NEUROSCIENCE OF HUMAN ATTACHMENT

EDITED BY: Anna Buchheim, Carol George, Harald Gündel and Roberto Viviani
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NEUROSCIENCE OF HUMAN ATTACHMENT

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Attachment and Exploration
Photo by Peter Buchheim

Attachment is a biologically emotion regulation based system guiding cognitive and emotional processes with respect to intimate and significant relationships. Secure relationships promote infants' exploration of the world and expand their mastery of the environment. Adverse attachment experiences like, maltreatment, loss, and separation have long been known to have enduring unfavorable effects on human mental health. Research on the neurobiological basis of attachment started with animal studies focusing on emotional deprivation and its behavioral, molecular and endocrine consequences.

The present book presents an interdisciplinary synthesis of existing knowledge and new perspectives on the human neuroscience of attachment, showing the tremendous development of this field. The following chapters include innovative studies that are representative of the broad spectrum of current approaches. These involve both differing neurobiological types of substrates using measures like fMRI, EEG, psychophysiology, endocrine parameters, and genetic polymorphisms, as well as psychometric approaches to classify attachment patterns in individuals. The findings we have acquired in the meanwhile on the neural substrates of attachment in healthy subjects lay the foundation of studies with clinical groups. The final section of the book addresses evidence on changes in the functioning of these neural substrates in psychopathology.

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EDITORIAL
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Editorial: Neuroscience of Human Attachment

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Keywords: attachment, attachment measures, human neuroscience, psychophysiology, EEG/ERP, fMRI, oxytocin, genetic markers

Editorial on the Research Topic

Neuroscience of Human Attachment

The Research Topic "Neuroscience of Human Attachment" includes innovative papers representing a broad spectrum of contemporary approaches to the investigation of biologically based systems that guide cognitive and emotional processes associated with intimate and significant relationships. This spectrum includes studies and theoretical reviews that discuss neurobiological substrates (fMRI, EEG, psychophysiology, endocrine parameters, genetic polymorphisms) using a range of psychometric approaches to attachment assessment [interview like e.g., the Adult Attachment Interview (AAI) (George et al., unpublished manuscript; Main and Goldwyn, unpublished manuscript), free response like e.g., the Adult Attachment Projective Picture System (AAP) (George and West, 2012), self-report questionnaire like e.g., the Relationship Scales Questionnaire].

The first group of papers explored the identification of neural activation response patterns to different relationship-based stimuli presented in an fMRI context. Heckendorf et al. examined the effects of subliminal threatening primes on responses to the presentation of familiar and unfamiliar faces. Their study showed enhanced activity in social cognition areas in the posterior temporal/anterior parietal lobes in response to viewing unfamiliar faces, indicating increased effortful processing. Labek et al. showed the involvement of similar social cognitive cortical areas in response to viewing AAP attachment stimuli as compared with carefully matched control pictures. Interestingly, Davidovic et al. full the same neural system was also active in response to tactile pleasant skin strokes (i.e., caress-like). These studies replicate findings regarding the dual role of perceptual networks in social cognition and draw attention to issues that are currently debated in neurobiological models of empathy and mentalization (Keysers et al., 2010).

The second group of papers investigated neural responses associated with individual differences in attachment. This section begins with a review paper by Gander and Buchheim that describes infant and adult attachment group differences in physiological responsiveness, such as adrenocortical activity, heart rate and skin conductance, and frontal electroencephalographic (EEG) asymmetry. The authors demonstrate the role of secure attachment, as compared with insecure attachment, as a physiological reactivity buffer to stress responses, noting also that investigations examining the most extreme forms of insecurity (disorganized and unresolved attachment) are still lacking. With regard to insecure adult attachment, Wichmann et al. demonstrated using a Reaction Time paradigm that statements derived from insecure AAP responses (typically describing unpleasant, unsatisfying, or conflictual themes) required significantly greater "unconscious" processing time as compared with sentences derived from secure responses.

Several studies specifically investigated the footprint of so called insecure dismissing attachment, the insecure attachment group characterized by regulation strategies that transform or divert conscious attention away from (i.e., avoid) conflictual attachment experience and affect.

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Kungl et al. studied the neural substrates of emotion regulation by assessing state and trait dependent EEG asymmetries in healthy adolescents judged dismissing on the AAI. The results showed elevated right-frontal brain activity and reduced right parietal brain activity, validating on the neural level the tendencies of these individuals for avoidance/redirection strategies. The ERP findings from the same study group by Leyh et al. confirmed the association of dismissing attachment with insufficient emotion regulation strategies as evidenced by reduced P3 amplitudes presented in a negative emotional context. Krause et al. applied an fMRI approach from the burgeoning field of resting connectivity using an auditing paradigm (excerpts from AAI narratives) to assess the association between a previously described social aversion network and dismissing attachment. These studies taken together suggest that avoidant strategies may be the result of recruitment of neural substrates associated with social withdrawal or dysfunctional emotion regulation.

A long-standing and important debate in the attachment field concerns demonstrated inconsistencies between self-report and narrative interview adult attachment assessment measures. Using fMRI, Yaseen et al. confirmed network pattern outcome differences associated with these two measurement types. Individual differences in scores from a self-report measure (Relationship Scales Questionnaire) were preferentially associated with changes in the activity of dorsal, cognitive/executive function-related networks while individual differences assessed through an interview assessment AAI were associated with modulation of activity of the antagonist "default system" network (Buckner and Carroll, 2007). This finding also suggests that different dimensions of attachment may associated with different emotion regulation strategies. Schneider-Hassloff et al. used electrophysiological approach to assess emotion regulation functioning (associated in other studies with the dorsal network) in relation to mother-child interaction patterns. They report evidence for a neurobiological signature of these patterns in a response inhibition task. The developmental lens adopted by these researchers (as compared with the personality perspective) was important in these studies. They sought evidence for the influence of adaptive emotion regulation strategies, thought to originate in early development, as characterized by effective and balanced recruitment of cognitive processes for top-down control, a central issue in the clinical neurosciences of affect (Ochsner and Gross, 2005; Messina et al., 2016). This developmental perspective is also central to the study by Zimmermann and Spangler. These authors investigated the role of genetic predisposition in modulating emotion regulation and attachment patterns of adolescents using the Late Childhood Attachment Interview (LCAI). Their results showed an interaction between the participants' attachment pattern with mother and a polymorphism of the serotonin transporter promoter region (5-HTTLPR), which has been shown in previous studies to modulate response to early adversity (Canli and Lesch, 2007).

A third group of studies importantly included participants from patient groups, acknowledging that adverse attachment experiences such as maltreatment, loss, and separation have long been known to have enduring consequences on human mental health. These studies addressed the issue of whether neural correlates of differing attachment patterns can shed light on psychopathology using the AAP (Krause et al.; Buchheim et al.; Jobst et al.). Krause et al. reported a significant increase of the neuropeptide oxytocin (OT—the "hormone of affiliation)" after administering the AAP to lactating mothers in a subclinical group. Although plasma OT was independent of the mothers' attachment representations, the finding that secure mothers showed a decrease of cortisol release after the AAP confirms the buffering effect of attachment security on a neuroendocrine level.

The neural patterns associated with attachment in an fMRI study with Borderline Personality Disorder (BPD) were examined using a paradigm that instructed participants to tell AAP stories in the scanner. The results showed significant differences between patients and control. Buchheim et al. found that unresolved attachment in both patients and controls demonstrated enhanced amygdala activation, but only the controls showed frontal activations (DLPFC, RCZ) and top down control. This finding points to possible neural mechanisms in BPD patients with unresolved attachment trauma (the majority attachment pattern associated with BPD in the literature) and their inability to regulate attachment distress. This finding was confirmed also in an OT study by Jobst et al. who demonstrated that only BPD patients with unresolved attachment (assessed with the AAP) showed lower OT in plasma over the course of an exclusion paradigm (cyberball), which again emphasizes the putative mechanisms underlying patients' interpersonal dysregulation.

The final paper reviews attachment, neurobiology and psychosis. Debbané et al. proposed a sophisticated model illustrating five neurobiological pathways through which attachment adversity may augment risk for psychosis.

We invited authors for this Research Topic in Frontiers in Human Neuroscience to submit original research or reviews that addressed topics in the neurobiological domain related to any aspect of attachment that would highlight promising avenues for basic research in developmental psychopathology or the translation of attachment studies into the clinical setting. The authors were using different methodological approaches to respond to this topic. As a result, we achieved an exciting interdisciplinary synthesis of existing knowledge and new perspectives on the human neuroscience of attachment that demonstrates the tremendous development in this field from the seminal first works by Hofer (1994) and Insel and Young (2001). These findings regarding the neural substrates of attachment in healthy individuals lay the foundation of future studies to address a wider range of clinical groups than reported here and the transgenerational transmission of attachment in low and high-risk groups. As a next step, we would like to encourage attachment researchers to evaluate the effectiveness of preventive programs and established interventions (Buchheim et al., 2012) with neurobiological or genetic approaches.

AUTHOR CONTRIBUTIONS

All authors (AB, CG, HG, RV) have contributed to this Editorial. AB and RV have drafted the Editorial, CG and HG provided intellectual contributions in commenting and revising the manuscript. AB edited its final version.

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ORIGINAL RESEARCH
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Neural Processing of Familiar and Unfamiliar Children's Faces: Effects of Experienced Love Withdrawal, but No Effects of Neutral and Threatening Priming

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In the face of a potential threat to his or her child, a parent's caregiving system becomes activated, motivating the parent to protect and care for the child. However, the neural correlates of these responses are not yet well understood. The current study was a pilot study to investigate the processing of subliminally presented threatening primes and their effects on neural responses to familiar and unfamiliar children's faces. In addition, we studied potential moderating effects of empathy and childhood experiences of love-withdrawal. A total of 45 students participated in an fMRI experiment in which they were shown pictures of familiar children (pictures morphed to resemble the participant like an own child would) and unfamiliar children preceded by neutral and threatening primes. Participants completed a modified version of the Children's Report of Parental Behavior Inventory to measure parental love withdrawal, and the Empathic Concern scale of the Interpersonal Reactivity Index to measure affective empathy. Contrary to our expectations, we did not find evidence for subliminal priming effects. However, we did find enhanced activity in the right inferior frontal gyrus (IFG; involved in self-referential processing) and in face processing areas (infero-lateral occipital cortex and fusiform areas) in response to the familiar child, indicating preferential processing of these faces. Effects of familiarity in face processing areas were larger for participants reporting more love withdrawal, suggesting enhanced attention to and processing of these highly attachment relevant stimuli. Unfamiliar faces elicited enhanced activity in bilateral superior temporal gyrus (STG) and other regions associated with theory of mind (ToM), which may indicate more effortful ToM processing of these faces. We discuss the potential difference between a familiarity and a caregiving effect triggered by the morphed faces, and emphasize the need for replication in parents with pictures of their "real" own child.

Keywords: threat, priming, face processing, superior temporal gyrus, inferior frontal gyrus, love withdrawal

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Abbreviations: fMRI, Functional magnetic resonance imaging; ROI, Region of interest; IFG, Inferior frontal gyrus; MFG, Middle frontal gyrus; STG, Superior temporal gyrus; ToM, Theory of mind.

INTRODUCTION

In the face of a potential threat or danger in the environment, a parent's caregiving system may become activated when his or her child or a stimulus reminiscent of that child (such as crying or a picture of the child's face) is present and the threat is not overwhelmingly strong (Mikulincer et al., 2005; George and Solomon, 2008; Swain et al., 2014). Even when a parent is not consciously aware of a threatening stimulus in the environment, he or she might still process this threatening stimulus to some extent, which could lead to specific parental behaviors (with accompanying changes in brain activity) to protect and care for the child (Bowlby, 1988; Bakermans-Kranenburg and van IJzendoorn, in preparation). It has been argued that the caregiving system is complementary to the attachment system (George and Solomon, 2008; Strathearn et al., 2009), and is not restricted to the parent-child relationship but rather extends to other intimate relationships such as the relationships with siblings or partners (e.g., Mikulincer et al., 2005). In the current study we focus on the neural processing of familiar and unfamiliar faces after subliminal neutral or threatening primes. The familiar faces were created by morphing a child's face with the participant's own face to suggest familiarity and potentially biological relatedness in order to trigger the caregiving system.

Individuals may be able to process affective information, especially potentially threatening stimuli, fast and automatically, and possibly even without conscious awareness (Whalen et al., 1998; Globisch et al., 1999; Mikulincer et al., 2005). Since it may take hundreds of milliseconds to consciously perceive a potential threat (Koch and Tsuchiya, 2007), a system in the human brain that can react to potential threats before conscious awareness seems advantageous from an evolutionary perspective, as it enables a fast reaction that can preserve oneself or one's offspring from danger or death. Subliminal primes can be used to examine the preconscious processing of threat-related information. In some previous studies, researchers found evidence for the human brain's capacity to process threat-related visual stimuli without conscious awareness. For example, in one study participants rated neutral stimuli (the target) more positively when these stimuli were preceded by a subliminal prime depicting a happy face and more negatively when targets were preceded by a prime depicting an angry face (Almeida et al., 2013). Brain imaging studies also found some evidence for the brain's ability to process threatening stimuli without conscious awareness. In these studies, researchers mainly focused on amygdala activity in response to subliminally presented angry or fearful faces. The amygdala is a subcortical structure commonly associated with the processing of emotional, especially threat-related, content (LeDoux, 1998). Briefly presented fearful (Whalen et al., 1998) and angry (Morris et al., 1998) faces evoked right amygdala activity.

However, in some studies no evidence for the existence of such an automatic processing system of threat-related stimuli was found. For example, in earlier studies with threat-related stimuli presented in supraliminal and subliminal conditions, enhanced amygdala activity was found in the supraliminal, but not in the subliminal condition (Pessoa et al., 2006; Hoffmann et al., 2012). Importantly, not everyone may respond to emotional or threatening information in the same way, and such moderating effects may explain inconsistent findings for main effects of threat-related stimuli. Considering parental responses or responses to biologically related or otherwise familiar others in threatening contexts, factors such as empathy and individuals' own childhood experiences with their attachment figures may influence how they react to a potential threat to offspring or other familiar persons.

With regard to empathy, which has been defined as the capacity to experience and understand the emotional states of others (Eres et al., 2015), cognitive (understand), affective (experience) and imitative (action) components can be distinguished (Klimecki and Singer, 2013). In the current study, we are mainly interested in the affective component of empathy, which refers to how we feel when we imagine the emotions of another person in a particular situation (i.e., when we "put ourselves in the other person's shoes"). This affective component refers to a mature affective response that is experienced with a certain distance to the person empathized with rather than the more primitive and potentially dysfunctional copying of the target's affective response or distress (Davis, 1983; De Corte et al., 2007). In previous research, viewing a beloved person in pain elicited activity in brain areas associated with affective dimensions of pain (e.g., dorsal anterior cingulate cortex, dACC, see Lieberman and Eisenberger, 2015), with stronger effects in participants with high scores on empathic concern (Singer et al., 2004). In addition, observing someone experiencing "social pain" (i.e., being socially excluded) elicited brain activity in similar areas (e.g., anterior insula, anterior cingulate cortex) in highly empathic but not in less empathic participants (Masten et al., 2011). Because pain, whether social or physical, results from a harmful stimulus in the environment, we may, extrapolating from these results, expect that highly empathic individuals will react stronger to a potential threat to their child or a familiar other. It should be noted, however, that the intensity of the threat could modulate responses of caregiving and protection, since overwhelmingly strong threats might turn the focus away from the other—even when it is offspring—to protecting oneself (Mikulincer et al., 2005). However, the stimuli used in the current study depict moderate rather than extreme threats.

Childhood experiences with parental love-withdrawal may also shape caregiving and protective responses to offspring or familiar others when confronted with a threat. Although the neural correlates of individual differences in caregiving and protective responses are poorly understood (but see Swain et al., 2014), the presence of a threat may affect the way parents perceive and respond to their child differently based on their own childhood experiences with protective or neglectful attachment figures. Love withdrawal is a parental disciplinary strategy in which the parent's love and affection is conditional on the child's behavior and success. Excessive use of love withdrawal is considered psychological maltreatment (Euser et al., 2010) and experiences of love withdrawal have been associated with long-lasting negative outcomes, like fear of failure, low self-esteem, low emotional well-being, and a negative view of parent-child relationships as well as insecure attachment (Bowlby, 1973/1985, p. 243; Assor et al., 2004; Goldstein and Heaven, 2000; Elliot and Thrash, 2004; Renk et al., 2006). Thus, experiencing love-withdrawal has consequences extending beyond the parent-child relationship, affecting ones beliefs about relationships as well as more generalized socio-emotional processes. That personal characteristics and belief systems formed within the parent-child relationship can affect responses to other significant others has convincingly been shown by, e.g., Mikulincer et al. (2005). These authors showed experimentally how feelings of more secure attachment facilitate supporting partners in distress. Previous research has associated childhood experiences of love withdrawal not only with changes in the (neural) processing of and responding to socio-emotional information, including faces (Huffmeijer et al., 2011), but also with changes in effects of external influences, including oxytocin administration, on these processes (Van IJzendoorn et al., 2011; Bakermans-Kranenburg et al., 2012; Huffmeijer et al., 2013).

The present study was a pilot for research to be conducted with mothers, and examined in young-adult females without children of their own whether subliminally presented threatening primes would evoke the expected changes in brain activity in the amygdala and would differentially affect (the neural correlates of) protective responses to pictures of a familiar and an unfamiliar child. In addition, we examined whether these effects would be moderated by empathic concern and self-reported childhood experiences of love-withdrawal. In order to provide a “proof of concept”, we used a homogenous student sample without children. We mimicked maternal reactions by presenting as “own child” the picture of a child face modified to resemble the participant’s face, and combined this with primes depicting neutral and threatening scenes to evoke (the neural correlates of) protective responses. Facial resemblance is a very important cue for kinship (Bressan and Grassi, 2004; Maloney and Dal Martello, 2006) and has been shown to increase “parental” responses such as willingness to invest in a child (e.g., DeBruine, 2004; Platek et al., 2004). Thus, using pictures of children facially resembling the participants (by use of morphing, see “Materials and Methods” Section) is probably the most accurate imitation of an “own” child in participants without children of their own. However, we cannot exclude the possibility that the morphed faces will only be perceived as familiar rather than suggesting biological relatedness.

We focused our analyses on brain regions known to be involved in the processing of threat and face familiarity: the amygdala (involved in threat detection as well as more general salience detection, and responsive to face familiarity in previous studies [Natu and O’Toole, 2011]), inferior frontal gyrus (IFG, implicated in the processing of familiar faces, see for a review Devue and Brédart, 2011; Platek et al., 2008; implicated in affective empathy, Shamay-Tsoory, 2011, and considered part of the mirror neuron system, e.g., Kilner et al., 2009), and superior temporal gyrus (STG, found to be activated in response to unfamiliar compared to personally familiar faces, see Ramon et al., 2015, and involved in Theory of Mind [ToM]). Importantly, these areas have not only been associated with the neural processing of threat and/or familiarity, but the functions mediated by these regions (such as ToM, empathy, affect regulation and mirroring) are also considered critical for parental behavior and involvement (Swain et al., 2014). We expected enhanced amygdala activity in response to threatening primes relative to neutral primes. We expected empathy to moderate this effect, with enhanced amygdala activity in highly empathic individuals. In addition, we hypothesized that IFG activity would be elevated in response to familiar-looking compared to unfamiliar-looking faces, and, conversely, that STG activity would be elevated in reaction to unfamiliar compared to familiar-looking faces. We explored potential moderating effects of experiences of love withdrawal, which might moderate effects of face familiarity or might be associated with the strength of a priming effect on familiar faces in particular. We chose to focus on a limited number of regions of interest (ROIs) to retain sufficient statistical power for testing *a priori* hypotheses, but, as interesting or unexpected effects might occur in other brain regions, we also conducted whole-brain analyses to explore changes in brain activity as a result of the primes, familiarity, empathy, and parental love withdrawal.

MATERIALS AND METHODS

Participants

A total of 49 female undergraduate and graduate students aged 18–28 years ($M = 21.73$, $SD = 2.55$) were invited for two experimental sessions, separated by approximately 4 weeks. The second session was included to study test-retest reliability of fMRI data (to be reported elsewhere); the current study uses data from the first session only. Exclusion criteria were MRI contraindications, pregnancy, current psychiatric and neurological disorders, severe head injury, current alcohol or drug abuse, and chronic use of medication (except contraceptives). Data of four participants were excluded from analysis because of excessive head movements (>3 mm; $n = 3$) or falling asleep during fMRI acquisition ($n = 1$). Our final sample therefore included 45 participants with an average age of 21.82 years ($SD = 2.61$, range: 18–28). The study was approved by the Ethics Committee of the Leiden University Medical Center. All participants signed informed consent at the beginning of the first session and were rewarded with 40€ for participation. None of these participants’ structural MRI scans showed any anomalies.

Procedure

Participants’ handedness was assessed using van Strien’s (1992) Handedness Questionnaire prior to the first session. Participants were asked to abstain from alcohol and excessive physical activity during the last 24 h and from caffeine during the last 12 h before the start of the session. At the beginning of the session participants completed questionnaires on empathy and parental use of love withdrawal. Subsequently, the MRI procedure was explained and participants were placed in the MRI scanner. Foam inserts were placed between the head coil and the participant's head to minimize head movements. Within the scanner, participants completed a priming task (see below), during which visual stimuli were projected onto a screen placed outside the opening of the scanner bore. Participants viewed the screen through a mirror fixed to the head coil. At the end of the second session participants were debriefed about the nature of the priming task.

Questionnaires

Handedness Questionnaire

This questionnaire consists of 10 items with regard to hand preference during execution of several tasks (e.g., "Which hand do you use to hold scissors?") scored on a 3-point scale (left hand, both hands, right hand) ranging from −1 to 1. Total scores can thus vary between −10 and +10. Individuals with a score of +8 or higher are classified as strongly right-handed, whereas individuals scoring −8 or lower are classified as strongly left-handed. Individuals with scores between −8 and +8 are classified as ambidexter (van Strien, 2003). According to this definition, in the current sample, 23 participants were strongly right-handed, 19 were strongly left-handed, and three were ambidexter. We oversampled left-handed participants in order to examine the potential influence of left-handedness on neural activity (to be reported elsewhere).

Children's Report of Parental Behavior Inventory

Participants completed a modified version of the 30-item Children's Report of Parental Behavior Inventory (CRPBI-30, Schludermann and Schludermann, 1983; Beyers and Goossens, 2003), containing the items of the Acceptance and Psychological Control scales from the original questionnaire and several extra items to measure love withdrawal. The 11-item Love Withdrawal scale consisted of all five items that constitute the Withdrawal of Relations subscale of the 108-item CRPBI (3 of which are also included in the Psychological Control scale of the CRPBI-30; Schludermann and Schludermann, 1983), two items that were adapted from this same questionnaire, and four items that were adapted from the Parental Discipline Questionnaire (PDQ, Hoffman and Saltzstein, 1967; Patrick and Gibbs, 2007). Participants rated how well each item described their mother and father separately (e.g., "My mother was a person who if I'd hurt her feelings, stopped talking to me until I please her again") on a 5-point Likert scale, ranging from ("not at all") to ("very well"). We only included the 11-items of the Love Withdrawal subscale in our analyses. Scores for maternal and paternal love withdrawal were summed. After winsorizing the score of one outlier ($z = 3.61$; the new score was computed as the highest score occurring in the rest of the sample plus the difference between the highest and next-highest score, see Tabachnick and Fidell, 2001), the scores were normally distributed with an average score of 18.72 ($SD = 6.15$). Internal consistency of this questionnaire was high (Cronbach's alpha = 0.91). Adequate validity and reliability of the CRPBI and its subscales were demonstrated (Schludermann and Schludermann, 1983, 1988; Locke and Prinz, 2002) and the Love Withdrawal subscale as used in this study was implemented in earlier research on the consequences of maternal love withdrawal in young adults (Huffmeijer et al., 2011).

Interpersonal Reactivity Index

To measure empathy, participants completed the 28-item Interpersonal Reactivity Index, a well validated questionnaire measuring four distinct aspects of empathy (Perspective Taking, Fantasy, Empathic Concern, and Personal Distress; Davis, 1983; De Corte et al., 2007). In the current analyses, we only administered the seven-items of the Empathic Concern subscale, since we were interested in the emotional component of empathy. Participants rated how well each of the items described themselves on a 5-point Likert scale, ranging from 0 ("does not describe me well") to 4 ("describes me very well"). The data were normally distributed and did not contain any outliers. On average, participants scored 19.36 ($SD = 3.53$) on the Empathic Concern scale. The internal consistency was acceptable ($\alpha = 0.67$).

Scores on Love Withdrawal and Empathic Concern were not correlated ($r = 0.00$) and could therefore be included as independent predictors in the same analyses.

Experimental Task

In the scanner, subjects completed a priming task consisting of 234 trials. The priming task was set up in an event-related design. E-prime Software (Psychology Software Tools, 2012) was used for stimulus presentation. All stimuli were shown in the center of the screen on a black background. Forward and backward masking of the primes, using a picture showing a colored, circular pattern, was used on all trials to prevent conscious perception of the primes. The mask matched the dimensions and average luminosity of the primes. During each trial, a fixation cross was presented for 1800–10,600 ms, followed by the mask (presented for 484 ms), a prime (i.e., a neutral or threatening picture) that was presented for 16 ms, and again the mask (presented for 100 ms). Subsequently, an unfamiliar-looking, a familiar-looking or a scrambled face was presented for 2000 ms. Thus, there were six conditions: a familiar-looking face presented after a neutral prime (neutral-familiar), a familiar-looking face presented after a threatening prime (threat-familiar), an unfamiliar-looking face presented after a neutral prime (neutral-unfamiliar), an unfamiliar-looking face presented after a threatening prime (threat-unfamiliar), a scrambled face presented after a neutral prime (neutral-scrambled), and a scrambled face presented after a threatening prime (threat-scrambled). Stimulus sequences (mask-prime-mask-[scrambled] face) were presented in quasi-random order, with the restriction that the same prime could not be presented more than twice in a row, the same face could not be repeated more than four times in a row, and the same condition could not repeat more than twice. In all, 13 neutral and 13 threatening primes were each presented three times with each face, resulting in 39 (3 × 13) trials per condition. To ensure that participants remained alert during the task, they had to press a button in order to continue the task after every 11–13 trials. The average duration of the task was 23 min.

Primes

The stimuli used as primes were developed by Nummenmaa et al. (2008). To enable comparability between neutral and threatening primes, these authors created pairs of photographs depicting a neutral and a threatening scene, respectively. Each pair was matched on luminosity, global energy, contrast density, and complexity, and showed the same persons in comparable proximity to each other. Each photograph portrayed two persons. On threatening photographs, interpersonal attack scenes (e.g., one person strangling the other) were shown, whereas non-emotional situations (e.g., two persons having a conversation) were depicted on neutral photographs.

We selected 13 pairs out of the 37 pairs of threatening and neutral pictures (Nummenmaa et al., 2008): an independent sample of 15 participants were presented with the pictures for 16 ms, with forward and backward masking as described above, and asked to press one button if they were sure a neutral picture had been presented, a second button if they were sure a threatening picture had been presented (they were instructed to press these buttons only if they had seen the picture and were sure of its contents), and a third button if they had not seen the picture or were unsure of its contents. This was done to test whether the neutral and threatening pictures were visible for the participants when these pictures were presented for 16 ms. Ideally, the participants should not be able to consciously perceive and identify the pictures, since our goal was to investigate subliminal processing of neutral and threatening stimuli. Therefore, only pictures that were not identified as neutral or threatening above chance levels (i.e., pictures for which significantly more than 50% of participants answered "unsure") were selected for use in the current study. Another independent sample of 28 participants was used to rate the 13 pairs of pictures for valence and arousal. Threatening photographs ($M = 8.40$, $SD = 0.22$) were rated as significantly more negative than neutral photographs ($M = 4.48$, $SD = 0.60$; $t_{(12)} = -23.90$, $p < 0.01$, $d = -8.67$), on a scale ranging from 1 ("positive") to 9 ("negative"). Moreover, on a scale ranging from 1 ("affected") to 9 ("calm"), threatening primes ($M = 3.43$, $SD = 0.41$) evoked significantly more arousal than neutral primes ($M = 7.31$, $SD = 0.33$; $t_{(12)} = 21.62$, $p < 0.01$, $d = 10.43$).

At the end of the second session, participants in the current study were asked whether they had seen any of the pictures presented in between the masks (i.e., the primes). Twenty-six participants (58%) indicated that they had noticed the pictures. Subsequently, these participants were asked to indicate which of several items (e.g., "truck", "adults") they had seen in the pictures. Some of these items had actually been present in the pictures, others had not. None of the participants performed above chance level, the participants selected seen and unseen items with equal probability.

Facial Stimuli

Pictures of unfamiliar- and familiar-looking children were created by morphing the photograph of a child's face (unfamiliar to the participant) with: (i) a photograph of an unknown female's face and (ii) a photograph of the participant's own face. Prior to the first session, participants were asked to provide a full-color digital photograph of themselves that met the following criteria: picture on a light and uniform background, showing their face (full frontal) and neck only, with a neutral facial expression, and no piercings, make-up or glasses. Full color, full frontal photographs of two female faces (both Caucasian and unfamiliar to the participant, aged 24 and 25 year, neutral facial expression, no jewelry or glasses) were used to create the unfamiliar-looking morphs. For half of the participants, female face 1 was used to create the unfamiliar-looking morph for session one and female face 2 was used to create the unfamiliar-looking morph for session two, and for the other half vice versa. Full color, full frontal photographs of six 9–11 year old children (three boys and three girls, all Caucasian [but slightly varying in skin color], all unfamiliar to the participants, with neutral facial expression, no jewelry or glasses) were available for morphing. For half the participants ($n = 21$ for the current sample) morphs were created with the picture of a female child and for the other half ($n = 24$ for the current sample) morphs were created with the picture of a male child. Within genders, the child that best matched the participant's skin color and face-shape was selected for ease of morphing. Both unfamiliar-looking and familiar-looking morphs were created with the photograph of the same child. One familiar-looking and two-unfamiliar-looking morphs were created for the two sessions. We did not use the same unfamiliar-morph for both sessions, since this would have led to increased familiarity with the unfamiliar-looking face in session two compared to session one.

Prior to morphing, all photographs were resized to 448 × 560 pixels and edited using Adobe Photoshop CS: External features (i.e., hair and ears) were removed and the pictures were framed on a black background. Morphing was then performed using Fantamorph 5 Deluxe, such that the picture of the familiar-looking child consisted for 50% of the participant's face and for 50% of an unknown child's face, and the picture of the unfamiliar-looking child consisted for 50% of the unknown female's face and for 50% of the child's face. The resulting pictures appear to present children slightly older than the 9–11 year olds used for morphing. An independent sample of 15 participants rated the age of the unfamiliar-looking morphs as 13.80 years ($SD = 1.66$) and the familiar-looking morphs as 14.40 years ($SD = 1.60$) on average ($p > 0.05$). Finally, a scrambled face was created for each participant from the familiar-looking morph by randomly rearranging blocks of 9 × 9 pixels using Matlab R2012B.

At the end of the second session, participants in the current study evaluated how much the familiar-looking and unfamiliar-looking faces used during the priming task resembled themselves on a scale ranging from 0% resemblance to 100% resemblance.

On average, the participants reported a similarity of 38.07% ($SD = 13.38\%$) with the familiar and 6.40% ($SD = 6.84\%$) with the unfamiliar morphs. The difference in perceived similarity was significant with a large effect size ($t_{(44)} = 15.82$, $p < 0.01$, $d = 2.98$).

Image Acquisition

Images were acquired at the Leiden University Medical Center on a 3-T Philips Achieva MRI system (Philips Medical Systems, Best, Netherlands) with a 32-channel SENSE (Sensitivity Encoding) head coil. An event-related design with 680 T2*-weighted whole-brain echo planar images (EPI, repetition time (TR) = 2200 ms, echo time (TE) = 30 ms., flip angle = 80°, 38 transverse slices, descending acquisition order, voxelsize = $2.75 \times 2.75 \times 3.025$ mm^3 with a 10% interslice gap, field of view (FOV) = $220 \times 114.675 \times 220$ mm^3) was used for the functional scans. To avoid magnetic saturation effects, the first four functional scans were discarded. In addition, an anatomical 3D T1-weighted scan (TR = 9.825 ms, TE = 4.605 ms, flip angle = 8°, 140 transverse slices, voxelsize $0.875 \times 0.875 \times 1.2$ mm^3, FOV = $224 \times 168 \times 177.333$ mm^3) and a high-resolution T2*-weighted EPI-image (TR = 2200 ms, TE = 30 ms, flip angle = 80°, 84 transverse slices, voxel size = $1.964 \times 1.964 \times 2$ mm^3, FOV = $220 \times 168 \times 220$ mm^3) were obtained for coregistration purposes.

fMRI Data Analysis

Data-analyses were performed using FSL (FMRIB's Software Library[1]) FEAT (FMRI Expert Analysis Tool) version 5.0.4, part of Jenkinson et al. (2012) and Smith et al. (2004). The following pre-statistics processing steps were carried out: motion correction using MCFLIRT (Jenkinson et al., 2002), non-brain removal (BET; Smith, 2002), spatial smoothing using a Gaussian kernel with a full-width-at-half-maximum of 6 mm, and high-pass temporal filtering with a high-pass filter cutoff of 100 s.

Functional images were registered to the high-resolution EPI-image, which was then registered to the 3D T1-weighted scan, and then to the 2 mm isotropic MNI-152 standard space image (T1 standard brain averaged over 152 subjects; Montreal Neurological Institute, Montreal, QC, Canada; Jenkinson et al., 2002). Functional activity in response to the stimuli was investigated using general linear model analysis in native space. Because primes and masks were presented for very short durations and time-locked to the presentation of the faces, hemodynamic responses to the individual stimuli within a mask-prime-mask-face sequence overlap extensively and sum to a total, summed hemodynamic response to the stimulus sequence. Assuming that responses to the masks in a given brain area do not vary systematically across the different conditions (as these are defined by different types of primes and the faces, but the masks are always the same), this summed response may vary depending on the response to the primes and faces. We thus treated the presentation of mask-prime-mask-face as a single stimulation period, and thus the different conditions (threat-familiar, threat-unfamiliar, threat-scrambled, neutral-familiar, neutral-unfamiliar, and neutral-scrambled) and the participants' responses were modeled as seven explanatory variables using the Custom (3 column format) wave function and convolved with a double gamma hemodynamic response function. The temporal derivatives of the explanatory variables were included in the model, yielding 14 regressors. Subsequently, individual lower-level contrast images (see below) were submitted to higher-level mixed effects (FLAME 1 + 2) group ROI and whole-brain analyses. Group means for ROIs and whole-brain analyses were tested using F-tests. All statistical images were thresholded using clusters determined by $Z > 2.3$ (F-values are automatically converted to z-statistics) and a cluster-corrected significance threshold of $p < 0.05$ (Worsley, 2001)[2].

Before evaluating our main hypotheses, a preliminary analysis was conducted to check whether faces activated known face processing areas such as the fusiform gyrus more than scrambled stimuli. For this purpose, the contrast face (i.e., neutral-familiar, neutral-unfamiliar, threat-familiar, threat-unfamiliar) > scrambled face was tested. In the preliminary analysis, no confound regressors or continuous predictors were added to the model and only whole-brain analysis was conducted. Results of the preliminary analysis, showing that the facial stimuli reliably activated face processing areas as expected, can be found in the Supplementary Materials.

To evaluate our main hypotheses, separate whole-brain and ROI-analyses were performed to test for: (i) differences in brain activity in response to stimulus sequences in which faces were presented with a neutral prime and sequences in which faces were presented with a threatening prime; (ii) differences in brain activity in response to familiar and unfamiliar faces; and (iii) interactions between the type of face and the type of prime. For these analyses, five contrasts of interest were calculated: (1) familiar (threat-familiar and neutral-familiar) vs. unfamiliar (threat-unfamiliar and neutral-unfamiliar); (2) threatening (threat-familiar and threat-unfamiliar) vs. neutral (neutral-familiar and neutral-unfamiliar); (3) (threat-familiar vs. neutral-familiar) vs. (threat-unfamiliar vs. neutral-unfamiliar); (4) threat-familiar vs. neutral-familiar; and (5) threat-unfamiliar vs. neutral-unfamiliar. The first contrast tested for differences in brain activity in response to viewing familiar-looking faces

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[1] www.fmrib.ox.ac.uk/fsl

[2] Due to the large number of voxels analyzed, multiple testing is a well-known problem inherent to fMRI research. We chose to use cluster-extent based correction to correct for multiple testing. This correction procedure combines a threshold for results at individual voxels (i.e., for a cluster of voxels to be considered significantly activated all z-values at individual voxels within that cluster must exceed a certain value, in this case 2.3; t- and F-values are automatically converted to z-values) with requirements for the size of the cluster (i.e., a cluster is only considered significant if it consists of a sufficient number of voxels), in such a way that the probability of finding active clusters under the null hypothesis is smaller than 0.05 (i.e., α). To offer some indication of the robustness of statistical findings it is common to report the z- and p-values (α) employed in the cluster-based correction procedure, as well as the cluster size (in number of voxels) of significant clusters and the maximum z-value (i.e., Z-max) found among individual voxels in each significant cluster.

compared to unfamiliar-looking faces. Because the type of face presented may be expected to affect only the hemodynamic response to the face stimulus (as the prime is presented before it), the areas identified respond differently to familiar and unfamiliar faces. The second contrast tested for effects of the primes, i.e., differences in brain activity in response to presentation of sequences including neutral primes compared to sequences including threatening primes. Because the type of prime presented could theoretically affect the hemodynamic response to both the prime itself and the face stimulus, this contrast will identify both brain regions that respond differentially to the neutral and threatening primes (i.e., areas involved in processing the primes) and brain areas that respond differently to faces (regardless of whether this was a familiar or unfamiliar face) depending on the type of prime (i.e., a priming effect on face processing). In case of significant effects, comparisons to sequences including a scrambled stimulus instead of a face are used to distinguish between these two options. The third contrast tested for the interaction (i.e., variation in the effect of familiarity depending on the type of prime and/or variation in the effect of priming depending on face familiarity), and significant results for contrasts 4 and 5 were only interpreted in areas where contrast 3 was significant. F-tests were used to evaluate the hypotheses of the whole-brain and ROI-analyses. Scores on love withdrawal and empathic concern were included as continuous predictors and handedness was added to the model as a confound regressor.

The ROI analyses were performed on bilateral amygdala, bilateral inferior frontal gyrus (IFG) and bilateral STG to test our *a priori* hypotheses. Three higher-level analyses, restricted to bilateral amygdala, IFG and STG respectively, were conducted to investigate activity in these regions with maximized statistical power by limiting the number of statistical tests to the investigated ROI. The Harvard-Oxford Subcortical Structures Atlas was used to define the ROI for the amygdala and the Harvard-Oxford Cortical Structures Atlas (both implemented in FSL version 5.0.4) was used to define ROIs for the IFG and the STG. Three masks were created in 2 mm isotropic MNI-152 standard space (Jenkinson et al., 2002), consisting of voxels belonging to the left or right amygdala, IFG and STG respectively with a probability of at least 25%. Exploratory whole-brain analyses were performed to investigate brain activity in regions other than the *a priori* ROIs.

As use of caffeine may have an influence on brain activity as measured with fMRI (Liu et al., 2004; Liau et al., 2008; Perthen et al., 2008; Chen and Parrish, 2009), we reran the ROI and whole brain analyses testing effects of face and prime type excluding participants ($n = 7$) who did not comply with the request to abstain from caffeine during the last 12 h before the study. Using this sensitivity analysis, we evaluated whether effects in the total sample were replicated in the sample without caffeine-using respondents.

RESULTS

All significant clusters were defined by $Z > 2.3$ and a cluster-corrected significance threshold of $p < 0.05$ (Worsley, 2001).

ROI Analyses

Significant effects of face familiarity were found in both the IFG and STG (see **Figure 1**): familiar-looking faces elicited greater brain activity than unfamiliar-looking faces in the right IFG (size = 220, *Z-max* = 4.54, MNI coordinates *x, y, z* (mm) = 46, 26, 22), whereas unfamiliar-looking faces elicited greater brain activity than familiar-looking faces in bilateral STG (cluster 1 [left]: size = 304, *Z-max* = 4.1, MNI coordinates *x, y, z* (mm) = −62, −32, 14, cluster 2 [right]: size = 182, *Z-max* = 3.53, MNI coordinates *x, y, z* (mm) = 64, −26, 10). No effects of familiarity were found in the amygdala, and we did not find significant activity differences between stimuli preceded by

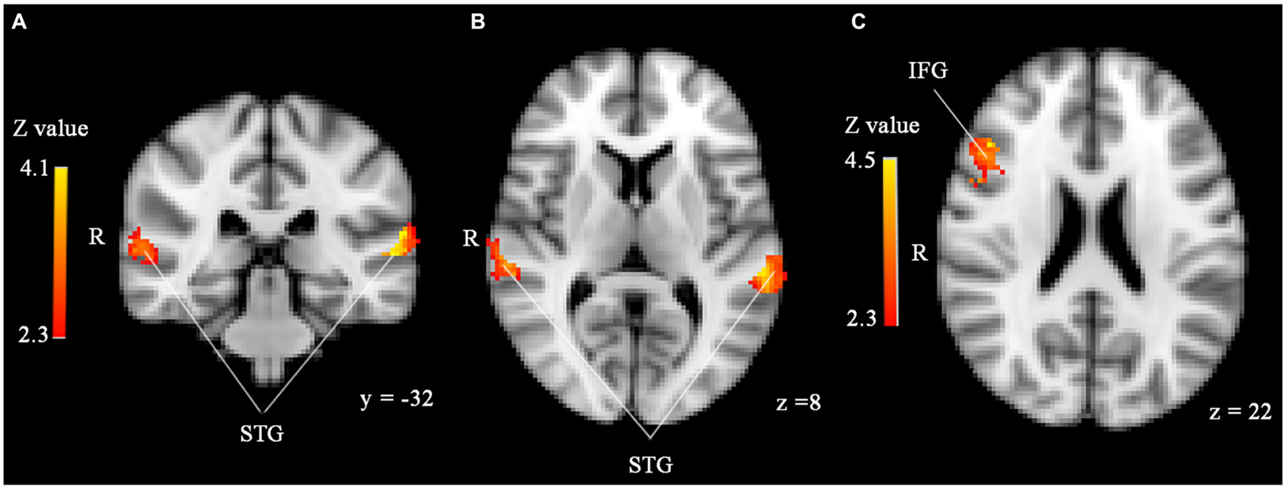

FIGURE 1 | (A,B) Significantly enhanced activity in bilateral superior temporal gyrus (STG) in response to unfamiliar compared to familiar faces in the sample with 45 participants. **(C)** Significantly enhanced activity in right inferior frontal gyrus (IFG) in response to familiar compared to unfamiliar faces. ROI analyses, $p < 0.05$, corrected by cluster threshold ($Z > 2.3$).

threatening and neutral primes or any familiarity*prime type interaction in any of the ROIs. Love withdrawal and empathic concern did not affect brain activity in any of the ROIs either.

Whole-Brain Analyses

To explore effects of threat priming and familiarity in regions outside our regions of interest, we performed whole-brain analyses. Results of these analyses revealed more widespread effects of face familiarity on brain activity (see **Table 1**). As illustrated in **Figure 2**, familiar-looking faces elicited greater brain activity in a cluster including not only the right IFG, but also parts of the right middle frontal gyrus (MFG), frontal pole, and insular cortex (cluster 2: size = 1559, peak *Z-max* = 4.54, MNI coordinates *x, y, z* (mm) = 46, 26, 22; see **Figure 2**). We also found increased activity in response to familiar- compared to unfamiliar-looking faces in bilateral clusters including the occipital pole, infero-lateral occipital cortex, and the temporo-occipital fusiform gyrus (cluster 3 [right]: size = 1627, peak *Z-max* = 4.63, MNI coordinates *x, y, z* (mm) = 40, −72, −10, cluster 1 [left]: size = 1182, peak *Z-max* = 4.29, MNI coordinates *x, y, z* (mm) = −30, −90, 6).

In addition, love withdrawal interacted with the effect of familiarity in a partially overlapping cluster including the right infero-lateral occipital cortex, occipital fusiform gyrus, and occipital pole (size = 1008, peak *Z-max* = 4.22, MNI coordinates *x, y, z* (mm) = 34, −80, 0). As illustrated in **Figure 3**, the effect of familiarity was larger (i.e., a larger difference in brain activity in response to familiar-looking compared to unfamiliar-looking faces) for participants reporting more love withdrawal.

Unfamiliar-looking faces compared to familiar-looking faces evoked increased activity bilaterally in clusters including not only

TABLE 1 | MNI Coordinates and *Z*-max values for regions with significant main effects for face familiarity and for regions in which love withdrawal and empathic concern interact with effects of face familiarity.

Experimental effect	Cluster number	Size (# voxels)	Region	*Z-max*	MNI coordinates for *Z*-max		
					x	***y***	***z***
Familiar > unfamiliar	3	1627	Right infero-lateral occipital cortex	4.63	40	−72	−10
	2	1559	Right MFG	4.54	46	26	22
	1	1182	Left infero-lateral occipital cortex	4.29	−30	−90	6
Unfamiliar > familiar	4	2815	Left planum temporale	4.57	−56	−30	10
	3	1794	Right postcentral gyrus	3.86	24	−34	60
	2	1504	Right planum temporale	4.09	48	−30	16
	1	765	Cuneus	3.85	0	−78	26
Familiar > unfamiliar^{LW+}	1	1008	Right infero-lateral occipital cortex	4.22	34	−80	0
Familiar > unfamiliar^{EC+}	1	593	Left frontal pole	3.68	−22	56	36

Note: Familiar > unfamiliar^{LW+}, Positive correlation between love-withdrawal and the activity difference in response to familiar and unfamiliar (i.e., familiar > unfamiliar) faces. Familiar > unfamiliar^{EC+}, Positive correlation between empathic concern and the activity difference in response to familiar and unfamiliar (i.e., familiar > unfamiliar) faces.

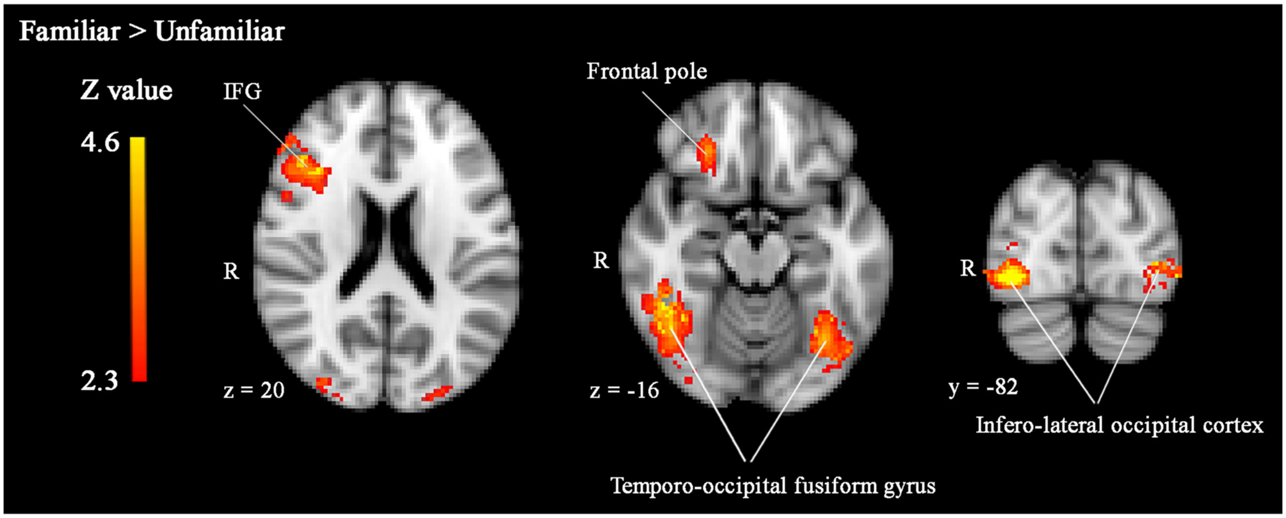

FIGURE 2 | Significantly enhanced activity in right IFG, bilateral temporo-occipital fusiform gyrus, and infero-lateral occipital cortex in response to familiar compared to unfamiliar faces. Whole-brain analyses, $p < 0.05$, corrected by cluster threshold ($Z > 2.3$).

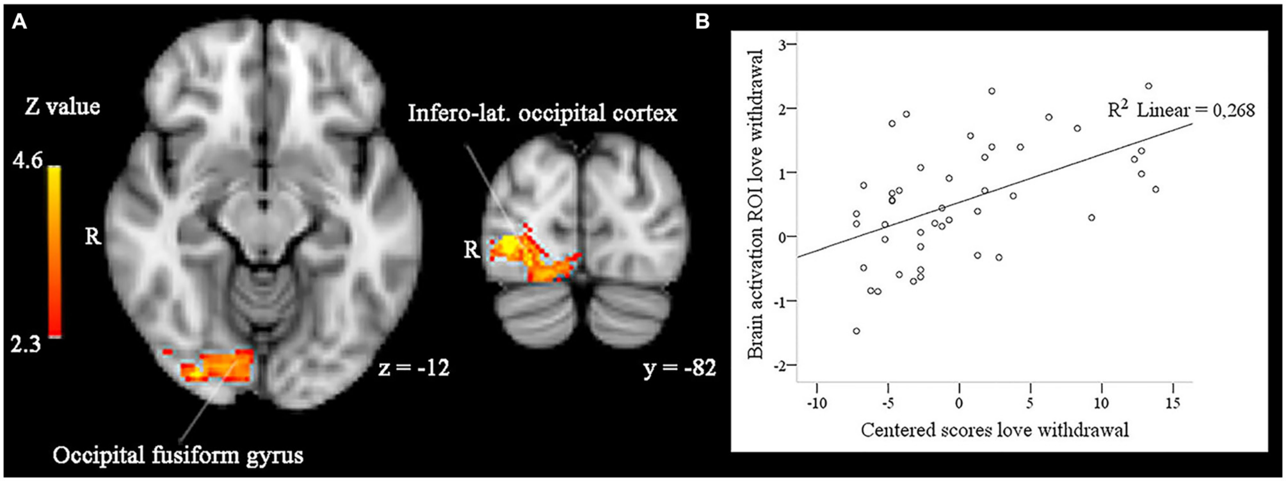

FIGURE 3 | (A) In right infero-lateral occipital cortex and right occipital fusiform gyrus the effect of face familiarity (enhanced activity to familiar compared to unfamiliar faces) is significantly and positively related to participants' scores on love withdrawal in whole-brain analyses, $p < 0.05$, corrected by cluster threshold ($Z > 2.3$). **(B)** Scatterplot between the activity difference (familiar > unfamiliar) found in these areas and participants' centered scores on love withdrawal.

the STG, but also the posterior division of the supramarginal gyrus, and the parietal operculum, and extending anteriorly into the planum temporale (cluster 4 [left]: size = 2815, peak Z-*max* = 4.57, MNI coordinates x, y, z (mm) = −56, −30, 10; cluster 2 [right]: size = 1504, peak Z-*max* = 4.09, MNI coordinates x, y, z (mm) = 48, −30, 16). In addition, unfamiliar-looking faces compared to familiar-looking faces elicited heightened activity in a cluster including the right postcentral gyrus, right superior parietal lobe, and bilateral precuneus (cluster 3: size = 1794, peak Z-*max* = 3.86, MNI coordinates x, y, z (mm) = 24, −34, 60) and in bilateral cuneus (cluster 1: size = 765, peak Z-*max* = 3.85, MNI coordinates x, y, z (mm) = 0, −78, 26). These clusters are presented in **Figure 4**.

Empathic concern interacted with face familiarity in a frontal area (frontal pole: size = 593, peak Z-*max* = 3.68, MNI coordinates x, y, z (mm) = −22, 56, 36) far at the outside of the brain and not overlapping with any of the significant clusters described above, suggesting artifactual activity.

Similar to the ROI analyses, the whole-brain analyses did not reveal any significant activity differences between

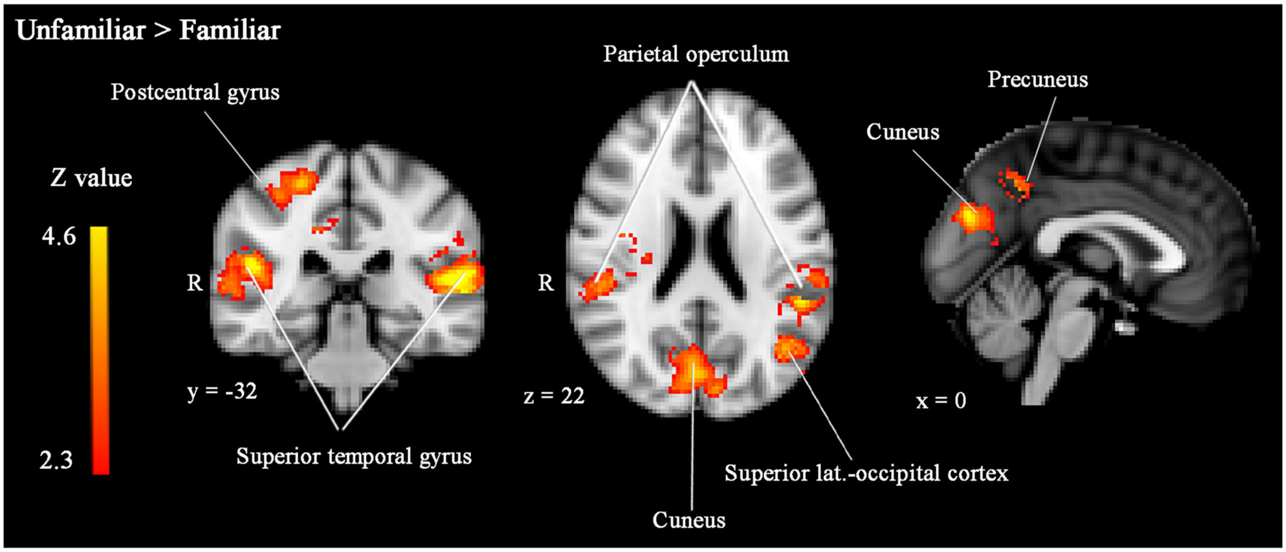

FIGURE 4 | Significantly enhanced activity in bilateral STG, right postcentral gyrus, bilateral parietal operculum, left superior lateral occipital cortex, bilateral cuneus and left precuneus in response to unfamiliar compared to familiar faces. Whole-brain analyses, $p < 0.05$, corrected by cluster threshold ($Z > 2.3$).

stimuli preceded by threatening and neutral primes or any familiarity*prime type interaction.

Analyses with 38 Participants

The clusters that we found in the ROI and whole-brain analyses in the total sample of 45 participants were largely replicated with the 38 participants who abstained from caffeine use. In the smaller sample, however, familiar-looking compared to unfamiliar-looking faces evoked enhanced activity only in right occipital pole, infero-lateral occipital cortex, and temporo-occipital fusiform gyrus and not bilaterally as in the sample with 45 participants. This small difference may be due to lower statistical power in the smaller sample.

DISCUSSION

In this study, we investigated the processing of subliminally presented threatening primes and their effects on neural responses to pictures of a familiar (and potentially "own") and unfamiliar child in a homogenous student sample. In addition, we studied moderating effects of empathy and experiences of love-withdrawal. Since we were particularly interested in parental protective reactions in the presence a potential threat, we combined pictures of faces of familiar-looking children with primes that depicted threatening scenes. Contrary to our expectations, we did not find evidence of a priming effect, nor of any interaction between empathy or experienced love withdrawal and priming. The primes used in our study depicted fairly complex neutral and threatening scenes, showing multiple people and objects. It is possible that these images were too complex for the brain to extract the threatening or neutral content fast and efficiently, and that preconscious processing of the threat thus did not occur. Earlier studies on subliminal priming usually used less complex stimuli (e.g., fearful or angry facial expressions; e.g., Morris et al., 1998; Whalen et al., 1998; Almeida et al., 2013). However, if the brain possesses a specialized threat-detection system to enable fast and automatic responses to environmental threats, we would expect such a system to be able to process threatening stimuli with various contents and complexities.

An absence of priming effects on face processing may not only be due to the complexity of the scenes used as primes. It is also possible that the scenes did not induce protective reactions. It seems natural, however, that parents or adults in general look after children when they witness or expect threatening events and their own survival is not immediately at stake. Although caregiving responses may be weaker when the child is not in distress (i.e., crying) or when the threat is aimed at the adult, the hypothesis that neural differences can be observed if the subliminal threat is really processed may still be warranted. Interestingly, results of some recent studies actually do not provide much support for the existence of a human brain system capable of preconscious processing of threatening information (see Pessoa and Adolphs, 2010; Hoffmann et al., 2012). It should be noted that in earlier studies of "subliminal" processing of affective information primes were often presented for 30 ms or longer (Morris et al., 1998; Whalen et al., 1998; Dimberg et al., 2000; Li et al., 2008). Participants differ in their sensitivity to threatening stimuli, but reliable detection of fearful faces has been observed with presentation durations of only 17 ms (Pessoa et al., 2005). This suggests that priming may not have been completely subliminal in the previous experiments with prime presentations of approximately 30 ms. Obviously, what is needed is replication of our study with subliminal stimuli of varying duration and involving a more direct threat to the child or, alternatively, with supraliminal threat stimuli.

We also investigated the effects of face familiarity on neural activity. As hypothesized, we found enhanced activity in response to familiar-looking faces in the IFG, extending into the MFG and insular cortex. Enhanced activity in IFG and MFG is frequently seen in familiar face processing (Gobbini and Haxby, 2006; Platek and Kemp, 2009; Taylor et al., 2009). In addition, enhanced activity of these brain areas is frequently found in response to pictures or videos of an own vs. other/unfamiliar child (Bartels and Zeki, 2004; Noriuchi et al., 2008; Kuo et al., 2012; Wittfoth-Schardt et al., 2012). These effects may be associated with the role of these brain areas in self-referential processing: when confronted with (the face of) someone who physically resembles the self (whether due to kinship or otherwise) concepts relating to the self are automatically activated. This human tendency to extrapolate from physical, "outer", resemblance to psychological, "inner", resemblance plays an important role in the understanding (including empathic understanding) of others (see for a review Devue and Brédart, 2011) Importantly, these as well as other processes in which the IFG and insula have an important role (e.g., emotion-regulation) are very important for parental behavior. In fact, Swain et al. (2014) have given these areas an important role in their model of the "parental brain". We also found enhanced activity in occipital and temporal (i.e., occipital pole, infero-lateral occipital cortex, and fusiform gyrus) areas involved in visual, and, more specifically, face processing (Haxby et al., 2000; Natu and O'Toole, 2011). Our findings suggest preferential processing of the familiar-looking faces. Both of these effects fit well with known processing advantages of stimuli associated with own compared to unfamiliar children in parents (Leibenluft et al., 2004).

Love withdrawal moderated the effect of familiarity in right hemisphere face processing areas (infero-lateral occipital cortex and occipital fusiform gyrus). Participants reporting more love withdrawal showed larger differences in brain activity in response to familiar-looking vs. unfamiliar-looking faces. Interestingly, changes in the neural processing of facial stimuli in young adults reporting high maternal love withdrawal have been observed before (e.g., Huffmeijer et al., 2011). Experiences of love withdrawal create a mental link between behavior and relational consequences, and they compromise the security of the parent-child attachment relationship, which becomes conditional on the child's behavior (Goldstein and Heaven, 2000; Assor et al., 2004; Elliot and Thrash, 2004; Renk et al., 2006). We suggest that the increased salience and relevance of the parent-child relationship may generalize to relationships more generally and increase the processing of information relevant to those relationships, in particular relationships with other family members, including own children. The enhanced brain activity seen in participants with high scores on love withdrawal to familiar-looking faces, designed to appeal to a kinship bond, may be a neural signature of this processing enhancement.

In contrast to familiar-looking faces, unfamiliar-looking faces enhanced activity in bilateral STG, and in whole brain analyses this activity extended anteriorly from the planum temporale into the parietal operculum and the posterior part of the supramarginal gyrus. In addition, unfamiliar-looking faces elicited enhanced activity in the right postcentral gyrus, right superior parietal lobe, and bilateral cuneus and precuneus. These regions are part of the brain's socio-emotional networks and they are, in particular the superior temporal sulcus (STS), involved in ToM processes. ToM refers to the cognitive capacity to attribute mental states (e.g., desires, intentions) to others and to predict others' behaviors from these mental states (Frith and Frith, 1999; Schurz et al., 2014). Although contrasting results exist in the literature (Leibenluft et al., 2004), several previous studies have observed decreased activity in the STS in response to familiar faces (Ramon et al., 2015) and to pictures of mothers' own children (Bartels and Zeki, 2004) compared to unfamiliar faces. Decreased activity in brain areas supporting ToM in response to familiar compared to unfamiliar faces may be explained by reduced effort, i.e., due to for example self-referential processing (see above) it is easier to estimate the mental state of someone familiar or similar to the self and by a lower need to investigate the social validity, i.e., a reduced need to thoroughly assess/estimate the mental state or intentions of familiar persons, as suggested by Bartels and Zeki (2004).

Future research should also take some limitations of the current study into account. The most important limitation is of course the use of morphed faces instead of faces of own offspring. The difference between the "own" and unfamiliar children's faces was physical resemblance (looking familiar). Although the participants reported afterwards that the familiar faces were much more similar to their own faces than the unfamiliar faces and physical resemblance is a kinship cue, replication with faces of real offspring is needed to disentangle effects of biological relatedness and familiarity or physical resemblance in the absence of a kinship bond. Second, the current design did not allow for separate modeling of hemodynamic responses to primes and faces. Because primes and masks were presented for very short durations and time-locked to the presentation of the faces, hemodynamic responses to the individual stimuli within a mask-prime-mask-face sequence overlapped extensively, requiring the modeling of a single, summed hemodynamic response to each stimulus sequence. Although all relevant processes (processing of the primes, processing of the faces, and effects of priming on face processing) could be separated by comparing responses to the different stimulus sequence conditions, it is worthwhile to consider the inclusion of conditions in which either the prime or the face is omitted from the stimulus sequence. Although this would lengthen the paradigm, such a design would allow for separate modeling of responses to primes and faces which may lead to a less complicated analysis approach. Third, we used self-report questionnaires to investigate parental love withdrawal and empathy. There are obvious limitations to the accuracy and reliability of participants' self-reports. Furthermore, we chose to focus our analyses on the affective component of empathy captured by the Empathic Concern scale of the Interpersonal Reactivity Index (IRI). Future studies may also focus on other empathy dimensions, such as the cognitive component or the tendency to experience personal distress. In addition, the participants in our sample reported relatively low levels of experiences of love withdrawal and were generally psychologically healthy. It may be interesting to replicate the study within clinical samples, e.g., in parents reporting experiences of (emotional) abuse or those with post-traumatic stress symptoms. These experiences and symptoms have been related to hyper-vigilance and arousal (van Harmelen et al., 2013; Stark et al., 2015), and individuals with post-traumatic symptoms in particular seem to have enhanced amygdala responses to threat (Stark et al., 2015). Thus, they may be more sensitive to (supraliminally or subliminally presented) threat primes, which may lead to altered priming effects. Third, as this was a pilot study focusing on women without children, for which pictures of an "own" child were artificially created, future studies should certainly focus on parents' neural responses to their own and unfamiliar children in the presence and absence of threat. As we found no evidence of subliminal priming effects, replication studies might want to modify the priming design. Less complex stimuli (e.g., angry or fearful vs. neutral faces) could be used, as the neutral and threatening primes used in our study were perhaps too complex. Primes could also be presented supraliminally. In fact, ideally the primes should be both sub- and supraliminally, to directly compare brain activity seen in both conditions and to shed light on the possibility of subliminal threat processing. Finally, a behavioral measure (e.g., reaction time) of the priming effect could be included to directly compare changes in brain activity to changes in behavior.

So far, our results question the effectiveness of subliminal threat-priming. As others have questioned the existence of a fast and automatic threat processing system, too (see Pessoa and Adolphs, 2010; Hoffmann et al., 2012), we feel that this is an important issue that deserves attention in future research. In addition, our results again illustrate the profound impact that experienced parenting strategies such as love withdrawal may have, even at the level of neural information processing. Although changes in neural activity and the preferential processing of familiar vs. unfamiliar faces are not inherently adaptive and desirable or maladaptive and undesirable (as this ultimately depends on the characteristics and demands of the situation or context in which they occur), parental use of love withdrawal may generally be considered undesirable because of its behavioral consequences (see e.g., Assor et al., 2004; Renk et al., 2006). It certainly has to be considered insensitive parental behavior that elevates the chance for an insecure attachment relationship to develop (Bowlby, 1973/1985). The fact that even relatively "mild" negative parenting experiences, such as the levels of love withdrawal reported by our participants, are associated with changes in very basic neural processes only adds to the importance of the early parenting environment and attachment relationship for individual development.

AUTHOR CONTRIBUTIONS

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

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fnhum.2016.00231/abstract

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Neural Correlates of the Appraisal of Attachment Scenes in Healthy Controls and Social Cognition—An fMRI Study

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The human attachment system is activated in situations of danger such as potential separation, threats of loss of a significant other and potential insecurity on the availability of the attachment figure. To date, however, a precise characterization of the neural correlates of the attachment system in healthy individuals is lacking. This functional magnetic resonance imaging (fMRI) study aims at characterizing the distinctive neural substrates activated by the exposure to attachment vs. non-attachment scenes. Healthy participants ($N = 25$) were presented scenes from the Adult Attachment Projective Picture System (AAP), a validated set of standardized attachment-related pictures extended by a control picture stimulus set consisting of scenes without attachment-related content. When compared to the control neutral pictures, attachment scenes activated the inferior parietal lobes (IPLs), the middle temporal gyrus (MTG), and the anterior medial prefrontal cortex (mPFC). These areas are associated with reasoning about mental representations, semantic memory of social knowledge, and social cognition. This neural activation pattern confirms the distinctive quality of this stimulus set, and suggests its use as a potential neuroimaging probe to assess social cognition/mentalizing related to attachment in healthy and clinical populations.

Keywords: attachment, fMRI, social cognition, mentalizing, temporo-parietal-junction

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INTRODUCTION

The human attachment system is a behavioral system that is responsible for triggering specific responses when situations arise that signal potential physical or psychological danger or stress. In this respect, the human attachment system differs from other related innate attachment systems, such as the caregiving, affiliative, and romantic/sexual systems. Attachment theory is rooted within an evolutionary context and may be viewed as one of the motivational systems that have the function to maximize the chances of survival. When activated, the attachment system motivates behaviors that aim at responding the child's need for protection or support, such as seeking the proximity of the caregiver (Bowlby, 1969, 1973, 1980).

Several neuroimaging studies have investigated the neural correlates of the caregiving (e.g., Bartels and Zeki, 2004; Leibenluft et al., 2004; Nitschke et al., 2004; Lenzi et al., 2009; Riem et al., 2012; Wittfoth-Schardt et al., 2012), the affiliative (e.g., Vrtička et al., 2008) and the romantic/sexual system (e.g., Bartels and Zeki, 2000, 2004; Gillath et al., 2005; Coan et al., 2006).

These studies have used various approaches to identify the neural correlates of distinctive attachment-related systems, such as pictures or video clips of one's own vs. unknown children, pictures of romantic partners, have one's hand held while being subjected to painful stimuli, or thinking about relationship scenarios. Notwithstanding the differences in methods and aims, several studies have reported a shared neural activity for the romantic and maternal attachment in regions associated with reward and motivation (ventral striatum, the putamen and the globus pallidus) and affective processing (orbitofrontal cortex).

However, much less is known about the neural correlates of the attachment system related to own representations. In the present study, we investigated the neural substrates activated by appraising situations that potentially activate the attachment system in the healthy adult.

In the child, the attachment system is activated on the one hand by attachment-related threats (for example, when infants are separated from their caregivers), and on the other hand by situations that are inherently threatening or increase the likelihood of danger (such as isolation, illness, injury; see Bowlby, 1969, 1973, 1980). In the adult, the attachment system may be activated by attachment-related stress, such as the loss of a loved one, and by a wider set of emotional or interpersonal situations. This activation is mediated by mental representations or schemata that encode past experiences of interactions with attachment figures in times of threat, of the availability or the intentions of attachment-figures, of the capacity of the attachment-figure to respond to our needs. Thus, according to attachment theory, in the adult responses to stimuli of social nature may also be organized by the attachment system when these stimuli are appraised through the appropriate schemata.

This fact is exploited by diagnostic instruments, such as the Adult Attachment Projective Picture System (AAP; George and West, 2001, 2012; Buchheim et al., 2006, 2008), that aim at characterizing in the adult the quality of the responses triggered by the activation of the attachment system. In the AAP interview, individuals are presented with scenes depicting attachment relationships or potential relationships in the presence of figural elements alluding to threatening conditions such as illness, separation, loneliness, or death. The quality of the attachment-related response of the individual is assessed through a semi-structured interview that measures the individual's attachment representations activated by these scenes.

To characterize the neural substrates activated by the exposure to the attachment scenes of the AAP and that are involved in processing these stimuli we developed a new set of control pictures that depicted almost the identical scenes, except for the replacement of the threatening figural elements with others of a more neutral nature (for example, see **Figure 1**). In developing these control pictures we made every effort to create scenes portraying social interactions and in which individuals appeared as possessing a purpose and/or mental activity, as in the original AAP scenes. The function of these control pictures was not one of offering impoverished scenes of human interaction, or individuals without a discernible mental content; instead, we attempted to recreate scenic elements of similar complexity as in the original AAP set, but without the reference to the cues that may activate the attachment system. Activated neural correlates were sought that emerged in the comparison between the exposure to the attachment scenes of the AAP diagnostic interview and the modified neutral scenes as a control condition.

The present study belongs to the set of studies that investigate the neural correlates of the own representations of attachment with respect to attachment related threats or loss of the reference person and insecurity about its permanence or availability (Buchheim et al., 2006, 2008, 2012, 2013). To date, these studies have instructed the participants to tell narratives to the AAP pictures in the functional magnetic resonance imaging (fMRI) environment or they used individualized text passages from the AAP interview to activate the attachment system. These studies intended to characterize differences between healthy participants and patient groups, such as depressives or individuals suffering from borderline personality disorder at a neural level. While these studies have successfully identified differences between healthy controls and patients, it has been difficult to interpret the data univocally in the absence of an adequate control stimulus set. Therefore, the present study is also meant as a methodological development to achieve improved specificity in the detection of the substrates associated with the attachment-related cues.

One issue raised by these studies is the involvement of areas, such as the right temporo-parietal-junction (TPJ; Buchheim et al., 2008), which in other studies has been shown to be part of a network underlying social cognition, and is often activated in response to social inputs, like social interactions (Frith and Frith, 2003). In the studies of the human attachment system (Buchheim et al., 2008), these areas are more often active in the presence of scenes depicting two interacting individuals (dyadic scenes) than in scenes showing only one person (monadic scenes). In attachment theory, social cognition abilities are considered essential to interact suitably with the attachment figure. These abilities are needed to make appropriate attributions about the mental states of others that may explain their behavior in the interaction. Especially in times of need or in the presence of threats, what individuals know about the mental state of attachment figures is important to behave so as to obtain proximity and care (see Bowlby, 1969, 1973, 1980). Recruitment of brain areas associated with social cognition (e.g., temporal poles, TPJ, posterior superior temporal sulcus), has been reported in few other studies of attachment (Leibenluft et al., 2004). The more complex interpersonal nature/information of the dyadic scenes may indicate the need for greater cognitive processing and could be particularly effective in eliciting schematic representations of social interactions.

A further issue arising from the comparison with studies of different forms of attachment is the predominantly negative valence of stimuli activating the human attachment system. This contrasts with the generally appetitive nature of stimuli activating the affiliative, caregiving, and romantic systems. Processing of stimuli of negative emotional valence is often associated with the activation of the amygdala (Davis and Whalen, 2001; Adolphs et al., 2005). This activation, however, may be related to the generally high arousing nature of these stimuli (Adolphs, 2010). Strathearn and Kim (2013) reported amygdala responses to positively or negatively valenced cues (own vs. unknown child, happy, sad, neutral faces) modulated by personal relevance. To address this issue, we characterized the amount of negative valence and arousal in our stimulus set relative to other sets commonly used in neuroimaging studies, and examined the activation of the amygdala with region-of-interest (ROI) analyses.

MATERIALS AND METHODS

The study protocol was approved by the Ethical Committee of the Medical University of Innsbruck and was in compliance with National legislation, the principles expressed in the Declaration of Helsinki, and the Code of Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association. All participants gave written informed consent.

Participants

A sample of $N = 25$ healthy volunteers were recruited at Leopold-Franzens University in Innsbruck (age mean/SD 22.7/1.8, age range: 19–26, 12 females, see **Table 1**). Depressiveness was measured with a computerized German Version of the Centre for Epidemiologic Studies Depression Scale (CES-D, Radloff, 1977; German Version: Hautzinger and Bailer, 1993). The present and long-lasting anxiety levels were assessed by the State-Trait Anxiety Inventory (STAI, Spielberger et al., 1970; German Version: Laux et al., 1981) All participants had scores in a subclinical range. Finally participants were assessed with the International Neuropsychiatric Interview (M.I.N.I. 5.0.0, Sheehan et al., 1998, German version) to exclude previous psychiatric or psychological illnesses.

TABLE 1 | Participants.

	n = 25
Age mean (std. dev.)	22.7 (1.8)
Female (%)	12 (48)
Male (%)	13 (52)
ADS (std. dev.)	10.08 (10.39)
STAI-S (std. dev.)	35.60 (11.55)
STAI-T (std. dev.)	35.68 (11.36)

Stimulus Material

The stimulus material consisted of attachment-related pictures (AAP© George and West, 2012) and their modified neutral counterparts as a control condition. The AAP, an established and validated interview to assess attachment representations, is comprised of eight black and white line drawn pictures: seven attachment-related drawings and one neutral scene used as a warm-up. The attachment-related pictures are designed to activate the attachment system and to elicit mental engagement with attachment-related experiences (such as loneliness, helplessness, loss following illness, separation, solitude, death, and abuse). These drawings contain no facial expressions, and figures are drawn in summary strokes without precise details, but include the essential characteristics to recognize the attachment context. Drawings portray adult-adult dyads, adult-child dyads, adults alone, and children alone and capture attachment across the life span, infancy to old age.

For the control condition, pictures of attachment scenes from the AAP (George and West, 2012) were expanded with a set of carefully matched control scenes of non-attachment "neutral" character (**Figure 1**). The control battery consisted of eight line drawings of non-attachment pictures developed by the first author. In the control set, allusions to

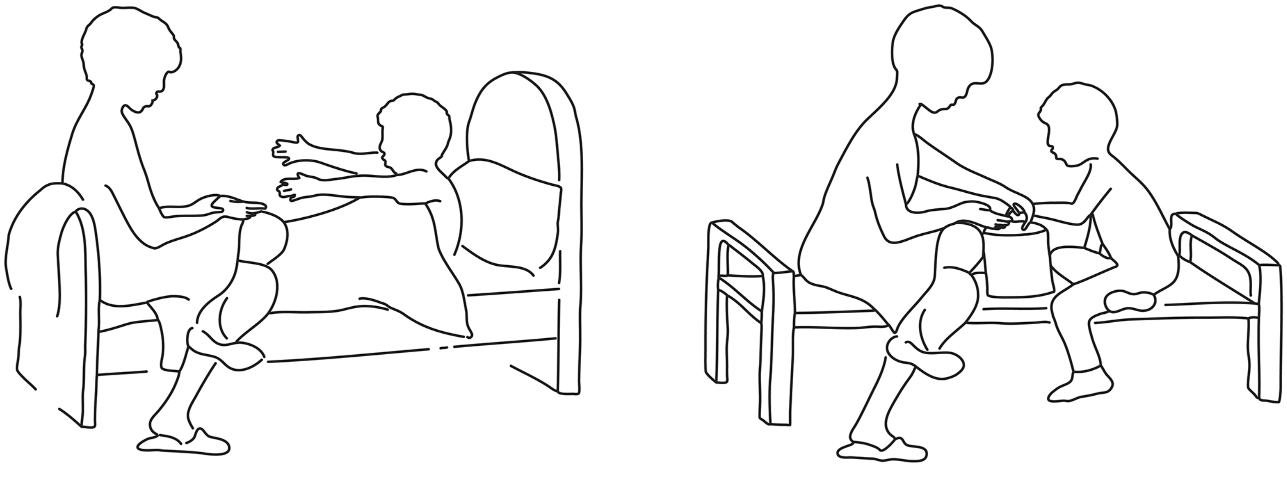

FIGURE 1 | Example of an original attachment-related scene of the Adult Attachment Projective Picture System (AAP) (left) and the newly created corresponding control scene (right).

loneliness, potential rejection, death or illness, etc., were removed while replicating objects/characters, spatial structure and object configuration as closely as possible. Therefore, elements such as the monadic or dyadic nature of the scene, the age of the individuals depicted in it, etc., was precisely matched in the control picture set. The control scenes had the same size and were aligned with the corresponding AAP pictures. Care was given to prepare all pictures, attachment-related and non-attachment related, with the same stroke width, thickness, and size to make them formally identical. Since the original AAP warm-up scene contains no attachment-related content, we created a matched attachment-related scene (the picture of two children playing ball was transformed into a scene of potential separation). In total, there were 16 pictures, eight for each condition.

Validation of the Stimulus Material

To validate the stimulus set, a preliminary behavioral study was conducted on a separate group of 97 healthy subjects (age mean/SD 23.15/5.12, 72 females). In this preliminary study, all scenes (attachment-related and control) were rated according to the dimensions valence and arousal through the self-assessment manikin (SAM) scales developed by Bradley and Lang (1994). This pictorial rating system records self-assessments of experienced emotion, rated according to icons depicting a 5-point scale along the dimensions affective valence and arousal. This rating system was developed to assess sets of standardized stimuli for experimental investigations that are widely used in neuroimaging investigations of emotion (International Affective Picture System [IAPS], Lang et al., 2008). Hence, the collection of these validation data makes it possible to compare the present stimulus set with other visual stimulus sets used in the neuroimaging literature.

Valence ratings of the attachment-related pictures (mean score = 1.85, SD = 1.00) were significantly more negative in comparison to the ratings of neutral pictures (mean score = 3.75, SD = 0.98; $T = -37.971$, $p < 0.000$). Attachment-related pictures were rated of higher arousal (mean score = 3.06, SD = 1.18) than neutral pictures (mean score = 2.28, SD = 1.08; $T = 13.577$, $p < 0.000$; Knoll, 2015). These results confirmed that the new control picture-set significantly differed from the original AAP-set. However, it also suggested that the attachment-related pictures differed from typical negatively valenced visual stimuli used in previous neuroimaging studies. In those studies, the arousal of negatively valenced scenes may be higher than the arousal of the attachment-related scenes in the AAP set. **Figure 2** shows the combination of the arousal and valence scores of the pictures in our set, plotted in a two-dimensional affective space representing the valence-arousal relationship. The gray dots show the arousal and valence of the IAPS, which is the source of material often used in neuroimaging studies (Lang et al., 2008). This plot shows the association of extreme valence scores (either positive or negative) with high arousal scores in the IAPS. In our picture set, negative emotional scores (in red) were not associated with arousal values substantially above the middle line. As in the IAPS set, there was an association of degree of negative valence in the attachment-related pictures with the level of arousal; however, the arousal levels were consistently less than what one would expect for pictures of comparable negative valence.

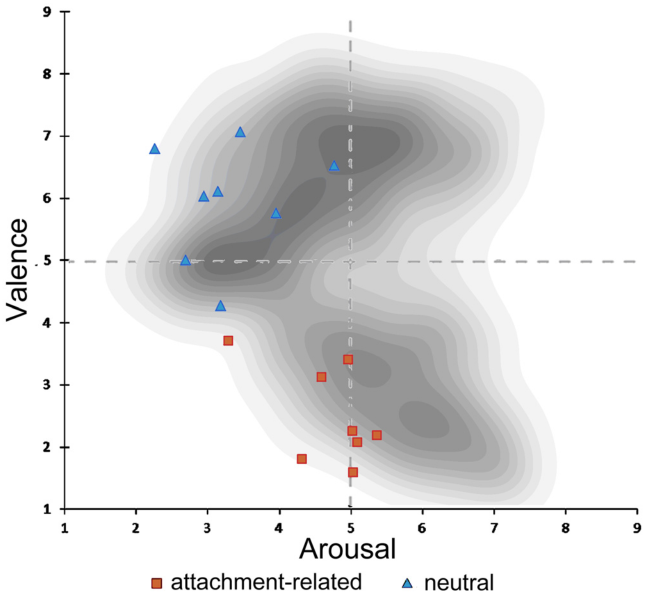

FIGURE 2 | Illustration of the two-dimensional affective space of the International Affective Picture System (IAPS) pictures. In shades of gray, density of pictures in the original IAPS database in relation to valence and arousal. Rating of valence and arousal of the attachment-related scenes (red dots); rating of the neutral scenes (blue dots).

fMRI Data Acquisition, Preprocessing, and Statistical Modelling

Participants were placed supine in the scanner, wearing earplugs to muffle noise. Head fixation was assured through a foam rubber device mounted on the head coil. Data were acquired using a T2*-weighted echo planar imaging (EPI) sequence on a 3T Siemens Verio scanner (repetition time (TR)/echo time (TE) 2900/30 ms, transversal acquisitions, phase encoding anterior-posterior, field of view (FOV) 1260 * 1260, slice thickness 2.5 mm with a gap of 1 mm, giving a voxel size of 1.88 × 1.88 × 3.5 mm, flip angle 90°, pixel bandwidth 1680 Hz). Data were acquired in two separate runs, each of which contained eight trials in which a scene was shown for 15 s, followed by a fixation cross for further 15 s Participants were instructed to pay attention to the persons depicted in scenes. Each run contained eight trials, equally divided into two of the two types of scenes (attachment-related or control). Scenes constituting the control version of the original attachment-related AAP scenes were shown in different runs, so that each run contained exposure to the whole set of eight scenes (attachment-related or control). To avoid systematic effects, the sequence in which scenes were recruited in the two runs was systematically changed across subjects.

Data were analyzed after realignment, normalization (resampling size, 2 mm isotropic) and smoothing (8 mm full width at half maximum (FWHM)) with the software package

SPM8[1]. Contrasts of interest were estimated at the first level within each participant separately, and brought to the second level to account for the random effect of subjects. We report effects at $p < 0.05$, cluster-level corrected, with clusters defined by the threshold $p < 0.001$, uncorrected.

The data were analyzed with a model in which the blocks during which pictures were displayed were convolved with a standard blood oxygen level dependent (BOLD) hemodynamic function to account for the delay of onset of the signal. A design matrix was constructed containing two factors of two levels each: attachment/control and monadic/dyadic. Appropriate contrasts were taken to the second level to estimate the effects of attachment and its interaction with the monadic or dyadic nature of the pictures.

RESULTS

In the contrast attachment vs. neutral we found a statistical significant activation in the left inferior parietal lobe (IPL)/temporo-parietal junction (TPJ) (MNI coordinates $x, y, z = -46, -52, 42$, $t = 6.67$, number of voxels in cluster $k = 833$, $p < 0.001$, cluster-level corrected), in the left middle temporal gyrus (MTG) ($x, y, z = -66, -24, -12$, $t = 5.10$, $k = 258$, $p = 0.005$). These clusters were accompanied by less pronounced activations on the opposite side, which failed to reach significance after correction (IPL: $x, y, z = 62, -54, 36,$

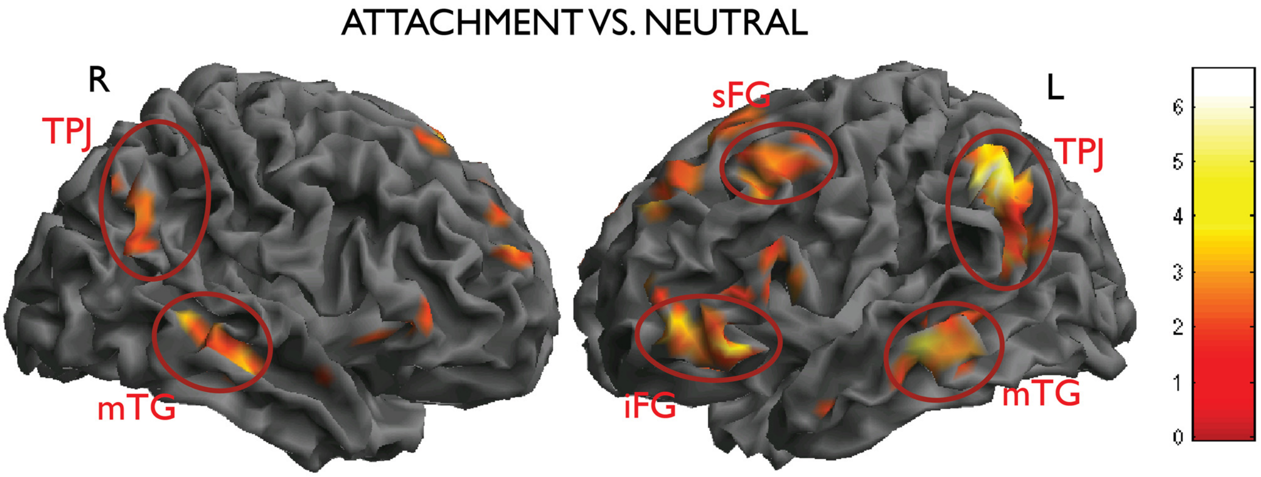

FIGURE 3 | Activations from the main contrast of interest attachment vs. neutral (left inferior parietal lobe (IPL)/temporo-parietal junction (TPJ), middle temporal gyrus (MTG), the left superior and inferior frontal gyri (SFG and IFG), picture on the right side; right IPL and MTG, picture on the left side). Data thresholded at $p < 0.005$, uncorrected, for display purposes.

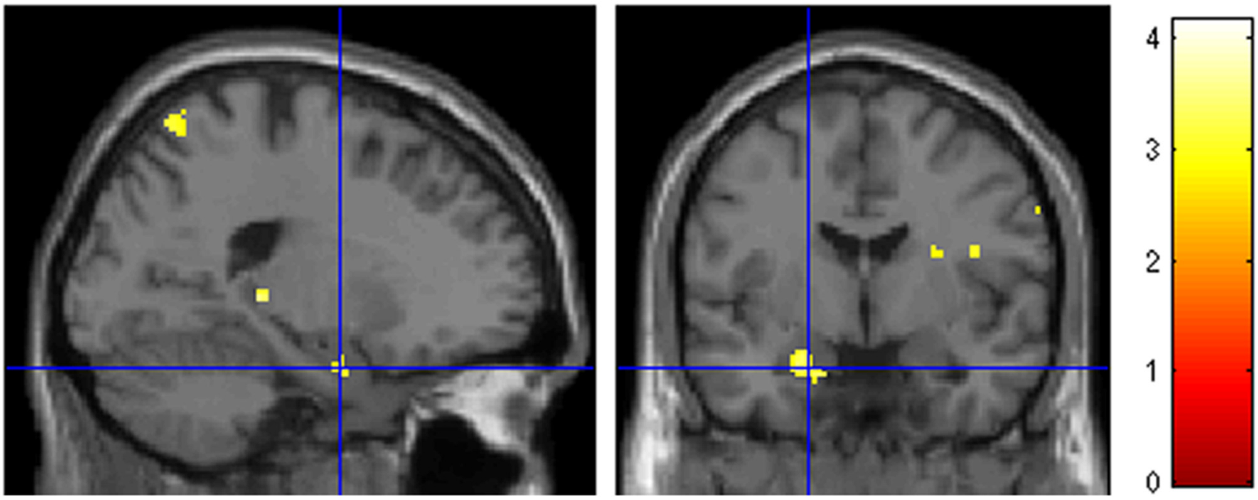

FIGURE 4 | Deactivation of the amygdala in the main contrast attachment vs. neutral pictures. Same display threshold as in the previous Figure ($p < 0.005$).

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[1] http://www.fil.ion.ucl.ac.uk/spm/

$t = 4.69$, $k = 54$, n.s.; MTG, *x, y, z* = 52, −20, −16, $t = 4.98$, $k = 64$, n.s.). In the prefrontal lobes, the left superior and inferior frontal gyri (SFG and IFG) and the anterior medial prefrontal cortex (mPFC) were also activated in this contrast (*x, y, z* = −42, 16, 56, $t = 5.40$, $k = 273$, $p = 0.004$; *x, y, z*; **Figure 3**).

A question of interest was the involvement of the amygdala, given the combination of marked negative emotional valence and low arousal values of these pictures demonstrated by the behavioral validation study (see **Figure 2** in the "Materials and Methods" Section). There was a bilateral light deactivation of the amygdala in the contrast attachment vs. neutral, which however was not significant after correction (*x, y, z* = −24, −2, −24, $t = -3.55$; *x, y, z* = 22, 0, −22, $t = -2.54$; **Figure 4**).

A second contrast of interest investigated the modulation of the effect of attachment by type of scenes (dyadic or monadic). In the contrast attach vs. control within the dyadic scenes group, the right temporo-parietal region was activated more strongly (effect within dyadic scenes: *x, y, z* = 56, −52, 34, $t = 5.75$, $k = 517$, $p < 0.001$; effect within monadic scenes: *x, y, z* = 54, −64, 40, $t = 3.84$, $k = 19$, n.s.; interaction: *x, y, z* = 62, −32, 16, $t = 4.33$, $k = 47$, n.s; see **Figure 3**, top row). An interaction between the two factors attachment/neutral × dyadic/monadic was observed in the occipital lobes bilaterally (*x, y, z* = 48, −78, 6, $t = 5.44$, $k = 123$, $p = 0.079$; *x, y, z* = −40, −80, −6, $t = 4.63$, $k = 139$, $p = 0.050$).

There was no significant interaction in the opposite direction, i.e., for effects of attachment that were larger in the monadic than in the dyadic group. As one may see from **Figure 5** (bottom row), this was due to effects of similar intensity within both picture types in the areas activated by attachment, such as the TPJ on the left. Also the apparent higher activation in the left IFG in the monadic group, visible in the bottom row of **Figure 3**, failed to achieve significance (*x, y, z* = −36, 38, 2, $t = 3.19$).

DISCUSSION

The main contrast of interest of our study revealed the activation of areas of predominantly associative nature, such as the IPL and the MTG, in association with attachment-related stimuli. These findings replicate those of previous studies in which the AAP pictures were used in comparisons between healthy participants and patients (Buchheim et al., 2006, 2008). Activations in the anterior insula have a similar interpretation but have been more explicitly associated with emotional representations (Gu et al., 2013). This pattern of activation contrasts with those commonly obtained in studies of negatively valenced visual stimuli, which are characteristically more arousing and activate limbic structures such as the amygdala (for a quantitative review, see Costafreda et al., 2008). The activation of these limbic structures has been shown to be related to the early automatic processing of sensory aspects of the stimulus (Morris et al., 1999), which trigger arousal levels favoring its attentional prioritization for further processing (Vuilleumier, 2005). The lack of recruitment of these circuits in the present study suggests that appraisal of attachment content recruited processes that differed from those typically associated with the exposure to negatively valenced stimuli in many previous neuroimaging studies. Activation of the amygdala in studies of attachment styles that used facial expression stimuli may have detected differences in arousal and emotional reactivity (Vrtička et al., 2008).

