and $\geq$0.75 for the borderline personality traits scale (20). Moreover, for the total sample, the test-retest estimates of reliability (ICCs) ranged from 0.75 to 0.94 for specific scales. Regarding the criterion-related validity, ROC analyses were completed in the course of the main study. The AUCs for the major depressive disorder scale and for the borderline personality traits scale were both 0.91 (20).

## Ethical Considerations

The Institutional Review Board of the Rivière-des-Prairies Mental Health Hospital (CIUSSS du Nord-de-l'Île-de-Montréal) approved the research protocol of this study. All participants and their parents gave their written informed consent.



# DMDD Questionnaire

File No:_____ Interviewer's Name:_____ Interview Date |__|__|__|__|__|__|__|__|

Age: |____|____|

Gender: T1____ T2____

**Interviewer: Specify to the adolescent that the questions are about the past 12 months**

**Codes: No (0) Yes (1) Not applicable (X)**

| | | | |
|---|---|---|---|
| **1.** A1 | Have you had temper outbursts where you have been verbally abusive or performed physical aggression towards property or people? **If yes (≥ 2 times), ask questions 2 to 10 If no or 1 time, apply code X to questions 2 à 10** | | ____ |
| **2.** A2 | Do you feel like you were over-reacting to the situation or provocation that triggered your temper outburst? | | ____ |
| **3.** C | Do you experience temper outbursts three times a week or more? | | ____ |
| **4.** D1 | Almost every day, do you feel between your temper outbursts: | irritable? | ____ |
| | | angry? | ____ |
| | | sad? | ____ |
| | **If no to question 4, apply code X to Q5 and go to the question 6** | | |
| **5.** D2 | Do people around you, such as your parents, your teachers or other teenagers notice that you feel irritable, angry or sad? | | ____ |
| **6.** E1 | Have your temper outbursts been lasting for at least one year? | | ____ |
| | **Inverted item: No (1), Yes (0)** | | |
| **7.** E2 | Within the past year, was there a period of at least three months when you did not experience any temper outburst? | | ____ |
| **8.** F1 | Do your temper outbursts happen: | at home? | ____ |
| | | at school? | ____ |
| | | With your friends? | ____ |
| **9.** H | Did your temper outbursts start before age 10? | | ____ |
| **10.** F2 | Do your temper outbursts get you in trouble: | at home? | ____ |
| | | at school? | ____ |
| | | With your friends? | ____ |

The DMDD Questionnaire was developed in French and English by Drs. Jean-Jacques Breton, Lise Bergeron et Réal Labelle (2011). For research or clinical information, contact Dr. R. Labelle, Email: labelle.real@uqam.ca.

**FIGURE 1 |** DMDD Questionnaire.

## Statistical Analyses

All analyses were run on the IBM SPSS Statistics 23 application. First, descriptive analyses were carried out to see how the sample was distributed over the questionnaire scores and criteria. Then, Cronbach's alpha coefficient (25) and its confidence intervals (26) were calculated to verify the internal consistency of the DMDD Questionnaire (22, 27). A coefficient $\geq$0.70 suggests acceptable internal consistency (28, 29). Finally, Pearson's correlation

coefficients were calculated between the DMDD score and the scores obtained for depressive symptoms and borderline personality traits. The statistical power test showed that these analyses reached the recommended power (80%) to detect medium or large effects as defined by Cohen (30).

# RESULTS

## First Objective

The DMDD Questionnaire was developed in 2011 by Breton, Bergeron and Labelle (31). Their objective was to construct a decision-support tool for the psychiatric evaluation of children with both behavioral and emotional symptoms. Moreover, they wanted to collect data on this new and controversial diagnosis. They took the criteria proposed by the DSM-5 Task Force and formulated them in the form of simple questions to be put directly to adolescents during an interview. The questionnaire comprises ten "yes/no" questions. It may be administered by a nurse, a psychologist or a trained research assistant and allows the interviewer to clarify time frames and provide synonyms and examples, if needed. The questions were initially drafted in English by Breton using the same wording as that used by the Task Force in their criteria. Then, Breton, Bergeron and Labelle (31) each drafted and revised a French version and a consensus was reached on the final formulation of each question. Finally, a professional translator was tasked with verifying the equivalence between the French and the English versions. This questionnaire has been presented in **Figure 1**.

## Second Objective

### Descriptive Statistics

The clinic sample was composed of 56 youths (29.2%) 12 or 13 years old and 136 youths (70.8%) 14 or 15 years old. There were more girls (55.2%) than boys (44.8%) and more French speakers (85.4%) than English speakers (14.6%). In this sample, 41.7% of the adolescents answered "no" to the first question on the questionnaire and therefore did not complete the remaining questions. Conversely, two adolescents (1%) met all the criteria measured by the DMDD Questionnaire and obtained a score of 10/10. Twelve participants (6.3%) met nine or more criteria and 11 (5.7%) met the three main criteria of DMDD (A, C and D), which suggested the likely presence of DMDD.

Frequencies for the DMDD Questionnaire items are given for presence (criteria A, C, and D) and severity (criteria E and H) of symptoms and for adaptation problems in different settings (criterion F). The results presented in **Table 2** show that few youths (5.7%) presented the key DMDD symptoms (criteria A, C, and D). As expected, when the number of criteria to be met increased, the percentage of youths that met all of them fell. In this regard, the addition of the timing criterion (criteria E and H) resulted in a considerable drop in the number of youths that did so.

**TABLE 2 |** Frequency of DMDD questionnaire items based on DSM-5 criteria.

| DSM-5 criteria | Convenience sample ($n$ = 192) | |
|---|---|---|
| | *n* | % |
| $A_{1,2}$, C, $D_{1,2}$ intense temper outbursts three times a week and irritable mood in between | 11 | 5.7 |
| $A_{1,2}$, C, $D_{1,2}$ and $E_{1,2}$ symptoms present for a year with no asymptomatic period | 4 | 2.1 |
| $A_{1,2}$, C, $D_{1,2}$, $E_{1,2}$ and H onset of symptoms before age 10 | 2 | 1 |
| $A_{1,2}$, C, $D_{1,2}$, $E_{1,2}$, H et $F_{1,2}$ symptoms present and causing problems in different settings | 2 | 1 |

*Frequency for each criterion. A1, 58.3%; A2, 37.0%; C, 13.0 %; D1irr, 24.5%; D1ang, 21.4%; D1sad, 20.3%; D2, 42.7%; E1, 45.3%; E2, 26.6%; F1hom, 54.2%; F1sch, 24.0%; F1fri =15.6%; H, 25.0%; F2hom, 44.3%; F2sch, 17.2%; F2fri, 8.9%.*

### Internal Consistency

The internal consistency of the construct was the only index of reliability of the DMDD Questionnaire measured. The alpha was 0.90 for this sample and the 95% confidence intervals are 0.88–0.92.

### Concurrent Validity

The association between the continuous measure of DMDD and the other continuous measures of mental health problem was assessed for the sample. First, the correlation coefficients revealed a significant link between DMDD and, respectively, depressive symptoms ($r = 0.310$, $p = 0.001$ for the DIA-R and $r = 0.144$, $p = 0.049$ for the K-SADS-PL) and borderline personality traits ($r = 0.427$, $p = 0.001$ for the DIA-R and $r = 0.261$, $p = 0.001$ for the Ab-DIB).

# DISCUSSION

This is the first study of a brief questionnaire that allows obtaining information from adolescents regarding the principal DMDD criteria. The content of the instrument's items was initially developed based on DSM-5 criteria and expert judgment to ensure that this new instrument covered the theoretical concepts of DMDD in English and French. The reliability and concurrent validity indices suggest that the questionnaire may be used in a clinical context.

In addition, our results show that DMDD is relatively rare. Overall, 12 participants or 6.3% of the sample scored at least nine out 10 on the questionnaire, and almost as many met criteria A, C and D (5.7%). These figures fall within the prevalence estimated in the general population according to the DSM-5 (2–5%) (2) but are lower than those usually observed in clinical settings (13, 32, 33) probably due to differences in DMDD measures (9, 34). When time criteria were added (symptoms present for a year with no asymptomatic period of more than 3 months), the percentage dropped to 2.1%. We therefore suggest to clinicians who might use this questionnaire to suspect the presence of DMDD if the respondent scores nine or more or answers "yes" on the items regarding the symptoms of DMDD (criteria A, C, D, and questions 1–5).

In general, this first step in the validation of the DMDD Questionnaire shows that the instrument possesses satisfactory

initials psychometric properties. The construct's internal consistency is the questionnaire's only reliability index. From an interpretative perspective, the questionnaire's structure, which includes a main question (Q1) and nine contingency items, is largely conducive to the high degree of consistency observed relative to dimensional scales without this contingency. However, it is important to underscore that the alpha coefficient obtained (0.90) suggests an acceptable internal consistency (>0.70) (27). It should also be noted that some authors raise few limitations associated with the use of sum scores as in the calculation of Cronbach's alpha (35, 36). It is however possible to use sum scores insofar as a factorial analysis carried out in the preliminary analyzes of this study showed that a single factor is present in the DMDD Questionnaire. Also, since it is a screening tool and not an accurate diagnostic tool, it seems acceptable to use the sum score in this initial validation study (35). Being aware of all these limitations, we cannot reach a firm conclusion regarding internal consistency. Still, these initial results push us toward a future study that will allow us to do a more solid validation on another sample.

The results regarding concurrent validity to examine the relationship between the DSM-5 DMDD criteria and two related constructs suggests that the DMDD criteria in adolescence are significantly associated with depressive symptoms and borderline personality traits. Classifying DMDD in the DSM-5 category of depressive disorders reflects the fact that youths that present these symptoms generally develop depressive or anxiety disorders as they approach adulthood (3–5). Additionally, part of the convergence between DMDD and depression can also be explained by the fact that irritability and negative mood are symptoms of depression that are also found in youth (2). The significant correlation between the DSM-5 DMDD criteria and borderline personality traits is interesting as well. Perepletchikova, Nathanson (37) hypothesized a link between these two constructs, noting that the two disorders shared the core element of emotional dysregulation. This hypothesis enabled these authors to develop a treatment based on dialectical behavior therapy for DMDD. Moreover, Guilé, Boissel (38) reported that the presence of externalizing disorders in childhood predicted borderline personality traits in early adolescence, whereas depression in adolescence predicted borderline personality traits in adulthood. This concurs with the portrait of DMDD, namely, childhood marked by excessive temper outbursts and adolescence marked by depressive symptoms. Hence, it is reasonable to think that the trajectory proposed by these authors applies here. Especially since our research on the DMDD Questionnaire indicates a possible association between DMDD, depressive symptoms, and borderline personality traits in adolescence. Future research should validate this hypothesis. Studying the relationship between these concepts could help steer the treatment options for these youths.

These findings also have practical implications. From a clinical viewpoint, the questionnaire is useful in that it takes little time to administer. It is all the more useful since the rates of comorbidity in DMDD are high (2). A decision support tool is therefore relevant. Furthermore, the items are put directly to the adolescent in English or French. In addition, compared with the DMDD module of the K-SADS-PL (10), the DMDD Questionnaire proposes a small number of clear, easy-to-understand items regarding DMDD alone. What's more, the score yielded by the questionnaire gives an idea of the number of symptoms and timing elements that correspond to the diagnostic criteria. The instrument thus makes a contribution above and beyond the K-SADS's utility.