The most prominent among the association areas activated by the attachment-related content was the TPJ, a region that numerous previous studies have identified as a neural correlate of theory of mind tasks and social cognition (for reviews, see Gallagher and Frith, 2003; Saxe and Kanwisher, 2003; Decety and Lamm, 2007; Van Overwalle, 2009; Saxe, 2010; Carter and Huettel, 2013). Theory of mind is a construct that refers to the cognitive capacity to form a representation of other people's beliefs and intentions (Premack and Woodruff, 1978; Baron-Cohen, 1997). Neuroimaging studies have investigated this construct through story comprehension tasks that require the correct attribution of beliefs after changes in the environment (Mar, 2011). Social cognition is a label that more generically refers to the adequate perception and evaluation of social stimuli and the processing of information about social interactions, including their affective components. Functional neuroimaging studies have associated social cognition processes with an extensive network of areas, which, beside the TPJ, also includes the middle temporal sulcus, the temporal poles, and the mPFC (Frith and Frith, 2012).

Neuroimaging studies of theory of mind have reported that left TPJ activations are more common when processing different subjective perspectives, whereas the right parietal junction was more specifically activated by processing states like beliefs (Perner et al., 2006). In the present study, dyadic pictures activated the TPJ on both sides, while monadic pictures activated this structure only on the left. This result is consistent with a more complex representation of beliefs and mental states in the presence of interactions between participants in the scenes, relative to pictures where the mental state of the individual in the scene could be inferred directly from pictorial elements such as her body posture (Peelen and Downing, 2007).

In attachment theory, the concept of mentalization refers to the capacity of the individual to understand one's own and other people's actions in the light of intentions, personal desires, needs or beliefs (Fonagy and Target, 2005). To predict behavior on the basis of mental states, the current literature divide mentalization processes in emotional and cognitive aspects. Emotional mentalizing abilities are referred to the ability to empathize emotionally like representations of intentions and believes. Emotional contagion/mentalization processes are thought to involve a network of brain area e.g., IFG and the IFL (Shamay-Tsoory, 2011) while cognitive mentalization processes activate brain regions like e.g., the TPJ (Saxe, 2006; Vrtička and Vuilleumier, 2012) or superior temporal sulcus (Frith and Frith, 2003). In the AAP interview, participants are invited to develop narratives over the motives, feelings and thoughts of the individuals depicted in the scenes. Activation of the neural substrates of social cognition in the present study suggests that the healthy participants in

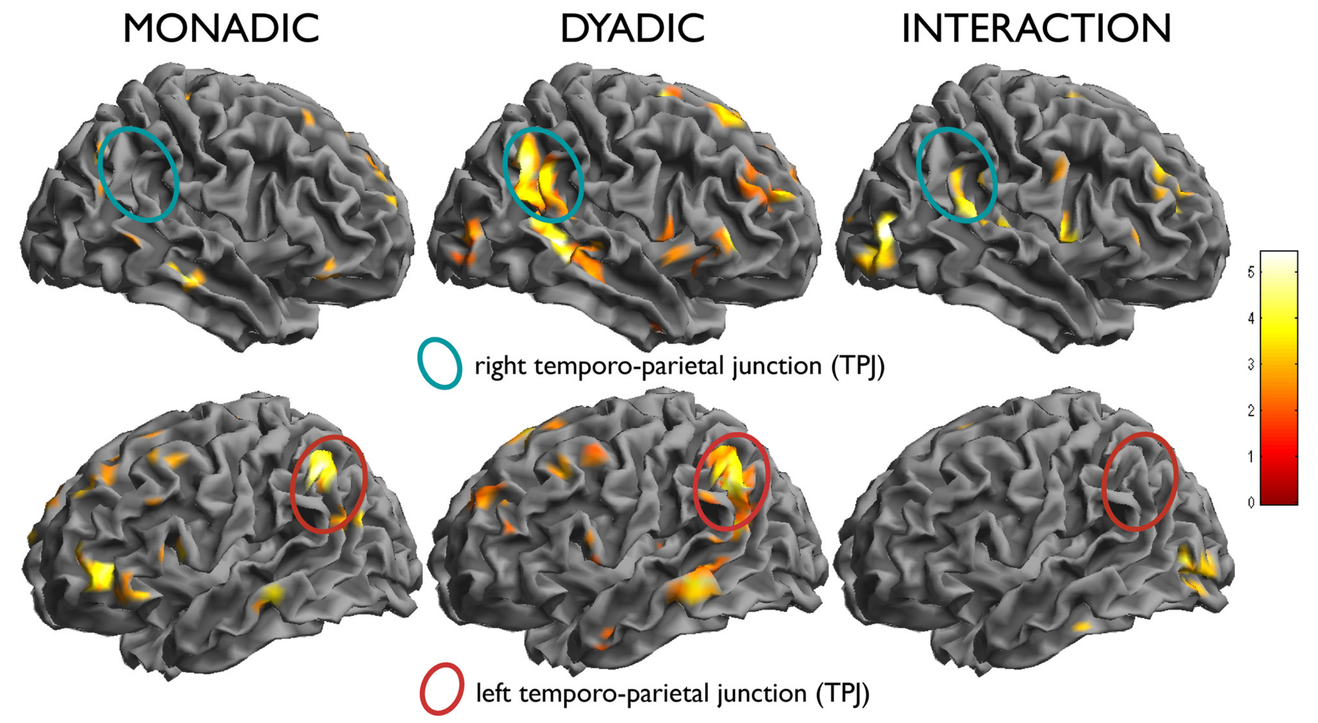

FIGURE 5 | In the left column, effect of the simple effect attach vs. control within monadic scenes, and in the middle column, within dyadic scenes. Note the activation of the left temporo-parietal region in both (bottom row), and the selective activation of the right counterpart in the dyadic scenes (top row). In the right column, test of the interaction attachment/control × dyadic/monadic, showing the differential effect in the right TPJ.

our sample spontaneously reacted to attachment scenes by elaborating such motives, especially in the presence of dyadic scenes.

Mentalization is an important individual trait that maybe associated with better affect- and self-regulation capacity (Fonagy and Luyten, 2009; Viviani et al., 2011). Dysfunction of self-regulation is crucial especially in the context of social relationships (Posner et al., 2002) Mentalization capacities in the adult are considered to develop from the internalization in childhood of the capacity for containment of the attachment figure. This containment enables the child to experience its own emotions without being overwhelmed by them (Fonagy et al., 1995; Bateman and Fonagy, 2004). In the theory underlying the AAI interview, this capacity is referred to as "reflective functioning" (Fonagy et al., 1998). Neuroimaging studies attempting to locate the neural correlates of mentalization have reported activations in the left MTG and IFG, two foci that were active also in the present study (Nolte et al., 2012).

In the alternative DSM-5 model for personality disorders (see "Results" Section), personality functioning (Criterion A) was included to assess the level of functional impairment associated with personality disorders (DSM-5; American Psychiatric Association, 2013). The level of personality functioning scale (LPFS; Bender et al., 2011) conceptualizes intrapersonal (identity, self-direction) and interpersonal (empathy, intimacy) components of the underlying personality structure. Hence, the ability to understand oneself and the social and internal world of others in terms of mental states are viewed as an essential trait of personality disorders. Here, working models of attachment theory and implicit representations of others represent a key theoretical and empirical issue (Skodol et al., 2011). Reflecting the increasing recognition of the importance of personality functioning, fMRI studies are beginning to apply assays eliciting activation in areas associated with representations of self (Doering et al., 2012) and empathy (Dziobek et al., 2008; Fan et al., 2011; Decety et al., 2013; Mier et al., 2013) to assess functional differences in personality disorders.

In summary, the present study provided evidence that exposure to the attachment scenes activated a cortical network that is recruited to represent the mental states of oneself and of others. These results are consistent with attachment theory, according to which the capacity to correctly interpret and process social cues from the attachment figure is important for responding appropriately in attachment relationships, thus ensuring security and proximity to the attachment figure. Our results suggest that while exposure to attachment-related themes, especially depicting interactions, specific processing takes place in brain areas associated with social cognition. The recruitment of social cognition-related areas while assessing attachment related pictures may be used in future studies to further explore its potential in detecting individual differences in mentalization capacities. By comparing the results of this and other functional assays, fMRI may contribute to clarifying the constructs involved in personality functioning.

AUTHOR CONTRIBUTIONS

The study was conceptualized by KL, AB, RV. The study setup and data collection were organized and conducted by KL, RV, ERG, MV. fMRI analyses was performed by KL and RV. KL and RV performed the statistical data analysis and contributed substantially to the result interpretation. AB and ERG provided important intellectual contribution in commenting and revising the manuscript. KL, RV, and AB wrote the manuscript and edited its final version.

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Posterior Superior Temporal Sulcus Responses Predict Perceived Pleasantness of Skin Stroking

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Love and affection is expressed through a range of physically intimate gestures, including caresses. Recent studies suggest that posterior temporal lobe areas typically associated with visual processing of social cues also respond to interpersonal touch. Here, we asked whether these areas are selective to caress-like skin stroking. We collected functional magnetic resonance imaging data from 23 healthy participants and compared brain responses to skin stroking and vibration. We did not find any significant differences between stroking and vibration in the posterior temporal lobe; however, right posterior superior temporal sulcus (pSTS) responses predicted healthy participant's perceived pleasantness of skin stroking, but not vibration. These findings link right pSTS responses to individual variability in perceived pleasantness of caress-like tactile stimuli. We speculate that the right pSTS may play a role in the translation of tactile stimuli into positively valenced, socially relevant interpersonal touch and that this system may be affected in disorders associated with impaired attachment.

Keywords: brain, fMRI, socio-emotional, tactile, posterior superior temporal sulcus

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INTRODUCTION

Expressions of nurturing socio-affiliative behaviors, such as love and affection, are a cornerstone in the development of attachment. Specifically, animal research emphasizes the life-long effects of physical maternal care, including licking and grooming, on nervous system maturation and behavior (Weaver et al., 2004). Indeed, interpersonal touch plays a particularly important role in brain development across a range of species (Ardiel and Rankin, 2010), and is a primary channel mediating social bonding and secure attachment in primates across the lifespan (Harlow, 1958; Dunbar, 2010; Walker and McGlone, 2013).

The temporal lobes contain key nodes of the circuitry supporting social cognition, essential for accurate perception of social cues and healthy development of attachment (Adolphs, 2009; Vrticka and Vuilleumier, 2012; Nolte et al., 2013). The posterior superior temporal sulcus (pSTS) has been identified as particularly sensitive to visually presented social information (Yang et al., 2015). A growing number of studies suggest that the pSTS may also contain multisensory circuits (Beauchamp, 2010), including areas responding to tactile stimulation (Beauchamp et al., 2008). Given the profound role interpersonal touch plays in social interactions and attachment (McGlone et al., 2014), it seems likely that the pSTS may be selectively sensitive to socially relevant tactile information. Indeed, recent studies show that caress-like gentle skin stroking of the forearm activates the right pSTS (Gordon et al., 2013; Voos et al., 2013; Björnsdotter et al., 2014). Moreover, pSTS responses to skin stroking show sex-specific developmental effects (Björnsdotter et al., 2014), correlate inversely with autistic traits (Voos et al., 2013) and are reduced in individuals diagnosed with autism spectrum disorder (Kaiser et al., 2015). Taken together, these findings demonstrate a role of the pSTS in tactile processing, but also link temporal lobe functionality to individual variability in social behavior.

Already at the level of the skin, specific peripheral nerves in the form of small-diameter, unmyelinated C tactile (CT) afferents signal socio-affective dimensions of touch (Löken et al., 2009; Björnsdotter et al., 2010; Morrison, 2012; Ackerley et al., 2014). Contrary to large-diameter myelinated mechanoreceptive (Aβ) afferents, CT nerve fibers respond particularly well to gentle, caress-like slow skin stroking (Löken et al., 2009; Ackerley et al., 2014) but poorly to rapid skin deformation such as vibrotactile stimuli (Bessou et al., 1971; Olausson et al., 2002). Physical touch mediates social bonding and attachment in primates (Harlow, 1958; Dunbar, 2010), and the CT system is posited to play a particularly important role in the development of attachment (McGlone et al., 2014). Moreover, pure CT stimulation evokes a vaguely pleasant percept (Olausson et al., 2002), and CT afferent firing frequency correlates with perceived pleasantness of skin stroking (Löken et al., 2009; Ackerley et al., 2014).

Consistent with a socio-affective role of the CT system, previous studies suggest that posterior temporal lobe regions responsive to touch may be selective to the type of skin stroking that vigorously activates CT afferents. Stroking of the hairy skin of the arm elicits more activity than that of the glabrous skin of the palm (Gordon et al., 2013; Björnsdotter et al., 2014) which is not innervated by CT afferents (Björnsdotter et al., 2010). Also, the STS is more responsive to slow than fast skin strokes (Voos et al., 2013). However, the extent to which the STS is selective to CT targeted stimulation is unclear; specifically, the STS is known to respond to skin vibration (Beauchamp et al., 2008), which poorly activates CT afferents (Bessou et al., 1971; Olausson et al., 2002). In the current study, we therefore used functional magnetic resonance imaging (fMRI) to contrast brain responses to skin stroking and vibration in healthy participants.

In addition to having dissimilar effects on Aβ and CT afferents, skin vibration is an artificial type of touch that is not associated with social processes. The right pSTS is selectively responsive to point-light displays of biological motion, including depictions of human movements compared to randomly moving dots (Grossman and Blake, 2002). Similar to such displays, purposeful gentle skin stroking is an inherently social stimulus, in contrast to vibration, which can be considered an unnatural, non-social type of touch. Consistent with previous studies showing selective activations of the posterior temporal lobe to socially relevant touch (Gordon et al., 2013; Voos et al., 2013; Björnsdotter et al., 2014), we hypothesized that the pSTS would respond more to skin stroking than to skin vibration. Superior temporal cortex activity is also modulated by a wide array of factors related to individual variability, such as social impairment (Kaiser et al., 2010), autism diagnosis (Björnsdotter et al., 2016), perceived level of animacy (Kuzmanovic et al., 2014), and plasma oxytocin (Lancaster et al., 2015). Specifically, temporal responses to skin stroking are affected by age and gender (Björnsdotter et al., 2014), autistic traits (Voos et al., 2013), and autism diagnosis (Kaiser et al., 2015). Here, we asked whether pSTS activity may also be modulated by individual percepts of the affective quality of tactile stimulation. In line with previous studies of the CT system (Olausson et al., 2002; Löken et al., 2009; Ackerley et al., 2014), we therefore asked the participants to rate the perceived pleasantness of the tactile stimuli. Consistent with the role of the pSTS in processing socially relevant touch (Gordon et al., 2013; Voos et al., 2013; Björnsdotter et al., 2014), we hypothesized that pleasantness ratings of skin stroking, but not vibration, would correlate with pSTS responses.

MATERIALS AND METHODS

Participants

Participants were recruited through university advertisements. Twenty-three subjects (11 males, mean age 25 years, range 19–38 years) participated in the study. All subjects were right handed as assessed through the Edinburgh Handedness Inventory, and healthy. Ethical approval was obtained by the ethics board of the Gothenburg University, and the study was performed in line with the guidelines of the Declaration of Helsinki (1996). Participants were compensated with 200 Swedish crowns per hour.

Tactile Stimuli and Experimental Protocol

A trained experimenter (author MD; female, aged 44) applied the stimuli by hand, guided by visual cues. The experimenter was invisible to the participants throughout the scanning session. Gentle skin stroking was applied by a 6-cm wide artist's brush at a speed of 2 cm/s across a distance of 10 cm, in a proximal to distal direction on the right anterolateral surface of the thigh. Vibration (100 Hz) was delivered with a device consisting of a rectangular piece (40 mm × 12 mm × 7 mm) of balsa wood connected to a piezo-element (Piezo Systems Inc., Cambridge, MA, USA).

Each tactile stimulus lasted for 15 s and the stimuli were administered in a pseudo-randomized order. The order of the stimuli was visible only to the experimenter who administered the touch. Each block contained one stroking stimulus, one vibration stimulus, and a behavioral assessment (**Figure 1**). In the behavioral assessment, participants were asked to rate the perceived pleasantness of the last stimulus on a visual analog scale (VAS) presented on a screen visible for the participant through a mirror attached to the head coil. The scale was visible for 15 s, during which the participants could move a cursor using buttons. The cursor was initially placed at the center marked 'neutral,' and the endpoints of the VAS were 'unpleasant' ('obehagligt' in original Swedish language) and 'pleasant' ('behagligt' in original Swedish language). The visual cues and VAS scales were presented using custom designed Matlab scripts, which were synchronized with scanner data collection. Participants were instructed to focus on the screen throughout the experiment. For statistical assessment, the scale was subsequently converted to the range -5 to 5, and the average value was computed across all blocks for stroking and vibration, respectively. The scanning session

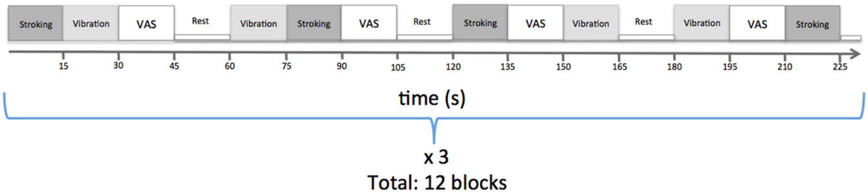

FIGURE 1 | Experimental paradigm.

comprised one run with 12 blocks, each block separated by a 15 s rest period (**Figure 1**).

MRI Acquisition

Magnetic resonance imaging was performed on a Philips Gyroscan 3T Achieva, software release 3.2, (Philips, Eindhoven, The Netherlands). The scanner's two channel parallel transmit was used for improved signal homogeneity over the field of view and the subject's head was firmly supported with cushions in the head coil (32 channel SENSE, same manufacturer as the scanner). A T1-weighted scan (3D T1-TFE) was performed as anatomical reference (parameters: flip angle 8°, $TE = 4.0$ ms, $TR = 8.4$ ms, SENSE factor 2.7, TFE factor 240, 170 sagittal slices with scan resolution 1.0 mm × 1.0 mm × 1.0 mm). Functional data comprised 245 volume images of the brain (parameters: single shot gradient echo, echo planar imaging with flip angle 90°, $TE = 35$ ms, $TR = 3000$ ms, SENSE factor 1.8, 40 axial slices without slice gap and with scan resolution 2.8 mm × 2.8 mm × 2.8 mm), acquired after four discarded dummy scans.

Data Pre-processing

All spatial preprocessing and statistical analyses of anatomical and functional images were performed using SPM8[1]. The anatomical images were segmented into gray matter, white matter, and cerebrospinal fluid images. The gray matter images were used to determine the 12-parameter affine transformation onto the standard stereotactic MNI (Montreal Neurological Institute) space. Functional data preprocessing included slice time correction, realignment to the first volume of the first run (using a 6-degree rigid spatial transform), co-registration to anatomical images, transformation to MNI space using the parameters obtained from transformation of gray matter images, resampling to 2 mm × 2 mm × 2 mm voxels and smoothing with a 6-mm full width at half maximum Gaussian kernel. In addition, motion artifacts were examined using the Artifact Detection Toolbox (ART)[2]. Volumes in which global signal deviated more than two standard deviations (SDs) from the mean signal or in which the difference in motion between two neighboring volumes exceeded 1 mm (across rotational or translation directions) were marked as outlier volumes. Smoothed functional images were band pass-filtered with a 128 s high pass filter.

General Linear Modeling

Four regressors corresponding to the four conditions (stroking, vibration, VAS rating for stroking, and VAS rating for vibration) were modeled using a boxcar function with 1 during the 15 s stimulus conditions and 0 otherwise, convolved with a canonical hemodynamic response function. The design matrix also included motion parameters and outlier volumes as regressors of no interest. The mean number of outliers per participant was 1.91 ($SD = 2.66$, range = 0–8). There was no significant difference in number of outliers between stroking and vibration ($p = 0.3$). Parameter estimates of blood-oxygen level dependent (BOLD) responses (β-values) were calculated for each tactile condition (stroking and vibration) and for the difference between conditions. These were passed to a second level mixed effect group analysis. As there are sex-specific age-effects on brain responses to tactile stimuli (Björnsdotter et al., 2014), we included gender and age as covariates.

We examined the main effect for each of the two tactile stimuli, as well as the contrast between them. The resulting statistical maps were thresholded at whole-brain family-wise error (FWE) corrected $p < 0.05$ and cluster size > 5.

Region-of-Interest (ROI) Analyses

We conducted ROI analyses in the right pSTS, with Talairach space coordinates reported in the seminal paper on temporal processing of CT targeted touch ([57, −55, 13]; Gordon et al., 2013). Here, we converted the coordinates to MNI space in GingerAle (Laird et al., 2011), resulting in [55, −53, 15], and constructed the right pSTS ROI as a sphere with radius 8 mm centered on this coordinate. Within this ROI, we applied small volume correction (SVC) for multiple comparisons at pFWE < 0.05.

Correlation Analyses

We assessed brain-behavior links in the form of correlations between brain responses and participants' pleasantness ratings. Specifically, we assessed the correlations between β-values for each tactile condition and the respective pleasantness ratings. First, we used the MarsBaR toolbox[3] to extract average β-values for stroking and vibration from the right pSTS ROI and computed the correlations between these values and the pleasantness ratings. Second, we conducted an exploratory group-level, whole brain, random effects analysis to examine

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[1] http://www.fil.ion.ucl.ac.uk/spm/

[2] http://www.nitrc.org/projects/artifact_detect/

[3] http://marsbar.sourceforge.net/

voxel-wise correlations between ratings and brain responses to stroking and vibration, respectively, including age and gender as a covariates. The results were reported at an uncorrected $p < 0.001$ and cluster size > 5.

RESULTS

Behavioral Ratings

Skin stroking ratings ranged from neutral to very pleasant (**Figure 2A**), and vibration ratings ranged from slightly unpleasant to slightly pleasant (**Figure 2B**). The group mean pleasantness ratings were 1.9 ($SD = 1.1$) and 0.4 ($SD = 0.9$) for skin stroking and vibration, respectively. Within subjects, the SDs of the pleasantness ratings were small, ranging from 0.1 to 1.8 for skin stroking and 0.1 to 1.1 for vibration. Participants experienced stroking as more pleasant than vibration (paired samples t-test, $p < 0.001$). Stroking, but not vibration, was rated significantly higher than 0 ('neutral'; $p < 0.001$ and $p = 0.08$, for stroking and vibration, respectively).

Neuroimaging

Main Effects of Tactile Stimuli

For the main effects of skin stroking and vibration, respectively, we found activations in a range of somatosensory areas previously associated with tactile stimulation, such as bilateral secondary somatosensory cortex and contralateral primary somatosensory cortex (**Figure 3**; **Table 1**). However, we did not find any significant activation of the pSTS for skin stroking, even at the lower threshold of $p < 0.001$ or within the right pSTS ROI.

Effects of Skin Stroking vs. Vibration

We found multiple of brain regions in which stroking elicited a significantly larger response than vibration (**Table 1**). However, we found no significant differences between skin stroking and vibration in the STS, at the lower threshold of $p < 0.001$ or within the right pSTS ROI. Also, no region with significantly larger responses for vibration than skin stroking was found.

Correlation Analysis

The analysis examining the correlation between right pSTS ROI β-values and pleasantness ratings showed a significant positive correlation for stroking ($r = 0.444$, $p = 0.034$) (**Figure 2A**). For vibration, the correlation was not significant ($r = -0.098$, $p = 0.657$) (**Figure 2B**). Consistently, a one-tailed t-test on the z-transformed correlation coefficients showed that the skin stroking correlation coefficient was significantly larger than the vibration coefficient ($p = 0.034$).

The whole-brain exploratory analysis revealed a number of regions exhibiting a correlation between brain responses and pleasantness ratings for stroking (uncorrected $p < 0.001$) (**Table 1**). Of these, a cluster with a peak in the superior temporal gyrus, extending well into the STS, was the largest (**Figure 2C**). No voxels passed the threshold for vibration.

DISCUSSION

We examined the extent to which posterior temporal lobe responses are selective to socio-affective touch by comparing activity elicited by skin stroking and skin vibration. Contrary to our hypothesis, we found no significant differences between skin stroking and vibration. However, right pSTS responses correlated significantly with participants' perceived pleasantness of skin stroking, but not vibration. These results suggest that right pSTS responses may indeed be selective to skin stroking, but also that pSTS activity is modulated by individual variability in perceived affective quality of touch.

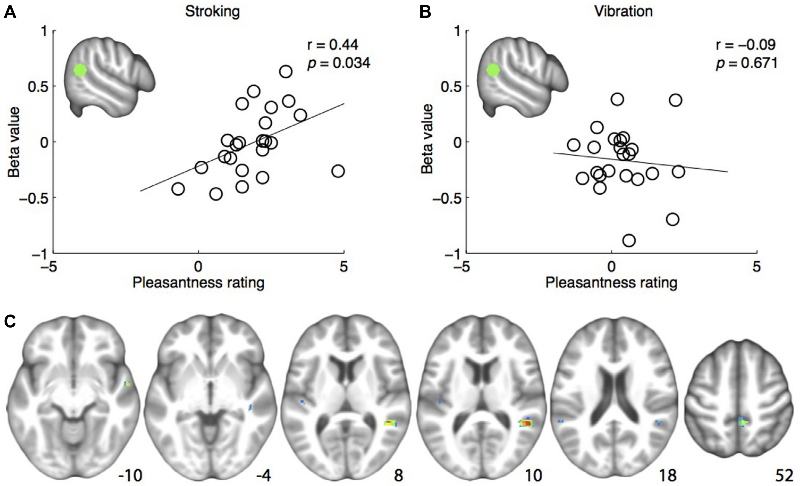

FIGURE 2 | (A) Positive correlation between pleasantness ratings and brain responses to skin stroking in the pre-defined right posterior superior temporal sulcus region-of-interest (rpSTS) (indicated in green). **(B)** No correlation between pleasantness ratings and brain responses to skin vibration in the rpSTS. **(C)** Whole-brain correlations between brain responses to skin stroking and pleasantness ratings, shown at $p < 0.001$. Coordinates are indicated in Montreal Neurological Institute (MNI) space.

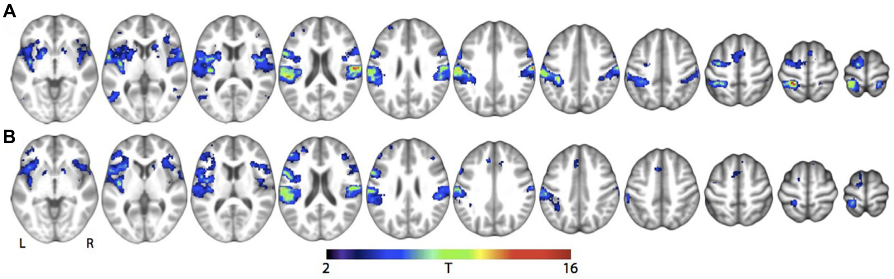

FIGURE 3 | Main effect of tactile stimulation vs. rest for (A) Skin stroking and (B) Skin vibration. Results are shown at whole-brain $p < 0.001$, uncorrected for multiple comparisons.

Our study did not replicate previous findings of significant group level pSTS responses to skin stroking, and skin stroking did not elicit significantly more temporal lobe activity than vibration on the group level. However, the finding of a positive correlation between pleasantness ratings and pSTS responses to skin stroking, but not vibration, suggests that the lacking group level effects may be partially due to statistical issues. Specifically, we applied voxelwise correction for multiple comparisons, which was recently demonstrated to be substantially more conservative than clusterwise correction (Eklund et al., 2016) used in previous

TABLE 1 | Results from the whole brain analyses.

	Region		Peak *z*-value	*x*	*y*	*Z*	Nr voxels
Stroking	Left	Postcentral gyrus	7.30	−24	−42	62	1548
	Right	Postcentral gyrus	6.80	56	−18	18	503
	Right	Insula	6.11	40	−2	14	48
	Left	Superior frontal gyrus	5.91	−14	−10	72	14
	Left	Inferior frontal gyrus	5.76	−56	8	22	89
	Left	Precentral gyrus	5.43	−34	−10	56	19
	Left	Lentiform nucleus	5.34	−20	6	−6	8
	Right	Inferior frontal gyrus	5.14	60	10	30	5
	Right	Superior temporal gyrus	5.09	60	6	2	5
Vibration	Left	Postcentral gyrus	6.60	−60	−18	16	563
	Left	Inferior frontal gyrus	5.85	−56	8	24	112
	Right	Postcentral gyrus	5.84	50	−16	18	142
	Left	Insula	5.71	−40	−12	4	52
	Left	Undefined	5.36	−54	10	4	15
	Left	Postcentral gyrus	5.25	−22	−40	68	13
	Left	Inferior frontal gyrus	5.23	−40	16	−4	21
Stroking> Vibration	Left	Postcentral gyrus	6.13	−54	−22	36	132
	Left	Inferior frontal gyrus	5.78	−58	6	30	17
	Left	Postcentral gyrus	5.65	−24	−48	68	146
	Right	Postcentral gyrus	5.63	20	−44	70	20
	Left	Precentral gyrus	5.58	−34	−10	56	9
	Right	Precentral gyrus	5.45	56	−18	36	17
	Right	Postcentral gyrus	5.44	54	−16	24	29
Stroking – Rating[1] Correlation	Right	Superior temporal gyrus	4.44	50	−44	10	137
	Right	Middle temporal gyrus	4.08	58	−4	−10	18
	Right	Paracentral lobule	4.03	6	−44	52	72
	Right	Insula	3.39	42	−28	−4	9
	Left	Superior temporal gyrus	3.35	−56	−42	18	15
	Left	Superior temporal gyrus	3.24	−44	−24	8	5

Results are assessed at family-wise error corrected $p < 0.05$, unless otherwise specified.

[1] *Reported at $p < 0.001$, uncorrected for multiple comparisons.*

studies (Gordon et al., 2013; Voos et al., 2013; Björnsdotter et al., 2014). As such, there may have been STS effects that would have survived a less stringent initial threshold (of e.g., $p < 0.005$) with clusterwise correction for multiple comparisons, but that did not pass our least stringent voxelwise threshold ($p < 0.001$). In the current study, we did not assess the effects using less stringent criteria due to the high risk of obtaining type I errors (Eklund et al., 2016). The experimental design, in which stroking and vibration stimuli were interleaved with no interstimulus interval, is less likely to have caused the lacking effect: this design was successfully applied in a similar previous study (Morrison et al., 2011), albeit using a larger number of stimuli repetitions but also substantially fewer participants, and we identified condition differences across a large number of other brain regions previously associated with tactile stimulation at the highly conservative threshold of whole-brain pFWE < 0.05.

In light of potential statistical processing differences, our finding that pSTS responses to skin stroking, but not to vibration, correlate with pleasantness ratings is highly consistent with previous findings of a selective role of the right pSTS in processing socially relevant tactile cues (Gordon et al., 2013; Voos et al., 2013; Björnsdotter et al., 2014). Although vibrotactile stimulation may be linked to social processing – the vibration probe was manually applied by the experimenter, and vibration is becoming increasingly associated with communication through cell phones (Drouin et al., 2012) – our data did not reveal any significant effects in relation to skin vibration. However, since vibrotactile stimuli is known to activate the temporal lobe (Beauchamp et al., 2008), we speculate that paradigms specifically interrogating social processes linked to vibration, such as the behavioral response to the regular repeated buzz of a cell phone call, may detect such effects. Similarly, the current study did not attempt to dissociate social and CT-mediated touch processing, as gentle skin stroking is both the preferred CT stimulus and an inherently social type of touch. Instead, future studies using factorial designs including social/non-social and CT/non-CT mediated touch are required to establish whether the observed effects are related to the social component of touch or to the CT system.

The finding of a correlation between brain responses to skin stroking and pleasantness ratings supports the previously demonstrated link between variability in pSTS processing and social behavior. The superior temporal cortex is modulated by an astonishing variety of individual parameters, including task performance (Herrington et al., 2011), cognitive ability (Rutherford and Troje, 2012), social impairment (Kaiser et al., 2010), perceived animacy (Kuzmanovic et al., 2014), motor skills (Freitag et al., 2008), serotonin transporter genotype (Fisher et al., 2015), and plasma oxytocin (Lancaster et al., 2015). In line with these findings, we speculate that the demonstrated correlation may reflect a range of individual factors related to socio-affective sensory dimensions, rather than varying levels of peripheral input or low-level processing. For instance, early experiences such as frequency of maternal touch (Brauer et al., 2016), attachment-related stress (Nolte et al., 2013), and a range of other attachment-related processes (Vrticka and Vuilleumier, 2012) influence the functioning of social brain regions such as the STS. Since we did not assess these measures in the current study, future studies are needed to disentangle the relative contributions of such factors, as well as to identify additional brain circuits that may contribute to the coding of affective aspects of touch.

Conforming to previous research on the CT system (Löken et al., 2009; Morrison et al., 2011), we asked participants to rate the tactile experience in terms of pleasantness. The term ‘pleasant’ is not sufficiently concise to allow a precise interpretation, however; for example, interpersonal touch may feel pleasant in terms of sensory hedonics (such as ‘softness’) but unpleasant in terms of social aspects (such as ‘unfamiliarity’) (Gentsch et al., 2015). Hence, it is not clear whether the demonstrated correlation reflects a sensory-hedonic or social-affective dimension of the tactile sensation. Since the pSTS is robustly linked to social (Adolphs, 2009), rather than emotional or hedonic processing, we speculate that the observed correlation is primarily governed by a social-affective dimension.

Given the role of the pSTS in integrating sensory and social information (Yang et al., 2015), we further propose that the pSTS may play a role in the translation of neutral tactile stimuli into positively valenced, socially relevant touch. As such, this system may be affected in psychiatric conditions associated with altered social behavior and impaired attachment, including autism spectrum disorder (ASD). Consistent with this notion, just-published findings show reduced right pSTS responses to skin stroking in children with ASD (Kaiser et al., 2015). Socially relevant tactile behaviors extend well beyond skin stroking and caressing, however, including hugging, kissing, tickling, and so on; further studies are required to elucidate any generalized role of the temporal lobes across such behaviors.

CONCLUSION

Our results support a role for the posterior temporal lobe in processing socio-affective dimensions of touch. Specifically, our study supports the notion that socio-affective touch may be selectively processed in the temporal lobe; however, our results also suggest that any selectivity is contingent on top-down effects related to subjectively perceived qualities of the tactile stimulation.

AUTHOR CONTRIBUTIONS

MD and EJ designed the study and collected data. MD and MB performed the analyses. All authors participated in the interpretation of the data. MD an MB drafted the article. All authors contributed to the final revision of the article.

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Attachment classification, psychophysiology and frontal EEG asymmetry across the lifespan: a review

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In recent years research on physiological response and frontal electroencephalographic (EEG) asymmetry in different patterns of infant and adult attachment has increased. We review research findings regarding associations between attachment classifications and frontal EEG asymmetry, the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenocortical axis (HPA). Studies indicate that insecure attachment is related to a heightened adrenocortical activity, heart rate and skin conductance in response to stress, which is consistent with the hypothesis that attachment insecurity leads to impaired emotion regulation. Research on frontal EEG asymmetry also shows a clear difference in the emotional arousal between the attachment groups evidenced by specific frontal asymmetry changes. Furthermore, we discuss neurophysiological evidence of attachment organization and present up-to-date findings of EEG-research with adults. Based on the overall patterns of results presented in this article we identify some major areas of interest and directions for future research.

Keywords: psychophysiology, heart rate, cortisol reactivity, skin conductance, EEG asymmetry, prefrontal cortex

ATTACHMENT AND PSYCHOPHYSIOLOGY: AN INTRODUCTION INTO THE FIELD

According to Bowlby (1969) attachment is a biobehavioral state in which several physiological and behavioral systems are organized in order to provide an individual with a certain sense of security and intimacy with significant others. As attachment behaviors seem to be approach and withdrawal behaviors, Bowlby assumed that attachment behaviors are associated with approach and withdrawal mechanisms. For example, children around 6–9 months withdraw from the negative stimulus and approach their caregivers for security (Marvin and Britner, 1999). Bowlby defined these behavioral systems as biological systems that work along with physiological processes. It is assumed that individuals correct and adjust their approach and withdrawal behaviors by learning to manage their environments and maintain the homeostatic balance within the physiological system when they are emotionally aroused (Bowlby, 1969; Bretherton, 1995; Solomon and George, 1999). Mental representations of early attachment relationships shape emotional and cognitive information, which affects our attention and memory as well as our emotional reactivity of the central nervous system. In order to maintain organization within the attachment system, emotional reactivity is then regulated within the central nervous system (Main et al., 1985; Bretherton, 1993). Attachment is associated with different ways to regulate emotions and thus some researchers have actually argued that the attachment system is in itself an emotion regulation device (Vrtička and Vuilleumier, 2012). It has been hypothesized that attachment relationships (at least those with secure attachment classification) have a regulatory effect on individuals' affective and physiological responses to distress (Diamond, 2001; Gross, 2007).

Research employing physiological measures and electroencephalographic (EEG) techniques in children, adolescents and adults has flourished in recent years due to increased interest in understanding psychological states and behavior associated with attachment. The psychophysiological approach focuses on the measurement of physiological correlates of observed behavioral responses and the way in which individual differences in physiological response predispose specific behavior. In the present review we aim to present research findings regarding associations between attachment classifications and frontal EEG asymmetry, the autonomic nervous system (ANS) and the hypothalamic-pituitary-adrenocortical axis (HPA) across the lifespan. We included studies that report on participants' reactions to scenarios involving behaviors that are relevant for attachment purposes like sequences of separation and reunion. Furthermore we discuss reactions as a function of an individual's attachment classification. As our review is limited to prefrontal activation using EEG, we excluded studies presenting functional neuroimaging data (for further details on fMRI data, see Vrtička and Vuilleumier, 2012).

Before launching into specific areas of neurophysiological attachment research, it is necessary to point out that there are different ways of measuring attachment. In infants, the most commonly used is the Strange Situation procedure, where infants are classified into secure, insecure-avoidant, insecure-ambivalent

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Abbreviations: ANS, autonomic nervous system; HPA, hypothalamic-pituitary-adrenocortical axis; AAI, adult attachment interview; AAP, adult attachment projective picture system.

and disorganized attachment groups. Securely attached infants have confidence in their caregiver's availability and they actively seek them for comfort and use them as a safe haven. Insecure-avoidant infants expect rejection from their caregiver and consequently avoid their caregiver to effectively reduce anticipated conflict or rejection. Insecure-ambivalent infants are uncertain about their caregiver's response so they demonstrate passive or angry resistant behavior that serves to establish proximity to their caregiver. Disorganized infants have been unpredictably frightened by their caregiver. They are caught in a conflict when confronted with a situation that normally elicits attachment behavior. Many of them show signs of fear, freezing or disorientation during the Strange Situation procedure (Kobak and Madsen, 2008).

In adults there are two major approaches, namely self-report measurements and narrative methods. Although they both measure and classify attachment groups, they define the construct in a different way. Self-report questionnaires either assess categories of attachment style or they measure the degree to which dimensions of attachment styles are present (Ravitz et al., 2010). The outcome of self-report items is a product of thoughts about attachment that have entered the consciousness of a person and therefore reflect how the individual wishes to represent him- or herself towards others. Several self-report measurements like for example the Adult Attachment Questionnaire and the Experiences in Close Relationships converge on two dimensions of insecurity. Attachment anxiety refers to individuals with a negative sense of the self. They tend to expect separation, abandonment or insufficient love and they are preoccupied with the availability and responsiveness of others. Furthermore, they tend to maximize negative experiences, they are hypervigilant to potential threat and they demonstrate a hyperactivation of attachment behavior. In contrast, attachment avoidance refers to individuals with a negative sense of others. They are characterized by self-reliance, an avoidance of intimate relationships and they devaluate the importance of close relationships. In addition, they minimize feelings of distress and deactivate attachment behavior. Some instruments like for example the Relationship questionnaire allow deriving categories from these dimensional scales. According the Bartholomew and Horowitz's four category model these categories correspond to combinations of extreme positions on the aforementioned two dimensions. A secure attachment style is defined as a relative absence of attachment avoidance and attachment anxiety. A preoccupied/ambivalent attachment style is characterized by high attachment anxiety and low attachment avoidance. Individuals with an avoidant attachment style have low attachment anxiety and high attachment avoidance. Finally the fearful attachment style is conceptualized as high insecurity on both attachment avoidance and anxiety (Bartholomew and Horowitz, 1991).

In contrast to self-report measures narrative instruments like the Adult Attachment Interview (AAI) and the Adult Attachment Projective Picture System (AAP) do not rely on conscious self-evaluation and they allow analyzing unconscious defensive processes. The AAI is a semi-structured interview that measures the representation of attachment experiences in the mind of individuals. Individuals are asked to retrieve attachment-related autobiographical memories from early childhood and evaluate these memories from their current perspective (Hesse, 2008). According to the AAI there are four main adult attachment representations: Secure-autonomous (F), insecure-dismissing (Ds), insecure-preoccupied (E) and unresolved (U). Secure individuals (F) are able to reflect and integrate positive and negative experiences with their caregivers and their evaluation of attachment experiences is coherent. They have a so called "internalized secure base" which can be interpreted as the ability to internally and mentally explore thoughts and feelings. In contrast to them, insecure-dismissing individuals (Ds) tend to idealize or devaluate their attachment experiences by deactivation of attachment distress. Insecure-preoccupied (E) individuals are enmeshed with their caregivers and they show anger and low autonomy in their narrative evaluation. Finally, the unresolved category (U) refers to individuals who show a breakdown of defensive and coping strategies when talking about traumatic experiences like loss and abuse. Their evaluation is incoherent and often includes fearful affect (Buchheim and George, 2011, 2012). The AAP (George and West, 2012) is an established and validated interview to assess attachment representations, based on a set of eight picture stimuli. The stimuli are line drawings of a neutral scene and seven attachment scenes (e.g., illness, separation, solitude, death, and threat). The AAP classification system designates the four main adult attachment representations identified using the AAI classification system (secure, dismissing, preoccupied, unresolved). The AAP narratives of secure individuals (F) demonstrate the ability and willingness to think about attachment distress. In their stories characters reach out to attachment figures for comfort, they show a lot of constructive actions and they often describe mutual enjoyment in their relationships to others. The insecure-dismissing (Ds) group is characterized by a predominance of deactivating defensive processes that emphasize distance in relationships. Their narratives often focus on achievement and exploration. Attachment relationships usually provide functional care or they are described as authoritarian. The AAP stories of insecure-preoccupied (E) individuals include a lot of material that confuses and obscure attachment relationships. They typically concentrate on emotions related to problems, their responses have several undecided themes or story endings and they often focus on the past rather than on the present. This confusion in the story line is also reflected in the blurring of the hypothetical story with personal experiences. The unresolved attachment (U) refers to a group of individuals who are not able to contain and reorganize stories including features that evidence danger, helplessness, failed protection or isolation. Unresolved individuals become momentarily flooded by their attachment fears that cannot be reorganized in the narratives (George and West, 2012). In sum, attachment style as measured by self-report questionnaires is a product of thoughts that enter an individual's consciousness whereas developmental attachment patterns assessed by narrative techniques are based on the evaluation of defensive processes. A large body of research confirms a low correlation between self-report and interview results suggesting that they both assess different facets of attachment (Ravitz et al., 2010). Therefore, we can assume that despite they are theoretically related, attachment style and developmental attachment patterns are not the same constructs.

In the field of neurophysiological attachment research, there are studies measuring autonomic activity, which provides an index of physiological arousal like increased heart rate, skin conductance (electrodermal activity) or respiration. The ANS can be divided into the parasympathetic and sympathetic branches, which characterize different stress responses. The parasympathetic branch regulates organ functions. It is responsible for maintaining normal growth, restoration of internal organs, rest-and-digest and feed-and-breed situations. The sympathetic branch is the dominant branch in stress situations and stimulates acceleration in heart rate, increased sweating and blood pressure. In times of intense stress individuals redistribute metabolic resources to deal with external threat. On a physiological level this leads to an activation of the sympathetic nervous system accompanied by some degree of deactivation of the parasympathetic nervous system. As attachment relationships have a regulatory effect on the physiological and psychological response to stress, it is expected that the presence of attachment figures lead to an attenuated activity of the sympathetic nervous system (Diamond, 2001). Other studies measure the activity of the HPA like cortisol change during tasks designed to provoke stress (Phillips et al., 2006; Fox and Hane, 2008). According to Hennessy (1997) hormones that are released by stress-induced HPA activity do not only support the formation of social bonds but they are also influenced by proximity to and separation from social partners. Thus it is important to consider the relational context of support provision and an individual's interpretation of relational context in order to interpret reactivity to different types of tasks which are performed in social contexts. In order to accurately capture an individual's HPA response, it is necessary to measure cortisol in salvia or plasma 15–30 min after the completion of the procedure as the cortisol response takes place over a much longer time course than other physiological systems. For analyzing cortisol recovery after a stressful task, samples are usually taken 60 min after the procedure (Laurent and Powers, 2007). From an attachment perspective, it can be assumed that a secure attachment buffers physiological reactivity in response to stressors as these individuals can balance exploration and attachment, they are more open in their emotional expressions and they can use attachment figures as a safe haven. In contrast, insecure attachment is related to deficits in emotion regulation as they either deactivate attachment distress (in case of the avoidant/dismissing group) or they show low autonomy and feelings of anger (ambivalent/preoccupied group). Thus it is expected that these individuals show a heightened physiological reactivity in response to attachment-related stressors. The disorganized/unresolved group demonstrate a breakdown of defensive and coping strategies, suggesting that they might display the highest physiological arousal.

In addition to psychophysiological attachment research, a growing body of work is examining frontal EEG asymmetry and its relation to attachment. Research in that field indicates that there is a relation between approach/withdrawal tendencies and hemispheric asymmetries in EEG activity at frontal electrode sites. Left and right cerebral hemispheres are also involved in the experience and/or expression of different emotions (Fox and Davidson, 1984; Fox, 1991). The main focus of attachment studies is on the hemispheric asymmetry in EEG power in the general range of 3–12 Hz over the frontal region. A particular emphasis is on the "alpha" band (6–9 Hz). Activity in this band has been seen as being inversely related to cortical activity over a given scalp region. The model of Fox and Davidson (1984) proposes that the right frontal activation might be associated with withdrawal behaviors and the expression of negative affect and the left frontal activation might be associated with approach behaviors and the expression of positive affect. A decrement in left frontal activation indicates an absence of the expression of positive affect. A decrement in the right frontal activation it is associated with an absence of the expression of negative affect. In the study of Davidson and Fox (1982) the brain activity of 10 month old infants was recorded while watching videotape segments of an actress who was spontaneously generating a happy or a sad facial expression. In two studies the infants displayed a greater activation of the left frontal than the right frontal area in response to the happy segments as evidenced by lower alpha power on the right side. Other studies found the same asymmetry in frontal EEG activity when infants respond to sweet and sour tastes (Davidson and Fox, 1989) and when mothers or a stranger approach the infant (Fox and Davidson, 1984). Pizzagalli et al. (2005) also argue that resting left prefrontal dominance in the EEG activity might be associated with the propensity of developing approach-related tendencies. These study results suggest that there is an association between the regulation of approach and withdrawal mechanisms within the prefrontal cortex and attachment dependent emotion regulation. In line with the aforementioned hypothesis on physiological correlates, we expect clear differences in the emotional arousal between the attachment groups evidenced by specific frontal asymmetry changes.

PSYCHOPHYSIOLOGY AND ATTACHMENT CLASSIFICATIONS

Various data from different studies suggest that there is an association between the regulation of approach and withdrawal mechanisms within the prefrontal cortex, physiological arousal and emotion regulation that is related to attachment issues (Fox et al., 1992; George et al., 1999; Dawson et al., 2001; Roisman et al., 2004; Schieche and Spangler, 2005; Zelenko et al., 2005; Feldman et al., 2011). In this review we report on participants' reaction to scenarios involving behaviors that are relevant for attachment purposes like sequences of separation and reunion. Furthermore we discuss reactions as a function of an individual's attachment classification. In the following paragraphs we summarize studies on cardiovascular and galvanic skin response, adrenocortical activity and EEG asymmetry for the different attachment classifications across the life span.

CARDIOVASCULAR AND GALVANIC SKIN RESPONSE

Infants gain security from being physically close to a caring caregiver. When growing up children are expected to move from this behavioral level to an internal mental representation of the attachment figure (Main et al., 1985; Marvin and Britner, 1999). It is assumed that the more adaptive strategy of securely attached individuals leads to a lower physiological arousal in heart rate and skin conductance. This might contribute to their ability to deal with negative information in emotional processing (Dozier and Kobak, 1992; Spangler and Grossmann, 1993; Stanley, 2006). In infants, Sroufe and Waters (1977) investigated heart rate changes in the Strange Situation and found that although all attachment groups showed increased heart rate upon separation secure infants managed to recover their heart rate after reunion within less than 1 min after contact with their mothers and heart rate deceleration when they returned to play. In accordance to these results, Donovan and Leavitt (1985) also found acceleratory trends of the heart rate in secure infants. Furthermore, they found out that secure infants displayed heart rate deceleration when the unfamiliar adult approached. This might indicate their ability to direct their attention and orient to a stranger. Interestingly, the heart rate of mothers and secure infants paralleled each other, which might be caused by the mother's involvement in her infant's behavior. Zelenko et al. (2005) also found that mothers showed acceleration during separation and deceleration upon reunion that paralleled with that of their secure infants. In contrast to other attachment groups, mothers of securely attached infants displayed a heart rate decrease after they successfully calmed their infants. In a recent study, Feldman et al. (2011) also found a concordance between maternal and infant heart rate. Especially during episodes of affect and vocal synchrony infant and maternal heart rate increased similarly compared to non-synchronous moments.

When a secure strategy fails to gain support and comfort from an attachment figure, individuals develop secondary strategies to regulate the attachment system. Insecurely avoidant/dismissing individuals use deactivating strategies which are characterized by a suppression of emotions and masking of negative affect during attachment related situations. Conversely, insecurely ambivalent/preoccupied individuals are enmeshed with their caregivers and they commonly use hyperactivating strategies indicating that they show more negative affect and less autonomy in attachment related situations (Dozier and Kobak, 1992; Roisman, 2007).

Looking at innovative studies on heart rate and skin conductance in infants, researchers have argued that insecure infants are highly aroused during separation and reunion (Sroufe and Waters, 1977; Dozier and Kobak, 1992; Roisman et al., 2004; Diamond et al., 2006). Sroufe and Waters (1977) reported about the reunion session in the Strange Situation. In contrast to securely attached infants, ambivalent infants were put down before the recovery of their heart rate and so their heart rate was still elevated while playing. Avoidant infants also showed an increased heart rate from beginning of separation long into the reunion. Avoidant infants, on the other hand, minimize the display of negative emotions and thus might be protected against elevated cardiovascular reactivity in response to stressful situations. A recent study by Hill-Soderlund et al. (2008) examined the role of physiology in avoidant infants in comparison to secure infants in the Strange Situation. As the authors expected infants with an avoidant pattern of attachment exhibited a greater vagal withdrawal which indicates greater allostatic load. Surprisingly, they could not find a greater vagal withdrawal during the reunion episode in avoidant infants, although they are expected to be more actively engaged in minimizing their distress. Thus, the primary caregiver probably provides some sort of regulatory repair (Hofer, 2006).

From studies with disorganized infants during the Strange Situation we know that they suffer from tremendous stress as indicated by their increased heart rate and skin conductance when they are alone in the room and in the presence of a caregiver. Spangler and Grossmann (1993) analyzed the cardiovascular response of six disorganized infants. Their results indicate that disorganized infants have a significantly higher acceleration in their heart rate when they are alone in the room compared to the other infants. In accordance to these results, Willemsen-Swinkels et al. (2000) found an association between a disorganized pattern of attachment and an increase in heart rate during parting with the caregiver and a decrease in heart rate during reunion.

A number of researchers have examined the physiological response of adults during the AAI (George et al., 1996). Adults with the classification secure give open, coherent and consistent accounts of their childhood memories, regardless of whether they were positive or negative. They are able to integrate their various experiences into a unitary whole and to reflect upon their accounts during their interviews. These individuals have free access to the topics asked about and show a feeling for balance. It is suggested that a "secure" discourse can be understood in terms of a capacity for fluidly shifting attention between memories and maintenance of coherent discourse with the interviewer. Study results indicate that individuals with a secure attachment representation show a lower increase in skin conductance levels from baseline to questions asking them to recall experiences of separation, rejection and threat compared to the other groups (Dozier and Kobak, 1992, 1993; Roisman et al., 2004).

Dozier and Kobak (1992) found that adults with deactivating strategies (i.e., individuals who often report very positive relationships with their parents, play down the significance of their early attachment experiences and show lacks of concrete episodes) show a marked increase in skin conductance levels and heart rate from baseline to questions asking them to recall experiences of rejection, threat and separation from their parents. Individuals with hyperactivating strategies (i.e., individuals who show negative involvement and excessive detail when reporting relationships with their parents which is generally associated with the preoccupied group) also display higher skin conductance and heart rate when questioned about separation or threatened separation from caregivers (Dozier and Kobak, 1993; Roisman, 2007; Holland and Roisman, 2010).

Beijersbergen et al. (2008) did one of the few studies that investigated physiological reactivity in adolescents during the AAI and a family interaction task. Dismissing adolescents did not seem to be more stressed than secure adolescents in the AAI as indicated by their cardiovascular response. The authors assume that they are probably less open to the challenge of the AAI and can cope with the interview in a somewhat superficial manner. However, they exhibited an increased heart rate and electrodermal activity during the direct interaction task with their mother when trying to find a consensus in an area of disagreement indicating that it seems impossible for them to be uninvolved in direct interaction.

Differences in adult regulation patterns can not only be observed in the AAI but also in other situations where individuals activate their attachment system (Feeney and Cassidy, 2003). For example, Roisman (2007) examined psychophysiological profiles of secure and insecurely attached individuals (classified by the AAI) during marital interactions. During areas of disagreement with their (pre) marital partners, securely attached adults had the lowest increase in electrodermal reactivity indicating their ability to share their thoughts and opinions with their partners. The insecure-dismissing adults demonstrated heightened electrodermal reactivity while they attempted to resolve the conflict in their relationship. The author linked this physiological response to emotional inhibition which means that they want to avoid their spouses when called to resolve problems. This heightened electrodermal reactivity could also be found for general stressors (Carpenter and Kirkpatrick, 1996; Diamond et al., 2006; Kim, 2006; Kidd et al., 2011; Ablow et al., 2013). Compared to the insecure-dismissing group, Roisman (2007) found that insecure-preoccupied individuals displayed an even higher heart rate while conversing with their partners suggesting an emotional overinvolvement.

Although some studies investigated skin conductance and heart rate during the AAI and conflict interaction tasks, most of them focus on secure and insecure attachment. One of the few studies including the unresolved attachment group found no differences in cardiovascular response and skin conductance level between resolved ($N = 108$) and unresolved ($N = 23$) adolescents during the AAI (Beijersbergen et al., 2008). The authors argue that this might be due to the way they measured physiological reactivity as they only focused on reactivity during the trauma, loss and abuse questions although that may also be discussed in other questions. Furthermore, the breakdown in strategy might be very brief so that the physiological changes may also be more momentary than during the entire response to the questions. Stanley (2006) examined skin conductance in unresolved adults (assessed with the AAP, George et al., 1999; George and West, 2012) while watching separation and reunion scenes. The unresolved group showed significantly higher arousal than the secure and preoccupied groups as measured by skin conductance. Interestingly their level of arousal increased during the reunion, which coincides with reports that with increasing exposure to reunion episodes the unresolved group might become dysregulated (Creasey, 2002). Until now it is still unclear how much intensity would be needed to cause dysregulation.

ADRENOCORTICAL ACTIVITY

According to Hertsgaard et al. (1995) assessing the cortisol level in attachment research can be very useful as the neuroendocrine system might be stimulated when individuals have inadequate coping behaviors or coping sources are not available. Studies on attachment classification and adrenocortical response mainly focus on stress reactivity after a stressful event. Various studies have examined cortisol levels of infants after Strange Situation procedure. For example, Spangler and Grossmann (1993) collected salvia samples immediately before the Strange Situation procedure as well as 15 and 30 min after the end of the Strange Situation procedure. They found a small decrease in the cortisol response for secure infants 30 min after the end of the Strange Situation procedure. It is assumed that securely attached infants have a more adaptive behavioral strategy in response to stressors and thus they display no or only little adrenocortical activity during the procedure. This finding is consistent among a series of infant studies (Gunnar et al., 1996; Spangler and Schieche, 1998). However, adrenocortical responses among insecurely attached infants during the Strange Situation are inconsistent. Spangler and Grossmann (1993) found an increased cortisol level in both insecure-avoidant and insecure-ambivalent infants, whereas Spangler and Schieche (1998) could only observe an increase in the insecure-ambivalent group. In line with that, also Luijk et al. (2010) found higher cortisol levels after the Strange Situation in ambivalent infants. The authors suggest that the "maximizing" strategies (i.e., they maximize their behavior while they are the same time unable to find a state of homeostasis in interaction with their caregiver) of ambivalent infants, lead to a higher physiological arousal than the "minimizing" strategies of avoidant infants (Cassidy and Berlin, 1994). One possible explanation for the aforementioned inconsistences among infant studies is that behavioral factors might be involved the infant's cortisol response to stress. A number of studies have explored the relationship between inhibition of exploratory behavior and adrenocortical activation during stressful situations. In sum, the findings suggest that inhibition in exploratory behavior leads to adrenocortical activation in stressful situations only in insecure but not in secure infants (Gunnar et al., 1996; Nachmias et al., 1996; Spangler and Schieche, 1998). These effects during the Strange Situation could be replicated in other stressful situations like baby examination with inoculation (Gunnar et al., 1996) or a confrontation with other arousing stimuli (Nachmias et al., 1996).

Furthermore, it is suggested that adrenocortical activity is also influenced by the quality of the caregiver (Gunnar et al., 1992; Spangler et al., 1994). For example, Schieche and Spangler (2005) explored the influence of maternal behavior, infant-mother attachment and inhibition of exploratory behavior on the cortisol level during a problem-solving task in toddlers. In their study, elevated cortisol was associated with low task orientation and exploration in infants. These characteristics were in turn related to low supportive maternal presence and a reduced quality of maternal assistance during the challenge task. In line with other findings adrenocortical activation was not found in infants with low inhibition in exploratory behavior. Among the highly inhibited infants, those with a secure attachment classification showed the usual circadian pattern, i.e., a decrease in cortisol from task onset to 30 min after the task.

Although many infants develop organized strategies to manage stressful events in the presence of their primary caregiver, some display a breakdown of strategy which is associated with specific parenting behaviors such as maltreatment, abuse or neglect.

Adrenocortical response of these disorganized infants has been investigated in only very few studies. In the study of Hertsgaard et al. (1995) adrenocortical activity came out most clearly for the six disorganized infants. They found the highest cortisol concentration in 19 month old toddlers who were classified as having disorganized attachments. Also, Gunnar et al. (1996) observed a significantly higher cortisol level in disorganized infants after the Strange Situation. Bernard and Dozier (2010) were the first to investigate infants' cortisol changes during the Strange Situation and a comparison laboratory task (i.e., play). Disorganized infants displayed increases in cortisol that were significantly different than changes elicited during the free play task. These differences were not found in the organized attachment groups which support the hypothesis that adequate maternal care buffers an infant's stress reactivity. Even though these preliminary studies offer exciting data of the effects of maternal care on an infant's stress response, it will be important for future research to examine what particular aspects of maternal care are associated with adrenocortical response to stress.

To date there has been little research on adult attachment and cortisol response. Usually the adrenocortical activity in adults is assessed in the laboratory, comparing stress reactivity between individuals among the different attachment groups. One of the first studies measuring attachment and cortisol response was done by Powers et al. (2006). The authors assessed attachment in 124 adult dating couples with the Experiences in Close Relationships Questionnaire which represents a continuous measure of attachment anxiety and avoidance. They measured their cortisol response during a relationship conflict task. They collected samples 20, 30, 45 and 60 min after the conflict task to analyze stress recovery of the participants. The authors argue that measuring cortisol level after 60 min is an adequate time for cortisol recovery. Their findings demonstrate that insecure-avoidant attachment style in females predicted greater HPA reactivity during the conflict interaction task with their partners. However, avoidant women could recover very quickly. Interestingly the authors found that in men, in contrast to women, insecure-anxious attachment style correlated with higher stress reactivity and it also took them longer to return to the baseline after the conflict. Laurent and Powers (2007) expanded this research by examining moderating effects within the couples. Their results indicate that an avoidant attachment style in both partners leads to an increase in woman's cortisol response during the conflict interaction task. The authors argue that the mutual avoidance makes it difficult for the partners to negotiate their conflict and the woman's sense of responsibility for doing it might generate a stress response even though she appears disengaged.

Another study by Quirin et al. (2008) investigated the cortisol response during an acute stressor consisting of a cognitive task with an unpredictable and uncontrollable noise in 48 healthy women. Results demonstrate that attachment anxiety was associated with heightened cortisol to acute stress. Although some studies were done for stressful events and attachment, only very little is known about regarding the association between attachment and cortisol response over the course of the day. To our knowledge there is only one study by Kidd et al. (2013) examining this relationship and they found that individuals with a preoccupied attachment style who are characterized by high anxiety and low avoidance have the highest cortisol level throughout the day. One explanation for this result might be that hypervigilant strategies lead to anticipatory stress appraisals for upcoming events and an inability to downregulate subjective and physiological response.

All of the aforementioned studies employed self-report questionnaires to assess attachment style. There is only one study by Rifkin-Graboi assessing attachment and HPA activity using the AAI. This study investigated relations between attachment and cortisol levels during daily life and interpersonal laboratory challenges wherein college aged men were asked to respond to hypothetical situations concerning separation, abandonment and loss. Results show that dismissing subjects show comparatively higher cortisol during the challenges than the other attachment groups. Unfortunately, current research still lacks data on unresolved attachment status in adults.

FRONTAL EEG ASYMMETRY

In the last two decades researchers have started to recognize the central role of the prefrontal cortex in the regulation and expression of emotion. As mentioned in the introduction, right frontal activation in infants and adults is associated with "withdrawal" emotions like distress and sadness, whereas left frontal activation is related to "approach" emotions like joy and interest (Dawson et al., 2001). It is assumed that securely attached individuals show a flexibility of the prefrontal emotion regulation mechanisms. Studies on insecure attachment show that the activation of the right frontal brain areas, usually seen in the insecure-ambivalent/preoccupied group, is associated with the full expression of distress. The activation of the left hemisphere, displayed by the insecure-avoidant/dismissing group, might signal the inhibition of emotional attachment behavior like crying (Calkins et al., 1996; Rognoni et al., 2008; Behrens et al., 2011).

Several studies examined EEG asymmetry and its relation to attachment in human infants in Ainsworth's Strange Situation (Calkins and Fox, 1992; Dawson et al., 1992, 2001). Various data from a number of different studies have implicated that securely attached infants are more positive, are less stressed in separation segments and engaged their parents in interaction more often (Davidson and Fox, 1989; Fox et al., 1992; Diener et al., 2002). Spangler and Grossmann (1993) examined behavioral organization in securely and insecurely attached infants using the Strange Situation. Their results indicate that when securely attached infants approached their caregivers for comfort during reunion, mothers managed to calm and soothe their infants with their presence (Braungart and Stifter, 1991). Davidson and Fox (1989) studied EEG asymmetry in 13 month old infants and found out that infants with right frontal activation were more likely to cry at maternal separation than those who displayed left frontal dominance. This finding was replicated in another study by Fox et al. (1992) that recorded EEG during brief maternal separation in two sessions and found again that infants exhibiting right frontal activation were more likely to cry at separation from their mothers. These findings suggest that right frontal activation, commonly seen in ambivalent infants, might be associated with a lower threshold for the expression of negative affect. In contrast, left frontal activation, commonly seen in avoidant infants, might be associated with a higher threshold and a disposition to express more positive emotions.

Other evidence for this model stems from studies on EEG asymmetry in infants of depressed mothers. Dawson and her colleagues (Dawson et al., 1992, 2001; Dawson, 1994) found differences in EEG asymmetry between secure infants of depressed and non-depressed mothers in the Strange Situation experiment. Those who were classified as securely attached to their non-depressed mothers showed significantly greater right frontal activity whereas securely attached infants of depressed mothers showed greater left frontal activity when the mother walked to the door. Ordinarily, sadness and withdrawal (i.e., the activation of the right prefrontal region) would be expected at parental separation. This might lead to the hypothesis that infants of depressed mothers who show left frontal activity (i.e., positive emotion and approach) when their mothers walk to the door, inhibit their negative emotions. Another interesting area of research is the study of the relationship between the level of exploratory behavior, the attachment organization and the EEG asymmetry in infants (Calkins and Fox, 1992; Fox et al., 1994; Calkins et al., 1996). Calkins and Fox (1992) examined the relationship among infant temperament, security of attachment and exploratory behavior at 24 months. In their study, 34 infants were classified as secure, 7 as avoidant and 9 as ambivalent. The authors conceptualized the term behavioral inhibition in exploratory behavior as the infant's tendency to show negative affect in response to new people, places and events. This tendency is displayed by long latencies to approach the unfamiliar adult, high amounts of time spent in proximity to the mother as well as facial and vocal displays of negative affect. In contrast to that, uninhibited exploratory behavior in infants means that they are quick to explore the novel room, approach the stranger with no apparent distress and spending only little time with their mothers. Results indicate that avoidant infants are likely to be uninhibited in their exploratory behavior whereas ambivalent infants are likely to be inhibited in their exploratory behavior. Securely attached infants tend to display behavior in the mean. In a subsequent study, Calkins et al. (1996) extended these findings by examining the role of behavioral profiles (high/low motor activity and positive/negative affect) and brain electrical activity in 4 month old infants to predict inhibited and uninhibited exploratory behavior at 14 month of age. It was hypothesized that the behavioral profiles of infants are associated with particular profiles of brain electrical activity and response to novelty. Results demonstrate that infants with high frequencies of motor activity and negative affect display greater right frontal activation at 9 months. In the laboratory situation they showed more inhibited exploratory behavior, they spent more time in proximity to the mother and it took them longer to approach the unfamiliar adult. Furthermore their mothers reported that they have more social fear than the low motor and positive affect group. This finding is consistent with previous findings (Davidson and Fox, 1989; Spangler and Grossmann, 1993).

An area of most interest with respect to emotion regulation is EEG asymmetry in disorganized patterns of attachment. It is hypothesized that in contrast to the other attachment groups these infants do not manage to create the best possible proximity to an attachment figure because their parents are extremely insensitive or even frightening. This leads to a temporary breakdown in the infant's strategy to keep close to the attachment figure. They segregate emotions into a separate system and dysregulate when the attachment system is overstressed (Main and Solomon, 1990). This dysregulation might be observed in the prefrontal mechanisms. For example, Dawson et al. (2001) examined EEG asymmetry in disorganized children during the Strange Situation and found that these children had higher activity in both the left and the right prefrontal cortex. Dawson interpreted these results as the intensity the children were experiencing and also as a reaction of the prefrontal cortex to dysregulation. As the intensity of the attachment increased, children with that attachment representation tend to over react.

A lot of studies in adults focus on EEG asymmetry during emotion perception among individuals with different attachment patterns. There is growing evidence that left frontal activation at rest and in response to emotional stimuli is associated with approach system and positive emotion, whereas right frontal activation is related with the withdrawal system and negative emotions. Regarding this aspect, it is assumed that attachment patterns might have a strong impact on individual affective dimensions and modulate the underlying neural activity (Rognoni et al., 2008). Results from studies on EEG asymmetry and insecurely attached adults indicate that dismissing individuals have higher left than right activity in the prefrontal cortex during a baseline measure (Stanley, 2006). It is suggested that even though they are stressed during a baseline measure they tend to explore and approach so that they can deal with the negative emotionality (Braungart and Stifter, 1991; Spangler and Grossmann, 1993). A growing body of research also supports the presumption that this attachment group processes positive stimuli related to close relationships and intimacy as less arousing and thus activates withdrawal neural circuits. However, when confronted with unpleasant stimuli they either activate approach-related neural circuits (i.e., activation of the left hemisphere) or deactivate withdrawal-related right hemisphere circuits, depending on the attachment activation of the stimuli. On the other hand, preoccupied individuals show the opposite tendency by enhancing withdrawal neural circuits in response to fear and stimulating the approach circuits in response to happiness (Calkins et al., 1996; Schmidt et al., 1999; Buss et al., 2003; Rognoni et al., 2008).

A couple of studies have investigated adult attachment and hemispheric asymmetries during visual stimuli. Rognoni et al. (2008) examined whether adult attachment styles using several self-report measures influence subjective and neurophysiological aspects of emotion. The subjects watched emotional video-clips that induced happiness, fear and sadness with attachment-related content. Results reveal that fearful individuals responded with less arousing subjective experience and right frontal asymmetry to positive stimuli whereas preoccupied individuals showed higher arousal feelings and wider frontal left activation. Interestingly the authors observed opposite patterns in response to fear. This lower level of arousal in fearful adults suggest that they restrictively experience positive affect and this could be related to the lower involvement of the left hemisphere in processing positive information. The enhanced right prefrontal activation shown in the preoccupied group when confronted with the fearful stimuli is in line with previous findings of children who exhibit fearful and shy behavior at rest and during stressful tasks and separation (Calkins et al., 1996; Buss et al., 2003). These results are consistent with other studies that examined how attachment styles modulate brain responses to emotional stimuli. For example, Zilber et al. (2007) examined whether adult attachment styles modulate the processing of emotional stimuli. To assess attachment-related social information processing they used scalp-recorded event-related potentials (ERP) while participants watched unpleasant, pleasant and neutral pictures. The ERP waveforms consist of positive and negative components which allow measuring the processing of emotional stimuli. One of these components is the late positive potential (LPP) which is very strong when individuals watch emotionally arousing pictures. It is assumed that the further from neutral a stimulus is perceived to be, the larger is the resulting LPP amplitude. Their main result was that the difference in LPP amplitudes between negative and neutral pictures was found to be the greatest for individuals scoring high on attachment anxiety. These findings were extended by Chavis and Kisley (2012) who also considered the emotion bias of individuals with different attachment styles. They measured ERP during an affective oddball paradigm in which participants viewed positive, negative and neutral images of people. The authors found that avoidantly-attached adults displayed a bias towards more neural activation in response to negative images suggesting a greater motivational relevance of negative stimuli. From an attachment perspective their favoring of negative over positive social stimuli could be a reason for their interpersonal withdrawal. In contrast to them anxiously-attached adults demonstrated a bias towards neural activation in response to positive images which appears to be related to a greater motivational relevance of positive stimuli. The behavior of striving for interpersonal closeness in anxiously-attached individuals might be reflective of their motivational balance favoring positive social stimuli. Compared to the two insecure attachment groups, the secure groups did not favor either positive or negative categories.

In a very recent study by Escobar et al. (2013) this processing of emotional information was further examined by exploring ERP correlates of facial emotion recognition in adolescents with different attachment styles. The authors were especially interested in the P1 component which can be modulated by stimulus type (e.g., comparing faces to words) and the N170 component which is more strongly triggered with facial stimuli than with object or word stimuli. Results show that the insecurely attached adults exhibited larger P1 for face stimuli and attenuated the N170 component over the right hemisphere. These results could indicate that this group does not differentiate between emotions when looking at facial stimuli. This was also observed in another study by Dan and Raz (2012) in which adults with an insecure attachment style were slower and less accurate at differentiating angry from neutral faces. Furthermore, the larger face-elicited P1 in the insecure group might suggest a general state of higher vigilance and the larger N170 when viewing negative face stimuli might relate to their proneness to a negative bias.

All of the above adult studies employ self-report measures and unfamiliar face stimuli. One of the few studies using narrative technique for assessing attachment representation was done by Behrens et al. (2011). The authors explored whether neurophysiological responses to photographs of the own child differed based on attachment status. EEG response records to a total of 100 images of the participant's parents and child (25 each of positive, negative, neutral and personal) were analyzed among three mothers with three different attachment patterns (preoccupied, dismissing and secure) classified with the AAI (George et al., 1996). The dismissing mother showed significantly stronger left hemisphere activation across all image types whereas the preoccupied mother displayed significantly stronger right hemisphere activation for all images except the neutral ones during which the activation in both hemispheres did not differ. The mother with the secure pattern of attachment showed greater left hemisphere activation for all but parental personal images during which activation did not differ between the two hemispheres. Since this pilot study includes only three participants, a replication of these findings using a larger sample is necessary to draw further conclusions about EEG response to attachment-related visual stimuli.

A relatively new area of research is the study of how attachment classifications influence behavior and psychophysiology to social vs. nonsocial situations and stimuli (Vrtička and Vuilleumier, 2012). A recent study by Verbeke et al. (2014) measured resting-state cortical brain activity using EEG in 35 participants when they were alone in the room (condition 1) and when they were together (condition 2). Individuals who scored higher on anxious attachment style experienced an enhanced alpha, beta and theta power when they were together with another person during the resting session. Interestingly, these results did not occur in the avoidant group. During the task-free resting state procedure implemented in this study, adults with an anxious attachment style fail to have their need for approval met and consequently they become preoccupied with what other people might think about them. The enhanced alpha power observed in anxiously-attached adults might provide protection for this internal information processing by blocking external interferences of the surrounding sensory input. For a deeper analysis of these differences, future research could add further biomarkers like heart rate or skin conductance.

Studies using narrative techniques to measure prefrontal activation in a standardized social context are a very new field of research. Two recent publications studied neural correlates of attachment representations during a virtual game involving unfamiliar peers. White et al. (2012) measured ERPs during the Cyberball experiment, a ball toss game where participants play with two peers online who first include and later exclude the participant. The results show that an insecure-dismissing attachment is related to negative left frontal slow wave during rejection. This wave form may suggest a bias to expect more extensive or lasting exclusion from the group and thus entail a more negative appraisal of the interaction and less approach motivation. In accordance with other findings, the dismissing

Table 1 | Studies on cardiovascular response in different attachment groups.

	Study	**N**	**Participants**	**Gender**	**Attachment measures**
Infants	Sroufe and Waters (1977)		Individual case studies	Mixed	Strange situation
	Donovan and Leavitt (1985)	29	22 B[a], 4 A[b], 3 C[c]	Mixed	Strange situation
	Spangler and Grossmann (1993)	41	18 B, 6 A, 6 D[d]	Mixed	Strange situation
	Willemsen-Swinkels et al. (2000)	82	32 children with pervasive developmental disorder, 22 with developmental language disorder and 28 within the normal range	Mixed	Strange situation
	Izard et al. (1991)	54	40 B, 8 A, 6 C	Mixed	Strange situation
	Fox (1985)	60	43 B, 16 A, 1 C	Mixed	Strange situation
	Spangler et al. (2002)	Series of studies	Mothers and infants	Mixed	Strange situation
	Burgess et al. (2003)	140	140 mothers and infants	Mixed	Strange situation, behavioral inhibition, play with unfamiliar peers
	Tharner et al. (2013)	450	450 mothers and infants	Mixed	Shortened strange situation
	Zelenko et al. (2005)	41	23 B, 6 A, 12 C	Mixed	Strange situation
Children	Stevenson-Hinde and Marshall (1999)	126	38 B, 6 A, 8 C	Mixed	Strange situation
	Stevenson-Hinde and Marshall (1999)	126	38 B, 6 A, 8 C	Mixed	Modified strange situation
	Oosterman and Schuengel (2007a)	50	50 parents and their children	Mixed	Observational inhibition scale, separation and reunion procedure
	Oosterman and Schuengel (2007b)	110	60 foster children and 50 control children with their caregivers	Mixed	Modified strange situation
Parents	Donovan and Leavitt (1978)	22	22 mothers and their infants	Female	Physiological reaction to infant's signals during the feeding session
	Wiesenfeld et al. (1981)	32	16 mothers and 16 fathers with their infants	Mixed	Audio cry segments of own and unfamiliar infants
	Wiesenfeld and Klorman (1978)	17	17 mothers	Female	Videotaped smile and cry segments of own and unfamiliar infants
	Donovan and Leavitt (1989)	48	48 mothers	Female	Response to infant cries
	Donovan et al. (1990)	66	66 mothers	Female	Response to infant cries
	Feldman et al. (2011)	43	43 mothers and infants	Mixed	Face-to face interactions during free play
	Hill-Soderlund et al. (2008)	132	132 mothers and their infants	Mixed	Strange situation
	Donovan et al. (1997)	38	38 mothers	Female	Response to infant cries
Adults	Spitzer et al. (1992)	131	131 adults	Mixed	Response to stressors in social situations
	Palestrini et al. (2005)	17	17 dogs and their owners	Mixed	Modification of strange situation (strange environment)
	Roisman (2007)	80	40 younger engaged couples, 40 mature married couples	Mixed	AAI[e]; conversation about areas of disagreement with their partners
	Fontana et al. (1999)	60	60 undergraduate women	Female	Stressful tasks with and without social support
	Sbarra and Borelli (2013)	89	89 adults	Mixed	Self-report adult attachment style; divorce-related mental recall task
	Kim (2006)	66	33 college couples	Mixed	7 point Likert scale on attachment styles; distress inducing film clips; discussion scenarios
	Carpenter and Kirkpatrick (1996)	34	34 college women	Female	Questionnaire on attachment style; stressful situation with or without presence of romantic partner
	Ablow et al. (2013)	53	53 women	Female	Infant cry segments, AAI[e]

[a]B, secure attachment; [b]A, avoidant insecure attachment; [c]C, ambivalent attachment; [d]D, disorganized attachment; [e]AAI, adult attachment interview.

subjects also underreported subjective distress on self-report although the demonstrated neural activity that is related to an elevated level of distress (Dozier and Kobak, 1992; Roisman et al., 2004). In a subsequent study, White et al. (2013) analyzed neural responses to the reunion phase in the Cyberball experiment. Compared to secure participants, the dismissing group demonstrated a greater increment in the N2 during reunion with excluders suggesting that their expectations for being rejected are more strongly violated by a re-initiation of fair play that follows the exclusion phase. In other words, these individuals tend to have continued expectations of rejection even though they were re-included by their peers.

CONCLUSION AND DIRECTIONS FOR FUTURE RESEARCH

Over the last twenty years the psychobiological research on attachment has increased dramatically. The study of neurobiological underpinnings of attachment and its impact on a range of social and affective behaviors is a relatively new field of research. Vrtička and Vuilleumier (2012) published the first review in the field of neuroscience and attachment focusing mainly on fMRI results. In the present review we intended to make an important addition to that by discussing EEG and psychophysiological data from attachment research. Furthermore we provided an overview on recent studies on cardiovascular reactivity (see **Table 1**), galvanic skin response (see **Table 2**), adrenocortical activity (see **Table 3**) and on EEG asymmetry (see **Table 4**) among the four attachment classifications across the life span.

In summary, studies using physiological parameters support the hypothesis that a secure attachment representation buffers physiological reactivity in response to stressors. Securely attached individuals are characterized by open, flexible emotional expressions, they are better able to balance exploration (i.e., autonomy strivings) and attachment (i.e., relatedness) and they show a greater openness to explore their own thoughts and feelings. On a physiological level they respond with less cortisol increase, lower skin conductance and more flexible prefrontal mechanisms during attachment-related stimuli compared to the other attachment groups. However, it is still unknown in how far attachment security and physiological functioning are stable at the different stages of development from childhood to adulthood. Investigating childhood and later adult attachment and analyze their influence on adult psychobiological processes could make a significant contribution towards understanding psychophysiology of human attachment.

In contrast to securely-attached infants and adults, those with an insecure attachment show a heightened physiological reactivity to stress, which is consistent with the hypothesis that attachment insecurity is associated with deficits in emotion regulation. During the Strange Situation, ambivalent infants have higher cortisol level and they tend to show more right prefrontal activity, whereas avoidant infants have increased heart rate from separation long into reunion, an increased cortisol level and they tend to exhibit more left prefrontal activity which is associated with the inhibition of emotional attachment behavior like crying. These findings especially among the avoidant attachment pattern are particularly notable as this group typically shows low levels of subjective distress. This discrepancy between physiological reaction and subjective distress was also observed in adults with an insecure-dismissing classification as indicated by their low level of self-reported stress. Thus a central question for future research is whether there is a failure to experience subjective distress or a failure to report it. Although physiological results would actually support the latter explanation, it will be necessary to closer investigate the mechanisms underlying the lack of correspondence between physiological and subjective responses to stress (Diamond and Fagundes, 2010).

Another important issue regarding the study of neurophysiological correlates is that the majority of neurophysiological studies of adult attachment have used

Table 2 | Studies on electrodermal reactivity in different attachment groups.

	Study	N	Participants	Gender	Attachment measures
Adolescents	Beijersbergen et al. (2008)	156	156 adolescents	Mixed	AAI[a]; conflict interaction task
Parents	Frodi et al. (1978)	128	64 parents	Mixed	Videotaped crying segments of normal and premature infant
Adults	Boukydis and Burgess (1982)	72	36 couples	Mixed	Audio cry segments of infants
	Dozier and Kobak (1992, 1993)	50	50 students	Mixed	AAI
	Roisman et al. (2004)	60	60 adults	Mixed	AAI
	Diamond et al. (2006)	148	148 adults	Mixed	Confrontation with psychological stressors; discussion of attachment-related issues
	Kiss et al. (2011)	82	82 adults	Mixed	Trust game; ECR[b] scale
	Davydov et al. (2011)	26	26 female students	Female	Emotional film clips
	Holland and Roisman (2010)	114	115 couples at T1[c], 57 couples at T2[d]	Mixed	AAI; conflict resolution task; self-reports about relationships
	Rochman et al. (2008)	27	27 university students	Mixed	Self-report on unresolved anger towards an attachment figure; sadness-anger induction
	Groh and Roisman (2009)	60	60 undergraduate students	Mixed	Attachment script assessment; audio cry and laughter segments of infants; emotional experience questionnaire

[a] AAI, adult attachment interview; [b] ECR, experiences in close relationships; [c] T1, time 1 refers to the first assessment; [d] T2, time 2 refers to the second assessment one year later.

Table 3 | Adrenocortical response in different attachment groups.

	Study	N	Participants	Gender	Attachment measures
Infants	Gunnar et al. (1989)	66	37 B[a], 10 A[b], 16 C[c], 3 D[d]	Mixed	Strange situation
	Gunnar et al. (1996)	73	73 infants	Mixed	Strange situation; clinic exam-inoculation situation
	Nachmias et al. (1996)	77	48 B, 12 C, 13 A, 4 D	Mixed	Strange situation; parent-reported behavioral inhibition
	Spangler and Grossmann (1993)	41	18 B, 6 A, 6 D	Mixed	Strange situation
	Hertsgaard et al. (1995)	38	17 B, 5 A, 1 C, 11 D	Mixed	Strange situation
	Roque et al. (2012)	51	51 infants	Mixed	Positive and negative emotional situations in natural setting;
	Bernard and Dozier (2010)	32	32 infants	Mixed	Strange situation; play
	Luijk et al. (2010)	369	369 infants	Mixed	CIDIe for depression; strange Situation
	Spangler and Schieche (1998)	106	66 B, 21 A, 15 C,	Mixed	Strange situation; maternal report on behavioral inhibition
Toddlers	Schieche and Spangler (2005)	76	23 B, 19 A, 11 C, 23 D	Mixed	Strange situation; problem-solving task; toddler temperament scale
Adults	Quirin et al. (2008)	48	48 women	Female	Laboratory stress task
	Pruessner et al. (2004)	120	120 college students	Mixed	Mental arithmetic task, parental bonding index (PBI)f
	Powers et al. (2006)	248	124 dating couples	Mixed	Conflict negotiation task; ECRg
	Kirschbaum et al. (1995)	66	66 adults	Mixed	Public speaking task with or without social support
	Kidd et al. (2011)	498	498 adults	Mixed	Relationship questionnaire; behavioral tasks; word/color interference task; mirror tracing task
	Laurent and Powers (2007)	398	199 couples	Mixed	ECR; emotionality, activity and sociability questionnaire for temperament; conflict discussion with partner
	Rifkin-Graboi (2008)	73	73 students	Male	AAIh; daily life and interpersonal laboratory challenges
	Kidd et al. (2013)	1807	1807 adults	Mixed	Relationship questionnaire

[a]B, secure attachment; [b]A, avoidant insecure attachment; [c]C, ambivalent attachment; [d]D, disorganized attachment; [e]CIDI, composite international diagnostic interview; [f]ECR, experiences in close relationships; [g]AAI, adult attachment interview.

self-report measures (Carpenter and Kirkpatrick, 1996; Pruessner et al., 2004; Kim, 2006; Laurent and Powers, 2007; Rochman et al., 2008; Kiss et al., 2011; Dan and Raz, 2012; Sbarra and Borelli, 2013), whereas only a handful of studies have used a narrative approach towards attachment like the AAI or the AAP (Beijersbergen et al., 2008; Fraedrich et al., 2010; Holland and Roisman, 2010; Behrens et al., 2011). Although both approaches have their roots in a common theoretical tradition, the distinctions between these assessments should be discussed. As already mentioned in the introductory section, self-report measures on attachment are commonly used to assess adult romantic relationships by asking about a person's feelings and behaviors in the context of close relationships. In contrast to them narrative instruments measure attachment representations and they allow an analysis of unconscious defensive processes—a dimension that is not included in self-report measures. When those two approaches are compared, it becomes apparent that the measures are not interchangeable which raises practical questions why they lead to divergent results and which one can accurately capture the constructs fundamental to Bowlby's attachment theory. Therefore, Roisman et al. (2007) suggest that due to the small overlap between these two attachment measurement traditions, AAI and self-report literatures should not be cited and discussed as if these measures were interchangeable. An important issue for future research will be a neurophysiological distinctive comparison between infant attachment, adult attachment and caregiving patterns to find out more about the underlying mechanisms at different stages of our lives, which shape our emotional and physiological regulation.

A relatively untapped area of research is that of neurophysiological correlates of unresolved attachment pattern in adults. Although there are a couple of studies on infants, there is a lack of studies for adolescents and adults. From studies with unresolved infants during the Strange Situation we know that they suffer from tremendous stress as indicated by their high cortisol level, their increased heart rate and skin conductance when they are alone in the room. Interestingly they also show a higher activity in both hemispheres during the procedure, which might be an indicator of their segregation. In one of the few studies that investigated physiological response in disorganized adults, Stanley (2006) found a higher arousal as measured by skin conductance while watching video clips on reunion scenes, which might be a signal for their dysregulation. However, Beijersbergen et al. (2008) could not find any significant

Table 4 | Prefrontal EEG asymmetry in different attachment groups.

	Study	N	Participants	Gender	Attachment measures
Infants	Davidson and Fox (1989)	13	13 infants	Mixed	Periods of maternal approach and separation
	Fox et al. (1992)	46	(1) 33 infants (2) 13 infants	Mixed	(1) Separation responses at 12 and 24 months of age (2) longitudinal separation distress
	Dawson et al. (1992, 2001)	26	26 mothers (12 with elevated depressive symptoms) and their infants	Mixed	Strange situation
	Calkins and Fox (1992)	52	52 infants	Mixed	Strange situation; assessment of temperament and inhibition
	Calkins et al. (1996)	207	207 mothers and their infants	Mixed	Visual, auditory, olfactory stimuli; infant behavior questionnaire; toddler behavior questionnaire; free play
	Hane and Fox (2006)	185	185 infants (61 control, 67 high degrees of negative reactivity, 57 high degrees of positive reactivity	Mixed	Reactivity paradigm; laboratory temperament assessment battery; early social communication scale; maternal caregiving behavior during routine activities in the home
Children	Davis O'hara (2003)	67	67 children (5–7 years)	Mixed	CBQ[a]; separation anxiety test, three stimulus situations (post-maternal separation, happy/sad and separation/reunion)
Adolescents	White et al. (2012)	23	13 secure, 10 dismissing	Mixed	CAI[b]; cyberball social exclusion task; need threat scale
	White et al. (2013)	23	13 secure, 10 dismissing	Mixed	CAI[b]; cyberball social exclusion task; need threat scale
	Escobar et al. (2013)	40	20 secure, 15 dismissing, 5 preoccupied	Mixed	FFI[c]; modified dual valence task; sociodemographic questionnaire
Adults	Stanley (2006)	124	124 college students	Mixed	AAP[d]; video clips of separation and reunion
	Zilber et al. (2007)	44	44 undergraduate students	Mixed	ECR[e]; response to 60 images (pleasant, unpleasant, neutral)
	Rognoni et al. (2008)	39	9 avoidant, 14 free, 9 preoccupied, 7 fearful	Mixed	Film stimuli with emotional content; relationship questionnaire; ECR[e]; adult attachment scale
	Behrens et al. (2011)	3	Case study: 3 mothers and their infants	Mixed	AAI[f]; response to 100 images (positive, negative, neutral, personal)
	Fraedrich et al. (2010)	16	16 mothers	Female	AAP[d]; presentation of pictures which show infant faces expressing a positive, negative and neutral emotion
	Chavis and Kisley (2012)	42	14 avoidant, 12 anxious, 15 secure	Mixed	ECR[e]; response to 45 images (positive, negative, neutral)
	Weisman et al. (2012)	65	65 adults: new parents, new lovers and romantically unattached singles	Mixed	Response to images of a familiar/unfamiliar infant face and neutral stimuli
	Dan and Raz (2012)	50	50 undergraduate students	Mixed	ECR[e]; response to images of angry and neutral faces
	Verbeke et al., 2014	35	35 undergraduate students	Female	Attachment styles questionnaire; task-free resting-state under condition A[g] and condition B[h]

[a] CBQ, child behavior questionnaire; [b] CAI, child attachment interview; [c] FFI, friends and family interview; [d] AAP, adult attachment projective picture system; [e] ECR, experiences in close relationships; [f] AAI, adult attachment interview; [g] condition A, participants sit isolated in a dimly lit EEG lab; hcondition B, two participants sit together in a dimly lit EEG lab.

difference in physiological response during the AAI between the resolved and the unresolved group. Future work should focus on that research topic. At present it is still unclear, how much intensity is needed to cause dysregulation in adults and how they react on a physiological level. Therefore, future research should attempt to identify and connect the moment of breakdown with the recordings of physiological reactivity. Our suggestion would be to use the AAP as stimulus material, since that measure was successfully used in experimental settings (like fMRI) assessing neural correlates of resolved and unresolved attachment in different clinical groups compared to healthy participants (Buchheim et al., 2006a,b, 2008, 2012; Buchheim and George, 2011).

Although psychophysiological attachment research remains an active area, there certainly remain some outstanding questions and limitations concerning the methodology. The first consideration refers to the measurement and interpretation of physiological responses such as the autonomic and HPA axis activity. When measuring adrenocortical activity, researchers must carefully think about the time of the day for their sample collection as there are changes due to circadian rhythms. In addition, some research questions require a recording of physiological data during a baseline level to analyze phasic responses. This can be particularly challenging in experiments including infants and young children as they cannot be instructed to sit quietly for a baseline recording. Therefore, researchers usually record physiological responses when the participants are not responding to a strong stimulus which is not equivalent to a baseline measure in adults. In this respect also underlying physiological mechanisms like for example the degree of vagal control of the heart might have a significant influence on the magnitude of physiological response (Fox and Hane, 2008). The second consideration refers to methodological challenges and constraints involved in the recording of infant EEG. These include environmental challenges like setting up an infant-friendly and interference-free lab but also task-related challenges like designing age-appropriate stimuli and paradigms (Hoehl and Wahl, 2012). Although investigating the correlates of frontal EEG asymmetry among the attachment groups is still an active area of research, overarching developmental model of EEG asymmetry has not been developed yet (Saby and Marshall, 2012). Integrating the previously mentioned findings into such a conceptual model that also considers possible neurophysiological origins of the observed asymmetries and their association to affective processes would be an interesting avenue for future research.