**TABLE 3 |** Pearson's correlations for concurrent validity.

| Criterion score | Symbols | DIA-R depression symptoms | K-SADS depression symptoms | DIA-R borderline traits | Ab-DIB borderline traits |
|---|---|---|---|---|---|
| | *r* coefficient | 0.310** | 0.144* | 0.427** | 0.261** |
| | Sig. (two-tailed) | 0.001 | 0.049 | 0.001 | 0.001 |
| | *N* | 192 | 187 | 192 | 191 |
| Confidence interval | Lower | 0.176 | −0.004 | 0.298 | 0.123 |
| | Upper | 0.440 | 0.281 | 0.525 | 0.397 |

*r = 0.10 is a weak correlation; r = 0.30 is a moderate correlation; r = 0.50 is a strong correlation. 95% bootstrap confidence intervals. **Correlation significant at 0.01 (two-tailed); *Correlation significant at 0.05 (two-tailed).*

Our study has limitations. First, the DMDD Questionnaire is a decision-support instrument and, by definition, cannot serve as the basis for rendering a psychiatric diagnosis. It could serve as a brief questionnaire administered prior to a complete psychiatric evaluation. Second, this exploratory study represents a first step in the psychometric validation of the instrument. While the criteria selected remain pertinent, the absence of another measure to evaluate DMDD based on DSM-5 criteria restricts the possibility of comparing the questionnaire against an external validation criterion that refers to this construct. Once again, we have to keep in mind that the K-SADS-PL with the DMDD module was published after our study was carried out (10). Third, the initial study design did not allow evaluating the questionnaire's test-retest reliability. Fourth, we did not use or develop a version of the DMDD Questionnaire for parents. Fifth, the instrument's comprehensibility of some questions was not examined. Sixth, the convenience sample was not representative of all adolescents with DMDD symptoms from the clinical population. The absence of representativeness limits the extent to which we can generalize the results to this population. Finally, although the results suggest a possible relationship between DMDD criteria and depressive symptoms and borderline personality traits, the correlation coefficients remain modest, the level varying from low to moderate (see **Table 3**). Note that although the correlations are present, some might say that there is a reasonable doubt as to whether they are real (39). Future studies will be necessary to establish more robust calculations in relation to the validity and reliability of this questionnaire.

In summary, the results suggest that the DMDD Questionnaire presents adequate initial psychometric properties when used with adolescents from clinical settings. The results allow clinicians and researchers to use a practical, brief questionnaire based on DSM-5 criteria as a decision-support

tool. Finally, this study supports the presence of association between the DSM-5 DMDD criteria and depressive symptoms and, to our knowledge, this is the first study to show that DMDD could be associated with borderline personality traits.

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board of the Rivière-des-Prairies Mental Health Hospital (CIUSSS du Nord-de-l'Île-de-Montréal). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

RL, LB, and J-JB contributed to the conception and design of the DMDD Questionnaire and the study. CB organized the database and performed the statistical analysis. J-MG helped interpret the data. AB wrote the first draft of the manuscript as part of her thesis. RL and LB drafted sections of the manuscript. All authors contributed to the manuscript's revision and read and approved the submitted version. The Canadian French and English versions of the DMDD Questionnaire are available for use from RL.

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# Radical Acceptance of Reality: Putting DBT®-A Skill Groups Online During the COVID-19 Pandemic: A Qualitative Study

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**Introduction:** Emotion dysregulation is a common challenge pertaining to numerous psychiatric disorders in adolescence and is associated with increased morbidity and mortality. Dialectical Behavior Therapy for Adolescents (DBT®-A) has been shown to be an effective treatment, especially in the reduction of self-harm and suicidality. Measures in relation to the COVID-19 pandemic set strict limits on physical contacts with patients. In order to continuously provide evidence-based specialized care to patients suffering from emotion dysregulation, we offered two online DBT®-A skill groups in a video-group-call format.

**Objective:** We aimed at assessing our online DBT®-A skills groups, collect according up- and downsides, and form a basis for advancement of this form of treatment provision. Also, the impact of the COVID-19 pandemic on patients was assessed.

**Methods:** A physical DBT®-A skill group was switched to a video-group-call format and a second group was initiated *de novo online*. After five sessions, patients engaged in structured group discussions to reflect experiences. Discussion content was analyzed via Inductive Category Formation within the Framework of Qualitative Content Analysis.

**Results:** Patients unanimously found the COVID-19 pandemic challenging, but also reported differentially on its impact. Downsides were balanced by subjective "gains" in time and a perceived reduction in stress. Technical problems of the online format were discussed, but did not limit the positive experience of still receiving treatment. Patients of both online DBT®-A skill groups valued the offer, felt connected, and reported benefits from the treatment. The *transition* group additionally discussed changes in structure and content of the group sessions after the switch to online meetings and reflected differential functions of the group.

**Discussion:** Although the sample size is small, and conclusions are drawn from Inductive Qualitative Content Analysis, the presented results are of interest. In our investigation, video-group-calls were both safe and beneficial for patients. This alternative

to physical meetings is not only interesting for further waves of the current pandemic but also for service provision in remote areas with limited access to specialized care. Further research is needed to challenge and refine our results and to explore extensions to "basic" video-group-calls, such as "break-out sessions," blended therapy, or real-time supervision within an online session.

**Keywords: DBT-A, skills group, COVID-19, emotion dysregulation, teletherapy, online, video**

## INTRODUCTION

Emotion dysregulation is seen as a trans-diagnostic factor with negative impact on various domains of psychopathology in adolescents (1), although specifics could be identified in the subgroup of patients suffering from borderline personality disorder (BPD) (2). Deficits in emotion regulation are associated with social impairment (3) and, consequently, contribute negatively to the level of psychosocial functioning. Additionally, typical behavioral manifestations of emotion dysregulation, such as self-harm, suicidal ideation, eating disorder behaviors, or substance (ab)use, are associated with increased morbidity and mortality (4–7). According to international standards, Dialectical Behavior Therapy for Adolescents (DBT®-A) is an evidence-based treatment for these patients, especially concerning the reduction of self-harm (8–11). DBT-A is a manualized treatment tailored for application in outpatient settings (12–14). Full DBT®-A treatment comprises weekly individual sessions, concurrent participation in a DBT®-A skills group, telephone coaching, consultation team, and family work (13, 15). Specific strategies taught within the skills group component of DBT®-A are mindfulness, distress tolerance, interpersonal effectiveness, emotion regulation, and "walking the middle path" (strategies connecting teens and caregivers).

In integrating the above with results from first observations on the impact of the COVID-19 pandemic on patients suffering from mental health disorders, the continued provision of evidence-based care is of utmost importance. So far, data clearly indicate disproportional consequences of the COVID-19 pandemic (16–18), even a potentially increased suicide risk (18), and an increase of adversities (19) in patients suffering from mental health disorders.

Owing to restrictions set to ensure minimum spreading of SARS-CoV-2, not only in everyday life, but also in clinical routine suffered critical cuts. Limits especially concerned physical contacts, which were reduced to an absolute minimum (i.e., emergency presentations in the psychiatric context). Given the need to continuously serve patients despite these restrictions, a lot of effort went into provision of services through other means of care, such as telehealth interventions (20). In the need of the moment and given changes in several legal regulations, many departments of child and adolescent psychiatry conducted an *ad hoc* switch from face-to-face to teletherapy to continuously serve their current outpatients (21). Although the preexisting body of literature on telemental health, many countries stepped into this venture without preparation because of lack of legal frameworks and lacking prior approval on the conductance of teletherapy by legal authorities and professional organizations (22). Even in countries with regulations and formal licensing procedures, such as the United States, many therapists were unexperienced in using telemental health (23). Sampaio et al. could show that around half of the mental health professionals in their survey were concerned about data safety when using telemental health.

In order to ensure continuation of high-quality, evidence-based services, especially in expectance of further waves of the current pandemic, we aimed at systematically evaluating patients' experiences with our DBT-A skill group in the newly established video group call format via structured group discussions and consecutive qualitative analyses[1]. Sampaio et al. argued that around 50% of mental health professionals expressed concerns about their ability to handle emergency situations in a telemental health setting (23), which is of special interest for our research because the population investigated herein were "at risk" patients (self-harm, suicidality).

Little et al. (24) argued that qualitative methodology is suitable to address and assess patients' perceptions of DBT®. Since presentation, discussion and training of behavioral, cognitive, and emotional skills serve as one of the main therapeutic tools in overcoming pervasive emotion dysregulation (25, 26), we decided to focus on this component. Also, Linehan et al. (27) could show that skills training alone leads to better results concerning the frequency of self-harm than individual DBT®, as well as overall similar rates concerning other symptoms of BPD addressed within therapy (e.g., suicidal ideations, suicide attempts). The aim of this small open trial was, thus, to assess practicability and record potential adverse effects of DBT®-A skills training in a video group call format. Thoughts and ideas expressed by our patients, as well as insights gained in the process, were deemed to form the base for further steps, especially concerning positive lessons, but also flipsides of this form of treatment conductance. Although this is especially relevant in case of further waves of the COVID-19 pandemic, results might also be helpful concerning potential applications in other situations, such as service provision in remote areas with limited access to specialized care.

## MATERIALS AND METHODS

### Participants

Of five patients participating in our *physical* group, four decided to continue online. All four patients completed the online "cycle."

[1]All patients also had individual therapy, which was not evaluated within this study.

Although all patients gave consent to study participation, only three engaged in the investigative group discussion (one patient had a colliding appointment).

Six patients showed interest and started in our second *de novo online* group. Of these six patients, one dropped out after two sessions because she felt the content was not the right fit for her, and one left the group after three sessions because of repeated technical problems (unstable internet connection). The remaining four patients gave consent to study participation, but only three were online at the time of the investigative group discussion. One patient had technical problems during the discussion and, thus, could not continuously contribute. Concerning dropouts, we saw no difference to our *physical* groups. The dropout rates we observed in our sample were at the lower end of rates reported in other studies (28, 29). Also, dropout rates were equal in both online groups, which is of interest because the module, and thus, content differed. This is in line with the observations of Landes et al. (28).

All patients received concurrent psychiatric treatment (case management and psychopharmaceuticals) and individual psychotherapy before, as well as during the COVID-19 pandemic (during lockdown per telephone or video call). Patients were between 14 and 18 years old and mainly female. The leading diagnoses were BPD, depressive disorder, or anxiety disorder (diagnoses according to ICD-10). Non-BPD patients met at least three BPD criteria.

## Procedure

Given the need to continuously offer specialized care in times of COVID-19-associated restrictions on physical contact, our clinic's DBT®-A team decided to create an online offer. DBT®-A skill group sessions were conducted in a video group call format. Skype for Business (Skype Communications SARL, Luxembourg) was used as platform conforming to Austrian data safeguarding measures. The respective session link was always sent via email a day before the session.