Studying the neurophysiology of human attachment has broadened the understanding of the manner in which attachment represents a buffer or a moderator of initial physiological disposition. This also leads to the assumption that the early caregiving environment has an influence on the physiological processes that underlie individual differences in reactivity. The emerging body of psychobiological research on attachment provides us a promising insight into the interplay of biology and the environment and how they influence the human personality.

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A Reaction Time Experiment on Adult Attachment: The Development of a Measure for Neurophysiological Settings

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In the last few decades, there has been an increase of experimental research on automatic unconscious processes concerning the evaluation of the self and others. Previous research investigated implicit aspects of romantic attachment using self-report measures as explicit instruments for assessing attachment style. There is a lack of experimental procedures feasible for neurobiological settings. We developed a reaction time (RT) experiment using a narrative attachment measure with an implicit nature and were interested to capture automatic processes, when the individuals' attachment system is activated. We aimed to combine attachment methodology with knowledge from implicit measures by using a decision RT paradigm. This should serve as a means to capture implicit aspects of attachment. This experiment evaluated participants' response to prototypic attachment sentences in association with their own attachment classification, measured with the Adult Attachment Projective Picture System (AAP). First the AAP was administered as the standardized interview procedure to 30 healthy participants, which were classified into a secure or insecure group. In the following experimental session, both experimenter and participants were blind with respect to classifications. One hundred twenty eight prototypically secure or insecure sentences related to the eight pictures of the AAP were presented to the participants. Their response and RTs were recorded. Based on the response (accept, reject) a continuous security scale was defined. Both the AAP classification and security scale were related to the RTs. Differentiated study hypotheses were confirmed for insecure sentences, which were accepted faster by participants from the insecure attachment group (or with lower security scale), and rejected faster by participants from secure attachment group (or with higher security scale). The elaborating unconscious processes were more activated by insecure sentences with potential attachment conflicts. The introduced paradigm is able to contribute to an experimental approach in attachment research. The RT analysis with the narrative procedure might be of interest for a broader variety of questions in experimental and neurophysiological settings to capture unconscious processes in

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association with internal working models of attachment. An electrophysiological model based on preliminary research is proposed for assessing the preconscious neuronal network related to secure or insecure attachment representations.

Keywords: adult attachment projective picture system, reaction times, decision task

INTRODUCTION

Attachment theory is an evolutionary-based theory of a specific type of intimate human social relationship conceived to have a major developmental influence from "the cradle to the grave" (Bowlby, 1969, 1973). According to attachment theory, the foundation of the attachment relationship is a biologically based behavioral system that evolved in ways that influence and organize motivational, cognitive, emotional and memory processes. These processes are organized in early infancy with respect to significant caregiving figures that extend into adulthood. Bowlby (1980) conceived attachment as a key mechanism related to maintaining biological homeostasis, including the modulation of physiological stress and mental health. Researchers have found physiological correlates of attachment and the affective components of relationships in nonhuman species and humans. Mental representations of early attachment relationships shape emotional and cognitive information, which affects our attention and memory. In order to maintain organization within the attachment system, emotional reactivity is then regulated within the central nervous system (Bretherton, 1993; Main, 1995). Over the decades, psychobiological attachment research with infants and adults has increased dramatically (Coan, 2008; Gander and Buchheim, 2015). Attachment patterns have been linked to different ways to emotion regulation processes and some researchers even argued that the attachment system is in itself an emotion regulation device (Vrtička and Vuilleumier, 2012).

Most recent findings on attachment and neurobiology in functional magnetic neuroimaging (fMRI) showed that researchers investigated very different systems, often by very different means and a variety of paradigms, ranging from the presentation of individual photos of loved and unknown faces to more complex approaches (e.g., reflecting on attachment-relevant events, priming experiments, talking about attachment-relevant situations; see overview Buchheim and George, 2012). At present, the delineation of a neuronal network of attachment is not possible yet. However, there is evidence across fMRI studies that brain regions like the amygdala and orbito/prefrontal cortices are involved in processing attachment-related stimuli. In addition, convergent research results suggest that when caregiving is addressed, dopamine-associated regions of the reward system are active that differ from the neural correlates of the postulated "attachment circuitry" (Buchheim et al., 2010).

Several neurophysiological studies of adult attachment assessing the autonomic nervous system, the hypothalamic-pituitary-adrenocortical axis or frontal electroencephalography (EEG) asymmetry used self-report measures (Carpenter and Kirkpatrick, 1996; Kim, 2006; Laurent and Powers, 2007; Rochman et al., 2008; Zhang et al., 2008; Kiss et al., 2011; Dan and Raz, 2012), while other studies used narrative interview measures of attachment such as the Adult Attachment Interview (AAI) and the Adult Attachment Projective Picture System (AAP; Beijersbergen et al., 2008; Buchheim et al., 2009; Fraedrich et al., 2010; Holland and Roisman, 2010; Behrens et al., 2011; Leyh et al., 2016).

The self-report questionnaire instruments are conceived as personality constructs and assess the subjective evaluation of attachment styles with reported patterns monitored by conscious processing of feelings and experiences related to desires and worries regarding a romantic partner; these measures typically differentiate secure from insecure avoidant or anxious attachment styles (Ravitz et al., 2010). By contrast, developmental attachment measures such as the AAI (George et al., 1985–1996; unpublished manuscript) or AAP (George et al., 1999) are designed to activate the individuals attachment system by introducing attachment-related topics (e.g., separation, illness, abuse and death), and assess attachment representations (secure, insecure-dismissing, insecure-preoccupied and unresolved trauma) based on the analysis of discourse patterns of verbatim transcripts. Interview discourse analysis is less concerned with a specified response (as compared with attachment style measures) as how experiences and feelings are described.

In a very recent fMRI study, Yaseen et al. (2016) investigated the comparison of brain activity correlating with self-report (Relationship Scales Questionnaire, RSQ) vs. a narrative attachment measure (AAI) during conscious appraisal of an attachment figure. Interestingly the two measures elicited different brain responses. While the AAI appeared to disproportionately correlate with conscious appraisal associated activity in Default Mode Network (DMN) and *subcortical* structures, the RSQ seemed to tap Executive Frontal Network (EFN) structures more extensively. The authors suggested, that the AAI captured more interoceptive, "core-self"-related processes, while the RSQ assessed higher-order cognitions involved in attachment. The authors recommended in their conclusions, that the AAP might be an appropriate alternative in this kind of research, since this measure consists of a set of pictures feasible to present during an experimental setting.

Abbreviations: AAP, Adult Attachment Projective Picture System; AAP-RC, Adult Attachment Projective Relationship Choices Version 1; AAP-RC 2.0, Adult Attachment Projective Relationship Choices Version 2; ART, Attachment Reaction Times; Ds, dismissing attachment; E, preoccupied attachment; EEG, Electroencephalography; ERP, Event related potential; F, secure attachment; fMRI, Functional magnetic resonance imaging; RT, reaction times; U, unresolved trauma.

The feasibility of the AAP measure as an attachment-activating stimulus in a neurobiological context (fMRI, neuroendocrinology) has been established in diverse experimental settings in clinical and nonclinical groups (e.g., Buchheim et al., 2006, 2008, 2009, 2012). Participants in these different settings were instructed to tell stories to the AAP picture stimuli in the fMRI environment (Buchheim et al., 2006, 2008) or were presented individualized sentences constructed from their own AAP responses in the fMRI setting (Buchheim et al., 2012).

In the context of a double-blind study with a neuroendocrine research question, we modified the AAP task for a double blind controlled study comparing the effects of oxytocin to a placebo condition. The AAP picture presentations were accompanied by prototypical phrases constructed to represent one of the four established attachment categories (i.e., a generalized attachment-sentence schema for each attachment group). The participants were instructed to rank these phrases from the most to the least appropriate for each presentation. The most interesting finding from this study was that insecurely attached individuals at baseline decided that secure attachment sentences were most appropriate for them under the oxytocin condition (Buchheim et al., 2009). This attachment experiment was a first attempt to assess a combination of conscious and unconscious processes in a self-report perception task. In this present study, we sought to improve on this approach by using this methodology in a reaction time (RT) paradigm. The research question was to examine if the RTs differed with respect to an individual's attachment representation in order to provide a paradigm to use in a neurobiological setting, like an EEG experiment.

One interesting development in the past few years has been experimental research using the Implicit Association Task (IAT), the goal of which was to explore the domain of automatic cognitive processes concerning the evaluation of the self and others (Lane et al., 2007). The IAT task is based on the measurement of RTs and answers in combination with a target category, for example gender stereotyping and the self. Implicit measures have been successful in predicting verbal behavior, group membership, sexual behavior, and evaluative judgments (Gawronski, 2002) or personality (Grumm and von Collani, 2007).

RT research has a long experimental tradition in psychology, beginning with the experiments by Helmholtz (1850). Helmholtz was interested in the time relations structured by the nervous systems of living beings not just from a physiological but also from a psychological point of view. In fact, at the time at which he performed his time experiments in frogs, Helmholtz carried out similar studies in human beings (Schmidgen, 2002).

RT experiments are relatively inexpensive to execute and results are easy to obtain, even though the conclusive interpretations are still under discussion. According to Harris et al. (2014) RT experiments have become a standard paradigm for measuring behavioral reactions without taking into account underlying mental processes. Harris et al. (2014) suggested a sophisticated way to improve the analysis and interpretations of RT paradigms.

The idea behind the measurement of RT is that it can be used as a measure in social cognition research, as an index of the complexity of the underlying mental processes. Results showed for example, that more complex processes are associated with longer elaboration/RTs (Rösler, 1993). Moreover, RT experiments have a predictive value for social decisions and have been used successfully in IAT clinical and social experiments (Lane et al., 2007). It was possible to differentiate groups with and without disorders using the IAT in reliable experiments about self-judgments (Gemar et al., 2001). RT measures were also used to understand semantic priming. Reactions were more quickly facilitated when categories were closely related and shared the same reaction as compared to categories that did not share the same reaction. Attribution measures can be interpreted as a measure of relative identity with the objects (Lane et al., 2007). The association of the self as a target category and an attitude dimension provides a measure of implicit self-esteem; it describes the strength between associations of the self and another category. Studies show that emotional relevant primes have an effect on memory performance. One study showed that memory performance was impaired in borderline patients when negatively valued interference was presented (Mensebach et al., 2009). A recent study on autobiographical memories reported that past intentions could be reliably identified with high accuracy using a RT measure (Zangrossi et al., 2015).

A central concept of attachment theory is that individuals develop internal working models, that include expectations about the self, and significant others outside of conscious awareness (Bowlby, 1969, 1973, 1980; Bretherton, 1985). Furthermore, internal working model content is believed to include knowledge about concrete details of interpersonal experiences as well as the associated affect (Bretherton, 1985). In general, psychoanalytic theory suggests to divide the mind into three different levels: the conscious mind includes everything we are aware of and represents our mental processing that we think of and talk about rationally. A part of this includes memory structures, which are considered not always to be part of consciousness, but can be retrieved and brought into awareness, called preconscious. The unconscious mind constitutes a reservoir of feelings, thoughts, urges and memories that exist outside of conscious awareness. From a psychoanalytic point of view, most of these contents are unacceptable or unpleasant and represent feelings of pain, anxiety or individual conflicts. Unconscious processes are considered to influence our behavior and experience, even though we are unaware of these underlying influences (Freud, 1915/2001). As mentioned above internal working models are also thought to work primarily outside of conscious awareness (unconsciously) and guide attention, interpretation, and memory of attachment experiences and emotions. This allows individuals to generate expectations about the future concerning interpersonal interactions and to develop plans relating to them (Bowlby, 1969, 1973, 1980; Bretherton, 1985, 1990). Bowlby (1980) examined possible memory constructs and unconscious processes to explain misrepresentations of mental functioning and behavior, informed by mid-20th century advances in cognitive psychology (Bowlby, 1980). He suggested conscious representations of what parents made the child believe are stored in the semantic memory, while the defensively excluded and traumatic attachment experiences are stored in the episodic memory. Emotional schemata are part of episodic memories and, over time, these schemata can grow into explicit models of the self and the attachment figure (Liotti, 1999). According to information processing theory, the term "unconscious" describes the product of the perceptual systems that work unattended or unrehearsed. Thus from this perspective, nonconscious mental life is identified with early preattentive perceptual processes such as e.g., pattern or face recognition. One of the most common forms of preconscious processing is priming. When investigating the label "automatic", some processes are intended, others require recent conscious and intentional processing of related information (Bargh et al., 2012). In the following, we use the term "unconscious" in association with the internal working models of attachment and "preconscious" when relating to information processing theory or neurobiological models.

There are several recent studies investigating implicit aspects of romantic attachment using self-report measures as explicit instruments for assessing attachment style (Marks and Vicary, 2015; De Carli et al., 2016). In the present study, we were interested to capture automatic processes in the moment the attachment system is activated by using a narrative attachment measure with an implicit nature. The AAP is designed to activate the individual's attachment system and emphasizes the evaluation of unconscious defensive processes in the narratives. In this study, we intended to combine attachment methodology with knowledge from implicit measures by using a RT paradigm.

The general question for this study addressed how a person accepts or rejects prototypic sentences belonging to the two major attachment categories (secure and insecure) using a modified version of the AAP (Buchheim et al., 2009) in a RT paradigm. All participants were administered the standard AAP interview before the experiments started in order to assess their individual attachment representation. The participants did not get any information about their attachment representation during the whole assessments. The experimental design is described in the "Materials and Methods" Section in detail. In short, participants were presented pictures from the AAP accompanied with sentences representing different attachment patterns while assessing how long it took for them to make a decision (i.e., accept or not accept).

(1) We expected that participants would accept the prototypic sentences from the experiment more frequently when these sentences match with their own adult attachment classification.
(2) We expected group differences in reaction speed between participants with secure or insecure adult attachment classification assessed in the previous AAP interview. These expectations were differentiated for four possible configurations of the stimulus (secure, insecure) and the reaction (acceptance, rejection). Comparing both groups, we expected that

    (2a) secure sentences will be accepted faster by securely attached participants,
    (2b) secure sentences will be rejected faster by insecurely attached participants,
    (2c) insecure sentences will be accepted faster by insecurely attached participants,
    (2d) insecure sentences will be rejected faster by securely attached participants.

(3) The preference of secure or insecure prototypes in the experimental procedure was expressed by the continuous Adult Attachment Projective Relationship Choices Version 2 (AAP-RC) security scale (see below). We expected following correlations of the security scale with the reaction speed: the higher the security scale, . . .

    (3a) . . . the faster the acceptance of secure sentences,
    (3b) . . . the slower the rejection of secure sentences,
    (3c) . . . the slower the acceptance of insecure sentences,
    (3d) . . . the faster the rejection of insecure sentences.

MATERIALS AND METHODS

Adult Attachment Projective Picture System (AAP)

The AAP (George and West, 2012) assesses the attachment status in adults using a standardized set of eight picture stimuli. The stimuli are line drawings that include a warm-up scene and seven attachment scenes of individuals in conceptually-defined attachment situations. Four so called "alone pictures" depict scenes of a single person with no other persons visible in the picture. Three so called "dyadic pictures" depict scenes of two or more persons in a potential attachment dyad. The scenes portray characters in different age groups across the life span (e.g., child to old age). The drawings contain only as much details necessary to connote the situation. Features indicating details such as emotion, ethnicity and gender are obscure. Stimulus presentation is standardized so as to introduce increasingly distressing attachment scenes. Participants are asked to tell a story to each picture using a standardized set of instructions: "What is going on in the picture, what led up to this scene, what are the characters thinking or feeling, and what might happen next." AAP administration is done in person on an individual basis in a quiet location with no distraction and typically takes 30 min. The stories are audio-recorded and analyses are done from verbatim transcripts.

Each stimulus response is coded for attachment related content and defensive processes. Content coding evaluates representation of the presence and degree of integration (as defined by attachment research) of attachment relationships in the response, the actual coding dimensions of which are evaluated on different dimensions for the alone and dyadic pictures. Alone response content is evaluated on two dimensions. The agency of self is defined as the degree to which the character can seek and effectively use attachment figures. The connectedness is defined as the degree to which the character is portrayed as seeking proximity to others. Dyadic response content is evaluated for synchrony, a single dimension that captures the quality of agency of self and connectedness used for the alone pictures. Synchrony is defined as the degree to which responses depict attachment figure sensitivity in the context of distress themes (e.g., a child is sick) or mutual enjoyment in the context of togetherness themes (e.g., couple goes on a trip). Defensive processes are coded for the three standard attachment-defined defenses (Solomon et al., 1995): deactivation (distanced attention from attachment), cognitive disconnection (close attention to and confusion by attachment) and segregated systems (attachment fear and dysregulation).

The AAP designates four attachment classifications based on the evaluation of response content and defensive processes coding patterns across the entire set of seven attachment stories. Individuals are judged secure (F) when the coding patterns demonstrate that attachment figures are present and self and attachment figures manifest integrated interaction (sensitivity, relationship repair, thoughtful action and mutual enjoyment). Defensive processes, which can be depicted in any of the three defense, help integrate and maintain relationships, and manage attachment fears. Individuals with insecure-dismissing (Ds) or insecure-preoccupied (E) attachment are characterized by relative absence of integration, sensitivity and mutual enjoyment in their responses. Descriptions of the alone characters range from themes that portray taking simple action (reactive problem solving behavior without thoughtful consideration) to evidence, that characters cannot move forward. Attachment figures, if included, are described in ways ranging from functional roles without comfort (e.g., just give the sick boy soup), unable to respond (e.g., the mother refuses to hug the child), punishing and sometimes harsh (e.g., an enraged parent who is drunk and abusive). Connections with others, if described, are typically shift to interactions with non-attachment figures (e.g., police, nurse, soccer coach). The dismissing group is characterized by defensive processes, that deactivate attachment needs and shift attention away from attachment distress and themes (e.g., by rejection, power, achievement). The preoccupied group is characterized by defensive processes, that disconnect attachment needs and relationships (i.e., deconstruct the details) shifting attention to elements of frustration and anger, or distorting or blurring story characters and events (e.g., the child is waking up or going to bed; someone died—cannot specify who). Individuals are judged as insecure-unresolved with regard to trauma (U) when they remain dysregulated and overwhelmed by dangerous or threatening story elements (e.g., being frightened, assault, isolation, helplessness). One or more of their stories are void of the content and defensive processing features associated with integration, functional care, or attachment figure or other people providing care. For more complete details of the coding system and classification, see the monograph (George and West, 2012).

Multiple studies have demonstrated excellent convergent validity of the AAP with the AAI (George et al., 1985–1996), test-retest reliability, inter-judge reliability, and discriminant validity in community samples and clinical patients. Results from a large-scale psychometric investigation, including 144 adult participants demonstrated excellent inter-judge reliability; the concordance rate for two judges on the four-group classifications were 90%, κ = 0.85, test-retest reliability (after 3 months 84% remained in the same attachment category; κ = 0.78) and discriminant validity. To evaluate the convergent validity, AAP classifications were compared to independent AAI classifications. The concordance rates for the four-group classifications were 90%, κ = 0.84, and for the two groups ("secure" vs. "insecure") even 97%, κ = 0.89 (George and West, 2001, 2012; Buchheim and George, 2011).

Development of the AAP Reaction Time Paradigm

Buchheim et al. (2009) developed and used the first experimental adaption of the AAP in a double-blind, placebo-controlled within-subject experimental design. These researchers developed the AAP-RC stimulus set, which is comprised of a set of statements that represent attachment-related sentences that describe the AAP picture stimuli. The statements were schematic descriptions of secure, dismissing, preoccupied, and unresolved attachment stories, as determined by two expert AAP judges (AB, CG) who collectively had experience with over 300 AAP transcripts. Attachment statements described common story response situations. The study compared participant responses to the statement in an oxytocin and a placebo condition. The eight AAP picture stimuli were presented over four sequences, always presented in each sequence in the standardized order. Each of the 32 picture presentations was accompanied by four prototype phrases each of them representing one of the four established attachment categories. The participants were instructed to rank these phrases from the most to the least appropriate for each presentation. The phrases were presented in a randomized balanced sequence in order to minimize simple memory effects across test sessions.

The present study used a modified version of the Buchheim et al. (2009) prototype sentences. Sentences were revised to improve the content and to control for the sentence length. In each group of length-adjusted sentences, all four sentences consisted of the same number of German words in order to minimize the effect of the sentence length on RTs. The modified system of 128 sentences is called Adult Attachment Projective Relationship Choices Version 2 (AAP-RC 2.0). The AAP-RC evaluation procedure uses all eight AAP drawings, including the first dyadic "warm-up" picture with two playing children. Hence, 64 sentences relate to the alone pictures and 64 sentences to the dyadic ones. The revised sentences were rated for content by three certified AAP judges. **Table 1** shows example sets of four sentences that represent four attachment categories for two selected AAP picture stimuli. **Figure 1** demonstrates an example how

TABLE 1 | Examples of prototypical sentences from the Adult Attachment Projective Relationship Choices Version 2 (AAP-RC 2.0) instrument.

Prototypical sentences from the AAP-RC	Attachment classification
AAP picture "Bed"	
A child is put to bed by his mother and she sings a nice comforting lullaby for him.	**F**—secure
A child is put to bed by his mother and she gives him a toy and walks out.	**Ds**—dismissing
A child is put to bed by his mother and she is angry because he was too naughty.	**E**—preoccupied
A child is put to bed by his mother and she is helpless due to the child's nightmare.	**U**—unresolved trauma
AAP picture "Departure"	
A couple bids farewell and is looking forward to being together soon again.	**F**—secure
A couple bids farewell and he is ruminating about his upcoming business meeting.	**Ds**—dismissing
A couple bids farewell and she is very angry about his surprising departure.	**E**—preoccupied
A couple bids farewell and she threatens to hurt herself if he leaves her.	**U**—unresolved trauma

a stimulus sentence was presented on the PC screen to the participant. The experimental procedure consisted of 128 such screen sequences.

The RT paradigm used in this study followed Bem's (1981) procedure for RT analysis for gender role schemas. The procedure was to record answers and to assess the time the participants needed to react. The Bem's (1981) study showed that schema consistent judgments were more quick when the stimuli presented during a selection task matched participants' gender role schema. We chose this approach because gender role schemas, like attachment representations, are conceived as stable views of self that develop in early childhood that automatically monitor, modulate attentional shifts and appraise new experiences (Bretherton, 1990). Classical experimental designs of self-concept tests using randomized stimulus sequences like the IAT (Gawronski, 2002) could not be used because attachment assessments such as the AAP must adhere to the procedural order in which stimuli are presented (George and West, 2012).

In the current study in the context of a diploma thesis (Wichmann, 2011, unpublished diploma thesis), we first administered the AAP and next presented the AAP-RC 2.0. We conducted an Attachment Reaction Time analysis (ART) for the experimental condition. The AAP was administered by a trained interviewer (TW). AAP verbatim protocols were coded by a certified AAP judge (AB). The structure of the administration procedure was as follows: the entire series of AAP picture stimuli were presented 16 times and each series was composed of eight pictures in the standardized AAP administration order. Each picture presentation was accompanied by one stimulus sentence, which was related to one of the four attachment representations. The experimental procedure contained a measure for the individual responses (yes/no) to the prototypical sentences and the recorded RTs.

The interview and the experimental task took place in the same office. The experimental condition was conducted using a computer. The computer was a table mounted Dell computer with no internet-connection and no additionally installed software. The program used for the presentation and RT measurement was *E-Prime* (Schneider et al., 2002). Participants were alone in the room. Room lighting was artificial and participants sat 0.5 m from the monitor. Answer responses were given via the computer keyboard. At the beginning of the experiment the participants were told to put the index fingers of their hands on the keys: Y for "yes" and the key N for "no". The keys were marked with a red label. The participants had to press a key to move on with the task. A short practice task was given before to ensure that the participants had understood the task. The practice task included three attachment neutral stimuli with drawings produced in a style similar to the AAP pictures. All instructions were given on the computer screen and, if necessary, explained a second time after the test run.

Participants were told that the task was a speed task so as to avoid participant reflection and distraction. It was emphasized that there were no right or wrong answers, and that responses were simply their preferences. The timing of the presented sentence order (**Figure 1**) was as follows: 1st a fixation cross (1 s); 2nd the sentence (2 s); 3rd a countdown (1.5 s) and 4th the picture along with the decision task. AAP RC sentences were shown one at a time, next showing an AAP picture, with a "3-2-1" countdown shown between the sentence and the picture. The labels "Yes" and "No" were presented on the side of the monitor, analogs to the keys, during the decision tasks. The picture was displayed on the screen until a decision was made. The experiment continued only after a decision was made. We presented the participants first the sentence and then the picture so as to eliminate bias produced by different reading speed. The four attachment categories were presented each with four prototype sentences per picture. The order of attachment representations within the sentence was randomized. In sum there were 128 choices to be made. The choices were forced choice subjective selections, representing their acceptance (yes) or rejection (no) of an AAP RC sentence (see **Table 2**). Task scores are based on counts of agreements and rejections by four attachment representations.

Participants

Participants were asked for voluntary participation. The sample was comprised of 30 students from the University of Innsbruck (17 women, 13 men; sample mean age: 26.8, SD = 3.4). The participants reported no neurological conditions and were not in psychological or psychiatric treatment. All had normal or corrected eye vision. The study was conducted according to the Helsinki Declaration with informed consent

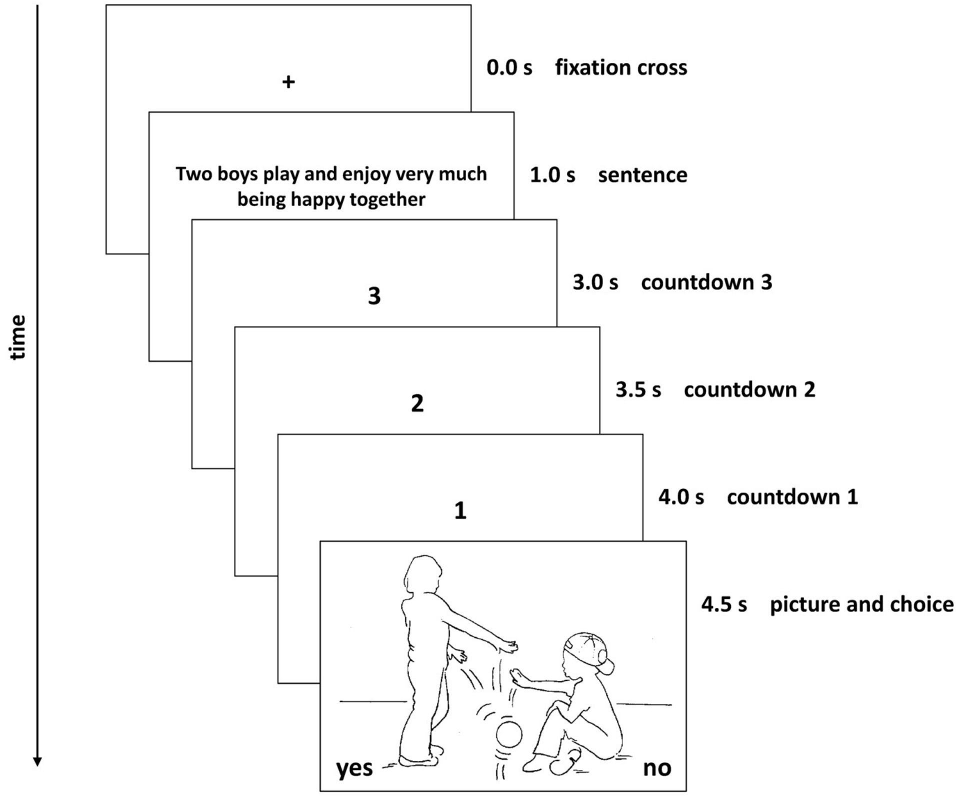

FIGURE 1 | One of the 128 screen sequences presented in the course of the experimental procedure.

received from all participants. All participants completed the study.

RESULTS

The reported results concern three methodical approaches: the AAP attachment classification assessment; the computerized experimental method AAP-RC; and the ART experiment. The results first describe the findings associated with each of the measures used in the study and second report the relations among them. There were no missing data.

Adult Attachment Projective Picture System (AAP): Distribution of Attachment Classifications

The attachment classification distribution was as follows: 10 (33%) F, 12 (40%) Ds, 6 (20%) E, and 2 (7%) U. Because of the small frequencies in especially the preoccupied and unresolved groups, insecure classifications were collapsed together and data analyses compared only secure (*n* = 10, 33%) vs. insecure attachment (*n* = 20, 67%).

TABLE 2 | Schema of evaluation of the AAP-RC 2.0 by a test person.

Test person	F secure	Ds dismissing	E preoccupied	U unresolved trauma	Total
Yes	a	b	c	d	r
No	32 – a	32 – b	32 – c	32 – d	128 – r
Total	32	32	32	32	128

Relationship Choices, Version 2.0 (AAP-RC): Psychometrical Analysis and Security Index

Reactions to AAP-RC stimuli in the ART test were coded dichotomously as yes (endorsement, acceptance) or no (rejection). The frequencies *a, b, c, d* shown in **Table 2** represent numbers of accepted sequences belonging to the four attachment prototypes. The sets of 32 dichotomous items related to the attachment prototypes F, Ds, E, U, as well as the joint set of 96 insecure type items can be understood as a scale in the psychometric sense. These values of Cronbach α were satisfactory for the secure scale (0.77), for the U scale (0.82) for the joint insecure scale (0.88). However, they were *not* satisfactory for the Ds scale (0.64) and for the E scale (0.66). The correlation structure was investigated by means of the item-scale correlations and corrected item-scale correlations. The correlation structure was satisfactory for the system of two scales, secure and insecure. However, it was *not* satisfactory for the more detailed system of four scales F, Ds, E, U.

Guided by the referred psychometric results, we have decided to base the analyses of AAP-RC on the secure-insecure dichotomy. In respect of this aspect we have defined a *security index* expressing the degree of security vs. insecurity by the formula (see **Table 2**): $a/r = a/(a + b + c + d)$. The index is a proportion of accepted secure sentences related to all accepted sentences, ranging from 0.00 (completely insecure) to 1.00 (completely secure). By the random answering independent of sentence prototype, it would oscillate around 0.25. The analogously constructed complementary insecurity index $(b + c + d)/(a + b + c + d)$ is mathematically redundant; summing up to one, both indices contain the same information. Hence, the following analyses utilize the *security index* as a central measure.

Adult Attachment Reaction Time (ART): Reaction Time Analysis

The program *E-Prime* stored the dichotomous reaction and the needed RT in milliseconds. The hierarchically structured data sample consisted of 30 persons × 128 sentences = 3840 pairs of reactions and RTs.

Figure 2A: the average RT was about 1 s, ranging from 0 up to 15 s; exact values of measures and statistics see in **Table 3**. As commonly experienced by the duration time data, the distribution was skewed and its normality was rejected by the Kolmogorov-Smirnov test.

Figure 2B: this was the case after applying the frequently recommended logarithmic transformation. Additional problems were caused by some extreme outlier values. Similarly, other transformations considered by Harris et al. (2014) did not lead to satisfactory results in this case.

Figure 2C: transformation based on quantiles in the total pooled sample of 3840 measurements resulted in a close approximation to the normal distribution; the variable was transformed by the linear function $s_{(z)} = 50–10z$. The resulting variable is interpreted as the *speed* of the reaction. However, there were striking differences in the RTs between the 30 study participants, on an average ranging from 0.32 s up to 2.41 s. The reaction speed differed significantly by ANOVA ($F_{(29,3810)} = 74.17$, $p < 0.001$; $\eta^2 = 0.36$); a considerable portion of measurement variance was explained by the individual basic reaction speed.

Figure 2D: in regard to excluding the bias by individual basic reaction speed, we have normalized speed values intra-individually. The RTs for a test person were replaced by ranks 1 for the slowest reaction to 128 for the quickest one, and transformed to the s (speed) values according to the quantiles of the normal distribution $N(50,10)$[1]. Because of the subsample sizes $n = 128$, the density curve of the obtained empirical distribution is less smooth than the previous one. Nevertheless, it is very close to the normal distribution $N(50,10)$, and its normality in the sample of 3840 observations was *not* rejected by the exact Kolmogorov-Smirnov test.

The tests of study hypotheses (correlations, *t*-tests) were based on the last described intra-individually normalized speed values. The $N = 3840$ single values were aggregated to the intra-individual means for each of $N = 30$ study participants. Particularly, the following four aggregated values were relevant: speed of "yes" reactions to secure sentences; speed of "no" reactions to secure sentences; speed of "yes" reactions to insecure sentences; and, speed of "no" reactions to insecure sentences.

Convergent Validity Between the AAP Interview and the AAP-RC Security Index

The convergent validity of the AAP-RC security index was examined by its comparison with the secure and insecure attachment classifications (**Figure 3**). Mean of the AAP-RC security index in the secure group ($n = 10$, $M = 0.432$, SD = 0.105) was greater than the mean in the insecure group ($n = 20$, $M = 0.293$, SD = 0.087); this difference was significant according to the two-sided two-group *t*-test: $t_{(28)} = 3.866$, $p = 0.001$, Cohen's $d = 1.50$ indicated a strong effect.

The predictability of attachment classifications on the basis of the security index in the attachment RT experiment was estimated by the discriminant analysis. The cross-validated classification was used, which is by small sample sizes particularly important (see "discriminant—cross-validation" in the IBM SPSS software system). The procedure recommended predicting AAP classification as secure when the security index exceeded the threshold 0.362 shown by horizontal line in **Figure 3**. Appling this threshold, 8 of 10 secure participants and 16 of 20 insecure participants were recognized correctly; the prediction was successful in 80% of cases in both groups.

Reaction Time to Accept or Reject Secure or Insecure Prototype Sentences

For each participant, the set of 128 measurements was divided by sentence prototype stimulus (secure, insecure) and his/her answer reaction (yes, no) into 2 × 2 = 4 subsets, as described above (see "Adult Attachment Reaction Time (ART): Reaction Time Analysis" Section). Within each subset, the intra-individual mean values of speed were computed, resulting in the speed values of the following four stimulus-reaction combinations: (1) accept secure sentences; (2) reject secure sentences; (3) accept insecure sentences; and (4) reject insecure sentences. These computations were based (a) on all 128 sentences and alternatively; (b) on 64 sentences relating to the alone pictures; and (c) on 64 sentences relating to the dyadic pictures.

These speed variables were compared by ANOVAs for 2 × 2 repeated measures in the whole sample of $N = 30$ participants. Results of analyses based on all, alone and dyadic stimuli are shown in **Table 4**: (a) The analysis based on the complete material has shown that the *interaction of sentence prototype and answer* was significant ($p = 0.011$), whereas both main effects were not. As can be seen, participants

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[1] Technical note on ties: the ties were resolved by the replacing values by the average quantile value. For instance, by the subject p09, the first three quickest reactions needed the same time 0.185 s. Without ties, the ranks 1, 2 and 3 would correspond to the speed scores 76.6, 72.7 and 70.6. Because of ties, the mean value of three of these scores 73.3 was considered, rather than 72.2 corresponding to the mean rank 2.0. Resolving ties in this way, the intra-individual mean value was exactly 50.000 for each participant, the intra-individual standard deviations were very close to the value 10.000 (9.981–9.989), depending on the number of ties.

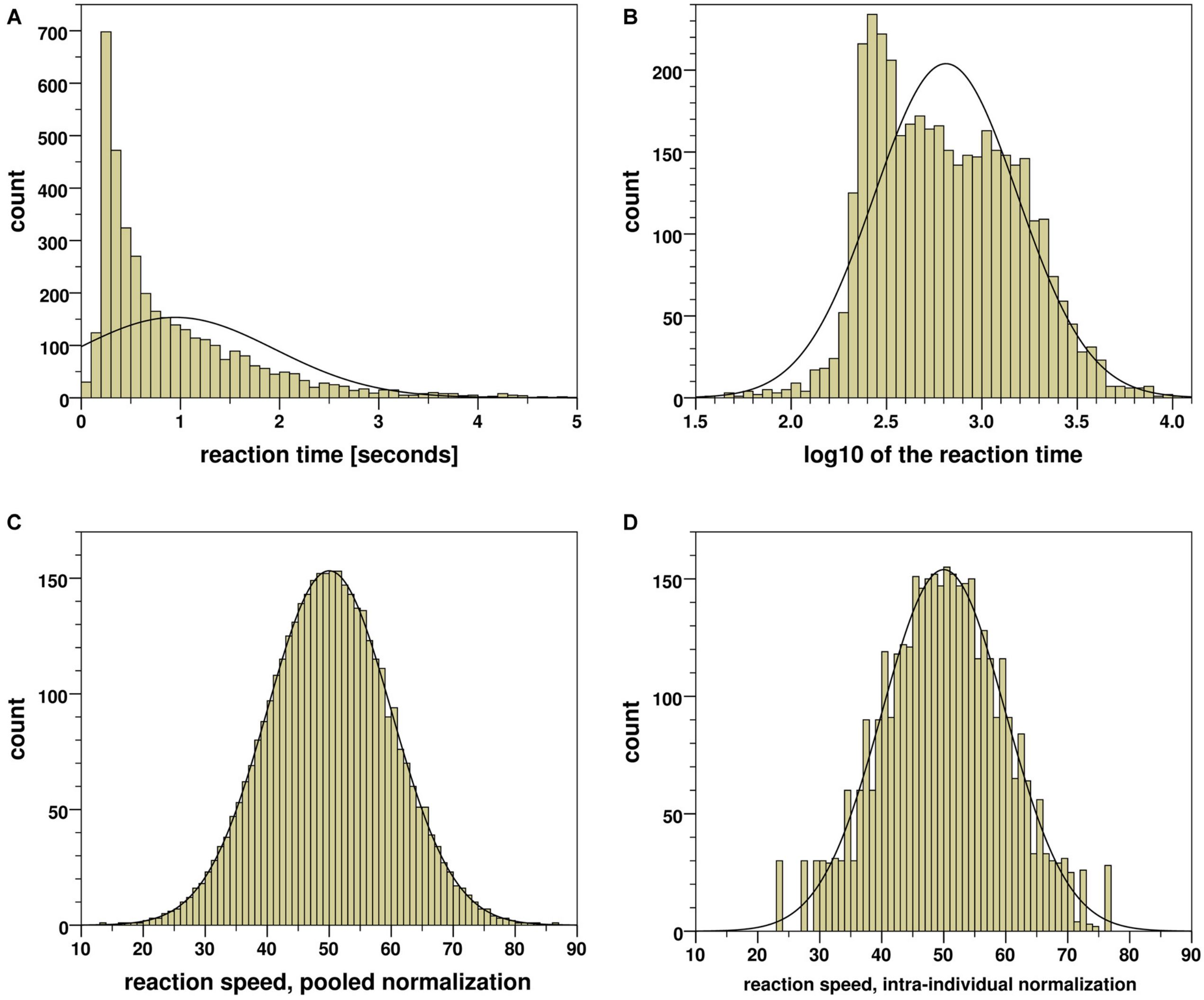

FIGURE 2 | Distribution of reaction time (RT), *N* = 3840 measurements. (A) Original observation (range 0–15 s), **(B)** logarithmic transformation, **(C)** pooled normalization, **(D)** intra-individual normalization.

answered more quickly to "yes to secure" and "no to insecure" and more slowly to "no to secure" and "yes to insecure". It means that the "secure-conform" answers were given more quickly than "insecure-conform" ones. (b) For the alone pictures, none of the three ANOVA effects was significant. (c) For the dyadic pictures, the *interaction* effect ($p = 0.005$) and the main effect *sentence prototype* ($p = 0.020$) were significant. The highest speed was observed for the combination "yes to secure"; the lowest

TABLE 3 | Kolmogorov-Smirnov test of normality of the reaction time (RT) distribution.

	Reaction time [ms]	log$_{10}$(time[s])	Speed pooled normalization	Speed, intra-individual normalization
See Figure:	**2A**	**2B**	**2C**	**2D**
N	3840	3840	3840	3840
M	949	2.811	50.0000	50.0000
SD	999	0.376	9.9996	9.9507
KS statistic[1]	0.195	0.060	0.002	0.005
p	$p < 0.001$	$p < 0.001$	1.000	1.000

[1] *The largest absolute difference between empirical and theoretical distribution, exact two-tailed test.*

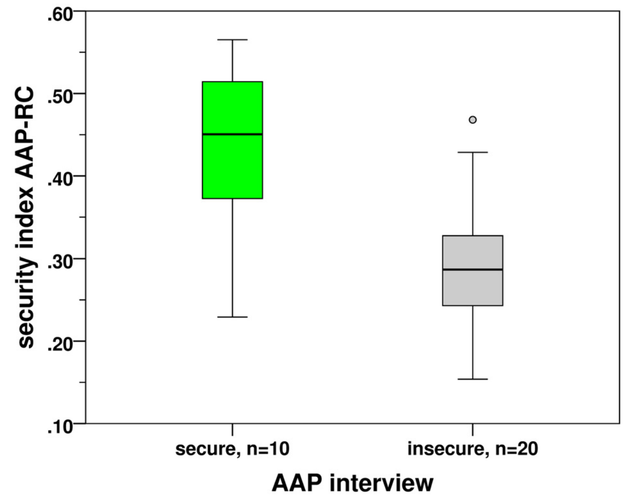

FIGURE 3 | Adult attachment projective relationship choices version 1 (AAP-RC) security index in attachment groups by AAP.

speed and hence the highest time needed to answer was observed for the combination "yes to insecure".

Reaction Times in Secure and Insecure Attachment Groups According to AAP

The four speed variables (1–4) described in "Reaction Time to Accept or Reject Secure or Insecure Prototype Sentences" Section were compared between secure and insecure AAP attachment classification groups. As shown in **Table 5**, the significant group differences were found for "RC-insecure" prototype sentences:

1. The insecure participants *accepted* the RC-insecure sentences more quickly than the secure participants.
2. The secure participants *rejected* the RC-insecure sentences more quickly than insecure participants.

The first result was also confirmed for both subsets of alone and dyadic sentences. The second result was confirmed for sentences connected to the dyadic pictures. In sum, the differences between the secure and the insecure attachment group according to the AAP were significantly manifest for the RC-insecure sentences.

Reaction Times in Correlation to the Security Index AAP-RC in ART

The AAP-RC security index (see "Relationship Choices, version 2.0 (AAP-RC): Psychometrical Analysis and Security Index" Section) ranges from completely insecure (0.0) to completely secure (1.0) reactions to the 128 stimuli. The correlations of the AAP-RC security index with variables concerning the reaction speed by four stimulus-reaction pairings are shown in **Figures 4A–D**.

(A) The RT speed of acceptance of secure sentences (**Figure 4A**) was *not* significantly correlated with the security index; according to ART both rather securely or insecurely attached persons reacted comparable quick in this case.

(B) The rejection speed of secure sentences (**Figure 4B**) was negatively correlated with the security index; the rather insecurely attached persons rejected the secure sentences more quickly.

(C) The acceptance speed of insecure sentences (**Figure 4C**) was negatively correlated with the security index; the rather insecurely attached persons accepted the insecure sentences more quickly.

(D) The rejection speed of insecure sentences (**Figure 4D**) was positively correlated with the security index; the rather securely attached persons rejected the insecure sentences more quickly.

Summarizing, the results of the experiment—especially for insecure prototype sentences—indicate a consistency between the attachment preferences and the higher speed of the corresponding reaction. The complete results of the experiment are summarized visually in **Figures 4A–D**, which underlines the consistency of the different results.

DISCUSSION

Discussion of the Methodology and Results

Bowlby (1980) proposed that inner working models of attachment function automatically and outside of conscious awareness. RT analyses are a way to observe the implicit automatic reactions. Pietromonaco and Barrett (2000) recommend the use of implicit measures like RTs to capture the unconscious parts of attachment, which are obscured when relying on self-report measures. Therefore we chose a narrative attachment measure, the AAP, designed to elicit unconscious elements by focusing on defensive processes, in combination with a RT measure. Our results reflect that implicit methodology can bring new and interesting insights in attachment related processes in the domain of neuroscience of human attachment.

Participants in our study were tested in an attachment RT experiment using the AAP picture stimuli accompanied by prototypic sentences representing different attachment representations (AAP-RC). Participants were not informed about their attachment classification prior to beginning the experimental session; therefore their reaction to the sentences was considered to be automatic and outside of conscious appraisal (i.e., unconscious). We hypothesized that the participants would accept the prototype sentences in the attachment RT paradigm: (1) more frequently; (2) more quickly when sentences matched with their own representations of attachment classification; and (3) that this would correspond with their attachment prototype preferences in the RT experiment (ART). Overall most of our expected results were confirmed for secure vs. insecure attachment groups.

The distribution of attachment classifications in our sample showed an overrepresentation of dismissing participants as compared to the distributions in samples with healthy controls (Bakermans-Kranenburg and van Ijzendoorn, 2009). Therefore, one caveat of our study is that we did not have a representative distribution of attachment classifications. Another caveat is the small sample size. The consequence was that data analyses

TABLE 4 | Speed of yes/no answers to secure/insecure prototype sentences.

	PROTOTYPE × ANSWER				**ANOVA**		
	Secure yes ***M*** ***(SD)***	**Secure no** ***M*** ***(SD)***	**Insecure yes** ***M*** ***(SD)***	**Insecure no** ***M*** ***(SD)***	**Effect prototype** $F_{(1,29)}$ p	**Effect answer** $F_{(1,29)}$ p	**Effect interaction** $F_{(1,29)}$ p
All stimuli	51.25	48.89	48.85	50.05	2.290	1.026	**7.320**
	(2.90)	(2.90)	(2.16)	(1.30)	0.141	0.319	**0.011**
Alone stimuli	49.53	48.89	49.71	50.29	1.661	0.002	0.641
	(4.17)	(4.90)	(3.55)	(1.81)	0.208	0.968	0.430
Dyadic stimuli^x	52.14	49.40	47.50	49.81	**6.089**	0.278	**9.258**
	(3.83)	(5.71)	(2.91)	(1.84)	**0.020**	0.603	**0.005**

Repeated measures in the sample of N = 30 participants. Bold: significant effects. ^{x}sample n = 28, df = 1, 27.

for separate attachment groups was not possible and we were confined to comparisons of participants with secure and insecure attachment representations. This remains a challenge for our next studies.

Item-scale analyses confirmed the internal consistency for the secure and insecure scales. Discriminant analysis showed that AAP-AAP RC 2.0 convergence prediction was successful in 80% of the cases in both groups; 8 of 10 secure and 16 of 20 insecure participants. Although a 100% correspondence was not reached, there was a sufficient agreement in this study to demonstrate the validity of the paradigm. This association was stronger, for example, than the results of studies that correlated narrative and self-report attachment measures (e.g., Roisman, 2007).

Given that participants did not know their own attachment classifications by the standard AAP procedure, we can assume that they were not guided by informed conscious appraisals of attachment while evaluating the prototype sentences, rather by unconscious processes. The fact that the different measures showed a considerable convergence supports the conclusion that we were able to capture both conscious and unconscious automatic reactions to attachment related stimuli. The average RTs differed significantly between the study participants. The considerable portion of variance of the originally measured RTs is explained by the individual basic speed of reactions to the presented stimuli. This empirically found fact can be caused by different plausible reasons, like overall speed or slowness of mental processes of the subject, extended rational reasoning on the presented sentences, or intensive imagination triggered by them.

With regard to the RT results, we found that all participants had a tendency to answer "yes" to secure and "no" to insecure sentences quickly and more slowly when the cases were inverted (i.e., "no" to secure and "yes" to insecure). ANOVA did not show significant results for both main factors sentence prototype stimulus and answer reaction; the *interaction effect prototype and answer* was significant however. The participants accepted secure prototype sentences and rejected the insecure prototype sentences more quickly. One possible explanation of this finding is social desirability, because the perception of secure sentences could be expected to be ideal. This is in line with findings by De Carli et al. (2016). In their IAT study about caregiving and attachment, which they proposed as two different systems, the authors found that adult attachment style had a role in shaping the implicit attitude, but not the explicit attitude, concerning the category "mother." The explicit attitude did not appear to be influenced in that study by experimental manipulation or the

TABLE 5 | Speed of answers in participants with secure and insecure attachment according to the AAP classification.

AAP-RC 2.0		**AAP secure *n* = 10**		**AAP insecure *n* = 20**		**Cohen effect size**	**Two-group t-test**	
Prototype	**Answer**	***M***	***(SD)***	***M***	***(SD)***	***d***	$t_{(28)}$	***p***
All stimuli								
Secure	Yes	51.34	(2.81)	51.20	(3.01)	+0.05	+0.123	0.903
Secure	No	47.65	(5.90)	49.51	(3.08)	−0.44	−1.139	0.265
Insecure	Yes	47.00	(2.46)	*49.77	(1.24)	**−1.60**	**−4.134**	**0.000**
Insecure	No	*50.73	(0.86)	49.71	(1.37)	**+0.84**	**+2.164**	**0.039**
Alone stimuli								
Secure	Yes	49.80	(3.11)	49.39	(4.68)	+0.10	+0.250	0.804
Secure	No	47.06	(5.45)	49.81	(4.46)	−0.57	−1.475	0.151
Insecure	Yes	47.70	(3.68)	*50.72	(3.11)	**−0.91**	**−2.359**	**0.026**
Insecure	No	50.56	(1.60)	50.16	(1.94)	+0.22	+0.565	0.576
Dyadic stimuli								
Secure	Yes	52.03	(3.77)	52.19	(3.95)	−0.04	−0.108	0.915
Secure	No^x	49.75	(7.01)	49.26	(5.3ß)	+0.08	+0.201	0.842
Insecure	Yes	45.91	(3.76)	*48.29	(2.07)	**−0.87**	**−2.256**	**0.032**
Insecure	No	*50.82	(1.47)	49.30	(1.82)	**+0.88**	**+2.277**	**0.031**

*Group comparison. Bold: significant t-test. *significantly higher group mean. ^{x}sample n = 28, AAP secure n = 8, df = 26.*

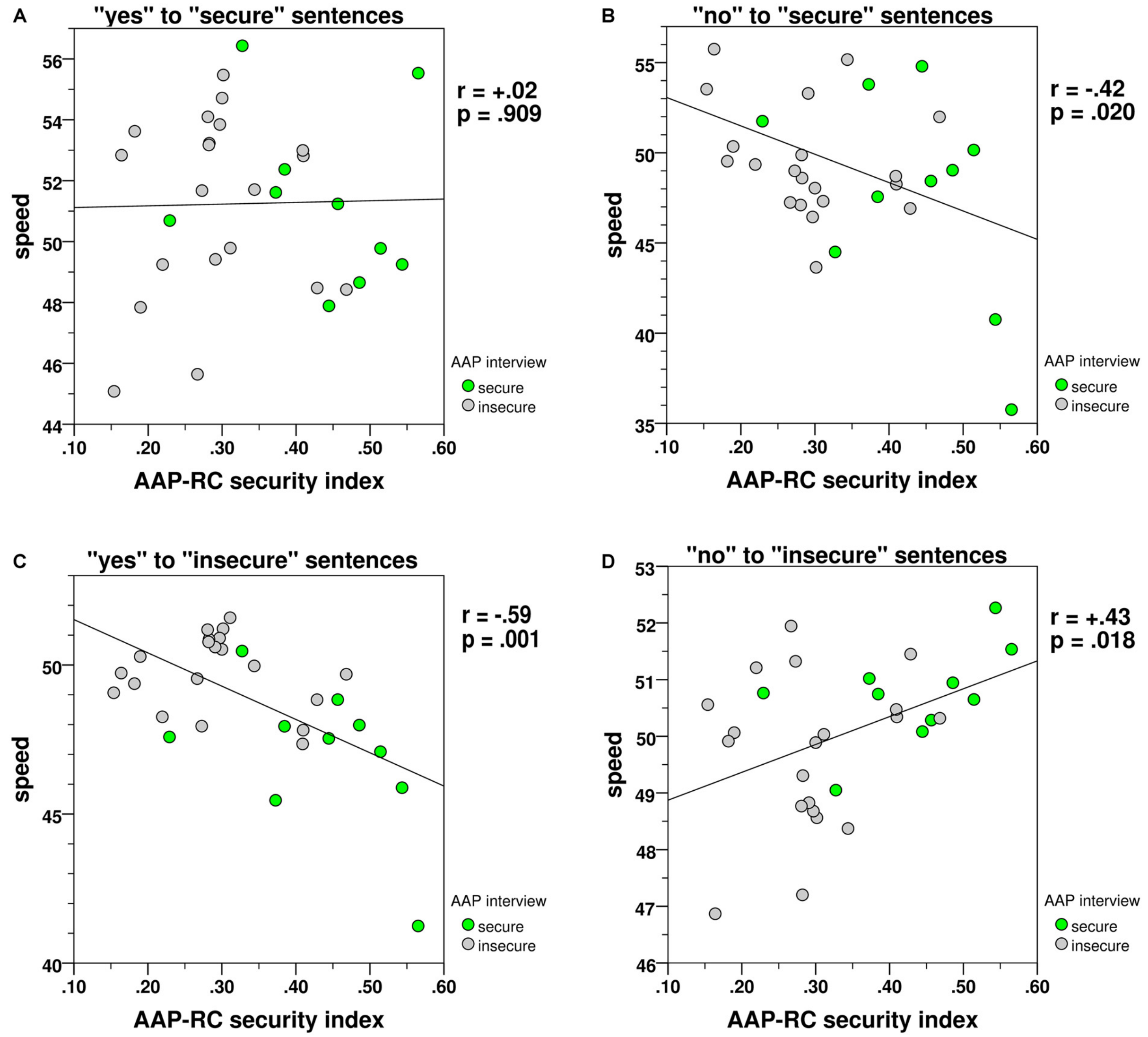

FIGURE 4 | Correlations between AAP-RC security-insecurity index and reaction speed. (A) Accepted secure sentences, **(B)** rejected secure sentences, **(C)** accepted insecure sentences, **(D)** rejected insecure sentences.

participants' attachment style. The authors discussed that this can be explained by social desirability, because the perception of mother is expected to be mostly positive. In sum the IAT findings of De Carli et al. (2016) in the context of the transmission of attachment are in line with our results by showing that the participants preferred a particular style of caregiving coherent with their own attachment style. However the authors pointed out that their attachment measure was a self-report instrument that captured explicit thoughts only. However a notable strength in our study is that we used a free-response narrative attachment assessment measure, which seems to be more appropriate for this kind of experimental approach because of its implicit nature. Yet the role of social desirability should be clarified in future studies.

Despite the results, that all participants in our study accepted the prototype secure sentences faster than insecure prototypes, there were significant differences between the two adult attachment groups. Secure participants accepted more prototype secure sentences and showed faster RTs than insecure participants. Insecure participants accepted more insecure sentences, and did so faster than secure participants. This result underscores the presence of automatic unconscious detection and appraisal processes when responding to attachment relevant information.

Parallel patterns were found in the AAP-RC with the RTs in the experiment. Participants with higher preference for secure prototype secure sentences rejected insecure sentences more quickly. Participants with higher preference for insecure prototype sentences accepted insecure sentences more quickly and rejected secure ones more quickly.

Our differential hypotheses addressed secure and insecure prototype sentences. Findings supported our hypotheses, and we confirmed all hypotheses concerning the insecure prototypes. In other words: "*accept secure and reject insecure*" goes *fast*, and "*reject secure and accept insecure*" goes *slow*. It seems that the "insecure-type" reactions demand more time.

In a study by Rösler (1993), more complex processes took longer elaboration time than more simple ones. What makes the insecure reaction more demanding than the secure one in our study? We can nearly exclude that the linguistic or cognitive complexity would play a role: the grouped sentences had the same length and they were clear and understandable. However, the complexity of the relationship related decision processes might differ. It is reasonable then to conclude that the differences were due to story content. George and West (2012) described, how different insecure attachment representations are connected to different defensive mechanisms. The insecure attachment prototypes have the potential to address inner conflicts (e.g., ambivalence or deactivation of attachment relevant information), which must be recognized first, and then accepted or rejected. This unconscious process might request the additional "working time"[2].

Our findings are in line with those of Vrtička et al.'s (2012) study of attachment style. These researchers used an explicit choice paradigm and found distinct effects of attachment avoidance and anxiety on subjective emotional judgments. Their results supported the assumption that anxious attachment is associated with a hyperactivating tendency for the appraisal of social threat, but may also involve an ambivalence influencing the judgment of information. Although, the authors did not use a RT experiment, their results support thinking that proposes that insecure attachment seems to need more mental elaboration time.

Therefore we could have assumed in our study that individuals with preoccupied attachment representations associated with heightened emotional reactivity would show different RT patterns compared to dismissing individuals, characterized by deactivating attachment related emotions. This important differentiation should be the next step in future studies with a larger sample size.

According to previous research with the AAP we might have also expected particularly differentiated results for the analyses based on "alone pictures" compared to "dyadic" ones. Alone pictures represent scenarios of emptiness and loneliness and seem to elicit high affective arousal in participants (Buchheim and George, 2011). However the results of the present study showed that insecure individuals needed longer elaboration times confronted with the dyadic pictures. This type of sentences (like in the AAP picture of the couple in the scenario "departure") represents explicit attachment related scenarios between two or more persons (potential separation, need for care). We might conclude that insecure individuals needed more elaboration time for processing these attachment related conflicts. The observed differences should be verified in further investigations using a larger sample.

In sum, high security index scores were associated with prompt rejection of insecure prototype sentences. Lower security index scores were associated with prompt acceptance of insecure sentences, as well as rejection of secure sentences. Some other hypotheses could not be confirmed significantly; there were no contrary findings nevertheless. We might have demonstrated that the secure vs. insecure attachment classification groupings could be observed with the implicit measure, by observing the activation of inner working model in "real time."

Our results support the conceptualization of inner working models of attachment as guiding attention and interpretation outside of conscious awareness and the coherency of the association between mental representation and interpretation of attachment situations (Bowlby, 1980).

From a methodological perspective, we suggest that the observation of RTs is valuable to complement the spectrum of mainstream measures in human neuroscience, like brain mapping or EEG analyses. These highly advanced measures focus on brain localizations and processes associated with different psychological tasks and events. The RT approach investigates the overall time of participants to specific stimuli analogous to the time complexity theory in computer science (Sedgewick and Wayne, 2011). The more operations are needed for the problem solution, the more time is needed. The time needed for the problem solution might then constitute an operationalization of the problem complexity and depends on numerous biasing factors. Human processing time consists of the individual's basal or momentary reaction speed including external disturbing influences, which could cause long outlier RTs. The data-analytic procedure proposed in this article was designed with the aim to be robust against the mentioned biasing factors and could be a fruitful additional approach in an EEG analysis when using a similar paradigm.

Limitations

The size of our sample of 30 participants was sufficient, albeit small, for the experimental investigation of the RT phenomena. The number of 128 attachment prototype sentences was considerably larger than the sample size; this circumstance limited the use of more advanced psychometrical analyses (e.g., factor analysis). Similarly, the sample sizes and the distribution of four particular attachment groups led us to the decision to confine the analyses to the two basic attachment classifications secure and insecure. In fact, secure vs. insecure analyses are often chosen as a comparison in the field of attachment. However as we discussed it would have been valuable to differentiate the insecure attachment groups and the individuals' RTs. This aspect should be tested in further research.

In sum the present study served as a pilot study to test its feasibility in healthy participants. The next steps are the

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[2] An analogous approach is being used in the computer science: the complexity of a problem is classically operationalized by the number of needed steps of the problem solving algorithm, and consequently by the time demanded for the problem solution; see Sedgewick and Wayne (2011).

application of the RT experiment in clinical studies with a larger sample. Moreover, the AAP measure is constructed and validated for adults and adolescents only, so the application is limited to that age group and not feasible for children, where other measures should be used, like the Separation Anxiety Test (Klagsburn and Bowlby, 1976).

Despite these limitations, the study has shown that the concept of immediate reactions to stimulus sentence could be beneficial for experimental attachment research contributing to measure the intensity of unconscious processes empirically. As a following research step, we intend using psychometric procedures to continue and improve the development of the AAP-RC instrument in order to implement it in a neurobiological setting.

Outlook: Neurobiological Model Using the Reaction Time Experiment on Adult Attachment

In the presented study, we have seen that stimuli with more distressing attachment content might need a longer RT for its elaboration than stimuli with more harmonious content. Future studies need to replicate these findings using larger samples. A further next step is to adapt the experiment for an EEG setting, which could give further insight into the neural mechanisms of potential response delays during an implicit task.

One of the most interesting areas in the research of preconscious perception is the investigation of early brain potentials. Until now, there are only a small number of studies examining the perception of emotional stimuli in individuals with different attachment patterns. In an EEG setting the N1 potential, which is also called N170 component, is considered to be a very sensitive representation of early perceptual processing. Spatio-temporal analyses of brain activity patterns during the first 200 ms after stimulus presentation have characterized the timing of attentional selection processes and different stages of feature encoding and pattern analyses (Hillyard et al., 1998). In an attachment study on *face recognition* Zhang et al. (2008) reported distinct differences in N1 activation using self-reports. The perception of angry faces was followed by high N1 amplitudes in anxious and secure individuals in contrast to the smaller amplitudes in avoidant individuals. Given that N1 is considered to be an index of the level of attention, the authors suggested that individuals with anxious attachment "use most, and avoidant individuals use least attentional resources to face stimuli than secure individuals". The authors considered these differences as the results of automatic processes in association with conscious and preconscious emotional information processing. In contrast to the latter study Fraedrich et al. (2010) focused on event-related potentials (ERPs) in mothers during the perception of infant emotions by presenting positive, negative and neutral facial expressions as well as non-facial stimuli within an oddball paradigm. Dismissing mothers exhibited elevated N170 amplitudes for *facial* target stimuli within conditions that contained frequent non-facial stimuli. In summary, the findings suggested that insecure mothers require more cognitive resources to process infant faces, while secure mothers allocate more attention to infant faces and clearly show a perceptual bias toward social information. The differences between the study results of Zhang et al. (2008) and Fraedrich et al. (2010) might be due to the different stimulus material.

In a very recent study by Leyh et al. (2016), the association between maternal attachment representation and brain activity (ERPs) underlying the perception of infant emotions was examined. Securely attached mothers recognized emotions of infants more accurately than insecurely attached mothers. ERPs yielded amplified N170 amplitudes for insecure mothers when focusing on negative infant emotions. Secure mothers showed enlarged P3 amplitudes to target emotion expressions of infants compared to insecure mothers, especially within conditions with frequent negative infant emotions. In these conditions, P3 latencies were prolonged in insecure mothers.

One potential limitation of attachment research of preconscious perception with the help of the early brain potentials so far might be the predominant focus on *face processing* as the stimulus material. Neural processing in secure and insecure subjects were not examined by attachment related material directly linked to the individuals' own attachment representations using a paradigm where spontaneous preferences had to be given in a defined time frame.

In a recently published article by Matheus-Roth et al. (2016) early occipital ERP's (e.g., P100 and N170) have been shown to be sensitive for a "preference" for stimuli with alcohol association in patients with alcohol dependance. The authors used a Go-NoGo paradigm with three visual stimuli: tea, juice and beer. The N170 amplitudes were elevated in response to the alcohol-related (beer) stimuli in the NoGo condition in these patients compared to controls. The patients had to react to the frequent tea stimuli and ignore the beer and the juice stimuli. While the higher N170 component correlated with a relapse within the following 3-month, the shorter P100 latencies were related to higher depression scores. The latencies of these early ERPs represent the "RTs" of the brain, presumably independent of deliberate influence. In another study, the so called "mismatch negativity" (MMN) has been demonstrated to react pre-attentively to syntactic or semantic errors (Menning et al., 2005). The authors used an auditory oddball design with frequent standard sentences to elicit a memory trace, which was interrupted by rare deviant (erroneous) sentences. Moreover, Hietanen and Nummenmaa (2011) revealed that N170 is sensitive to stimuli of naked bodies. In their studies it is even greater for nudes than to faces. Overall N170 seems to be an indicator for the preconscious individual importance of visual stimuli.

Finally the analysis of P300 component—an indicator for emotional operations—might reveal interesting results (Nieuwenhuis et al., 2005; Schupp et al., 2007; Flaisch et al., 2008). However, assuming that P300 is a correlate of conscious perception (Dehaene et al., 2006), more early EEG components like cited above should be considered first to capturing modes of more unconscious processes.

In sum these neurophysiological and the other cited attachment studies investigating implicit aspects of romantic attachment using self-report measures as explicit instruments for assessing attachment style (Marks and Vicary, 2015; De Carli et al., 2016) suggest that early visual and auditory stimuli could be used as a change detector of emotionally preferred stimuli. Thus, transposed to our tested and validated AAP RT paradigm, we would expect that the specific (secure or insecure) attachment system paves the way for a specific ERP, e.g., higher amplitudes or shorter latencies of the N170 or P300 to individual preferred stimuli which represent the own attachment representation. One advantage of our paradigm would be to use attachment related material linked to the individuals' inner working models of attachment in a RT setting. This might extend previous studies in healthy samples and may provide some feasibility for clinical studies.

The measures based on RT reflect the overall activity of the brain needed for the elaboration of different stimuli. The results of the referred study suggested that the overall time needed for the processing of "unpleasant", discomforting stimuli was higher than for "pleasant", comforting ones. The fact that RT showed convergence with the individual' inner working model of attachment in our study, has the potential to contribute to the validity of neurobiological experiments, like EEG. Therefore RT analysis with the proposed evaluation procedures might be of interest for a broader variety of questions concerning attachment in experimental and neurophysiological settings to capture automatic, unconscious processes in association with internal working models of attachment.

AUTHOR CONTRIBUTIONS

The study was conceptualized by AB, CG, TW and DP. The attachment experiment was developed by AB. The study setup and data collection were organized and conducted by TW. Coding of attachment interviews were conducted by AB. DP performed the statistical data analysis and contributed substantially to the result interpretation. DP developed the statistical procedure for RT analyses. CG, DP, TW, HM, IS and AB provided important intellectual contribution in commenting and revising the manuscript. AB, DP and TW wrote major parts of the manuscript and edited its final version.

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Attachment Representations and Brain Asymmetry during the Processing of Autobiographical Emotional Memories in Late Adolescence

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Frontal and parietal asymmetries have repeatedly been shown to be related to specific functional mechanisms involved in emotion regulation. From a developmental perspective, attachment representations based on experiences with the caregiver are theorized to serve regulatory functions and influence how individuals deal with emotionally challenging situations throughout the life span. This study aimed to investigate neural substrates of emotion regulation by assessing state- and trait dependent EEG asymmetries in secure, insecure-dismissing and insecure-preoccupied subjects. The sample consisted of 40 late adolescents. The Adult Attachment Interview was administered and they were asked to report upon personally highly salient emotional memories related to anger, happiness and sadness. EEG was recorded at rest and during the retrieval of each of these emotional memories, and frontal and parietal hemispheric asymmetry were analyzed. We found attachment representations to differentially affect both the frontal and parietal organization of hemispheric asymmetry at rest and (for parietal region only) during the retrieval of emotional memories. During rest, insecure-dismissing subjects showed an elevated right-frontal brain activity and a reduced right-parietal brain activity. We interpret this finding in light of a disposition to use withdrawal strategies and low trait arousal in insecure-dismissing subjects. Emotional memory retrieval did not affect frontal asymmetry. However, both insecure groups showed an increase in right-sided parietal activity indicating increased arousal during the emotional task as compared to the resting state suggesting that their emotion regulation capability was especially challenged by the retrieval of emotional memories while securely attached subjects maintained a state of moderate arousal. The specific neurophysiological pattern of insecure-dismissing subjects is discussed with regard to a vulnerability to affective disorders.

Keywords: attachment, EEG, hemispheric asymmetry, emotional memory, late adolescence

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INTRODUCTION

A central tenet of attachment theory is that depending on the caregiver's availability and responsiveness children form expectations about how they can rely on the caregiver in the face of stress and consequently develop individual ways to regulate behavior in emotionally challenging situations (Bowlby, 1969; Ainsworth et al., 1974). For example, when the caregiver poorly or inappropriately responds to the child's signals of distress, the child may learn to avoid expressing negative affect in the future. These experiences are believed to result in a so-called inner working model of attachment that serves regulatory functions throughout the life span (Bowlby, 1982; Bretherton and Munholland, 2008). Applying a developmental perspective, the current study set out to investigate how in late adolescence working models of attachment influence hemispheric brain activity related to emotional processing at rest and during the retrieval of autobiographic emotional events that have occurred beyond childhood. This research is important, as biological substrates of emotion regulation capacities may reveal dysfunctional processes that are not inferable via narratives or self-report. Importantly, in adolescence, the generation of a meaningful life story emerges (Habermas and Bluck, 2000). The effective conscious recollection of personally salient emotional memories plays a major part in this development and is linked to psychological growth and well-being (Singer et al., 2013). Moreover, the "the updating of prior emotional memories through a process of reconsolidation" can be seen as a core element of different psychotherapeutic approaches as it enables the incorporation of new experiences, and thus, supports healthy development (Lane et al., 2015, p. 1). With this study we aim to add to current knowledge on processes involved in emotional memory retrieval with special regard to individual differences related to attachment.

While in early childhood individual patterns of attachment come to light by assessing children's behavioral organization in stressful situations (e.g., the Strange Situation Procedure, Ainsworth and Wittig, 1969) with increasing age, behavioral differences become more subtle. By late childhood, inner working models of attachment are believed to be reflected in narratives about attachment related topics, and would typically be assessed by using interview measures. The Adult Attachment Interview (AAI, Main et al., 2002) reveals classifications of attachment that are based on explicit assumptions about securely, insecure-dismissing and insecure-preoccupied individuals' way to access and regulate their emotions. As theorized by Main et al. (1985) when asked about his or her experiences with the caregiver, a securely attached person is capable of freely evaluating and openly communicating pleasant and unpleasant emotions. Irrespective of their valence, he or she can reflect upon his or her experiences and integrate them as important aspects of the past and current self. In contrast, insecurely attached persons are unable to present a coherent life history with regard to attachment related issues. Presumably due to having experienced an irresponsive caregiver that did not provide the opportunity to communicate various aspects of emotions, insecure-dismissing individuals appear to only have limited access to their feelings and are less capable of perceiving and expressing emotional information. As a consequence, using a rather unconscious defensive process, they tend to idealize attachment experiences or present them as less meaningful to their development. In contrast to these de-activating strategies, insecure-preoccupied individuals seem to be overwhelmed by their emotions, especially regarding anger. At the same time they make contradictory statements leading to an incoherent narrative reflective of their deficits to integrate conflicting emotions. Instead they appear to be ambivalent, entangled and highly affected when reporting about their past. The insecure-preoccupied state of mind is thought to be a result of inconsistent responsiveness of the caregiver during the early years (Cassidy and Berlin, 1994).

Attachment and Emotion Regulation

Furthermore, it is assumed that regulatory capacities of grown-up individuals with different attachment representations not only apply to the retrieval of childhood experiences but that they also result in a certain predisposition to respond to various kinds of emotional challenges (Spangler and Zimmermann, 1999; Cassidy, 2008). As such, inner working models of attachment affect, for example, how emotional stimuli are perceived and interpreted and, by doing so, shape how the individual experiences his or her inner and outer world, hence guiding subsequent behavior. Indeed, insecurely attached individuals have been found to show deficits in the processing of emotional stimuli. For example, studies using self-report of attachment have found heightened or reduced attention in insecure-ambivalent[1] and insecure-avoidant subjects, respectively, when compared to secure ones (Hazan and Shaver, 1994; Simpson et al., 1996; Cooper et al., 1998). Using the AAI, Spangler and Zimmermann (1999) found insecure-dismissing adolescents failing to show typical mimic responses to emotional film clips, indicating reduced emotional expressiveness. Interestingly, on a declarative level they were also found to report reduced attention to negative stimuli (Spangler and Zimmermann, 1999). Also, empirical evidence suggests that insecurely attached mothers are less accurate in identifying infant emotion and process infants' negative emotional expressions in a specific way (e.g., Spangler et al., 2010). In this line, a number of ERP studies report evidence of attachment related differences in the neural processing of emotional stimuli. For example, analyzing ERP responses to infant emotional faces studies using narrative measures of attachment found neural correlates associated with attentional processing (i.e., N200, P3) to be less prominent in insecure mothers (Fraedrich et al., 2010; Leyh et al., 2016a). Accordingly, studies using self-report measures of attachment found decreased ERP amplitudes in response to emotional faces in avoidant subjects (Zhang et al., 2008), as well as a response bias in favor of positive stimuli (Chavis and Kisley, 2012), while others found insecurely attached individuals to be less able to accurately discriminate between different facial emotion expressions on a neurophysiological level (Escobar et al., 2013; for a review also see Gander and Buchheim, 2015).

There also is evidence for attachment differences in adolescents' emotion regulation behavior and adrenocortical regulation in specific problem-solving and emotion eliciting tasks (e.g., Zimmermann et al., 2001; Spangler and Zimmermann, 2014) as well as in individuals' physiological reactivity during family conflict interaction (Beijersbergen et al.,

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[1] Note that the terms "-ambivalent" and "-avoidant" apply to studies using self-report measures but refer to the terms "-preoccupied" and "-dismissing", respectively, that are commonly used in studies using narrative measures of attachment.

2008). For example, Beijersbergen et al. (2008) found insecure-dismissing subjects to elicit increased heart rate reactivity when their emotion regulation strategies were challenged during the interaction, however, their defensive mechanisms seem to work well during the retrieval of caregiving experiences (but see Roisman et al., 2004). Taken together, including physiological measures when investigating psychological processes appears to reveal insecurely attached individuals' struggle to effectively regulate affective states which would not be accessible by verbal communication only.

In sum, these findings, together with numerous other studies provide strong evidence that patterns of attachment account for variability in adolescents' and adults' emotion regulation strategies on both a behavioral as well as a psycho-biological level (also see Spangler and Zimmermann, 1999; Gander and Buchheim, 2015).

The Role of Hemispheric Asymmetries in Emotion Regulation

During the last decade the use of EEG as a measure of the brain's responses to emotional stimuli and its activity during emotional tasks has gained great popularity. To date, there is a still increasing number of neurophysiological studies investigating the neural circuits underlying differences regarding securely and insecurely attached individuals' processing of emotions. One common approach in the EEG literature is the use of EEG asymmetries reflecting the functional involvement of both hemispheres during an extended recording episode which is associated with well-grounded theoretical models. Beside the measurement of individual affective dispositions, EEG asymmetries are also modulated by, for example, the induction of certain emotions, thus, serving as a trait as well as a state variable, respectively (e.g., Coan and Allen, 2003). Regarding both of these aspects of emotion regulation, ongoing alpha power[2] (8–13 Hz) at rest and its moderation by emotional content are the major focus of the current study.

Left and right frontal cerebral regions have shown to be differentially involved in the processing of different types of emotion (e.g., Coan and Allen, 2004). More precisely, relatively increased left frontal brain activity (LFA) is conceived as being associated with positive affect and increased approach-oriented behaviors. On the other hand, relatively increased right frontal brain activity (RFA) is thought to reflect a motivational tendency to use withdrawal strategies to regulate emotions and is associated with negative affect (Davidson and Fox, 1982; Davidson, 1993). The model has repeatedly been confirmed by studies in both infants and adults (see Davidson, 2004; Marshall and Fox, 2007).

While there has been considerable research on frontal EEG asymmetry, somewhat less is known about the role of parietal brain asymmetry in emotion processing. However, EEG asymmetry scores at parietal cortical areas –with special regard to the right hemisphere- are assumed to reflect additional aspects of the neural processing of emotions, namely the arousal component related to affective states (Heller, 1990). For example, involving a posterior brain system enhanced arousal is thought to typically elicit relatively increased right parietal activity (RPA) (Heller et al., 1997). Furthermore, the role of relatively decreased RPA as a psychophysiological indicator of risk for depression is strongly undermined by empirical evidence (reviewed in Stewart et al., 2011). These findings go along well as they suggest reduced RPA in depressed individuals to indicate low emotional arousal, which itself is commonly associated with the disorder (Mennella et al., 2015). To sum up, both frontal and parietal regions seem to be involved in emotion regulation; however, they appear to be distinctively related to different components of affect.

Attachment and Hemispheric Asymmetries

To date, there are a few studies that have investigated the association between attachment and EEG asymmetries. However, most of them refer to asymmetrical patterns of ERP waveforms elicited during emotion perception (for a review see Gander and Buchheim, 2015). As an exception, in her infant study, Dawson et al. (2001) found that in interaction with their mothers insecurely attached infants exhibited reduced LFA, which is interpreted in line with a hypo-activation of the attachment system. Investigating this linkage in an adult sample, Rognoni et al. (2008) identified specific patterns of frontal cerebral asymmetry varying as a function of attachment style assessed by questionnaire. In particular, they found attachment insecurity to be associated with greater RFA and security with greater LFA in a resting state indicating avoidance and approach motivation, respectively. Furthermore, attachment groups, on a neural level, differentially responded to emotional stimuli (Rognoni et al., 2008). Accordingly, using the Adult Attachment Projective, Fraedrich et al. (2010) reported further evidence suggesting increased RFA in insecurely attached subjects, however, they could not replicate Rognoni et al.'s (2008) findings with regard to statistical significance (Fraedrich et al., 2010). Regarding attachment and hemispheric asymmetry in parietal regions, Rognoni et al. (2008) briefly reported not to have found any effects. Apart from this, to the best of our knowledge there is no study investigating attachment related differences with regard to parietal asymmetry.

Regarding task specificity, it is suggested, that associations between an individual's emotion-regulatory capability and hemispheric asymmetries can best be inferred by assessing EEG within an emotional context (e.g., Coan and Allen, 2003; Dennis and Solomon, 2010) or by inducing an affective state as recommended by Mennella et al. (2015). Drawing on a number of inconsistent findings regarding both frontal and parietal asymmetries, they summarize several studies indicating that resting state assessments may not be powerful enough to reliably elicit individual differences in brain activity. Furthermore, they suggest using emotional tasks that especially activate brain regions of interest. In particular, differences in the parietal region may best be observed when using imagery tasks (Mennella et al.,

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[2] Alpha power is an indicator of neural deactivation (Lindsley and Wicke, 1974), and thus, speaking about brain activity in a given hemisphere, the alpha power score needs to be inverted.

2015). From an attachment theory perspective, the attachment system gets activated in emotionally challenging situations. Thus, it would only be plausible that differences in EEG asymmetries especially come to light during affect regulation. With attachment security as being reflected in a coherent report of one's attachment history (Main et al., 1985), we assumed that differences in asymmetrical brain activity may be most prominent when inducing an affective state that is linked to highly salient autobiographical memories. While there is evidence, that depending on their mental representation of attachment security, individuals elicit different psychophysiological reaction when talking about their childhood experiences (Roisman et al., 2004), we are not aware of any study that has investigated this effect using EEG measures when processing personally meaningful experiences.

Furthermore, it should be noted that many EEG studies on attachment rely on self-report measures, however, they assess different aspects of attachment than interview measures that take into account mental processes operating on a rather subconscious level. Indeed, correlations between these two measurements is only small (Roisman et al., 2007). Possibly due to the fact that the AAI as well as the EEG are both time consuming methods and, in addition, both require particular expertise for analysis, neurophysiological studies using narratives to assess individual representations of attachment are rather sparse. This void in the literature is addressed in the current study.

Hypotheses

Drawing from empirical evidence and theoretical assumptions reported above, we expected hemispheric asymmetries to be affected by an individual's attachment representation at rest as well as during the retrieval of personally salient emotional memories (resembling a trait and a state marker, respectively).

Regarding frontal asymmetry at rest we hypothesized that insecure-dismissing attached subjects would show relatively increased RFA linked to a motivational tendency of withdraw and avoidance (Davidson, 2004) as compared to securely attached ones. With regard to parietal asymmetry linked to arousal (Heller et al., 1997), we hypothesized that insecure-dismissing subjects would show a pattern of hypo-arousal as indicated by reduced RPA while insecure-preoccupied subjects, assumed to have a lower threshold to distress, may show the opposite pattern. For securely attached subjects, however, we expected a more regulated pattern falling in between the hypo- and hyper-activating disposition expected in the insecure-dismissing and the insecure-preoccupied group, respectively.

Furthermore, our study particularly aimed to investigate attachment related differences in state dependent hemispheric asymmetry patterns. In this regard we expected that the retrieval of personally salient emotional memories would affect brain activity patterns, and, as attachment is associated with how individuals regulate their affective states we expected the effect to vary as a function of attachment. Thus, when comparing brain activity at rest (trait) to emotional memory retrieval (state), we hypothesized that insecurely attached subjects would show increased RPA indicating increased arousal during emotional memory retrieval as compared to hemispheric parietal activity at rest. This pattern reflecting a restricted capability to effectively regulate their affective states was not expected in securely attached subjects.

MATERIALS AND METHODS

Participants

The sample consisted of fourty-two late adolescents (22 female, 20 male) ranging from 17 to 22 years of age ($M = 19.46$, $SD = 1.27$). Participants were recruited with flyers to take part in a larger study including three laboratory visits. They were compensated 40 Euros in total. The current paper refers to data collected at the first and second laboratory assessment[3].

Right-handedness was a selection criterion and all participants completed the Edinburgh Handedness Inventory (EHI, Oldfield, 1971) upon arrival. Twenty-nine percent of the participants were currently attending school while the rest has already graduated but was not yet enrolled at University. Two participants were excluded from further analysis due to non-compliance with the study procedure and insufficient artifact-free EEG data. Thus, data from 40 participants were used for statistical analysis.

Procedure

On arrival participants gave written consent. The first laboratory visit included the assessment of attachment representations, handedness and autobiographical emotional experiences. Within a few weeks, at the second laboratory visit, neurophysiological data were collected using stimuli extracted from participants' specifications about their emotional experiences reported earlier. Each laboratory assessment lasted approximately 2.5 h.

Materials

Assessment of Attachment Representations

Attachment representation was assessed by the AAI (George et al., 1985), a semi-structured interview focusing on significant caregiving experiences and attachment relevant situations in childhood. Furthermore, it targets the evaluation of these experiences as well as the current relationship to the primary caregivers[4]. Transcripts of these interviews were coded in accordance with Main et al. (2002). The judgment of narrative coherence, idealization and derogation of parents and/or attachment, as well as current preoccupying anger and passivity of speech results in one of the three main attachment categories: Secure (F), Insecure-Dismissing (Ds), Insecure-Preoccupied (E). The AAI's reliability and validity is well established (for a review see Hesse, 2008).

In the present study the German translation of the original English AAI protocol was used (Gloger-Tippelt, 2001). The AAIs in this sample were conducted by the first author and a psychology student after receiving extensive training. Interviews were audio-taped, transcribed and all personal information about the participants was removed from the

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[3] See Leyh et al. (2016b) for a description of the third laboratory assessment.

[4] The description of the AAI-procedure used here was drawn from Leyh et al. (2016b).

transcripts. The transcripts were coded by a certified coder[5]. To test reliability 10 randomly selected AAIs were coded by a second certified coder[6]. Coding agreement was 90% ($\kappa = 0.84$, $p \leq 0.001$).

Emotional Memory

Subsequently to the AAI assessment participants were asked to memorize and write down three personally meaningful events. In particular, they were successively instructed to describe three single events representing their happiest, saddest and most infuriating personal experience during adolescence (starting by age 10). Descriptions were required to be detailed, including antecedences and outcomes of the situation. Finally, participants were asked to sum up each story in one phrase that was later used as a cue to the emotional experience described (e.g., "death of my grandfather"). These phrases were included in the EEG experiment aiming to help participants to retrieve the emotional memory and, by doing so, trigger the associated affective state.

Neurophysiological Assessment

EEG Procedure

For the EEG assessment, participants were seated in a comfortable chair in a dimly lit, electrically and acoustically shielded cabin. Asymmetrical brain activity was measured during two pseudo-randomized blocks: (1) Resting state EEG asymmetries were measured during two four minute episodes (initial resting state, final resting state), separated by the emotional memory retrieval experiment followed by an ERP paradigm on emotional face processing, which is not included in the current paper. We assessed brain activity during both an initial as well as a final resting state to control whether effects were especially due to the retrieval of emotional memories and thus limited to the intermediating experimental manipulation[7]. During the resting state episodes, participants were instructed to close their eyes, sit quietly and stay calm to avoid movement artifacts. (2) To measure asymmetrical brain activity while retrieving emotional memories, participants were presented with each single phrase cuing their self-reported autobiographical emotional experiences. Phrase stimuli appeared in white fonts on a 19″ black screen with a viewing distance of 115 cm and stimulus presentation was controlled by the experimental software Inquisit (Millisecond Software, Seattle, WA, USA). Each of the three emotional memory retrieval episodes (happiness, sadness, anger) lasted 4 min with phrase stimuli staying on screen the whole time. The order of stimulus presentation was pseudo-randomized. Preceding each of the three emotional memory retrieval episodes a written instruction appeared on screen. More precisely, the instruction page said that participants will be confronted with the phrase they provided during the first assessment and that indicated their happiest, saddest and most infuriating memory, respectively. Moreover, participants were instructed to sit still and to recall the respective situation and, by doing so, they were asked to put their selves back in the corresponding affective state. After reading the instructions, participants could start the respective emotional memory retrieval episode by pressing a button. Throughout the whole assessment participants were monitored via a frontal camera to ensure that they did not move and (during emotional memory retrieval) direct their focus to the screen.

EEG Recording

Recording and analyzing of the EEG was performed using BrainVision software (Brain Products, Gilching, Germany). The ERP experiment that was conducted at the same measuring point but not included in the current study required the use of numerous additional electrodes. Thus, a total of 60 active electrodes[8] based on Ag/AgCl sensors were placed 5 mm in diameter according to the international 10–20 system. To assess eye movements EOG was recorded from electrodes placed below and above the left eye, as well as next to each eye's outer canthus. The ground electrode was placed at Afz and FCz served as the online reference channel. Signals were acquired using BrainAmp Standard amplifier (Brain Products, Gilching, Germany) that recorded frequencies ranging from 0.016 to 1000 Hz with a resolution of 0.1 μV per bit and a measurement range of ±3.28 mV. They were digitized using a 16 bit A/D converter.

EEG Data Reduction and Analysis

For offline processing data were re-referenced to the mastoids and a 115.2 Hz, 24 dB/oct high-cut off filter was applied before downsampling the data to 256 Hz. Saccadic eye movements or eye blinks were corrected according to the Gratton & Cole Procedure (Gratton et al., 1983). EEG-signals were segmented into 2 s intervals. Segments with muscular and other artifacts were removed using a semiautomatic procedure. More precisely, the maximal allowed voltage step was 50.00 μV, the maximal allowed absolute difference of two values in one segment was 300.00 μV and amplitudes were only allowed in the range between −70.00 and +70.00 μV. Also, minimum activity was set to 0.10 μV. In the analysis of artifact-free segments a Hanning window with 50% overlap of each epoch was used to prevent spurious estimates of spectral power. For each resting episode segments were averaged and FFT analyses with a resolution of 0.5 Hz were performed. Subsequently, alpha power (8–13 Hz) was extracted from the spectrum as the sum of according frequency bins. Finally, following a common approach by Coan and Allen (2004) data were log-transformed and alpha power of left electrode sites were subtracted from homologous right sites leading to a frontal (ln[F4]–ln[F3]) and a parietal (ln[P4]–ln[P3]) asymmetry score. These two pairs of electrodes correspond to regions commonly studied in the hemispheric asymmetry literature and, for reasons of comparability, their selection was informed by previous studies

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[5] Johanna Behringer, Institute of Psychology, University of Erlangen-Nuremberg, Germany.

[6] Kathrin Beck, Institute fuer Therapieforschung, Munich, Germany.

[7] We are aware that the collection of ERP data on emotional face processing may have had effects on brain activity during the final resting state. However, our results show that brain activity in the final resting state did not differ from the initial resting state with regard to statistical significance (see Results), suggesting there were no spill-over effects due to the second paradigm.

[8] AF4, AF8, C1, C2, C3, C4, C5, C6, CP1, CP2, CP3, CP4, CP5, CP6, CPz, Cz, F1, F2, F3, F4, F5, F6, F7, F8, FC1, FC2, FC3, FC4, FC5, FC6, FT10, FT7, FT8, FT9, Fz, O1, O2, Oz, P1, P2, P3, P4, P5, P6, P7, P8, PO10, PO3, PO4, PO7, PO8, PO9, POz, Pz, T7, T8, TP10, TP7, TP8, TP9.

(Bruder et al., 1997; Dawson et al., 2001; Coan and Allen, 2003; Shankman et al., 2005; Dennis and Solomon, 2010). It is important to note that since spectral power and neural processing are inversely related, increasing EEG asymmetry scores (referring to relatively increased alpha power in the right hemisphere) are reflective of decreasing RFA and RPA, respectively.

Statistical Analyses

To compare attachment groups regarding EEG asymmetries during the initial resting state we used repeated measures MANOVAs with attachment (secure, insecure-dismissing, insecure-preoccupied) as the between-subjects factors and region (frontal, parietal) as the repeated factor. Furthermore, for each, the frontal and the parietal region, we conducted analyses to examine the impact of retrieval of emotional memories on EEG asymmetry with regard to attachment representations. Therefore, repeated measures MANOVAs were performed including regional asymmetry scores during both resting state episodes and the three episodes, during which emotional memory retrieval took place. More precisely, condition (initial resting state, sadness, anger, happiness, final resting state) was included as the repeated measure factor and attachment (secure, insecure-dismissing, insecure-preoccupied) was used as the between-subjects factor. All *post hoc* pairwise comparisons were performed using LSD. When the sphericity assumption was violated, degrees of freedom were computed applying Greenhouse–Geisser adjustments to the degrees of freedom.

RESULTS

Handedness

We calculated a laterality quotient [(R–L)/(R+L)] as a measure of handedness in accordance with Oldfield (1971). It was confirmed that there were no left-handers in the sample (laterality quotient: $M = 0.74$, $SD = 0.23$), however, one participant's laterality score equaled zero. Pearson correlations revealed that right-hand dominance was negatively related to frontal EEG asymmetry scores during four out of the five conditions (*rs* ranging from –0.42 to –0.31, $ps < 0.05$). Including the laterality quotient as a covariate did not change the results of our analyses in terms of significance.

Attachment Representation

Scoring of the AAIs resulted in the following distribution of attachment representations: There were 21 persons with a secure attachment representation and 19 with an insecure one, among the latter 14 persons had an insecure-dismissing and five persons had an insecure-preoccupied attachment representation.

Preliminary analyses showed that attachment representation was not associated with subjects' age and education. However, there was a significant association between attachment and gender ($\chi^2 = 10.3$, $p = 0.006$). A closer inspection of the data showed that males were more frequently found in the insecure-dismissing (11 of 14) and less frequently in the secure group (5 of 16), while there was no difference within the insecure-preoccupied group (2 boys, 3 girls). Therefore, gender was used as a covariate in all analyses regarding attachment.

EEG Asymmetries: Differences between the Attachment Groups

EEG Asymmetries in the Initial Rest State

First, we tested whether groups with different attachment representations differed regarding frontal and parietal cerebral asymmetries at rest. The RM- MANOVA with asymmetry scores calculated from brain activity during the initial resting state at each region (frontal, parietal) revealed no main effects neither for region nor attachment. However, there was a significant interaction between attachment and region, $F(2,36) = 15.65$, $p < 0.001$, $\eta^2 = 0.465$.