Patients of the current DBT®-A skill group and patients new to DBT®-A, as well as all respective parents/guardians, were asked individually, per telephone or video call, whether they would participate in an online format. Two separate DBT®-A online skill groups were offered. Group 1 was transited from an existing *physical* group to online meetings after a COVID-19-associated break of 3 weeks (time needed for organization, preparation of technology, checking compliance to data safety regulations). Group 2 was initiated *de novo online* 3 weeks after the onset of Group 1. Lockdown measures were still active at the time.

Two group discussions, conceptualized to evaluate each of the online DBT®-A skill groups, were conducted online via Cisco WebEx (Webex Communications Deutschland GmbH, Germany).

Ethical approval for this investigation was granted by the institutional review board of the Medical University of Vienna (#1540/2020), and patients and guardians gave written consent prior to study participation.

**TABLE 1** | Session structure.

| Topic | Time |
|---|---|
| Greetings and quick evaluation of acute needs | 5' |
| Mindfulness | 5' |
| . Exercise | (2') |
| . Reflection | (3') |
| Collection of "hot topics" (specific needs in relation to the dynamic of the COVID-19 pandemic) | 5' |
| Recap | 10' |
| . "Challenge" (therapeutic homework) | (5') |
| . "Skills of the week" (top skills applied) | (5') |
| New content (following the current module, integrating specific needs addressed during collection of "hot topics") | 20' |
| Assignment and explanation of "challenge" for the upcoming | 5' |
| Mindfulness in the sense of reflection of the current session | 5' |
| Buffer | 5' |

## Description of Treatment

DBT®-A skill group contracts were adapted so as to suit online sessions and were signed by all patients. The following methods and materials were used: (1) presentation of content by skill trainers, (2) group discussions engaging all patients, (3) chat function where applicable (e.g., group tasks), (4) worksheets (distributed via email), (5) shared files for continued group work (e.g., collective PowerPoint presentations for collection of skills manageable within the set restrictions, which were conducted with enthusiasm and creativity by the patients and the trainers, and which were presented and discussed in the next session), and (6) peer feedback. Session structure was defined so as to follow the same basic routine for both groups, although specific content varied between the two groups. This variation was owed to the fact that the first of the two online DBT®-A skill groups was transited from an existing *physical* group and, thus, already had prior knowledge on a range of skills, while the second group started *de novo online*. In order to follow the need of the moment, we decided to align content around the current module (group 1 → emotion regulation, group 2 → distress tolerance), but integrate specific content according to patients' current needs, thus, sometimes giving the group the lead and reacting spontaneously including skills from other modules. Basic session structure and specific content per group and appointment for the first five sessions (evaluation after session 5) are listed in **Tables 1**, **2**, respectively. Upon onset of the online format, the DBT®-A team was unsure about session length (presence groups lasted for 90 min including a 15-min break), so that this was openly discussed with participants from group 1, who by then all had experience with distance learning. Consensus was reached at a session length of 60 min. In order to ensure patient safety, each patient had to name a contact (mostly parent) beforehand, who could be reached in case of emergency (this emergency procedure actually never had to be used). Contact details of patients and emergency contacts were kept "ready to use" by both skill trainers. Additionally, patients were informed that in case of emergency (acute tension, need for immediate support/action)

**TABLE 2 |** Specific session content.

| Appointment | Content |
|---|---|
| **Group 1 (*transition* group)** | |
| 1 | . "Update" after pandemic-associated 3-week break<br>. Collection of current needs<br>. Explanation of structure of online sessions<br>. Short discussion about session length<br>. Evaluation of current survival skills (idea that some might not be applicable during lockdown)<br>. Group discussion (recap from prior modules) concerning survival skills<br>"challenge" → revision of individual crisis survival kits |
| 2 | . Introduction to module "emotion regulation"<br>. Understanding emotions<br>. Group discussion concerning specific emotions<br>. Specific skill: *ABC PLEASE*<br>. Specific skill: *accepting reality*<br>"Challenge" → practice *ABC PLEASE* |
| 3 | . Specific skill: *opposite action*<br>. Specific skill: *focusing on positive events*<br>. Group work (using the chat)—collection of current (or potential) positive events<br>. Mindfulness story ("bean exercise")<br>"Challenge" → collection of "beans" and contribution to shared file (collection of positive events) |
| 4 | . Specific skill: *check the facts*<br>. "Guide to" dialectics<br>. Group discussion concerning specific skill: *thinking and acting dialectically*<br>"Challenge" → *re-phrasing dialectically* |
| 5 | . Specific skill: *wave skill*<br>. "Expert" discussion (one patient already had experience with the wave skill)<br>. "Guide to" validation<br>. Specific skill: *validation of self* (followed by group discussion)<br>"Challenge" → "fairness" and *validation of self* |
| **Group 2 (*de novo online* group)** | |
| 1 | . Introduction/getting to know each other online<br>. Explanation of structure of online sessions<br>. Collection of current needs<br>. Collection of strategies applied so far (and labeling of specific skills)<br>. "Guide to" understanding tension and early warning signs<br>. Introduction to survival skills<br>. Specific skill: *self-sooth with the six senses*<br>. specific skill: *PLEASE*<br>"Challenge" → experimenting with at least one (max 3) six sense skills at medium tension, observation of *PLEASE* |
| 2 | . Recap of early warning signs<br>. "Hot chair"<br>. "Guide to" mindfulness<br>. What and how skills<br>. Exercise: description of picture<br>. Specific skill: *IMPROVE the moment*<br>"Challenge" → experimenting with at least one further six *sense skill*, *IMPROVE the moment*, collection of individual early warning signs |
| 3 | . Coordinative exercise<br>. Specific skill: *accepting reality*<br>. Specific skill: *focusing on positive events*<br>. Group work (using the chat)—collection of current (or potential) positive events<br>. Mindfulness story ("bean exercise")<br>"Challenge" → collection of "beans," contribution to shared file (collection of positive events), "first draft" of individual crisis survival kits |
| 4 | . Coordinative exercise<br>. Crisis survival kits<br>. Specific skill: *wise mind ACCEPTS*<br>. Recap of specific skill: *PLEASE*<br>Challenge" → *PLEASE* and *wise mind ACCEPTS* |
| 5 | . "Cognitive" exercise<br>. Discussion of vulnerability<br>. "Guide to" validation<br>. Specific skill: *validation of self* (followed by group discussion)<br>"Challenge" → "fairness" and *validation of self* |