Figure 1 shows and LSD *post hoc* comparisons ($p < 0.05$) confirmed, that along with our expectations frontal asymmetry scores for the insecure-dismissing group were decreased and negative ($M = –0.10$, $SD = 0.18$) as compared to the secure group ($M = 0.03$, $SD = 0.20$), $p = 0.033$, as well as to the insecure-preoccupied group ($M = 0.11$, $SD = 0.19$), $p = 0.026$. The mean difference between the latter two groups was not significant. This finding indicates that in comparison to both the other two attachment groups the insecure-dismissing group was more likely to show increased RFA at rest.

Regarding the parietal region, LSD *post hoc* comparisons ($p < 0.05$) of the three attachment groups' EEG asymmetries during the initial resting state revealed the opposite pattern. As can be seen in **Figure 2**, parietal asymmetry scores at rest were significantly increased in the insecure-dismissing group ($M = 0.59$, $SD = 0.30$) as compared to the secure ($M = 0.15$, $SD = 0.21$), $p < 0.001$, as well as to the preoccupied group ($M = 0.15$, $SD = 0.32$), $p = 0.005$, while, again, there was no significant difference between the latter two groups. In other words, at rest, the insecure-dismissing group showed reduced RPA in the parietal region as compared to the secure and the insecure-preoccupied group.

EEG Asymmetries during Emotional Memory Retrieval

To test whether emotional memory retrieval differentially impacted frontal asymmetry depending on attachment (see **Figure 2**), a RM-MANOVA with attachment as the group factor was performed on asymmetry scores calculated from frontal brain activity during each of the five conditions. However, there neither were significant main effects nor a significant interaction between attachment and condition.

In the next step, we tested whether attachment groups differed with regard to the impact emotional memory retrieval had on parietal asymmetry scores. Here, the respective RM-MANOVA revealed a main effect for attachment, $F(2,36) = 8.64$, $p = 0.001$, $\eta^2 = 0.324$, which was qualified by an interaction between attachment and emotional condition, $F(5.09,91.55)$[9] $= 3.11$, $p = 0.012$, $\eta^2 = 0.147$, indicating that parietal asymmetry scores differentially varied with condition depending on attachment

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[9] Degrees of freedom corrected according to Greenhouse–Geisser.

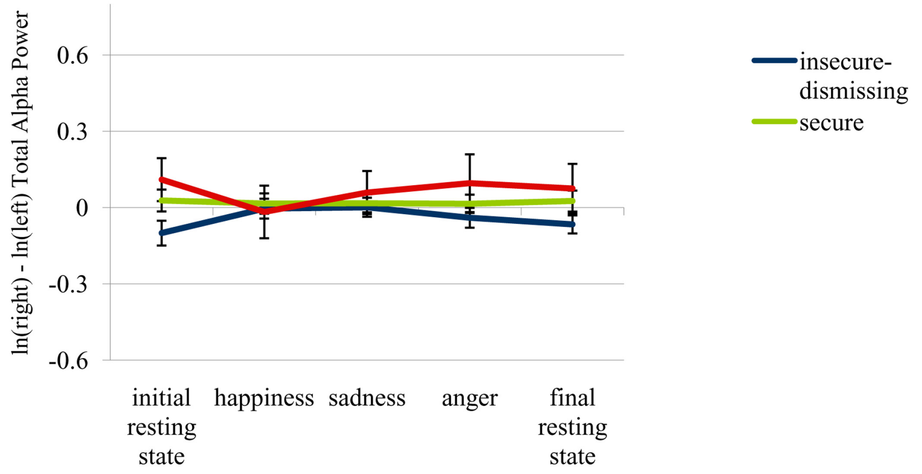

FIGURE 1 | Frontal EEG asymmetry scores in the insecure-preoccupied, secure and insecure-dismissing attachment group during each condition. Means and standard errors. Note that episodes inducing happiness, sadness, and anger did not necessarily appear in this order as emotional conditions were counterbalanced between subjects. Lower values are indicative of increased relative right frontal brain activity (RFA).

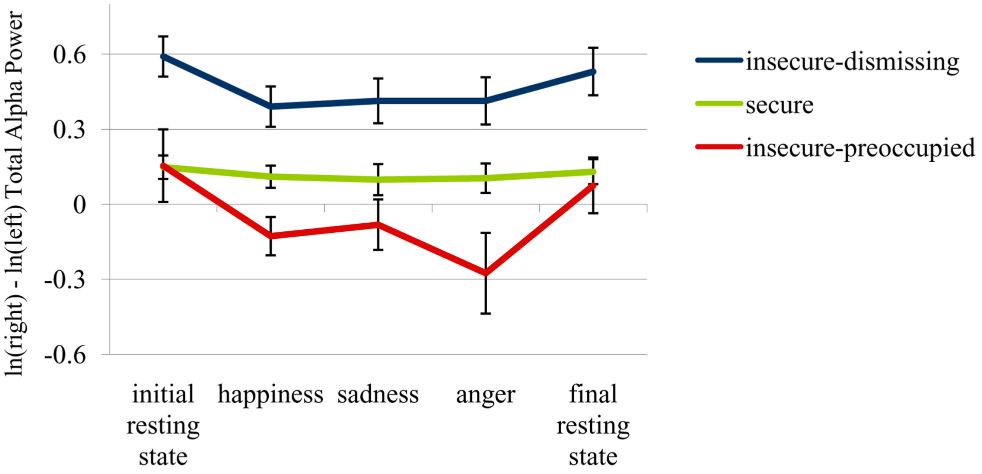

FIGURE 2 | Parietal EEG asymmetry scores in the insecure-preoccupied, secure and insecure-dismissing attachment group during each condition. Means and standard errors. Note that episodes inducing happiness, sadness, and anger did not necessarily appear in this order as emotional conditions were counterbalanced between subjects. Lower values are indicative of increased relative right parietal brain activity (RPA).

status. These attachment specific patterns are visualized by the graph in **Figure 2**.

Table 1 shows and LSD *post hoc* tests ($p < 0.05$) confirmed that insecure-dismissing subjects' parietal asymmetry scores were relatively decreased (inferring an increase in RPA) during each of the emotional retrieval conditions as compared to the initial resting state.

Insecure-dismissing subjects' parietal asymmetry scores during the emotional retrieval conditions did not differ from each other. However, they were significantly lower during each of the emotional conditions as compared to the final resting state, which -with regard to brain activity- itself did not differ from the initial resting state. Thus, there seems to be a "back-to baseline-recovery" following performance of the emotional task in this group. A very similar pattern emerged for the insecure-preoccupied attachment group, who also showed lower parietal asymmetry scores during each of the emotional conditions (which again did not differ from each other) as compared to the initial resting state. The "back-to-baseline-recovery" in insecure-preoccupied subjects, however, was only significant for the anger condition. In contrast to the two insecure groups, parietal asymmetry scores in securely attached subjects did not indicate any changes in hemispheric activity depending on experimental manipulation. LSD *post hoc* testing confirmed there were no significant differences between any of the five conditions in this group.

In addition to these attachment-related patterns, **Figure 2** also indicates differences between the three groups with regard

TABLE 1 | Parietal asymmetry scores during rest and emotional memory retrieval by attachment group.

Attachment Group	Condition *M (SD)*					*n*
	Initial resting state	Happiness	Sadness	Anger	Final resting state	
Secure	$0.15\ (0.21)^{a}{}_{1}$	$0.11\ (0.20)^{a}{}_{1}$	$0.10\ (0.28)^{a}{}_{1}$	$0.10\ (0.27)^{a}{}_{1}$	$0.13\ (0.23)^{a}{}_{1}$	21
Insecure-dismissing	$0.59\ (0.30)^{a}{}_{2}$	$0.39\ (0.30)^{b}{}_{2}$	$0.41\ (0.33)^{b}{}_{2}$	$0.41\ (0.35)^{b}{}_{1}$	$0.53\ (0.36)^{a}{}_{2}$	14
Insecure-preoccupied	$0.15\ (0.32)^{a}{}_{1}$	$-0.13\ (0.17)^{bc}{}_{3}$	$-0.14\ (0.22)^{bc}{}_{1}$	$-0.28\ (0.36)^{b}{}_{2}$	$0.02\ (0.25)^{ac}{}_{1}$	5

Means, standard deviations, and statistical significance. Columns: Different Numbers ($_{1-3}$) indicate that the difference between attachment groups was significant within the respective condition, $p < 0.05$ in post hoc testing (LSD). Lines: Different letters ($^{a-c}$) indicate that the difference between conditions was significant within the respective attachment group.

to hemispheric brain activity across conditions (indicated by the main effect). **Table 1** shows that in the insecure-dismissing group parietal asymmetry scores were significantly higher than in the other two groups during each resting state and each emotional memory retrieval condition (LSD-*post hoc* comparison, $p < 0.05$), except for the difference between the insecure-dismissing and secure group in the anger condition, which did not reach statistical significance. In the insecure-preoccupied group, parietal asymmetry scores were significantly lower than in the dismissing group. These differences were consistent over all conditions. Insecure-preoccupied subjects also showed lower parietal asymmetry scores when compared to the secure group, but only in the happiness and the anger retrieval condition.

DISCUSSION

In this study, we were looking at attachment-related differences in EEG asymmetries at rest and during the retrieval of emotional memories. Thereby, we focused on both frontal and parietal asymmetries assuming to find differential patterns with regard to attachment in both regions.

Attachment and Frontal EEG Asymmetry

Trait Dependent Frontal EEG Asymmetry

Concerning differences in frontal EEG asymmetries we found a specific pattern of hemispheric activation across the three attachment groups. As expected, we found relatively increased RFA in subjects with an insecure-dismissing attachment representation as compared to those with a secure attachment representation during the initial resting state. In consistency with the approach/withdraw model applied to frontal EEG asymmetry numerous other studies have found relatively increased RFA to be associated with negative affect and withdrawal tendencies (e.g., Hane et al., 2008; also see Davidson, 1992). This interpretation fits well with the phenomenon of insecure-dismissing attachment. According to attachment theory, repeatedly experiencing an irresponsive or rejecting caregiver a child learns to avoid the expression of negative affect (Bowlby, 1969). Assuming stability of the internal working models of attachment from childhood into adulthood, insecure-dismissing adolescents and adults tend to withdraw from negative stimuli as an adaptive strategy to regulate their emotions by, for example, paying less attention to negative stimuli (Hazan and Shaver, 1994; Simpson et al., 1996; Cooper et al., 1998). In line with our finding, Rognoni et al. (2008) found an increase in resting RFA in avoidantly attached subjects as assessed via self-report. Also, Dawson et al. (2001) found insecurely attached children to show decreased left frontal asymmetry as compared to securely attached ones. Taken together our findings provide further evidence for a stable pattern of greater withdrawal (or less approach) motivated tendencies in insecure-dismissing subjects to show on a neurophysiological level. Noteably, there is strong evidence that this frontal hemispheric pattern is associated with emotional disorders like depression in infants and adults (for a review see Thibodeau et al., 2006).

Regarding the insecure-preoccupied group we did not find an elevated RFA, which is in contrast to Rognoni et al.'s (2008) study, who found this pattern in both insecure as compared to the secure groups. However, we found insecure-preoccupied subjects to show relatively increased LFA during rest. Even though the difference to the secure group failed to reach significance (perhaps partially due to the small size of the sub-sample) this finding points in the right direction as it is theoretically well founded. Insecure-preoccupied subjects tend to hyper-activate the attachment system and report about childhood experiences eliciting highly intense emotions. Indeed, left frontal hemisphere activation is associated with approach-related motivation, coping and proactive social behavior (Davidson, 1992; Master et al., 2009; Licata et al., 2015). However, relatively increased LFA has also been found in dispositional anger which can be regarded an approach related tendency as well (Harmon-Jones and Allen, 1998). Thus, insecure-preoccupied subjects' frontal asymmetry scores at rest may indicate that they are more prone to approach rather than withdraw from emotional challenges. However, this tendency may be rather accompanied by negative emotions like anger, which may contribute to the assumption that attempts to resolve their entanglement rather tend to fail.

The secure group's frontal asymmetry scores were distributed around zero indicating rather symmetrical brain activity during rest. This is in agreement with Rognoni et al.'s (2008) findings. It could be interpreted in light of securely attached persons' flexibility to differentially react to various environmental challenges without being predisposed to withdraw or approach.

State Dependent Frontal EEG Asymmetry

While attachment-related differences in frontal asymmetry could be well identified during rest, significant differences between attachment groups could not be found during phases of emotional memory retrieval intended to induce specific affective states. It could be assumed that attachment differences in frontal asymmetry scores rather represent a trait variable and thus are less affected by the experimentally induced affective state. Indeed, frontal asymmetry have shown to be unaffected by emotional valence in other studies using emotional tasks as well (e.g., Hagemann et al., 2005; Feng et al., 2012; Mennella et al., 2015). Moreover, in the current study the main effect for attachment diminished for frontal asymmetry during the retrieval of emotional memories. Thus, it may also be that the high emotional involvement induced by all three types of memories activated and deactivated the approach/withdrawal system in a more complex way obliterating previous differences between attachment groups. Future research may address this issue by, for example, examining whether the nature of the emotional memory may account for this non-finding. It could be possible, that specifically focusing on attachment relevant memories is a more powerful approach to elicit differences in emotional memory processing with regard to attachment security.

Attachment and Parietal EEG Asymmetry

Trait Dependent Parietal EEG Asymmetry

Regarding the parietal region, we found that, during a resting state, insecure-dismissing subjects elicited significantly higher asymmetry scores as compared to secure and insecure-preoccupied subject (reflecting decreased RPA in insecure-dismissing individuals) which is in line with our hypothesis. Such right-sided parietal hypo-activity has repeatedly been related to reduced arousal and low emotionality (Shankman et al., 2005; Hayden et al., 2008). This neurophysiological evidence fits with the assumption of insecure-dismissing subjects to be predisposed to show inattentiveness to emotional stimuli. Concluding from our findings this inattentiveness may result from a larger threshold to be emotionally affected due to trait hypo-arousal, which is in line with Kobak and Sceery (1988), who claimed that the insecure-dismissing attachment pattern is characterized by hypo-activation of emotions.

Notably, it has been suggested that relatively decreased RPA represents an endo-phenotype for depression (Bruder et al., 1997; Kentgen et al., 2000; also see Stewart et al., 2011). Indeed, as shown in an overview by Dozier et al. (2008) there is abundant evidence linking insecure attachment to the development of affective disorders in adulthood. This also includes the insecure-dismissing state of mind. Moreover, Duggal et al. (2001) reported that insecure attachment (both resistant and avoidant) predicted depression in adolescence. According to Fonagy et al. (1996) parents of depressed persons were rated as less supportive and more rejecting. Taking the developmental perspective, experiences with an irresponsive and rejecting caregiver may lead to an inner working model of the self as not loved and unworthy and may hinder the child to develop appropriate emotion regulation strategies. Low self-esteem as well as a restricted ability for emotional regulation are regarded as risk factors for the development of depression (e.g., McCauley et al., 2001). Thus, our finding on decreased RPA (as well as increased RFA) in insecure-dismissing subjects may represent the biological substrate that signifies vulnerability to depression in these individuals.

While decreased RPA during rest was found in the insecure-dismissing group, individuals with a secure and insecure-preoccupied attachment representation did not differ with respect to parietal asymmetry during rest. This similarity between secure and insecure-preoccupied attachment groups applies to our findings on frontal asymmetry as well, indicating a common trait-like emotional system in both groups that clearly differs from insecure-dismissing subjects. According to Kobak and Sceery (1988) a main difference between insecure-dismissing and preoccupied persons relates to the activation of emotions. While the insecure-dismissing pattern is characterized by emotional hypo-activation, hyper-activation is typical for the insecure-preoccupied pattern. Thus, although pre-occupied persons have difficulties to regulate emotions appropriately, a high sensitivity or attentiveness to emotional information may be assumed for them comparable to secure persons.

Regarding this assumption our findings can be interpreted in line with the "right-hemisphere hypotheses" that claims that the right hemisphere is especially involved in the automatic generation of emotional responses (Gainotti, 2000; Hagemann et al., 2005; for a review see Borod, 1993). Testing the hypotheses, Hagemann et al. (2005) found greater right-sided activity to be associated with the intensity of felt emotions and that this cortical activity pattern was especially evident in the parietal region.

Thus, it might be that our finding on increased resting RPA in secure and insecure-preoccupied as compared to insecure-dismissing individuals indicates a trait-like sensitivity to emotional information while their decreased RFA reflects both their tendencies to explore affective states instead of using withdrawal strategies.

State Dependent Parietal EEG Asymmetry

As expected, we found emotional memory retrieval to affect parietal hemispheric asymmetry, but again, this finding was given irrespective of emotional valence. Thus, the valence or type of the retrieved memory did not systematically affect brain processing in the parietal region and inter-individual differences of attachment groups remained relatively stable or –with regard to the insecure-preoccupied group- became even more pronounced (at least for anger and happiness). Regarding the "right-hemisphere hypotheses" mentioned above, our non-findings of an effect of emotional valence are in line with empirical evidence that suggests that impairments in the right cortical region have tremendous effects on both positive and negative emotional responses (for a review see Borod, 1993).

More interestingly, there appeared to be a shift towards lower parietal asymmetry scores during the emotional memory retrieval task in both insecure groups but not in the secure group. Interestingly, a comparable shift has also been found in anxious individuals during a fear inducing narrative task (Heller et al., 1997). This decrease in right-sided alpha power is reflective of an increase in RPA that can be interpreted as enhanced arousal (Heller et al., 1997; Metzger et al., 2004).

Notably, we found that by the final episode at rest (following the retrieval of emotional memories), parietal asymmetry scores in insecure subjects have increased again showing this specific pattern of brain activity to be clearly state-dependent.

Our findings suggest that parietal asymmetry during emotional memory retrieval may be indicative of one's ability to effectively regulate emotions. Both insecure attachment groups characterized by a restricted ability to regulate emotions, albeit in a very different way, show an increase of RPA, that could not be observed in the secure subjects characterized by high emotional regulation capacities. Interestingly, during the retrieval of happiness and anger (but not sadness) evoking memories, the difference between the insecure-preoccupied and the secure group reached significance. As we assume both of these affective states to be more likely to elicit increased arousal as compared to sadness, they seem to be more powerful in the detection of trait-dependent arousal-related cerebral differences between attachment groups.

In sum, these findings lead to the conclusion that in our study insecurely attached individuals were more affected by the memory retrieval task, probably because confrontation with highly salient emotions provided a greater challenge to their restricted emotion regulation capacities. Interestingly, both insecurely attached groups, the insecure-dismissing as well as the insecure-preoccupied one, showed this shift, even though they started at different baselines. Thus, they may differ from one another with respect to attention and sensitivity to emotional information, however, when directly confronted with personally highly salient emotions induced by experimental induction, on a neurophysiological level, they appear to respond very similar, as both their regulation strategies are rather ineffective. Interestingly, Beijersbergen et al. (2008) found that while during the AAI insecure-dismissing attached adolescents were capable of remaining a physiological state that was comparable to that of secure ones, their emotion regulation capacities were highly challenged during a family interaction task as indicated by increased heart rate reactivity. Thus, including our findings it can be suggested that the effectiveness of emotion regulation strategies typical for insecurely attached individuals are strongly depends on the nature of the emotional challenge.

The pattern of the securely attached group's hemispheric brain activity during emotional memory retrieval is quite different. According to attachment theory they are expected to be sensitive and attentive to emotional information, still, emotional memory retrieval did not affect parietal hemispheric activity (no increased arousal) in this group. Indeed, this may be due to their high capacity to regulate emotional states. Equally important,securely attached individuals by theory are capable of freely evaluating meaningful experiences and report them in a coherent manner. In a recent study, Spangler and Zimmermann (2014) found young adolescents with a history of secure attachment to be more aware of their emotions as compared to subjects with an insecure attachment history. Furthermore, they were found to be more capable of communicating affective states as well as using social emotion regulation strategies. These competencies may lead to a more effective integration of highly salient experiences, and thus, may account for their well-regulated affective state during emotional memory retrieval. Finally, emotional memory retrieval in our study may have been less challenging for securely attached individuals.

Taken together, it seems that, while the differences in parietal asymmetry during resting state reflect differences between the attachment groups with respect to sensitivity to emotional information, the differences in parietal asymmetry during emotional memory retrieval appear to rather reflect differences in emotion regulation capabilities specific for the attachment groups.

Regarding our methodological approach of including both the frontal and parietal asymmetries in our analyses, it is noteworthy to mention, that we have found effects of attachment to be more pronounced at parietal sites and that the right hemisphere seems to play a prominent role in affect regulation, which has been suggested and discussed in other studies (see Hagemann et al., 2005).

CONCLUSION

Summing up, differences in attachment representations were found to affect both the frontal and parietal organization of hemispheric asymmetry at rest and (for parietal region only) during the retrieval of emotional memories, however, irrespective of valence.

More precisely, during a resting state we found insecure-dismissing subjects to show increased RFA and at the same time a decrease in RPA. This finding on trait-like hemispheric asymmetries in insecure-dismissing subjects corresponds to their disposition to show –on the one hand- tendencies to withdraw rather than approach, and –on the other hand- lower state-like arousal in comparison to the other attachment groups. Notably, this specific pattern in hemispheric asymmetries has also been found to be stable in dysphoric individuals (Mennella et al., 2015), and thus, may indicate of an increased vulnerability to depression in insecure-dismissing subjects.

Moreover, when compared to the secure group, insecure-dismissing and insecure-preoccupied subjects showed reduced and enhanced state-dependent arousal, respectively, as indicated by parietal asymmetry scores during emotional memory retrieval. At the same time, both insecurely attached groups seemed to rather use state-dependent dysfunctional strategies to regulate affective states related to personally highly salient emotional experiences. This assumption was concluded since when unlike securely attached individuals they showed a clear shift in RPA towards increased arousal during the emotional task. These specific neurophysiological substrates indicating less effective emotion regulation may again be viewed as a vulnerability to develop an affective disorder in insecurely attached individuals.

LIMITATIONS

The strength of this study lies in the application of an emotional imagery task that we assume a valid measure to probe the neural substrates of emotion regulation as subjects chose upon a personally highly salient emotional memory. However, it is crucial to note that there was no control condition, in which participants were exposed to an autobiographical episode with a neutral valence. Still, it may be hard to isolate a salient neutral memory that is not contaminated by any emotional tone. This is why we chose to compare neural activation during emotional memory retrieval with pre- and post-measurement resting state conditions. In future studies, it could be useful to differentiate between attachment related and non-attachment related emotional memories. Thereby, one may be more successful in eliciting attachment related differences in frontal hemispheric asymmetry during the processing of emotional information. Such approach would also shed light on the generalizability of our findings to attachment related differences in emotion regulation in late adolescence. Furthermore, even though the distribution of attachment classification is in agreement with meta-analytic findings (Van IJzendoorn, 1995), our analyses are restricted to reduced statistical power with regard to the small sample size, in particular that of the insecure-preoccupied group. Also, since this was the first study of its kind, future studies are needed to replicate and potentially extend our findings. Another limitation of this study is that the design does not allow to draw upon assumptions on the causal mechanisms between neural measures and emotion regulation strategies associated with different attachment representations. While associations between frontal asymmetry and attachment as well as maternal depressive symptoms have already been found in young children (e.g., Field et al., 1995; Dawson et al., 1997; Dawson et al., 2001), a recent study's findings suggest that frontal hemispheric asymmetry may be less influenced by environmental factors (Licata et al., 2015). It would be very interesting to apply a longitudinal approach to attachment related emotion regulation strategies and the neural circuits that are associated with the phenomenon beyond childhood.

ETHICS STATEMENT

The study was conducted in accordance with the Code of Ethics of the German Psychological Association (from 09/28/2004), which is essentially based on the Code of Ethics of the APA (Ethical Principles of Psychologists and Code of Conduct, American Psychologist, 2002, 57, 1060–1073). According to the rules of the German Research Foundation, it was not required to apply for a formal vote for this study, because (1) the participants were healthy (no patient groups), (2) no invasive methods were used, and (3) their participation did not present any risk to the participants. Finally (4), for studies using ERP assessments, a formal vote is only required if subjects' age is either below 14 or above 65 years.

The participants were informed about the study's aims and methods. In addition, they were informed that (1) their participation is voluntary and that they can withdraw from it any time without stating reasons, and (2) that the data were treated according to the data protection law and saved anonymously. Each participant signed the informed consent form before participation.

AUTHOR CONTRIBUTIONS

MK: collection, design, analysis and interpretation of data, literature research, writing. RL: concept, design, collection, analysis, and interpretation of data, literature research. GS: concept, design, supervision, writing, critical review.

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Attachment Representation Moderates the Influence of Emotional Context on Information Processing

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The induction of emotional states has repeatedly been shown to affect cognitive processing capacities. At a neurophysiological level, P3 amplitude responses that are associated with attention allocation have been found to be reduced to task-relevant stimuli during emotional conditions as compared to neutral conditions suggesting a draining impact of emotion on cognitive resources. Attachment theory claims that how individuals regulate their emotions is guided by an internal working model (IWM) of attachment that has formed early in life. While securely attached individuals are capable of freely evaluating their emotions insecurely attached ones tend to either suppress or heighten the emotional experience in a regulatory effort. To explore how attachment quality moderates the impact of emotional contexts on information processing event-related potentials (ERPs) in 41 individuals were assessed. Subjects were instructed to detect neutral target letters within an oddball paradigm. Various images taken from the International Affective Picture System (IAPS) served as background pictures and represented negative, positive and neutral task-irrelevant contexts. Attachment representation was assessed using the Adult Attachment Interview (AAI) and individuals were assigned to one of three categories (secure, insecure-dismissing, insecure-preoccupied). At a behavioral level, the study revealed that negative emotionally conditions were associated with the detection of less target stimuli in insecure-dismissing subjects. Accordingly, ERPs yielded reduced P3 amplitudes in insecure-dismissing subjects when given a negative emotional context. We interpret these findings in terms of less sufficient emotion regulation strategies in insecure-dismissing subjects at the cost of accurate behavioral performance. The study suggests that attachment representation differentially moderates the relationship between emotional contexts and information processing most evident in insecure-dismissing subjects.

Keywords: attachment, emotion, P3, ERP, EEG, IAPS

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INTRODUCTION

The first central key for the development into a social human being capable to interact properly with others is the attachment formed between a child and his or her primary caregiver (Sroufe, 1988). The caregiver is obliged to convey security and protection, and invite for exploration. Nevertheless, caregivers differ in their ability to handle infant emotions, what is most obvious in situations eliciting distress or anxiety. Parental sensitivity provides a developmental context for the child in which felt security is reliably balanced through the attachment figure (Ainsworth et al., 1978). Attachment theory postulates that these dyadic experiences of emotion regulation become internalized with time, resulting in internal working models (IWMs) of attachment (Bretherton and Munholland, 2008), which can be assigned to three prototypical patterns. Securely attached individuals have IWMs of their caregiver as available and responsive to their emotional needs and of the self as being worthy of love. In contrast, insecurely attached individuals have IWMs of their attachment figure as unavailable (insecure-dismissing) or unpredictable in behavior (insecure-insecure-preoccupied) and the self as being unworthy of love. IWMs resulting from different experiences are assumed to be carried over into adulthood and influence the way individuals organize their feelings, thoughts and behaviors in attachment-relevant situations (e.g., Bowlby, 1969) and especially how they handle their emotions (Cassidy, 1994). In particular, it has been theorized that securely attached individuals have free access to both negative and positive emotions. They are able to perceive and express their emotional state, which allows them a flexible evaluation and regulation within an emotional context. In contrast, insecurely attached individuals show deficits in their emotion regulation capacities. According to attachment theory insecure-dismissing subjects tend to hypo-activate emotional states as they have experienced rejection to expressed negative emotions earlier in life. Finally, based on the experience of a caregiver who only inconsistently responded to their psychological needs, insecure-preoccupied subjects are easily over-whelmed by negative emotions that—once activated—tend to dominate their mental state. The association between attachment security and a flexible regulation of emotions has been well established, including contexts that are not directly linked to the original attachment dyad (e.g., Kobak and Sceery, 1988; Zimmermann et al., 2001). In addition, attachment-related differences in emotional processing have been found to be evident on subconscious levels measured by biological markers such as endocrinological (e.g., Spangler and Grossmann, 1993), neurophysiological (e.g., Dawson et al., 2001) or electromyographic (e.g., Spangler et al., 2010) responses.

While during infancy and early childhood individual differences in IWMs of attachment are assessed by standardized observation of attachment behavior towards the caregiver (e.g., in the strange situation; Ainsworth et al., 1978), in adulthood they are assessed on a representational level. This can be done explicitly by the use of self-report questionnaires (e.g., Fraley et al., 2000) or implicitly by the use of the Adult Attachment Interview (AAI; George et al., 1985) or the Adult Attachment Projective (AAP; George et al., 1999).[1] Self-report measures—mainly used within the social psychology tradition of attachment research—focus on believes about personal attachment relationships. In contrast, the assessment of attachment representation by the AAI and the AAP, developed within the developmental psychology tradition, is based on the coherence of mind in talking about one's own attachment history (AAI) and the coherence of narratives elicited through attachment relevant pictures (AAP), respectively. Indeed, associations between explicit and implicit methods of adult attachment are only modest (de Haas et al., 1994; Crowell and Treboux, 1995). Focusing on experiences with primary caregivers and giving details on how emotions in attachment-related situations are regulated by an individual (e.g., Allen and Miga, 2010), the AAI is often marked as the gold standard.

Early childhood appears to be a critical period for the development of the IWM of attachment. At the same time, the first 2 years of life are crucial for the human brains' structural development. In this developmental period neural circuits become organized and adjusted to the child's environment (Rutter, 2002). This is why during the early years these neuronal changes are highly affected by experiences with the attachment figure (Luby et al., 2012; Whittle et al., 2015). In adulthood, cross-sectional studies have shown that individuals with different attachment qualities, presumably resulting from attachment experiences during early development, differ regarding the neural processing of emotional information as assessed by brain imaging and EEG measures (e.g., Schore, 1994; Vrtička et al., 2008; Zhang et al., 2008; Suslow et al., 2009; Dan and Raz, 2012; Leyh et al., 2016; for a review, also see Gander and Buchheim, 2015). For example, using a self-report measure Vrtička et al. (2008) found avoidant attachment, associated with low emotional availability of the attachment figure, to be related to lower responses of the primary somatosensory cortex to masked sad faces. The authors interpreted the finding as a habitual unwillingness to deal with a partner's distress and his or her needs for proximity. Furthermore, anxious attachment was related to a left amygdala response evoked by angry faces when associated with negative feedback. Several studies indicate that at an automatic processing level individuals with anxious attachment quality are more responsive to emotional facial signals than securely attached individuals (Vrtička et al., 2008; Donges et al., 2012).

Neurophysiological activation underlying social-emotional processes can best be investigated by using event-related potentials (ERPs) because of their high temporal resolution. Currently available ERP studies provide evidence of attachment-related differences in neuronal processing of facial emotions (Zhang et al., 2008; Fraedrich et al., 2010; Escobar et al., 2013; Leyh et al., 2016). While early ERP responses usually index bottom-up sensory mechanisms, which are sensitive to stimuli characteristics and therefore indicate pre-attentional processes, top-down control mechanisms occur at later processing stage and reflect in mid-latency ERP responses (>300 ms) interpreted as correlates of attention allocation, arousal, control and/or awareness (Polich, 2007). There is convincing evidence that later ERP components are modulated by attachment representation. According to Zhang et al. (2008), avoidantly attached subjects, in response to emotional facial expressions,

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[1] To distinguish between explicitly and implicitly assessed attachment categories, we used the different terminology that commonly applies to both approaches: avoidant (explicit measures) vs. insecure-dismissing (implicit measure).

again had lower N400, which is negative going component associated with semantic integration (Kutas and Federmeier, 2009). Moreover, evidence suggests that mothers with insecure attachment representation show lower P3 amplitudes than securely attached mothers after presentation of infant emotion pictures (Fraedrich et al., 2010; Leyh et al., 2016). The P3 component reflects task characteristics like cognitive demand (Isreal et al., 1980) and task difficulty (Polich, 1987). It is influenced by stimulus novelty (Polich, 2007) as well as subjects' arousal level (Kahneman, 1973). The underlying processes are thought to be the inhibition of extraneous neural processes associated with attention allocation and memory (Polich, 2007). In combination with imaging studies it can be assumed that the dampened neural response to infant emotion pictures reported above indicates deficits in perception of and responsiveness to emotional stimuli in insecure-dismissing subjects. However, it is still unclear how neural processing is altered in insecure-preoccupied attached subjects. It remains open whether restrictions in neurophysiological processing are also given in subjects with an insecure-preoccupied attachment representation, as due to the small group sizes this group frequently has neither been included in systematic analyses nor has it been combined with the insecure-dismissing group to form a group of insecure subjects (e.g., Leyh et al., 2016).

Taken together, these findings suggest that experimental paradigms targeting the processing of social-emotional stimuli are capable of activating the attachment system as they have repeatedly shown to reveal attachment related differences at both the behavioral as well as the neurophysiological level. From an attachment theory perspective this makes perfect sense, as especially situations triggering negative emotions with a need for emotional regulation are believed to activate the attachment system, hence, shedding light on individual strategies to handle these emotions. However, the studies reported above have solely focused on altered processing of emotional information with regard to attachment rather than looking at how emotional contexts affect individual processing of neutral information. Indeed, such knowledge would be highly relevant for understanding an individual's functioning in everyday life in the face of emotional stressors. Addressing this void in the literature the main objective of the current study was to investigate whether emotional contexts influence the neuronal processing of neutral (non-emotional) information depending on attachment.

The studies reported above provide evidence on the influence of attachment qualities on the processing of emotional information which can be expected on the base of assumptions guided by attachment theory. Based on these findings it can be assumed that effects of attachment quality on cognitive processing are also evident when challenging subjects' capacities of emotional regulation by embedding neutral task-relevant information in emotional (especially negative) contexts. In insecure subjects inefficient attempts to regulate negative emotions provoked by a negative emotional context may lead to an enhanced allocation of cognitive resources to the processing of the task-irrelevant emotional information. Consequently, there may be a lack of cognitive capacities needed to effectively process task-relevant information.

Regardless of attachment, Meinhardt and Pekrun (2003) investigated the impact of emotions on attentional resource allocation in an ERP-experiment by combining auditory and visual stimulation. They examined the P3 in an oddball task using auditory stimuli during presentation of positive, negative or neutral emotional pictures or by imagination of emotional events. They found that the P3 amplitude to auditory stimuli was reduced during emotional compared to neutral conditions. This supports that emotional states influence cognitive processing. Furthermore, Albert et al. (2010) showed the impact of emotional contexts on response inhibition to neutral stimuli in an ERP-experiment using a Go/No-go task. They presented two different letters (as Go and No-go-stimuli) on the background of positive, negative and neutral pictures, and found a modulating effect of emotional contexts on the no-go P3. Larger frontocentral no-go P3 amplitudes and stronger anterior cingulate cortex activation were found to stimuli that required withholding a pre-potent response during positive contexts compared to negative contexts. This shows on a neuronal level that more inhibitory control is necessary to withhold a pre-potent response in positive contexts.

As differences in the quality of attachment are associated with the ability to efficiently regulate emotions, attachment representation might, consequently, be an important moderator between task-irrelevant emotional contexts and the processing of neutral, task-relevant information. Thus, the current study aimed to test this assumption by investigating the role of attachment on cognitive performance in emotional and neutral contexts as indexed by the ERP- component P3, using an oddball paradigm.

Securely attached individuals are assumed to be more capable to effectively regulate emotional states, expectably enabling them to dedicate more cognitive resources to a given task. By theory, a securely attached individual's regulatory capability especially comes to light when dealing with negative emotions. Consequently, the impact of negative emotional contexts on task relevant processing of embedded neutral information might be less intense. Thus, we hypothesized that especially negative emotional contexts reduce P3 amplitudes during information processing in insecure-dismissing and presumably insecure-preoccupied attached individuals, compared to securely attached individuals.

MATERIALS AND METHODS

Participants

The sample consisted of 42 right-handed young adults (22 female, 20 male) ranging from 17 to 22 years ($M = 19.46$, $SD = 1.27$). One and five of the participants have graduated from secondary school after 9 years (low level) and 10 years (medium level). Twelve participants were striving for a high level graduation (after 12 or 13 years), 24 already had graduated on this level. One participant dropped out before the completion of the study. Thus, data from 41 individuals was used for statistical analysis. Participants were recruited with flyers to take part in a larger overall study, which included three laboratory visits and they were compensated 40 € in total.

Measures

The current article refers to data collected at the first and third laboratory assessment. At the first laboratory visit attachment representation (AAI; George et al., 1985) and handedness (EHI; Oldfield, 1971) were assessed. Right-handedness was confirmed in all individuals. Within a few weeks, there were two further laboratory assessments to collect neurophysiological data using various paradigms. The current article refers to the investigation of relations between attachment representations and ERP data assessed during the final laboratory visit.[2]

Adult Attachment Interview

Attachment representation was assessed by the AAI (George et al., 1985), a semi-structured interview focusing on significant childhood experiences, attachment relevant situations in childhood, the evaluation of these experiences as well as the current relationship to the primary caregivers. Transcripts of these interviews were coded on the basis of Main et al. (2002) manual. The judgment of the narrative coherence, idealization and derogation of parents and/or attachment, as well as current preoccupying anger and passivity of speech results in one of the three main attachment categories: Secure (F), Insecure-Dismissing (Ds), Insecure-Preoccupied (E). The AAI's reliability and validity is well established (for a review, see Gloger-Tippelt, 2001).

In the present study, the German translation of the original English AAI protocol was used (Gloger-Tippelt, 2001). The AAIs were conducted by the third author and a psychology student after receiving extensive training. Interviews were audio-taped, transcribed and all personal information about the participants was removed from the transcripts. The transcripts were coded by a certified coder.[3] To test reliability 10 randomly selected AAIs were coded by a second certified coder.[4] Coding agreement was 90% ($\kappa = 0.84$, $p \leq 0.001$).

ERP Experiment

Stimuli

Oddball stimuli consisted of one out of two white letters, a frequently shown "M" (80%; standard stimulus) and a rarely shown "W" (20%; target stimulus). To increase perceptibility they were shown against a black square sized 2.7 cm × 2.7 cm. Nine pictures taken from the International Affective Picture System (IAPS; Lang et al., 2008) were used as context pictures. They were sized 38.6 cm × 29 cm filling the whole visual background of the 19" screen. Background pictures were presented with subtending 10.2° by 7.8° of visual angle, oddball stimuli with 0.45° by 0.45° of visual angle. Background context pictures were selected from the IAPS on the basis of normative valence ratings (vr). Selection criteria were as follows: negative: vr < 1.98 (PR = 05); neutral: $4.7 \leq \text{vr} \leq 5.3$; negative: vr < 7.57 (PR = 95). The range of the vr of the pictures used was between 1.52 and 1.80 for negative pictures (IAPS No. 3015, 3060, and 3530), between 5.12 and 5.33 for neutral pictures (IAPS No. 2745.1, 5530, and 7493), and between 8.24 and 8.59 for positive pictures (IAPS No. 1710, 2058, and 2165). The mean arousal ratings of the pictures varied as expected, with highest arousal for negative pictures (5.90 to 7.12) and lowest for neutral ones (2.87 to 3.41) and in-between values for positive pictures (5.05 to 5.31). Between conditions, background pictures were matched in mean luminance and spatial frequency using parameter values provided by Delplanque et al. (2007). Mean luminance for positive, neutral and negative pictures were 95, 97, and 113, respectively. There was no significant difference among them ($F_{(2,6)} = 0.46$, ns). Differences regarding the spatial frequency were tested for nine frequency bands (from < 2 to 256–512 cycles per image) and each type of layer (grayscale, red, green, blue) in a multivariate analysis of variance (MANOVA). There was no effect for valence ($F < 1$; ns).

Procedure

During the ERP experiment, participants were seated in a dimly lit, electrical and acoustically shielded cabin in a comfortable chair. The monitor presenting the stimuli was placed in a viewing distance of 115 cm. Prior to the oddball experiment participants were instructed to press a button as fast as possible when detecting the target stimulus ("W"). The task was performed during three emotional context conditions (negative, positive, neutral) that were generated by IAPS stimuli appearing on the screen as background pictures. Emotional context conditions were presented in randomized order and consisted of 390 trials (312 standard/78 target) per condition. Within each emotional context condition there were three blocks (130 trials) each presenting one of three negative, positive, or neutral background pictures, respectively. Each block started with the presentation of three additional standard trials. The order of background pictures within each condition was randomized across subjects. During each block the respective context background picture remained on screen. In every single trial oddball stimuli appeared at the center of the screen against the respective background picture, thus, being embedded in it. This simultaneous presentation of stimuli and background pictures remained on screen for 200 ms followed by an inter-stimulus interval of 1300 ms, during which the oddball stimuli, the white letter, disappeared. After each block participants were asked to push a button to continue the experiment.

The stimulus presentation was controlled by the experimental software Inquisit (Millisecond Software, Seattle, WA, USA). The behavioral responses following standard and target stimuli (button press) were registered in ms after stimulus onset. Correct responses were defined as button press after target presentation.

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[2] During the second laboratory assessment further EEG experiments were conducted to investigate hemispheric asymmetries (see also Kungl et al., under review) and facial emotion processing.

[3] Johanna Behringer, Institute of Psychology, University of Erlangen-Nuremberg, Germany.

[4] Kathrin Beck, Institute fuer Therapieforschung, Munich, Germany.

Data Recording and Analysis

EEG was recorded according to the international 10–20 system with active electrodes based on high-quality Ag/AgCl sensors 5 mm in diameter from 60 electrode sites[5] while keeping impedances below 25 kΩ. To assess eye movements additional electrodes were placed below and above the left eye, as well as next to the outer canthi. The ground electrode was placed at AFz and data was referenced to activity recorded from electrode site FCz. Signals were acquired using BrainAmp Standard amplifier (Brain Products, Gilching, Germany) allowing for the recording of frequencies ranging from 0.016 to 1000 Hz with a resolution of 0.1 μV per bit and a measurement range of ±3.28 mV. Sampling rate for all channels was set to 500 Hz and signals were digitized using a 16 bit A/D converter. Recording and analyzing of the EEG was performed using BrainVision Software (Brain Products, Gilching, Germany).

During offline-processing the EEG signal was re-referenced to the average of the mastoids and digitally filtered using a 0.1 Hz high pass and a 30 Hz low pass filter with a 24 dB/oct gradient. The EEG signal then was segmented into epochs ranging from 200 ms pre- to 700 ms after stimulus onset. The pre-stimulus window of 200 ms was used for baseline-correction. To correct for saccadic eye movements or eye blinks the Gratton and Cole Procedure was applied (Gratton et al., 1983). Further artifacts were removed semi-automatically allowing for voltage steps of 50 μV between sampling points and a voltage threshold of ±70 μV.

Finally, standard and target stimuli segments were averaged for each participant and condition. Based on previous literature and a visual inspection of the grand average waveforms, the P3 was scored as the maximum positive peak between 330 and 600 ms after stimulus onset at midline electrodes Fz, Cz, Pz. With brain activity decreasing from parietal to frontal scalp it was found to show typical scalp topography (Johnson, 1993). In addition, to test whether the effects are consistent and not restrict to the midline channel, lateral electrodes on the parietal site were also included (P3, P1, P2, and P4). Number of correct responses and response latencies (ms) of behavioral responses to target and standard stimuli were stored by the experimental software.

Statistical Analysis

Number of correct responses and reaction times to targets as well as false alarms were analyzed by a two-way MANOVA with a repeated measure factor for context and an independent factor for attachment representation.

To examine the impact of attachment representation on P3 amplitude responses repeated measure MANOVAs were conducted with repeated measure factors for electrode (midline: Fz, Cz, Pz; parietal: P3, P1, Pz, P2, P4), stimulus type (standard vs. target), context (negative, neutral, positive) and an independent factor for attachment representation (secure, insecure-dismissing, insecure-preoccupied). The main focus of analysis was on effects concerning attachment, hence only significant effects including attachment security are reported in detail. Attachment relevant effects were further analyzed *post hoc* using LSD tests. Due to the small sample size of the insecure-preoccupied group, analyses of variances were additionally tested without this group, hereby restricting the analysis on a comparison of the secure and insecure dismissing group.

RESULTS

Attachment Representation

The scoring of the AAIs resulted in the following distribution of attachment representations: There were 22 persons with a secure attachment representation and 19 with an insecure one, among the latter 14 persons had an insecure-dismissing and 5 persons had an insecure-preoccupied attachment representation.

Preliminary analyses showed that attachment representation was not associated with the subjects' age and education ($F_{(2,39)} < 1$, ns). Mean ages were 19.4, 19.6 and 19.4 years for the secure, the insecure-dismissing and the insecure-preoccupied group, respectively. The respective levels of education (on a four-point scale) were 3.5, 3.4, and 3.4. However, there was a significant association between attachment and gender ($\chi^2 = 10.1$, $p < 0.01$). A nearer inspection of the data showed that boys were more frequently found in the insecure-dismissing (11 of 14) and less frequently in secure pattern (6 of 16), while there was no difference within the insecure-preoccupied group (two boys, three girls). Therefore, gender was used as a covariate in the analyses regarding attachment.

Behavioral Data

The attachment × emotional context repeated measure MANOVA for correct target responses with gender as a covariate did not show main effects, but resulted in a significant interaction between emotional context and attachment representation ($F_{(4,72)} = 2.65$, $p \leq 0.05$, $\eta^2 = 0.13$; see **Figure 1**). This interaction was also found after exclusion of the insecure-preoccupied group ($F_{(2,64)} = 4.04$, $p < 0.05$, $\eta^2 = 0.11$). LSD *post hoc* tests ($p < 0.05$) showed that effects of emotional context were only given for insecure-dismissing subjects. These subjects detected fewer targets in the negative emotional context than in neutral or positive contexts (see **Figure 1**). In addition, the number of correct target responses in the negative emotional context was lower in the insecure-dismissing group than each of the other groups. There were no significant effects for false alarms and response times to target (for the means, see **Table 1**).

P3

The grand average waveforms of the P3 responses of the three groups of attachment representations are shown in **Figure 2** for each of the three electrode positions (Fz, Cz, Pz) and separately for positive, neutral and negative emotional context. Comparing the responses to the target and standard stimuli the grand means show the typical response pattern of an oddball paradigm with the typical P3 deflection for the target stimuli. In addition,

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[5] F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, T8, TP9, CP5, CP1, CP2, CP6, TP10, P7, P3, Pz, P4, P8, PO9, O1, Oz, O2, PO10, AF4, AF8, F5, F1, F2, F6, FT9, FT7, FC3, FC4, FT8, FT10, C5, C1, C2, C6, TP7, CP3, CPz, CP4, TP8, P5, P1, P2, P6, PO7, PO3, POz, PO4, PO8.

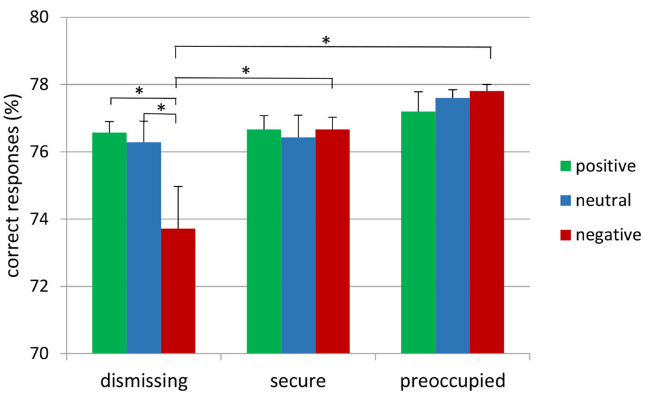

FIGURE 1 | Frequency of correct responses to target stimulus presented on the background of negative, neutral and positive background stimuli in secure, insecure-dismissing and insecure-preoccupied subjects (asterisks indicate significant differences, *$p < 0.05$).

Figure 3 clearly indicates differences in the P3 deflection between the attachment groups.

The four-way repeated measure MANOVA for P3 amplitude responses with the factors electrodes (midline: Pz, Cz, Fz), context, stimulus type, and attachment and with gender as a covariate resulted in a significant main effect for electrode ($F_{(2,74)} = 12.87$, $p \leq 0.001$, $\eta^2 = 0.26$) stimulus type ($F_{(1,37)} = 11.95$, $p \leq 0.001$, $\eta^2 = 0.24$), qualified by a significant two-way interaction between electrode and stimulus type ($F_{(2,74)} = 16.61$, $p \leq 0.001$, $\eta^2 = 0.31$) and by a significant three-way interaction between context, stimulus type and attachment ($F_{(4,74)} = 2.72$, $p \leq 0.05$, $\eta^2 = 0.13$). This three-way interaction including attachment remained significant after exclusion of the preoccupied group ($F_{(2,66)} = 3.54$, $p \leq 0.05$, $\eta^2 = 0.10$). The first three effects including stimulus type and electrode effect (higher amplitudes for target stimuli, increasing amplitudes from Fz to Cz to Pz) depicts the typical P3 effect with an increasing effect from the frontal to the parietal brain area. Regarding the three-way interaction between stimulus type, emotional context, and attachment, *post hoc* multiple LSD comparisons revealed an effect of emotional context only in the insecure-dismissing group in which the P3 amplitude was significantly lower in the negative emotional context than in the positive emotional context. In addition, the P3 amplitudes of the insecure-dismissing group in the negative emotional context were significantly lower than the amplitudes of the secure group.

The four-way repeated measure MANOVA for P3 amplitude responses with the factors electrodes (parietal: P3, P1, Pz, P2, P4), context, stimulus type, and attachment and with gender as a covariate resulted in a significant main effect for electrode ($F_{(4,148)} = 3.45$, $p \leq 0.01$, $\eta^2 = 0.09$) stimulus type ($F_{(1,37)} = 26.26$, $p \leq 0.001$, $\eta^2 = 0.42$), qualified by a significant two-way interaction between electrode and stimulus type ($F_{(4,148)} = 4.48$, $p \leq 0.01$, $\eta^2 = 0.11$) and by a significant three-way interaction between context, stimulus type and attachment ($F_{(4,148)} = 2.57$, $p \leq 0.05$, $\eta^2 = 0.12$). The first three effects including stimulus type and electrode effect depicts the typical P3 effect regarding central and lateral brain areas with higher amplitudes for target stimuli with the highest amplitude at Pz and decreasing amplitudes at lateral sites P1 and P2 and still more decreasing at P3 and P4 (see **Table 2**). Regarding the three-way interaction between stimulus type, emotional context, and attachment, *post hoc* multiple LSD comparisons revealed an effect of emotional context only in the insecure-dismissing group in which the P3 amplitude was significantly lower in the negative emotional context than in the neutral and positive emotional context. In addition, the P3 amplitudes of the insecure-dismissing group in the negative and neutral emotional context were significantly lower than the amplitudes of the secure group.

After exclusion of the preoccupied group the three-way interaction between emotional context, stimulus type, and attachment failed to reach significance. Instead there was a main effect of attachment ($F_{(1,33)} = 5.48$, $p \leq 0.05$, $\eta^2 = 0.14$) qualified by a two-way interaction between stimulus type and attachment ($F_{(1,33)} = 4.55$, $p \leq 0.05$, $\eta^2 = 0.12$). As can be seen from **Table 2**, the P3 amplitude in response to target is higher in secure than in insecure-dismissing subjects.

TABLE 1 | Frequency of correct responses and false alarms as well as response times depending on emotional context and attachment representation.

	Emotional context		
	Positive	**Neutral**	**Negative**
Correct responses			
Secure	76.7 (1.6)	76.4 (3.0)	76.7 (1.7)
Insecure-dismissing	76.6 (1.2)	76.3 (2.3)	73.7 (4.7)
Insecure-preoccupied	77.2 (1.2)	77.6 (0.5)	77.8 (0.5)
False alarms			
Secure	1.2 (1.7)	1.7 (2.1)	1.0 (1.6)
Insecure-dismissing	0.9 (1.3)	1.5 (1.4)	1.9 (1.9)
Insecure-preoccupied	0.2 (0.4)	0.6 (1.3)	1.2 (2.7)
Response time			
Secure	507.5 (57.3)	520.3 (66.3)	511.3 (58.8)
Insecure-dismissing	502.6 (61.2)	506.7 (58.6)	519.7 (53.2)
Insecure-preoccupied	480.6 (34.1)	499.8 (26.2)	495.2 (42.4)

Means and standard deviations.

DISCUSSION

The current study aimed to link attachment representation to cognitive and emotional information processing on a behavioral and neurophysiological level. At the behavioral level, subjects with insecure-dismissing attachment representation responded less frequently with correct responses to targets in negative contexts than securely or insecure-preoccupied attached subjects, which indicates that they recognized fewer target stimuli. On a neurophysiological level, ERP-data showed that subjects with insecure-dismissing attachment representation had smaller P3 amplitudes to target stimuli when they were embedded within a negative as compared to a neutral and positive context, which was not the case in the secure and insecure-preoccupied attachment groups. These findings support the hypothesis that attachment representation moderates the association between emotion and information processing.

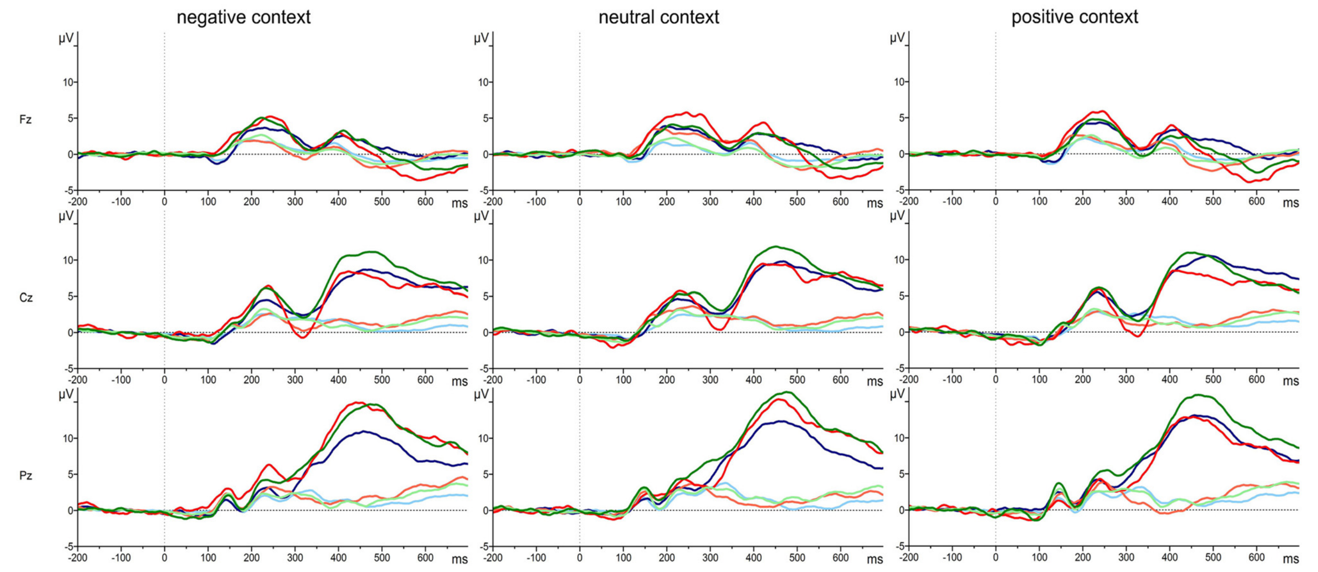

FIGURE 2 | Grand average waveforms of P3 responses to target stimuli (dark colored lines) and standard stimuli (light colored lines) in positive, neutral and negative emotional context for Fz, Cz and Pz in persons with a secure (green line), insecure-dismissing (blue line) or insecure-preoccupied attachment representation (red line).

Behavioral Results

In the present study, negative emotional context reduced hit rates to neutral stimuli in insecure-dismissing compared to securely attached subjects. Similar findings have been reported in several studies showing restrictions in processing negative facial expressions shown by avoidantly attached subjects as assessed by self-report questionnaire. For example, Dan and Raz (2012) investigated responses to angry and neutral faces in subjects with different attachment qualities. They reported slower response times in trials with angry faces as compared to trials with neutral faces in subjects with an avoidant attachment. These differences were not found in the secure or anxious attachment groups. Similarly, Escobar et al. (2013) reported slower reaction times to stimuli with negative valence in insecurely attached adolescents as compared to securely attached ones. Effects on both response times and correct answers were reported by Fraedrich et al. (2010) who reported shorter response times after presentation of negative faces in secure as compared to insecure-dismissing mothers and a smaller amount of false alarms (i.e., less errors) in secure mothers.

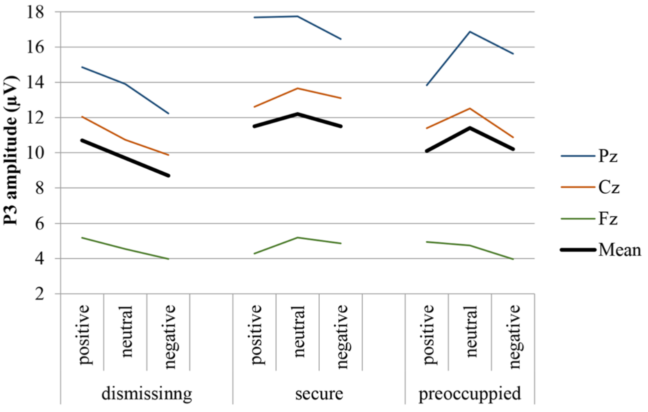

FIGURE 3 | P3 response (Fz, Cz, Pz, and mean) to target stimulus presented on the background of negative, neutral and positive stimuli in secure, insecure-dismissing and insecure-preoccupied subjects.

Although the present study did not replicate the findings regarding response times, the fewer correct answers in insecure-dismissing subjects as compared to the other attachment groups depicts a restricted processing ability in the context of negative emotion. Presumably the present stimulus, either "W" or "M" may invite for faster responses with the side-effect of a higher error-rate, while decisions on facial valence are more complex. Consequently, subjects take more time but have lower error-rates.

These findings are in line with theoretical assumptions from attachment theory postulating deficits in emotional regulation abilities in insecure-dismissing individuals in distressing or threatening situations, in which the attachment system is activated. This is explained by the child's experiences with the caregiver. While sensitive responding to the infant's emotional expression and emotional needs in mothers facilitates the development of emotional competences and finally contributes to the development of a secure infant-mother attachment, infants of insensitive or rejecting mothers are restricted in the development of emotional regulation strategies, their ability recognize emotions, to express and communicate their needs and to refer

TABLE 2 | P3 amplitudes (μV) to target stimuli depending on emotional context and attachment representation.

	Insecure-dismissing			Secure			Insecure-preoccupied		
	Positive	**Neutral**	**Negative**	**Positive**	**Neutral**	**Negative**	**Positive**	**Neutral**	**Negative**
Fc	5.18	4.55	3.98	4.28	5.19	4.87	4.95	4.75	3.96
Cz	12.04	10.73	9.87	12.61	13.66	13.10	11.40	12.51	10.88
Pz	14.86	13.90	12.24	17.68	17.75	16.47	13.83	16.88	15.63
P1	13.45	12.53	10.77	15.71	15.48	14.74	13.55	16.08	15.74
P2	13.94	12.88	11.21	17.27	16.46	15.94	11.91	14.39	13.72
P3	10.69	10.16	8.61	14.64	14.09	13.36	11.13	13.01	12.15
P4	11.60	10.29	9.15	13.85	13.96	12.90	9.85	11.60	11.40

to the caregiver as a source of emotional support. For example, a restricted ability in emotion recognition in insecure-dismissing subjects was also found in behavioral studies with children or adolescents (e.g., Spangler and Zimmermann, 1999; Steele et al., 2008). During the AAI, insecure-dismissing individuals lack to produce coherent answers when confronted with questions regarding emotional experiences during their childhood. This seems to indicate restricted processing of emotional information (Main et al., 2002).

P3 Results

First of all, the pattern of the P3 responses along the midline (frontal, central and parietal) demonstrating decreasing P3 amplitude responses from frontal to central to parietal areas as well as the pattern of the P3 amplitude responses along the parietal line (central and lateral) demonstrating higher central and lower lateral amplitudes were as expected from research literature and verify the validity of the assessment.

In the current study, attachment groups differed significantly with regard to the P3 ERP component. Individuals with an insecure-dismissing attachment representation showed significantly smaller P3 amplitudes to target stimuli when embedded within negative as compared to neutral or positive emotional contexts. In addition, the P3 amplitudes of insecure-dismissing subjects during negative contexts were smaller than those of secure subjects. This pattern was found independent of the location of the electrodes included, both for the amplitudes along the midline (Pz, Cz, Fz) and the amplitudes along the parietal line (P3, P1, Pz, P2, P4).

According to Polich (2007) the P3 amplitude is hypothesized to index allocation of attentional resources. Thus, the P3 amplitude typically increases for infrequently appearing oddball stimuli. This is especially true when task conditions are undemanding. However, an increase in task requirements appears to occupy cognitive resources leading to smaller P3 amplitude responses (Polich, 1987; Kok, 2001). Similarly, evidence suggests that events independent of the oddball task (i.e., engagement in a secondary task) draw upon attentional ressources resulting in smaller P3 amplitude responses (e.g., Isreal et al., 1980).

Transferring the attention allocation theory of Polich (2007) to the present study, it can be concluded that negative emotional contexts drain on information processing in insecure-dismissing individuals. Thus, the smaller amplitudes in the P3 of insecure-dismissing subjects in negative contexts in our study may reflect lower engagement in target stimulus processing. It can be assumed that top-down processes modulating the P3 come along with a concurrent neurophysiological activation that suppresses target detection in negative contexts (also see Vrtička et al., 2008). Indeed, as reported above, few studies including the current paper found insecure-dismissing (or avoidant) subjects to show behavioral deficits associated with stimuli of negative valence as well (e.g., Dan and Raz, 2012; Escobar et al., 2013). This interpretation is supported by the above reported behavioral deficits of insecure-dismissing attached individuals in recognizing targets embedded within a negative context. From this perspective, the reported neurophysiological processes involved in the processing of task-irrelevant information might contribute to attachment related differences in behavioral target detection within negative contexts.

Similarly, differences between insecure-dismissing and secure individuals in the P3 amplitude in response to faces of different valence were also found by Fraedrich et al. (2010) in a study with mothers looking at positive, neutral and negative infant faces. In addition, Leyh et al. (2016) found an elevated P3 positivity during perception of infant emotional faces in securely compared to insecure mothers. More precisely, they found higher P3 amplitudes in secure mothers when asked to focus on positive or negative faces and when asked to differentiate neutral faces from negative faces. According to Polich (2007) this indicates that insecure mothers allocated fewer attentional resources to recognize emotional faces, which could be interpreted as a defensive effort in light of emotional information. The heightened allocation of attentional resources found in secure as compared to insecure mothers may explain why securely attached mothers are more sensitive to their infants' signals of emotional needs. The main difference between the study of Fraedrich et al. (2010) and the current study was that in the former one, subjects were asked to draw attention to emotional expressions while in the current study attention had to be focused on a neutral stimulus while ignoring the emotional context. Nevertheless, there were similar results indicating reduced P3 responses associated with negative emotions in insecure-dismissing subjects.

The findings of other studies were somewhat different to the findings of this study. Zhang et al. (2008) did not find associations between attachment quality and the P3 amplitude in general. Only avoidant attachment was associated with lower P3 amplitude responses and a later component, namely the N400, associated with semantic integration. Mark et al. (2012) investigated ERP responses to sad and angry faces depending on dimensions of secure, anxious and avoidant attachment. They did not assess group comparisons between secure and insecure attachment, but calculated associations between ERP responses and the attachment scales. While their findings did not suggest any association between facial emotional processing and avoidant attachment, P3 amplitude was positively associated with anxious attachment and negatively with secure attachment. These effects, however, did not reach significance after controlling for trait anxiety.

A reason for the different findings of Zhang et al. (2008) as well as Mark et al. (2012) may be the attachment assessment procedure, as these two studies—in contrast to the current study as well as the studies by Fraedrich et al. (2010) and Leyh et al. (2016)—used self-report measures.

In sum, interpreting the current findings of insecure-dismissing subjects' dampened P3 amplitude responses to target stimuli in negative contexts in terms of reduced attentional processing capacities well fits with the behavioral findings in the current study. More precisely, this study suggests that the insecure-dismissing group may allocate more attention resources to task-irrelevant negative emotional information, presumably in a defensive regulatory effort, which may in turn contribute to poorer task performance at a behavioral level. This interpretation is supported by previous studies cited above reporting restrictions in the ability to recognize and to regulate negative emotions in infants and adolescents with a history of insecure attachment relationships.

While securely attached subjects significantly differed in neural processing from subjects with an insecure-dismissing attachment relationship, we did not find differential processing patterns when comparing secure and insecure-preoccupied subjects. There are several explanations for this non-finding. Firstly, due to the very different modes of emotional regulation associated with the two different insecure attachment patterns and also due to the explanation of their determinants (Cassidy and Berlin, 1994) similar neurophysiological responses would not be expected anyway. For example, Mark et al. (2012) found an association between the P3 amplitude and anxious attachment, but not with avoidant attachment.

Secondly, from a methodological perspective the relatively low number of insecure-preoccupied subjects in our study (which could be expected with respect to known normative distribution of attachment patterns) may have resulted in low statistical power, which makes further neurophysiological studies of this attachment subgroup necessary. Moreover, data inspection revealed that the mean scores of the insecure-preoccupied subjects actually lie between the secure and insecure-dismissing ones, with being more similar to the secure subjects.

Due to the small number of preoccupied subjects we, additionally, calculated the analyses of variance after exclusion of the preoccupied group. In most cases, the findings regarding attachment representation remained essentially the same. Only for the ERP analyses along the parietal line, the interaction between emotional context and attachment for the target stimuli disappeared, and a main effect of attachment in response to target stimuli was found indicating that insecure subjects allocated fewer attentional resources not only in a negative emotional context, but in general. This is in line with Fraedrich et al. (2010) who found a smaller P3 response in dismissing mothers to infant faces of any valence. It may be that in dismissing subjects the processing of social or emotional information during an oddball task requires additional resources, in general, which decreases available attentional resources in this attachment group, resulting in decreased P3 amplitudes. From this perspective the supposed modulating effect of attachment might already be present at an earlier stage of regulation regarding emotional tension induced by the experimental task *per se*.

In summary, the present study shows that the attachment representation influences neurophysiological processing of task-relevant stimuli embedded within emotional contexts. This finding provides further empirical evidence for the assumption that the inner working model of attachment influences perception, processing and interpretation of emotional cues (Spangler and Zimmermann, 1999). As the assessment of attachment by the AAI focuses on experiences with the primary caregiver our findings suggest that the early attachment relationship or the attachment history with the caregiver has an impact on neurophysiological processing of emotional information. Support comes from few studies, presenting results that early interaction with the primary caregiver affect the development of brain structures significantly (Rutter, 2002; Luby et al., 2012).

Furthermore, this study combines a neurophysiological approach with the assessment of attachment on a representational level, in contrast to other studies (Zhang et al., 2008; Dan and Raz, 2012; Mark et al., 2012) that assessed attachment style by self-report questionnaires. This further shows that associations between attachment and neurophysiological processes may depend on the measure used for assessment of attachment. The AAI assesses attachment qualities implicitly on a representational level. Thereby, it focuses on experiences with primary caregivers and gives details on how an individual regulates its emotions regarding attachment related situations (e.g., Allen and Miga, 2010). Using the AAI may be the most effective way to gain information about emotion regulation in early childhood retrospectively. Indeed, this developmental phase is especially sensitive to neurophysiological alterations induced by parenting behavior as the brain undergoes many plastic changes. To further study the developmental trajectory of attachment development associated with neuronal insights later in life, the AAI seems to be relevant because of its developmental implications. Future research could also add behavioral assessments to investigate the generalizability of the effects to daily social interactions.

The present study investigated neural processing of neutral targets in emotional contexts to study how attachment moderates the link between processing of task-irrelevant stimuli in the environment (here: the emotional context) and task relevant information processing. In contrast, most other studies focus on facial expressions to investigate emotion perception in others (Green et al., 2007; Milanak and Berenbaum, 2014). This limits comparisons to the effects of other studies on attachment and emotion processing. Moreover, in the present study, pictures showing emotional contexts did not necessarily include socially relevant situations. The question remains, if effects became stronger when real social situations or even better a live social interaction would be presented. This also assigns to the neutral stimuli "W" and "M" which usually do not have any significant meaning in our daily life. While the focus of the study was to investigate the impact of emotional surroundings on neutral targets, the ecological validity should be enhanced for further studies by using socially relevant situations as context and more relevant objects, like familiar persons or objects with emotional relevance as targets.

Limitations

Some limitations have to be considered in this study. First, the sample size of the study is limited, and second, the sample size of the different attachment groups varies considerably. Specifically, the insecure-preoccupied group is rather small. It should be noted that the distribution found in this study corresponds with the typical distribution found in several studies (for e meta-analysis, see van IJzendoorn, 1995). This may suggest using non-parametric procedures for hypothesis testing. However, using nonparametric procedures would restrict possibilities for multifactorial designs. Therefore, we nevertheless used parametric procedures. Although the insecure-preoccupied groups is quite small ($n = 5$), we nevertheless included this group into the study and into the statistical analyses in order to provide at least the descriptive information about this group for the interested reader. As the main findings of this study mainly refer to differences between the insecure-dismissing and the secure group, we did not make specific conclusions regarding the insecure-preoccupied group. Moreover additional analyses without the insecure-preoccupied groups resulted in the same effects.

CONCLUSION

Our findings support assumptions about moderation of emotional information processing by differences in attachment representation. Specifically it has been shown that negative emotional information restricts cognitive emotional processing in insecure-dismissing subjects. This indicates that it is sufficient to alter context information to influence neural processing in insecure-dismissing subjects in contrast to varying emotional content of stimuli in the focus of attention. However, in the case of insecure-preoccupied subjects it remains vague to which extent neural processing is altered by varying emotional contexts.

ETHICS STATEMENT

The study was conducted in accordance with the Code of Ethics of the German Psychological Association (from 09/28/2004), which is essentially based on the Code of Ethics of the APA (Ethical Principles of Psychologists and Code of Conduct, American Psychologist, 2002, 57, 1060-1073). According to the rules of the German Research Foundation, it was not required to apply for a formal vote for this study; because (1) the participants were healthy (no patient groups); (2) we did not use invasive methods; and (3) there participation did not provide any risk to the subjects. Finally (4), for studies using ERP assessments, a formal vote only is required if the subjects are younger than 14 years and older than 65 years.

Informed Consent

The participants were informed about the aims of the study and about the methods used. In addition, they were informed that (1) their participation was voluntary and that they at any point of time had the right to withdraw the participation and (2) that the data were treated according to the data protection law, and that they were saved anonymously. Each participant signed the informed consent form before participation.

AUTHOR CONTRIBUTIONS

RL: concept, design, collection, analysis and interpretation of data, literature research, writing. CH: analysis and interpretation of data, literature research writing, critical review. MTK: collection, analysis and interpretation of data, writing, critical review. GS: concept, design, supervision, writing, critical review.

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frontiers in Human Neuroscience

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Dismissing Attachment Characteristics Dynamically Modulate Brain Networks Subserving Social Aversion

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Attachment patterns influence actions, thoughts and feeling through a person's "inner working model". Speech charged with attachment-dependent content was proposed to modulate the activation of cognitive-emotional schemata in listeners. We performed a 7 Tesla rest-task-rest functional magnetic resonance imaging (fMRI)-experiment, presenting auditory narratives prototypical of dismissing attachment representations to investigate their effect on 23 healthy males. We then examined effects of participants' attachment style and childhood trauma on brain state changes using seed-based functional connectivity (FC) analyses, and finally tested whether subjective differences in responsivity to narratives could be predicted by baseline network states. In comparison to a baseline state, we observed increased FC in a previously described "social aversion network" including dorsal anterior cingulated cortex (dACC) and left anterior middle temporal gyrus (aMTG) specifically after exposure to insecure-dismissing attachment narratives. Increased dACC-seeded FC within the social aversion network was positively related to the participants' avoidant attachment style and presence of a history of childhood trauma. Anxious attachment style on the other hand was positively correlated with FC between the dACC and a region outside of the "social aversion network", namely the dorsolateral prefrontal cortex, which suggests decreased network segregation as a function of anxious attachment. Finally, the extent of subjective experience of friendliness towards the dismissing narrative was predicted by low baseline FC-values between hippocampus and inferior parietal lobule (IPL). Taken together, our study demonstrates an activation of networks related to social aversion in terms of increased connectivity after listening to insecure-dismissing attachment narratives. A causal interrelation of brain state changes and subsequent changes in social reactivity was further supported by our observation of direct prediction of neuronal responses by individual attachment and trauma characteristics and reversely prediction of subjective experience by intrinsic functional connections.

We consider these findings of activation of within-network and between-network connectivity modulated by inter-individual differences as substantial for the understanding of interpersonal processes, particularly in clinical settings.

Keywords: functional connectivity, individual differences, attachment, cognitive schema, resting-state

INTRODUCTION

The perception of an interpersonal encounter and thus the brain's dynamic response to it depends on many aspects, including the listener's past experiences, their current mood, attitudes, attention and cognitive performance. The basis for certain patterns of interpersonal behavior is already formed in early childhood. Individuals begin to develop an "internal working model" (IWM) of relational expectations combined with a set of likely responses towards interactions with others. These may in part find their origin in experiences with caregivers in early childhood (Bowlby, 1969/1982, 1973, 1980, 1988). This individual IWM forms their attachment representation, that influences interpersonal behavior such as approach/avoidance towards another individual or friendly/hostile reactions towards someone else. Different childhood or life experiences therefore lead to discernible types of attachment representations and corroborating expressions in behavior and discourse (e.g., Cassidy, 2008).

According to this theory of attachment, "attachment representations" can be discerned into secure and different insecure types (Hesse, 2008). Interestingly, attachment representations are part of our communication style and it has been shown that secure and insecure attachment representations can be differentiated based on the coherence level of a person's speech (Hesse, 2008). Typically, securely attached individuals report past experiences in a coherent manner whereas narratives of insecure individuals are characterized by an incoherent discourse. Broadly, insecure attachment types can be subdivided in insecure-dismissing (or avoidant) and insecure-preoccupied (or anxious) styles, according to classification by the adult attachment interview (AAI) or questionaires such as the Experience in Close Relationships Questionnaire (ECR; Ehrenthal et al., 2009). Individuals with an insecure-preoccupied attachment representation tend to have long conversational turns and focus on affective aspects of experiences such as helplessness and anger. In contrast, insecure-dismissing individuals, report fragmented or abstract recollections of memories with significant others, which may even contradict previous statements (George et al., 1985; Buchheim and Mergenthaler, 2000; Hesse, 2008).[1] The specific discourse characteristic of attachment-representations is known to influence the counterpart, by activation of certain schemata underpinning interpersonal disposition. Schemata are patterns of thought and behavior including internal representations of oneself, others and the environment. Their activation, as explained in the cognitive model of depression (Beck, 1967), can be seen as a psychopathologically relevant "carry-over" effect of an environmental trigger. Moreover, once activated by a salient internal or external stimulus, schemata influence the subsequent processing of social information and for instance, compromise mentalization capacities (Nolte et al., 2013). Furthermore, they impact attention towards negative or positive stimuli, which may bias processing and memory formation of new incoming information (Disner et al., 2011).

Investigating the influence of attachment representations on subsequent mental states, Kirchmann et al. (2011) revealed carry-over effects of prototypical audio narratives of different attachment representations (secure, insecure-dismissing and insecure-preoccupied) on self-reported well-being and interpersonal dispositions of the listener conceptualized as countertransference (see below). These conscious and unconscious responses were not only influenced by the content of the narrative but, more importantly, also by the different characteristic speech patterns of the securely and insecurely individuals whose recorded narratives were used as stimuli (Martin et al., 2007).

The "classical" concept of countertransference was first defined by the psychoanalyst Freud as "...the patient's influence on [the therapist's] unconscious feelings..." (Freud, 1910/1957, p. 144) resulting from the patient's influence on the therapist. Freud (1910/1957, 1912/1959) considered countertransference as an unrequested process, which is associated to unresolved conflicts of the clinician. However, subsequent authors emphasized the importance of countertransference reactions for the therapeutic process and broadened the definition to the therapist's emotions towards the patient comprising, to differing degrees, also an objective aspect not depending on the therapist's own intrapsychic conflicts, but instead a response which the patient evokes in others and is thus related to the patient's behavior (e.g., Winnicott, 1949; Heimann, 1950; Kernberg, 1965; Gabbard, 2001). Generally, countertransference reactions can be seen as one's feelings towards the counterpart.

In a review article, Vrtička and Vuilleumier (2012) emphasized that in a novel interpersonal situation the first mental reaction is an affective evaluation of the situation, which is underpinned by the recruitment of specific brain networks important for the processing of social context. The first rapid or automatic processing of such a situation includes the decision to approach or avoid a stimulus or person. Brain regions important for social approach comprise ventral tegmental area (VTA), pituitary/hypothalamus, striatum, and ventral medial orbitofrontal cortex (OFC). Regions associated with fear and

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[1] It must be pointed out that the attachment terminology is quite complex. Talking about attachment *representation* (e.g., assessed by the AAI) the terms "(insecure-) dismissing" for individuals scoring high on avoidance scales and "(insecure-) preoccupied" for individuals scoring high on anxiety scales or preoccupation with anger are used. Talking about the attachment *style* (and therefore self-reported aspects) the terms "(insecure-) avoidant" and "(insecure-) anxious" are used.

negative affect such as amygdala, hippocampus, insula, anterior cingulate cortex (ACC), and anterior temporal pole (ATP) are activated by aversive social events (Vrtička and Vuilleumier, 2012). The activation of these regions varies with individual differences: individuals with an insecure-avoidant attachment, for example, showed decreased activation in dorsal ACC in situations of social exclusion (DeWall et al., 2012) as well as weaker responses to sad and fearful faces (Zhang et al., 2008; Suslow et al., 2009). An insecure-anxious attachment style, in contrast, has been associated with an increased activation of the "social aversion system" in response to negative social cues (e.g., Lemche et al., 2006; Vrtička et al., 2008; DeWall et al., 2012). Furthermore, suppression of resting state activity has been observed in affective, empathy and default mode brain networks following emotional movie clips, emotional biographic narratives or social stress respectively (Eryilmaz et al., 2011; Vaisvaser et al., 2013; Borchardt et al., 2015), suggesting that emotional or social stress "carry-over" effects are associated with temporary alterations of the brain's dynamic baseline. Consequently, such a shift in baseline intrinsic connection would have an effect on individual responses towards explicit subsequent situations.

Whether speech patterns characteristic of insecure attachment style really have similar effects on brain dynamics during rest, which could explain reactive avoidant or approaching behavioral tendencies, has not been investigated so far.

For the current study, we hypothesized that exposure to discourse characterized by an avoidant attachment representation may similarly influence intrinsic brain dynamics during rest between brain regions important for avoidant or approaching behavior, in contrast to speech characterized by a secure attachment style. Taken together, with neurophysiological and psychological evidence for considerable carry-over effects, this may provide a neuronal trace of what is described as schema activation in cognitive behavioral psychotherapy (Disner et al., 2011). Such influence on subsequent behavior and psychological states is thought to be mediated by prolonged changes of the intrinsic functional network architecture, which can be investigated using resting-state functional magnetic resonance imaging (fMRI). Importantly, we hypothesize that such effects are subject to inter-individual variability which can be best explained by the individual's own attachment style. Individuals with an insecure attachment style, characterized by attachment anxiety and avoidance are thought to be more susceptible to behavioral changes and resting-state connectivity changes in a network relevant to process experience of social aversion.

Therefore, we investigated for the first time effects of attachment on subsequent resting-state brain responsivity and their modulation by individuals' attachment styles.

MATERIALS AND METHODS

Participants

Twenty three healthy male, right-handed participants (mean age: 29.8 years, SD: 3.5 years) underwent fMRI.

All participants were screened for psychiatric, neurological or medical illness using the Mini-International Neuropsychiatric Interview (MINI), the Hamilton Depression Scale (HAM-D) and the Young Mania Rating Scale (YMRS) to ensure the absence of any psychiatric disorders (Sheehan et al., 1998) according to ICD-10 criteria. In addition to psychopathology, exclusion criteria included ineligibility to undergo MRI.

The study was approved by the institutional review board of the University of Magdeburg, Germany, and all participants provided written informed consent according to the Declaration of Helsinki.

Stimuli for the fMRI Experiment

Every participant listened to three narratives, characteristic for secure, insecure-dismissing and insecure-preoccupied attachment representation. These narratives were based on the AAI (George et al., 1985). Questions of this semi-structured interview focus on relevant past attachment situations with caregivers, potential losses and traumata—mainly in early childhood. The used narratives are prototypical excerpts of question 3 and 4 from the AAI in which the interviewees are asked to describe characteristic relationship examples with their father and mother in childhood. They belong to the AAI categories dismissing (Ds1/2), preoccupied (E2) and secure-autonomous (F3). To avoid the impact of different vocal qualities and to ensure anonymity of the interviewees, participants listened to recordings of the transcripts recited by AB. These stimuli have been validated and utilized in prior research by Martin et al. (2007) and Kirchmann et al. (2011). In these studies, the length of the narratives differed largely. To avoid possible confounds due to different length of the original narratives, the two longer recordings were shortened to a duration of 4:58 min (insecure-preoccupied) and 4:08 min (secure-autonomous) to match the naturally shorter dismissing narrative (3:46 min). During the process of shortening of the audio stimuli, attention was paid to preserve attachment specific content and speech characteristics (which was cross-checked by a reliable and experienced AAI rater).

Data Acquisition and Procedure

Ultra-high field fMRI was chosen for its capacity to measure high spatial resolutions, which are very beneficial for the investigation of subcortical nuclear structures, highly relevant for affective and social processing (Walter et al., 2008b; Metzger et al., 2013a).

Resting-state BOLD data were acquired on a 7 T whole body MR system (Siemens, Erlangen, Germany) with a 32-channel receiver coil, using an EPI sequence (TR 2.61 s, TE 22 ms, 240 time points, 50 slices, voxel size 1.6 mm isotropic, flip angle 90°). Reconstruction of functional imaging data included a distortion correction and an inbuilt online-motion correction (Zaitsev et al., 2004; Speck et al., 2008). Motion corrected during this procedure was recorded for further analysis. Additionally residual motion was estimated using DPARSFA V2.3 (Yan and Zang, 2010; Song et al., 2011) motion detection.

T1-weighted anatomical reference data were imaged using 3D-MPRAGE (1 mm isotropic resolution, TE 2.01 s, TI 1050 ms, TR 1700 ms, flip angle 5°). The participants were instructed to lay still inside the scanner and for the resting-state scans in specific with their eyes closed without thinking of anyhing particular but without falling asleep. Motion was minimized using soft pads fitted over the ears and participants were given ear-plugs to minimize noise.

We conducted a rest-task-rest design (**Figure 1**) with a 10 min baseline resting-state scan at the beginning. The aim of this design was to compare a baseline resting-state condition to a second resting-state scan, acquired directly after the short task of passive listening. A rest-task-rest design (Barnes et al., 2009) was used to provide the most naturalistic scenario for the presentation of the stimuli with the aim to elicit a natural response from the participants. The benefit for such a design lies in the free manipulation of brain activity during the actual stimulation, which avoids a necessity to arrange stimulation parallel to EPI noise, especially for longer auditory sequences. Secondly, the activation of schema-like processes might be more realistic if the actual social context is presented as naturalistic as possible, which is more difficult if repeated short sequences are required for an event related general linear model (GLM)-based analysis. Furthermore, we deemed this paradigm optimal to capture prolonged carry-over effects, which were thought to emerge after narrative exposure. Before each intervention, the participants had to complete a distractor task, which consisted of easy arithmetic problems (90 s) to ensure comparable baseline conditions. After this, they passively listened to the first narrative. Then we obtained 10 min post-task resting-state data. Afterwards, the participants were asked to rate their feelings and the narrative they had listened to with the questionnaires described below. This procedure was conducted three times so that every participant listened to all of the three narratives in one fMRI session. To control for order effects, the order of narrative presentation was randomized over participants.

Questionnaires

The German version of the revised Experience in Close Relationships Questionnaire (ECR; Ehrenthal et al., 2009) was used to assess participants' individual attachment style like avoidance and attachment anxiety. The Questionnaire contains 36 items estimating a persons' needs, thoughts and behavior in relationships (e.g., "Just when my partner starts to get close to me I find myself pulling away.") on a 7-point Likert scale ("not at all" to "exactly), including an attachment avoidance scale and an attachment anxiety scale.

As traumatic experiences in childhood play a substantial role in the development of different attachment styles, we utilized the German version of the Childhood Trauma Questionnaire (CTQ, Wingenfeld et al., 2010) to assess child maltreatment in our participants. The CTQ is a questionnaire with 28 items evaluating emotional, physical and sexual abuse and emotional and physical neglect on a 5-point Likert scale ("not at all" to "very often").

Furthermore, we used a scale to assess countertransference reactions (one's feelings towards the counterpart) of positive and negative quality based upon Mertens (2005) theoretical model of unconsciously elicited relational responses. This 16-item countertransference questionnaire was adapted from Martin et al. (2007). Sample items are: "Would you like to be a friend of this person?" or "Can you imagine how this person is feeling?" Participants had the possibility to rate with "rather yes", "rather no" or "neither yes or no", where high scores indicate a high tendency for social interaction.

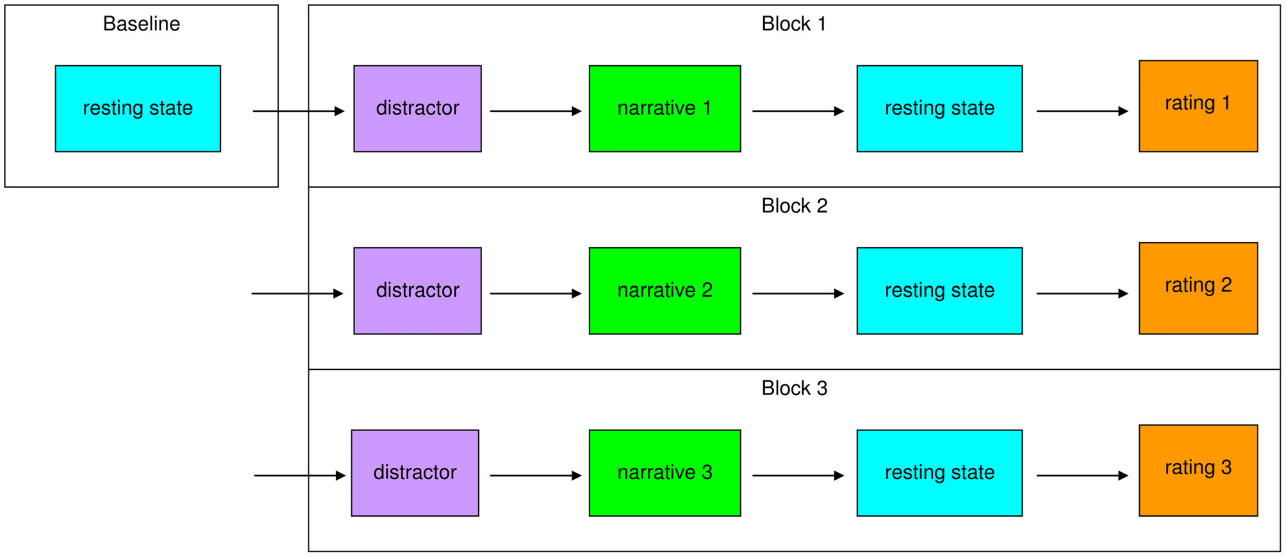

FIGURE 1 | Study design. First, a 10 min baseline resting-state was measured. After a distractor (90 s), participants listened to the first narrative. Then a 10 min post-task resting-state was measured. Afterwards participants rated the narrative and their feelings. The block distractor–narrative–resting-state–rating was conducted for a second and third time, so every subject listened to all three narratives (secure, insecure-preoccupied, insecure-dismissing) in a randomized order over subjects.

To evaluate changes in participants' wellbeing, we asked participants to complete the German Well-being scale ("Befindlichkeitsskala", Bf-S', Zerssen, 1976) at baseline and after every narrative. This well-established state-measurement starts with the sentence "At the moment I feel . . ." and consists of 28 pairs of extremes, e.g., "pessimistic" or "optimistic" or "neither nor", where high scores indicate low well-being.

The Impact Message Inventory (IMI, Fingerle, 1998) is related to the interpersonal circumplex model and assesses someone's reaction when being confronted with a person ("When I would be with this person, I would . . ."). In the current study the 8 item-subscale "friendly" was used. Participants evaluated their interpersonal reactions to the person listened to on a 4-point Likert scale ("not at all" to "exactly"). High scores indicate high estimation of friendliness.

The well-being scale was measured at baseline as well as after every narrative presentation. IMI and countertransference scale were measured after narrative presentation.

Data Preprocessing and Functional Connectivity Analysis

Preprocessing was performed using SPM12 (Wellcome Trust Center for Neuroimaging, London, England; Friston et al., 1994), running under Matlab R2009a. Time series were slice-time acquisition corrected, realigned, coregistered to participant's anatomical T1-weighted image (segmented and normalized into MNI space), normalized to MNI-space and smoothed (resampled to 2 mm cubic voxels) with a Gaussian kernel of $6 \times 6 \times 6$ mm^3 full-width-half-maximum. Since an online motion correction was applied, we requested residual head motion to be lower than 1.0 mm and 1.0 degree. One participant was excluded due to excessive movement, apparently uncontrollable by the correction algorithm. The instantaneous head displacement, also known as frame-wise displacement (FD), was calculated from derivatives of the six rigid-body realignment parameters estimated during standard volume realignment of the motion corrected data. Motion-induced artifacts were then minimized through censoring of motion confounded time points (i.e., "scrubbing"), presented by Power et al. (2012). The volume and its time-adjacent volume with larger head displacement ($FD > 0.5$ mm) were removed in the present study. After this, functional connectivity (FC) analysis was performed. This step was performed after preprocessing, which included deletion of the first 10 time points and temporal filtering (0.01–0.08 Hz) and regression of nuisance covariates (white matter, cerebrospinal fluid, motion and global signal) using DPARSFA V2.3 (Yan and Zang, 2010; Song et al., 2011).

Brain regions of the "social aversion network" (Vrtička and Vuilleumier, 2012) were selected as seed regions of interest (ROIs): amygdala, hippocampus and dorsal anterior cingulate cortex (dACC) of the baseline and dismissing condition. The ROI for hippocampus ($x = -22$, $y = -20$, $z = -26$, 8 mm sphere) has been described by Andrews-Hanna et al. (2010). The amygdala-ROI was based on the AAL atlas. For ACC-ROI, we used a modified version of the AAL atlas, containing a higher level of parcelling in cingulate cortex (Tzourio-Mazoyer et al., 2002; Yu et al., 2011; Lord et al., 2012).

Inter-individual differences: for every participant, correlation coefficients between the mean time course of each seed ROI and the time course of every voxel in the brain were calculated and then converted into three-dimensional zFC maps, using Fisher's r-to-z transformation. Individuals' zFC maps were entered into a paired *t*-test in SPM12 to determine the effect of narratives on seed-driven FC. We conducted a paired *t*-test to compare baseline to the narrative condition. A multiple regression analysis was performed to test for a correlation of post-narrative states with the individual scores of the questionnaires in the different scanning conditions for dACC, amygdala and hippocampus.

We further tested if subjective ratings of friendliness and countertransference following the dismissing narrative were also predictable from participants' baseline resting state networks. This correlation analysis, in contrast to the above correlation of acute brain changes as a function of attachment trait markers, tested the inverse association of individual predisposition as represented in participants' brain network states towards subsequent behavioral responsivity. We focused on subjective responses of friendliness after the dismissing state as it most strongly differed from secure conditions and the prediction of subsequent responsivity by baseline resting state connectivity followed a similar approach proposed by Metzger et al. (2013b) on participants' behavioral reactivity towards pharmacological challenge. Again, a multiple regression analysis was performed to test for a correlation of post-narrative states with the individual scores of the questionnaires in the different scanning conditions for dACC, amygdala and hippocampus.

Changes from baseline were assessed using a paired *t*-test and multiple comparisons were corrected using false discovery rate (FDR, peak-level p-value = 0.05) on the whole brain level. The same correction was used for prediction of friendliness scores after the dismissing narrative by baseline connectivity within the "social aversion network".

Statistical analyses were carried out using SPSS 20. A full factorial model was used to assess the effect of narrative type on individual wellbeing, friendliness and countertransference reactions. Correlation analyses were conducted for the scales of ECR and CTQ.

RESULTS

Behavioral Effects of Narratives and Correlation of Attachment Style and Childhood Trauma

A significant difference of evaluated friendliness was found between dismissing narratives when compared to preoccupied and secure ones (dismissing-preoccupied $p = 0.022$; dismissing-secure $p < 0.001$), but not between preoccupied and secure (preoccupied-secure $p = 0.188$; **Figure 2A**). This was paralleled by lowest tendency to engage in potential social interaction (measured with the countertransference-scale) with the dismissing prototype when compared to the preoccupied ($p = 0.003$) and to the secure narrative ($p = 0.002$; **Figure 2B**).

These specific reactions appeared in the absence of significant changes of wellbeing between conditions

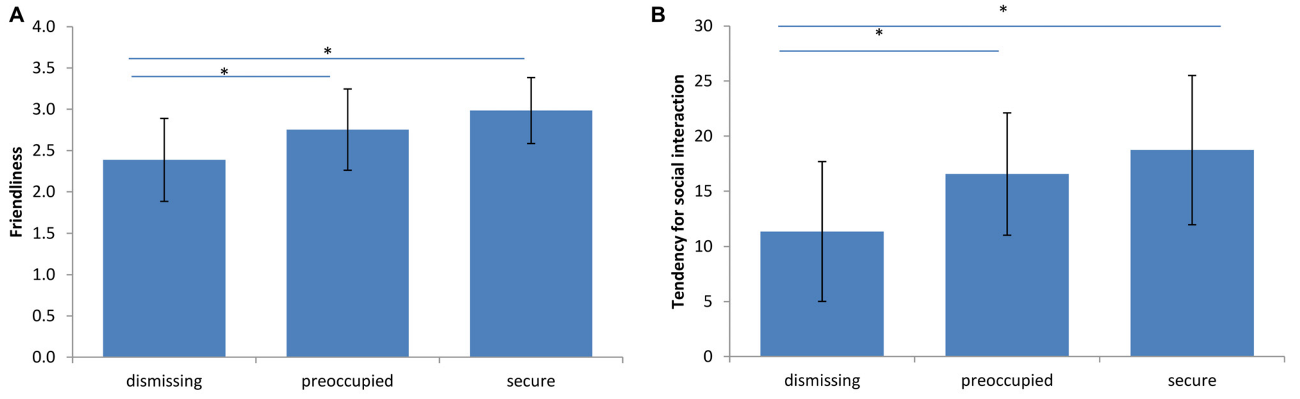

FIGURE 2 | Behavioral effects of narratives. (A) Friendliness. A significant effect of narrative on countertransference reactions was observed ($n = 23$, $^*p < 0.03$, $F_{(2,19)} = 11.73$). The dismissing narrative was rated as the least friendly. The bars represent the standard deviation between subjects. **(B)** Tendency for social interaction. A significant effect of narrative on countertransference reactions was observed ($n = 23$, $^*p < 0.004$, $F_{(2,19)} = 11.30$). The participants showed the lowest tendency for potential social interaction with the dismissing narrative. The bars represent the standard deviation between participants.

(dismissing-preoccupied $p = 1.00$, dismissing-secure $p = 0.29$, preoccupied-secure $p = 1.00$).

A significant positive correlation was found for the sum score of the CTQ with attachment anxiety ($r = 0.66$, $p < 0.002$) and attachment avoidance ($r = 0.59$, $p < 0.006$; **Figure 3**). Regarding the CTQ subscales, emotional abuse and emotional neglect both correlated positively with attachment anxiety (emotional abuse—attachment anxiety: $r = 0.49$, $p = 0.026$; emotional neglect—attachment anxiety: $r = 0.44$, $p = 0.046$) and attachment avoidance (emotional abuse—attachment avoidance: $r = 0.59$, $p = 0.005$; emotional neglect—attachment avoidance: $r = 0.62$, $p = 0.003$). As the subscales physical abuse, sexual abuse and physical neglect were not normally distributed, we conducted for theses scales the non-parametric Spearman's rho—test. Physical abuse and physical neglect showed a positive correlation with attachment anxiety (physical abuse—attachment avoidance: $r = 0.61$, $p = 0.003$; physical neglect—attachment avoidance: $r = 0.60$, $p = 0.005$).

We did not find any significant correlations of HAM-D and YMRS with the CTQ total score and its subscores (HAMD-CTQ totalscore: $r = 0.18$, $p = 0.434$; YMRS-CTQ totalscore: $r = -0.25$, $p = 0.283$).

For descriptive statistics see **Table 1**.

fMRI Results

Main Effects of the Dismissing Narrative

Changes in FC of the "social aversion network" were found when comparing between baseline and exposure to the dismissing narrative, but not in response to the other two narratives:

A stronger FC between dACC was found towards another component of the "social aversion network", namely the left anterior middle temporal gyrus (aMTG; $x = -50$, $y = -6$, $z = -24$, left dACC: $Z = 5.1$, $k = 8$, $p < 0.05$, corrected; right dACC: $Z = 4.9$, $k = 6$, $p < 0.05$, corrected) after the dismissing condition compared to baseline resting-state (**Figure 4A**). A direct comparison of FC between dACC and anterior MTG between all conditions further revealed that this FC was significantly increased for dismissing against secure narrative conditions but not between secure and preoccupied (**Figure 4B**).

We found no significant changes of FC for amygdala or hippocampus.

Inter-Individual Differences

FC of dACC was then investigated to mediate effects of behavioral variability across participants related to attachment characteristics.

The main effect of dismissing narratives, FC between dACC and aMTG was further specifically correlated with attachment avoidance ($r = 0.34$), also when compared to effects of attachment anxiety ($x = -56$, $y = -8$, $z = -24$; $Z = 3.7$, $k = 18$, $p < 0.001$, uncorrected; **Figure 5A**). This was also the case for FC between dACC and left medial prefrontal cortex (MPFC; $x = -18$, $y = 38$, $z = 52$; $Z = 3.8$, $k = 21$, $p < 0.001$, uncorrected, $r = 0.34$; **Figure 5B**).

Inversely, FC between left dACC and right DLPFC specifically correlated negatively with attachment anxiety ($r = 0.54$) when compared to attachment avoidance ($x = 26$, $y = 62$, $z = 18$; $Z = 4.1$, $k = 40$, $p < 0.001$, uncorrected; **Figure 5C**).

In contrast, FC between right dACC and right hippocampus ($x = 30$, $y = -10$, $z = -24$) after the dismissing narrative correlated positively ($r = 0.69$) with attachment avoidance scores ($Z = 3.6$, $k = 12$, $p < 0.001$, uncorrected; **Figure 5D**), however this effect was not revealed specific by direct comparison with attachment anxiety.

Childhood Trauma Related Influences on Regions Involved in Social Aversion

Baseline FC of aMTG, as a target region for amygdala seeded FC, was positively correlated with participants ($n = 20$ due to missing CTQ data) CTQ total score ($p = 0.008$, $k = 43$, small volume corrected for an AAL-derived MTG ROI; **Figure 6**). To gain a deeper insight into the effect of the subscales of the CTQ, we conducted multiple regression analyses with the same ROI and

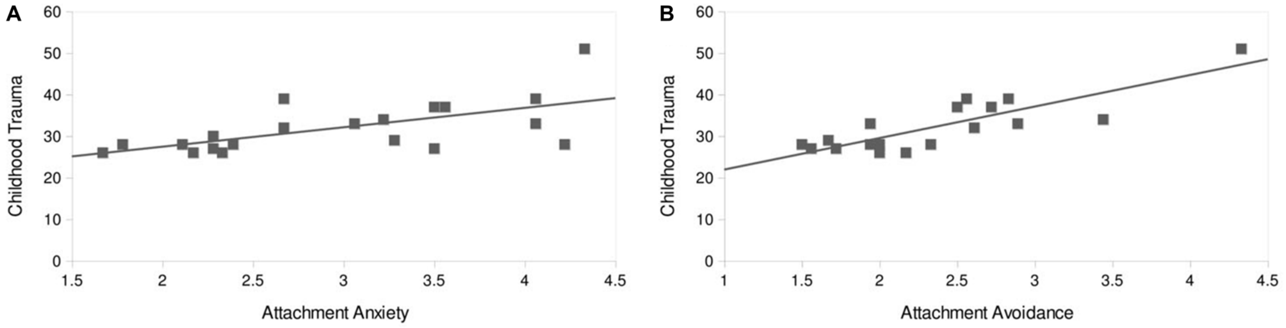

FIGURE 3 | Correlation of attachment characteristics with childhood trauma score. Childhood Trauma Questionnaire (CTQ) score correlates positively with attachment anxiety ($r = 0.66$, $p < 0.002$; **A**) and attachment avoidance ($r = 0.59$, $p < 0.006$; **B**).

the scores of the CTQ subscales. The subscale physical neglect is driving the effect ($p < 0.001$, $k = 102$, small volume corrected for an AAL-derived MTG ROI) followed by emotional neglect ($p = 0.010$, $k = 39$, small volume corrected for an AAL-derived MTG ROI) and emotional abuse ($p = 0.048$, $k = 21$, small volume corrected for an AAL-derived MTG ROI).

Baseline Network Prediction of Subjective Response

In a *post hoc* analysis, the general predisposition to experiencing aversion following dismissing narrative was further examined using baseline resting-state measures. An exploratory multiple regression analysis with friendliness and countertransference scores recorded for the dismissing condition as a predictor was performed for baseline resting-state connectivity of dACC, amygdala and hippocampus. A significant negative correlation ($p < 0.05$, corrected, $Z = 5.17$, $k = 9$, $r = -0.86$) was found for FC between left hippocampus and right inferior parietal lobule (IPL; $x = 38$, $y = -40$, $z = 50$) with subjective friendliness ratings. Participants with high FC between these two regions at baseline reported low subjective friendliness ratings of the subsequent dismissing narrative (**Figure 7**).

For the countertransference scores, we found no significant correlations.

DISCUSSION

We demonstrated that FC in a "social aversion network" was increased specifically after presentation of the prototypical narrative of a person with insecure-dismissing attachment representation. This key finding mirrors the behavioral countertransference reactions of listeners towards insecure-dismissing attachment characterized by the lowest rating of friendliness and tendency for social interaction

TABLE 1 | Descriptive statistics.

		Mean	Std	95% Confidence interval
Wellbeing (Bf-S)	Dismissing	36.74	11.15	31.91–41.56
	Preoccupied	35.10	7.98	31.65–38.56
	Secure	33.87	9.14	29.92–37.82
IMI (friendly)	Dismissing	2.39	0.50	2.17–2.60
	Preoccupied	2.75	0.49	2.54–3.00
	Secure	2.98	0.40	2.81–3.16
Counter-transference	Dismissing	11.35	6.34	8.61–14.09
	Preoccupied	16.57	5.54	14.17–18.97
	Secure	18.74	6.76	15.81–21.66
Childhood Trauma Questionnaire	Sum score	32.38	6.51	29.42–35.34
	Emotional abuse	6.38	1.53	5.68–7.08
	Physical abuse	5.71	1.49	5.04–6.39
	Sexual abuse	5.33	1.53	4.64–6.03
	Emotional neglect	8.10	2.39	7.01–9.18
	Physical neglect	6.19	1.94	5.31–7.07
Attachment Anxiety (ECR)		2.93	0.85	2.57–3.30
Attachment Avoidance (ECR)		2.31	0.70	2.01–2.61
Hamilton Depression Scale (Ham-D)		0.74	1.20	0.22–1.26
Young Mania Rating Scale		0.48	1.04	0.03–0.93

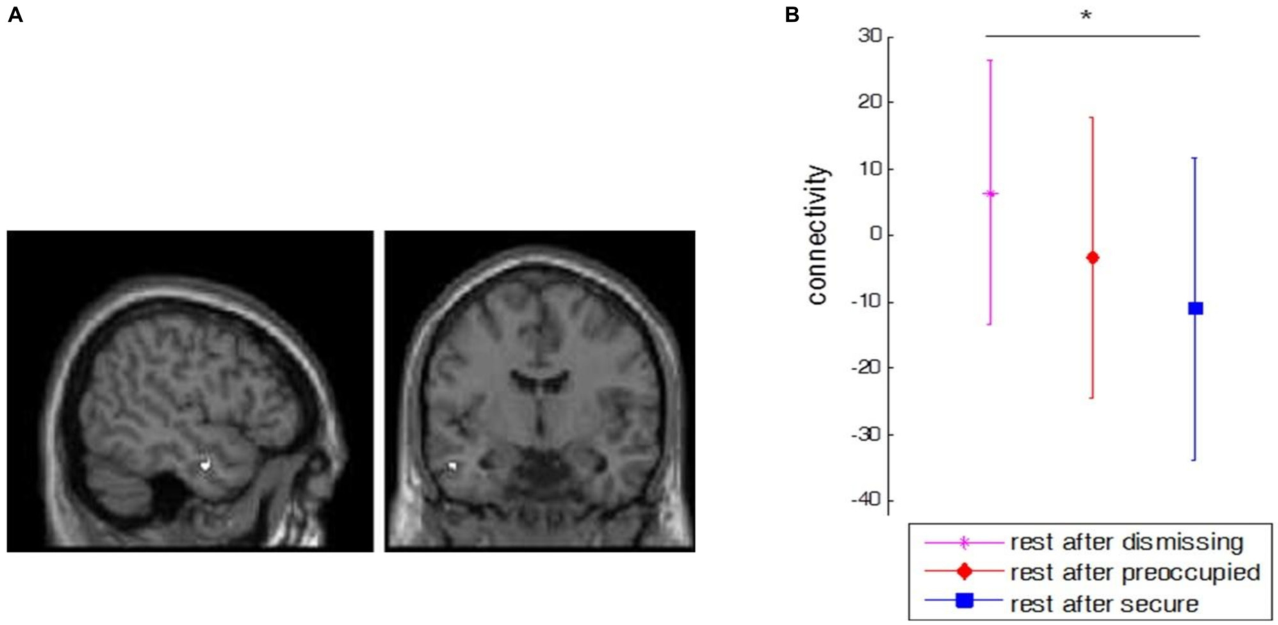

FIGURE 4 | Main effect of dismissing narrative. (A) Depicted is the increase in functional connectivity (FC) between left dorsal anterior cingulated cortex (dACC; seed region) and left anterior middle temporal gyrus (aMTG; $x = -50$, $y = -6$, $z = -24$) after the dismissing narrative compared to baseline ($p < 0.05$, corrected, $Z = 5.1$, $k = 8$). The same peak coordinates were found for right dACC ($p < 0.05$, corrected, $Z = 4.9$, $k = 6$). **(B)** Comparison of FC between the seed dACC and anterior MTG between all narrative conditions. The bars represent the standard deviation between subjects. The black star indicates a significant difference ($p < 0.01$) between dismissing and secure conditions.

(countertransference-reactions)—in comparison to the secure and the insecure-preoccupied narrative.

Particularly, the connectivity of the dACC with the hippocampus as well as the aMTG and MPFC showed a positive correlation with participants' own individual attachment *avoidance* levels. Furthermore, participants' attachment *anxiety* was correlated with dACC connectivity to the DLPFC which is outside the postulated "social aversion network". In the same direction the participants' general susceptibility towards dismissing content as expressed by subjective evaluations of *friendliness* was correlated with FC between another major region of the "social aversion network", the hippocampus, and the MPFC and parietal cortex, which are also not part of the "social aversion network". Together, these findings support the hypothesis that listening to dismissing attachment narratives leads to a specific increase of FC within the "social aversion network"—while interactions of these nodes with regions outside this network, such as DLPFC and parietal cortex are mediated especially by the listener's attachment *anxiety* and evaluation of *friendliness*.

Activation of the "Social Aversion Network"

Our findings are in line with the interpretation that listening particularly to the dismissing narrative triggers a prolonged activation of the "social aversion network" in healthy participants related to a schema activation as described in depressed patients (Disner et al., 2011). This set of interconnected brain regions directly relates to self-reported avoidance and to anxiety and friendliness indices in the current sample via the recruitment of additional brain regions. This interpretation is furthermore supported by the corroborating behavioral results which highlight a reactivity pattern indicative of "disengagement" from someone else's narrative when characteristic of a dismissing attachment representation.

Recent neuroimaging findings suggest that the dACC plays a key role in processing social aversion, e.g., social exclusion induced by the cyberball paradigm (DeWall et al., 2012). Furthermore, Buchheim et al. (2008) reported an increased activity in the dACC in response to talking to attachment-related pictures representing loneliness in patients with borderline personality disorder who are characterized by a predominance of insecure unresolved attachment representations with respect to attachment trauma. Gillath et al. (2005) found increased activity in ATP, hippocampus and dACC of anxiously attached participants when thinking about negative emotions. While activity in OFC was decreased when suppressing these negative thoughts, activity in ATP and OFC was even inversely correlated (Gillath et al., 2005). Moreover, ATP was found to be an important neural correlate of sadness and grief states (Lévesque et al., 2003; Kersting et al., 2009). Vrtička and Vuilleumier (2012) emphasized not only the important role of the "social aversion network" for the processing of social context, but also that of regions

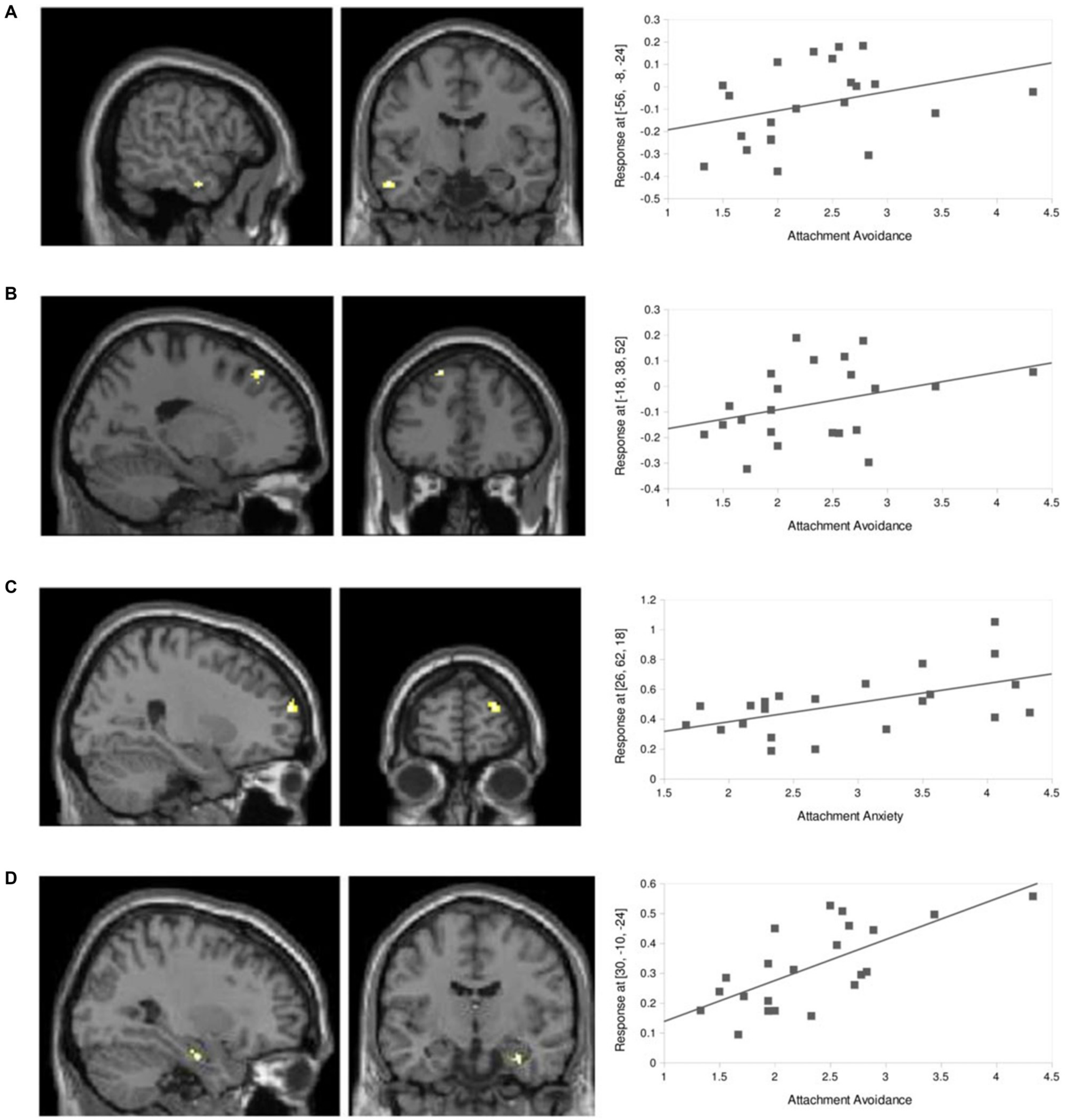

FIGURE 5 | Inter-individual differences. (A) FC between right dACC and aMTG ($x = -56$, $y = -8$, $z = -24$) after the dismissing narrative showed a positive correlation with attachment avoidance ($Z = 3.7$, $k = 18$, $p < 0.001$, uncorrected, $r = 0.34$). **(B)** FC between right dACC and MPFC ($x = -18$, $y = 38$, $z = 52$) after the dismissing narrative showed a positive correlation with attachment avoidance ($Z = 3.8$, $k = 21$, $p < 0.001$, uncorrected, $r = 0.34$). **(C)** FC between left dACC and right DLPFC ($x = 26$, $y = 62$, $z = 18$) after the dismissing narrative showed a positive correlation with attachment anxiety ($p < 0.001$, uncorrected, $Z = 4.1$, $k = 40$, $r = 0.54$). **(D)** FC between right dACC and right hippocampus ($x = 30$, $y = -10$, $z = -24$) after the dismissing narrative showed a positive correlation with attachment avoidance ($p < 0.001$, uncorrected, $Z = 3.6$, $k = 12$, $r = 0.69$).

essential for social approach and for more controlled cognitive reappraisal processes such as the prefrontal cortex (Vrtička and Vuilleumier, 2012).

We found that these important regions within the "social aversion network", dACC and aMTG, show a higher FC after listening to the dismissing narrative implying a detachment

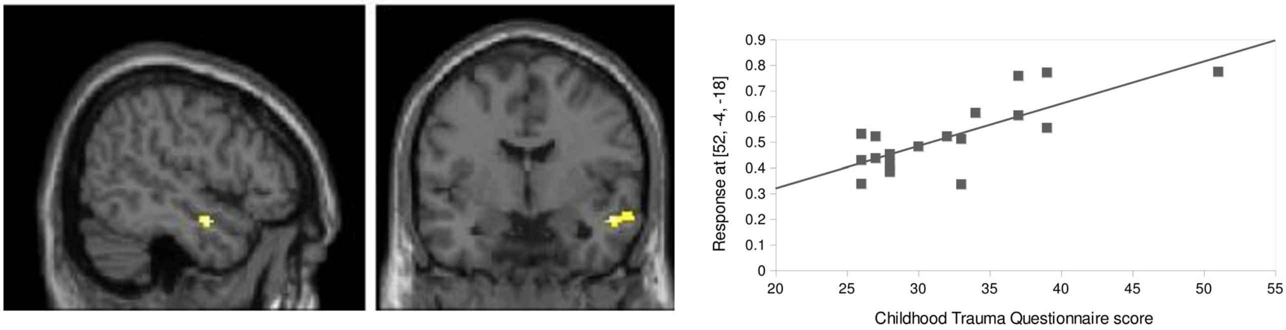

FIGURE 6 | Childhood trauma related influences. FC between right amygdala and right aMTG (*x* = 52, *y* = −4, *z* = −18) at baseline showed a positive correlation with CTQ total score ($r = 0.79$, $p = 0.008$, $k = 43$, small volume corrected for an AAL-derived MTG ROI on a cluster level).

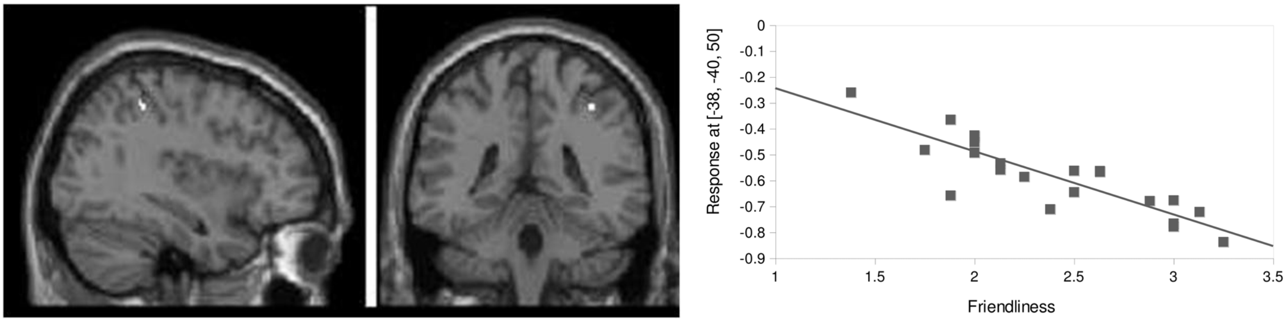

FIGURE 7 | Baseline prediction by friendliness scores. FC between left hippocampus and left inferior parietal lobule (IPL; *x* = 38, *y* = −40, *z* = 50) correlated negatively with friendliness ratings ($p < 0.05$, corrected, $Z = 5.17$, $k = 9$, $r = -0.86$).

of speech patterns characteristic for dismissing attachment representation.

Inter-Individual Differences

Attachment avoidance correlated with the FC between dACC and aMTG after the dismissing narrative. This correlation was specific for the listener's own attachment avoidance as compared to attachment anxiety. This supports the activation or increased intrinsic connectivity within the "social aversion network" as a function of sensitivity to dismissing content.

A positive correlation of FC between dACC and hippocampus, another constituent of the "social aversion network", was observed for resting state conditions following the dismissing narrative, however, this correlation could not be rendered significantly different when corrected for attachment anxiety. Such a distinct correlation for attachment avoidance was further the case for FC between dACC and MPFC after the dismissing narrative, however this was not predicted by our hypothesis given that MPFC had been assigned to a network subserving mental state representation. There is previous evidence for co-activation of ACC and MPFC during thought suppression in attachment avoidant individuals (Gillath et al., 2005). Gillath et al. (2005) also found ATP, dACC and hippocampus to be correlated with attachment anxiety, while we could not reproduce this finding.

We did however find specific effects for attachment anxiety, also when directly comparing with correlations of attachment avoidance: attachment anxiety influenced the change of connectivity in reaction to the preceding dismissing narrative between the "social aversion network" and dorsolateral prefrontal cortex. Of note, no effect of attachment anxiety on connectivity with other regions associated with amygdala processing such as the ventrolateral prefrontal cortex was found. Whether the DLPFC indeed plays a mediating role between social aversion and other crucial social-cognitive processes, such as for instance monitoring social processes, may remain a speculative interpretation at least on the basis of our data. The comparably low level of social threat experiences after the narrative may have led to an increased activation of neural structures underpinning successful reappraisal of potentially distressing information in anxious individuals rather than to an active induction of anxiety and thus changes of amygdala connectivity. Recently, Silvers et al. (2014) found that high intensity threats lead to stronger DLPFC activation compared to those of lower intensity. Similarly, individuals with high attachment anxiety may have interpreted the dismissing narrative as more intense and thus reacted with increased, yet still effective, reappraisal strategies (Silvers et al., 2014).

Following Ochsner et al. (2012) correlations after dismissing narratives with ventrolateral and DLPFC regions suggest an increased call for regions associated with explicit regulation of affective states in order to keep homeostasis or a healthy state, which is especially relevant since we measured healthy partipants. Although the direct function cannot be inferred from resting state network connectivity, this suggests that participants who currently show higher levels of attachment anxiety specifically need more regulatory resources to maintain homeostasis following dismissing narratives.

While DLPFC activation was related to threat (Silvers et al., 2014), activation of the ventral lateral prefrontal cortex during social feedback processing was found to correlate with attachment anxiety (Vrtička et al., 2014). To our knowledge, literature on DLPFC, especially in its modulation of connectivity with dACC during attachment processing is missing. Therefore, more work will be needed to explore this particular finding in the future.

Childhood Trauma Related Influences on Regions Involved in Social Aversion

As experiences in childhood play an important role in the development of attachment style and childhood maltreatment is associated with an insecure attachment style (e.g., Cassidy, 2008), we expected CTQ scores to correlate with attachment avoidance and attachment anxiety scores measured with the ECR.

Interestingly, CTQ scores correlated with FC between regions within the "social aversion network", namely amygdala and aMTG, at baseline. It is well known, that the amygdala is involved in the processing of fear and stress-related experiences (e.g., Keifer et al., 2015). Marusak et al. (2015) for example could show a "higher conflict-related amygdala reactivity" whereas in a more specific attachment context, Lemche et al. (2006) found an increased amygdala response to negative sentences with attachment content, which was also correlated with attachment insecurity. Examining intra- and extra-amygdaloid paths in healthy participants with and without early life stress (using the CTQ as a measure), Grant et al. (2015) found that participants with early life stress showed very complex and "atypical" amygdaloid connectivity compared to participants without early life stress. Furthermore, individuals with a history of childhood maltreatment (measured with the CTQ) were found to show a higher amygdala responsiveness to threat-related facial expressions, which is underlying one aspect of vulnerability for affective disorders and post-traumatic stress disorder (Dannlowski et al., 2012). These findings underpin the relevance of the amygdala and its connections to the "social aversion network" in the context of childhood trauma, attachment style and psychiatric disorders. In general, disturbances in network reactivity related to childhood trauma, which might result for instance in a higher activity of the "social aversion network", seem likely as childhood trauma results in disturbances of brain development and traumatic experiences are consequently incorporated in brain connectivity (Glaser, 2014).

Regarding the CTQ subscales, in our sample the subscale physical neglect is driving the effect followed by emotional neglect and emotional abuse in contrast to other studies where the emotional subscales often showed the strongest effects (e.g., Dannlowski et al., 2012).

In the current study, we found a correlation of aMTG in its FC (after dismissing states) to dACC with attachment avoidance and further a correlation of aMTG FC (at baseline) to amygdala with CTQ. We further observed correlations between attachment avoidance and CTQ. Further studies should thus try to directly address this complex interrelation and potential underlying circuits by focusing more directly on this task-rest relationship.

Baseline Network Prediction of Subjective Response

In addition to changes in the "social aversion network" following the dismissing narrative and the accompanying inter-individual differences in attachment avoidance, we also observed a relevance of connectivity of a constituent of the "aversion network", namely hippocampus, for individual predisposition to react to the dismissing narrative. Resting-state FC between hippocampus and IPL at baseline was negatively correlated with the friendliness perception regarding the speaker in the dismissing narrative (note that all three narratives were conveyed by the same person, thus differences in perception are due to content but not the speaker). The importance of the structures involved here would be in line with previous associations of subjective reactivity towards stressful social situations. Furthermore, Hertzman and Boyce (2010) or Letourneau et al. (2014) for example describe long-term-changes in the hypothalamic–pituitary–adrenal (HPA) system, the main component of stress response, related to the quality of early caregiving. This is an evidence for brain and body changes in individuals with a history of neglect or maltreatment, as often seen in insecure and disorganized individuals. As the hippocampus is strongly connected to the hypothalamus-pituitary-adrenal-axis it plays an important role in the evaluation of stressful social encounters (Foley and Kirschbaum, 2010) while the IPL is essential in social perception processes, e.g., in the distinction between self and other (Ruby and Decety, 2004; Lawrence et al., 2006). The association of their interconnectivity, especially as a baseline feature characterizing participants with stronger responsiveness to dismissing attachment information is novel and suggests further investigations of the link between IWMs of attachment and social stress systems.

Clinical Implications

By means of understanding the neural correlates and etiological factors of affective disorders as well as different processes and impacts on outcome of psychotherapy, attachment characteristics, childhood trauma and countertransference reactions are meaningful aspects to be considered. According to Beck's cognitive model of depression (Beck, 1967), depressive symptoms are induced and maintained when certain environmental triggers activate specific schemata stored in a person with an individual vulnerability. Significant factors of vulnerability are childhood maltreatment and attachment characteristics (e.g., Gilbert et al., 2009; Strauss, 2011). For the latter, a moderate increase of attachment security was found after psychotherapy (Kirchmann et al., 2012). In our study, we found carry-over effects similar to schema activation and countertransference reactions induced by narratives characteristic for attachment representations. Schema activation is not only fundamental for the understanding of depression (Clark et al., 1999), but attachment-related schemata are also expected to appear in the therapeutic alliance and influence therapy outcome substantially (e.g., Blatt et al., 2008; Muller, 2010; Schauenburg et al., 2010). The activation of the "social aversion network" after the dismissing narrative therefore is an important insight and needs to be considered especially in therapeutic relationships as the awareness of these mechanisms can be beneficial for the process of psychotherapy.

Brain networks involved in affective and anxiety disorders include for example ACC, hippocampus and amygdala (e.g., Disner et al., 2011; Nolte et al., 2011; Grotegerd et al., 2014). The understanding of these brain networks can be a clinically helpful step towards neuroimaging markers assessing the individual vulnerability for affective disorders.

Limitations

Some limitations need to be considered. Firstly, while the sample size is quite large compared to other group analysis performed at high magnetic fields so far (Metzger et al., 2010) it is relatively small and suggests a cautious interpretation of the results. Secondly, all participants were young (mean age: 29.8 years) males. We chose to include only males to avoid sex differences and hormonal variations. At this point sex differences in attachment contexts are not fully understood and therefore we wanted to avoid this complicating factor. However, Ehrenthal et al. (2009) reported no differences in gender regarding levels of attachment anxiety and avoidance for the German version of the revised ECR. Nevertheless, the results cannot be generalized to females. Thirdly, although there was an attachment-related effect of the stimuli shown in prior research (Martin et al., 2007; Kirchmann et al., 2011) on a behavioral level, an additional effect of emotional arousal induced by the content of the stimuli cannot be excluded and needs to be considered when interpreting the results.

Furthermore, high field investigations are of particular danger to incomplete brain coverage due to signal losses. We therefore ensured that all regions of the "social aversion network" were covered. The small voxel sizes chosen here further add to signal rescue due to minimizing intra-voxel dephazing (Walter et al., 2008b). Nevertheless, some parts of hypothalamic areas were not covered in all participants. Given that this region is crucially involved in processing social interactions (Walter et al., 2008a), at least partial involvement of this region cannot be fully excluded. Higher spatial resolution would in part have resolved the issue of signal losses in hypothalamus (Metzger et al., 2010) but would have led to either restricted coverages or largely increased repetition times. New methods such as multiband EPI (Feinberg and Setsompop, 2013) may solve this issue for future studies.

CONCLUSION

To conclude, this study revealed prolonged changes in brain activity in a network processing social aversion. This network was particularly activated after stimulation with dismissing attachment content and therefore may be seen as a representation of the neuronal correlates of schema activation—reflecting previous findings on a behavioral level (Martin et al., 2007; Kirchmann et al., 2011). Importantly, this activation of within-network and between-network connections was modulated by inter-individual differences of self-reported attachment avoidance and attachment anxiety respectively. To our knowledge, our study is the first to establish the effect of complex emotional inductions related to characteristic attachment speech patterns on specific and temporally robust FC changes. These findings have implications for the understanding of interpersonal processes, particularly in clinical settings, especially the process of psychotherapy, where an activation of attachment-related schemata of both patient and clinician are likely to occur (e.g., Blatt et al., 2008; Muller, 2010; Schauenburg et al., 2010).

AUTHOR CONTRIBUTIONS

ALK, BS, HK, AB, CDM, TN and MW did substantial work on the design of the study. AB, BS and HK provided the narratives and previous experiences with the design. ALK and MW were responsible for the data acquisition. ALK, VB, ML, M-JvT, LRD, TN and MW contributed to data anlaysis and interpretation of the data. ALK, VB, M-JvT, TN and MW drafted the work and all co-authors were revising and improving it critically. All co-authors approved the final version and agree to be accountable for all aspects of the work.

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Comparison of Brain Activity Correlating with Self-Report versus Narrative Attachment Measures during Conscious Appraisal of an Attachment Figure

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Objectives: The Adult Attachment Interview (AAI) has been the gold standard of attachment assessment, but requires special training. The Relationship Scales Questionnaire (RSQ) is a widely used self-report measure. We investigate how each correlates with brain activity during appraisal of subjects' mothers.

Methods: Twenty-eight women were scored on the AAI, RSQ, and mood measures. During functional magnetic resonance imaging, subjects viewed their mothers in neutral-, valence-, and salience-rating conditions. We identified regions where contrasts in brain activity between appraisal and neutral viewing conditions correlated with each measure of attachment after covarying for mood. AAI and RSQ measures were then compared in terms of the extent to which regions of correlating brain activity overlapped with "default mode network" (DMN) vs. executive frontal network (EFN) masks and cortical vs. subcortical masks. Additionally, interactions with mood were examined.

Results: Salience and valence processing associated with increased thalamo-striatal, posterior cingulate, and visual cortex activity. Salience processing decreased PFC activity, whereas valence processing increased left insula activity. Activity correlating with AAI vs. RSQ measures demonstrated significantly more DMN and subcortical involvement. Interactions with mood were observed in the middle temporal gyrus and precuneus for both measures.

Conclusion: The AAI appears to disproportionately correlate with conscious appraisal associated activity in DMN and subcortical structures, while the RSQ appears to tap EFN structures more extensively. Thus, the AAI may assess more interoceptive, 'core-self'-related processes, while the RSQ captures higher-order cognitions involved in attachment. Shared interaction effects between mood and AAI and RSQ-measures may suggest that processes tapped by each belong to a common system.

Keywords: attachment, attachment measures, adult attachment, AAI, RSQ, fMRI

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INTRODUCTION

Attachment and its Role in Psychotherapy Research

Measuring patient changes has been a longstanding challenge for psychotherapy outcome research, and patient personality in addition to symptomatology and functioning is an important consideration in the assessment of patient change (Strupp et al., 1997). Since the publication of Strupp et al.'s (1997) volume on assessment of patient change in psychotherapy, there have been many significant contributions to the domain of personality measurement in the context of psychotherapy research. Recently, Dimaggio et al. (2013) organized a special issue for *Psychotherapy Research* in which this subject matter received considerable attention. In this issue, they once again drew attention to attachment theory as a valuable approach to understanding personality. Attachment characteristics may themselves be important treatment targets (Taylor et al., 2015). Change in attachment characteristics may be a particularly important outcome in therapies aimed at long-term change in personality functioning (for example, transference and schema focused therapies; Giesen-Bloo et al., 2006; Levy et al., 2006; Doering et al., 2010). Attachment characteristics are thus important personality traits that bear on the assessment and understanding of treatment efficacy as direct measures thereof, but also in numerous other ways. Studies examining attachment characteristics' bearing on psychotherapy include investigations of: (1) patient factors in treatment efficacy (Wei et al., 2004), (2) patient factors in treatment process (Mallinckrodt, 2000; Mallinckrodt et al., 2005), (3) therapist factors in treatment efficacy (Bruck et al., 2006), (4) therapist factors in treatment process and alliance formation (Sauer et al., 2003), and (5) patient-therapist matching (Wiseman and Tishby, 2014).

For research to proceed in these domains, understanding measures of attachment is imperative. Furthermore, as neuroscience becomes increasingly able to inform psychotherapy research (Weingarten and Strauman, 2015), and even psychotherapy design (Alexopoulos and Arean, 2014), an understanding of the neural activity correlates of specific attachment measures (and ultimately the neural bases of their meaning) during psychotherapy relevant tasks such as attachment figure appraisal is necessary if this fundamental domain is to be included in the conversation.

The Constructs of Attachment and Their Neural Bases

Attachment characteristics are thought to be relatively stable traits that develop in infancy, arising from the patterns of interaction between the infant and its caregivers (typically most importantly the mother), who serve as primary attachment figures. They describe a working model of others and their response to one's distress that in turn guides one's own patterns of behavior in response to distress (Wallin, 2007). The development of attachment is, therefore, a complex phenomenon that combines in a programmatic and cyclical way exteroceptive processes (oriented to perception and processing of external stimuli–in particular, detection of goals, threats, and attachment figures' affective responses), and interoceptive processes (oriented to perception and processing of internal states–in particular core affect generation, regulation, and recognition), to modulate responses to environmental stimuli according to attachment figure responses (Vrticka and Vuilleumier, 2012). (see **Figure 1**).

Ultimately, this iterative process should, on the neural level, involve networks that function to evaluate basic affects as well as those that are involved in mental state representations and affect regulation (Vrticka and Vuilleumier, 2012). Indeed, recent work has emphasized and begun to clarify the structures of interacting distributed brain networks whose activity generates mental experience (Pessoa, 2008; Spreng et al., 2013). Such work has emerged from a basic division between anticorrelated networks of brain activity: the primarily lateral, primarily exteroceptive task-positive networks, active during task performance, and the primarily medial, primarily interoceptive task negative network, active when individuals are not engaged in a particular task (Fox et al., 2005). Moreover, as recent work by Dr. Ochsner's group on elements of affective response shows, some of the integration of medial cortical structures in cognitive control (task-positive) networks may be a function of necessary involvement of interoception in many cognitive control tasks (Satpute et al., 2013).

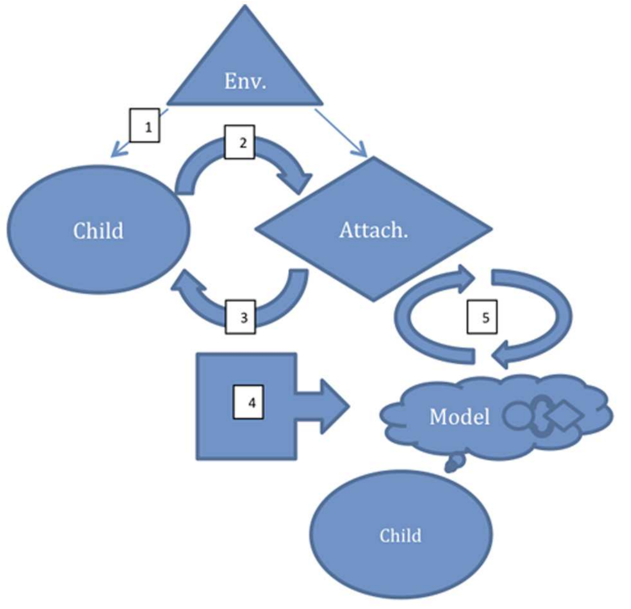


FIGURE 1 | A schematic model of the development of an internal working model for attachment. (1) Perception of an external stimulus as one that should be approached or avoided. (2) Affective/behavioral response to stimulus (influencing the attachment figure). (3) Perception of attachment figure response to the environmental stimulus-affective/behavioral response pair. (4) Recursion of the cycle resulting in modeling/prediction of the attachment figure's responses to such affect/behavior. (5) Generation of a behavioral responses matching the model with actual attachment figure response as the initiating external stimulus; comparison of predicted and actual response refines model. Env, environmental stimulus; Attach, Attachment figure.

As the development of attachment results from recursive interplay between interoceptive and exteroceptive processes, it might be expected that neural activity that is involved in tasks pertinent to attachment representations and that varies with attachment characteristics (i.e., correlates with attachment measures) should link multiple interacting networks at different levels (Vrticka and Vuilleumier, 2012). In particular, networks involved in the generation of basic affects [most directly, the 'PANIC' system, described by Panksepp, responsible for separation distress (Panksepp, 2005)] and valence systems (Lindquist et al., 2015), as well as networks involved in tasks of social cognition such as recognition of others' affects and empathy (Bernhardt and Singer, 2012) should be involved in attachment processes. Finally the activity patterns of affect-regulating circuits linking cortical regulatory structures to subcortical and cortical affect generating structures in negative feedback loops may vary with attachment characteristics. Indirect evidence for this is provided, for example, by Borchardt et al. (2015) study of resting state network connectivity pattern changes in response to narratives characteristic of different prototypical attachment representations; there they found decreased network connectivity for the supplemental motor area (implicated in empathic processes) following attention to biographical narratives presented in a dismissing attachment manner (Borchardt et al., 2015).

The mental phenomena emergent from these patterns of brain activity are working models of self in relation to others—interpersonal schemas. As Safran (1990) has elegantly described, interpersonal schemas, a critical treatment target of cognitive behavioral therapies, may be more rigorously and fruitfully understood as elaborations of attachment characteristics defining these working models in terms of generalized scripts for interpersonal interaction. Such scripts describe a pattern of cognitive attributions or appraisals regarding relation of other to self *and* affective/behavioral responses adapted to preserve interpersonal relatedness based on that attributional frame. Such appraisals and affective/behavioral responses constitute central elements of what therapy might work on.

The general valence of the script, schema or working model may then be thought of as a level of attachment security (vs. fearfulness/disorganization). Where attachment is secure, there is a working expectation that appeals for relatedness will produce a positive and adequate response from the attachment figure. Such an expectation is based on a globally positive sense of self and other. Disner et al. (2011) suggest that in depression negative schema valence is a product of an imbalance of influence favoring subcortical/emotion processing regions over top-down cognitive control networks. Similarly, on a neural level, the association between attachment security and valence system function has been documented in a number of studies. Correlations between anterior cingulate gyrus (valence system) activity in response to attachment related stimuli has been correlated with attachment security in studies using narrative measures (AAI coherence of mind; Galynker et al., 2012), as well as with self-report attachment measures (DeWall et al., 2012), and indirect proxies such as romantic relationship length (Eisenberger et al., 2011). Anterior cingulate activity in response to attachment-relevant stimuli has likewise been correlated with level of (Zhang et al., 2011) and improvements in (Buchheim et al., 2012) depression.

The general tendency of the script, schema, or working model to ascribe low or high salience to interpersonal relatedness and accordingly to regulate intensity of interpersonal relatedness downward (deactivating) or upward (activating) may then be thought of as the 'dismissiveness versus preoccupation' attachment characteristic (Mikulincer et al., 2003). Previous studies (using the RSQ) have found attachment dismissiveness to correlate negatively with primary somatosensory and lateral prefrontal cortex (PFC) activity in response to sad faces (Suslow et al., 2009) and to associate with reduced processing of performance-incongruent social feedback among adolescents in medial and subcortical emotion processing structures (amygdala, caudate, anterior cingulate and insula; Vrticka et al., 2014). Similarly, listening to biographical narratives characteristic of dismissive attachment appeared to reduce subsequent functional connectivity in an empathy-associated network hub (Borchardt et al., 2015). Thus, at one end of the spectrum, persons with dismissive attachment have hypoactive attention and response to emotional input from others, while at the other end those with preoccupied attachment tend to over-respond.

Measurement of Attachment

Assessments of adult attachment fall into two basic categories: observer-rated narrative measures of verbal behavior in response to a variety of stimuli, and self-report scales (Roisman et al., 2007). The Adult Attachment interview (AAI), belonging to the former category, is considered to be the gold standard of adult attachment assessment, but, being an extensive semi-structured interview requiring high-level training to administer and score, it is expensive, complex, and time consuming. The AAI assessment of attachment is based on verbal behavior, and examines attachment as manifested by the pragmatic structuring (Grice, 1975) of verbal behavior rather than by its overt content (George et al., 1996). As such, it is regarded as assessing implicit processes (Jacobvitz et al., 2002).

In contrast, the Relationship Scales Questionnaire (RSQ) is a popular self-report assessment of attachment which is quick and simple to score. However, it appears to measure different constructs from the AAI despite similarities in nomenclature. For example, Roisman et al. (2007) report that AAI security associates with the "Big Five" personality trait of *conscientiousness*, while RSQ security associates most strongly with *extroversion* and low levels of *neuroticism*. The RSQ assessment of attachment is based on the subjects' overt, explicit representations and assessments of their behavior in relationships. Further, while the RSQ inquires about subjects' experiences with relationships in general, the AAI focuses on subjects' verbalizations of recollections of childhood experiences with their parents (George et al., 1996).

Measurement of Attachment Dimensions

In this study we consider a dimensional approach, which characterizes attachment along two distinct dimensions—security-fearfulness and dismissiveness-preoccupation (Stein et al., 2002) that are equivalent to the anxiety (vs. security) and avoidance (vs. preoccupation) dimensions argued for by Kurdek (2002) for the RSQ.

The AAI conceptualization of security (vs. fearfulness/ disorganization) is centered on the ability to maintain narrative organization and coherence in recounting memories of early attachment relationships (George et al., 1996) whereas the RSQ conceptualization of security (vs. fearfulness; Griffin and Bartholomew, 1994a) centers on self-report of trust in and comfort with attachment relationships (e.g., "I am comfortable depending on other people." and "I am comfortable having other people depend on me."; Kurdek, 2002). Both these approaches might be viewed as reflecting the global valence of the working model of self-other relations. The AAI approach, however, emphasizes narrative coherence as a marker of organization of the relational working model. Ethologically based attachment theory posits an over-all positive valence of primary self-other relation development through the 'good enough mother' who provides an adequately attuned and responsive holding environment for the developing infant as a baseline condition for development of a coherent and organized attachment representation (Winnicott, 1960). Thus, the AAI-approach to attachment security may be viewed as reflecting positive valence of self-other relational models implicitly. The RSQ approach, on the other hand, might be viewed as reflecting positive valence of self-other relational models as represented in explicit attributions.

The AAI conception of dismissiveness (vs. preoccupation) focuses on subjects' verbal behavior, which deemphasizes relationships by providing inadequate, unconvincing, or even contradictory experiential evidence for qualitative assessments of those relationships (e.g., "My mother was wonderful; we did the usual things...I don't remember anything in particular."). At the other extreme, the AAI conception of preoccupation as manifest in verbal behavior focuses on over-emphasis of relationships in angry contexts through such features as over-inclusiveness, calling on the interviewer to join the speaker in the experience recounted, and re-living of these experiences. The RSQ conception of dismissiveness, on the other hand, focuses on low (vs. high) subjective desire for attachment and emotional proximity (e.g., "I am comfortable without close emotional relationships."; Kurdek, 2002). Both these approaches might be viewed as reflecting diminished salience of self-other relations at the dismissive end of the spectrum. Again, the AAI might be understood as reflecting the behaviorally implicit salience, while the RSQ reflects the cognitively explicit salience of self-other relations.

While the face validity of the RSQ is quite strong, correlations between the RSQ (and other self-report scales of adult attachment) and the AAI (and other observer-rated measures of adult attachment) have been consistently low (Roisman et al., 2007). Nonetheless, both AAI and RSQ demonstrate predictive validity for behavioral observations predicted by attachment theory (Shaver and Mikulincer, 2004; Roisman et al., 2007; Ravitz et al., 2010). Thus, current evidence suggests that each assesses independent but clinically meaningful aspects of adult attachment.

Study Aims

Understanding how these divergent but meaningful measures of attachment correlate with neural activity associated with processes pertinent to psychotherapy may thus shed light on the aspects of attachment they capture and explain what it means to find change in repeated measurement on these measures over the course of psychotherapy. In the present study, we examine the neural activity specific to conscious appraisal of subjects' mothers (using the contrast between active appraisal and neutral viewing conditions) and aim to clarify how different approaches to measuring attachment might correlate with different elements of that brain activity.

Namely, insofar as the AAI (both in theory and overtly) relies on implicit markers of attachment representation, and thus is liable to assess primarily the implicit (affective/behavioral response) processes involved in the function of the internal attachment model, our first hypothesis is that this measure will correlate with brain activity associated with implicit/interoceptive brain function; we expect distribution of this activity to be preferentially associated with default mode network (DMN) and subcortical structures (Northoff et al., 2006; Northoff and Panksepp, 2008; Sajonz et al., 2010; Oosterwijk et al., 2015).

As the RSQ overtly captures conscious/explicit attributions, and thus is liable to assess primarily the explicit processes involved in the function of the internal attachment model, our second hypothesis is that RSQ measures will correlate with brain activity primarily in regions associated with conscious/expressive brain function and thus will preferentially identify executive frontal network (EFN) and generally cortical rather than subcortical structures (Northoff et al., 2006; Northoff and Panksepp, 2008; Sajonz et al., 2010; Oosterwijk et al., 2015).

To this end we examine the distributions of brain activity specific to conscious appraisal of a primary attachment figure correlating with the AAI and RSQ measures in relation to their basis in DMN vs. EFN networks as well as cortical vs. subcortical regional masks.

Further, we explore how brain activity specifically involved during explicit appraisal of a primary attachment figure varies with attachment security (vs. fearfulness/disorganization) and dismissiveness (vs. preoccupation), and how these dimensions interact with negative mood.

This study reanalyzes raw imaging data previously analyzed using other approaches in other publications. (Zhang et al., 2011; Galynker et al., 2012)

MATERIALS AND METHODS

Participants

The study was approved by the Beth Israel Medical Center Institutional Review Board. All participants gave and signed a statement of informed consent. Basic study methodology has been previously described (Zhang et al., 2011; Galynker et al., 2012) and is reviewed below.

Physically healthy unmedicated depressed and non-depressed participants were recruited through online advertisements (craigslist.org), and screened by telephone and then in person by trained researchers. Participants were right-handed females aged 18–30 years who were able to understand and sign the informed consent and raised (birth to at least 14 years old) in a household with their biological mother. Potential subjects with current and lifetime substance abuse, history of head trauma or mental retardation, history of Schizophrenia, Schizoaffective Disorder, OCD, current suicidality or serious medical illness, or past year use of psychotropic medications were excluded.

Instruments and Subject Evaluations

The Mini-International Neuropsychiatric Interview (MINI), a short structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders, was used to establish subjects' clinical diagnosis of depression and exclude other major psychiatric disorders (Sheehan et al., 1997, 1998). All MINI evaluations were conducted in the research office at the Beth Israel Medical Center 1–4 weeks prior to the scan.

Measures of Mood

The Beck Depression Inventory II (BDI-II) was used to assess depression (Beck et al., 1996a). Cronbach's alpha for the BDI-II was 0.92 for outpatients and 0.93 for a non-clinical sample (Beck et al., 1996b).

The Beck Anxiety Inventory (BAI) was used to assess anxiety (Beck et al., 1988). Cronbach's alpha for the BAI was 0.94 for outpatients (Fydrich et al., 1992) and 0.92 for a non-clinical sample (Osman, 1993).

As BDI and BAI scores in our sample were highly correlated ($r = 0.85$) a composite score of depression and anxiety (BDI + BAI) was used in subsequent analyses as a control for mood. At a cut score of 15, this composite measure had 100% sensitivity and 93% specificity for MINI diagnosis of depression in the study sample.

Measures of Attachment

Attachment characteristics were assessed with the *Adult Attachment Interview (AAI)* and the *Relationship Scales Questionnaire-General (RSQ)*.

The *AAI* is a validated narrative assessment of attachment based on a structured semi-clinical interview focusing on early attachment experiences and their effects (George et al., 1996). AAI interviews were administered, videotaped, and transcribed by trained baccalaureate level research assistants. Research assistants were trained by an AAI-institute trained MEd researcher. Research assistants watched videotaped AAI interviews and performed practice interviews prior to interviewing study subjects. Interview transcripts were scored by AAI-training institute trained and certified PhD psychologist raters (Bakermans-Kranenburg and van Ijzendoorn, 1993).

From these interviews, and following the approach of Roisman et al. (2007) in their comparison of the AAI and RSQ, the Coherence of Mind index is derived as a measure of *attachment security*, with values ranging from 1 to 9. Scores (henceforth referred to as 'AAI security scores') 6–9 indicate secure attachment, scores 1–3 indicate insecure attachment and scores 4–5 are indeterminate (George et al., 1996). The coherence of mind index provides a conceptually unified core index of the implicit aspect of attachment security (George et al., 1996; Roisman et al., 2007).

A rating of *dismissiveness* ranging from −2 (most preoccupied) to +2 (most dismissing) was assigned based on attachment categorizations using the D/E/F/U/CC categorization system (George et al., 1996). Subjects' categorical attachment type ratings and their derived 'dismissiveness' scale scores are shown in Supplementary Table S1. Subjects classified with an F subtype were scored between −1 and +1 on the Dismissiveness scale based on the description of the various F subtypes as either resembling the D (dismissing) type (+1), the E (enmeshed/preoccupied) type (−1), or the prototypical secure type (0). Subjects with a D-categorization were scored +2, and subjects with an E-categorization were scored −2. Subjects with a U (unresolved) or CC (cannot classify) categorization were scored according to the dominant D/E/F category accompanying the CC or U designation.

The RSQ is a well-validated 30-item, 5-point Likert scale, self-report questionnaire. From this scale, four subscale scores are derived – Secure, Fearful, Dismissing, and Preoccupied (Griffin and Bartholomew, 1994b; Kurdek, 2002). Using these subscale scores, composite dimensional Security and Dismissiveness scores were derived by subtracting Fearful from Secure score, and by subtracting Preoccupied from Dismissing score, respectively. This approach has yielded good reliability with Cronbach's alphas of 0.85 and 0.81, respectively (Roisman et al., 2007).

Mood and attachment assessments were administered on the morning of the scan at the Hatch Imaging Center at Columbia Presbyterian Medical Center.

Scanning Protocol

Stimuli were color photographs of the subject's mother (M), a close female friend (F) and two strangers, one age matched to the mother and the other to the friend (S1 and S2). In the present study, however, data from friend and stranger stimuli was not used. The subject selected the photographs (straight on, shoulders up, taken within the past year) as most characteristic of the person being represented. Stranger photographs were selected from other subjects' mother and friend photographs. Four different photographs of each person were provided. All images were processed using Photoshop to conform to approximately uniform head size, brightness, and contrast, and backgrounds were blacked-out.

There were four 12.6-min fMRI scans per subject. Each scan consisted of three blocks. For each block one of three tasks was defined for the subject with a written prompt. At the beginning of each block, this prompt was shown for 10 s. The prompts were: "How much can you relate to this picture?" (Relatedness task), "How pleasant do you feel when you look at this picture?" (Valence task), and "Press any button when you see the picture" (Passive/Neutral task). Each block consisted of 16 trials, with a picture viewed through goggles for 4 s. During this time subjects used their right hands to rate pictures according to the prompt by a recorded button-press. Ratings were on a 1–4 Likert (1–2 = negative to neutral, 3–4 = positive-very positive). Pictures were followed by a fixation-cross viewed passively by the subject for 10 s. Both type of picture and sequence of task were pseudo-randomized.

fMRI Acquisition, Experimental Paradigm, and First Level Analysis

Scanning was performed on a Philips Intera 3T scanner using a Philips SENSE head coil (gradient echo EPI, TR/TE = 2 s/25 ms, 77° flip angle. Voxel size was 2 mm × 2 mm × 3 mm). Functional imaging data were preprocessed and analyzed with FSL (FMRIB Software Library; Smith et al., 2004). Motion correction parameters and global average of the BOLD for white matter were entered as covariates to control for movement and global BOLD signal fluctuation. Images were smoothed with a 9-mm FWHM Gaussian kernel.

Having found Mother stimulus to be the most pertinent in assessing attachment-related brain activity (Zhang et al., 2011; Galynker et al., 2012), in the present study, only data from viewing mother images was used. Thus, there were three relevant event related models: viewing images of mother (M) in each of three viewing conditions (Salience, Valence, and Neutral viewing). The models were convolved with the canonical hemodynamic response function. Two contrasts, Salience minus Neutral (henceforth referred to as Salience for concision), and Valence minus Neutral (henceforth referred to as Valence for concision) were applied and were averaged using fixed effects analysis. These served as the fMRI input for subsequent regression analyses. Significance of main-effects of contrast ROIs in whole brain analysis was assessed using FSL using a primary threshold $p = 0.01$, and a cluster-size probability threshold of $p = 0.05$, which provides cluster-extent based probability thresholding to correct for multiple comparisons.

fMRI Second Level Analysis

We examined two regression models on the main effects of two contrasts for Mother images: Salience-Neutral task, and Valence-Neutral task, regressing each attachment measure against voxel contrast for the two contrasts above. Thus there were four regression models in total with two predictors of interest each, generating eight sets of ROIs:

(1a) AAI secure, covaried for AAI dismissing and BDI + BAI scores, (1b) AAI dismissing, covaried for AAI secure and BDI + BAI scores, (2a) RSQ secure, covaried for RSQ dismissing and BDI + BAI scores and (2b) RSQ dismissing, covaried for RSQ secure and BDI + BAI scores, regressed against Salience and Valence contrasts, respectively. Again, significance of ROIs in these whole brain analyses was assessed using FSL cluster-extent probability thresholding with a primary threshold $p = 0.01$, and a cluster-size probability threshold of $p = 0.05$.

Analysis of ROI Distribution

To assess the distributions of AAI- and RSQ-correlated regions, the above ROIs (threshold voxel z-score > 1.96) derived from the second level analyses were intersected with Allen et al. (2011) anatomical masks for the internally oriented DMN, versus the more externally oriented, higher order processing, EFN (see Supplementary Figure S1). Additionally, the above ROIs were intersected with anatomical masks for cortical versus subcortical structures, generated using the Harvard-Oxford anatomical atlas (Desikan et al., 2006; see Supplementary Table S2). The proportion of AAI- and RSQ-correlated voxels falling within each pair of masks was then compared to the proportional distribution of available voxels between masks (i.e., DMN mask Voxel Count : EFN mask Voxel Count, and Cortical Mask Voxel Count : Subcortical Mask Voxel Count) using a χ^2 test for each pair-wise comparison. For example, if two masks are of equal size, a null result for the AAI would find approximately equal numbers of voxels in the intersection of the AAI ROIs with each mask. On the other hand if the AAI measured properties more strongly associated with activity in the network represented by the first mask than the second, the intersection of AAI ROIs with the first mask would be significantly larger than with the second.

Exploratory Analysis of Interaction Effects

For the exploratory analysis of interaction effects between mood and attachment measures, mood and attachment measures were median-centered and the relevant interaction term was added to each of the above models; for example, 'Mood x AAI security' was added to the model with Mood, AAI security, and AAI dismissiveness as covariates. Again, significance of ROIs in these whole brain analyses was assessed using FSL cluster-extent probability thresholding with a primary threshold $p = 0.01$, and a cluster-size probability threshold of $p = 0.05$.

RESULTS

Sample Characteristics

The demographic and behavioral characteristics of the study sample have been described previously (Zhang et al., 2011; Galynker et al., 2012) and are summarized in **Table 1**.

Measures of Attachment

For both the AAI and RSQ, attachment security and dismissiveness were independent of one another (correlations near zero), and both have moderate negative correlations with depression/anxiety. See **Table 2**.

Main Effects of Contrasts

Active salience processing associated with bilateral decreases in orbital PFC and posterior cingulate activity, and increases in thalamo-striatal activity and cerebellar and visual cortex (Brodmann Area 18) activity compared to passive viewing. *Active valence processing* also associated with bilateral increase in thalamo-striatal activity, posterior cingulate and visual cortex activity (Brodmann Areas 18, 19), cerebellar activity, and also notably associated with increased left insula activity compared to passive viewing, but was not associated with relative suppression of PFC activity. See **Figure 2**.

TABLE 1 | Behavioral and demographic characteristics of the sample.

Subject characteristics		
Socio-demographic characteristics	**Mean**	***SD***
Age (years)	24.5	2.9
Years of education	16.6	2.0
% of days in past year having contact with Mother[1]	49	39
Race/Ethnicity	***N***	**%**
Caucasian	21	75
African American	1	3.6
Hispanic/Latino	3	10.7
Asian	2	7.1
Other[2]	1	3.6
Behavioral characteristics	**Mean**	***SD***
Mother salience rating	3.6	0.6
Mother valence rating	3.4	0.8

[1] *% of the 365 days of the past year on which subject spoke with or saw Mother.*
[2] *Pacific Islander, Alaskan Native or Native American.*

DMN vs. EFN Activity Correlating Significantly with Attachment Measures

The DMN mask comprises 24287 voxels while the EFN network mask comprises 13841 voxels. Thus there is a 64:36 ratio of DMN to EFN voxels. Globally, looking at all activity significantly correlated with AAI measures (with threshold voxel z-score > 1.96 applied to the ROIs), there are 2898 voxels that fall within the DMN mask and 794 that fall within the EFN mask. Thus, in the AAI ROIs, DMN voxels are found at a 78:22 ratio to EFN voxels—significantly greater than the anatomical proportion [$\chi^2(1) = 348$, two-tailed $p < 0.0001$]. On the other hand, with respect to all activity significantly correlated with RSQ measures, there are 2396 voxels that fall within the DMN mask and 1763 that fall within the EFN mask. Thus, in the RSQ ROIs, DMN voxels are found at a 58:42 ratio to EFN voxels—significantly lower than the anatomical proportion [$\chi^2(1) = 68$, two-tailed $p < 0.0001$]. The results were similar, and significant at $p < 0.0001$, when AAI and RSQ Secure-Fearful and Dismissing-Preoccupied dimensions were compared separately, with the exception of RSQ security where the proportion was nearly identical to the anatomical proportion. See **Figure 3** for a qualitative visual summary, and see **Figure 4** for quantification of DMN vs. EFN distributions.

Cortical vs. Subcortical Activity Correlating Significantly with Attachment Measures

Globally, looking at all activity significantly correlated with AAI measures vs. all activity significantly correlated with RSQ measures, the proportion of subcortically vs. cortically located activity was significantly higher than the anatomical proportion of subcortical vs. cortical voxels (15% subcortical vs. 85% cortical) for the AAI (31% subcortical vs. 69% cortical, χ^2 782.20, $p < 0.0001$), while the proportion was significantly lower than the anatomical proportion of subcortical vs. cortical voxels (3% subcortical vs. 97% cortical, χ^2 851.30, $p < 0.0001$) for the RSQ.

However, this global finding was not repeated uniformly across attachment dimensions. Cortical versus subcortical distributions did not differ significantly between AAI and RSQ in the Secure-Fearful dimension, with both measures having overwhelmingly cortical activity associations (99.8 and 99.4% of significant voxels, respectively, $p > 0.05$ for comparison of AAI vs. RSQ proportions, $p < 0.0001$ for both comparisons with the anatomical proportion). In the Dismissing-Preoccupied dimension, however, the global results were repeated with 37% of AAI vs. 5% of RSQ correlated activity within the subcortical mask (two-tailed $p < 0.0001$ for both comparisons with the anatomical proportion). See **Figure 5**.

Specific Brain Structure Activities Correlating with AAI and RSQ Measures of Attachment

Coordinates of all peak voxels significant at the $p < 0.005$ level in clusters with extent based significance $p < 0.05$ are listed in Supplementary Tables S3–S5.

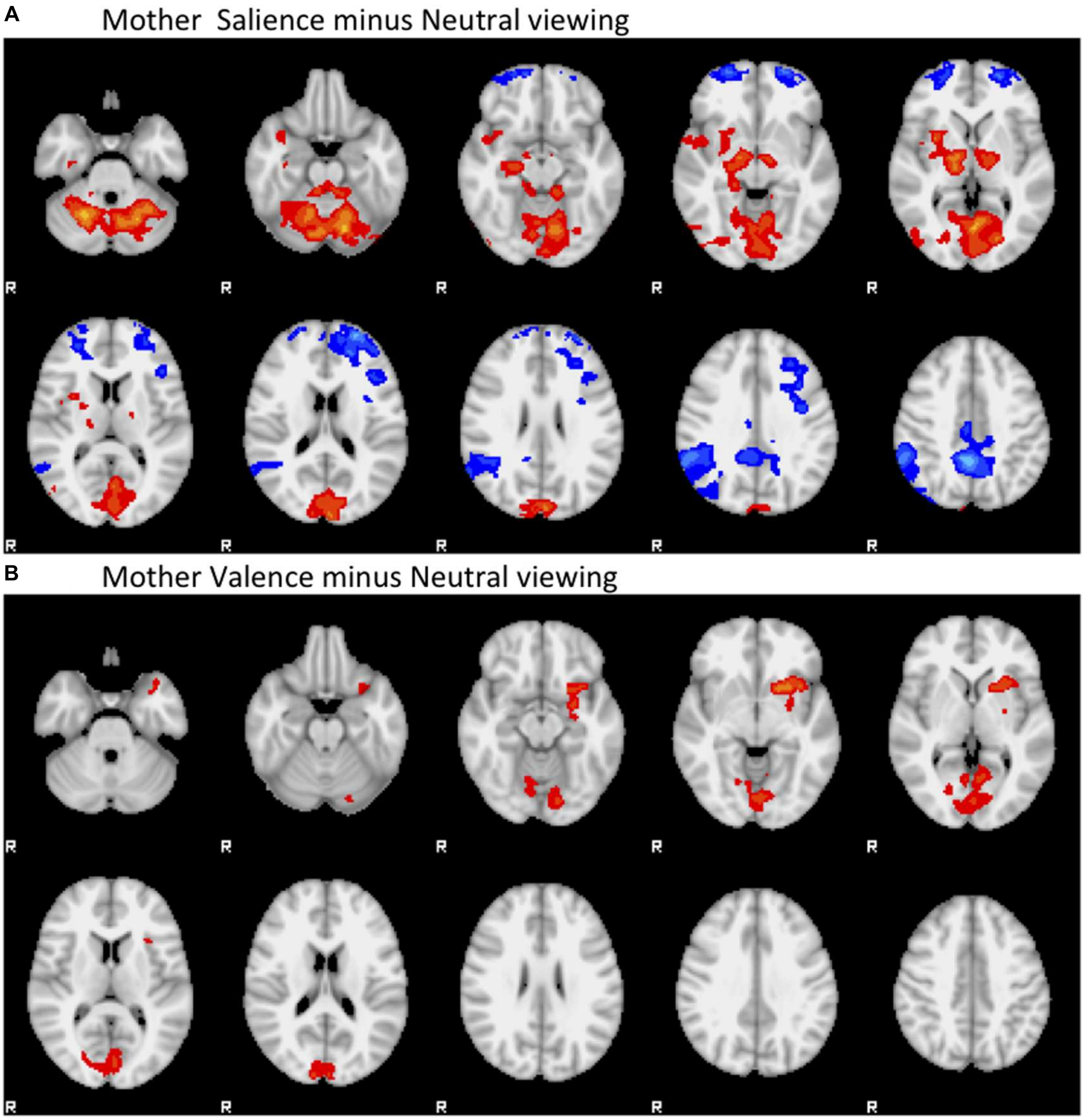
AAI security was significantly correlated with activity in the right parahippocampal gyrus—a brain region associated with social cognition including empathy and the interpretation of non-verbal communication (Vollm et al., 2006; Rankin et al., 2009), as well as the right posterior cingulate and fusiform gyri—brain regions associated with empathy (Vollm et al., 2006), and facial recognition (Haxby et al., 2000), respectively. It was anti-correlated with activity in the cuneus bilaterally—an occipital brain region found to be activated by explicit attention to negative affect (Sander et al., 2005).

Relationship Scales Questionnaire security on the other hand was significantly anti-correlated with right middle temporal gyrus and left lateral PFC activity—brain regions associated with semantic processing of visual emotional cues, and explicit affect

TABLE 2 | Pairwise Intercorrelations of AAI and RSQ attachment measures, and correlations with Depression/Anxiety.

Inter-Correlations of attachment measures

	AAI secure	**AAI dismissing**	**RSQ secure-fearful**	**RSQ dismissing-preoccupied**	**Depression and Anxiety (BDI + BAI)**
AAI secure	1				−0.29
AAI dismissing	0.09	1			−0.36
RSQ secure-fearful	0.25	0.03	1		−0.47
RSQ dismissing-preoccupied	0.22	0.05	−0.05	1	−0.18


A Mother Salience minus Neutral viewing

B Mother Valence minus Neutral viewing

FIGURE 2 | Main Effects of contrast. (A) Mother Salience minus Neutral viewing. **(B)** Mother Valence minus Neutral viewing. Negative contrasts are colored in the blue range, positive contrasts are colored in the red range. Contrasts start at $Z = 1.96$, colored dark blue or dark red, and range up to $Z = 6$, colored cyan or yellow.

regulation, respectively (Ochsner and Gross, 2005; Ochsner et al., 2012).

Adult Attachment Interview dismissiveness was significantly correlated with activity in the right cuneus and left lingual gyrus—an area associated with facial recognition, as well as the thalamus bilaterally—a subcortical region involved in affective processing, including maternal response to infant distress (Noriuchi et al., 2008; Diener et al., 2012). AAI dismissiveness also demonstrated significant negative correlations with activity in the corpus callosum—the major inter-hemispheric tract of white matter fibers, left medial frontal gyrus, and right anterior cingulate—a region involved in negative affect regulation (Etkin et al., 2011), as well as the parahippocampal gyri, and bilateral temporal lobe white matter tracts.

Relationship Scales Questionnaire dismissiveness, demonstrated significant negative correlations with cerebellar activity, left superior temporal gyrus, right anterior cingulate and right cuneus activity.

Exploratory Comparison of Interaction Effects between Mood and AAI vs. RSQ Measures of Attachment

Interaction effects with mood were found for both the AAI and RSQ, primarily in brain regions involved in regulation of affect as well as semantic processing and memory. AAI measures of attachment characteristics demonstrated interactions with mood in brain regions involved in regulation of affect as well as visual attention to affective stimuli and memory retrieval.

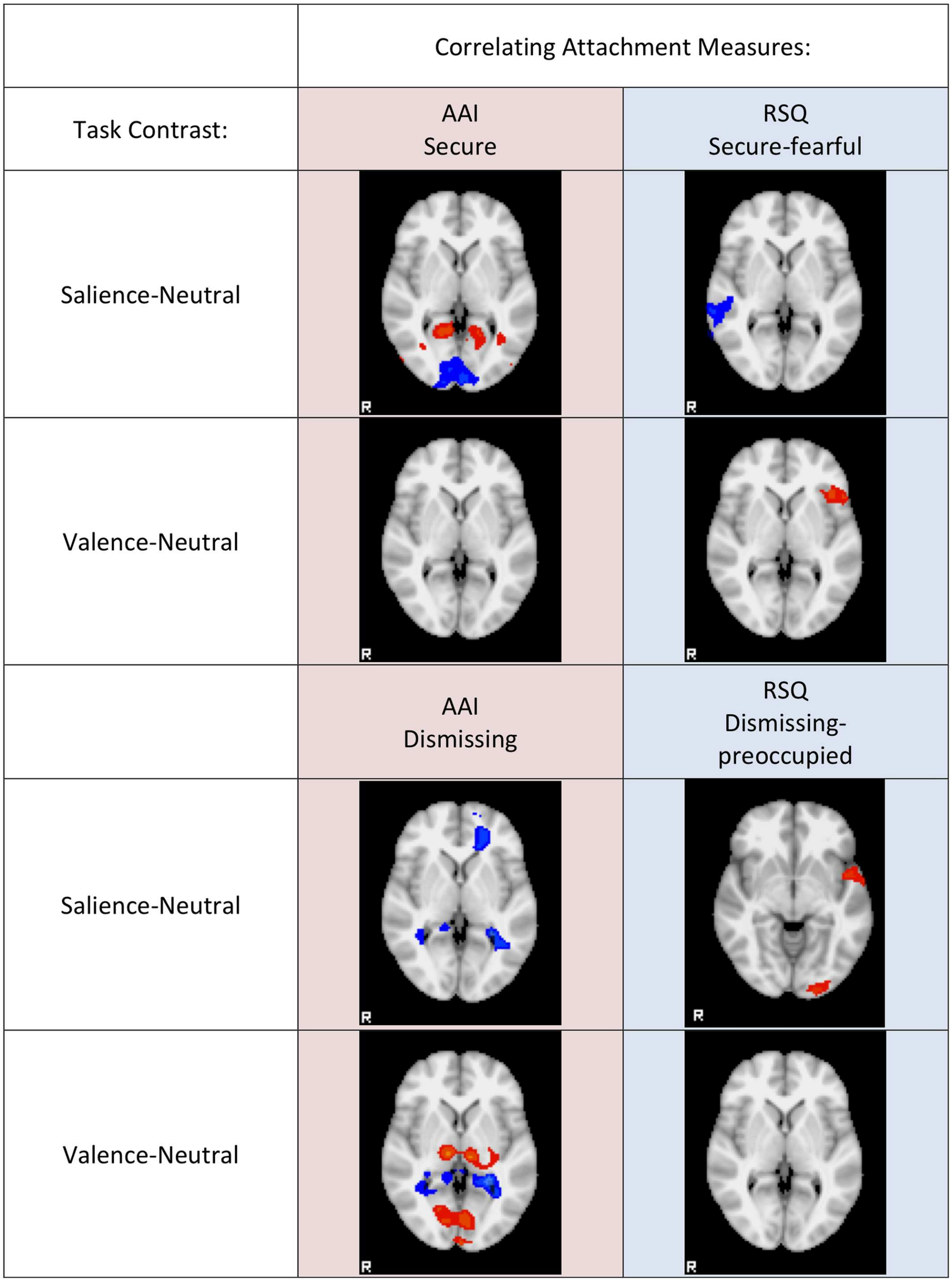


FIGURE 3 | Qualitative Visual summary. Representative slices are shown for each Attachment measure (columns) regression against Mother viewing task contrast (rows). Negative correlations are colored in the blue range, positive correlations are colored in the red range. Correlation *z*-scores start at $Z = 1.96$ colored dark blue or dark red, and range up to $Z = 6$, colored cyan or yellow.

AAI security demonstrated enhancing interactions with negative mood in the caudate tail—a region involved in guiding visual attention (Yamamoto et al., 2012), and in the right temporal lobe. A negative interaction was found in the right cuneus—where activity is associated with attention to negative affect (Sander et al., 2005)—suggesting that heightened activity in this region associated with dysphoric mood is attenuated by more secure attachment. A negative interaction was found in the right superior frontal gyrus as well—where activity is associated with conscious regulation of affect (Beauregard et al., 2001)—suggesting, perhaps, that securely attached subjects were less able to regulate affect during maternal appraisal when depressed.

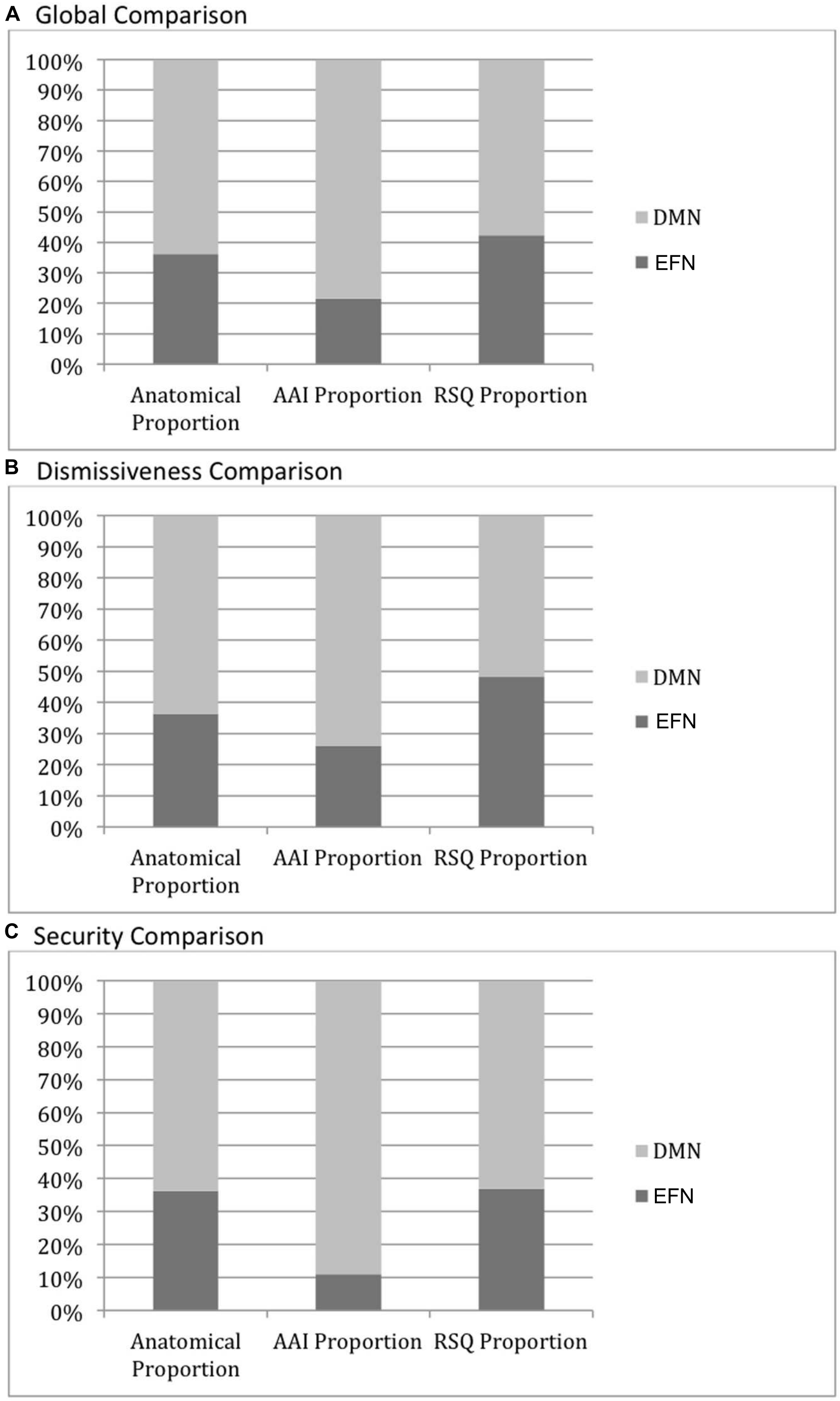


FIGURE 4 | Default mode network (DMN) vs. executive frontal network (EFN) cortical activity distributions. The leftmost columns in each graph show the proportion of voxels in the DMN (light gray) vs. EFN (dark gray) masks, illustrating the relative size of each mask and the null-hypothesis distribution of voxels associated with each measure. The AAI and RSQ columns show the proportion of voxels significantly correlating with those measures falling within each mask. **(A)** DMN vs. EFN cortical activity: Global Comparison–all AAI/RSQ significant voxels. All pairwise proportion comparisons differ significantly at $p < 0.0001$. **(B)** DMN vs. EFN cortical activity: Dismissiveness Comparison–only AAI/RSQ Dismissiveness-measure significant voxels. All pairwise proportion comparisons differ significantly at $p < 0.0001$. **(C)** DMN vs. EFN cortical activity: Security Comparison–only AAI/RSQ Security-measure significant voxels. All pairwise proportion comparisons differ significantly at $p < 0.0001$ except RSQ vs. Anatomical ($p > 0.05$).

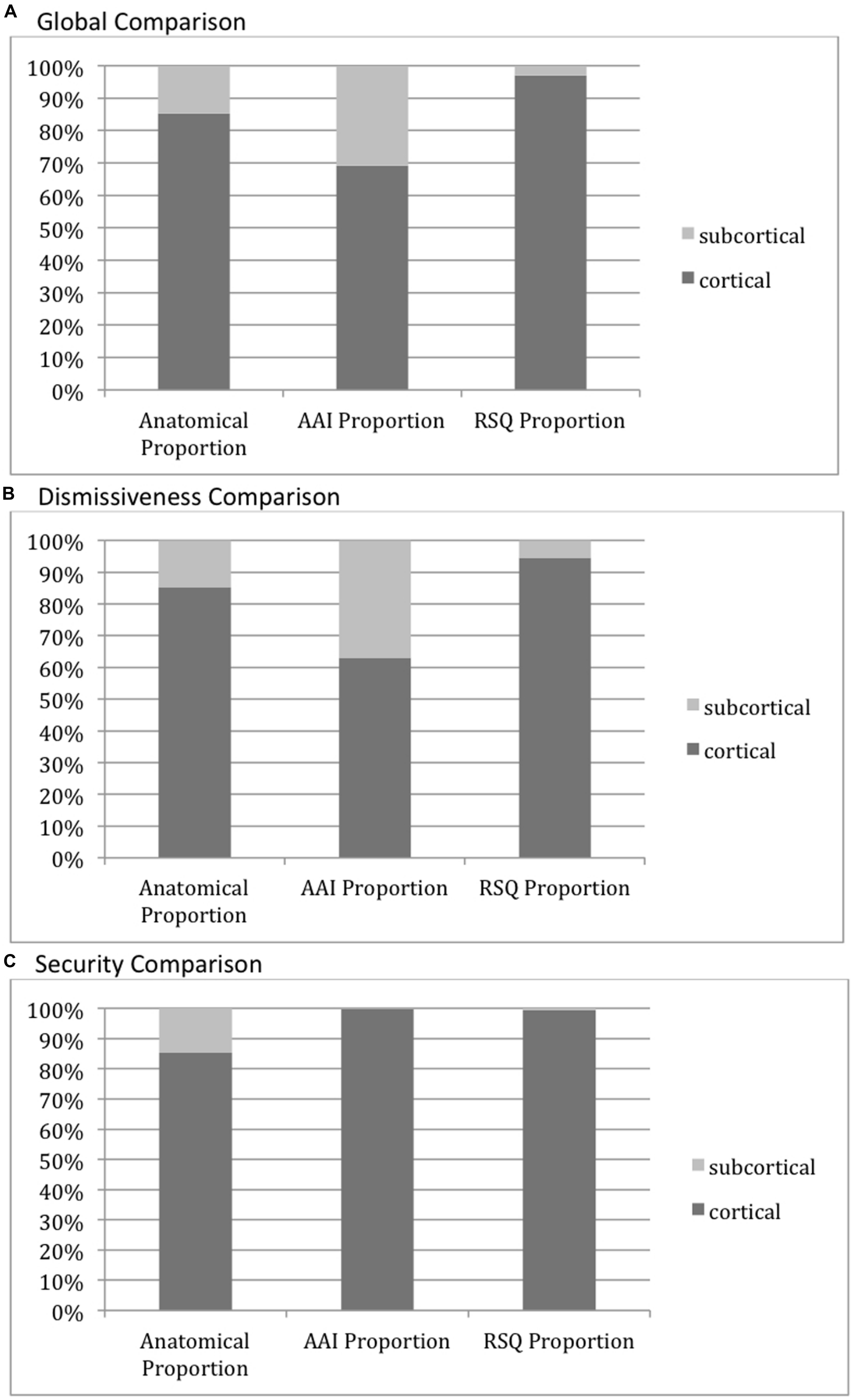


FIGURE 5 | Cortical vs. Subcortical activity distributions. The leftmost columns in each graph show the proportion of voxels in the cortical (dark gray) versus subcortical (light gray) anatomical masks, illustrating the relative size of each mask and the null-hypothesis distribution of voxels associated with each measure. The AAI and RSQ columns show the proportion of voxels significantly correlating with those measures falling within each anatomical mask. **(A)** Cortical vs. Subcortical activity: Global Comparison–all AAI/RSQ significant voxels. All pairwise proportion comparisons differ significantly at $p < 0.0001$. **(B)** Cortical vs. Subcortical activity: Dismissiveness Comparison–only AAI/RSQ Dismissiveness-measure significant voxels. All pairwise proportion comparisons differ significantly at $p < 0.0001$. **(C)** Cortical vs. Subcortical activity: Security Comparison–only AAI/RSQ Security-measure significant voxels. Pairwise proportion comparisons with anatomical proportion differ significantly at $p < 0.0001$. AAI vs. RSQ proportions do not differ significantly.

Finally, AAI security demonstrated a negative interaction with mood in the right middle temporal gyrus, a region associated with semantic processing of emotional visual stimuli (Ochsner and Gross, 2005).

Negative interaction effects were also found between mood and AAI dismissiveness in the right medial frontal gyrus, and bilateral medial somatosensory association cortices including the precuneus; these areas have been associated with affect regulation, and self-related mental imagery and episodic memory retrieval, respectively (Cavanna and Trimble, 2006; Fransson and Marrelec, 2008).

For RSQ measures of attachment styles, interaction effects were also found in brain regions associated with semantic processing, memory, and affect regulation. RSQ security demonstrated positive interactions with mood in Wernicke's area. As with AAI measures, RSQ security demonstrated negative interactions with mood in the right precuneus and middle temporal gyri. RSQ dismissiveness also demonstrated negative interactions with mood in the precuneus, as well as neighboring somatosensory association cortex areas. Surprisingly, RSQ dismissiveness also demonstrated an enhancing interaction with dysphoric mood in the supplementary motor area—a brain region that has been implicated in empathy (Borchardt et al., 2015).

Significant clusters are illustrated in Supplementary Figure S2. Coordinates of all peak voxels significant at the $p < 0.005$ level in clusters with extent based significance $p < 0.05$ are listed in Supplementary Table S6.

DISCUSSION

We commonly ask patients how they felt toward or were made to feel by others, especially significant others, with whom attachment plays an important relationship-shaping role, such as parents, romantic partners, children, and ourselves (as their therapists; Schore, 2003). Thus, the conscious appraisal of attachment figures' affective significance is a task with substantial ecological validity for a wide variety of psychotherapies, as making emotional appraisals conscious and explicit is a highly prevalent process in many. The process of such conscious affective appraisal is liable both to be influenced by attachment configuration and to be a therapeutic factor in the psychotherapy process (Schore, 2003).

This study is the first to compare self-report (explicit) and observer-rated narrative (implicit) measures of adult attachment in terms of brain activity. We compared the distributions of brain regions where activity associated with appraisal of a primary attachment figure correlated with either the AAI—an observer rated narrative measure, relying on non-conscious manifestation of attachment representations in verbal behavior, or, the RSQ—a self-report measure of adult attachment relying on conscious appraisal of attachment styles. Further, we examined the correlations between neural activity associated with explicit attachment-figure appraisal and attachment-dimensions as measured by the AAI and RSQ, as well as their interactions with negative mood.

Our results are pertinent to psychotherapy research in a number of ways. First, we obtain findings supporting the supposition that implicit and explicit assessments of attachment do in fact correspond to assessment of implicit and explicit components of the complex mental functions characterizing attachment configurations, with AAI assessment of attachment representation correlating with activity preferentially distributed in brain regions (the DMN and subcortical structures) associated with interoceptive and core affective experience, and RSQ assessed attachment style measures correlating with activity preferentially distributed in brain regions associated with exteroceptive and higher-order explicit processing of such affective information (EFN networks and cortical structures; Northoff et al., 2006; Sajonz et al., 2010). Second, we identify neural substrates whose activity during explicit appraisal of attachment-related affect is sensitive to variation with specific measures and dimensions of attachment characteristics. Finally, we demonstrate regions where negative mood and attachment characteristics interact in their effects on brain activity during attachment-figure appraisal.