one of the two trainers would continue the session alone, and the other would be available in a separate online meeting or via telephone.[2] Sessions were prepared in a separate, weekly online meeting by the two DBT®-A skill trainers. Each session was followed by a reflection of the trainers directly after the end of the respective session. Supervision via telephone conference by an external supervisor was well-established and continued during the pandemic crisis and the according DBT®-A online format.

## Study Design

To our knowledge, a video group call format of a DBT® (-A) skill group has not yet been evaluated, so this investigation was set up as an exploratory pilot study. Due to the novelty of the situation, only limited prior knowledge on its effects on adolescents suffering from mental health disorders (especially emotion dysregulation, self-harm, and suicidal ideations), and a limited number of participants, we opted for a purely qualitative evaluation in the form of online group discussions and according analyses. Separate discussions were planned for each of the two online DBT®-A skills groups at our clinic after five sessions of skill training. Details of the study were explained to patients and guardians separate from details concerning the skill training sessions, and written informed consent was obtained. The group discussion sessions were configurated by a qualified research fellow and senior resident in Child and Adolescent Psychiatry, who was not involved in the treatment of the respective patients. Session links were sent per email to all participants by one of the skill trainers. At the beginning of the group discussion sessions, both skill trainers were present and introduced the moderator of the discussion. The skills trainers then logged out of the respective session and stayed available as background support per telephone or video call for any acute situations or technical problems. Immediately after the end of the respective discussions, the moderator left the meeting, and the skill trainers took over to resume and round up.

[2]We twice had to make use of this option. In both cases (once in group 1 and once in group 2), patients could be reached on their smartphones and rejoined the running session.

## Measurements

Discussions were conceptualized, moderated, and analyzed by a qualified research fellow and senior resident in Child and Adolescent Psychiatry, who was not involved in the treatment of the respective patients. The format of a group discussion, due to the shared background of the patients following the ideas of Bohnsack (30), was chosen because perceptions and opinions of participants were interpreted as being results of the process of the groups *per se* and were, thus, deemed to be best accessible via discussion within the established groups. Discussions followed the structure *stimulus* → *discussion* → *"exmanent" questioning*[3] → *directive phase* → *protocol*. Stimuli are understood as input material to start off the process of discussion. Most frequently, statements, videos, audio files, or pictures are being used. The main discussion is understood as exchange between the participants without intervention of the moderator. When the discussion is "exhausted," i.e., there are no more novel contributions or long pauses, the moderator steps in to ask questions that have not been addressed by the participants, but are of relevance for the research in question. The directive phase of the discussion serves clarification; contradictory statements are being picked up by the moderator, and participants are asked for further input.

The stimulus presented in this study were verbal captions of the current situation and varied slightly between the two groups, so as to additionally encompass the fact that the *transition* group already had a good working alliance before the start of the online treatment, while the *de novo online* group had to manage this process online.

## Data Analysis

In light of the novelty of the situation and the consequent lack of prior information, in-depth qualitative analysis of discussion content was open and exploratory, applying Inductive Category Formation within the framework of Qualitative Content Analysis (Mayring) (31). Analysis was supported by the standard computerized qualitative data analysis tool ATLAS.ti 8 (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany). A summary description of the according analytical steps is presented in **Table 3**.

**TABLE 3 |** Summary description of Inductive Category Formation (Qualitative Content Analysis) (31).

| Step | Content |
|---|---|
| Step 1 | Research of literature (theoretical background), formulation of research question(s) |
| Step 2 | Establishment of selection criterion, definition of categories, and level of abstraction |
| Step 3 | Working through the material "line by line" → either formulation of new categories or subsumption |
| Step 4 | Revision of categories and rules after 10%–50% of the material |
| Step 5 | Final working through the material |
| Step 6 | Building of main categories |
| Step 7 | Going back to the material to back-check categories |
| Step 8 | Final results and interpretation |

# RESULTS

Content of the group discussions varied between the two groups, whereby group 1 engaged in a more in-depth discussion on specifics of teletherapy and benefits from the skill group, in general, and especially in times of the COVID-19 pandemic, while group 2 stayed on a more superficial level and rather focused on differential impacts of the pandemic.

## Perceived Impact of the Pandemic

Patients of both groups unanimously agreed upon the challenging character of the current situation and the need to engage in adjustment processes ["It, like, happened all at once, it was simply there, it was so overwhelming."].[4] Both groups expressed up- and downsides of lockdown measures and associated restrictions. Main themes on the positive side were the feeling of having more time (for relaxation, for reflection, for the family) ["All of a sudden I had time, time that I never had before."] and experiencing less stress. Patients also mentioned the perception of now valuing things more ("little" things, freedom, contacts) ["I've learned to appreciate every-day life things a lot more."], and the feeling of confronting and experimenting more (affective states, emotions and respective skills); in their view mainly attributed to fewer distractions ["The situation implied that I could not run away from my feelings that much, because I just had less distraction. Obviously, that wasn't always comfortable, but it made me get to know my emotions and deal with them."]. Flipsides named were restrictions concerning typically applied coping strategies, boredom, self-isolation ["It was just so easy to self-isolate."], decreased mood, less drive, and the missing of physical contacts (both in the sense of seeing them for real and being touched) with friends.