In accordance with our first hypothesis, brain activity correlating with AAI measures of attachment was found disproportionately in DMN and subcortical brain regions, as would be expected for the measure assessing the pre-conscious/interoceptive aspects of attachment. In accordance with our second hypothesis, brain activity correlating with RSQ measures of attachment was found preferentially in Attentional/Frontal control areas with very little involvement of subcortical structures, as might be expected for this instrument measuring conscious/explicit aspects of attachment.

Furthermore, these findings generally held across orthogonal dimensions of attachment—the Secure-Fearful/Disorganized and Dismissing-Preoccupied dimensions—indicating that these findings are independent of rotation of attachment dimensions.

We found that RSQ-assessed attachment security was significantly anti-correlated with activity in the right middle temporal gyrus (involved in semantic processing of visual emotional cues) and in the left lateral PFC (involved in explicit affect regulation) during deliberate appraisal of subjects' mothers (Ochsner and Gross, 2005; Ochsner et al., 2012). This reduction in activity among more RSQ-securely attached subjects may indicate less effortful explicit processing of relational information. This is consistent with the teleology of secure attachment as resulting in a working model of the attachment figure as reliable and safe and thus requiring less explicit self-regulation of affect to be (mentally) approached. AAI-assessed security on the other hand was associated with enhanced activity in midline regions involved in empathy suggesting more active implicit processing of relational information. This finding is consistent with the etiology of secure attachment as the product of an empathic relationship between parent and offspring.

Interactions with severity of dysphoric mood were found for both the AAI and RSQ, primarily in brain regions involved in regulation of affect as well as semantic processing and memory. Negative interactions between attachment security and dysphoric mood were found for both AAI and RSQ measures in the middle temporal gyrus—a region associated with facial memory (Brent et al., 2016) and facial affect processing (Pohl et al., 2013). Notably this region is also involved in preferential parental responses to their own over others' infants (Atzil et al., 2012). Negative interaction effects on activity in this region suggest that reduction of activity here associated with depression (Vizueta et al., 2012) may be heightened by less secure and more preoccupied attachment characteristics.

Notably, also, both AAI and RSQ measures of dismissiveness exhibited negative interactions with mood in the precuneus. This brain region has been found to be an important hub of the DMN where it may serve to integrate self-referential thought and episodic memory retrieval (Fransson and Marrelec, 2008). Such a function seems to be highly pertinent to the conscious appraisal of the affective impact of attachment figure images. This negative interaction effect may be due to opposing cognitive biases associated with dismissing attachment and depression. Dismissing vs. preoccupied attachment is characterized by inhibited vs. enhanced recall of negative valence interactions on the one hand, and derogation of the value (positive valence) of connection on the other. Meanwhile depression is characterized by an attentional bias for negative information. Thus, perhaps, increased recall of negative interactions with attachment figures by depressed subjects as they attempt to evaluate the affective impact of attachment figure images is attenuated by more dismissing attachment and amplified by more preoccupied attachment.

These findings have both theoretical and practical implications. On a theoretical level, our results provide evidence that the overt contents of AAI and RSQ assessments match the actual constructs assessed by each. That is, the implicit assessment (AAI) overtly assesses non-conscious/implicit processes which are products of a "core self," while the self-report scale (RSQ) assesses (necessarily) conscious/explicit appraisals of emotion and behavior, and thus produces an assessment of "higher-order" cognitive aspects of relational function (Northoff et al., 2006; Sajonz et al., 2010). Moreover, these "higher-order" aspects of adult attachment are likely to be developmentally secondary to the AAI-assessed ones. Because of the iterative pattern of brain development, with globally burgeoning development in infancy, and continuing development through late adolescence (Shaw et al., 2008; Gilmore et al., 2012; Alcauter et al., 2014), the trajectory of development of core vs. higher-order self-functions is best examined through cognitive/behavioral rather than anatomical measures. In terms of cognitive/behavioral measures, a developmental hierarchy, with the emergence of, implicit core cognitive processes followed by explicit higher-order cognitive processes in childhood cognitive/behavioral maturation has been documented (Case, 1991; Howe et al., 1994; Howe and Courage, 1997). Thus, the attachment phenomena assessed by the RSQ may be viewed as the developmentally secondary and more externally oriented outcomes of the more primary internally oriented phenomena assessed by the AAI. Such a view would predict both the observed clinical relevance of both measures, and the limited correlations observed between them, as common primary processes are liable to find divergent secondary cognitive and behavioral expressions (Allen et al., 1998).

Considering attachment security as a dimension of relational script valence, one might relate this dimension to brain activity as a product of the intrinsic responsivities of positive vs. negative valence systems and compensatory activity of the systems that regulate them, as suggested, for example, by Disner et al. (2011) in relation to depression. In light of our findings, the AAI might be understood as more strongly related to those intrinsic responsivities while the RSQ might be understood as more strongly related to the activity of the regulatory system. Both systems, however, might be psychotherapeutic targets as well as moderators of intervention efficacy.

Considering attachment dismissiveness (avoidance) as a dimension of relational script salience, one might relate this dimension to brain activity as a product of the intrinsic responsivities of positive *and* negative valence systems and systems regulating attention to positive and negative social cues. Again, our findings suggest that the AAI measure might be considered as more strongly related to primary affective responsivity, while the RSQ might be considered as more strongly related to activity of the systems responsible for regulating attention to social information.

Our findings may thus also have important practical implications for psychotherapy study design and interpretation. For example, attachment characteristics are developed early in life and are largely conserved (Waters et al., 2000); this makes attachment a strong target for investigation as moderator of change processes and treatment outcomes in psychotherapy.

Several studies have examined moderation of psychotherapeutic outcomes by attachment characteristics, e.g., (McBride et al., 2006; Bagby et al., 2008). McBride et al. (2006) using the RSQ, found that with increasingly avoidant attachment, cognitive-behavioral therapy demonstrated increasing advantage over interpersonal psychotherapy in the treatment of major depression. Our findings bear on the interpretation of these results, given the author's use of the RSQ. The observed interaction between attachment and treatment modality might be predicted on two distinct (though not mutually exclusive) theoretical grounds, as the authors note in their discussion. Namely, interpersonal therapy, by focusing on close relationships, might be too emotionally threatening to persons with high attachment avoidance, and thus elicit excess distress, or it may be cognitively dissonant for persons who explicitly devalue close relationships and result in poor treatment alliance (which has been robustly demonstrated to be an important predictor of treatment outcome; Horvath and Symonds, 1991). Our findings would support the latter interpretation based on the authors' use of the RSQ and its primarily lateral cortical activity associations. Replication of McBride et al.'s (2006) findings using the AAI, which we found to associate significantly with medial and subcortical brain activity and thus be more liable to reflect core generation and regulation of emotion, might more strongly support the 'excess emotional threat' interpretation of their results.

Increases in attachment security can be important outcomes in psychotherapy (Travis et al., 2001; Levy et al., 2006). Moreover, such changes may be particular to the type of psychotherapy (Levy et al., 2006). Thus, in assessing the relative efficacy of specific therapeutic modalities in effecting attachment changes, the mechanism of action at the neuroactivity level should be related to the measure of outcome at the neuroactivity level. For example, transference focused therapy (TFP) focuses heavily on the development of reflective function (increasing interoception) as its mechanism of action (Clarkin et al., 2007). In turn, reflective function relies primarily on midline cortical structures (Buckner and Carroll, 2007). Thus our findings would indicate use of the AAI rather than the RSQ to assess attachment changes (Levy et al., 2006) in TFP. In contrast, schema focused therapy places significant emphasis on cognitive restructuring of patient schemata (Young et al., 2003; Kellogg and Young, 2006). Such deliberate cognitive restructuring may rely more prominently on processes such as deliberate reappraisals of negative emotions that bring in exteroceptively derived 'factual data' (e.g., 'Mary always smiles when she sees me'). Such deliberate reappraisals rely heavily on lateral prefrontal cortical activity and activity in the area of the temporoparietal junction (Ochsner et al., 2002; Buhle et al., 2014). One might therefore predict that RSQ assessment of attachment change would be more sensitive to effects of such a treatment than an implicit/projective measure such as the AAI. Furthermore, these lateral cortical regions (subserving exteroceptive, RSQ-assessed relational functions) demonstrate significant and evolutionarily conserved connectivity (Mars et al., 2013) to the medial PFC (subserving interoceptive, AAI-assessed relational functions). Thus, one might expect RSQ-assessed changes in attachment to mediate AAI-assessed changes following cognitive therapies, and the reverse to be observed following transference or emotion focused therapies.

On the other hand, both therapies might be characterized by a common factor of repeated exposure to interactions that would be perceived attachment threats (e.g., presaging rejection or abandonment) in the context of an insecure script. By a process of reversal learning, given a strong working alliance where the feared rejection or abandonment is seen not to occur, such repeated exposure might decouple the interaction from the threat response. This learning might be driven in different stages by changes in explicit regulatory strategy and by attenuation of core affective responsiveness (or both processes may occur in simultaneous and complementary fashion). To understand how such changes occur over time, tasks and biological measurement that probe both regulatory functions and core affective responses should be used along with attachment measures such as the RSQ and the AAI, which might reflect, respectively, the contributions of each of these domains.

Limitations

This study has a number of important limitations that should be considered in interpreting the findings. First, we examine only one narrative and one self-report measure of attachment. A detailed discussion of the range of adult attachment measures is beyond the scope of this paper, and so, the reader should note that there are several excellent reviews of adult attachment measures, Ravitz et al. (2010) being the most recent, to our knowledge. It is nonetheless worth considering here some other important exemplars of narrative and self-report measures of adult attachment. Among *narrative* measures of attachment, the Adult Attachment Projective (AAP; George and West, 2001) is the most prominent alternative to the AAI, and relies on analysis of narrative interpretations of a standardized set of attachment-related images (Ravitz et al., 2010). This feature has made it particularly valuable in the study of brain processes involved in adult attachment as AAP stimuli are easily presented during fMRI scanning. (See, for example, several of the articles in this special issue of Frontiers as well as (Buchheim et al., 2006, 2008). It is worth noting, however, that there is very strong convergence between AAI and AAP assessments (Ravitz et al., 2010), so our results for the AAI might be expected to apply to the AAP as well. Among *self-report* assessments of adult attachment, a recent meta-analysis comparing five commonly used dimensional measures, not including the RSQ, found the Revised Experiences in Close Relationships scale, which focuses on attachment in partnered (i.e., romantic) relationships, to have superior reliability with a stable two-factor structure (anxiety and avoidance) akin to our security and dismissiveness dimensions for the RSQ (Graham and Unterschute, 2015). Given modest correlations among self-report measures, it is possible that our results for the RSQ might not apply to other measures.

In addition to the limitation of using only one self-report and one narrative attachment measure, we also report on only one of several possible dimensional approaches to characterization of these assessments. Others have proposed other methods for assessment of attachment dimensions in the RSQ and AAI. However, our results document similar DMN versus EFN activity distributions across orthogonal dimensions within a measure but different distributions between measures. This suggests that the limitation involved in our choice of attachment dimension extraction from the measures used is more pertinent to the consideration of specific individual structures' functional relations to a given measure than to the global comparison of the AAI versus the RSQ's patterns of association with brain activity. In addition, it should be noted that dimensional approaches to interaction effects are sensitive to transpositions of the dimensional measures; to mitigate this issue we median centered our measures for interaction effect analyses so that zero would correspond approximately to the cut point between categorical notions of symptomatic and asymptomatic. However, in samples with different median scores, different results might be obtained.

A second limitation of the current study is the lack of assessment and control for the extent to which subjects' mothers were their primary attachment figures. However, the requirement that subjects have been raised in a household with their mothers from birth until at least age thirteen significantly mitigates this limitation.

A third limitation is the absence of systematic activation of the attachment system by any threatening or distressing stimulus in the scanning paradigm, as such stimuli have been found to increase the salience of attachment figures (Mikulincer et al., 2002). While the cold and isolated conditions of an fMRI scan might serve this purpose, some studies suggest more attachment-specific stressors may be needed (Nolte et al., 2013).

Finally generalizability is limited both by the small sample size and the restriction to women aged 18–30 years.

CONCLUSION

The AAI and RSQ measure different aspects of attachment with highly divergent associated brain activity. The AAI taps DMN and subcortical structure activity more extensively, while the RSQ taps EFN activity more extensively. Thus, the AAI may assess non-conscious 'core-self' and interceptive processes in attachment figure appraisal, while the RSQ captures higher-order cognitive aspects that integrate externally derived information. Common effects of AAI- and RSQ-measured attachment security on the impact of mood on deliberate affective appraisal of an attachment figure are consistent with the notion that the 'core-self'-related and higher-order cognition-related processes tapped by each measure do indeed belong to a common attachment network.

AUTHOR CONTRIBUTIONS

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

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fnhum.2016.00090

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frontiers in Human Neuroscience

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Emotional Availability Modulates Electrophysiological Correlates of Executive Functions in Preschool Children

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Executive functions (EFs) – a set of cognitive control abilities – mediate resilience to stress and are associated with academic achievement and health throughout life. They are crucially linked to prefrontal cortex function as well as to other cortical and subcortical brain functions, which are maturing throughout childhood at different rates. Recent behavioral research suggested that children's EFs were related to parenting quality and child attachment security, but the neural correlates of these associations are unknown. With this study we tested in 4- to 6-year-old healthy children ($N = 27$) how emotional availability (EA) of the mother-child-interaction was associated with behavioral and electrophysiological correlates of response inhibition (a core EF) in a Go/Nogo task, using event-related potential recordings (ERPs), and with behavioral performance in a Delay of Gratification (DoG) and a Head-Toes-Knees-Shoulders task (HTKS). Our data showed that the Go/Nogo task modulated children's ERP components resembling adult electrophysiological indices of response inhibition - the N2 and P3/LPC ERPs-, but the children's N2 and P3/LPC ERPs showed longer latencies. Higher maternal autonomy-fostering behavior and greater child responsiveness were significantly associated with smaller children's N2 Go/Nogo effects at fronto-central and parietal sites and with greater Go/Nogo effects in the N2 time window at occipital sites, over and above children's age and intelligence. Additionally, greater maternal sensitivity and a higher dyadic EA quality of the mother-child-interaction went along with greater occipital Go/Nogo effects in the N2 time window, but this effect clearly diminished when we controlled for children's age and intelligence. Higher maternal autonomy-support was also positively associated with better HTKS performance, and higher dyadic EA quality went along with higher HTKS and DoG scores. However, no significant associations were found between EA variables and the behavioral response inhibition measures of the Go/Nogo task. Our results suggest that parenting qualities modulate the functionality of neural circuits involved in response inhibition, an important component of EFs. This finding, thus, indicates that parent–child interactions shape the neurocognitive development underlying EFs.

Keywords: executive function, EEG, Go/Nogo, child development, emotional availability, autonomy support, parenting, parent–child interaction

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INTRODUCTION

Parenting and the quality of parent–child relationship are crucial for children's emotional development and the establishment of attachment patterns (Bowlby, 1969; Ainsworth and Bell, 1970). However, there is growing evidence that the quality of parent–child relationship also shapes children's EFs skills (e.g., Belsky et al., 2007; Bernier et al., 2010, 2012; Blair et al., 2011; Dilworth-Bart, 2012; Towe-Goodman et al., 2014; Bindman et al., 2015). The term EFs refers to higher-order cognitive skills, that allow for flexible, adaptive and goal-oriented behavior (e.g., Norman and Shallice, 1986). EFs have considerable impact on personal well-being over the life course and on societal prosperity: They are considered as "vital for human autonomy" and are associated with social competence, academic achievements, socioeconomic status, stress coping, health-related behaviors (e.g., substance abuse), physical and mental health, and criminality (e.g., Mischel et al., 1989; Morgan and Lilienfeld, 2000; Royall et al., 2002; Blair and Razza, 2007; Best et al., 2011; Moffitt et al., 2011; McClelland et al., 2014).

According to a predominant theory of EF, proposed by Miyake et al. (2000), the EF construct comprises three separable, but interrelated components – i.e., working memory updating, inhibition, and shifting. The interrelations between the dissociable components point to a "common mechanism across different EFs" (Miyake et al., 2000). There is not yet a consensus about the quality of this common EF mechanism. Several researchers have suggested that an attention system constitutes the core of EFs, e.g., as proposed in the framework of the supervisory attentional system (Norman and Shallice, 1986), the theory of the executive attention network (Rueda et al., 2004; Posner and Rothbart, 2007) and in the concept of the controlled attention system (Engle et al., 1999).

Zelazo and Müller (2002) put forward to additionally distinguish between 'cool' and 'hot' EF (Zelazo and Carlson, 2012). 'Cool' EFs refer to abstract, affectively neutral contexts, while 'hot' EFs involve the top-down control of motivation and affect. Different brain areas are assumed to subserve 'cool' and 'hot' EFs: 'Cool' EFs possibly recruit the lateral prefrontal cortex and 'hot' EFs orbitofrontal and other medial prefrontal cortex areas (Zelazo and Carlson, 2012).

Executive functions were originally conceptualized as exclusively frontal cortex function. However, lesion and neuroimaging studies revealed that the frontal cortex is neither specific nor sufficient for executive functioning and that EFs involve an extended network encompassing frontal, parietal, temporal, and occipital cortices as well as subcortical areas (Alvarez and Emory, 2006). The interpretation of these findings is nevertheless complicated by the fact that EFs control the production of activities and thereby interact with and depend on other processes such as for instance perception or memory (Royall et al., 2002; Alvarez and Emory, 2006). This issue leads to the so-called task impurity problem in the measurement of EFs: Tasks that are designed to measure EF proficiency not only involve the target EF, but other cognitive processes as well (Miyake et al., 2000).

The prefrontal cortex matures at a slower rate than most other brain areas, with highest plasticity until age 7, and its maturation protracts into young adulthood (Huttenlocher and Dabholkar, 1997; Gogtay et al., 2004). A similar developmental pattern has been observed for EFs. EFs develop over childhood and adolescence into adulthood (Garon et al., 2008; Best and Miller, 2010) and show moderate stability over the life course (e.g., Mischel et al., 1989; Casey et al., 2011). It is assumed that brain maturation parallels the evolution of children's EF abilities (e.g., Garon et al., 2008; Best and Miller, 2010). A comparative study with human infants and primates provided evidence that brain maturation of prefrontal cortices likely underlies the developmental improvements in EFs during the first year of life (Diamond and Goldman-Rakic, 1989). Infancy and early childhood are considered pivotal for the EF development (Garon et al., 2008; Best and Miller, 2010). Rudiments of the EF components inhibition, working memory updating and shifting, as well as of voluntary attention are present as from the first year of life (Garon et al., 2008). Rapid growth of EF occurs in preschool and early school years, and children become able to deal with more complex EF tasks (Garon et al., 2008; Best and Miller, 2010). From 3 to 5 years of age all three EF components (i.e., inhibition, working memory updating, shifting) improve significantly (e.g., Carlson, 2005; Garon et al., 2008). The observed EF improvements could be either attributed to quantitative changes in each EF component and/or to changes in the underlying common factor, as was put forward by Garon et al. (2008), for instance.

Mammalian brain maturation is not solely genetically determined, but relies upon appropriate, species-typical stimulation from the environment (experience-expectant maturation) and it is shaped by environmental stimuli, that may be unique to an individual (experience-dependent maturation; Greenough et al., 1987). Animal studies revealed that variations in the environment have a strong impact upon animal's brain structure, with varying effects at different ages (e.g., Kolb et al., 1998). However, not only the physical environment, but also the emotional quality of caregivers' interactions with the child are important for brain and cognitive-emotional development (Harlow and Harlow, 1962). With regard to humans, children's brain structure and functioning is affected by adverse rearing conditions (e.g., Sheridan et al., 2012), and ordinary variations in maternal sensitivity and intrusiveness are associated with differences in children's frontal brain activity (Hane and Fox, 2006). Developmental research, in particular attachment theory, highlighted the importance of the caregiver–child relationship on children's cognitive, social, and emotional growth (Harrist and Waugh, 2002; Sroufe, 2005; Waller et al., 2015). It has been assumed that caregivers initially serve as external regulators of the infant and facilitate the progression from external to internal regulation, depending on parental sensitivity to the child (e.g., Kopp, 1982). Parental sensitivity, defined as prompt, contingent, and appropriate response to infant's behavior, is closely linked to child attachment security (e.g., Bowlby, 1969; Blehar et al., 1977).

Abbreviations: HTKS, Head–Toes–Knees–Shoulders Task; DoG, delay of gratification task; EF, executive function; EA, emotional availability; EA CS, EA clinical screener; ERP, event-related potentials; LPC, late positive complex; M, mean.

A secure attachment provides the child with a secure base for competent exploration of the environment (Ainsworth and Bell, 1970). The opportunity for exploration likely allows the child to develop and practice self-controlled actions (see e.g., Bernier et al., 2012). Child attachment security is not only determined by parental sensitivity, but also by parental autonomy-support (Whipple et al., 2011) and mind-mindedness (Meins et al., 2001). Mind-mindedness describes the parental tendency to perceive the child as individual with own mental states, and to appropriately comment on the child's mental states (Meins et al., 2001). Autonomy-support is defined as the parental tendency to recognize and value children's needs, to support their choices and their independent problem-solving. It involves scaffolding behavior that offers age-appropriate problem-solving strategies to the child. Carlson (2003) proposed that maternal sensitivity, mind-mindedness and autonomy-support might be crucial facilitators of children's EF development.

As outlined above, individual differences in EFs may be accounted for by genetic and/or (social) environmental factors. Twin and genetic association studies suggest that EFs are under considerable genetic control (Friedman et al., 2009; Barnes et al., 2011). Similar results were obtained for the attention network (Fan et al., 2001; Barnes et al., 2011).

However, the social environment proved to be relevant for EF proficiency as well, as revealed in several cross-sectional or longitudinal studies that investigated home environment characteristics and different aspects of parenting in their relation to children's EF:

Lower socioeconomic status (operationalized as maternal education and household income) was significantly associated with worse performance in EF tasks in children (at ages 4–5; Dilworth-Bart, 2012). Parental education (but not occupation or income-to-needs ratio) accounted for about 12% of variance in EF performance in children (mean age 5 years), with lower parental education predicting lower EF task scores (Noble et al., 2005).

Maternal sensitivity at 1 or 2 year(s) predicted EF capacity in children at ages 18 months to 3 years (Bernier et al., 2010, 2012; Towe-Goodman et al., 2014). Similarly, greater maternal sensitivity at 54 months and at 6 years was associated with better attentional control at ages 6 and 9 (Belsky et al., 2007), and greater maternal responsiveness at 22 months (albeit not at 9 nor 14 months) was related to higher effortful control (a construct overlapping with EFs) in children aged 22 and 33 months (Kochanska et al., 2000). Father's sensitive caregiving (Bernier et al., 2012; Towe-Goodman et al., 2014), maternal scaffolding (Bibok et al., 2009; Hughes and Ensor, 2009; Hammond et al., 2012) and maternal mind-mindedness (Bernier et al., 2010, 2012) were significantly associated with children's EF outcomes. The latter also predicted EF improvements between 18 and 26 months better than other parenting variables (Bernier et al., 2010). In studies that investigated parenting multidimensionally, attachment security, and maternal autonomy-support emerged to be most predictive for EF performance (Bernier et al., 2010, 2012; Bindman et al., 2015). Child attachment security at ages 12 and 18 months also predicted DoG proficiency in a 'hot' EF task in 6-year-olds (Jacobsen et al., 1997) and higher maternal responsiveness and autonomy-support across the first 3 years were significantly related to more proficient DoG at 54 months (Razza and Raymond, 2013; Bindman et al., 2015).

While the importance of attachment-related experiences for EF development has been demonstrated in several studies, little attention has been paid on whether and how these experiences are associated with EF-related neural processes in children. We hypothesized that the quality of parent–child interactions modulates neural processes that underlie children's EF performance. In the present study, we investigated how the quality of caregiver–child interactions is associated with behavioral and electrophysiological measures of EFs.

We chose EA as construct to assess the quality of the caregiver–child interactions. EA "refers to a dyad's capacity for emotional connection and the extent to which the connection is genuinely affectively positive and healthy and the extent to which the dyad can accommodate and downregulate negative affect" (Biringen and Easterbrooks, 2012b). The EA construct is considered to contain attachment as a component. EA focuses more on positive emotions compared to attachment theory and can be assessed across a broader range of situations (Biringen and Easterbrooks, 2012b). Several studies demonstrated that key aspects of the caregiver–child relationship can be measured by the EA scales in a reliable and valid manner (see e.g., Biringen and Easterbrooks, 2012b; Bornstein et al., 2012).

For the assessment of EFs, we chose behavioral tasks that are well established in developmental research: (a) The HTKS, that involves all three dimensions of EF and refers to the concept of 'cool' EF, (b) the DoG, that implicates impulse control and refers to 'hot' EF, and (c) the Go/Nogo task, that targets (behavioral) response inhibition and has been intensively studied in electrophysiological research. During the Go/Nogo task event-related potentials (ERPs) were recorded to reveal the electrophysiological correlates of EF.

The Go/Nogo task allows for the minimization of other cognitive and behavioral processes, thereby reducing the task-impurity problem. The Go/Nogo task involves two conditions: In the 'go' condition participants have to respond to a given target stimulus. In the 'nogo' condition subjects have to refrain from a response to a given stimulus. In electrophysiological studies in adult or adolescent participants the effect of response inhibition (Go/Nogo effect) was shown to be associated with two event-related potentials, the N2 and the P3 component (Kopp et al., 1996; Kiefer et al., 1998; Stroth et al., 2009). The N2 component is a negative ERP that peaks over fronto-central sites between 150 and 350 ms after stimulus presentation, with a larger amplitude in the 'nogo' condition compared to the 'go' condition. This N2 Go/Nogo effect is assumed to be associated with higher-order inhibitory processes (Eimer, 1993; Kiefer et al., 1998; Ruchsow et al., 2008) and/or conflict monitoring (Nieuwenhuis et al., 2003; Donkers and van Boxtel, 2004). Source analyses suggested that the 'nogo' N2 is generated in bilateral inferior frontal cortices (Kiefer et al., 1998). The P3 component, alternatively labeled as late positive complex (LPC), is a positive ERP that usually peaks between 300 and 600 ms after stimulus presentation. The 'go' P3 shows its maximum over centro-parietal sites, while the 'nogo' P3 is enlarged over fronto-central sites. According to source analysis the P3 Go/Nogo effect likely originates from anterior cingulate and motor cortex activity (Kiefer et al., 1998). The P3 is assumed to reflect attentional resource allocation engaged for the evaluation of stimuli, and to be related to working memory processes involving context updating and subsequent memory storage (Polich, 2007). Comparably to the N2, the P3 Go/Nogo effect is regarded as signature of response inhibition (Kiefer et al., 1998; Smith et al., 2008). On the basis of neuroimaging data a model for behavioral response inhibition was posited by Aron (2007): Successful inhibition possibly activates a fronto-subthalamic circuit (i.e., inferior frontal cortex and subthalamic nucleus) and subsequently leads to the inhibition of the primary motor cortex via basal ganglia/thalamo-cortical pathways.

Developmental neuroimaging and electrophysiological studies of response inhibition suggested immature prefrontal cortex functioning as well as different task strategies in early and middle childhood compared to adults (Bunge et al., 2002; Davis et al., 2003; Jonkman et al., 2003; Ciesielski et al., 2004; Jonkman, 2006). With regard to behavioral measures children usually preformed less accurate (Casey et al., 1997; Bunge et al., 2002; Davis et al., 2003; Jonkman et al., 2003; Ciesielski et al., 2004) and with slower reaction times (Bunge et al., 2002; Davis et al., 2003; Ciesielski et al., 2004; Lamm et al., 2006) than adults in response inhibition tasks. Electrophysiological research additionally revealed decreases in latencies and amplitude of the N2 (Davis et al., 2003; Jonkman et al., 2003; Jonkman, 2006; Lamm et al., 2006) and P3 (Davis et al., 2003) ERP components as a function of children's age. Decreases in 'nogo' N2 amplitude were associated with better EF performance over and above effects of age (Lamm et al., 2006). Absent 'nogo' P3 in children (ages 6–7, respectively, 9–10) was reported by Jonkman et al. (2003) and Jonkman (2006) and different P3 patterns in 6-year-old children compared to adults were observed by Davis et al. (2003). These developmental changes in the N2 and P3 components might reflect ongoing maturation of the prefrontal cortex.

Earlier ERP components than the N2 or P3, such as the N1 ERP component, are usually disregarded for the evaluation of response inhibition in Go/Nogo tasks. However, an enlargement of the N1 in the 'nogo' relative to the 'go' condition was observed by Filipović et al. (2000) and by Lavric et al. (2004). The N1 component is a negative ERP that peaks between 125 and 175 ms over parieto-occipital sites for visual stimuli (Harter et al., 1982; Luck et al., 1990). Focused attention leads to an enlargement of the N1 (e.g., Luck et al., 1990). It has been proposed that the enlarged N1 component refers to an early visual selection process and represents the orienting and/or recruiting of an attention system to a task-relevant location (Luck et al., 1990). It was assumed that the N1 'nogo' effect might trigger the later inhibitory process (Lavric et al., 2004) and might be more specifically related to the 'nogo' decision than later components (Filipović et al., 2000).

As outlined above, we aimed at investigating whether and how parenting is associated with EF-related neural processes in children, using ERP recordings. To our knowledge, this issue has so far not been addressed by other studies. We hypothesized that the quality of parent–child interactions modulates neural processes that underlie children's EF performance. In the present study, we investigated how the quality of caregiver–child interactions is associated with behavioral and electrophysiological measures of EFs. The interaction quality was assessed with the construct of EA. For the assessment of children's EF ability, the HTKS, DoG and Go/Nogo tasks were chosen. Children's ERPs were recorded during Go/Nogo performance. Children were 4- to 6-year-old. We hypothesized that the Go/Nogo effects on the N1, N2, and P3 ERP components are related to the behavioral EF task performance indicating that electrophysiological measures are indicative of response inhibition performance.

We also predicted that higher EA scores are associated with (a) better behavioral EF task performance and with (b) Go/Nogo effects of the ERP components N1, N2, and P3 that are indicative of more efficient EF skills.

MATERIALS AND METHODS

Participants

Data from 27 parent–child dyads were used for the analysis. Mean age of the children ($n = 27$, four sibling pairs) was 58.7 months ($SD = 6.6$, range 48.1–72.8; 48.2% girls). Mothers ($n = 23$) were between 29.4 and 48.6 years old ($M = 39.0$, $SD = 4.0$), and had either a master's degree (63.0%) or an otherwise completed professional education (37.0%). All mothers were married or living with the child's father.

Families were recruited in kindergartens of Ulm and Neu-Ulm (Germany). Inclusion criteria were children's age (48–73 months), mastery of the German language and absence of any known psychiatric or neurological disease or severe developmental delay according to parent report. A total of 36 children was recruited. For eight children EEG data were not available due to technical problems or due to discontinuation of the EEG experiment. These data sets were therefore excluded. One child was excluded because of low performance in the intelligence task (i.e., below two standard deviations according to normative, age-adjusted data (Bulheller and Häcker, 2002)). Mothers gave written informed consent and the study protocol was approved by the local ethics committee according to the declaration of Helsinki.

General Procedure

The current study involved two laboratory visits for the mother–child dyad, typically within 2 weeks. During the first visit children were administered several behavioral EF tasks and one intelligence test. In order to assess EA, mother and child engaged in free play and their interaction was videotaped. A questionnaire battery was delivered to the mother including reports on family demographics and child's behavior. During the second visit children participated in a Go/Nogo task, which measures EFs, and during which task-related electroencephalographic activity was recorded.

Assessment of Emotional Availability

Mothers and children were instructed to play at a table with toys in a typical manner, and to tidy the table at the end of the play. The duration of this free-play interaction was at least 20 min. The mother–child interaction was videotaped and the interactions were coded for maternal and child's behavior using the fourth edition of the EA scales (Biringen, 2008).

Emotional availability is a global measure of "dyadic or relational capacity for mutual emotional awareness, perception, experience, and expression" (Biringen et al., 2005; Biringen and Easterbrooks, 2012b). The EA measure has been empirically validated for parents of children aged 0–14 years (Biringen and Easterbrooks, 2012b). Its operationalization comprises four adult components (sensitivity, structuring, nonintrusiveness, nonhostility), two child components (responsiveness, involvement) and the EA CS. Adult sensitivity assesses warmth and attunement to emotional cues. Adult structuring refers to guidance of child's play and to setting limits, and it also involves autonomy-fostering behaviors. Encouragement of age-appropriate autonomy by the absence of interference, overprotection or withdrawal is operationalized as nonintrusiveness. Adult nonhostility describes the emotional range from absent hostility to covert or open hostile behavior. Child responsiveness is characterized as child's behavioral and emotional responsiveness comprising compliance. Lower scale points either indicate over- or under-responsiveness of the child. Child involvement describes child's initiative to engage the adult in the interaction. Finally, the EA CS is a global measure of the adult–child relationship quality, with an emphasis on adult sensitivity and child responsiveness (Biringen and Easterbrooks, 2012a,b).

The adult and child components are rated on a 7-point Likert-type scale (D-scores) and on a 29-point rating scale (T-scores), the latter are a sum of seven subscales. High scores represent the optimal level of EA and low scores indicate complicated EA. The EA CS ranges from 1 to 100 points; high EA CS scores (>80) indicate a dyadic EA. D-scores and T-scores were highly correlated ($\rho \geq 0.88$) and D-scores yielded results that were similar to those of the T-scores (data not shown).

However, as T-scores are assumed to "more fully capture the variability among cases" (Biringen and Easterbrooks, 2012a), further data analyses were based on T-scores. We additionally summed up the T-scores of the four adult and the two child EA scales to the variable "EA sum."

Emotional availability coding uses verbal and non-verbal indicators (like physical, facial, and vocal signals as well as displays of positive and negative emotions), with an emphasis on non-verbal cues. Coding was done by one research assistant who had obtained inter-rater reliability with Biringen. Five dyads were coded by a second trained assistant and inter-rater reliability was very good for five of the EA scales (adult structuring, adult nonintrusiveness, adult nonhostility, child responsiveness, child involvement; ICC > 0.89, $p < 0.01$), acceptable for adult sensitivity (ICC $= 0.67$, $p = 0.052$), but rather low for EA CS (ICC $= 0.55$, $p = 0.10$).

Emotional availability scores of one child were missing due to technical problems with the video equipment. We expected that EA is not stochastically independent for siblings; therefore we excluded one child of each sibling pair at random, resulting in a sample size of 22 dyads.

Behavioral Executive Functions Tasks

Head–toes–knees–shoulders task (HTKS)

The HTKS task is a measure of cognitively mediated behavioral self-regulation that involves attention, cognitive flexibility, working memory, and inhibitory control, i.e., components of EFs (Cameron Ponitz et al., 2008; McClelland et al., 2014). The task is appropriate for children aged 4–8 years. The HTKS comprises 30 test items, and scores range from 0 to 60. Higher scores imply higher levels of EFs. The HTKS is divided into three sections with 10 items each, and involves up to four paired behavioral rules ("touch your head/toes/knees/shoulders"): In the first section, children have to respond in a non-automatic way (i.e., touching their toes when told to touch their head, and vice versa), in the second section, a paired behavioral rule is added (i.e., touching their knees when told to touch their shoulders, and vice versa), and in the third section, the rules are changed by switching the pairings (i.e., toes go with shoulders and head goes with knees). The task was shown to be reliable and valid, to have good test–retest stability and to significantly predict academic achievements (McClelland and Cameron, 2012; McClelland et al., 2014). In this study, we administered the validated German version (von Suchodoletz et al., 2014).

Delay of gratification task (DoG)

The DoG task measures the child's ability to "[voluntarily postpone] immediately available gratification in order to attain delayed but more valued outcomes" (Mischel et al., 1989). The task was shown to be predictive for social and cognitive competence in later life (Mischel et al., 1989). The DoG is assumed to involve cognitive control of motivation and affect (Hongwanishkul et al., 2005).

In this study, children were first asked to choose their preferred candy (Smarties, lollipop, jelly babies), which was subsequently placed in front of them. The experimenter then explained to the children that their mother and the experimenter had to leave the child for a while and that the candy was meant for the child as a reward for waiting. Children were also told that they would receive a further candy portion if they waited until the return without leaving their chair, eating the candy or ringing the bell. The child was informed that it can shorten the waiting period by ringing the bell, but that then it would only receive one instead of two candy portions. Scores were the number of seconds waited (Mischel et al., 1989). Maximum duration of the task was 15 min.

Control Variables

Colored progressive matrices task (CPM)

Child's general intelligence was assessed with a non-verbal task, the Colored Progressive Matrices task (Raven et al., 1998; Bulheller and Häcker, 2002). The task contains 36 items, and the maximum score is 36. The percentile rank was computed for each child by use of normative, age-adjusted data (Bulheller and Häcker, 2002).

Children's age and *maternal education* were assessed in maternal reports on sociodemographic variables.

Strengths and difficulties questionnaire (SDQ)

The Strengths and Difficulties Questionnaire Version P4-16 (Goodman et al., 2000; Goodman, 2001), a brief behavioral screening instrument for children aged 4–16 years, was administered to the mothers. The SDQ measures psychopathology and prosocial behavior. The questionnaire contains 25 three-point items, that are divided between 5 subscales: "emotional symptoms," "conduct problems," "hyperactivity/inattention," "peer relationship problems," and "prosocial behavior." The first four subscales are summed up to generate a total difficulties score[1]. Children's behavior is classified according to the sum scores (of the subscales resp. the total difficulties score) into "normal," "borderline," and "abnormal" behavior. In a general population 80% of the children show "normal," 10% "borderline," and 10% "abnormal" behavior (Goodman et al., 2000).

EEG Experiment

Go/Nogo task

The Go/Nogo task requires inhibition of a prepared response, thereby implicating inhibitory control processes. In the 'go' condition the participant has to respond to a given target stimulus. In the 'nogo' condition the subject has to withhold a response to a given stimulus. The 'go' stimulus was a picture of a circular wooden board. The 'nogo' stimulus was a picture of a cookie, i.e., a rewarding cue, which should induce approach tendencies and render the suppression of the response more difficult (see Casey et al., 2011). 'Go' and 'nogo' stimuli were selected such that shape and color of the stimuli were highly similar in order to keep visual processing of the stimuli comparable. The stimulus size was 16 cm × 11 cm (410 × 314 pixel) for 'go' and 'nogo' stimuli. We presented the 'go' stimulus with a higher frequency than the 'nogo' stimulus (80 vs. 40 trials per condition), so that participants were used to prepare and execute a response in the majority of trials, which had to be withhold in the rare 'nogo' condition. Stimulus duration of both 'go' and 'nogo' stimuli was 750 ms, interstimulus interval varied between 1600 and 2000 ms ($M = 1800$ ms). Children were instructed to press a key as fast and as accurately as possible only when the wooden board ('go' stimulus) was presented, but to withhold a response upon the cookie ('nogo' stimulus).

As behavioral data, we recorded the response latency in the 'go' trials and the response accuracy for both 'go' and 'nogo' trials. Response accuracy is reported in terms of relative frequency of correct responses in the 'go' trials (hits) and relative frequency of incorrect responses in the 'nogo' trials (false alarms). Additionally, the sensitivity measure d', which is "defined as the separation, in standard deviation units, between a pair of hypothesized normal density functions representing the internally observed effects of signal plus noise, and noise alone" (Nevin, 1969), was calculated by subtracting z(false alarms) from z(hits), with z as "the inverse of the normal distribution function" (see e.g., Macmillan and Creelman, 2005). The measure d' hence captures performance independent of response biases according to signal detection theory (Green and Swets, 1966).

Additionally, a sum score, *EF sum*, of z-standardized HTKS, DoG and Go/Nogo d' scores was computed (for data reduction purposes). A factor analysis of the EF task scores was not appropriate due to the small sample size.

EEG recording and ERP extraction

Children were seated in a height-adjustable chair in a sound-attenuating, electrically shielded booth. EEG was continuously recorded using 39 channels mounted in an elastic cap (Easy Cap, Herrsching, Germany). Sintered Ag/AgCl-electrodes were positioned according to the extended 10–20 system. All electrodes were referenced to an electrode at the left earlobe. Eye movements were registered by vertical and horizontal electro-oculograms. Electrode impedances were kept below 5 kΩ. Electrical signals were continuously recorded with BrainAmp amplifiers (BrainProducts GmbH, Gilching, Germany) with a bandwidth of 0.01–100 Hz and a 50 Hz notch filter. The data were digitized at a sampling rate of 500 Hz. After data acquisition a Butterworth Zero Phase Filter (low cutoff: 0.20 Hz, 12 dB/oct; high cutoff: 30 Hz, 24 dB/oct) was applied to the data. EEG data were analyzed using BrainVision Analyzer 2.0 (BrainProducts GmbH, Gilching, Germany).

Continuous EEG was segmented from 150 before to 1000 ms after stimulus onset. Ocular artifacts were removed using a regression method proposed by Gratton et al. (1983) and segments were baseline corrected to an interval of 150–0 ms before stimulus onset. Artifacts were automatically rejected by use of following criteria: minimal allowed amplitude of -100 μV, maximal allowed amplitude of 100 μV and maximal allowed absolute difference of 180 μV. Afterward, data were manually checked whether all artifacts had been removed. Stimulus-locked event-related potentials (ERPs) were extracted by averaging artifact-free EEG segments for 'go'- and 'nogo'-trials separately. EEG epochs with delayed or erroneous responses were excluded from ERP analysis.

Statistical Analyses

ERP components

ERP components of interest were the N1, N2, and P3/LPC components. For statistical analyses, electrodes were selected in clusters over occipital, parietal, and fronto-central scalp regions, including lateral as well as midline electrodes in separate clusters, at which these components were typically largest (Coles and Rugg, 1995). Potentials were averaged across electrode sites within left and right hemisphere clusters, respectively: Left (O1) and right occipital (O2), left (cluster Par-left: P3, P7) and right parietal (cluster Par-right: P4, P8), left (cluster Fcentral-left: FC3, C3, CP3) and right fronto-central (cluster Fcentral-right: FC4, C4, CP4) as well as midline electrodes including occipital (Oz), parietal (Pz), and fronto-central (Cz) electrodes.

We identified an occipital N1 ERP component, a fronto-central N2 component and a parietal P3/LPC component.

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[1] http://www.sdqinfo.com/a0.html

We labeled the ERP components according to their order of appearance in time because ERP latencies vary with age (see e.g., Davis et al., 2003; Jonkman et al., 2003; Itier and Taylor, 2004; Jonkman, 2006; Lamm et al., 2006).

For statistical analyses, mean amplitudes within time windows centered at the corresponding peaks of these components were computed as dependent ERP variables. The N1 time window was defined as time period from 184 to 284 ms after stimulus presentation, the N2 time window lasted from 318 to 518 ms and the P3/LPC time window from 600 to 800 ms. ERP amplitudes in the N1, N2, and partially P3/LPC time window were found to be polarity inverted at fronto-central electrode sites compared with occipital and parietal sites, similarly to previous studies (Kiefer et al., 1998; Kaiser et al., 2003).

Mean potentials at all electrode sites (i.e., occipital, parietal, fronto-central, and midline electrodes) were analyzed in repeated measures analyses of variance (ANOVAs) for each ERP time window separately, in order to reveal significant differences between ‘go’ and ‘nogo’ condition for the selected electrodes/electrode clusters. The ANOVAs included two within-subject factors for the occipital and midline electrodes: Condition (‘go,’ ‘nogo’) and hemisphere/electrode sites (occipital: O1, O2; midline: Oz, Pz, Cz). For the parietal and fronto-central clusters three within-subject factors were included: Condition (‘go,’ ‘nogo’), hemisphere (left, right) and electrode sites (parietal: P3/P4, P7/P8; fronto-central: FC3/FC4, C3/C4, CP3/CP4). We only report the main effects of condition and the interaction effects of condition and hemisphere, in order to reduce the complexity of the result section. In case of significant interactions, follow-up analyses were conducted using *post hoc t*-tests.

For correlational analyses ERP Go/Nogo effects were computed by subtracting potentials of individual ‘nogo’ ERPs from those of ‘go’ ERPs.

Behavioral data

Statistical analyses of the behavioral data were performed using R 3.2.1[2]. Packages in use were “car” (Fox and Weisberg, 2011), “ez” (Lawrence, 2013), and “psych” (Revelle, 2015). Repeated measures analyses of variance with three within-subject factors were carried out using STATISTICA for Windows, Version 12[3].

Associations between Go/Nogo effects, behavioral measures of EFs and measures of EA were assessed in correlational analyses. Taking into account the small sample size, Spearman’s rho correlations were computed. In addition, partial correlations were performed to control for children’s age and children’s intelligence (CPM scores): Multiple regressions were computed with children’s age and children’s CPM scores as predictors, and for the residuals the Spearman’s rho correlations were computed. In the multiple regressions the variance inflation factor (i.e., a multicollinearity measure) was 1.48 and therefore did not exceed critical values [as commonly recommended (O’Brien, 2007)].

Alpha level of statistical significance was set at $p < 0.05$ for all analyses. Because of the exploratory nature of the analyses, no correction for multiple comparisons was applied.

RESULTS

Behavioral Executive Function Data

Mean values, standard deviations (SD) and observed ranges of HTKS, DoG, ‘go/nogo’ response accuracy, ‘go’ reaction time and children’s intelligence are presented in **Table 1**. Associations with children’s age are shown in the last column of **Table 1**. According to the SDQ children’s behavior was rated “normal” for 88.9% of the children and “abnormal” for 11.1%. The distribution of the SDQ ratings in our sample thereby indicated slightly lower levels of psychopathology compared to the general population (Goodman et al., 2000). Maternal education was not significantly associated with EF scores (Supplementary Table SI1), and this variable was excluded from the subsequent analyses. However, older children had significantly higher HTKS scores, more ‘go’ hits and a higher ‘go/nogo’ *d*′. With regard to the percentile rank of children’s intelligence no significant correlations were observed (Supplementary Table SI1).

Intercorrelations of the behavioral EF measures across the different tasks are shown in **Table 2**. Higher HTKS scores significantly correlated with higher DoG scores, i.e., a longer DoG waiting period, with more ‘go’ hits and a higher *d*′ in the Go/Nogo task, but not with ‘nogo’ false alarms; however, when controlling for children’s age and intelligence, higher HTKS scores were only significantly associated with less ‘nogo’ false alarms. Higher DoG scores were associated with more ‘go’ hits (significantly in the zero-order correlation analysis, but insignificantly when we controlled for children’s age and intelligence). Faster ‘go’ reaction times were significantly correlated with more ‘go’ hits (in both correlations).

Electrophysiological Data of the Go/Nogo Task

Grand-averaged ERPs at all analyzed 15 electrode sites are presented in **Figure 1**.

We observed a negative deflection at about 250 ms peaking most prominently at occipital sites, which was identified as N1

TABLE 1 | Descriptive information for the behavioral EF measures (*N* = 27).

Variable	*M*	*SD*	Observed range	Child’s age (ρ)
HTKS [scores]	34.48	16.47	0–57	0.60***
DoG [sec]	494.07	351.41	22–900	0.32
Go/Nogo *d*′	2.97	1.44	1.06–5.96	0.61***
Go Hits [rel.fr.]	0.90	0.10	0.59–1.00	0.69***
Nogo False alarms [rel.fr.]	0.16	0.13	0.00–0.48	–0.30
Go RT [ms]	715.37	100.57	546.89–968.26	–0.42*
EF sum [z-scores]	0.00	2.28	–4.16–3.88	0.64***
CPM [scores]	18.26	5.47	11–33	0.54**
CPM [pr]	69.26	26.52	24–100	0.21

HTKS, Head–Toes–Knees–Shoulders Task; DoG, delay of gratification task; EF sum, sum of z-standardized HTKS, DoG and Go/Nogo d′ scores; CPM, colored progressive matrices; rel.fr., relative frequency; pr, percentile rank; M, mean; SD, standard deviation; rho, Spearman’s rho correlation coefficient.

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

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[2] http://www.r-project.org/

[3] http://software.dell.com/products/statistica/

TABLE 2 | Intercorrelations of the behavioral EF measures ($N = 27$).

Variable	HTKS	DoG	Go/Nogo *d′*	Go Hits	Nogo FAs	Go RT
HTKS	–	0.42*	0.50**	0.66***	–0.37	–0.38
DoG	0.32	–	0.27	0.40*	–0.13	–0.05
Go/Nogo *d′*	0.23	0.10	–	0.80***	–0.82***	–0.37
Go Hits	0.31	0.37	0.61***	–	–0.41*	–0.56**
Nogo false alarms	–0.39*	–0.04	–0.81***	–0.45*	–	0.11
Go RT	–0.13	0.02	–0.14	–0.43*	0.05	–

Spearman's rho zero-order correlation coefficients are presented above the diagonal, below the diagonal the partial correlation coefficients, controlling for children's age and intelligence, are depicted.
*HTKS, Head–Toes–Knees–Shoulders task; DoG, delay of gratification task; FAs, false alarms; RT, reaction times; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.*

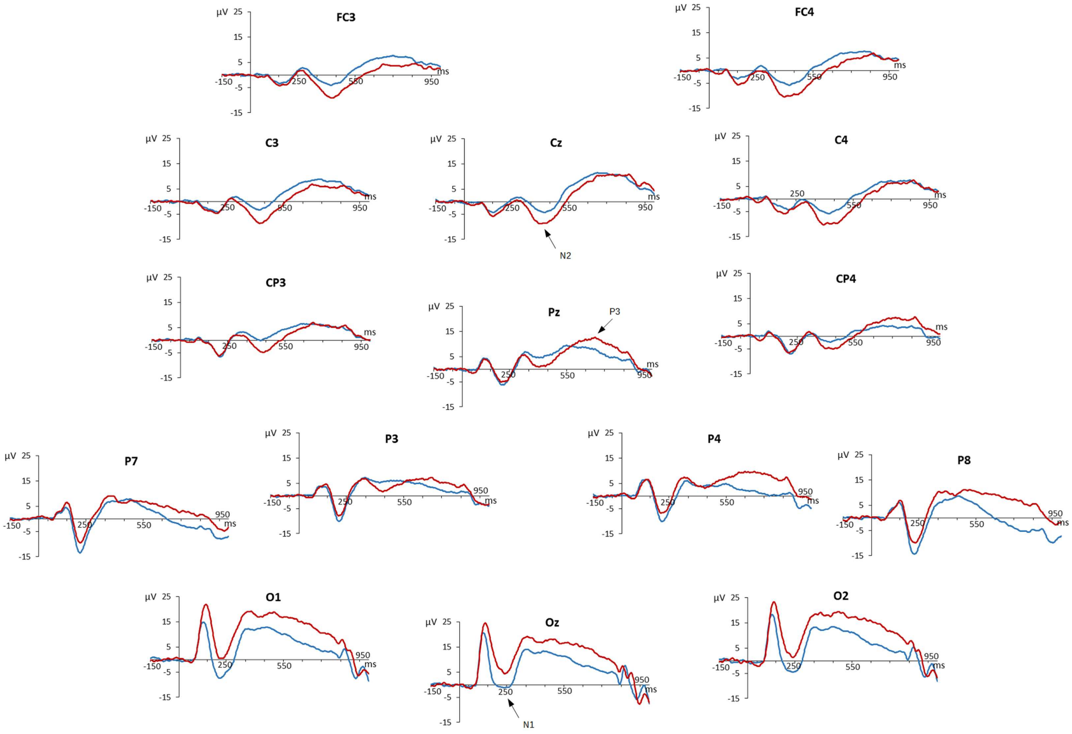

FIGURE 1 | Event-related potentials of the Go/Nogo task. Amplitudes (in millivolt) of grand average stimulus-locked waveforms are shown for all analyzed 15 electrode sites. Waveforms of 'go' trials are blue-colored, those of 'nogo' trials are red-colored.

ERP component. ERPs of 'go' and 'nogo' trials started to diverge at occipital recording sites with more positive ERPs for 'nogo' trials. This Go/Nogo effect at occipital electrodes remained visible throughout the entire recording epoch.

Later, an N2 ERP component peaking at about 420 ms was present at fronto-central, but also at parietal electrodes, with a more pronounced negativity for 'nogo' than for 'go' trials. Finally, a P3/LPC peaking at about 700 ms was observed at parietal sites with more positive potentials for 'nogo' than for 'go' trials.

Go/Nogo Effects

Mean numbers of artifact-free EEG segments with correct responses, which were included in the analyses, were 59.85 ($SD = 12.71$) for the 'go' condition and 27.26 ($SD = 6.33$) for the 'nogo' condition.

For the N1 time window (184–284 ms) we found significant differences between 'go' and 'nogo' condition (Go/Nogo effects) as indicated by a main effect of condition at occipital [$F(1,26) = 76.3$, $p < 0.001$], parietal [$F(1,26) = 10.5$, $p = 0.003$] and midline [$F(1,26) = 15.1$, $p < 0.001$] electrodes. No significant Go/Nogo effects on the N1 were observed at fronto-central electrodes [$F(1,26) = 1.5$, $p = 0.229$]. Significant condition × electrodes interaction effects were observed at midline electrodes [$F(2,52) = 47.2$, $p < 0.001$]. In *post hoc* tests significant Go/Nogo effects were observed for Oz [$t(26) = -8.1$, $p < 0.001$] and Cz [$t(26) = 2.5$, $p = 0.019$], but not for Pz [$t(26) = -0.9$, $p = 0.366$]. Although the interaction condition × hemisphere was not significant, we tested whether the condition effect was reliable over either hemisphere. This analysis revealed significant condition effects for O1 [$t(26) = -8.3$, $p < 0.001$], O2 [$t(26) = -7.6$, $p < 0.001$], Par-left [$t(26) = -3.3$, $p = 0.003$] and Par-right [$t(26) = -2.8$, $p = 0.009$]. At occipital and parietal electrodes, the 'nogo' condition elicited a more positive potential than the 'go' condition, and at the Cz electrode, the 'nogo' condition elicited a more negative potential than the 'go' condition.

For the N2 time window (318–518 ms) significant Go/Nogo effects were observed at occipital [$F(1,26) = 18.4$, $p < 0.001$] and fronto-central electrodes [$F(1,26) = 21.6$, $p < 0.001$]. Significant condition × hemisphere interaction effects were observed at parietal electrodes [$F(1,26) = 7.4$, $p = 0.012$] and significant condition × electrodes interaction effects were found at midline electrodes [$F(2,52) = 29.3$, $p < 0.001$]. In *post hoc* tests significant Go/Nogo effects were observed for Oz [$t(26) = -3.1$, $p = 0.005$], Cz [$t(26) = 4.6$, $p < 0.001$] and Pz [$t(26) = 2.1$, $p = 0.046$], but not for the clusters Par-left [$t(26) = 0.9$, $p = 0.398$] or Par-right [$t(26) = -1.8$, $p = 0.081$]. Although the interaction condition × hemisphere was not significant, we tested whether the condition effect was reliable over either hemisphere. This analysis revealed significant condition effects for O1 [$t(26) = -4.4$, $p < 0.001$], O2 [$t(26) = -3.9$, $p < 0.001$], Fcentral-left [$F(1,26) = 4.6$, $p < 0.001$] and Fcentral-right [$F(1,26) = 3.9$, $p < 0.001$]. At occipital electrodes, the 'nogo' condition elicited a more positive potential than the 'go' condition. At lateral and midline fronto-central as well as at midline parietal electrodes, the 'nogo' condition elicited a more negative potential than the 'go' condition.

For the P3/LPC time window (600–800 ms) we observed significant Go/Nogo effects at occipital [$F(1,26) = 35.1$, $p < 0.001$], parietal [$F(1,26) = 49.8$, $p < 0.001$] and midline electrodes [$F(1,26) = 8.0$, $p = 0.009$]. Significant condition × hemisphere interaction effects were observed at parietal electrodes [$F(1,26) = 15.2$, $p = 0.001$]. At midline electrodes, the interaction between condition and electrode sites was significant [$F(2,52) = 22.0$, $p < 0.001$]. In *post hoc* tests significant Go/Nogo effects were observed for Oz [$t(26) = -4.8$, $p < 0.001$], Pz [$t(26) = -2.8$, $p = 0.011$], the clusters Par-left [$t(26) = -3.4$, $p = 0.003$] and Par-right [$t(26) = -8.3$, $p < 0.001$], but not for Cz [$t(26) = 1.5$, $p = 0.160$]. Although the interaction condition × hemisphere was not significant, we tested whether the condition effect was reliable over either hemisphere. This analysis revealed significant condition effects for O1 [$t(26) = -6.0$, $p < 0.001$] and O2 [$t(26) = -5.5$, $p < 0.001$]. At occipital and parietal electrodes, the 'nogo' condition elicited a more positive potential than the 'go' condition.

In the following correlation analyses only the electrodes/electrodes clusters with significant Go/Nogo effects were included.

Relation of ERP Go/Nogo Effects to Behavioral Executive Function Measures and Demographic Variables

The descriptive statistics for the Go/Nogo effects is shown in **Table 3**. **Table 3** also presents the correlations between the ERP Go/Nogo effects and the behavioral EF variables.

Greater occipital N1 Go/Nogo effects (i.e., greater differences between 'go' and 'nogo' N1) were significantly associated with higher response accuracy (i.e., higher d', more hits, less false alarms) in the Go/Nogo paradigm. When we controlled for children's age and intelligence, this association was reduced to insignificance for false alarms, but remained significant for d' and hits.

With regard to the N2 time window, more 'go' hits were significantly associated with a greater Go/Nogo effect at the right occipital site, when we controlled for children's age and intelligence. No significant associations were observed for 'nogo' false alarms and 'go/nogo' d'. Faster 'go' reaction times were correlated with greater parietal N2 Go/Nogo effects when we controlled for children's age and intelligence, and with greater fronto-central N2 Go/Nogo effects in both correlational analyses.

Higher DoG scores were significantly related to greater Go/Nogo effects in the P3/LPC time window at occipital and parietal electrodes in both correlational designs. Greater parietal P3/LPC Go/Nogo effects were also significantly associated with more 'go' hits in both correlational designs.

A higher EF sum score (i.e., sum of z-standardized HTKS, DoG and 'go/nogo' d' scores) significantly went along with greater occipital Go/Nogo effects in the N1 and N2 time window and with greater parietal P3/LPC Go/Nogo effects in both correlational designs.

We observed a significant association between the left parietal N1 Go/Nogo effect and children's age (Par-left: $\rho = -0.43$, $p < 0.05$). Higher children's intelligence (percentile rank of CPM) was significantly correlated with greater occipital Go/Nogo effects in the N2 time window (O1: $\rho = -0.44$, $p < 0.05$; O2: $\rho = -0.42$, $p < 0.05$).

Emotional Availability

Descriptive statistics for the EA variables is shown in **Table 4**. T-scores ranged from 19 to 29, and EA CS ranged from 70 to 100. Adult structuring, adult nonintrusiveness and EA CS were significantly and positively correlated with children's percentile rank of intelligence (**Table 4**). The EA CS and the EA scales except nonhostility were strongly positively intercorrelated (Supplementary Table SI2).

Relation of Emotional Availability to Behavioral Executive Function Measures

We investigated the relations between EA variables and behavioral EF data. An overview of the results is presented in **Table 5**. Higher HTKS scores were significantly correlated with higher maternal nonintrusiveness and with a higher EA CS score in both correlational analyses. A higher EA CS score was also associated with a higher DoG score when we controlled for children's age and intelligence and with a higher EF sum score in both correlational analyses. We found no significant associations between EA variables and response accuracy or reaction time in the Go/Nogo task.

Emotional Availability and ERP Go/Nogo Effects

The relations between EA variables and Go/Nogo ERP effects were examined (see **Table 6** and Supplementary Table SI3, for

TABLE 3 | Descriptive information for the ERP Go/Nogo effects and their association with behavioral EF measures ($N = 27$).

Ele. Pos.	*CE M*	*CE SD*	HTKS	DoG	Go/Nogo d'	Go Hits	Nogo FAs	Go RT	EF sum
N1									
O1	–8.38	5.27	–0.18 (–0.02)	–0.19 (–0.00)	–0.47* (–0.24)	–0.32 (–0.18)	0.44* (0.27)	–0.04 (–0.14)	–0.42* (–0.16)
O2	–7.26	4.94	–0.36 (–0.28)	–0.13 (–0.01)	–0.53** (–0.40*)	–0.47* (–0.45*)	0.44* (0.35)	0.40* (0.34)	–0.47* (–0.35)
Oz	–7.21	4.63	–0.18 (–0.13)	–0.11 (–0.02)	–0.48* (–0.45*)	–0.37 (–0.43*)	0.43* (0.36)	0.02 (0.00)	–0.40* (–0.31)
Par-left	–2.53	3.95	–0.12 (0.11)	–0.01 (0.37)	–0.41* (–0.09)	–0.23 (0.22)	0.31 (0.05)	0.07 (–0.05)	–0.26 (0.13)
Par-right	–3.20	5.84	–0.14 (–0.03)	0.02 (0.36)	–0.39* (–0.07)	–0.21 (0.06)	0.32 (0.04)	0.17 (0.20)	–0.26 (0.13)
Cz	1.17	2.43	–0.20 (0.05)	0.04 (0.12)	–0.16 (0.09)	–0.29 (–0.13)	0.11 (–0.05)	0.14 (0.13)	–0.13 (0.08)
N2									
O1	–6.07	7.11	–0.16 (–0.06)	–0.15 (–0.19)	–0.28 (–0.10)	–0.35 (–0.31)	0.16 (0.06)	–0.11 (–0.27)	–0.31 (–0.26)
O2	–5.78	7.75	–0.28 (–0.18)	–0.28 (–0.35)	–0.36 (–0.23)	–0.45* (–0.42*)	0.19 (0.16)	0.07 (–0.16)	–0.44* (–0.43*)
Oz	–4.95	8.39	–0.18 (–0.08)	–0.19 (–0.23)	–0.31 (–0.19)	–0.32 (–0.35)	0.22 (0.12)	–0.05 (–0.22)	–0.36 (–0.31)
Pz	2.85	7.09	–0.02 (0.02)	–0.13 (–0.02)	–0.20 (–0.12)	–0.06 (0.07)	0.23 (0.08)	–0.33 (–0.52**)	–0.23 (–0.12)
Fcentral-left	3.93	4.48	0.06 (0.04)	–0.02 (0.05)	0.00 (0.04)	0.14 (0.20)	0.03 (–0.10)	–0.50** (–0.51**)	–0.03 (0.06)
Fcentral-right	3.49	4.65	0.11 (–0.01)	0.08 (0.04)	0.06 (0.08)	0.29 (0.19)	0.07 (0.07)	–0.21 (–0.20)	0.04 (0.06)
Cz	4.11	4.67	–0.13 (–0.15)	–0.12 (–0.04)	–0.10 (–0.05)	0.09 (0.19)	0.20 (0.10)	–0.52** (–0.58**)	–0.21 (–0.14)
P3									
O1	–7.82	6.84	0.03 (0.16)	–0.35 (–0.39*)	–0.06 (–0.04)	–0.20 (–0.20)	0.01 (–0.03)	–0.09 (–0.18)	–0.16 (–0.17)
O2	–8.12	7.74	–0.12 (–0.04)	–0.46* (–0.47*)	–0.02 (–0.03)	–0.25 (–0.37)	0.03 (–0.02)	–0.05 (–0.08)	–0.25 (–0.25)
Oz	–6.60	7.19	0.10 (0.08)	–0.35 (–0.39*)	–0.06 (–0.15)	–0.11 (–0.35)	0.08 (0.12)	–0.22 (–0.24)	–0.16 (–0.27)
Par-left	–3.77	5.84	–0.29 (–0.30)	–0.33 (–0.29)	–0.05 (–0.12)	–0.21 (–0.15)	0.02 (0.04)	–0.21 (–0.19)	–0.25 (–0.32)
Par-right	–8.74	5.50	–0.30 (–0.18)	–0.39* (–0.30)	–0.30 (–0.19)	–0.47* (–0.46*)	0.24 (0.17)	0.13 (0.03)	–0.42* (–0.29)
Pz	–3.97	7.49	–0.34 (–0.29)	–0.56** (–0.41*)	–0.33 (–0.18)	–0.39* (–0.27)	0.26 (0.16)	–0.09 (–0.26)	–0.52** (–0.48*)

*On the left mean values and standard deviations for the ERP Go/Nogo effects are presented. Right hand the Spearman's rho correlation coefficients for the association between Go/Nogo effects and behavioral EF variables are shown. In brackets the partial correlation coefficients, controlling for children's age and intelligence, are depicted. Ele.Pos., electrode position; CE, Go/Nogo effect; HTKS, Head–Toes–Knees–Shoulders task; DoG, delay of gratification task; FAs, false alarms; RT, reaction times; EF sum, sum of z-standardized HTKS, DoG and 'go/nogo' d' scores; *$p < 0.05$; **$p < 0.01$.*

an overview of the results). Our data revealed several significant associations between EA variables and the N2 Go/Nogo effect, but no significant relations were found between EA and N1 or P3/LPC Go/Nogo effects.

In more detail, greater maternal sensitivity and a higher EA CS score went along with greater occipital Go/Nogo effects in the N2 time window. However, this effect did not hold, when we controlled for children's age and intelligence. Higher maternal structuring and nonintrusiveness significantly correlated with greater occipital Go/Nogo effects in the N2 time window (in both correlational analyses). When we controlled for children's age and intelligence, we additionally found that smaller midline parietal N2 Go/Nogo effects were significantly related to higher maternal structuring and nonintrusiveness, and that smaller right fronto-central N2 Go/Nogo effects were associated with higher maternal structuring.

TABLE 4 | Descriptive information for the emotional availability variables ($N = 22$).

Variable	*M*	*SD*	Observed range	CPM pr [ρ]
Adult sensitivity	26.59	2.17	21.00–29.00	0.38
Adult structuring	26.50	2.72	19.00–29.00	0.43*
Adult non-intrusiveness	25.80	3.12	20.00–29.00	0.67***
Adult non-hostility	28.05	1.81	23.00–29.00	–0.16
Child responsiveness	26.27	2.57	21.00–29.00	0.38
Child involvement	26.27	2.61	22.00–29.00	0.29
EA sum	159.48	11.35	133.00–174.00	0.38
EA CS	84.41	9.76	70.00–100.00	0.43*

Means, standard deviations, and observed ranges are depicted for the emotional availability (EA) variables (T-scores and EA CS). On the right Spearman's rho correlation coefficients for the association between EA variables and the percentile rank of children's intelligence are shown.

*CPM, colored progressive matrices; M, mean; SD, standard deviation; pr, percentile rank; rho, Spearman's rho correlation coefficient; *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.*

Higher child responsiveness was significantly related to greater occipital Go/Nogo effects in the N2 time window in the zero-order correlation analysis, and when we controlled for children's age and intelligence, higher child responsiveness was associated with greater midline occipital Go/Nogo effects in the N2 time window, and with smaller midline parietal and fronto-central N2 Go/Nogo effects.

A higher EA sum score was significantly associated with greater occipital Go/Nogo effects in the N2 time window, even when we controlled for children's age and intelligence.

DISCUSSION

With this study, we aimed at investigating whether the quality of the mother–child interaction, assessed as EA, was associated with

TABLE 5 | Association between emotional availability and behavioral EF measures ($N = 22$).

	HTKS	DoG	Go/Nogo d'	Go hits	Nogo FAs	Go RT	EF sum
Adult sensitivity	0.28 (0.28)	0.22 (0.37)	0.00 (–0.16)	0.16 (–0.14)	0.13 (0.06)	0.07 (0.09)	0.24 (0.22)
Adult structuring	0.24 (0.25)	–0.12 (–0.01)	0.17 (0.07)	0.13 (0.07)	–0.09 (–0.19)	0.06 (0.14)	0.17 (0.15)
Adult non-intrusiveness	0.51* (0.48*)	0.04 (0.25)	0.19 (0.02)	0.36 (0.12)	0.06 (–0.12)	0.09 (0.38)	0.36 (0.39)
Adult non-hostility	0.16 (0.30)	0.17 (0.18)	0.06 (0.32)	0.12 (.27)	–0.04 (–0.23)	0.06 (–0.20)	0.21 (0.37)
Child responsiveness	0.17 (0.02)	–0.18 (–0.09)	0.08 (–0.05)	0.13 (–0.06)	0.15 (0.06)	0.16 (0.25)	0.08 (–0.05)
Child involvement	0.34 (0.16)	0.11 (0.21)	0.28 (0.27)	0.41 (0.22)	0.04 (–0.14)	–0.11 (–0.03)	0.33 (0.33)
EA sum	0.38 (0.27)	0.03 (0.11)	0.24 (0.10)	0.33 (0.13)	–0.01 (–0.07)	0.06 (0.07)	0.35 (0.26)
EA CS	0.43* (0.51*)	0.27 (0.47*)	0.20 (0.19)	0.32 (0.17)	–0.06 (–0.24)	0.04 (0.05)	0.43* (0.57**)

Spearman's rho correlation coefficients for the association between emotional availability (T-scores and EA CS) and behavioral EF measures are shown. In parentheses the partial correlation coefficients are shown, controlling for children's age and intelligence.

HTKS, Head–Toes–Knees–Shoulders task; DoG, delay of gratification task; FAs, false alarms; RT, reaction times; EF sum, sum of z-standardized HTKS, DoG and d' scores.

$^{*}p < 0.05$, $^{**}p < 0.01$.

behavioral and electrophysiological measures of EFs in preschool children. We administered behavioral EF tasks, the Go/Nogo, the HTKS and the DoG task, to preschool children, and recorded ERPs during the Go/Nogo task, which taps response inhibition.

Children's response accuracy in the Go/Nogo task highly correlated with HTKS performance, a measure of inhibition, shifting and working memory, and moderately correlated with DoG, a measure of impulse control. This result resembles the two factor structure of EFs in young children that was reported in Bernier et al. (2010, 2012). They found one factor loading on impulse control and one factor loading on working memory, shifting and inhibition, and a moderate correlation between these two factors. When we controlled for age and intelligence, the intercorrelations between the behavioral EF measures weakened. Additional data analyses (data not shown) indicated that the control for children's age, but not for intelligence, accounted for this effect. HTKS and response accuracy scores were highly correlated with age. We think that in consequence of the small sample size only few children were of similar age, and this resulted in little variation in task performance over and above age. In contrast, impulse control, as measured by means of the DoG, was not significantly related to age. Previous research revealed that the ability to delay gratification shows moderate stability from 4 years of age to adolescence into adulthood four decades later (Mischel et al., 1989; Casey et al., 2011). Impulse control might represent a relatively stable personality trait from early childhood on.

We observed significant occipital, parietal, and fronto-central Go/Nogo effects in the N1 and N2 time windows. Further, we observed significant occipital and parietal Go/Nogo effects in the P3/LPC time window, in contrast to Jonkman et al. (2003), who reported absent 'nogo' P3 effects in children, aged 6–7 (Jonkman, 2006) resp. 9–10 (Jonkman et al., 2003). We additionally found a longer P3/LPC latency in our sample (600–800 ms) compared to Jonkman (2006) (reporting 440–480 ms) and Jonkman et al. (2003) (reporting 300–600 ms). In our sample the ERP components N1, N2, and P3/LPC showed longer latencies than usually observed in adults. This finding concords with developmental electrophysiological research that revealed decreasing latencies with age (Davis et al., 2003; Jonkman et al., 2003; Jonkman, 2006; Lamm et al., 2006); the decreasing latency with increasing age is probably paralleled by increasing myelination during the development of children's cortices.

Furthermore, our results demonstrated that EA of the mother–child interaction is significantly associated with electrophysiological correlates of response inhibition during the Go/Nogo task in preschool children. However, our results yielded no significant associations between the behavioral response inhibition measures of the Go/Nogo task and the EA variables. Instead the EA variables maternal nonintrusiveness and EA CS were positively correlated with behavioral performance in the DoG and/or HTKS task.

Maternal structuring and maternal nonintrusiveness both refer to autonomy-fostering behaviors (Biringen and Easterbrooks, 2012b). High maternal structuring is characterized by adequate and consistent guidance and setting limits for the child, while high maternal nonintrusiveness encourages age-appropriate autonomy and simultaneously maintains an emotionally connected relationship. On the other hand, EFs are considered to be a crucial factor in human autonomy (Royall et al., 2002). It is an appealing notion, that parenting behavior which supports the child to practice autonomous actions, fosters EF proficiency. In support of this notion, previous developmental research depicted the importance of parental autonomy-support in the development of EF in children (Bernier et al., 2010, 2012; Bindman et al., 2015). Our data provide further evidence that maternal autonomy-support fosters EF skills in preschool children.

We found that children of higher autonomy-supportive mothers exhibited smaller fronto-central and parietal N2 Go/Nogo effects. The fronto-central N2 component is assumed to reflect higher-order inhibitory processes (Eimer, 1993; Kiefer et al., 1998) and/or conflict monitoring (Nieuwenhuis et al., 2003; Donkers and van Boxtel, 2004). Smaller fronto-central N2 Go/Nogo effects in a response inhibition task were related to increasing age in children (Davis et al., 2003; Jonkman et al., 2003; Jonkman, 2006). As we controlled for children's age and intelligence, our results cannot be attributed to age effects. In our task, smaller fronto-central and parietal N2 Go/Nogo

TABLE 6 | Association of emotional availability variables with N2 ERP Go/Nogo effects ($N = 22$).

Ele. Pos.	A-sensitivity	A-structuring	A-non-intrusiveness	A-non-hostility	C-responsiveness	C-involvement	EA sum	EA CS
N2								
O1	−0.48* (−0.25)	−0.54** (−0.47*)	−0.59** (−0.50*)	−0.21 (−0.30)	−0.50* (−0.39)	−0.25 (−0.13)	−0.54** (−0.45*)	−0.44* (−0.18)
O2	−0.48* (−0.26)	−0.55** (−0.43*)	−0.58** (−0.51*)	−0.23 (−0.31)	−0.49* (−0.35)	−0.28 (−0.17)	−0.53* (−0.46*)	−0.47* (−0.29)
Oz	−0.41 (−0.30)	−0.54** (−0.55**)	−0.49* (−0.60**)	−0.19 (−0.31)	−0.45* (−0.45*)	−0.21 (−0.21)	−0.48* (−0.53*)	−0.38 (−0.24)
Pz	−0.18 (−0.16)	−0.40 (−0.47*)	−0.31 (−0.44*)	0.03 (−0.08)	−0.37 (−0.46*)	−0.02 (−0.09)	−0.31 (−0.34)	−0.17 (−0.09)
Fcentral-left	0.02 (0.02)	−0.19 (−0.23)	−0.05 (−0.20)	0.10 (0.13)	−0.25 (−0.32)	−0.18 (−0.19)	−0.19 (−0.12)	−0.10 (−0.05)
Fcentral-right	−0.08 (−0.19)	−0.36 (−0.46*)	0.07 (−0.17)	0.28 (0.21)	−0.27 (−0.42)	−0.07 (−0.24)	−0.13 (−0.25)	−0.15 (−0.18)
Cz	−0.06 (−0.09)	−0.28 (−0.32)	−0.16 (−0.29)	0.18 (0.22)	−0.32 (−0.43*)	−0.13 (−0.23)	−0.21 (−0.20)	−0.19 (−0.22)

The Spearman's rho correlation coefficients for the association between N2 Go/Nogo effects and emotional availability variables are shown. In parentheses the partial correlation coefficients, controlling for children's age and intelligence, are presented.

Ele. Pos., electrode position; A, adult; C, child; $^{*}p < 0.05$; $^{**}p < 0.01$.

effects were also correlated with slower 'go' reaction times, and slower 'go' reaction times were in turn associated with less 'go' hits in our sample. However, a smaller fronto-central 'nogo' N2 amplitude was shown to be an indicator of better cognitive control over and above age (Lamm et al., 2006). Lamm et al. (2006) observed in children and adolescents that smaller fronto-central 'nogo' N2 amplitudes were associated with better performance in behavioral EF tasks, including a response inhibition task. Additionally, in a study with adolescents a reduced 'nogo' N2 amplitude was supposed to be an indicative of increased efficiency of the EF system (Stroth et al., 2009). We therefore postulate that higher maternal autonomy-support is related to electrophysiological indices of more efficient inhibitory control in our task over and above effects of children's age and intelligence.

The N2 component typically peaks at fronto-central sites extending to parietal sites in adults (Kiefer et al., 1998). In our sample, we additionally observed occipital Go/Nogo effects in the N2 time window, with inverted polarity. In adults, the source of the fronto-central N2 is probably located in the inferior frontal cortex (Kiefer et al., 1998). In children, the N2 component might be generated in orbitofrontal and cingulate cortex (Lamm et al., 2006). Immature functioning of fronto-parietal circuits in young children has been suggested by some researchers based on electrophysiological and neuroimaging study results (Bunge et al., 2002; Ciesielski et al., 2004). Ciesielski et al. (2004) reported more pronounced parietal than frontal ERPs in children, ages 6–12, during the performance in a Go/Nogo task. In the fMRI study of Bunge et al. (2002), 8- to 12-year-old children exhibited insignificant prefrontal activation in a Go/Nogo task, while adults most robustly activated right ventrolateral prefrontal cortex (when contrasting 'nogo' and neutral trials). However, in an fMRI study contrasting 'nogo' and 'go' condition, 7- to 12-year-old children activated the same locations in the bilateral prefrontal cortex compared to adults, but with an extended volume in the dorsal and lateral prefrontal cortices (Casey et al., 1997). Hence, research about Go/Nogo-related prefrontal cortex functioning in young children yielded conflicting results. It is possible that the observed frontal and parietal N2 ERP originated from the same sources in frontal (and cingulate) cortex. However, the occipital ERP effect in the N2 time window, which showed a reversed polarity compared with the parietal and fronto-central effects, was likely generated in a more posterior brain region. In our task right occipital Go/Nogo effects in the N2 time window were associated with response accuracy (i.e., 'go' hits), whereas fronto-central and midline parietal N2 Go/Nogo effects were related to 'go' reaction times. This divergent associations might hint to different generators. More 'go' hits went along with greater occipital Go/Nogo effects in the N2 time window predominantly in the right brain hemisphere. Based on neuroimaging studies, a right-lateralized ventral fronto-parietal network has been identified, that involves the temporoparietal junction and is activated by the detection of low-frequency stimuli, like the 'nogo' stimuli in our task, which reorient attention (Corbetta and Shulman, 2002). The detection of low-frequency stimuli co-activates the bilateral dorsal fronto-parietal network that involves posterior parietal cortices. This latter network is implicated in goal-oriented sustained attention to stimulus attributes and it is involved in the selection of appropriate hand-responses to stimuli. Its neural activity is modulated by behavioral relevance and can additionally involve occipital activations (Le et al., 1998; Corbetta and Shulman, 2002). The observed occipital Go/Nogo effects in the N2 time window might therefore be related to attentional processes, generated in posterior parietal areas. However, it is somewhat difficult to explain why these attentional modulations were only related to behavioral accuracy in 'go' trials, but not to that in 'nogo' trials as well. Possibly, the relation is more indirect: More accurate responding in 'go' trials can simultaneously increase the difficulty of withholding the response in 'nogo' trials, because there is an increased tendency to execute a motor response. Thus, higher accuracy in 'go' trials without increased false alarms in 'nogo' trials can already indicate better response inhibition as a consequence of a more efficient fronto-parietal attention network. With regard to the association between higher maternal autonomy-support and greater bilateral occipital Go/Nogo effects in the N2 time window, we therefore suppose that higher maternal autonomy-support promotes attentional mechanisms that are implicated in better response inhibition.

Additionally, we observed that child responsiveness was comparably related to the Go/Nogo effects in the N2 time window as was maternal autonomy-support, with higher responsive children showing smaller fronto-central and parietal, and greater occipital effects. Smaller fronto-central N2 Go/Nogo effects might be electrophysiological indices of more efficient inhibitory control (Lamm et al., 2006; Stroth et al., 2009), and greater occipital Go/Nogo effects in the N2 time window might reflect more effective attentional processes as discussed above. The EA scale 'child responsiveness' resembles the concepts of secure attachment and 'attachment-exploration balance' from attachment theory, and depicts the child's expression of healthy EA (Biringen and Easterbrooks, 2012b). A behavioral study reported that child attachment security predicts EF task performance (with regard to inhibition, working memory and shifting) in 3-year-olds (Bernier et al., 2012). Our results reveal for the first time the electrophysiological correlates that might underlie this association, and they provide further support that secure child attachment fosters EF-related proficiency.

Maternal sensitivity and EA CS went along with greater occipital Go/Nogo effects in the N2 time window. Maternal sensitivity in the EA framework resembles the attachment operationalization of maternal sensitivity, but emphasizes the quality of emotional exchanges and the dyadic nature to a higher extent (Biringen and Easterbrooks, 2012b). The EA CS is defined as summary of EA, stressing maternal sensitivity and child responsiveness. The association of both EA variables with the Go/Nogo effects in the N2 time window vanished when we controlled for children's age and intelligence. Additional data analyses (data not shown) indicated that children's intelligence accounted for this effect. Interestingly, children's intelligence moderately correlated with maternal sensitivity (insignificantly) and significantly with EA CS. Maternal structuring and nonintrusiveness showed comparable or even stronger, significant associations with children's intelligence. Our data thereby suggest that higher emotionally dyadic and autonomy-supportive mother–child-interactions promote children's general intelligence, and this conforms with the proposition by Harrist and Waugh (2002) that dyadic synchrony facilitates children's cognitive growth. Our results further suggest that maternal sensitivity compared to maternal autonomy-support affects children's task-related ERPs by cognitive mechanisms that are more closely related to general intelligence than to EFs. Nevertheless, these interpretations can only be considered tentative, particularly because inter-rater reliability for maternal sensitivity and EA CS was suboptimal.

Despite the significant associations between maternal autonomy-support and N2 Go/Nogo effects, we observed no comparable link to behavioral performance in the Go/Nogo task (neither for maternal autonomy-support nor for any other EA variable). Although autonomy-support was related to Go/Nogo effects in the N2 time window similarly to 'go' hits and to 'go' reaction times, there was no equivalent association with behavioral performance (i.e., more 'go' hits and slower 'go' reaction times). Two explanations for the missing association of maternal autonomy-support with behavioral measures of the Go/Nogo task are conceivable. One possible explanation would be that maternal autonomy-support fosters cognitive processes that annihilate each other with respect to behavioral performance. In fact, analyses of our behavioral data showed that more 'go' hits were moderately associated with faster, and not slower, reaction times in our sample. An alternative proposition would be that electrophysiological measures might reflect task-relevant cognitive processes with a higher sensitivity than behavioral outcomes (e.g., Stroth et al., 2009). Compensatory neural processes like higher activation (e.g., of fronto-central 'nogo' N2) or additional recruiting of other brain circuits could conceal behavioral consequences of suboptimal cognitive processing in children with less autonomy-supporting mothers. As a result, no behavioral differences would be observed depending on maternal autonomy-support. However, compensatory processes might break down if the cognitive load gets higher. The HTKS task can be regarded as a more complex and difficult task than the Go/Nogo task, because it involves shifting and working memory updating next to inhibition. We observed that children of less intrusive (i.e., more autonomy-supportive) mothers performed better in the HTKS task. This result could be interpreted in favor of our second explanation. It also dovetails with other research that demonstrated a positive association between maternal autonomy-support and performance in inhibition, shifting, and working memory tasks in 2- to 4-year-olds (Bernier et al., 2010, 2012; Bindman et al., 2015).

While the N2 Go/Nogo effects showed little association with response accuracy in our Go/Nogo task, occipital N1 Go/Nogo effects were significantly related to all response accuracy measures (i.e., 'go/nogo' d', 'go' hits, 'nogo' false alarms). The N1 component reflects focused attention and is presumably implicated in response inhibition (Luck et al., 1990; Filipović et al., 2000; Lavric et al., 2004). In the fMRI study by Bunge et al. (2002) behavioral accuracy was related to occipital, parietal, and temporal activation in children, and in adults only to occipital activation. A meta-analysis of fMRI studies revealed that successful response inhibition in a Go/Nogo paradigm activates bilateral occipital regions, next to right superior medial wall (pre-SMA) and precuneus (Simmonds et al., 2008). According to Friedman et al. (2009), variance in inhibition proficiency is mostly explained by the common EF factor, which might in turn be synonymic with an executive attention system (Norman and Shallice, 1986; Engle and Kane, 2004; Posner and Rothbart, 2007). We observed that better behavioral performance in the Go/Nogo task went along with greater occipital N1 Go/Nogo effects, i.e., a larger N1 amplitude for 'go' trials compared to 'nogo' trials. As a higher N1 amplitude indicates higher focused attention (Luck et al., 1990), we postulate that increased focused attention in the early visual processing of the 'go' stimulus is a prominent indicator of better behavioral accuracy in children, including not only more 'go' hits, but also less 'nogo' false alarms. Our results thereby suggest that children's focused attention plays a crucial role in successful response inhibition, because 'go' and 'nogo' stimuli were visually better differentiated. As inhibition is highly related to the common EF factor, our data are also in line with assumptions that attentional control might represent the common EF factor. Our results are also in line with findings that occipital activation (Bunge et al., 2002) and the N1 Go/Nogo effect (Filipović et al., 2000; Lavric et al., 2004) are important indicators of successful response inhibition in a Go/Nogo task. It should be noted that the occipital N1 Go/Nogo effects extended into the N2 and P3/LPC time windows as indicated by a slow positive potential shift of the 'nogo' amplitudes. To our knowledge, this occipital slow wave effect has not been reported before because previous work on Go/Nogo experiments focused on ERPs at parietal, central, and frontal electrodes. It is possible that this slow wave reflects sustained attentional processes underlying response inhibition.

N1 Go/Nogo effects were not related to EA variables, and the same applied to the P3/LPC Go/Nogo effects. The P3 Go/Nogo effect is assumed to be an indicative of response inhibition (Kiefer et al., 1998; Smith et al., 2008), and presumably related to motor inhibition and performance evaluation. We found that greater parietal and occipital Go/Nogo effects in the P3/LPC time window correlated with a higher DoG score. Our Go/Nogo task implicated response inhibition to an attractive 'nogo' stimulus (a cookie). Similarly, the DoG task demanded impulse control toward an appetizing stimulus. Our data suggest that individual differences in DoG performance are associated with variations in motor inhibition and performance evaluation. A greater parietal P3/LPC Go/Nogo effect was also correlated with more 'go' hits. In turn our behavioral data showed that more 'go' hits were associated with higher DoG scores. Our findings hence provide a link between behavioral as well as electrophysiological indices of better response accuracy and better performance in the DoG. With regard to the EA variables, we observed a moderately strong association between the dyadic quality of the mother–child-interaction (i.e., EA CS score) and the DoG score. Previous studies revealed that attachment security (Jacobsen et al., 1997), maternal responsiveness (Razza and Raymond, 2013), and autonomy-support (Razza and Raymond, 2013; Bindman et al., 2015) were associated with a higher ability to delay gratifications. Our results thereby partially support these previous findings. The ability to delay gratifications was originally considered as an indicator of impulse control, but recent research demonstrated that it is also an indicator of interpersonal trust (Michaelson et al., 2013). A secure child attachment as well as highly dyadic mother–child-interactions feed the child with experiences of predictable and trustworthy others, and this might increase the children's proclivity to postpone a gratification.

Limitations and Future Directions

Our sample included 4- to 6-year-old children, covering an age span, during which considerable growth in EFs is observed. As discussed above, the rather small sample size limited the detection of significant EF effects over and above age especially in tasks, in which performance was highly correlated with age. A replication study in a larger sample would be desirable.

Furthermore, we observed little variation in educational degree in our sample. Our sample comprised predominantly highly educated parents, restricting thereby the generalizability of our results.

Our study was cross-sectional in design, and it would be interesting to follow-up into adolescence how the subsequent development of electrophysiological EF measures is modulated by the interaction quality between parents and child. In addition, future studies could include distress (e.g., cortisol levels; see e.g., Blair et al., 2011) and genetic markers (Barnes et al., 2011) in the examination of the association between neural correlates of children's EFs and the early social environment.

CONCLUSION

The current study addressed – to our knowledge for the first time – whether the parent–child interaction quality is associated with electrophysiological correlates of EFs in preschool children. Maternal autonomy-support and child responsiveness were significantly related to Go/Nogo effects in the N2 time window indexing response inhibition, over and above effects of children's age and general intelligence. Our findings suggest that among other factors the quality of caregiver–child interaction shapes the functionality of the brain systems underlying EFs already during childhood. The present study therefore highlights the importance of parent–child interactions as a possible target of intervention programs aiming at improving EFs in children at risk.

AUTHOR CONTRIBUTIONS

HS-H supported data acquisition and study management, analyzed and interpreted the data, and drafted the manuscript.

AZ contributed to central parts of the study conception and design. She planned and coordinated the acquisition of the families as well as coordinated and managed data acquisition and performed data management. She also did the analysis of the mother–child-interactions and revised the manuscript. CM supported data acquisition and EEG data processing, and revised the manuscript. UZ, MK, and AK initiated and conceptualized the collaborative study, and revised the manuscript. MK furthermore contributed to data analyses and interpretation as well as to drafting the manuscript. All authors approved the final version and agreed to be accountable for all aspects of the work.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fnhum.2016.00299

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Effects of Gene × Attachment Interaction on Adolescents' Emotion Regulation and Aggressive Hostile Behavior Towards their Mothers during a Computer Game

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Adolescence is a time of increased emotionality and major changes in emotion regulation often elicited in autonomy-relevant situations. Both genetic as well as social factors may lead to inter-individual differences in emotional processes in adolescence. We investigated whether both 5-HTTLPR and attachment security influence adolescents' observed emotionality, emotional dysregulation, and their aggressive hostile autonomy while interacting with their mothers. Eighty-eight adolescents at age 12 were observed in interaction with their mothers during a standardized, emotion eliciting computer game task. They were genotyped for the 5-HTTLPR, a repeat polymorphism in the promoter region of the serotonin transporter gene. Concurrent attachment quality was assessed by the Late Childhood Attachment Interview (LCAI). Results revealed a significant gene × attachment effect showing that ss/sl carriers of 5-HTTLPR show increased emotional dysregulation and aggressive hostile autonomy towards their mothers. The results of the study suggest that secure attachment in adolescence moderates the genetically based higher tendency for emotional dysregulation and aggressive reactions to restrictions of autonomy during emotional social interactions with their mothers.

Keywords: 5-HTTLPR, attachment, emotionality, emotion regulation, adolescence, autonomy, aggression, gene × environment interaction

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INTRODUCTION

Adolescence, Autonomy, and Emotionality

Adolescence is characterized by increased emotionality and daily mood fluctuations especially in early adolescence (Larson et al., 2002; Maciejewski et al., 2015). This may be due to hormonal changes around puberty, brain development, cognitive, and social changes and stressors (Laursen, 1995; Forbes and Dahl, 2010; Somerville et al., 2010). Parallel, the elicitors of emotions change from childhood to adolescence. Social evaluation, especially by peers becomes a major elicitor of fear (Westenberg et al., 2004; Guyer et al., 2014). Autonomy restrictions, especially by parents, become major triggers (Laursen, 1995; Oudekerk et al., 2015) for impulsive anger, aggressive quarrel or sadness that also affects psychophysiological regulation during adolescent-parent interactions (Cook et al., 2015). Autonomy, the need for developing own goals and trying to reach them is a stage-salient issue for adolescents. Therefore, adolescents experience intense negative emotions when they are confronted with goal blocking in this domain.

These developmental changes and stage-salient issues challenge the adolescents' emotion regulation capacities but also that of their caregivers. Emotion regulation during adolescence becomes increasingly more effective and adaptive (Silk et al., 2003; Zimmermann and Iwanski, 2014). However, inter-individual differences in emotion regulation and emotional reactions to autonomy restrictions exist and partly are explained by genetic variations and social factors.

Genetic Effects on Emotionality, Emotion Regulation, and Aggression

Research on the associations between specific candidate genes and emotionality or emotion regulation has provided some evidence for the relevance of genetic polymorphisms of the serotonin system and the dopamine system in both domains (Munafò et al., 2008; Canli et al., 2009; Hawn et al., 2015). Canli and Lesch (2007) specifically emphasized the influence of the serotonin transporter 5-HTT gene on emotionality and emotion regulation. The 5-HTT polymorphism leads to differences in serotonin neurotransmission with the short (S) allele variants displaying significantly less 5-HTT binding in the brain than the homozygous long (L) variant (Murphy and Lesch, 2008). S-allele carrier show impaired functional integration of cortico-limbic connectivity and poorer inhibitory regulation via the prefrontal cortex that leads to an increased reactivity of the amygdala to emotionally provocative stimuli (Hariri and Holmes, 2006). In general, they seem to exhibit a higher emotional reactivity (i.e., a lower threshold to emotional stimuli and increased arousal) and a biased emotional information processing associated with an even higher baseline amygdala activity (Canli and Lesch, 2007). Fernàndez-Castillo and Cormand (2016) reported in their review, a clear link between the short allele variant and increased impulsivity and aggressiveness in humans. This might specifically be the case for impulsive aggression (Hennig et al., 2005). In a similar vein, Cyders and Smith (2008) proposed the idea that genetic polymorphisms affecting the serotonin and the dopamine system explain impulsive and rash reactions, especially in emotionally arousing situations. In summary, S-allele carriers seem to represent an emotional phenotype characterized by increased emotional reactivity and impaired capacity to regulate emotions, which finds its expression in impulsive aggressive actions on the behavioral level.

However, single genetic polymorphisms only explain parts of the variability of human traits or habitual patterns of emotionality and emotion regulation. Therefore, the interaction with other genetic variations and with environmental factors often moderates the effects of single genes on behavior. From a developmental perspective, a transactional model of genetic disposition, environmental factors, epigenetic changes, and the active role of the individual in selecting and shaping the environment is a more appropriate approach in understanding the development of emotion regulation (Sameroff, 2010). Thus, especially in adolescence possible effects of the individual genetic dispositions on eliciting specific responses in the social environment (e.g., their mothers) need to be considered. This includes, whether adolescent's genotype explains the eliciting of parenting (Oppenheimer et al., 2013) or whether mother's genotype explains variation in her sensitivity towards the adolescent in dyadic interactions (Bakermans-Kranenburg and van IJzendoorn, 2008), so that maternal genotype indirectly would explain differences in the adolescents' emotion regulation and autonomy.

Within the life span, emotion regulation in infancy starts with dominantly social emotion regulation where the infant depends on the caregiver's comfort and support. With increasing age, individual emotion regulation becomes more prominent and new emotion regulation strategies are integrated into the individual self-regulation repertoire (Zimmermann and Thompson, 2014). However, social and cultural factors moderate this process (Cole, 2014) and one of these central moderating factors is attachment.

Attachment and Emotion Regulation

The attachment system is a biologically based security regulation system that is activated by existential threat or intense negative emotions (Bowlby, 1980). Although initially developed in infancy, attachment can still be elicited and has regulatory functions during middle childhood, adolescence, and adulthood (Allen and Land, 2008; Grossmann et al., 2008; Bosmans and Kerns, 2015). However, in contrast to childhood, adolescents less often express their attachment needs by seeking proximity in time of distress (although they still do). More often, they show psychological proximity seeking by means of emotional communication with the caregiver when needed. By that, adolescents balance the stage-salient issue of autonomy development with maintaining attachment (Kobak et al., 1993; Allen and Land, 2008; Becker-Stoll et al., 2008). However, the importance of adolescents' verbal emotional communication with their caregiver for emotion regulation is obvious in the reduced adrenocortical activity in adolescents who have been able to talk to their mothers after having been stressed in the Trier Social Stress Test (Seltzer et al., 2012).

Attachment influences several domains of emotional development (Laible and Thompson, 1998; Spangler and Zimmermann, 1999; Steele et al., 2008). It is especially influential for emotion regulation (Cassidy, 1994) as attachment patterns represent specific organizations of interactive emotion regulation (Zimmermann, 1999) that develop early in ontogeny. Secure attachment during childhood and adolescence is characterized by the ability to effectively regulate negative emotions with the caregiver (effective social emotion regulation). In addition, securely attached children and adolescents do regulate their emotions individually as well. In contrast, insecure-avoidantly attached children or adolescents try to regulate negative emotions individually without the caregiver in emotionally stressful situations. However, their regulation attempts often remain ineffective. Children and adolescents with insecure-ambivalent attachment organization typically show social but ineffective emotion regulation patterns for negative emotions with the caregiver as the contact and communication with the caregiver does not effectively reduce their negative emotions. The central characteristic of disorganized attachment is the absence or a breakdown of a coherent attachment strategy regulating emotional challenges (Main and Solomon, 1990; George and Solomon, 1999).

There is ample empirical evidence that attachment in childhood and adolescence is associated with emotion regulation (Kobak et al., 1993; Cassidy, 1994; Zimmermann, 1999; Waters et al., 2010; Brumariu, 2015; Zimmer-Gembeck et al., 2015) and even has effects on emotion related psychophysiology (Gander and Buchheim, 2015) also in adolescents' interaction with their mothers (Spangler and Zimmermann, 2014).

Zimmermann et al. (2009) tested whether attachment and genetic variations of the 5-HTTLPR affect emotionality, emotion regulation, and aggression in early adolescence in a social talk show task eliciting social evaluative fear. They reported that S-allele-carriers of the 5-HTTLPR polymorphism were more aggressive and showed a higher emotional reactivity to restrictions of their autonomy. However, given secure concurrent attachment the S-allele- carriers of 5-HTTLPR showed more *agreeable autonomy* (i.e., assertion of own intentions with on-going communication with mother), whereas those with insecure attachment expressed more aggressive *hostile autonomy* (i.e., contradictions with verbal or physical aggression or emphasized refusal of further cooperation). Interestingly, there was no direct genetic or attachment effect on emotional expression, suggesting that eliciting negative emotions in adolescents works independently of attachment security and the serotonin transporter polymorphism. Thus, attachment and the 5-HTTLPR might be more influential on emotion regulation and hostile autonomy than on emotion expression, at least in a dominantly fear eliciting situation.

The current study tries to extend these results to a different situation that is dominantly eliciting anger. The main objective of the study was to investigate influences of adolescents' genetic differences of the 5-HTTLPR and concurrent attachment on their emotional reactivity, emotion regulation, and aggressive hostile autonomy. In addition, we wanted to examine whether mother's 5-HTTLPR explains her behavior towards the adolescent or explains the adolescent's behavior towards her. Similarly, we wanted to test possible eliciting effects of the adolescents' genotype on maternal behavior.

Similar to the study by Zimmermann et al. (2009), we expected no main effect of attachment and the 5-HTTLPR on emotionality as assessed in emotional expression. However, we expected that adolescents with both insecure attachment and the short S-allele would show more ineffective emotion regulation and aggressive hostile autonomy. Attachment security is expected to be a moderator of the genetic disposition associated with the 5-HTTLPR. This effect should be observed even when controlling for maternal intrusiveness as a concurrent environmental factor that differentially can elicit emotion dysregulation or hostile autonomy in the adolescent. In addition, we did expect that maternal 5-HTTLPR does not contribute to her intrusiveness or adolescents' emotion related behavior.

PROCEDURES AND METHODS

Participants

The current study was conducted as part of the 12-year longitudinal follow-up assessment of the Regensburg Longitudinal Study IV, a sample of originally 106 healthy German, Caucasian, low-risk infants (53 girls/53 boys), first assessed at 12 months of age. At the 12-year assessment, 96 early adolescents (49 girls/47 boys) and their mothers participated again in a series of tasks and interviews. According to maternal education assessed at follow-up, the families represent a wide range regarding their socioeconomic status, including 28% high school education (including university entrance certificate), 33% medium secondary school certificate, and 39% lower secondary education (most of them with additional vocational training).

The complete data set for this report was not available for all subjects due to missing values, which occurred because of technical problems with some video tapes, and in some cases due to the time schedule of families who had to leave before this task was completed. Therefore, specific statistical analyses include only a reduced sample size of $N = 88$.

Procedures

At the age of 12, adolescents came to the university lab together with their mothers. After obtaining informed consent from the parents, the adolescents were interviewed regarding their attachment pattern to both parents. Afterwards, the adolescents and their mothers participated in two standardized interaction tasks designed to induce negative emotions. In this article, we report the results of the second interaction task, the dyadic computer game task. The Ethics Committee of the German Psychological Association has positively evaluated and accepted the design of the study.

Computer Game

The dyadic computer game is a modification of a task used in adolescent aggression research to induce anger in children and adolescents and to observe their aggressive behavior (de Castro et al., 2003). In the adaptation used here, mother and adolescent together played a computer-based jump and run game, with the aim to free a princess ("Esmeralda") by controlling the play figure ("Quasimodo") through several levels. The adolescent had two keys to control the movements of the play figure and the mother had one key. Both were instructed how to play the game and informed that they should carefully avoid pressing the "Ctrl-Key" (available on both sides of the keyboard, next to mother's one key and next to the adolescent's two keys), as this will lead to a game crash. After a short exercise phase, both mother and adolescent played a manipulated version of the game, where shortly before they successfully reached the final aim of freeing the princess, the game stopped with a sound announcing a game crash and presenting the sentence "The Ctrl-Key has been pressed" on the screen. A short time after the computer crash the experimenter entered the room and started the original program. The adolescents' behavior and their mothers' behavior were coded for emotion expression, emotion regulation, and hostile autonomy before and after the manipulated game crash. Independent and reliable coders carried out all behavior analyses using a standardized observational system.

Measures

Twelve Year Measures of Emotion Expression, Emotion Regulation, and Hostile Autonomy

The analysis of the 12-year behavioral analysis included emotion expression, observed emotion regulation, and hostile autonomy of the adoelscent.

Emotion expression

Adolescents' negative emotions were coded by means of a second-by-second event-based coding system from their facial and verbal expressions before and after the manipulated game crash. Negative emotions included anger, sadness, fear, and uneasiness. Inter-rater reliability was good (kappa 0.75).

Emotion regulation

Emotion regulation included those behaviors that modulate or change the emotional arousal of the adolescent. The coding separates the observed emotion expression from the observed emotion regulation process (Cole et al., 2004). Similar to the approach used by Buss and Goldsmith (1998) coders assessed strategy use and emotion expression after strategy use separately and rated the effectiveness of each strategy use. Each emotion regulation behavior was coded as either *effective* when the adolescent did no longer express the emotion after a time interval of maximum 7 s, or as *ineffective* if the duration was longer. Shorter emotion expressions were not coded regarding regulation effectiveness. Inter-rater reliability was good (kappa 0.72).

Adolescents' Observed Hostile Autonomy

Autonomy represents the need for self-regulation achieved by being able to develop own goals or ideas for actions and striving to reach them. In the computer game task, autonomy was coded when the adolescent insisted on own ideas of playing the computer game or disagreed with his or her mother's suggestions, commands or comments of what to do next. Disagreements with the mother were coded as *hostile autonomy* when they were followed or accompanied by verbal or physical attacks of the mother or by an explicit refusal to cooperate for at least 3 s. Events also were coded as hostile autonomy when the adolescent expressed emotionally charged responses towards the mother in response to an earlier disagreement with her. Examples of such attacks are active or reactive verbal threats, threatening gestures, physical attacks, or ridiculing utterances. Possible elicitors were the mothers' tone of voice, her comments, or actions. Inter-rater reliability (kappa) was 0.84 for hostile autonomy.

Maternal Intrusiveness

Maternal intrusive behavior was defined as behavior inhibiting or undermining the adolescent's autonomy and felt competence during the game. Typical maternal intrusive behaviors in the computer game include all actions interfering with the adolescent's task activities, all derogating statements regarding the adolescent's performance putting or pressure or achievement demands on the adolescent. Raters coded the number of intrusive maternal utterances. The inter-rater agreement resulted in a kappa of 0.78.

Adolescent Attachment Security

Attachment was assessed by the Late Childhood Attachment Interview (LCAI; Zimmermann and Scheuerer-Englisch, 2000), a semi-structured interview that probes the individual's descriptions of the current relationship to both parents in attachment relevant situations and the attachment behavior towards the parents. The interviews were rated from videotapes with regard to attachment representations separately for attachment to mother and father and the adolescents' attachment behavior when distressed and upset on 5-point scales. In addition, adolescents' interview responses were coded regarding coherence with a categorical event-based system and regarding access to emotions. The adolescents' attachment behavior scale and the adolescents' attachment representations of mother scale were combined and utilized in the current study. Higher scores on this scale reflect seeking mother's proximity, support or comfort when experiencing negative emotions that the adolescent cannot regulate without help, and coherently reporting maternal support and emotional availability. Low scores reflect avoidance of the mother in times of distress, retreat, or pretending that no help is needed as well as reports of maternal rejection, lack of emotional availability or inability to sooth or regulate the adolescent effectively. The interviews were rated by an independent coder who did not know other data of this study. Reliability (kappa), established on 20 interviews from a different sample, was 0.93.

The validity of the LCAI has been demonstrated in previous studies. The attachment classification in the strange situation in infancy and the parent-child interaction in toddlerhood is significantly associated with secure attachment behavior in the LCAI. In addition, concurrent parenting, and later attachment representations in adolescence assessed with the Adult Attachment Interview (AAI) is significantly associated with the attachment representation of mother in the LCAI (Zimmermann et al., 2000; Grossmann et al., 2002a,b).

Molecular-Genetic Analyses

Genotyping for the 5-HTTLPR polymorphism was performed at the Institute of Medical Chemistry, Molecular Biology and Pathobiochemistry, Semmelweis University (Budapest, Hungary), by scientists blind to the psychological data. Genomic

DNA was isolated from buccal swabs using published procedures (Freeman et al., 1997).

The 5-HTTLPR variable number of tandem repeats (VNTR) polymorphism was investigated by employing two flanking primers for the polymerase chain reaction (sense primer: 5′ GGC GTT GCC GCT CTG AAT GC 3′, antisense primer: 5′ GAG GGA CTG AGC TGG ACA ACC AC 3′; thermocycling was initiated at 95°C for 10 min to activate HotStar DNA polymerase (Qiagen) followed by 35 cycles of 1 min denaturation at 95°C, 1 min of annealing at 65°C, and 1 min extension at 72°C, completed by 10 min of extension at 72°C. In both VNTR polymorphisms 50% of dGTP were replaced with dITP in order to avoid allelic drop-out in heterozygotes. The length of the generated PCR-amplicons directly reveals the repeat number (Ronai et al., 2001).

Task Duration

As mother-adolescent dyads differed somehow in the time they played the computer task, and in the time they spent discussing whose fault it was that the game crashed we also measured the task duration in seconds.

Statistical Analyses

Two-factorial genotype × attachment quality analyses of variance were applied to test the hypotheses of this study. For use as independent factors, the 5-HTTLPR polymorphism and the attachment measures were dichotomized. Subjects were grouped into carriers and non-carriers of a short allele (ss and sl vs. ll) of the 5-HTTLPR, based on theoretical considerations and sample characteristics. Many scientific studies and meta-analysis compare carriers of at least one s-allele with ll-allele carriers (e.g., Munafò et al., 2008) and contrast them regarding amygdala reactivity to emotional stimuli and functional differences in serotonin regulation (Canli and Lesch, 2007). Moreover, the relatively low frequency of ss carriers (20%) in this study as reported in the next section, would have led to inappropriately small cell sizes for the planned two-factor gene × attachment analysis of variance (ANOVA) design. Similarly, subjects were grouped according to their scores on the combined attachment measure into subjects with insecure attachment (score < 3; which include avoidant and ambivalent attachment patterns) vs. secure (score > 3; representing secure attachment behavior and representation). Maternal intrusiveness and duration of the interaction task were included as covariates in the ANOVAs for autonomy, emotion expression, and observed emotion regulation to control for potential influences of maternal behavior and differences in gaming speed.

RESULTS

Preliminary Analyses

The frequencies of the distribution of short and long allele variations of the 5-HTTLPR in the complete adolescent sample were 42% and 58%, respectively, which are comparable to the European population (Gelernter et al., 1997). The genotype frequencies were 35 (36%), 42 (44%), and 19 (20%) for the ll, ls, and ss genotypes, respectively. The 5-HTTLPR genotype distribution was in the Hardy-Weinberg equilibrium (χ^2 (2, N = 96) = 0.96, ns). The genotype frequencies for the mothers in this sample were 31 (32%), 50 (52%), and 15 (16%) for the ll, ls and ss genotypes, respectively. The carriers of the ss and sl genotype were grouped together to avoid too small cell sizes for two-factor ANOVAs.

The number and duration of negative emotional expressions clearly show that the computer task did elicit negative emotions in the adolescents. The adolescents' 5-HTTLPR-genotype status (ll vs. ss/sl) did not significantly differ with respect to maternal intrusiveness ($t_{(86)} = -0.26$, ns) or attachment security ($t_{(92)} = 0.16$, ns). However, adolescents with the long (ll) variant of the 5-HTTLPR-genotype were significantly faster (M = 149.3 s, SD = 50.2) in the computer game ($t_{(86)} = -2.4$, $p = 0.024$) compared to adolescents with at least one short (ss/sl) variant of the 5-HTTLPR-genotype (M = 180.0 s, SD = 66.7). Maternal 5-HTTLPR-genotype status (ll vs. ss/sl) did not significantly differ with respect to maternal intrusiveness ($t_{(86)} = -1.5$, ns) or adolescents' attachment security ($t_{(92)} = 0.15$, ns) or duration of the computer game ($t_{(86)} = 0.15$, ns).

These results indicate that neither the mothers' nor the adolescents' 5-HTTLPR variations were significantly associated with maternal intrusiveness or the adolescent's attachment security. In addition, there was no significant effect for adolescent's gender regarding 5-HTTLPR-genotype status (χ^2 (1, N = 96) = 0.63, ns), attachment security ($F_{(1,92)} = 3.1$, ns), or maternal intrusiveness ($F_{(1,86)} = 0.08$, ns). Moreover, gender was not significantly associated with adolescents' hostile autonomy in the computer game ($F_{(1,86)} = 0.09$, ns), the frequency of their observed effective ($F_{(1,87)} = 2.4$, ns) or observed ineffective emotion regulation ($F_{(1,87)} = 2.9$, ns). However, girls more frequently expressed negative emotions than boys ($F_{(1,87)} = 6.3$, $p = 0.014$; ($M_{\text{girls}} = 9.1$; SD = 7.9; $M_{\text{boys}} = 5.1$, SD = 5.6) and also showed a longer duration of expression of negative emotions ($F_{(1,86)} = 6.6$, $p = 0.012$; $M_{\text{girls}} = 26.0$ s; SD = 20.7; $M_{\text{boys}} = 13.3$ s, SD = 16.5) but did not spend more time playing.

Maternal intrusiveness was significantly associated with adolescent's hostile autonomy ($r_{(88)} = 0.57$, $p < 0.01$) and observed *ineffective* emotion regulation ($r_{(88)} = 0.33$, $p < 0.01$) but not with observed *effective* emotion regulation. For further statistical analyses, maternal intrusiveness, and duration of the computer game were included as covariates.

Gene-Attachment Interactions

First, we tested a possible influence of genotype and attachment security on emotion expression in the dyadic interaction task. A 5-HTTLPR (ll vs. sl/ls) × attachment (insecure vs. secure) ANOVA with frequency and duration of negative emotional expression as dependent variables and maternal intrusiveness and task duration as covariates did not result in significant main or interaction effects. Thus, there was no significant gene or attachment effect on the adolescents' emotional reactivity

TABLE 1 | Adolescents' observed negative emotionality and emotion regulation (Means and SE).

	ll 5-HTTLPR		ss/sl 5-HTTLPR	
	Insecure attachment (n = 17)	Secure attachment (n = 17)	Insecure attachment (n = 28)	Secure attachment (n = 25)
Negative emotionality				
Frequency	4.35 (0.84)	8.00 (1.99)	8.36 (1.49)	6.72 (1.27)
Duration (seconds)	11.83 (2.38)	21.56 (6.09)	25.15 (5.68)	21.05 (3.42)
Emotion regulation				
Effective	2.18 (0.40)	3.35 (0.67)	2.46 (0.38)	3.12 (0.47)
Ineffective	2.29 (0.68)	3.29 (0.83)	4.82 (0.83)	2.88 (0.42)

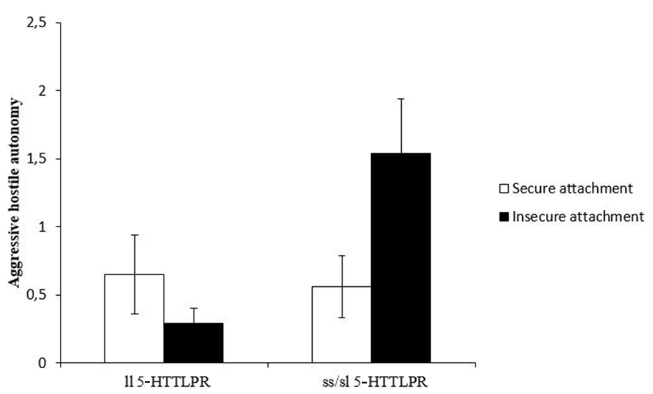

FIGURE 1 | Frequency (mean and SE) of adolescents' aggressive hostile autonomy behaviors in the computer game task while interacting with their mothers.

as observable in the negative emotional expressions (see **Table 1**).

Next, we examined the hypothesis of a possible gene-attachment interaction in explaining the adolescents' observed emotion regulation. A 5-HTTLPR (ll vs. sl/ls) × attachment (insecure vs. secure) ANOVA with the frequency of effective observed emotion regulation as dependent variables and maternal intrusiveness and task duration as covariates did not result in significant main or interaction effects for observed emotion regulation. The same analysis for ineffective observed emotion regulation did not reveal significant main effects for 5-HTTLPR ($F_{(1,87)}$ = 0.96, ns) and for attachment security ($F_{(1,87)}$ = 0.93, ns). However, the gene × attachment interaction effect nearly reached significance ($F_{(1,87)}$ = 3.9, p = 0.051). *Post hoc* t-tests revealed that adolescents with at least one short allele of the 5-HTTLPR who were in the secure attachment group showed significantly less observed *ineffective* emotion regulation ($t_{(39,8)}$ = 2.1, p = 0.04) compared to adolescents with the short allele of the 5-HTTLPR from the insecure attachment group (see **Table 1**). There was no significant attachment effect on ineffective emotion regulation for the homozygote long allele carriers. However, given insecure attachment, ll-carriers showed less ineffective emotion regulation compared to ss/sl- carriers ($t_{(42,8)}$ = 2.4, p = 0.023).

Finally, we examined the hypothesis of a possible gene-attachment interaction in explaining adolescents' hostile autonomy behavior. A 5-HTTLPR × attachment ANOVA with hostile autonomy as dependent variables and maternal intrusiveness and task duration as covariates revealed a significant main effect for the 5-HTTLPR polymorphism ($F_{(1,86)}$ = 4.5, p = 0.038), no significant main effect for attachment security ($F_{(1,86)}$ = 0.53, ns) but a significant interaction effect ($F_{(1,87)}$ = 5.2, p = 0.025) on hostile autonomy. As can be seen from **Figure 1**, the gene main effect indicates an increased frequency of hostile autonomy for short allele carriers of the 5-HTTLPR polymorphism. However, attachment security moderates this effect in two ways. Securely attached ss/sl carriers of the 5-HTTLPR polymorphism showed significantly less aggressive *hostile* autonomy ($t_{(42,7)}$ = −2.1, p = 0.041) compared to insecurely attached adolescents with the short variant of the 5-HTTLPR (see **Figure 1**). In addition, within the group of insecurely attached adolescents, ss/sl carriers show significantly increased rates of aggressive *hostile* autonomy compared to ll-carriers ($t_{(31,2)}$ = −3.0, p = 0.005). However, in the secure attachment group no significant 5-HTTLPR differences in hostile autonomy were found.

DISCUSSION

The primary goals of this study were to examine the interaction between molecular genetic polymorphisms of the serotonin transporter gene and attachment security in adolescence on emotionality, emotion regulation, and hostile autonomy as observed in an anger eliciting social context. Studies on the effects of the polymorphism in the promoter region of the serotonin transporter gene suggest an effect on emotional reactivity (i.e., amygdala activation) and attention to negative emotional stimuli and as a consequence, on emotion-regulation (Canli and Lesch, 2007; Canli et al., 2009; Hawn et al., 2015). However, surprisingly few genetic studies assess both emotionality and emotion regulation at the same time or include observable emotion regulation behavior as an outcome. As one of these few studies, Amstadter et al. (2012) showed that S-allele carriers gave up earlier during a frustrating task, an indirect hint for poor emotion regulation. However, the study did not report effects on emotionality. In this study, we successfully elicited negative emotions and coded emotional expression followed by the coding of effective or ineffective emotion regulation. Thus, the research is in line with suggestions for experimental emotion regulation research in developmental psychology (Cole et al., 2004). The task indeed did elicit negative emotions, which corroborates the internal validity of this task.

Replicating findings of a previous study (Zimmermann et al., 2009), neither the 5-HTTLPR polymorphism nor the attachment security predicted frequency or duration of negative emotional expression. Thus, the computer game task is comparably valid for all adolescents in eliciting negative emotionality when experiencing difficulties and failure in a dyadic computer game. In contrast to studies on amygdala activation, this study showed that the expressed negative emotionality seems to be independent of the serotonin transporter polymorphism. Oher studies report only more emotional expression in ss-carriers when combining positive and negative emotions (Gyurak et al., 2013). In addition, attachment security is associated with a wide range of open emotional expression, also of negative emotions, in contact with caregivers or with peers (Bretherton, 1990; Cassidy, 1994). Negative emotional expression would be restricted in insecure-avoidantly attached adolescents in interaction with the caregiver. However, as the computer task forces both adolescents and mothers to look at the screen and not to look at each other, display rules of insecurely attached adolescents might not influence emotional expression here. Similar attachment effects on emotion expression have been reported for adolescents' interactions with close friends during a computer based task (Zimmermann et al., 2001).

The effects on emotional dysregulation (i.e., inefficient emotion regulation) showed a clear gene-attachment interaction. Carriers of the short SERT allele only showed increased emotional dysregulation when insecurely attached but not when securely attached. Thus, secure attachment seems to buffer adolescents against an impulsive genetic disposition for emotional dysregulation. Similarly, s-carriers of the 5-HTTLPR only showed increased aggressive *hostile* autonomy when insecurely attached but not when securely attached. Thus, secure attachment is a buffer against an impulsive genetic disposition for impulsive aggressive behavior.

The study revealed a heightened emotional dysregulation, especially to restrictions of autonomy for short 5-HTT polymorphism carriers in adolescence, an age period in which autonomy restrictions typically elicit negative emotions and contribute to quarrels with parents (Laursen, 1995). Carriers of the short 5-HTT polymorphism were significantly more sensitive to maternal comments and restrictions of their autonomy regarding how to play the game, what to do next, who is to blame after the computer crash compared to ll-carriers. This led to more impulsive contradictions, aggressive assertiveness or attacks of the adolescents against their mother but only in case of insecure attachment. In contrast, secure attachment seems to buffer against this genetic tendency to contradict maternal comments or commands. Secure internal working models might contribute to the adolescents' expectations of trust towards their mother or an interpretation of her comments and commands as not undermining a general felt acceptance and security especially when emotionally challenged. The results also support the idea of differential susceptibility of adolescents who are carriers of the s-allele of the 5HTTLPR (Belsky, 2015). Within the group of ss/sl carriers, those with secure attachment did not show increased emotion dysregulation or aggressive hostile autonomy. The development of secure attachment in adolescence still depends on emotional available caregiving and support (Zimmermann, 1999; Allen and Land, 2008). Thus, short allele carriers seem to be more sensitive to effects of attachment security based on their attachment relevant caregiving experience. However, the results even speak more for a transactional developmental pattern. Differential susceptibility does not subsume the idea of an active individual. As attachment is a stable characteristic of the adolescent, the observed emotion dysregulation, and aggressive hostile autonomy is not only reactivity or sensitivity to the concomitant maternal comments as concurrent environment. Adolescent attachment moderates the responses the current environment and the genetic tendency associated with the s-allele.

Thus, at least in adolescence, the 5-HTTLPR does not seem to affect emotionality as observable in an increased frequency or duration of negative emotional expression but particularly in aggressive reactions to stage-salient emotional elicitors of negative emotions, such as restrictions of autonomy in adolescence (Laursen, 1995). The participants of this study were in early adolescence, an age with a lowered repertoire of emotion regulation strategies (Zimmermann and Iwanski, 2014). The many conflicts with parents at that age (Laursen et al., 1998) may increase the allostatic load of adolescents with the combination of the 5-HTTLPR S-allele and insecure attachment by a heightened physiological stress response (Cook et al., 2015) starting a maladaptive cascade which leads to an increased risk for psychopathology (Masten and Cicchetti, 2010). There is growing evidence 5-HTTLPR—environment interactions on the development of externalizing behavior in the last years (Brett et al., 2015; Cline et al., 2015).

Beside the effects on adolescent behavior the study also showed that mothers' 5-HTTLPR was not associated with her intrusive behavior towards the adolescent. In concordance with Bakermans-Kranenburg and van IJzendoorn (2008), mothers who are ss/sl carriers are not more intrusive, which suggests that we do not have the evidence of a specific genetic effect on mothers caregiving in this situation associated with the short allele of 5-HTTLPR. In addition, also adolescents who are ss/sl carriers did not significantly elicit more intrusive behavior in their mothers. Thus, we have not evidence of a genetic eliciting effect of the adolescent on this specific parenting behavior in this task. This further supports the idea that the moderation of adolescents' genotype (5-HTTLPR) by attachment is a sign of transactional processes in adolescence where attachment already is a characteristic of the person that influences the effect of genetic dispositions independent of the concurrent maternal caregiving environment.

Clearly, there are methodological limitations of this study. The sample size may have been too small to have enough power to detect more direct or interaction effects (Murphy and Lesch, 2008). As this was a longitudinal follow-up study, the sample size was somehow restricted which decreases statistical power. Extended replications with other age groups and in interaction with fathers or peers are required. In addition, the effects of other cumulative environmental risks (Caspi et al., 2003) or the interaction with other candidate genes clearly need to be considered. Moreover, from a transactional developmental perspective the direction of the effects might be more complex than has been studied here. Longitudinally, impulsive individuals also can elicit more negative evaluations and expectations in their social environment, which in turn increase the emotional dysregulation observed during interactions.

However, despite these limitation the study adds new evidence that attachment can moderate the effect of the short variant of the 5-HTTLPR on emotional dysregulation and impulsive aggression.

AUTHOR CONTRIBUTIONS

PZ and GS contributed to the design of the study, the data analysis, and the manuscript.

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Effects of the Adult Attachment Projective Picture System on Oxytocin and Cortisol Blood Levels in Mothers

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Oxytocin, a small neuropeptide of nine amino acids, has been characterized as the "hormone of affiliation" and is stimulated, for instance, in mothers when interacting with their offspring. Variations in maternal oxytocin levels were reported to predict differences in the quality of care provided by mothers. In this study, the Adult Attachment Projective Picture System (AAP) as a valid measure to assess attachment representations was used as an activating attachment-related stimulus. We investigated whether the AAP induces a release of oxytocin in mothers with a secure attachment representation and a stress-related cortisol response in mothers with an insecure attachment representation. Therefore, pre-post effects of AAP administration on plasma oxytocin and serum cortisol levels were investigated in $n = 44$ mothers 3 months after parturition. Oxytocin levels increased from pre to post in the significant majority of 73% participants ($p = 0.004$) and cortisol decreased in the significant majority of 73% participants ($p = 0.004$). Interestingly, no association between alterations in oxytocin and cortisol were found; this suggests taking a model of two independent processes into considerations. These results show that the AAP test procedure induces an oxytocin response. Concerning the results within the four AAP representation subgroups, our hypothesis of a particularly strong increase in oxytocin in secure mothers was not confirmed; however, in secure mothers we observed a particularly strong decrease in cortisol. Effect sizes are reported, allowing the replication of results in a larger study with sufficient sample size to draw final conclusions with respect to differences in OT and cortisol alterations depending on attachment representation. When interpreting the results, one should keep in mind that this study investigated lactating mothers. Thus, the generalizability of results is limited and future studies should investigate non-lactating healthy females as well as males and include a control stimulus condition.

Keywords: oxytocin, cortisol, attachment representation, stress, adult attachment projective picture system

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Abbreviations: AAP, Adult Attachment Projective Picture System; BPD, Borderline personality disorder; Ds, dismissing; E, preoccupied; F, secure; HPA, hypothalamus pituitary adrenal; SAM, sympathetic adrenal medullary; TSST, Trier Social Stress Test; U, unresolved.

INTRODUCTION

Attachment as a Biobehavioral System

Attachment is a state in which several physiological and behavioral systems are organized in order to provide an individual with a certain sense of security and protection with others (Bowlby, 1969). Bowlby defines these behavioral systems as biological systems that work along with physiological processes. Mental representations of early attachment relationships shape emotional and cognitive information, which affects the attention and memory as well as the emotional reactivity of our central nervous system. In order to maintain organization within the attachment system, emotional reactivity is regulated within the central nervous system (Main et al., 1985; Bretherton, 1993). Following Bowlby (1969) and Ainsworth et al. (1978), the assessment of developmental attachment places an emphasis on activating attachment and "seeing attachment in action" (i.e., in attachment activating contexts; Bowlby, 1969; Ainsworth et al., 1978). Over the last 20 years the psychobiological research on infant and adult attachment has increased dramatically. Attachment patterns have been linked to different ways to regulate emotions. Some researchers even argue that the attachment system is in itself a device of emotion regulation (Vrtička and Vuilleumier, 2012). Studies indicate that, in response to stress, the insecure attachment is related to a heightened adrenocortical activity, heart rate and skin conductance, which is consistent with the hypothesis that attachment insecurity leads to deficits in emotion regulation (Gander and Buchheim, 2015). The majority of neurophysiological studies of adult attachment use self-report measures (Carpenter and Kirkpatrick, 1996; Kim, 2006; Laurent and Powers, 2007; Rochman et al., 2008; Kiss et al., 2011; Dan and Raz, 2012). Only a few studies use narrative interview measures of attachment like the Adult Attachment Interview (AAI) and the Adult Attachment Projective Picture System (AAP; Beijersbergen et al., 2008; Buchheim et al., 2009; Fraedrich et al., 2010; Holland and Roisman, 2010; Behrens et al., 2011). Self-reports assess the subjective evaluation of attachment styles, primarily differentiating between secure and insecure avoidant or anxious attachment (Ravitz et al., 2010). On the other hand, the AAI or AAP are designed to activate an individual's internal working model of attachment by introducing attachment-related topics (e.g., separation, illness, abuse and death), and they assess attachment representations (e.g., secure, insecure-dismissing, insecure-preoccupied and unresolved trauma) based on the analysis of verbatim transcripts. The feasibility of the AAP measure as a stimulus in an attachment-related neurobiological context has been proven in diverse experimental settings in clinical and nonclinical groups (Buchheim et al., 2006a,b, 2008, 2009, 2012).

Oxytocin, Attachment and Caregiving

Oxytocin is a neuropeptide of nine aminoacids and is critically involved in both central and peripheral aspects of mammalian attachment and survival. The neuropeptide is mainly produced in the paraventricular and supraoptic nuclei of the hypothalamus. These nuclei project to the posterior pituitary gland. Here, oxytocin is stored coupled with neurophysin I as a precursor complex. Finally, oxytocin is cleaved and is released into the peripheral blood. Oxytocin induces well-described peripheral actions and the oxytocin neurons additionally project to important brain regions manifested in social and maternal behaviors (Braunstein et al., 1980; Insel, 1992; Gimpl and Fahrenholz, 2001; Bielsky and Young, 2004; Strathearn, 2011). Studies on humans and animals have shown that oxytocin mediates anxiolytic effects, and plasma levels are related to the reduction of anxiety and stress (Gimpl and Fahrenholz, 2001; Neumann and Landgraf, 2012). A substantial literature exists underscoring the role of oxytocin in regulating social behaviors (Gimpl and Fahrenholz, 2001; Feldman et al., 2010, 2011; Meyer-Lindenberg et al., 2011). A large number of studies have implicated oxytocin in maternal care (Pedersen et al., 2006), pair bonding (Ross et al., 2009), interpersonal trust (Kosfeld et al., 2005), emotion recognition (Gimpl and Fahrenholz, 2001; Lischke et al., 2012), and empathy (Hurlemann et al., 2010). Furthermore, oxytocin has been characterized as a "hormone of affiliation" and the oxytocinergic system has received attention as a key neural substrate of maternal caregiving, involved in the emergence and maintenance of maternal behaviors (Insel, 1992; Feldman et al., 2010, 2011). Prospective and cross-sectional studies have demonstrated that maternal oxytocin levels are systematically associated with naturally occurring variations in maternal behavior, with high plasma oxytocin levels during pregnancy and postpartum predicting increased maternal behavior in the postpartum months (Gordon et al., 2010; Atzil et al., 2011; Feldman et al., 2011). Interaction with their offspring, in the postpartum period further stimulated oxytocin response in mothers (Feldman et al., 2010, 2011), though significant inter-individual variations have been found in the oxytocin plasma levels (Strathearn, 2011; Strathearn et al., 2012). Additionally oxytocin plays a crucial role in bond formation between children and parents and social reciprocity. Parental oxytocin plasma level and early parental care patterns seemed to be associated with social reciprocity (Feldman et al., 2013; Waller et al., 2015). These natural variations in parental oxytocin responses may predict differences in the quality of maternal/paternal caregiving.

Oxytocin and Cortisol During Social Stress

Previous research mainly focused on attachment-related stress regulation and its effect on the reactivity of the hypothalamus pituitary adrenal (HPA) axis in adults using self-report measures (Heinrichs et al., 2003; Ditzen et al., 2007; Quirin et al., 2008). In addition, a few studies investigated adult attachment and the HPA-axis response during social stress (Gordon et al., 2010; Pierrehumbert et al., 2012). In these studies the interplay of oxytocin and cortisol in response to the Trier Social Stress Test (TSST) was investigated: Pierrehumbert et al. (2012) examined for the first time the interplay of attachment representation and plasma oxytocin and serum cortisol responses under stress in a mixed clinical and healthy sample ($N = 74$) using the TSST. Here, the AAI was used to determine attachment representations. Subjects with a secure attachment classification reported relatively low subjective stress; they presented a moderate response of cortisol and a high level of oxytocin after the TSST. Subjects with a dismissing classification reported moderate subjective stress; they presented an elevated cortisol response, and moderate levels of oxytocin due to social stress. Subjects with a preoccupied classification presented moderate levels of subjective stress, and of HPA response, and a relatively low level of oxytocin. Finally, participants with an unresolved classification presented a suppressed HPA axis response and moderate levels of oxytocin after TSST application (Pierrehumbert et al., 2012). However, using the TSST as a social challenge, an increase of plasma oxytocin in response to the acute social challenge test was not detectable (Ditzen et al., 2007). In this study, Ditzen et al. (2007) investigated the influence of couple interaction on cortisol and oxytocin responses to stress in women and revealed lower cortisol levels but no changes in oxytocin levels due to positive physical partner contact prior to the stress exposure (Ditzen et al., 2007). Ditzen et al. (2008) investigated the effects of the interplay of adult attachment and social support on psychological and cortisol responses to psychosocial stress using the TSST. State anxiety, mood and salivary cortisol levels were repeatedly assessed before and after stress. They found that social support alone reduced cortisol responses to stress (Ditzen et al., 2008). However, attachment seems to be a strong predictor of oxytocin and cortisol levels in the periphery, resulting in effects on state and trait anxiety. These data support the notion that attachment representations may affect stress responses and suggest a specific role of oxytocin in both the attachment and the stress system. These studies show that attachment representations are associated with characteristic oxytocin and cortisol responses in response to a social stress test.

While previous studies focused on the effects of social stress paradigms on cortisol and oxytocin responses, to our knowledge the direct effects of an attachment-related paradigm on peripheral oxytocin as well as cortisol levels before and after an attachment task have not been investigated so far. Therefore previous obtained data investigating the direct relation between attachment-related stress and peripheral oxytocin and cortisol levels seemed to be inconsistent and more research in this area is needed. According to that point, in this study we used the AAP to classify the mothers' attachment representations. Additionally, the AAP served as a stimulus to potentially activate the attachment and caregiving system, since attachment/caregiving situations are depicted in the AAP (see "Materials and Methods" Section). Following George and Solomon (2008) model, when the caregiving system is activated and the mother becomes distressed by the situation or the child, the mother's attachment system is also likely activated. Peripheral blood was collected to generate plasma and serum for the assessment of oxytocin and cortisol, respectively.

(i) We hypothesized an increase of oxytocin level after the AAP. (ii) We expected a possible change in the cortisol level. (iii) The investigation of attachment group differences was of exploratory nature. Nevertheless, we asumed a stronger oxytocin increase after the AAP in securely attached mothers compared to insecurely attached mothers and an increase in cortisol in the insecurely attached groups compared to the securely attached group.

MATERIALS AND METHODS

Participants

At the maternity ward of the university hospital Ulm, 1460 women who recently gave birth to a child constituted the pool of potential study participants. Exclusion criteria were age under 18, insufficient knowledge of the German language, and severe complications during parturition or severe health problems of mother or child, current drug consumption or psychotic disorders. Participants received 10 € as compensation. A total of 240 mothers provided written informed consent at t_0 and were invited for data assessment 3 months postpartum (t_1). As most mothers were still breastfeeding 3 months postpartum, we invited them to bring their infants along. In total, $n = 67$ mothers participated at t_1. The adult attachment representation was assessed with the AAP, and peripheral blood samples were collected by venipuncture before and after the AAP. Data of four cases had to be excluded from final analyses since infants became so unsettled that mothers were needed to breastfeed them during the AAP. For five mothers, AAP narratives were missing or incomplete due to technical problems (recording device did not work, or recordings had to low-noise). Another 14 women had to be excluded due to insufficient amount of blood for radio-immuno-assay (RIA) analyses. Thus, for t_1, the data of $n = 44$ mothers (age range 21.9–44.2 years, mean 33.6 years [SD 5.4 years]) was available (**Figure 1**). Participants received another 40 € as a compensation for the participation in t_1. The study was approved by the Ethics Committee of the Ulm University. Written informed consent was obtained from all subjects in accordance with the Declaration of Helsinki.

Attachment Measure

The Adult AAP System (George and West, 2012) assesses the attachment status in adults using a set of picture stimuli. The stimulus set includes eight line drawings, a warm-up picture and seven attachment scenes of individuals in attachment situations when they are alone or in potential attachment dyads. Participants are asked to tell a story to each picture. The stories are audio-recorded and analyses are done from verbatim transcripts. Each stimulus response is coded for attachment-related content and defensive processes. Pictures with a "alone scene" (i.e., stimuli that portray individuals alone) are evaluated for agency of self (internalized secure base, haven of safety in the context an attachment-caregiving relationship, capacity to act) and connectedness (i.e., desire and ability of the character in the story to be in a relationship defined by a behavioral system [e.g., attachment, caregiving, affiliative, sexual]). The dyadic pictures (i.e., stimuli that portray individuals in attachment-

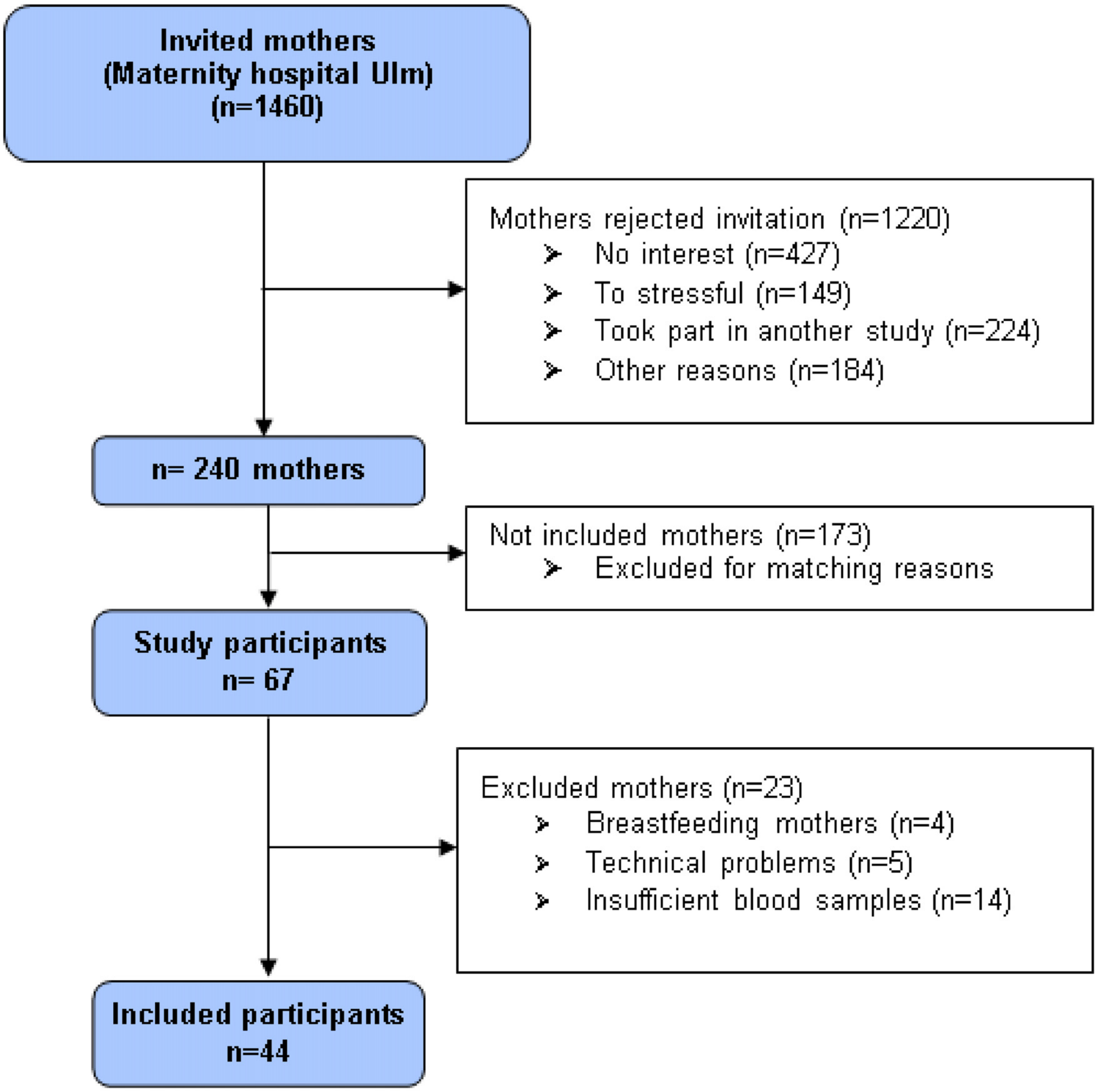

FIGURE 1 | Flowchart showing criteria of participants in- and exclusion.

caregiving dyads) are judged by their degree of synchrony in the interactions (i.e., synchrony is evaluated based on elements of partnership or elements of mutual enjoyment). The AAP evaluates the three forms of defensive processes: deactivation (avoidance), cognitive disconnection (ambivalence), and segregated systems (attachment fear and its resolution). The AAP designates four attachment classifications based on the analysis of the coding dimensions across the entire set of seven attachment stories. Individuals with secure attachment (F) show a high level of agency, connectedness and synchrony in attachment relationships in their narratives. If they use defensive strategies, they serve a more flexible integration at the representational level (high agency, e.g., thinking processes). Individuals with insecure-dismissing or insecure-preoccupied (E) attachment are characterized by functional or absent relationships in the stories. Those with dismissing representation rather use "deactivation" (represented, e.g., by rejection, power or achievement), whereas those with a preoccupied representation use a high amount of "cognitive disconnection" as a characteristic defense (represented, e.g., by conflicts, vagueness or anger). Individuals with unresolved trauma (U) are overwhelmed by topics related to attachment-related trauma (e.g., danger, isolation, fear or threat) and loss with no indications of the character's capacity to act, like protection from frightening and dangerous situations and no internalized available attachment figure providing comfort and security. For more complete details of the coding system and classification, see George and West (2012).

Studies provide evidence of excellent concurrent validity of the AAP with the AAI, test-retest reliability, inter-rater reliability and discriminant validity in healthy controls and clinical patients. Results from a large-scale psychometric investigation including 144 adult participants demonstrate excellent inter-judge reliability; the concordance rate for two judges on the four-group classifications were 90%, $\kappa = 0.85$, test-retest reliability (after 3 months 84% remained in the same attachment category; $\kappa = 0.78$) and discriminant validity. To evaluate the concurrent validity, AAP classifications were compared to independent AAI classifications. The concordance rates for the four-group classifications were 90%, $\kappa = 0.84$, and for the two groups (secure vs. insecure) even 97%, $\kappa = 0.89$ (George and West, 2001, 2012; Buchheim and George, 2011). All AAP protocols were analyzed by a highly experienced and reliable rater (A.B.). The personal codes of participants and time ("before" or "after" the AAP administration) were eliminated in the transcribed protocols. Hence, the judge was blind with respect to the time sequence and personal pairings.

Design

Mothers had their last meal 2–3 h before arriving in the laboratory between 12 pm and 1 pm. Mothers were allowed to have a regular breakfast, but they were asked to fast for at least 3 h prior to study participation. They were allowed to drink water only but no coffee or tea before and during the AAP. Mothers, who breastfed their child during the study procedures were excluded from the analysis due to the known effects of breastfeeding on the oxytocin levels. After arrival, mothers were asked to first take care of their babies (e.g., taking off warm cloth or blankets), then mothers were left alone for a short period (approximately 15–20 min) to bring the endocrine levels to a baseline level. Following this short resting period the first venipuncture and blood collection was performed. Afterwards mothers were introduced to the experimental procedures. In the AAP, participants were asked to tell a story for each AAP picture: "What is happening in the scene?", "What led up to the scene?", "What are the characters thinking or feeling?", "What might happen next?". The procedure lasted about 20 min (see "AAP Duration" Section below). Missing duration values were caused by incorrect settings of voice recorders. The AAP interviews were administered by trained psychologists in a standardized manner. Immediately following the attachment task, a second blood sample was collected again via venipuncture. Mothers were allowed to hold their babies in their arms. Mothers who needed to breastfeed during the AAP or during blood collection were excluded from further analyses. In the majority of cases, infants were sleeping in their baby carriages during the experiment. However, if infants became restless, mothers were allowed to hold them in their arms. After finishing the AAP procedure and the second blood sampling, snacks and water were offered and mothers were able to take care of their babies.

Blood Collection and Sample Preparation

Blood samples were drawn from antecubital veins into 7.5 ml vacutainer blood monovettes containing EDTA (Sarstedt, Germany) and 7.5 ml Z-Gel monovettes (Sarstedt, Germany). EDTA monovettes and tubes were ice-chilled and serum monovettes were stored at room temperature. EDTA monovettes were centrifuged at 4°C at 1.300 g for 15 min and serum monovettes were centrifuged at 4°C at 1.500 g for 10 min. Supernatants were stored at −80°C until further assay analysis. Aliquots of 250 μl were stored at −80°C until analyses.

Determination of Oxytocin and Cortisol Levels

Oxytocin was determined by standardized RIA (RIAgnosis, Max-Planck-Institute, University of Munich). Determination of cortisol (nmol/l) was realized using a chemiluminescence-immuno-assay CLIA (IBL international—Hamburg) at the Institute of Biopsychology, University of Dresden. Samples were shipped on dry ice. All procedures were performed according to the manufacturer's protocols.

Statistics

The study focused on the reactivity of oxytocin and cortisol levels in response to the AAP. For the original values of these two parameters, the normality assumptions for the pre values, post values, and pre-post differences were rejected both by the exact one-sample Kolmogorov-Smirnov test with Lilliefors correction and Shapiro-Wilks test. For the logarithmic values, the normality of pre-post differences by oxytocin remained rejected by both considered normality tests (see **Table 1**) and the requirements allowing the application of the paired t-test (or mathematically equivalent GLM models) were not satisfied.

Other strict monotone transformations like inverse or square root did not lead to the distribution desirably satisfying the test assumption as well. Hence, we decided to apply the conservative exact sign test. This test compares the number of participants with increased and decreased parameter values. Results of the sign test are robust, because they

TABLE 1 | Tests of normal distribution for oxytocin and cortisol levels (n = 44).

		Kolmogorov-Smirnov test (Lilliefors correction) *p*	Shapiro-Wilk test *p*
Oxytocin level	before AAP	<0.001	<0.001
	after AAP	<0.001	<0.001
	Pre-post difference	<0.001	<0.001
Cortisol level	before AAP	0.001	0.002
	after AAP	0.008	0.003
	pre-post difference	0.025	0.036
Logarithm of oxytocin level	before AAP	≥0.200	0.726
	after AAP	≥0.200	0.903
	pre-post difference	0.003	0.022
Logarithm of cortisol level	before AAP	0.120	0.241
	after AAP	0.048	0.012
	pre-post difference	≥0.200	0.719

Significant values indicate violations of the normality assumption.

are invariant to any strict monotone transformation. The association between increase:decrease ratios for oxytocin and cortisol were tested by the exact Fisher's test. The correlations between oxytocin levels, cortisol levels and psychometrical scales and subscales were tested by the Spearman's rank correlation coefficient. All these procedures are invariant to any strict monotone transformation of measured values as well. This implies that tests for originally measured and log-transformed values are mutually equal. In tables, we present means and standard deviations of originally measured hormone level values. These statistical examinations were performed by two-sided tests using the significance level $p = 0.05$. Statistical analyses were performed using the software system IBM SPSS 23.

RESULTS

AAP Duration

The observed mean duration of the AAP recordings was 17.5 min ($n = 35$; time range 9–34 min; $SD = 5.4$ min). No significant Spearman's correlation was found between the AAP duration on the one side and the pre and post values of the hormonal parameters oxytocin and cortisol on the other side ($n = 35$; oxytocin pre $r_s = 0.201$, $p = 0.248$; post $r_s = 0.278$, $p = 0.106$: cortisol pre $r_s = 0.185$, $p = 0.287$; post $r_s = 0.013$, $p = 0.941$). Furthermore, we found no significant differences in the duration of the AAP between the four different attachment representation groups (Kruskal-Wallis test, $\chi^2_{(3)} = 1.213$, Monte Carlo with 10^8 simulations: $p = 0.764$).

Attachment Representations

The four attachment representations in the study sample of $n = 44$ mothers were distributed as follows: F (secure) 9 (21%), Ds (dismissing) 16 (36%), E (preoccupied) 8 (18%), U (unresolved/disorganized) 11 (25%).

Oxytocin Plasma and Cortisol Serum Levels

On average, oxytocin levels increased from 0.83 pg/ml (*SD* 0.57, *SEM* 0.08) to 0.98 pg/ml (*SD* 0.75, *SEM* 0.11) from pre to post AAP. The pre and post mean values of oxytocin and standard errors of mean are shown in **Figure 2**. The average change of measured oxytocin levels was +0.15 pg/ml (*SD* 0.46, *SEM* 0.07); see **Figure 2** and the last row in **Table 2**. This increase was observed in the majority of mothers (73%); the increase:decrease relation 32:12 is significant by the exact sign test ($p = 0.004$, two-sided).

Cortisol levels decreased from 650.2 nmol/l (*SD* 213.8, *SEM* 32.2) to 568.7 nmol/l (*SD* 211.3, *SEM* 31.9). The average change in cortisol level was −81.5 nmol/l (*SD* 212.6, *SEM* 32.1); see **Figure 2** again and the last row in **Table 3**. A decrease of cortisol was observed by the majority of mothers (73%); the increase:decrease relation 12:32 is significant by the exact sign test ($p = 0.004$, two-sided).

A significant increase in oxytocin levels and a significant decrease in cortisol levels were found. However, the changes were not significantly associated, see **Figure 3**. The concurrent oxytocin increase and cortisol decrease - shown on the logarithm scales here - were observed by the majority of 23 participants (52%), the frequencies of all four combinations of oxytocin/cortisol changes are shown. The statistics and measures based on frequencies in this fourfold 2 × 2 table (23, 9, 9, 3) did not find any association between the increase/decrease of oxytocin and cortisol (Pearson $\chi^2_{(1)} = 1.213$; exact two-sided Fisher's test $p = 0.763$, Cramer's $V = 0.031$).

Oxytocin and Cortisol Levels in the Four Attachment Groups

The values of oxytocin and cortisol levels between the four AAP groups were compared by the non-parametric Kruskal-Wallis

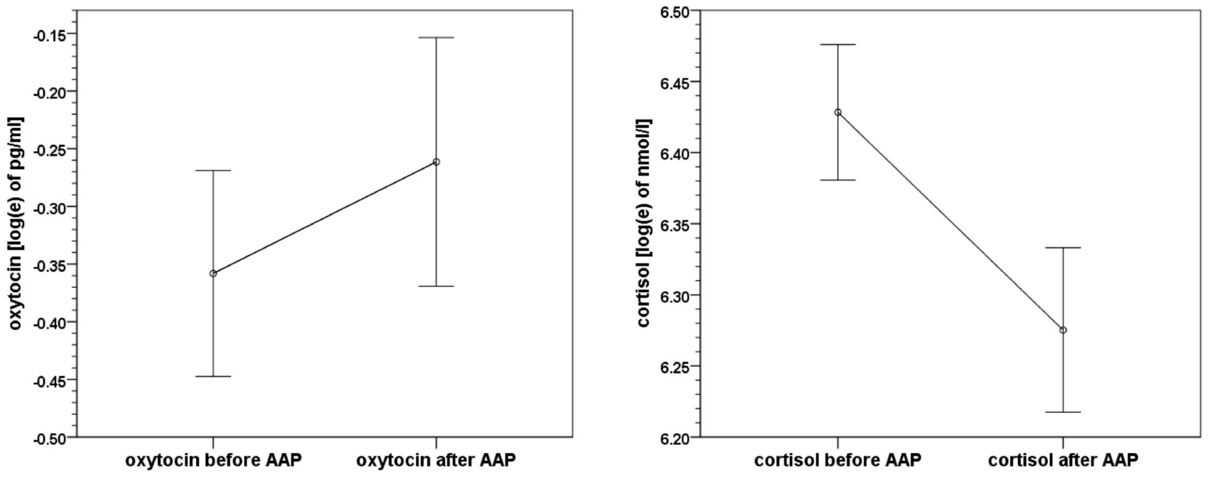

FIGURE 2 | Means and standard errors of mean of oxytocin and cortisol levels before and after the Attachment Projective Picture System (AAP) administration.

TABLE 2 | Oxytocin levels before and after the Adult Attachment Projective Picture System (AAP) in the sample and four attachment groups.

AAP	Sample size n	Oxytocin before m_1 s_1	Oxytocin after m_2 s_2	Oxytocin change m_c s_c	Paired effect size d_z	Exact sign test increase:decrease	p
F-secure	9	0.60	0.70	+0.10	+0.17	3:6	0.508
		0.27	*0.55*	*0.63*			
Ds-dismissing	16	1.05	1.16	+0.11	+0.47	13:3	0.021
		0.81	*0.97*	*0.24*			
E-preoccupied	8	0.57	0.70	+0.13	+0.40	7:1	0.070
		0.27	*0.37*	*0.32*			
U-disorganized	11	0.89	1.16	+0.26	+0.41	9:2	0.065
		0.34	*0.69*	*0.64*			
Whole sample	44	0.83	0.98	+0.15	+0.33	32:12	0.004
		0.57	*0.76*	*0.46*			

Oxytocin, plasma levels in pg/ml; m, s: means and standard deviations of pre, post and pre-post change values; $d_z = m_c/s_c$, paired effect size; p, two-sided exact sign test, reached significance level.

test, using the Monte Carlo approach with 10^7 simulations. No significant differences between attachment groups were found for the oxytocin pre values ($p = 0.055$), oxytocin post values ($p = 0.192$), cortisol pre values ($p = 0.537$) and cortisol post values ($p = 0.908$).

Contrary to our expectation, the increase in oxytocin within the secure group was observed only in 33% cases; in all three insecure groups its proportion was over 80% (see **Table 2**). Comparing these proportions mutually between groups, a general significant difference between the four groups was found (exact Fisher test for 4 × 2 table: $p = 0.046$). The mentioned increase proportion in the secure group was also significantly lower than the proportion in joint insecure groups (Fisher test for 2 × 2 table: $p = 0.007$ two-sided).

According to our expectation, the decrease of the cortisol level was prevailing by securely attachment mothers (100%, see **Table 3**). Comparing these proportions mutually between groups, no general significant difference between the four groups was found (exact Fisher test for 4 × 2 table: $p = 0.178$). As an exploratory result not corrected for the simultaneous inference, the significantly higher decrease proportion was found in the secure group (Fisher test for 2 × 2 table: $p = 0.047$ two-sided).

DISCUSSION

Oxytocin Increase, Attachment Stress and Attachment Representations

Increased oxytocin levels were observed after the AAP compared to baseline. This suggests, that the AAP is not only a valid instrument for assessing attachment representations, but may also activate a special pattern of physiological reactions in mothers, like increased oxytocin plasma levels after the AAP. Following studies of different patterns of physiological responsiveness associated with attachment groups (Dozier and Kobak, 1992), we expected different attachment representation to differ with respect to oxytocin. This expectation was not confirmed in this study: the increase in oxytocin was independent of the mother's attachment representation, but subsequent analyses showed that the effects were mainly driven by the

TABLE 3 | Cortisol levels before and after the AAP in the sample and four attachment groups.

AAP	Sample size n	Cortisol before m_1 s_1	Cortisol after m_2 s_2	Cortisol change effect size m_c s_c	Paired increase: d_z	Exact sign test decrease	p
F-secure	9	752	510	−242	−1.12	0:9	0.004
		255	*147*	*126*			
Ds-dismissing	16	624	558	−67	−0.40	6:10	0.454
		178	*147*	*167.5*			
E-preoccupied	8	681	597	−83	+0.49	2:6	0.289
		290	*272*	*171*			
U-disorganized	11	582	612	+29	+0.12	4:7	0.549
		148	*291*	*239.5*			
Whole sample	44	650	569	−82	−0.38	12:32	0.004
		214	*211*	*213*			

Cortisol, serum levels in nmol/l; m, s: means and standard deviations of pre, post and pre-post change values; $d_z = m_c/s_c$, paired effect size; p, two-sided exact sign test, reached significance level.

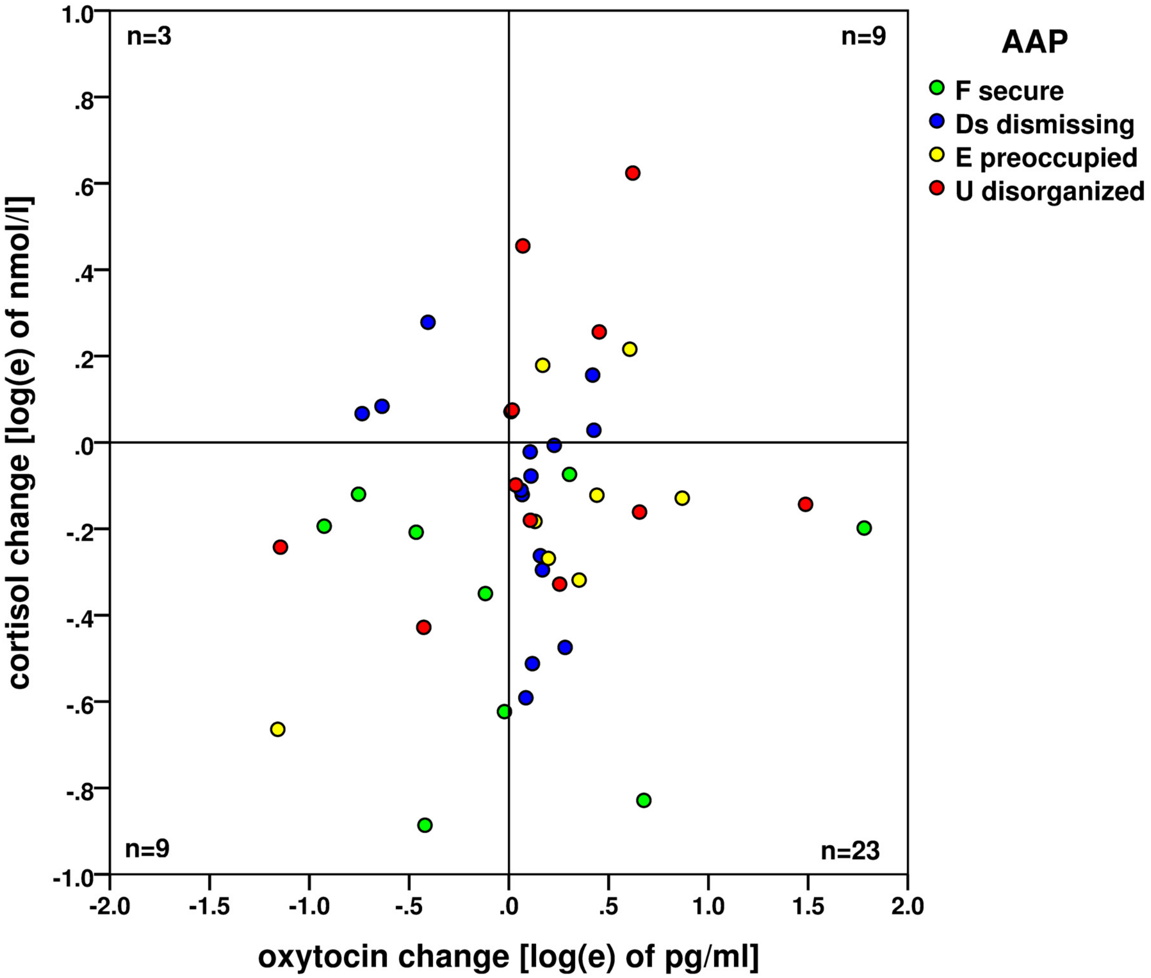

FIGURE 3 | Changes of oxytocin and cortisol levels (on the logarithm base *e* scale) before and after the AAP administration. No association (based on the case frequencies in four quadrants) between the oxytocin increase and cortisol decrease—both processes are likely independent. Attachment types are indicated by colored dots: green: (F) secure; blue (Ds) dismissing; yellow (E) preoccupied and red (U) disorganized.

insecure attachment groups which showed a significantly higher increase proportion of oxytocin compared to the secure group after the AAP. Thus, contrary to our initial expectation, secure mothers did not show higher oxytocin responses compared to insecure ones. Whereas the attachment-specific stimulus AAP may lead to an increase of circulating oxytocin in mothers, studies using specific social stress stimuli, like the TSST, revealed no changes in oxytocin levels in participants (Altemus et al., 2001; Ditzen et al., 2007; Cyranowski et al., 2008). In contrast, one study found higher oxytocin secretion in healthy women and men following psychosocial stress (TSST). According to this result oxytocin may provide an important protective mediator against the health-compromising effects of a stress exposure (Engert et al., 2016). Nevertheless, these results argue for our hypothesis that oxytocin release is sensitive to an attachment-specific stimulus, whereas social stress stimuli like the TSST seemed to induce different changes in oxytocin levels, revealing recent inconsistent results. It should be kept in mind, that lactating mothers indeed have a more sensitive oxytocin-system than other study participants. The direct comparison of oxytocin levels in our study and TSST studies with healthy participants should be discussed with caution. However, oxytocin itself is known to buffer stressful outcomes like the HPA axis activity (Gimpl and Fahrenholz, 2001), activated by psychosocial stress. We did not find an increase of cortisol responses using our attachment stimulus, suggesting that the AAP was more feasible for activating the oxytocin system in this pilot study. The increase in oxytocin was observed in all four attachment groups, contrary to the hypothesis of a higher oxytocin level in secure mothers compared to insecure ones. A study of Pierrehumbert et al. (2012) investigated oxytocin levels before and after the TSST stressor in association to attachment representations. They showed a broad range of the oxytocin level changes depending on the attachment classification: securely attached participants showed higher oxytocin levels after the stressor compared to the insecurely attached groups (Pierrehumbert et al., 2012).

Cortisol Decrease, Attachment Stress and Attachment Representations

This study found a decrease of cortisol levels after AAP administration compared to baseline. Moreover, we observed a decrease of cortisol levels after the attachment task especially in the participants with a secure attachment representation. Accordingly, the mothers classified as insecure did not show a significant cortisol decrease. These preliminary results indicate a stronger cortisol decrease in mothers with a secure attachment representation and correspond with the study of Pierrehumbert et al. (2012) who also demonstrated moderate stress reactivity in subjects with a secure attachment classification. Individuals with a secure classification revealed a low subjective stress sense and a moderate stress reactivity (Pierrehumbert et al., 2012). This study showed that attachment representations might affect stress responses independent of the used method (attachment stress or social stress). Despite the small sample size of the attachment groups, which does not allow for final conclusions, one possible explanation from an attachment perspective might be plausible: the secure group shows a flexible integration of attachment related themes in contrast to the insecure group, which was potentially reflected on a physiological level. Indeed, in individuals with secure attachment representations a high level of agency and connectedness was observed in the narratives (George and West, 2012). Thus, these individuals might have been more confident in the AAP task, while insecure individuals might have felt more stressed through the attachment task. As mentioned before we have to take into account that we have investigated lactating mothers in our study. It is already known, that the process of lactation after the birth of a child may influence the maternal oxytocin hormone system (Gimpl and Fahrenholz, 2001). Furthermore, oxytocin and cortisol can influence each other's releasing processes, especially in stressful or angst-inducing situations (Altemus et al., 2001; Tops et al., 2007). However, we found no significant association between hormonal changes of oxytocin and cortisol in our study setting. Consequently, more research is needed to get more detailed information about the HPA axis reaction in lactating mothers during an attachment stimulus. One possible approach should be the investigation of the stress system in non-lactating mothers during an attachment stimulus, evaluating the possible effect of lactation on HPA-axis response.

Study Limitations

The oxytocin increase after the AAP was observed in mothers 3 months postpartum. The question arises whether a similar effect would occur also at earlier or later time-points during mother-child relationship development. Clarifying these questions could generate new information about the development of mother-child attachment. In addition, due to small sample sizes of attachment groups and thus limited power, oxytocin-related differences caused by the different attachment representations might have not been detectable. This study investigated a particular sample of individuals, namely lactating mothers with newborns. It is known there are changes in maternal oxytocin responses during lactation (Salonia et al., 2005). Therefore, we excluded all breastfeeding mothers from our analyses. Furthermore, it remained unclear whether the oxytocin response may also be due to the mother-child-contact during the AAP, as mothers were allowed to be in visual or physical contact with their child during the experiments. Therefore, we cannot rule out the possibility that the mother-infant relationship might have triggered attachment-related feelings in all mothers independent of their individual attachment status. More research is needed to clarify this issue.

Blood samples were collected twice using venipuncture instead of using a venous catheter in order to avoid discomfort of the mothers due to the catheter when taking care of their babies. This approach was favored to maintain mother's flexibility in contact with their babies during the experimental setup. Although venipuncture induces a pain stimulus and therefore may result in acute effects on circulating stress hormones, recent studies indicate that blood sampling for most laboratory tests using either direct venous puncture or peripheral venous catheter reveal comparable results (Ortells-Abuye et al., 2014). For cortisol, resting time prior to the first blood sampling may take a minimum of 30 min, which should be ameliorated in further studies. Therefore, cortisol findings in this study should interpret with caution. Additionally, controlling for duration of the AAP revealed no significant effects on time-dependent hormone levels. Our aim was to perform the pre- and postmeasurements timely as exact as possible before and after the AAP interview. Because the duration of this interview is not constant by its nature the time interval between two measurements could not be constant as well. A main limitation of the study was the lack of placebo conditions where mothers were in contact with their child without the influence of the AAP. Due to our study design this additional condition was not possible to include.

The AAP is a valid measure to assess attachment representations and its feasibility as an activating stimulus in neurobiological studies was shown in several previous studies. In this study, we were not able to differentiate whether the maternal attachment or the maternal caregiving system was activated predominantly by the AAP. Since we have examined lactating mothers and the AAP presents several stimuli depicting parent-child interaction, we supposed that both systems might have been active during the task. Further, there is only limited work that distinguished mothers' attachment and caregiving assessments (George and Solomon, 1996, 2008). For mothers (and fathers as well), there is sometimes visible overlap between the AAP stories with their caregiving experiences. This is to be expected because the two systems mutually inform each other (George and Solomon, 2008). Activating the attachment system using the AAP, however, has been demonstrated to produce an overall representation of how children seek support from caregivers, irrespective of the overlaps. The AAP might also activate the caregiving system for many mothers, and moreover data show that the AAP is an overarching attachment system measure in different contexts (see also Isaacs et al., 2010).

Finally, the oxytocin effect could be caused by other factors than the AAP procedure; for instance, oxytocin release might have been stimulated by mother-child proximity and contact. Also the cortisol effects may be affected by other factors, like a stressful atmosphere by a crying child during the AAP or the relatively short habituation time before the basal blood collection. To answer this question, a control group of non-lactating mothers and a non-attachment related narrative task as a control condition (placebo group), are needed in future studies.

Conclusion

This study is the first to use the AAP as an instrument with the potential to activate the attachment and/or the caregiving system in an experimental setting. Measuring stress- and attachment-related hormones our results confirmed that the AAP, indeed, led to an increase in oxytocin levels. Oxytocin increase was similar in all attachment representation groups, but was mainly driven by the insecure attachment groups who showed a significantly higher increase proportion of oxytocin compared to the secure group after the AAP. Analogously, cortisol decrease was observed over all attachment groups, and was particularly pronounced within the secure attachment representation. A more detailed investigation of the differential effects of secure and insecure attachment was limited by the small sample sizes of the attachment subgroups. When interpreting these findings it should be kept in mind that the study investigated breastfeeding mothers. Nevertheless, the study indicates that the AAP might be able to induce an increase in oxytocin, although this has to be replicated in future studies with non-lactating mothers as well as males.

AUTHOR CONTRIBUTIONS

This study was a pilot study to a larger BMBF-funded project on "Stress resilience in the transgenerational transmission of childhood maltreatment". The pilot study was conceptualized by I-TK, AB, HG, CW and AK. The coding of attachment interviews were conducted by AB. The study setup and data collection were organized by KS, SK, AB, CW, CD-W, HG and AK. KS and A-LH conducted the AAP interviews. KS, A-LH, CD-W and SK controlled data entry and organized blood analyses. DP designed and performed the statistical data analyses; DP also contributed substantially to the psychological result interpretation. CW, I-TK, KS, A-LH and AK provided important intellectual contribution in commenting and revising the manuscript. SK, AB and DP wrote the manuscript and edited its final version. We would like to thank Traudl Hiller for substantial help in performing blood drawings and in the processing of blood samples.

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frontiers in Human Neuroscience

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Neural Response during the Activation of the Attachment System in Patients with Borderline Personality Disorder: An fMRI Study

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Individuals with borderline personality disorder (BPD) are characterized by emotional instability, impaired emotion regulation and unresolved attachment patterns associated with abusive childhood experiences. We investigated the neural response during the activation of the attachment system in BPD patients compared to healthy controls using functional magnetic resonance imaging (fMRI). Eleven female patients with BPD without posttraumatic stress disorder (PTSD) and 17 healthy female controls matched for age and education were telling stories in the scanner in response to the Adult Attachment Projective Picture System (AAP), an eight-picture set assessment of adult attachment. The picture set includes theoretically-derived attachment scenes, such as separation, death, threat and potential abuse. The picture presentation order is designed to gradually increase the activation of the attachment system. Each picture stimulus was presented for 2 min. Analyses examine group differences in attachment classifications and neural activation patterns over the course of the task. Unresolved attachment was associated with increasing amygdala activation over the course of the attachment task in patients as well as controls. Unresolved controls, but not patients, showed activation in the right dorsolateral prefrontal cortex (DLPFC) and the rostral cingulate zone (RCZ). We interpret this as a neural signature of BPD patients' inability to exert top-down control under conditions of attachment distress. These findings point to possible neural mechanisms for underlying affective dysregulation in BPD in the context of attachment trauma and fear.

Keywords: borderline personality disorder, emotional regulation, attachment system, amygdala, functional MRI

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Abbreviations: AAI, Adult Attachment Interview; ACC, anterior cingulate cortex; AAP, Adult Attachment Projective Picture System; BA, Brodmann area; BPD, Borderline personality disorder; CTR, controls; DLPFC, dorsolateral prefrontal cortex; IPDE, International Personality Disorder Examination; mPFC, medial prefrontal cortex; OFC, orbitofrontal cortex; PAT, patients; PFC, prefrontal cortex; PTSD, posttraumatic stress disorder; RCZ, rostral cingulate zone; SCID-I, Structured Clinical Interview for DSM-IV.

INTRODUCTION

Disturbances in the processing and regulation of emotions are core symptoms of borderline personality disorder (BPD; Leichsenring et al., 2011; Herpertz and Bertsch, 2015; Schulze et al., 2016). Emotional dysregulation is thought to result from increased impulsivity combined with the inability to modulate emotional responses (Linehan et al., 1994; Skodol et al., 2002; Lieb et al., 2004; Putnam and Silk, 2005; Conklin et al., 2006; Viviani et al., 2011; Mitchell et al., 2014; Scherpiet et al., 2014; Schmahl et al., 2014; Herpertz and Bertsch, 2015; van Zutphen et al., 2015).

Attachment theory provides a powerful framework for understanding links between close relationships, mental representations of attachment, and psychopathology (Westen et al., 2006; Bakermans-Kranenburg and van IJzendoorn, 2009). Early experiences of maltreatment, such as sexual and physical abuse and emotional neglect, are implicated in the etiology of BPD (Bandelow et al., 2005; Gunderson et al., 2006; Zanarini et al., 2006; van Dijke et al., 2011; Keinänen et al., 2012; Frías et al., 2016). Adverse attachment experiences, especially relationships trauma, are considered to be risk factors for poor emotion-regulation, functional impairment of mentalization, separation anxiety, and fear (Bowlby, 1973; Milrod et al., 2014; Mosquera et al., 2014; Brüne et al., 2016). The concept of adult attachment concerns an individual's current representational state with respect to early attachment relationships and their associated modes of defense and affect regulation. A large number of studies in adult attachment research have used the Adult Attachment Interview (AAI) or the Adult Attachment Projective Picture System (AAP) as narrative-based assessments of mental representations of attachment (George et al., 1984/1985/1996; Main and Goldwyn, 1995; George et al., 1999; George and West, 2001, 2012). Attachment classifications are derived from the analysis of narratives with three organized/resolved patterns (also termed attachment status), namely secure, dismissing, preoccupied and unresolved with respect to trauma or loss. Important for our study is the categorization into "resolved" (i.e., either secure, insecure dismissing, insecure-preoccupied) vs. "unresolved" attachment patterns in adults. The narratives of individuals who are unresolved demonstrate their inability to contain or integrate frightening thematic elements. These individuals, overwhelmed by trauma or loss, become dysregulated when attachment is activated during assessment. Dysregulation can be momentary or prolonged, but in either case the individual is unable to use defensive processes to remain organized and recover from conscious thoughts and feelings of frightening distress.

Insecure attachment patterns demonstrate risk for the maladaptive personality traits underlying BPD (Scott et al., 2009). BPD has been associated with increased occurrence of insecure and especially unresolved attachment representations (Agrawal et al., 2004; Bakermans-Kranenburg and van IJzendoorn, 2009; Buchheim and George, 2011). Unresolved attachment has been linked to psychological disorders, impaired cognitive functioning and trauma-related psychopathology (Fearon and Mansell, 2001; Nakash-Eisikovits et al., 2002; Lyons-Ruth and Jacobvitz, 2008; Joubert et al., 2012).

Emotional vulnerability in BPD patients may result from a marked sensitivity to emotional stimuli, an impairment of emotion regulation, or both (Gunderson and Lyons-Ruth, 2008). An attentional bias toward negative information in patients with BPD can be seen in neuroimaging data showing increased and prolonged amygdala responses (Herpertz et al., 2001; Donegan et al., 2003; Hazlett et al., 2012; Kamphausen et al., 2013; Schulze et al., 2016), and enhanced activity in the anterior insula (Schulze et al., 2011; Ruocco et al., 2013). Furthermore, study results indicate reductions in amygdala and hippocampal volume in BPD patients (Driessen et al., 2000; Schmahl et al., 2003, 2009; van Elst et al., 2003; Irle et al., 2005; O'Neill and Frodl, 2012; Rossi et al., 2012; O'Neill et al., 2013; Ruocco et al., 2013).

As emotion regulation is dependent on regions exerting cognitive control, like the dorsolateral prefrontal cortex (DLPFC) and medial prefrontal/anterior cingulate cortex (mPFC/ACC; for a review see Ochsner and Gross, 2005), a deficit in emotion regulation should be mediated by reduced activation in these regions in tasks affording emotion control. Studies using Positron emission tomography revealed hypometabolism in PFC of BPD patients compared with healthy controls (De La Fuente et al., 1997; Soloff et al., 2000) and enhanced activation of DLPFC when BPD patients were confronted with individual scripts that evoke personal memories of abandonment and abuse (Schmahl et al., 2003, 2004; Lang et al., 2012). In another study using magnetic resonance spectroscopy (van Elst et al., 2001), BPD patients showed a decreased level of N-acetyl aspartate, which suggests impaired neural functioning in the DLPFC. BPD patients showed metabolic alterations in the amygdala using proton magnetic resonance spectroscopy (Hoerst et al., 2010).

Moreover studies investigated brain activation during processing of autobiographical memory in BPD. One study examining unresolved as compared to resolved life events found, among other regions, increasing activation of amygdala and anterior cingulate cortex (Beblo et al., 2006). A follow up analysis from that study 1 year later reported substantial decrease of temporo-frontal activation during the recall of unresolved negative life, suggesting that these activations were not stable over time (Driessen et al., 2009). Mensebach et al. (2009), comparing episodic and semantic memory retrieval, demonstrated that BPD patients might need to engage larger brain areas to reach a level of performance in episodic and semantic retrieval tasks than comparable healthy controls. A recent study using a stimulus-driven Episodic Memory task showed that negative affective interference with cognitive processing differed in BPD patients compared to healthy controls (Soloff et al., 2015). This pattern was associated with functional abnormalities in brain networks reported to have structural or metabolic abnormalities, like the increased activation of the amygdala (Soloff et al., 2015).

In sum, emotion regulation and their neural correlates are impaired in BPD patients; for example, amygdala responses are prolonged and enhanced in particular during the presentation of emotional stimuli (for a review see Buchheim et al., 2013). Furthermore, traumatic experiences are considered as crucial in these processes. These impairments may be part of the neural mechanisms underlying emotional dysregulation in BPD patients (Kamphausen et al., 2013). Functional anomalies might also have an important impact on cognitive processes. A recent study of Enzi et al. (2013) demonstrated that impaired emotion processing seems to affect the reward system in patients with BPD. Moreover we can conclude, that patients with BPD have been shown to exhibit impaired neuronal activity in areas of the medial and lateral PFC that control and modulate emotional activation, thereby covering topdown processes. Functional neuroimaging studies examined prefrontal hypometabolism during regulatory control processes (O'Neill and Frodl, 2012), and a recent metaanalysis of functional magnetic resonance imaging (fMRI) studies across different stimulation procedures (Ruocco et al., 2013). These studies reported enhanced neuronal activity in the insula but reduced activity in the subgenual ACC and DLPFC in patients with BPD as compared with healthy subjects (O'Neill and Frodl, 2012; Ruocco et al., 2013).

The functional neuroimaging studies summarized above measured brain activation patterns in response to visual stimuli (pictures, faces) or passively presented scripts. Several studies have investigated the neural correlates of "social" attachment (i.e., defined loosely as individuals in intimate relationships) in healthy populations. The main paradigm in these studies is the presentation of pictures of the beloved sexual partner or their own infant by contrasting familiar vs. non-familiar stimuli (Bartels and Zeki, 2000, 2004; Leibenluft et al., 2004; Nitschke et al., 2004; Gillath et al., 2005; Coan et al., 2006; Lenzi et al., 2009; Riem et al., 2012; Wittfoth-Schardt et al., 2012). These studies have used various approaches to identify the neural correlates of distinctive attachment-related systems (caregiving or sexual system). Taking into account the differences in methods and aims, these studies have reported a common neural activity for the romantic and maternal attachment in regions associated with reward and motivation and affective processing. However, much less is known about the neural correlates of attachment representations, for example, when individuals are instructed to tell stories to attachment related pictures while being scanned in an fMRI environment.

Buchheim et al. (2006a,b) developed an fMRI paradigm to investigate the neural correlates of attachment representation while subjects tell stories to attachment pictures using the AAP stimuli (George et al., 1999; George and West, 2012). This validated narrative-based assessment is a set of stimuli and system of analysis that is theoretically derived using attachment theory, and not a traditional open-ended free-response measurement (i.e., subjective interpretation of emotional stimuli). The results of this pilot study showed unresolved attachment to be associated with increasing activation of the right amygdala, the left hippocampus and the right PFC over the course of the attachment task (i.e., from the first to the last attachment pictures).

The present study investigated neural correlates of attachment narratives in borderline patients using the same paradigm. In this article, we focus on differences between "unresolved" and "resolved" subjects. Our design permitted analysis related to other linguistic features of the AAP, which were reported elsewhere (Buchheim et al., 2008). Based on research linking BPD to unresolved attachment, we expected that amygdala activation in during the course of administering the attachment task (AAP) would be stronger in the patient group than the control group. We also expected that neural signs of emotion regulation in the cognitive control system (DLPFC and/or anterior cingulate) would decrease or be absent in the patient group.

MATERIALS AND METHODS

Participants

Thirteen female BPD inpatients were recruited from a psychiatric hospital (Psychosomatic and Psychiatric Hospital, Bad Wiessee, Germany) and compared to 21 healthy female volunteers recruited for the study by an advertisement in a local newspaper and leaflets distributed in the Hospital of the University of Ulm. The sample of the 17 healthy controls in this study included the 11 subjects of our pilot study (Buchheim et al., 2006b). Subjects were matched for age and education. Patients were treated on an average for 114 days (SD: 45.3, range 26–166 days) in the psychiatric hospital and had on an average 1.77 days of inpatient stays (range 1–4, median 1). They were assessed at the beginning of their treatment. All control subjects were physically healthy, without a history of psychiatric disorder and did not use any medication. Clinical diagnoses were assessed by a trained psychiatrist[1] using the Structured Clinical Interview for DSM-IV (SCID-I and SCID-II) and the International Personality Disorder Examination (IPDE). Exclusion criteria were left handedness, metal implants, language problems, and serious medical or neurological illness, including comorbid psychotic disorders and bipolar disorder. None of our patients met diagnostic criteria for posttraumatic stress disorder (PTSD) or dissociative disorder. Six subjects had to be excluded from our main analysis. Four controls were excluded for movement in the fMRI apparatus (>2 mm, see below). The only two patients who were classified as resolved were excluded from analysis because two subjects were not enough to allow any substantial group inferences. The final sample consisted of 11 BPD patients and 17 controls. Exclusion of the six subjects did not affect group homogeneity with respect to age (BPD, 27.8 years ± 6.7; controls, 28.4 years ± 7.5) and education (BPD, 10.8 years ± 1.4; controls, 10.9 years ± 1.6). Comorbidity

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[1] PM has been trained and certified for reliable diagnosis in the SCID-rating by Prof. Wittchen, Munich, Germany and by A. Loranger MD, New York, NY, USA regarding IPDE. In seven patients an experienced Master's level psychologist conducted a second SCID interview. Agreement between the raters was $\kappa = 1.0$ for both BPD and lifetime depressive episode.

in the final group included depression ($n = 6$), anxiety or panic disorder ($n = 2$), and somatoform disorder ($n = 3$). Five of the eleven patients were treated with psychotropic medication, including serotonin-reuptake inhibitors ($n = 2$), lithium ($n = 1$) and low doses of neuroleptics (perazin, promethazine and chlorprothixene, $n = 3$). After complete description of the study, participants provided written informed consent. The study was conducted in conformance with the Declaration of Helsinki. The protocol was approved by the local institutional ethics committee of the University of Ulm. Clinical characteristics of the sample are shown in **Table 1**.

Procedure and Measures

Attachment Stimulus Presentation and Attachment Coding

Participants were administered with the fMRI-adapted version of the Adult AAP (Buchheim et al., 2006a), a validated representational adult attachment measure. The measure is comprised of a set of eight drawings, one neutral scene and seven attachment scenes. The picture set includes scenes that depict events associated with attachment activation, such as illness, separation, solitude, death, and threat (Bowlby, 1973). The picture presentation order is designed to gradually increase the activation of the attachment distress (George et al., 1999; George and West, 2003), a methodological feature that has been validated using fMRI analysis (Buchheim et al., 2006b). Pictures are administered in the following sequence: Child at Window—a child looks out a window; Departure—an adult man and woman stand facing each other with suitcases positioned nearby; Bench—a youth sits alone on a bench; Bed—a child and woman sit opposite each other on the child's bed; Ambulance—a woman and a child watch someone being put on an ambulance stretcher; Cemetery—a man stands by a gravesite head stone; and Child in Corner—a child stands askance in a corner (example picture stimuli are provided in **Figure 1**).

AAP responses are classified on the basis of verbatim transcribed narratives. The coding system defines unresolved attachment as failure to contain frightening or threatening narrative material demonstrated, for example, by story elements representing attachment dysregulation, such as death, attack, abuse, or devastation (George et al., 1999; George and West, 2003; Buchheim and George, 2011). Resolved attachment is designated when the story material either does not include these elements, or if included, the narrative demonstrates emotional integration or mental organization. This requires the story characters to demonstrate the capacity to think through solutions that describe drawing on internalized attachment resources (the "internalized secure base"), seeking out attachment figures, the capacity for positive and constructive action, or others coming to provide comfort, explanation, or assistance to quell frightening distress (**Table 2**). Resolved attachment status groups include secure, dismissing, and preoccupied. Secure attachment is characterized by story elements that demonstrate the capacity to think about events and feelings, and expectations for comfort from or mutual enjoyment in attachment relationships. Dismissing attachment is characterized by evidence of physical and psychological distance from attachment figures and distress in story themes, often deflecting needs for care and the desire for attachment figures' comfort to other activities (e.g., achievement, peer relationship). Preoccupied attachment is characterized by representational confusion; the representation of people or events associated with story themes are diffused by vacillation among different and sometimes opposing ideas.

The psychometric properties of the AAP were established in an independent validity study with 144 subjects from a healthy community sample of non-patient subjects. This study demonstrated strong psychometric validity, including meeting psychometric standards for inter-judge reliability, test-retest reliability (after 3 months), discriminant validity, and convergent construct validity with another validated developmental attachment narrative assessment, the AAI (George et al., 1984/1985/1996; George and West, 2003, 2012).