## Technical Issues

Complaints about technical problems and specific challenges of teletherapy as such, especially video calls, did not relate to group membership. Only one patient (group 1) expressed frustration concerning problems with the internet connection, but said that this was easily circumventable by intermittent use of the chat function. Additionally, one patient from group 1 and one patient from group 2 expressed overall discomfort. Issues raised were irritation due to constantly seeing oneself (video in small display window) and the feeling of potentially being overheard by family members and consequently being less open. At the same time, both of these patients stated that they valued the offer as an alternative to not being able to receive specialized treatment at all. Both clearly stated to have benefitted a lot and would just prefer real-life contacts. On the other hand, one patient mentioned feeling more comfortable with the video call setting, due to not having to hide wounds and scars, because only her head and chest could be seen. This patient added that she found it easier

[3]"Exmanent" questioning translates into the moderator actively asking about topics that have not yet been addressed, but are relevant to the research question(s).

[4]For illustration, patient quotes are inserted in square brackets.

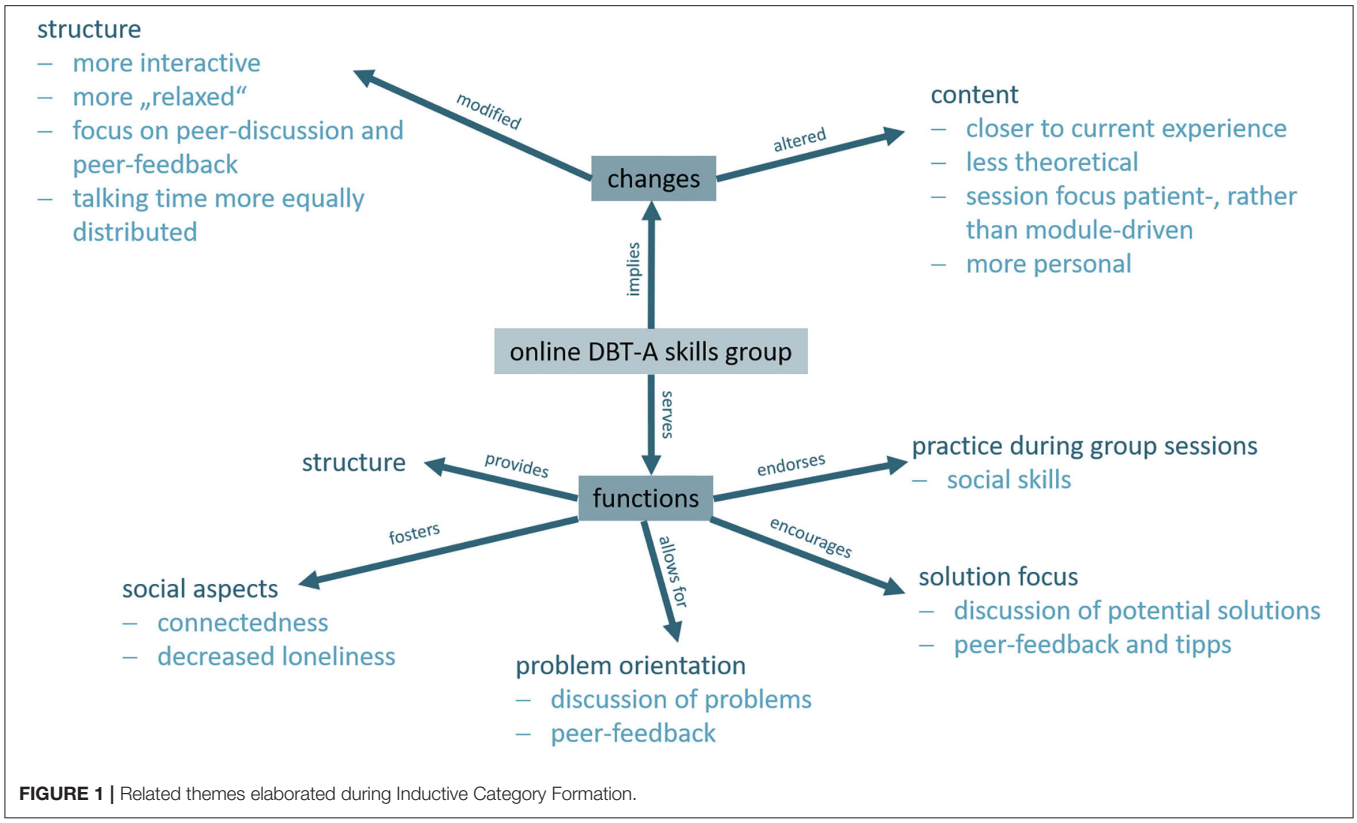


**FIGURE 1 |** Related themes elaborated during Inductive Category Formation.

to apply skills in case of distress during the sessions because of the opportunity to turn off the camera for a short time.

## Perceived Benefits

Patients reported on having learned to recognize and label different emotions and affective states, as well as behavioral patterns. They also valued the discussion of specific strategies to deal with according distress. Patients from both groups mentioned that they were able to amplify their coping repertoire. Additionally, the interactive character and the chance to give and receive peer feedback, which patients perceived as strongly supporting transfer into everyday application of specific skills, was mentioned as beneficial ["It was so positive that we could discuss ideas and provide potential solutions within the group, so we really could give and take."].

Reports from group 1 were more elaborated and integrated perceptions of differential changes in the structure and content of group sessions after the transition to the online format, as well as individually perceived functions of the group as such. To use the words of one of the patients, the group provided "familiarity within the unfamiliar." Details of the compiled categories are depicted in **Figure 1**. To summarize the analysis, patients of the *transition* group benefitted from continuation of established therapy and assigned a range of subjective functions of the group as such. The transition into an online setting worked for all of these patients and was reflected in the context of "change"; situational adaptions were mirrored in perceptions of changed structure and content of the group sessions. One of our patients summarized: "The mundane structure I was used to and, due to Corona, did not have anymore, was filled with this subtle but very helpful appointment."

Concerning the level of psychosocial functioning, all patients managed to stay socially integrated (with all limits imposed by the set restrictions) and to keep up with school, i.e., all patients made their grades; one even the school ending exam ("Matura").

# DISCUSSION

The COVID-19-pandemic had, and still has, a huge impact on people worldwide and not only demanded adaptions from individuals and systems but also required immense situational adjustment. Specific subpopulations, such as individuals suffering from psychiatric disorders, have been suspected to have an increased risk of deterioration in their mental health status, although limited data are available differentially evaluating potential consequences of the crisis (32, 33). All else put aside, current outpatients were confronted with the fact that measures set to ensure minimum spreading of SARS-CoV-2 imposed considerable changes in the availability of established treatment, ranging from treatment pause to an *ad hoc* switch to teletherapy (e.g., telephone, video calls). Data on the provision of DBT® and consequences for patients suffering from BPD during COVID-19 suggest serious consequences, especially reduced numbers treated and changes in structure and content of therapy (34). Although teletherapy generally seems to be beneficial (35, 36), many countries were unprepared for it due to lacking legal frameworks, lacking prior approval on the conductance of teletherapy by legal authorities and professional organizations,

and lacking clarity concerning cost coverage or reimbursement (22). Interestingly, even in countries with preexisting regulations on tele (mental) health, such as the United States, many mental health professionals had not used telemental health before the outbreak of the COVID-19 pandemic, whereby data safety and a lack of preparedness for handling emergency situations seem to have been the main concerns (23). Regulations in our country precluded video-calls as a legitimate treatment alternative so that the patients assessed in this study had no prior experience with teletherapeutic offers. When offered the option to participate in an internet-based video call format, only one patient from our ongoing *physical* group declined, so that we could assess the transition aspect—face to face switched to teletherapy—in this established group. Additionally, we invited patients new to us and to DBT-A to join a second *de novo online* skill group, which enabled us to assess the process of forming a group online and explore challenges in conveying DBT®-A skills via this format.

Concerning participation, we lost two patients due to dropouts. This number did not differ from recorded dropouts in our *physical* groups and is in line with rates reported in other studies (29).

Although this study is exploratory, and results are drawn from a small sample, we provided evidence for a differentiated view on the impact of the COVID-19 pandemic on adolescent psychiatric outpatients. Although perceiving the situation as challenging, patients not only named downsides but also numerous positive consequences during lockdown. Concerning technical aspects, the situation was challenging for both therapists and patients, although only one patient elaborated this aspect in the group discussion. As skill trainers, we decided to include the chat function of our video call platform to keep collaboration and exchange going in case of problems, which was valued by participants (e.g., a note that a patient will turn off the camera in case of the need to apply skills during the session, unstable internet connection, or quality problems with video and sound). Patients of the *transition* group could also be evaluated concerning the perception and acceptance of changes in content and structure. The feedback was very positive concerning both changes in content and structure. Patients stated that the sessions became more interactive than the physical meetings, and they especially valued extensive peer discussions and peer feedback, which we encouraged in order to give room for group exchange on pandemic-related topics. This "togetherness" was also directly addressed in the group discussions. Interestingly, also group 2, who only got to know each other online, stated feeling "connected" and also put emphasis on the group providing an anchor, something to hold onto.

Regarding patient safety, a meeting was arranged, and in consent with the patient, the patient's individual therapist was contacted in order to ensure continued treatment. One patient dropped out after the third session because her internet connection failed repeatedly, and she was neither able to interact, nor to follow the content.

Generalization of results is limited by the sample size and characteristics, the exploratory character, and the consequently applied qualitative methodology. Also, only five sessions of the online DBT®-A skill group have been evaluated.

Despite the abovementioned limitations, in our assessment, DBT®-A skill training via internet-based video group call proved to be safe and beneficial for adolescents with emotion dysregulation. This result is especially relevant since many therapists are concerned about their ability to handle emergency situations in a telemental health setting (23). Our results indicate that an online format might be an alternative to face-to-face group sessions if these are not possible. This is obviously interesting concerning future situations of quarantine, especially further waves of the current pandemic, but potentially also for service provision in remote areas, where highly specialized treatment often is not available.

In spite of the encouraging character of these results, further research is necessary to challenge and refine our findings, especially in the sense of a direct comparison of online vs. face-to-face DBT®-A skill groups, to assess suitability as alternative to or augmentation of face-to-face treatment in a more general context aside from quarantine. Despite the availability of smartphones and internet connection, technical difficulties, especially concerning speed and stability of the connection, have been raised by our patients, so that investment in enhancing availability of adequate technologies is necessary. Additionally, extensions of the video group call format, such as "break-out sessions" (i.e., parallel video sessions) for teamwork, real-time inclusion of an external supervisor or blended therapy has to be considered, in order to further test the potential of this format. Also, combinations with other technologies, such as virtual reality (e.g., Virtual Reality Mindfulness), should be explored within *online* DBT®(-A) (23).

## DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

## ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Review Board of the Medical University of Vienna. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

## AUTHOR CONTRIBUTIONS

MB, TG, and PP conceptualized the study. MB and VW conveyed the DBT-A treatment analyzed. TG planned and conducted the focus groups and according qualitative data analyses. MB, AB, OK, and PP all contributed to writing the manuscript. All authors contributed to the article and approved the submitted version.

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