In the present study, two blind, reliable AAP judges independently coded the AAP narratives of the stories that participants told in the scanner. There was unresolved-resolved agreement in 27 out of 28 cases (96%). The resulting inter-rater agreement was $\kappa = 0.93$, corresponding to "almost perfect agreement" by Landis and Koch (1977). AAP validity for scanner-produced stories was established through convergent classifications with the AAI, which were administered 1 month after fMRI AAP acquisition and classified by a blind trained reliable AAI judge. As also reported in a review on AAP classifications in different clinical groups (Buchheim and George, 2011), the correspondence between the AAP and AAI resolved vs. unresolved categories in this sample was $\kappa = 0.70$, corresponding to "substantial agreement" by Landis and Koch (1977).

TABLE 1 | Two-group-comparison of clinical scales.

	C Control ($n = 16$)		B Borderline ($n = 13$)		C×B effect size	Exact U-test	
Clinical scales	***M***	***SD***	***M***	***SD***	***d***	***Z***	***p***
GSI (SCL-90)	**0.22**	0.22	**1.48**	0.51	3.34	4.432	0.000
Barrett impulsivity scale	**67.38**	9.99	**85.23**	10.36	1.75	3.715	0.000
Dissociative experience scale	**4.23**	3.91	**15.66**	16.31	1.02	3.390	0.001

d, Cohen's effect size; Z and p, Exact two-tailed Mann-Whitney U-test.

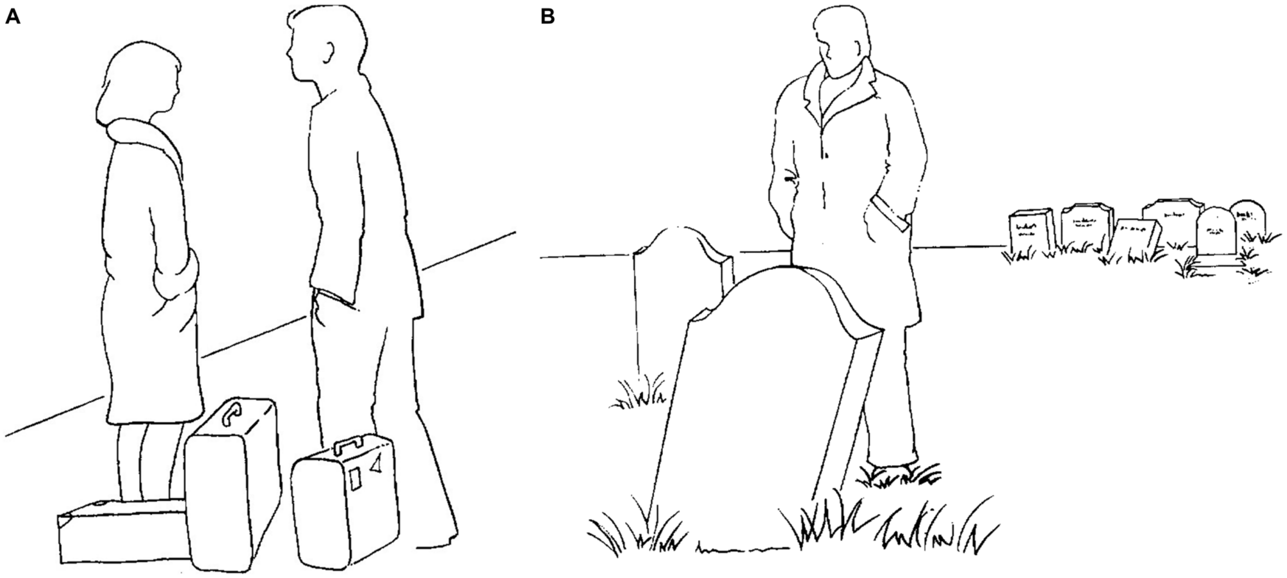

FIGURE 1 | (A) Picture "Departure" from the Adult Attachment Projective Picture System (AAP) © (George et al., 1999). **(B)** Picture "Cemetery" from the AAP © (George et al., 1999).

MRI Acquisition

Experimental procedure

Subjects were instructed in the AAP story telling task before they entered the scanner using two non-AAP "neutral" (i.e., not attachment related scenes) pictures. The pictures were same size and drawn in the same style as the stimuli in the AAP set. The goal was for subjects to understand the scope of the probes normally asked during in-person administration. The training procedure was repeated two more times, as needed to achieve this goal. The fMRI acquisition started with the original AAP picture presentation and instructions. During scanning, subjects were visually presented the standard AAP instruction at the introduction of the stimulus ("what led up to that scene, what are the characters thinking or feeling, and what might happen next?") for 10 s and a fixation cross for 10 s. Afterwards each AAP picture was presented (120 s) along the original order of the measure (described in the "Materials and Methods" Section). Subjects were asked to talk about the picture for at least 2

TABLE 2 | Transcript examples of a "resolved" and two "unresolved" stories to the AAP picture "Cemetery".

Resolved AAP story (Control)	Unresolved AAP story (Control)
"An elder man in the graveyard. The man is standing in front of his mother's tombstone. As he accidentally visited his hometown he also visited the graveyard and lays down a bunch of flowers to his mother. He is thinking about the past, how things had been when she was still alive, what she had pointed out to him for his live. He is very centered upon the past remembering many things and at the same time he is gathering courage for the future since he knows that life is transient. He is keeping to this task for a while; then he returns to his apartment lost in thought. The next day he is leaving his hometown after having visited some of his old friends and some of mother's neighbors to talk to".	"A man is standing besides a grave. His wife has recently died. She died suddenly in a car accident. The man is totally in despair. Once a week he is visiting her grave. He finds it difficult to say goodbye. He often talks to her. He communicates with her about whether he is doing things the right way and how hard it is for him to raise his three children all by himself. And how helpless the children are to have lost their mother too early. It's my impression that he needs a lot of time to come to terms with the situation".
	Unresolved AAP story (Borderline patient)
	"On a graveyard a man is standing by a grave he had been searching for many years. It's the grave of his parent, who gave their son up for adoption. Their son wants to finally say farewell to his biological parents and he wants to know where his roots are to be found. He is staying on the graveyard for a while, then moves on to an inn and gets drunk until the next evening hoping that in this way he could bury his past just like his parents are buried there. He feels suicidal and like an orphan with no roots. He will never return. He wants to erase the bad past with an adoptive family".

Note: Words representing attachment dysregulation are underlined.

min. A fixation cross was shown for 15 s after the picture presentation until beginning a new cycle of instruction and the next picture presentation. The total procedure included nine pictures, the two neutral and seven standard AAP attachment scenes.

Data acquisition

1.5 Tesla Siemens Magnetom Symphony scanner (Siemens, Erlangen, Germany), image size: 64 × 64 voxels, FOV of 192 mm, slice thickness 4 mm with 1 mm gap, 25 slices covering the whole brain, TE/TR 40 ms/2500 ms, total acquisition time 25 min (=598 volumes, one session). Instructions and pictures were shown with fMRI compatible video-goggles (Resonance Technologies, Northridge, CA, USA). Speech was digitally recorded beginning at the onset of each picture using an fMRI compatible microphone and saved digitally on a computer using Cool Edit Pro (Syntrillium Software Cop. Phoenix, Arizona). Head movement was minimized by using padded earphones fixating the head within the gradient insert coil.

Statistical Analysis and Image Analysis

Group differences of the behavioral attachment data were analyzed using the exact Mann-Whitney U-test and the Kruskal-Wallis H-test and (SPSS version 14). We used non-parametric tests because of the non-normal distribution of the dependent variables. Preprocessing and statistical analysis of fMRI data were carried out with SPM2[2] and MATLAB 6.1 (MathWorks, Natick, MA, USA). The first four functional images were discarded to account for equilibration effects. Individual functional images were corrected for motion artifacts by realignment to the first volume of each session. As noted earlier, we excluded four control subjects because of excessive head movement (>2 mm within a trial cycle) in order to minimize movement effects. Further preprocessing included spatial normalization (3 × 3 × 3 mm) and smoothing (FWHM 8 mm). The regression model for each subject was as follows: each of the nine pictures had three or two individual regressors with variable duration depending on the time of speech: Regressor 1, modeling the time from onset of picture till onset of speech; regressor 2, modeling the picture during speaking; and regressor 3, modeling the time from offset of speech till end of picture presentation (if the subject did talk for less than 2 min). Three more regressors were built, each modeling all nine pictures: Regressor 4, (onset of every single word of all pictures as a stick function); regressor 5, (instructions); and regressor 6, (all fixation crosses = base line). Regressors of interest were convolved with a function that modeled a prototypical hemodynamic response before inclusion into the regression model. A high-pass filter was set at a cutoff frequency of 240 s. Finally, six more regressors modeled residual motion. For each trial the variance of each voxel was estimated according to the General Linear Model Individual regionally specific effects of interest were calculated for each participant using linear contrasts, resulting in a *t*-statistic for every voxel.

The effects of interests in this study were narrative story responses to the seven attachment pictures. We calculated the contrast picture presentation for each subject during speech (regressor 2) + picture presentation before the subjects start to speak (regressor 1) vs. baseline (fixation cross), thereby including potential mental processes before the actual speaking phase starts. For each subject, contrasts for single pictures were calculated, that is, seven contrasts for the attachment pictures ordered 1–7.

A within subject repeated measures ANOVA with three groups (resolved healthy controls, unresolved healthy controls and unresolved BPD patients) and seven repeated measurements was calculated as a second level analysis in order to test for effects of group and attachment classification. The AAP is designed to activate the attachment system increasingly from picture 1–7. The contrast of interest within each group was labeled "AAP effect" (−3 −2 −1 0 1 2 3), in accordance with the results of our pilot study (Buchheim et al., 2006a). *t*-statistics for each voxel were set at a threshold of $p < 0.001$ uncorrected for multiple comparisons and a cluster threshold of $p < 0.05$. We allowed a small volume correction for regions of interest with family wise error correction of $p < 0.05$ for those regions for which we had *a priori* hypotheses (amygdala, DLPFC, dorsal anterior cingulate) using a radial sphere of 10 mm (amygdala) and 20 mm (DLPFC, dACC), respectively. Talairach and Tournoux (1988) and Duvernoy (1999) atlases were used to identify all brain areas.

RESULTS

Behavioral Data

Borderline patients differed significantly from controls in all clinical scales (**Table 1**). As expected, the majority of the BPD patients were judged unresolved (11/13, 85%) in the AAP. Ten of seventeen (59%) controls were judged resolved and seven (41%) were judged as unresolved. In the fMRI data analysis, we included 11 patients (all coded as unresolved) and 17 controls ($n = 7$ unresolved, $n = 10$ organized: $n = 6$ secure, $n = 4$ dismissing, no preoccupied subjects). The overall distribution of attachment status differed significantly between borderline patients and controls (Fisher's exact test, $p = 0.026$).

Neuroimaging Data

Both control and patient groups showed activations in bilateral occipital cortex, bilateral superior medial frontal cortex, bilateral precentral and left inferior frontal gyrus for the main effect of picture presentation and bilateral medial and superior temporal gyrus, bilateral precentral gyrus, medial occipital gyrus and cerebellum for the main effect of speech production.

The goal of the neuroimaging analysis was to examine the AAP effect (increasing attachment activation during the task) in control and borderline subjects. The first analysis examined the AAP effect for the control group. Three regions showed increasing activation during the task: right amygdala, right DLPFC and mPFC in the rostral cingulate zone (RCZ; **Table 3**). The second analysis compared all controls with

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[2] http://www.fil.ion.ucl.ac.uk

TABLE 3 | fMRI results.

Region	BA		Z	x	y	z
all CTRLs						
Amygdala		R	4.51	24	−3	−27
Dorsolateral prefrontal cortex	46	R	3.54	48	24	15
Medial prefrontal cortex	9		4.09	−3	33	33
CTRLs resolved						
Superior temporal sulcus	39	L	4.24	−51	−60	21
CTRLs unresolved						
Amygdala		R	4.60	24	3	−27
Dorsolateral prefrontal cortex	46	R	3.71	48	27	15
Superior frontal gyrus	6	R	4.26	21	15	63
all unresolved (CTRLs and PATs)						
Amygdala		R	4.42	24	3	−24
Superior temporal sulcus	39	R	3.87	57	−51	12
Medial prefrontal cortex	8	R	3.85	3	21	45
PATs unresolved						
Amygdala		R	3.66	21	−6	−21
Anterior cingulate cortex	32	R	3.70	3	21	33
Cingulate gyrus	24	R	3.58	3	−18	42
Superior temporal sulcus	39	R	3.99	60	−57	15
all CTRLs > PATs unresolved						
Medial prefrontal cortex	8	L	2.92*,#	−6	36	39
CTRLs resolved > PATs unresolved						
Medial prefrontal cortex	8	L	2.83*	−6	36	39
all unresolved (CTRLs and PATs) > CTRLs resolved						
Amygdala		R	3.15*,#	27	3	−21
CTRLs unresolved > CTRLs resolved						
Amygdala		R	3.41*,#	27	3	−24
Dorsolateral prefrontal cortex	46	R	2.51*	48	27	15
PATs unresolved > CTRLs resolved						
Amygdala		R	2.88*,#	21	−6	−21
CTRLs unresolved > PATs unresolved						
Dorsolateral prefrontal cortex	46	R	3.11*,#	48	24	15
Medial prefrontal cortex	8	L	2.44*	−6	36	39

*All results: $p < 0.001$ uncorrected for multiple comparisons at voxel level, $p < 0.05$ at cluster level; * $p < 0.05$ corrected for small volume and # additionally corrected for number of volumes of interest ($n = 6$); BA, Brodmann area; x, y, z, respective coordinates of MNI template.*

all patients. We found a significantly stronger activation of the RCZ in the healthy controls and a significantly stronger activation of the right amygdala in the patient group. The third analysis examined these three regions in order to understand the contribution of attachment status and diagnosis to these activations. This analysis was performed by contrasting the three subgroups of our sample with each other (**Figure 2**).

The results of these analyses are shown in **Table 3**. An AAP effect was found in the amygdala in both unresolved groups (unresolved controls and unresolved BPD patients). An AAP effect in the RCZ was found only in the controls (resolved and unresolved). An AAP effect in the right DLPFC was found only in the unresolved controls.

In order to check that our results are not solely due to *medication* effects, we performed an additional analysis including only patients taking no psychotropic drugs ($n = 6$). Results were the same: all CTRLs > unmedicated PATs unresolved: mPFC (−9, 36, −39, $Z = 3.63$); CTRLs resolved > unmedicated PATs unresolved: mPFC (−9, 36, −39, $Z = 3.54$); unmedicated PATs unresolved > CTRLs resolved: Amygdala (21, −6, −21, $Z = 3.39$); CTRLs unresolved > unmedicated PATs unresolved: DLPFC (48, 24, 15, $z = 2.53$).

DISCUSSION

The present study examined the neural correlates of attachment dysregulation in a group of BPD patients compared to controls. This study used a paradigm that evaluated neural response patterns while subjects told attachment stories in response to AAP stimuli in the fMRI scanner. The fMRI analysis model followed the logic of the design of the attachment measure. According to this logic, the picture presentation sequence increasingly activates the attachment distress. We labeled this increasing activation over the course of task as "AAP effect." Due to the fact that almost all BDP patients were classified as unresolved, we investigated only three classification groups: resolved controls, unresolved controls and unresolved BDP patients. There were three main imaging finding. First, all unresolved subjects (borderline and controls), but not the resolved controls, showed the AAP effect reflected in an increasing amygdala activation. Second, all controls (resolved and unresolved), but not the unresolved patients, showed the

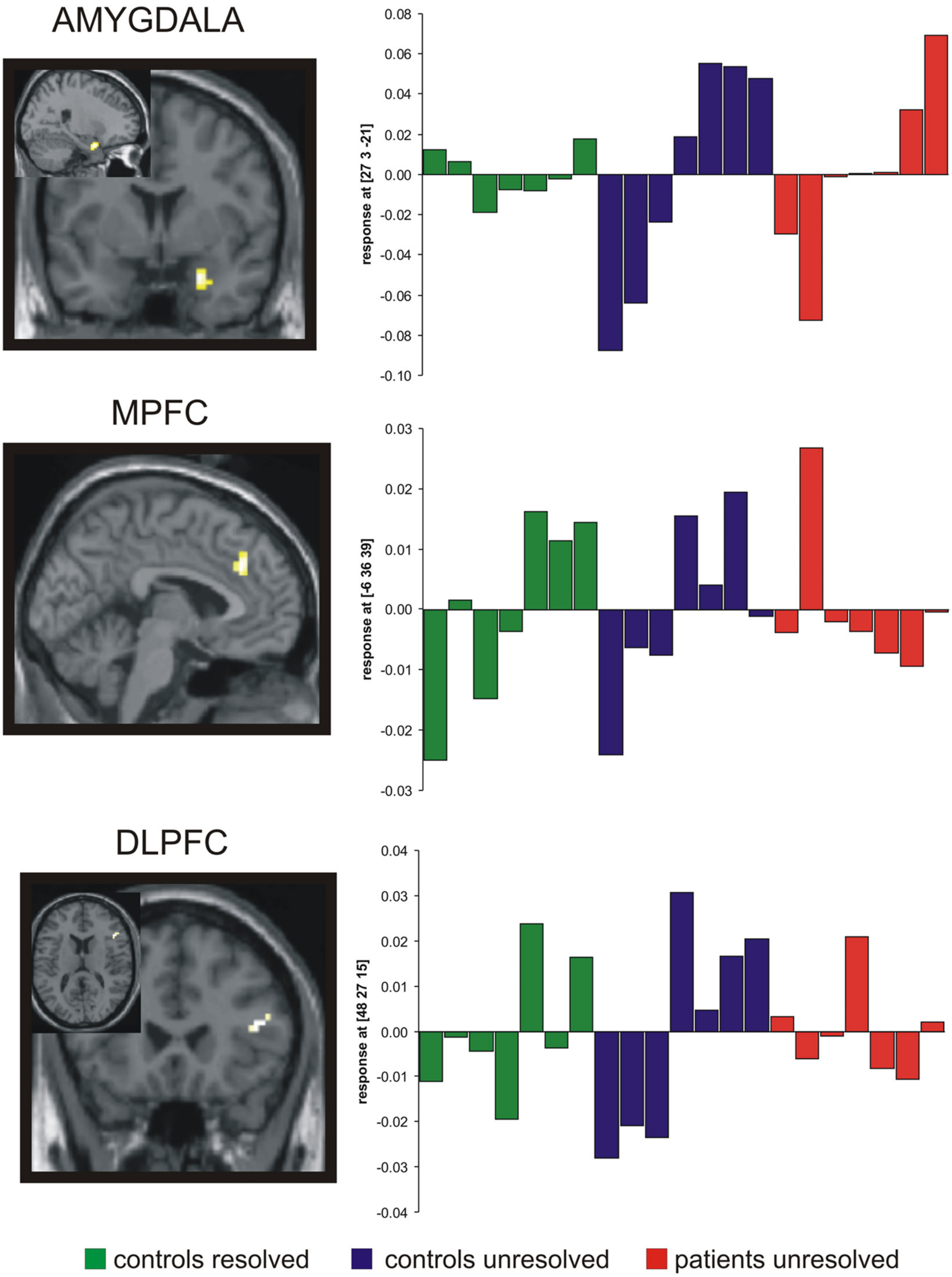

FIGURE 2 | Results of the functional magnetic resonance imaging (fMRI) analysis. A significant AAP effect (increasing activation along the task) was found in the amygdala for both, unresolved controls and patients, but not in the resolved controls. A significant AAP effect in the medial PFC was observed in both control groups, whereas the dorsolateral prefrontal cortex (DLPFC) exhibits an AAP effect only in the group of unresolved controls. All regions were significant in the respective interaction analyses (see **Table 3**). Images of statistic parametric mapping are projected onto sections of the standard T1 template of SPM 2. Plots of contrast estimates for each condition were shown on the right. Green bars, resolved controls; blue bars, unresolved controls; red bars, unresolved patients.

AAP effect in relation to increasing activation of the RCZ. Third, only the unresolved controls showed an AAP effect of increasing activation of the right DLPFC. This effect was not found in the resolved controls or the unresolved patients. We now discuss these results in the context of attachment research.

The predominant unresolved classification in the BPD patients was consistent with previous research (Fonagy et al., 2000; Agrawal et al., 2004; Bakermans-Kranenburg and van IJzendoorn, 2009; Buchheim and George, 2011). This was found using two independent attachment measures (AAI and AAP). How are these attachment findings related to the neural patterns found in the three groups (unresolved patients, unresolved and resolved controls)?

As shown in **Figure 2**, the AAP effect was present in the right amygdala in both unresolved groups. This finding strengthens the results of our pilot study with healthy subjects (Buchheim et al., 2006a). Amygdala activation has been found in other studies to be associated with a range of negative and positive emotional stimuli (Davis and Whalen, 2001). A recent study by White et al. (2014) demonstrated that the amygdala is responsive to animate and emotional stimuli. Moreover, the authors consider that the interaction between the various functions of the amygdala may need to be taken into account simultaneously to fully understand how they interact. Although amygdala activity has been suggested to be modulated by affective and non-affective factors, there is considerable controversy regarding its specific functional nature. Costafreda et al. (2008) examined the effects of experimental characteristics on the probability of detecting amygdala activity in a meta-analysis of 385 functional neuroimaging studies of emotional processing. The authors reported that all emotional stimuli were related to higher probability of amygdala activity than neutral stimuli. Comparable effects were detected for most negative and positive emotions, however there was a higher probability of activation for fear and disgust as compared to happiness (Costafreda et al., 2008). The stimuli used in the present study were not general emotional stimuli. The AAP picture stimuli were selected specifically because of their ability to activate attachment distress by introducing themes like, e.g., separation, loneliness, danger or loss. Therefore, we interpret this amygdala activation as a neural correlate of negative emotional arousal that is associated with dysregulated attachment fear that is evident in the unresolved verbatim narratives. In contrast, resolved controls do not show the AAP effect in the amygdala. Resolved attachment is defined by the ability to re-organize attachment related fearful and threatening themes emerging in their stories. This re-organization appears to have blocked the AAP effect in the amygdala. Attachment activation of resolved controls, therefore, is not dysregulated by the negative emotions associated with distress.

Increased amygdala activation in BPD patients has been found in a variety of passive stimulation paradigms and these findings are interpreted as heightened emotional sensitivity to aversive stimuli (Davis and Whalen, 2001; Herpertz et al., 2001; Donegan et al., 2003; Silbersweig et al., 2007; Hazlett et al., 2012; Kamphausen et al., 2013; Schulze et al., 2016). Our results are consistent with these findings. Moreover, they provide an empirical link to the frequently reported unresolved attachment found in BPD samples, as mentioned before (Agrawal et al., 2004; Bakermans-Kranenburg and van IJzendoorn, 2009; Buchheim and George, 2011). As the amygdala activation AAP effect was found in both our BPD and unresolved controls, the effect is likely to be related to adverse early experiences that are not necessarily specific to BPD diagnosis. In order to disentangle the contribution of attachment and diagnosis, it would be desirable to include a resolved BPD group. This was not possible in the current study because the small number of resolved BDP patients precluded such an analysis.

The RCZ showed the AAP effect in both control groups, resolved or unresolved. Studies in humans showed that the RCZ (the posterior MFC border zone between the medial areas BA8, BA6 and BA32' with some extension into BA24') is involved in monitoring for unfavorable outcomes, performance and conflict monitoring, and decision uncertainty (Carter et al., 1998; Botvinick et al., 1999; Ridderinkhof et al., 2004; Fan et al., 2008; Nee et al., 2011). A recent comprehensive review discussed the diverse functions of the RCZ and proposed that this diversity can be understood in terms of the allocation of control based on monitoring the expected value of control (Shenhav et al., 2013). Although a subgroup of the healthy participants showed the failure to reorganize their attachment distress in their narratives on a behavioral level (unresolved), they demonstrated the ability to control their distress on a neural level. As the attachment stories in our study include distressing and potentially threatening themes, one possible interpretation of this activation is that all control subjects monitored their stories for unfavorable outcomes, that is, how the story might continue (part of the instruction). This monitoring function seems to be impaired in the BPD patients of our sample. An alternative interpretation is that activation in this region simply reflects emotional involvement. However, this is unlikely given that the three groups showed a different pattern.

The AAP effect in the DLPFC was found only in the unresolved control group; it was not observed in the resolved controls or the unresolved patients. The right DLPFC has been described as being involved in cognitive control (Duncan and Owen, 2000), emotion regulation (Ochsner and Gross, 2005), and more generally in executive functions, regulatory mechanisms that help individuals cope with extraordinary affordances. Recent research findings suggested a regulatory hierarchy, whereby the DLPFC and areas of the anterior medio-PFC modulate the cingulate, which in turn modulates the amygdala and further subcortical areas (Meyer-Lindenberg et al., 2005; Buckholtz et al., 2007). Several neuroimaging studies described a dysfunction of the right DLPFC in BPD patients (De La Fuente et al., 1997; Soloff et al., 2000; Schmahl et al., 2003). One recent study reported that cortical thickness in the DLPFC of female BPD patients without PTSD correlated positively with emotion regulation scores, which was also positively associated with amygdala volume, as well as cortical thickness of the insula (Bruehl et al., 2013). These findings suggested possible compensatory mechanisms for the impaired emotion regulation. Resolved subjects in the present study demonstrated a low incidence of threatening situations in their narratives, suggesting that the cognitive control system was not increasingly engaged over the course of the task. Unresolved controls, however, had increasing affective involvement. We, therefore, interpret the accompanying right DLPFC activation as an effort in this group to cope with this increasing affective involvement.

BPD patients were showing the highest proportion of unresolved attachment patterns in this sample. The fMRI findings suggest that they were neither able to recruit the DLPFC (cognitive control) nor the RCZ (conflict monitoring) while being emotionally overwhelmed, as reflected in the enhanced amygdala activation. However this finding contrasts with some published neuroimaging studies of affective dysregulation in BPD, which used passive stimulation. Studies on functional correlates of response inhibition have demonstrated further evidence for functional impairments of prefrontal areas, particularly of the DLPFC, the rostral ACC, and the orbitofrontal cortex (OFC). Minzenberg et al. (2007) used for example an implicit affect regulation task (responses to threatening vs. neutral faces) and found specifically enhanced neural activation of the right amygdala in BPD along with attenuated activations of the rostral ACC. Although our interpretation of the different activation patterns shown in **Figure 2** cannot be directly proven, we suggest that we provided a novel and interesting approach to understanding emotional instability in BPD patients with respect to attachment on a neural basis. The participants in our task were actively talking about their subjective perception of attachment scenes reflecting their individual mental organization of these crucial topics in relation to their history of abuse, maltreatment and emotional neglect.

Limitations

There are several limitations to our study that need to be taken into account when interpreting our findings. First, the number of resolved BPD patients ($n = 2$) was too small to include in our analysis and moreover we were not able to recruit a larger sample of BPD patients willing to participate in such a demanding paradigm (talking in the fMRI scanner), which limits the generalization of our results. The attachment literature suggests, that unresolved attachment is the predominant classification group, therefore future research would require a substantially large sample in order to include resolved BPD subjects. Although this limits the interpretation of our data to a certain extent, we were able to meaningfully evaluate the results using the three-group designations afforded by the participant attachment distribution in the current study.

Second, we did not include a clinical control group. This leads to questions as to whether our results may also be present in patients with other psychiatric disorders and not specific to BPD.

Third, 5 out of 11 of the BPD subjects were under low dose medication. This could be a confounding factor in comparing patients and controls, although our control analyses of medication-free patients only speaks against this assumption.

Fourth, this study aimed to characterize differences between healthy participants and BPD patients using an attachment paradigm along the AAP system focusing on attachment related pictures only. Since this study has identified differences between controls and patients, it is rather difficult to interpret the data univocally in the absence of an adequate control stimulus set, which is the focus of a recent study with healthy controls (Labek et al., 2016). Moreover, it would have been appropriate to add an established emotion-inducing paradigm for comparing neural responses to attachment plus to emotional involvement and/or emotional regulation capacities. Strictly spoken without this contrasting paradigm we may not directly conclude that we have investigated emotional dysregulation in BPD patients compared to controls.

Fifth, all results were derived from the three group analyses. However, this might have inflated statistical results. Therefore, we also calculated separate analyses for those contrasts where only two groups were involved. All results remain significant, showing that increased degrees of freedom did not generally inflate our results. Only mPFC activation in the contrast comparing resolved controls and unresolved patients does not surpass additional small volume correction.

Finally, overt speech in the scanner always is accompanied with head movements. The head movement in this study was less than 2 mm, and we took steps to eliminate residual influences. These included dropping subjects, including movement parameters as a covariate of no interest, and modeling the onset of every spoken word.

Conclusions

Unresolved controls, but not patients, showed activation in the right DLPFC and the RCZ. We interpreted this as a neural signature of BPD patients' inability to exert top-down control under conditions of attachment distress. These findings point to possible neural mechanisms for underlying affective dysregulation in BPD in the context of attachment trauma and fear. We found that both increased emotional sensitivity, as well as impaired emotion regulation, may have contributed to affective dysregulation in unresolved BPD patients. Increased emotional sensitivity, as evidenced by an AAP effect in the right amygdala, might be explained in large part by their attachment pattern. An alteration of the cognitive control system (RCZ and right DLPFC) is found when unresolved attachment and diagnosis of BDP are present simultaneously. Modulation of BPD patients' responses in attachment situations during treatment and psychotherapy to patterns similar to those described in the control group might be an important indication of their increasing capacity to regulate attachment distress and to show sufficient cognitive control (Perez et al., 2016). Future studies may examine as to what extent psychotherapy has the potential to change brain activation from a more unresolved to a more resolved pattern.

AUTHOR CONTRIBUTIONS

The study was conceptualized by HW, AB, SE, CG, HK and MS. The study setup and data collection were organized and conducted by HW, AB, SE, MS, HK and PM. fMRI analyses was performed by HW and SE. Coding of attachment interviews were conducted by AB and CG. SE, HW and DP performed the statistical data analysis and contributed substantially to the result interpretation. HW, AB, SE, CG, and DP provided important intellectual contribution in commenting and revising the manuscript. AB, HW, SE, and CG wrote the manuscript and edited its final version.

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Lower Oxytocin Plasma Levels in Borderline Patients with Unresolved Attachment Representations

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Interpersonal problems and affective dysregulation are core characteristics of borderline personality disorder (BPD). BPD patients predominantly show unresolved attachment representations. The oxytocin (OT) system is associated with human social attachment and affiliative behavior, and OT dysregulation may be related to distinct attachment characteristics. Here, we investigated whether attachment representations are related to peripheral OT levels in BPD patients. Twenty-one female BPD patients and 20 age-, gender-, and education-matched healthy controls (HCs) were assessed with clinical scales and measures of interpersonal and attachment-related characteristics, including the Adult Attachment Projective Picture System (AAP). Plasma OT concentrations were measured prior to and during social exclusion in a virtual ball tossing game (Cyberball). The majority of BPD patients (63.2%) but no HCs showed unresolved (disorganized) attachment representations. In this subgroup of patients, baseline OT plasma levels were significantly lower than in BPD patients with organized attachment representations. This pilot study extends previous findings of altered OT regulation in BPD as a putative key mechanism underlying interpersonal dysregulation. Our results provide first evidence that altered OT plasma levels are related to disorganized attachment representations in BPD patients.

Keywords: oxytocin, attachment representation, borderline personality disorder, social exclusion, cyberball, social pain

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INTRODUCTION

Borderline personality disorder is characterized by a pervasive pattern of emotional instability, impulsivity, severe problems in social interactions, and disturbed self-image (Bohus et al., 2009; Leichsenring et al., 2011). Particularly dysfunctional interpersonal beliefs and behavior, such as interpersonal events like rejection or exclusion, have a high clinical relevance and result in

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Abbreviations: AAI, Adult Attachment Interview; AAP, Adult Attachment Projective Picture System; BDI-II, Beck Depression Inventory; BPD, Borderline personality disorder; BSL-23, Borderline-Symptom-List-23; CSF, cerebrospinal fluid; CTQ, Childhood Trauma Questionnaire; CV, interassay coefficient of variation; HAMD-24, Hamilton Depression Rating Scale; HC, healthy controls; NTQ, Needs-Threat-Questionnaire; OT, Oxytocin; RSQ, Rejection Sensitivity Questionnaire; SCID, Structural Clinical Interview for DSM-IV; SGA, second-generation antipsychotics; TSST, Trier Social Stress Test.

increasing aversive tension in BPD, which may lead to self-injurious behavior or dissociation (Herpertz, 1995; Stiglmayr et al., 2005; Gunderson and Lyons-Ruth, 2008). Interpersonal styles of BPD patients are characterized by a need for closeness and attention, combined with a fear of rejection and abandonment. Winter et al. (2015) found a negative evaluation bias for positive, self-referential information in BPD patients suggesting that they tend to refer information to themselves even if no explicit reference context is set. At the same time, BPD patients demonstrate significant impairments in making social judgments about others from their faces by judging them as less trustworthy and approachable than controls (Nicol et al., 2013). Moreover, Fertuck et al. (2009) reported an enhanced mental state discrimination based on the eye region of the face in BPD patients compared to HCs and considered this enhanced sensitivity as a potential basis for social impairment in BPD. Gunderson and Lyons-Ruth (2008) describe a genetically based hypersensitivity to interpersonal stressors in BPD patients: An interpersonal hypersensitivity phenotype may lead to characteristic interpersonal strategies and contradictory interpersonal features observed in adult BPD patients.

Stanley and Siever (2010) suggested that an altered regulation within the OT system might be an underlying mechanism for this interpersonal dysregulation in BPD, which might have developed because of or been enforced by adverse caretaking experiences in early childhood. Adverse early caretaking experiences, such as maltreatment, abuse, emotional neglect, separation, inconsistency, and invalidation, are thought to disrupt interpersonal attachment, leading to distinct attachment patterns (e.g., Lyons-Ruth and Jacobvitz, 2008). Current attachment representations of early experience can be assessed in adulthood by semi-structured interviews (Ravitz et al., 2010). These narrative assessments are typically used to divide individuals into groups with regard to representational security or insecurity, including individuals who are unresolved with regard to loss or physical or sexual abuse. More than 90% of adult BPD patients show insecure attachment classifications, and a high frequency of unresolved attachment representations predominates in some samples (Barone, 2003; Agrawal et al., 2004; Levy et al., 2006; Gunderson and Lyons-Ruth, 2008; Bakermans-Kranenburg and van IJzendoorn, 2009). Unresolved attachment, therefore, is of special importance in the development of BPD (Lyons-Ruth and Jacobvitz, 2008; Buchheim and George, 2011).

The neuropeptide OT has been hypothesized to play a crucial role in attachment, because it is involved in the regulation of human social behaviors such as mother-infant interaction, pair bonding, affiliative behavior, trust, and trustworthiness (Macdonald and Macdonald, 2010; Meyer-Lindenberg et al., 2011; Feldman, 2012). Intranasal administration of OT in healthy participants leads to enhanced theory of mind capacity, perception of attachment security, and relational trust and reduction of social stress (Kirsch et al., 2005; Kosfeld et al., 2005; Domes et al., 2007; Heinrichs and Domes, 2008; Buchheim et al., 2009; Zhong et al., 2012; Kumsta and Heinrichs, 2013). In BPD, OT dysregulation has been hypothesized to be one major neurobiological mechanism underlying interpersonal problems and hypersensitivity to social cues (Stanley and Siever, 2010; Meyer-Lindenberg et al., 2011). Intranasal OT was found to have stress-attenuating effects (reduced cortisol levels and reduced dysphoric mood) in 14 BPD patients during the TSST (Simeon et al., 2011). In neuroeconomic game paradigms, however, OT was found to exert different effects in BPD patients than in healthy participants, i.e., intranasal OT administration reduced trust and cooperation in 14 (four males) BPD patients and interpersonal trust in 13 (five males) BPD patients compared to HCs (Bartz et al., 2011; Ebert et al., 2013). These findings support the notion that sensitivity to social cues may be increased by OT, but the interpretation of these cues might be influenced by contextual (i.e., presence of a stranger versus friend) or individual (i.e., gender, attachment patterns, or the presence of psychiatric symptoms) factors (Olff et al., 2013). This might also be reflected in fewer prosocial behaviors in a study of non-verbal communicative signals in BDP during social interaction after OT administration (Brüne et al., 2015). However, another study showed that intranasal OT administration decreased the hypersensitivity to social threat in 40 female BPD patients, as measured by patterns of reflexive eye movements toward angry and fearful faces, and normalized amygdala activity (Bertsch et al., 2013). In addition, a recent study demonstrated that OT administration abolished the avoidant reaction to angry faces in 13 (five males) BPD (Brüne et al., 2013). Taken together, OT research is inconclusive and according to Brüne (2015) it seems oversimplified to render BPD an OT deficit syndrome (Stanley and Siever, 2010). Moreover it is still unclear whether OT should be used therapeutically as an add-on treatment in BPD patients (Eckstein and Hurlemann, 2013; Brüne, 2015). Inconsistent study results and effects of OT in BPD might be explained by inhomogenity and limitations of previous studies including mixed-sex and small size of samples as well as missing control for mestrual cycle in some cases.

Adverse attachment events during childhood, such as physical and sexual abuse by a significant caretaker, contribute to the development of BPD (Leichsenring et al., 2011), and maltreatment has been shown to be associated with altered OT regulation in children (Seltzer et al., 2014). The first study investigating OT plasma concentrations in 34 female BPD patients found lower plasma levels in patients than in HCs; levels were associated with childhood traumatization (Bertsch et al., 2012). A recent study by Jobst et al. (2014) showed lower OT plasma levels in 22 female BPD patients than in healthy individuals in response to a social exclusion situation, which constitutes a strong negative bonding stimulus in BPD (Jobst et al., 2014). These results converge with previous findings of an impaired social repair function in BPD when social cooperation is broken (King-Casas et al., 2008). The hypothesis of an altered regulation of endogenous OT in BPD is further supported by links to traumatic lifetime experiences: OT CSF levels of 22 women with childhood traumatization were negatively associated with trauma in a study categorizing participants into those with none-mild versus those with moderate-severe exposure to various forms of childhood abuse or neglect. The authors found inverse associations between CSF OT concentrations and both the number of exposure categories and the severity and duration of the abuse (Heim et al., 2009). Pierrehumbert et al.

(2010) found a positive correlation between OT release after a social stress situation (TSST) and childhood trauma in a mixed-sex sample. The study included participants with sexual abuse in childhood or adolescence as well as survivors of cancer in childhood or adolescence and a control group. Participants with a life-threatening illness during childhood showed higher OT levels than both abused and healthy participants (Pierrehumbert et al., 2010).

Several studies have focused on the link between affiliative behavior, attachment, and OT (Feldman, 2012; Stoesz et al., 2013). Studies on the role of OT for bonding difficulties report evidence of an effect of OT on human affiliation, because they observed that OT plasma levels across pregnancy and the postpartum period predicted mother–infant bonding (Feldman et al., 2007; Eapen et al., 2014). Moreover, intranasal OT administration increased the subjective experience of attachment security in 26 healthy male participants with insecure attachment representations (Buchheim et al., 2009), and adult attachment representations predicted OT and cortisol response to stress in both individuals with ($n = 46$) and those without ($n = 28$) childhood trauma (Pierrehumbert et al., 2012). Participants with preoccupied attachment showed low OT levels after the stress situation, whereas participants with unresolved attachment showed intermediate OT levels (Pierrehumbert et al., 2012). A recent pilot study ($n = 14$) used film clips of bonding or abandonment scenes to investigate OT plasma levels as a potential biomarker for alterations in the female attachment system. While lower OT plasma levels during abandonment scenes were positively correlated with posttraumatic stress symptoms, higher OT plasma levels during bonding scenes were negatively correlated with scores of dissociation and somatization (Munro et al., 2013).

To our knowledge, there is no study published investigating the association between attachment patterns in BPD patients and OT plasma concentrations. As the first analysis of our study was mainly focusing on differences in changes of peripheral OT levels after social exclusion between BPD patients and HCs (Jobst et al., 2014) irrespective of attachment representations, we re-analyzed our data here including the results of the AAP, a reliable and valid measure of adult attachment representations (George et al., 1999; George and West, 2011, 2012). We investigated attachment patterns in relation to both, general OT levels and their change during a social exclusion situation comparing BPD patients and HC. We hypothesized that alterations of OT levels observed in BPD patients would be especially pronounced in patients classified as unresolved, because this group is most frequently and seriously affected by early attachment trauma (Stalker and Davies, 1995; Bakermans-Kranenburg and van IJzendoorn, 2009) potentially disrupting a physiological development of OT regulation.

MATERIALS AND METHODS

Participants

Twenty-two female patients aged 19 to 46 years ($M = 30.0$ years, $SD = 7.95$) diagnosed with BPD and 21 HC aged 19 to 50 years ($M = 29.71$, $SD = 10.26$) matched for gender, age, and education participated in this study. BPD patients (8 inpatients and 14 outpatients) were recruited at the Department of Psychiatry and Psychotherapy at the Ludwig Maximilian University, Munich. BPD diagnoses and comorbid axis I and II diagnoses were assessed with the German Version of the SCID (SCID-I screening, SCID-II interview; First et al., 1995). Exclusion criteria were a comorbid diagnosis of substance dependence, schizophrenia, schizoaffective disorder, or bipolar disorder. All BPD patients met diagnostic criteria for BPD according to DSM-IV criteria. Comorbid diagnoses on SCID-I and -II were $M = 3.50$, $SD = 1.68$ (SCID-I: $M = 0.91$, $SD = 0.81$; range 0–3; SCID-II: $M = 2.59$, $SD = 1.44$, range 0–5). The following comorbid personality disorders were observed: Avoidant ($n = 11$), depressive ($n = 10$), anankastic ($n = 4$), negativistic ($n = 4$), paranoid ($n = 4$), dependent ($n = 2$), and histrionic ($n = 1$). Other comorbidities were major depressive disorder ($n = 5$) and eating disorder ($n = 3$). HC were recruited by advertisements in newspapers and posters on noticeboards. In HC, exclusion criteria were a current psychiatric disorder and a psychiatric and psychological treatment in the past 10 years, as confirmed with the SCID-I and -II screening instruments (First et al., 1995).

Most BPD patients received pharmacological treatment, as follows: Antidepressants ($n = 15$), SGA ($n = 14$), and mood stabilizers ($n = 8$). At the time of assessment, seven patients were taking sedative medication, and three patients were not taking any psychopharmacological drugs. All BPD patients were in current inpatient or outpatient psychotherapy.

The study was approved by the Institutional Review Board of the Faculty of Medicine at the University of Munich. All participants provided written informed consent. The study was part of a larger study investigating changes of neuropeptides during a social exclusion paradigm in patients with different psychiatric diagnoses. The results presented here are an extension of our previous study (Jobst et al., 2014).

Procedure and Measures

The experimental protocol included three separate sessions. At the first session, a screening interview was conducted to check for exclusion criteria, and participants were asked to provide informed consent. Moreover, participants completed German versions of a series of psychometric questionnaires: The BSL-23 (Bohus et al., 2009) to measure the severity of BPD symptoms; the BDI-II (Beck et al., 1996), and the 24-item HAMD-24 (Hamilton, 1960) to measure the severity of depression; the emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse subscales of the CTQ (Bernstein et al., 2003; Klinitzke et al., 2012), to assess traumatic experiences in childhood; and the RSQ (Downey and Feldman, 1996) to check for the grade of sensitivity to rejection.

At the second session, trained professionals at the Department of Psychiatry and Psychotherapy, Ludwig Maximilian University, Munich, administered the AAP (George et al., 1999; George and West, 2011, 2012). Administration lasted about 30 min. The AAP is a free-response measure comprising a set of eight line drawing stimuli, one showing a neutral scene and seven showing attachment scenes (e.g., illness, separation, solitude, death, and threat). Participants are asked to tell a story of what led up to a scene, what the characters are thinking or feeling, and what might happen next. Classifications are derived from evaluating response patterns on several response dimensions (agency of self, connectedness, synchrony, defensive processes) by using verbatim transcripts of audiotaped responses to the seven attachment-activating stimuli. The coding was performed by independent, trained raters at the Department of Psychology at the University of Innsbruck, Austria. Each participant was assigned to one of the four attachment classification groups "secure," "dismissing," "preoccupied," or "unresolved." The last three groups represent different types of attachment insecurity. Among these, unresolved representation is most frequently associated with early attachment trauma (Stalker and Davies, 1995) and is assigned when the response material demonstrates a failure to organize or contain representation indications of fear and dysregulation. On the basis of this differentiation, we defined two categorical pairs of representation types for comparison: (1) Secure vs. insecure, and (2) organized (resolved) vs. unresolved (disorganized). The psychometric properties of the AAP are excellent (George and West, 2012). Interrater reliability was found to be 90% ($k = 0.85$, $p < 0.001$, $n = 144$). Test–retest reliability was calculated on the basis of 69 participants who completed the AAP retest 3 months after the original AAP administration; 58 (84%) were classified in the same attachment group categories ($k = 0.78$, $p < 0.001$; 82% stability for secure, 96% stability for dismissing, 62% for preoccupied; 80% for unresolved). Verbal intelligence and social desirability are not related to AAP classifications (George and West, 2012). AAP convergence of classifications with the AAI (George et al., 1985; Main and Goldwyn, 1985–1994), the gold standard in the field of adult attachment assessment, was 84% for the four-group classification ($k = 0.71$, $p < 0.001$), 91% for the two-group classification ($k = 0.91$, $p < 0.001$), and 88% for the unresolved-resolved classification ($k = 0.75$, $p < 0.001$). The predictive validity of the AAP has been established for both clinical and healthy samples (Buchheim and George, 2011, 2012; George and West, 2012).

At the third session, plasma samples were taken for OT measurement before and after individuals participated in a social exclusion paradigm (Cyberball) in a standardized experimental setting, as previously reported (Jobst et al., 2014). In brief, through-the-wall blood drawings were performed by using a long catheter that ran through a soundproof lock to an adjacent laboratory. Participants had no visual contact with the investigators during the experiment. After baseline measurements had been taken, the Cyberball game was started on a computer screen positioned in front of the participants. The Cyberball paradigm is a virtual ball-tossing game played with two other virtual players and controlled by computer software (Williams and Jarvis, 2006). Participants were shown a statement on the computer screen that told them that they would take part in this virtual game with two other real players. Participants played one round of Cyberball, which lasted about three minutes. Participants were thrown the ball three times (10% of the throws) at the beginning of the round but were then excluded from the game without explanation and were able only to watch the other players.

During our study, we paid special attention to the stage of participants' menstrual cycle, because of neuroendocrine interactions with OT. Participants taking hormonal contraception were assessed during the 3rd and 18th day of the intake period, and those not taking hormonal contraception were assessed within the follicular phase, between the 5th and 12th day of the menstrual cycle, because gonadal hormones are more stable during this period (Salonia et al., 2005). Participants were told not to eat or drink one hour before hormonal measurement. All measurements took place in the morning between 8 and 11 a.m. to control for the circadian change in hormones.

Blood samples for OT measurement were collected at four time points: t0 (baseline), t1 (5 min after Cyberball), t2 (15 min after Cyberball), and t3 (40 min after Cyberball). Storage tubes were prepared in advance with aprotinin (500 IU/ml) in order to prevent OT degradation. Afterward, blood samples were centrifuged (1600*g*, 15 min), and plasma was stored at minus 80°C until the biochemical analyses. Analysis of plasma OT was performed by the Neurochemical Laboratory at the Department of Psychiatry, Ludwig Maximilian University, Munich, with a commercially available Enzyme Linked Immunosorbent Assay (ELISA) Kit (Enzo Life Sciences, Germany). Measurements were performed in duplicates. The inter-assay CV was below 17%, and the intra-assay CV was 15%. To control for stress reactivity, plasma cortisol was also measured; serum cortisol levels were determined with an immunoassay analyzer (Elecsys Cortisol Test; Roche Diagnostics, Mannheim, Germany), according to the manufacturer's instructions.

Emotional reactions to the social exclusion paradigm were measured with self-rating questionnaires, the NTQ (Williams et al., 2000), the Emotion Scale (Gross and Levenson, 1995) before and after Cyberball, as previously reported (Jobst et al., 2014). In addition, we asked the participants to assess aversive inner tension, expressed as a percentage of maximal tension before and after Cyberball.

Statistics

SPSS software version 17 was used for statistical analyses. Demographic and psychometric analyses were performed with χ^2-tests and independent sample *t*-tests. To analyze outcomes in the Cyberball paradigm, we used paired sample *t*-tests for the NTQ and rmANOVA for the emotion scale. For analysis of OT and cortisol levels as well as their changes during Cyberball, three repeated measure analyses of variance (rmANOVA) were conducted: (1) A group (HC vs. BPD) × time (before vs. after) rmANOVA (as reported in Jobst et al., 2014); (2) in BPD patients only a group (unresolved vs. other) × time (before vs. after) rmANOVA; and (3) in HC only a group (secure vs. insecure) × time (before vs. after) rmANOVA. In case of violation of sphericity assumption, Huynh–Feldt correction was used to present data. Moreover, we applied *post hoc* independent sample *t*-tests. Baseline OT plasma measurements showed a wide interindividual range of 164.4 pg/ml to 5092.4 pg/ml. Two BPD patients and two HC were excluded from statistical analysis, because their OT levels were higher than three standard deviations from the mean of the whole sample (outliers between 1271.2 and 5092.4 pg/ml). Regarding attachment representations, data for 19 BPD patients and 18 HC were available and included into further statistical analyses. Data samples for baseline OT showed normal distribution (Kolmogorov–Smirnov test). Correlation analyses were performed by Pearson correlation.

RESULTS

Demographic and Clinical Characteristics

Borderline personality disorder patients and HC did not differ significantly with regard to age and education. As expected, BPD patients showed significantly higher scores than HC for borderline and depressive symptoms (BSL-23, HAMD, and BDI-II). Also as expected, the BPD group showed higher CTQ scores, indicating early childhood trauma. On the basis of CTQ cut-off values defined by Bernstein and Fink (1998), the BPD patients in our sample reported moderate to severe traumatization. The CTQ scores of the control group were below cut-off values on all subscales. BPD patients also showed significantly higher scores of rejection sensitivity than controls, as assessed by the RSQ. There was no significant difference between BPD and HC as regards menstrual cycle and hormonal contraception. For an overview see **Table 1**.

Attachment, Clinical Variables, and Trauma

None of the BPD patients showed a secure attachment representation, whereas 8 HC (44.4%) were classified as secure. The attachment representations in the BPD group were as follows: 12 (63.2%) unresolved (disorganized), 4 (21.1%) dismissing, and 3 (15.8%) preoccupied, making a total of 36.8% with organized representation (dismissing and preoccupied together). Attachment representations among the HC were as follows: 8 (44.4 %) secure, 6 (33.3%) dismissing, 4 (22.2%) preoccupied, and none unresolved (disorganized). Secure and unresolved (disorganized) attachment representation differed significantly between BPD and HC (*secure*: $\chi^2 = 10.77$; df = 1; $p < 0.001$; *unresolved:* $\chi^2 = 16.83$; df = 1; $p < 0.001$), whereas dismissing and preoccupied representations did not (*dismissing*: $\chi^2 = 0.71$; df = 1; $p = 0.407$; *preoccupied*: $\chi^2 = 0.25$; df = 1; $p = 0.622$).

The group of organized and unresolved (disorganized) BPS patients showed no significant difference with regard to age, education, menstrual cycle, contraception, borderline symptoms (BSL-23), depressive symptoms (HAMD, BDI-II), and rejection sensitivity (RSQ) (overview **Table 2**). According to CTQ cut-off values, unresolved (disorganized) BPD patients reported severe traumatization on all trauma subscales, whereas organized BPD patients reported severe traumatization only on the subscales emotional abuse, emotional neglect, and physical neglect and mild traumatization on the subscales physical abuse and sexual abuse. The differences in the last two subscales were significant: On the physical abuse subscale, $n = 5$ (58.3%) patients in the unresolved (disorganized) group showed severe traumatization (cut-off score > 10) versus $n = 2$ (8.3%) in the organized group ($\chi^2 = 10.67$; df = 1; $p < 0.001$). On the sexual abuse subscale, $n = 3$ (12.5%) patients in the unresolved (disorganized) group showed severe traumatization (cut-off score > 8) vs. $n = 8$ (66.7%) in the organized group ($\chi^2 = 11.06$; df = 1; $p < 0.001$). HC with secure and insecure attachment representations did not differ with regard to age or education. However, insecure HC scored significantly higher on the HAMD ($t = 2.649$; df = 11.227; $p = 0.022$) than secure HC.

OT and Cortisol Plasma Levels

Though plasma OT levels showed a marked inter-individual variation, they were remarkably stable at an individual level.

Comparison of OT levels in BPD vs. HC

The rmANOVA comparing BPD patients and HC revealed a significant group (BPD vs. HC) × time (before vs. after) interaction when conducted over the first two time points ($F = 4.957$; df = 1; $p = 0.032$; **Figure 1**) and no significant group × time interaction when conducted over the four time points ($F = 1.467$; df = 2.427; $p = 0.234$): OT levels dropped after Cyberball from t0 to t1 in BPD whereas levels increased in HC (*post hoc* independent sample t-test: $t = 2.227$; df = 37; $p = 0.032$), as previously reported (Jobst et al., 2014).

Comparison of OT levels in BPD patients with unresolved vs. organized attachment patterns

As there were neither BPD patients with secure nor HCs with unresolved attachment, unresolved vs. organized attachment patterns were compared in BPD patients only and insecure vs. secure attachment patterns in HC only. For BPD patients, the respective rmANOVA showed a trend toward a significant group effect between BPD patients with unresolved (disorganized) and organized attachment ($F = 3.679$; df = 1; $p = 0.073$). BPD patients with unresolved (disorganized) attachment representations tended to show constantly lower OT levels compared to HC. *Post hoc* independent sample t-test showed significantly lower OT plasma concentrations at baseline in BPD patients with unresolved (disorganized) attachment than in BPD patients with an organized attachment representation ($t = 2.346$; df = 17; $p = 0.031$, $d = -1.078$; see **Figure 1**). There was no significant effect of time (before vs. after) in BPD ($F = 1.647$; df = 3; $p = 0.201$), nor a significant group (unresolved vs. organized) × time (before vs. after) interaction ($F = 0.361$; df = 2.453; $p = 0.742$); both groups showed a similar course of OT levels after social exclusion (**Figure 1**).

Comparison of OT levels in HC with insecure vs. secure attachment patterns

The respective rmANOVA for HC showed neither a significant effect of group (secure vs. insecure attachment pattern: $F = 0.012$; df = 1; $p = 0.916$) nor of time (before vs. after: $F = 0.587$; df = 3; $p = 0.627$) and no significant group × time interaction ($F = 0.450$; df = 3; $p = 0.718$).

TABLE 1 | Sample characteristics of patients with BPD and HC.

Characteristics	BPD patients ($n = 20$)	HC ($n = 19$)	*t*-test	*p*-value
	Mean *(SD)*[f]			
Age (in years)	29.85 (7.46)	30.42 (10.55)	0.20	0.847
Education (in years)	11.20 (1.70)	12.0 (1.53)	1.83	0.132
BSL-23[a]	2.07 (0.96)	0.08 (0.13)	−9.18	<0.001
BDI-II[b]	32.75 (14.28)	2.33 (3.0)	−9.30	<0.001
HAMD-24[c]	29.90 (12.04)	1.28 (1.57)	−10.20	<0.001
CTQ[d]				
Emotional abuse	17.89 (4.98)	8.22 (6.26)	−3.19	0.003
Physical abuse	10.80 (7.16)	5.56 (1.34)	−3.05	0.004
Sexual abuse	12.35 (8.39)	5.44 (2.20)	−3.39	0.002
Emotional neglect	18.30 (5.19)	7.94 (3.95)	−6.86	<0.001
Physical neglect	11.20 (4.4)	6.61 (2.59)	−3.96	<0.001
Global	15.00 (4.86)	6.76 (2.35)	−6.76	<0.001
RSQ[e]	17.92 (5.45)	5.98 (2.82)	−8.47	<0.001
Day of menstrual cycle	9.83 (4.15)	8.78 (3.62)	−0.813	0.422
Hormonal contraception	5 (22.7%)	10 (47.6%)	X^2: 2.931	0.091

No significant differences between patient and control groups in age and education. [a]BSL-23, Borderline Symptom List; [b]BDI-II, Beck Depression Inventory; [c]HAMD-24, Hamilton Depression Rating Scale; [d]CTQ, Childhood Trauma Questionnaire; [e]RSQ, Rejection Sensitivity Questionnaire; [f]SD, standard deviation.

TABLE 2 | Sample characteristics of BPD patients with organized or disorganized attachment representation.

Characteristics	Organized ($n = 7$)	Unresolved ($n = 12$)	*t*-test	*p*-value
	Mean *(SD)*[f]			
Age (in years)	25.14 (4.85)	31.75 (7.49)	−2.08	0.053
Education (in years)	12.0 (1.73)	10.83 (1.64)	1.47	0.161
BSL-23[a]	1.74 (1.09)	2.05 (1.11)	−0.60	0.558
BDI-II[b]	30.86 (16.82)	33.5 (13.91)	−0.371	0.716
HAMD-24[c]	27.86 (9.37)	30.42 (13.87)	−0.432	0.671
CTQ[d]				
Emotional abuse	16.0 (6.46)	19.0 (3.77)	−1.29	0.214
Physical abuse	8.57 (7.39)	12.58 (7.01)	−1.18	0.253
Sexual abuse	8.43 (7.46)	14.75 (8.66)	−1.61	0.126
Emotional neglect	16.86 (6.01)	18.58 (4.62)	−0.70	0.491
Physical neglect	10.43 (4.28)	11.17 (4.49)	−0.35	0.730
Global	12.06 (5.61)	15.22 (4.43)	−1.36	0.191
RSQ[e]	17.06 (4.46)	18.03 (6.23)	−0.36	0.727
Day of menstrual cycle	8.33 (2.81)	10.6 (5.04)	−1.064	0.333
Hormonal contraception	3 (42.4%)	1 (9.1%)	X^2: 3.273	0.195

[a]BSL-23, Borderline Symptom List; [b]BDI-II, Beck Depression Inventory; [c]HAMD-24, Hamilton Depression Rating Scale; [d]CTQ, Childhood Trauma Questionnaire; [e]RSQ, Rejection Sensitivity Questionnaire; [f]SD, standard deviation.

Comparison of cortisol levels between groups

Cortisol plasma levels were analyzed using rmANOVAs as described above. There were no significant effects of group or group × time interaction between BPD and HC, BPD patients with organized and unresolved (disorganized) attachment representation, and HC with secure and insecure attachment representation, respectively. There was a significant effect of time: Cortisol levels significantly decreased in BPD and HC (Jobst et al., 2014) and this decrease was not influenced by attachment representation. OT and cortisol plasma levels for all groups and time points are shown in **Table 3**.

Psychological Measures during Cyberball

The results of the psychological measures during Cyberball in BPD patients and HC have been published elsewhere (Jobst et al., 2014): To summarize, BPD patients felt more readily excluded, and the exclusion paradigm had a stronger negative impact on their needs than it did in HC (Needs-Threat-Questionnaire), but the social exclusion paradigm did not have impact on inner tension, neither in BPD, nor in HC. Negative emotions focused on other significantly increased in BPD (rmANOVA: time effect: $F = 6.065$; df = 1; $p = 0.019$; group effect: $F = 14.474$; df = 1;

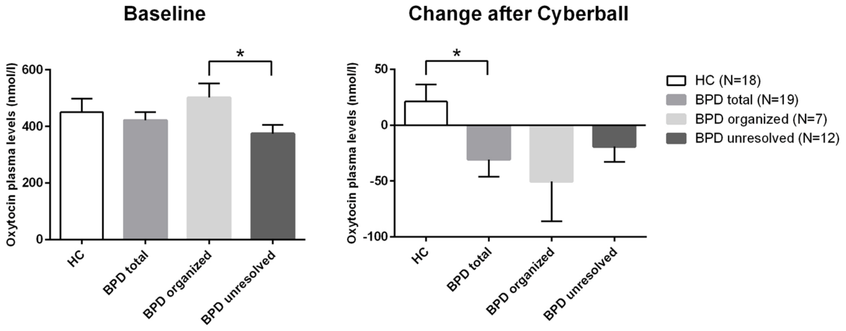

FIGURE 1 | Differences in baseline plasma OT levels and differences in the changes of plasma levels of OT over time (before and after Cyberball). *significant at $\alpha = 0.05$.

$p = 0.001$; group × time interaction: $F = 2.603$; df = 1; $p = 0.115$). *Post hoc* t-tests revealed that especially anger and contempt significantly increased in BPD (anger $t = -2.251$; df = 1; $p = 0.037$; contempt: $t = 2.480$; df = 18; $p = 0.023$), which was not the case in HC (Jobst et al., 2014).

We conducted additional analyses independently for BPD and HC regarding the association between attachment representation and psychological reactions toward social exclusion. BPD with organized and disorganized attachment representations felt disregarded ($t = 0.903$; df = 15; $p = 0.381$) and excluded ($t = 2.095$; df = 11.311; $p = 0.059$) to a comparable degree and judged ball ownership similarly ($t = 0.445$; df = 15; $p = 0.663$) and realistically (organized: 11.37%; disorganized: 9.85%). Moreover there was no significant difference between organized and disorganized BPD regarding the aversive impact triggered by the social exclusion (NTQ aversive impact factor: $t = 0.736$; df = 14; $p = 0.474$). Negative emotions focused on others increased in both the organized and disorganized group (rmANOVA: time effect: $F = 4.385$; df = 1; $p = 0.053$), but did not show differences between groups (group effect: $F = 0.128$ df = 1; $p = 0.725$) nor a significant group × time interaction ($F = 0.015$; df = 1; $p = 0.905$). However, contempt significantly increased in the organized group whereas this was not the case for the disorganized group (rmANOVA: time effect: $F = 9.120$; df = 1; $p = 0.008$; group effect: $F = 0.337$; df = 1; $p = 0.569$; group × time effect: $F = 3.446$; df = 1; $p = 0.082$). There was no such difference for anger. Inner tension did not differ between groups. Analysis between secure and insecure attached HC revealed no significant different emotional response to social exclusion: Both groups felt disregarded ($t = 1.065$; df = 16; $p = 0.303$) and excluded ($t = 1.056$; df = 16; $p = 0.306$) to a comparable degree and judged ball ownership similar ($t = -0.654$; df = 16; $p = 0.523$) and realistically (secure: 8%; insecure 10%). Both groups demonstrated a similarly aversive impact factor ($t = 0.565$; df = 16; $p = 0.580$). Change of other focused negative emotions and inner tension did not differ between groups.

DISCUSSION

Insecure and especially unresolved attachment representations are predominant patterns in patients with BPD. In the present study, we were able to replicate this finding on a behavioral level. Our main finding, however was, that BPD patients with unresolved attachment show significantly lower baseline OT plasma levels than BPD patients with organized attachment. These results extend previous findings of lower plasma OT

TABLE 3 | Oxytocin plasma levels in patients with BPD and HC according to attachment representation.

	BPD ($n = 19$)	**HC ($n = 18$)**	**BPD**		**HC**	
			Organized ($n = 7$)	**Unresolved ($n = 12$)**	**Secure ($n = 8$)**	**Insecure ($n = 10$)**
	Mean (*SD*)					
Oxytocin t1	421.67 (127.70)	450.26 (204.42)	502.14 (130.71)	374.73 (104.11)	443.21 (195.30)	455.89 (221.79)
Oxytocin t2	390.97 (130.70)	471.46 (240.63)	451.73 (186.02)	355.53 (73.21)	451.46 (225.54)	487.56 (263.01)
Oxytocin t3	399.19 (142.60)	468.19 (252.68)	480.60 (175.38)	351.70 (99.09)	466.55 (237.54)	469.50 (276.96)
Oxytocin t4	403.58 (128.54)	454.22 (233.85)	468.36 (133.92)	362.36 (111.91)	456.21 (214.54)	452.62 (259.80)
Cortisol t1	530.04 (236.08)	505.06 (170.52)	635.37 (298.52)	468.60 (188.24)	468.65 (208.98)	454.19 (120.35)
Cortisol t2	522.67 (243.70)	523.87 (185.45)	632.50 (299.91)	458.61 (170.06)	589.81 (223.08)	471.11 (138.41)
Cortisol t3	499.47 (246.31)	497.53 (195.64)	631.53 (312.10)	422.44 (169.03)	563.89 (244.15)	444.44 (137.44)
Cortisol t4	446.24 (221.78)	448.16 (198.26)	554.80 (286.38)	377.16 (144.61)	519.78 (239.67)	390.87 (146.30)

baseline levels in BPD than in HC and of a negative association between OT plasma levels and childhood trauma (Bertsch et al., 2012). The lower OT plasma levels in unresolved attached BPD seem to be plausible when taking into account that unresolved attachment trauma is associated with severe childhood trauma (Stalker and Davies, 1995; Bakermans-Kranenburg and van IJzendoorn, 2009). Accordingly, in our study BPD patients with unresolved attachment representations showed significantly more severe physical and sexual childhood abuse compared to BPD individuals with organized attachment. In our small sample, we could not find a direct association between childhood trauma (CTQ) and OT plasma levels, however, smaller OT recovery was associated with higher physical and emotional abuse (Jobst et al., 2014). Therefore it would be of major interest to investigate in future studies the association between childhood trauma, unresolved attachment representation, and OT in larger samples of BPD patients.

Oxytocin change after social exclusion (Cyberball) – a relevant social stimulus (Williams and Jarvis, 2006; Williams, 2007) that activates social pain in humans (Eisenberger et al., 2003) – did not differ in regard to attachment representations (not in BPD, nor in HC group). Both BPD patients with organized and those with unresolved attachment representations showed similar courses of OT after social exclusion; though we found lower OT plasma levels in BPD patients with unresolved attachment representations at every time point. Comparing BPD and HC group, change of OT plasma levels directly after social exclusion significantly differed as previously described (Jobst et al., 2014): After social exclusion OT plasma levels tended to decrease in BPD patients and tended to increase in HC and this different course was significant. Descriptively OT plasma levels were constantly lower in BPD patients than in HC. In accordance with other studies (Zöller et al., 2010; Zwolinski, 2012), the social exclusion paradigm did not elicit a neurobiological stress reaction, as central stress pathways might be inhibited due to the presence of a defensive response (emotional analgesia) (Bass et al., 2014).

Emotional responses to social exclusion differed between BPD and HC as previously described (Jobst et al., 2014). Attachment representation did not modify these responses besides a significant higher increase of contempt in the organized vs disorganized BPD group. We hypothesize that OT release after social exclusion might be understood as neuroendocrine reaction to broken relations. In this context, OT release may reduce social pain and induce pro-social orientation. In BPD patients, this OT reaction to social exclusion may be impaired, possibly corresponding to the general difficulty of BPD patients in repairing broken cooperation (King-Casas et al., 2008).

In previous studies, BPD patients responded to intranasal OT administration in the opposite way to HC, i.e., intranasal OT reduced trust in BPD but increased trust in HC (Bartz et al., 2011). Moreover, in depressed patients OT administration in addition to psychotherapy even increased fear during psychotherapy (Macdonald et al., 2013). Taking these results into consideration, another hypothesis seems plausible. Reduced OT levels in BPD as found in our study, and especially in BPD patients with unresolved attachment representations, might be the result of an altered OT system, most likely resulting from early caretaking experiences (Meaney, 2001; Champagne, 2008; Bertsch et al., 2013; Herpertz and Bertsch, 2015), so that the patients have a baseline state of "low OT." Lower OT levels in BPD compared to HCs might be specifically found in BPD with unresolved attachment representations but not in BPD with organized ones. Consequently, this "low OT state" might represent a protective state in which social pain might be more bearable, with reduced perception of negative emotions. OT administration might take the patients out of this state and consequently increase fear. Experiences occurring in sensitive periods in early development, especially traumatic childhood experiences, might critically modify epigenetic states of genes and influence the developing OT system and according to Kumsta and Heinrichs (2013) epigenetic modification of genes involved in OT signaling might therefore be involved in the mechanisms mediating the long-term influence of early adverse experiences on socio-behavioral outcomes. In this context the development of BPD might be understood as a result of early childhood maltreatment with the development of insecure attachment representations, which then contribute to Borderline symptoms in adulthood. This relationship might be neurobiologically mediated by epigenetic changes, which can be pictured by changes within the OT system. However, Brüne (2015) suggests that in the spectrum of childhood trauma, emotional neglect in early childhood may have a different impact on the OT system than, e.g., sexual abuse or later traumatic experiences in adolescence.

Our study has some limitations. These include a small sample size, pharmacological treatment in the BPD group, especially intake of neuroleptic medication, and failure to measure estrogen and progesterone levels. Due to the small sample size and exploratory character of this study, we did not control for influencing factors such as medication or depression. This should be re-analyzed within a larger sample. Moreover, the specificity of a dysregulated OT system to BPD patients is still unclear, as well as the interaction of OT with other neuromodulators, such as the endocannabinoid system, which has been found relevant for pain processing (Herpertz and Bertsch, 2015). The meaning and reliability of OT plasma levels with regard to central nervous system processes is still a matter of debate. Recently published articles argue that peripheral OT cannot give information about cognition, emotion and behavior (Meyer-Lindenberg et al., 2011; Quintana and Woolley, 2015; Leng and Ludwig, 2016; Walum et al., 2016). However, several studies also state the opposite and demonstrate an association between peripheral and central OT measures (Dal Monte et al., 2014; Carson et al., 2015; Freeman et al., 2016). Future research should clarify this controversy. Therefore our results have to be interpreted with caution. Another bias might result from the analysis of OT levels in a non-extracted plasma sample using a commercially available ELISA, which limits a direct comparison with other studies that used extracted samples and radioimmunoassays (Szeto et al., 2011).

In summary, this study demonstrates that BPD patients with unresolved attachment representations have significantly lower baseline OT plasma levels than BPD patients with organized attachment representations. However, this finding needs to be replicated in a larger sample.

AUTHOR CONTRIBUTIONS

Organized and designed the whole study setting and experiments: AJ, FP, PF, BR, AB. Coded, analyzed, and controlled the data and wrote most parts of the manuscript: AJ, FP, MG, AB. Performed and analyzed the experiments and data: MM, TD, CB-S, LS, NS, PZ.

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REVIEW
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Attachment, Neurobiology, and Mentalizing along the Psychosis Continuum

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In this review article, we outline the evidence linking attachment adversity to psychosis, from the premorbid stages of the disorder to its clinical forms. To better understand the neurobiological mechanisms through which insecure attachment may contribute to psychosis, we identify at least five neurobiological pathways linking attachment to risk for developing psychosis. Besides its well documented influence on the hypothalamic-pituary-adrenal (HPA) axis, insecure attachment may also contribute to neurodevelopmental risk through the dopaminergic and oxytonergic systems, as well as bear influence on neuroinflammation and oxidative stress responses. We further consider the neuroscientific and behavioral studies that underpin mentalization as a suite of processes potentially moderating the risk to transition to psychotic disorders. In particular, mentalization may help the individual compensate for endophenotypical impairments in the integration of sensory and metacognitive information. We propose a model where embodied mentalization would lie at the core of a protective, resilience response mitigating the adverse and potentially pathological influence of the neurodevelopmental cascade of risk for psychosis.

Keywords: schizophrenia, mentalizing, HPA, schizotypy, UHR, theory of mind, self

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INTRODUCTION

According to contemporary conceptualizations, psychosis is a neurodevelopmental disorder emerging during late adolescence and/or early adulthood and associated with the final stages of brain maturation. However, neuroscience research suggests that experiences of social adversity during early childhood, such as attachment-related trauma (Read et al., 2014), may independently contribute to alterations of neural development and brain dysmaturational processes during adolescence/early adulthood in those who go on to have psychosis (Brent et al., 2014b). Whilst basic neuroscience and novel brain imaging techniques have increasingly shed light on the neural correlates of psychosis vulnerability during the later stages of the psychosis risk period (Brent et al., 2013), there remains a great need to identify earlier (i.e., preadolescent and early adolescent) indicators of psychosis vulnerability. Importantly, the preponderance of youths at genetic or clinical high risk (CHR) for psychotic disorders will never transition to a first episode of psychosis (FEP), suggesting that illness onset may at least partly result from a breakdown of psychological mechanisms supporting resilience. The nature of such psychological mechanisms, potentially attenuating psychosis risk, remain incompletely understood.

Following the work of Brent et al. (2014a) and Brent and Fonagy (2014), we provide the theoretical basis to support further research regarding two inter-related, early putative protective factors: attachment security and mentalizing (a social cognitive capacity fostered by attachment security), which may together heighten resilience to developmental interpersonal stress and moderate the risk for psychosis onset. To frame our subsequent discussion, we begin with a consideration of the clinical phases associated with the emergence of psychosis.

The clinical course of psychotic disorders is commonly broken down into four phases (**Figure 1**): (1) the premorbid period, which is characterized by a wide-range of subtle physiological, neurocognitive and social impairments during preadolescent development that are thought to confer distal risk for schizophrenia (Seidman and Nordentoft, 2015); (2) the clinical high-risk (CHR), which encompasses a range of CHR states typically occurring during adolescence, or early adulthood (e.g., at-risk mental states (Yung et al., 2005), basic symptoms (Schultze-Lutter and Koch, 2010), ultra high-risk states (Miller et al., 2003), or significant functional decline in the context of genetic risk); (3) the first episode of psychosis (FEP), which marks the conversion to clinical psychosis; and (4) the post-conversion period, which can be divided into three developmental trajectories: remission, remission and relapse, and chronic disease.

Our specific interest concerns how the characteristics of the attachment environment may influence the trajectory of psychosis risk along its continuum of expression. We begin by highlighting the associations between trauma, insecure attachment, and psychosis. Second, we examine neurobiological links between early attachment trauma, stress, and social cognitive impairment. Lastly, we discuss the moderating role mentalization may play along the trajectory of risk for psychosis.

Our aim is not to construe a model of psychotic illnesses based solely on environmental risk factors (i.e., adverse attachment environment) acting in isolation, but rather to start fleshing out the kinds of transformations gene-environment interactions may incur during development, some of which appear to increase risk and probability to develop manifest psychotic disorders (van Os et al., 2010). We hope our review of the biological pathways upon which trauma, attachment and psychosis come together in gene-environment interactions and transactional processes may contribute to clarify which mechanisms may most likely lead to the emergence of psychotic disorders.

TRAUMA, ATTACHMENT, AND PSYCHOSIS

Is There Evidence for an Association Between Trauma and Psychosis Along the Continuum of Psychotic Expression?

There is strong evidence suggesting the importance of trauma as a risk factor for psychotic disorders (Read et al., 2005; Varese et al., 2012). High rates of childhood trauma have been observed across the psychosis continuum, particularly when experiences of emotional and physical neglect are also included in the analyses. Recent retrospective studies have reported childhood trauma rates as high as 82% (Duhig et al., 2015) and 85% (Larsson et al., 2013) among samples of individuals with psychosis. In these studies, emotional abuse and neglect were found to be the most representative traumatic experiences, followed by physical neglect, sexual abuse and physical abuse. An important methodological issue of studies examining the incidences of childhood abuse in adult psychosis samples pertains to the retrospective nature of their assessment, which may be confounded by both normal processes of forgetting, but also by specific processes characterizing psychotic illnesses such as paranoid delusional ideation and cognitive impairment. A number of recent studies have addressed these

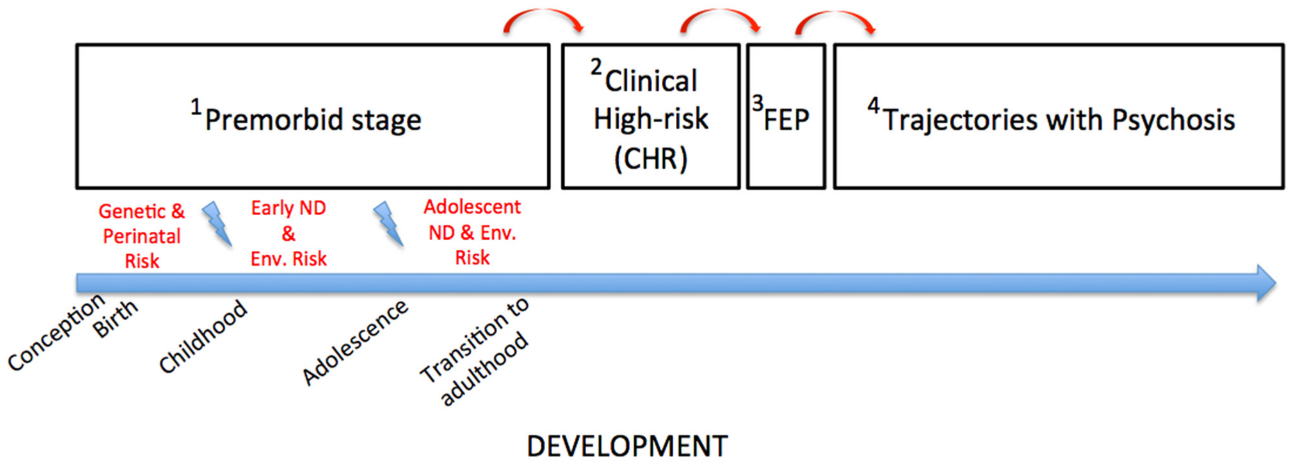

FIGURE 1 | The clinical developmental course of psychotic disorders, across the first two phases indicating increased vulnerability, and the last two phases charting the onset and development of the disorder. FEP, First-Episode Psychosis; ND, Neurodevelopment; Env, Environmental.

limitations. For example, Fisher et al. (2011) examined the reliability of retrospective assessments of childhood trauma among patients suffering from psychosis, finding high levels of concurrent validity with measures of parental bonding and good convergent validity with clinical case notes. Most importantly perhaps, prospective longitudinal studies of children have shown that exposure to traumatic experiences early in life is predictive of the development of psychotic experiences (PE) over time with specific associations reported in relation to severity of trauma (Kelleher et al., 2013) and childhood abuse characterized by harmful intentions (Arseneault et al., 2011).

The harmful intentions abused children face often originate from caregivers (Sedlak et al., 2010). A number of different clinical accounts describe the affective double bind that abused children face. Briefly, a child facing a threat or danger automatically activates attachment needs that trigger approach mechanisms to the caregiver to ensure security. In cases where the caregiver is also a source of neglect and/or abuse, the child will have to manage the potential threat associated with proximity to the caregiver. The threat can be managed by adopting a hypervigilant stance towards the caregiver (as in avoidant-fearful attachment), which translates the child's attempts to predict or control the threatening caregiver's states of mind. Alternatively, or in combination, the child may also manifest avoidance behavior characteristic of avoidant attachment, in order to keep the source of threat at bay. Liotti and Gumley (2008) observe that it is not uncommon for children to dissociate in the face of abusive threats. In doing so the child's attachment system is activated to maintain physical proximity and safety to the caregiver, whilst psychologically dissociating from the hostile images of the self that may populate the mind of the neglectful or abusing caregiver. This paradox lies at the core of the subjective experience of trauma; for some children, it can crystalize into disorganized attachment, which represents a combination of intense anxious and avoidant attachment strategies together with odd attachment behaviors which encapsulate the contradictory proximity-seeking and avoidant motivations of the child facing a maltreating caregiver (for example, walking backwards in the direction of the caregiver, to seek reassurance while avoiding visual and other straightforward contact; Fonagy et al., 2002).

Evidence suggests that traumatic experiences and sub-clinical psychotic manifestations are associated during childhood and adolescence. For example, Escher et al. (2002) found that 86.3% of a children sample reporting auditory verbal hallucinations (AVH; $n = 80$, mean age = 12.9 years) also reported experiencing traumatic and stressful life events in close temporal proximity to voice-hearing onset. Furthermore, prospective evidence links traumatic and stress-inducing events in childhood with the persistence and severity of auditory hallucinations, the emergence of new hallucinatory experiences in early adolescence, and the secondary development of delusional ideation (Bartels-Velthuis et al., 2012). Importantly, prospective studies in CHR populations have shown that childhood sexual trauma is predictive of conversion to a FEP, with individuals reporting high scores on sexual abuse questionnaires being 2–4 times more likely to transition into FEP compared to those with low scores (Bechdolf et al., 2010; Thompson et al., 2014).

Given the evidence linking adverse childhood experiences and the development of psychosis later in life (Read et al., 2014), and the association between early trauma and attachment insecurity, a number of authors have proposed that attachment security may be an environmental reliance factor, protecting against the likelihood that an underlying psychosis diathesis will become expressed (Read and Gumley, 2010). One possibility is that attachment security could foster protective psychological processes related to long-term adaptation, in the face of childhood traumatic events, while attachment insecurity may increase the risk of subsequent interpersonal dysfunction and psychopathological expression (Rutten et al., 2013).

Attachment and Interpersonal Functioning Along the Psychosis Continuum

Initial studies by Dozier (1990) and Dozier et al. (1991) observed that psychiatric groups display significantly greater levels of attachment insecurity compared to healthy controls, with individuals suffering from schizophrenia showing higher levels of insecure attachment (particularly dismissing-avoidant attachment) than those suffering from affective illnesses. Consistent with these findings, high rates of insecure attachment have also been reported in more recent studies of patients with chronic psychotic disorders (Mickelson et al., 1997), and FEP (MaBeth et al., 2011). Additionally, meta-analyses have shown associations between adult attachment avoidance and both positive and negative symptomatology, with more modest evidence for an association between positive symptoms and attachment anxiety/preoccupation (Berry et al., 2007b; Korver-Nieberg et al., 2013; Gumley et al., 2014). Thus, both early attachment and adult attachment, which traditionally show some continuity over development (Waters et al., 2000), relate to symptomatic expression of individuals with psychotic disorders in retrospective and prospective studies.

Attachment security has also been associated with several important clinical outcomes, such as enhanced help-seeking and treatment engagement, as well as stronger therapeutic alliance among individuals with established schizophrenia (Berry et al., 2007b). By contrast, insecure attachment (attachment avoidance in particular) has been linked with reduced help-seeking behaviors, poor use of treatment (Dozier et al., 1991), diminished therapeutic alliance (Berry et al., 2008) and increased service disengagement (Tait et al., 2004).

Among psychosis prone individuals, the majority of studies looking at attachment has focused on schizotypal traits in familial or psychometrically defined risk samples. Data from non-clinical samples suggest that insecure avoidant attachment is associated with subclinical psychotic symptoms (Korver-Nieberg et al., 2013). Positive schizotypy has been associated with both attachment avoidance (Berry et al., 2007a; MacBeth et al., 2008) and attachment anxiety (Berry et al., 2007a), while negative schizotypal symptoms have been specifically linked to attachment avoidance (Berry et al., 2006, 2007a; Tiliopoulos and Goodall, 2009). In a large community study, preoccupied attachment was associated to positive schizotypy, dismissing attachment was related to negative schizotypy and fearful attachment was related to both positive and negative schizotypy (Sheinbaum et al., 2013). Given that preoccupied attachment is characterized by hyper-activation of the attachment system (Shaver and Mikulincer, 2002), these findings support the possibility that disruptions in the regulation of negative emotion, and increased salience of threat-related cues and distress may contribute to the expression and maintenance of positive schizotypy. On the other hand, dismissing attachment, characterized by a deactivation of the attachment system (i.e., interpersonal distancing, etc.), is significantly associated with negative schizotypy (Sheinbaum et al., 2013), which may contribute to persistent social withdrawal and isolation. In a recent study with a large sample of undergraduate students, fearful attachment was found to mediate the relationship between physical/emotional trauma and both positive and negative schizotypy (Sheinbaum et al., 2014). The authors suggest that individuals with fearful attachment hold negative working models of both self and others, and resort to antagonistic approach and avoidance strategies, which may contribute to emotional and cognitive disorganization (Sheinbaum et al., 2014).

Despite the developing interest in interpersonal and social cognitive functioning in high-risk for psychosis studies, only a limited number of investigations to date have examined attachment among CHR samples. In one cross-sectional study using the self-report Revised Adult Attachment Scale (Collins, 1996), 80% of CHR young adults showed evidence of insecure attachment (Gajwani et al., 2013). Further, in a prospective study with a sample of 31 ARMS individuals (mean age = 15.7 years), Quijada et al. (2012) examined the relationship between baseline attachment, symptoms and social functioning after a 6-month psychosocial intervention. The majority of individuals in this ARMS sample was classified, on the basis of the observer-rated Relationships Questionnaire (Bartholomew and Horowitz, 1991), as fearfully attached (71%), followed by preoccupied (16.1%) and dismissing attachment (6.4%). Improvement in attenuated positive symptoms at 6 months was associated with baseline secure, preoccupied and dismissing attachment styles. According to Quijada et al. (2012), secure, preoccupied and dismissing attachment styles, all share the presence of at least one positive internal working model indicating that psychotherapeutic interventions, at least during the early stages of psychotic illnesses, may benefit from a positive internal working model, either of the self or of others. Further, these data suggest that individuals who hold negative internal models of both self and others in the context of fearful attachment relationships may be at greater risk for a poorer clinical course. In a follow-up study, patients with lower levels of fearful and dismissing/avoidant styles at baseline, displayed better clinical outcomes (positive, negative and total symptom scores), after the implementation of a psychosocial intervention at 12 months follow-up (Quijada et al., 2015).

Overall, the available literature appears to support the view that: (1) attachment insecurity is associated with psychosis and psychosis-like symptoms throughout childhood and adolescent development; (2) attachment classification is linked with treatment engagement and other clinical outcomes. Here, positive internal working models of self and/or other speak to a favorable disposition to respond to psychosocial treatment. At the neurobiological level of analysis, the impact of attachment on the potential routes sustaining a disposition to develop psychosis still require to be further characterized.

NEUROBIOLOGICAL TRAJECTORIES LINKING ATTACHMENT TO PSYCHOSIS VULNERABILITY

It has been proposed that psychotic disorders result from early (perinatal) and later (adolescence) biological insults that engender pathogenic processes altering the course of normal brain maturation (e.g., dendritic pruning) in late adolescence and young adulthood (Keshavan, 1999; Fatemi and Folsom, 2009). In the previous section we reviewed evidence suggesting that early trauma, together with insecure attachment, may affect the symptomatic course, therapeutic outcome, and interpersonal functioning associated with psychosis. This is not to say that insecure attachment is inherently maladaptive; as suggested above, insecure attachment in the context of trauma is a likely adaptive reaction (Chisholm, 1996; Ellis et al., 2011) to regulate distance and proximity to unpredictable and potentially harmful attachment figures. However, as suggested by studies on therapeutic outcomes, insecure attachment may hinder the development of alternative secure bonds to other individuals, thereby neutralizing potential psychosocial protective factors along the progression of the illness. As we will further develop in the third section, we also posit that attachment plays a critical role in the development of mentalizing, which may constitute a key protective social cognitive mechanism in psychosis-prone individuals.

In this section we will specifically focus on the links between the neurobiology of psychosis and attachment-related stress, which will highlight how the development of social cognition may be undermined in the course of childhood and adolescent development. We will survey five biological markers of psychosis (hypothalamic-pituitary-adrenal-axis (HPA-axis) hyperactivity, dopamine dysfunction, reduced oxytocin, neuroinflamation and oxidative stress) and how they may interact with developmental adversity to influence both childhood and adolescent neurodevelopmental disturbances associated with the illness. Although severe childhood abuse and emotional neglect have also been associated with non-schizophrenic illnesses such as borderline personality disorder (BPD) (Fonagy and Luyten, 2009, 2016), we highlight that in the developmental unfolding of psychosis, the pathogenic neurobiological impact of early attachment adversity, particularly during critical periods of neurodevelopment

(ND), may more severely affect brain regions sustaining the capacity to regulate self-generated experiences (body-states, thoughts, feelings). More specifically, echoing formulations from phenomenological psychiatry (Nelson et al., 2009; Sass, 2014), we suggest that social cognitive impairments in relation to self-generated bodily, affective and cognitive states along development, severely undermine the establishment of a coherent sense of self and promote a breakdown of self and reality monitoring.

HPA-Axis Hyperactivity and Psychosis

Early-life adversity has been found to significantly affect later life stress-responses by inducing long-term dysregulation of HPA-axis function, particularly in terms of elevated diurnal cortisol levels (Heim et al., 2008). Similarly to individuals suffering from depression and/or post-traumatic stress disorder, increases in glucocorticoid levels (cortisol in particular) have been reported in samples of patients suffering from schizophrenia compared to healthy controls, suggesting a potential relationship between early-life stress and psychosis (Ryan et al., 2004; Mondelli et al., 2010). Indeed, among patients with schizophrenia, those with a history of childhood abuse have been found to display significantly greater HPA-axis hyperactivity compared to non-abused controls (Braehler et al., 2005). Further, a more recent longitudinal study reported increased cortisol levels among CHR individuals who transitioned to a FEP, consistent with research on chronic samples (Walker et al., 2010).

At the neurobiological level, stress-based glucocorticoid exposure during critical periods of ND significantly affects the structure and function of brain regions with a high density of glucocorticoid receptors (e.g., hippocampus and prefrontal cortex) as well as regions sensitive to repeated neuronal excitation (e.g., amygdala; Teicher et al., 2003; McCrory et al., 2011). Functional and structural changes in these areas have an important influence on the disruption of cognitive processes associated with psychosis. For example, Aas et al. (2012) reported that childhood trauma was associated with smaller amygdala volume in a group of FEP subjects. Reduced amygdala volume also mediated the relationship between childhood trauma and impaired executive functioning. In addition, the disruptive effects of cortisol on prefrontal cortical activity have been linked with impaired higher order social cognitive processes (Arnsten, 2009). Specifically, acute stress has been shown to affect the dorsolateral and medial prefrontal cortex (mPFC), leading to a transient switch from flexible and reflective processing of social information, to a more automatic, action-based one (Fonagy and Luyten, 2009; Reyes et al., 2015). Additionally, chronic exposure to stress can produce extensive structural alterations in the PFC, including the loss of dendritic length, branching and spine density (Arnsten, 2009). Functional neuroimaging data from healthy participants suggest that the ventral and dorsal mPFC constitutes part of a wider network of cortical midline structures associated with self-referential and self-other discriminative processing (Brent et al., 2014b). Chronically elevated corticosterone levels in the context of adverse caregiving environments therefore may hinder the integrity of brain regions underpinning self-referential processing, leading to premorbid difficulties, in the capacity to differentiate between self and non-self cues, during middle childhood (Brent et al., 2014b). In line with two-hit neurodevelopmental conceptualizations of psychosis (Keshavan, 1999), adolescence-specific interpersonal stressors may thus further compromise the already vulnerable prefrontal self-processing network, leading to increased difficulties in self-reflective and self-monitoring processes as well as in other social-cognitive domains, and eventually to prodromal psychotic manifestations (Brent et al., 2014b). In this vein, psychosis would not directly emanate from HPA dysfunction; rather, the HPA dysfunction sustained by trauma and insecure attachment, would contribute in bringing the individual closer to the clinical threshold of psychotic breakdown. In contrast to exposure to trauma and neglect, supportive early social experiences associated with maternal care appear to promote the modulation HPA-axis-based threat reactivity, thus fostering flexibility and resilience in the face of novel stress-inducing social situations (Gunnar and Quevedo, 2007). By undermining the neural integrity of brain regions sustaining flexible and robust emotion regulation, as well as self-referential and metacognitive processing, the early disruption of the stress regulatory system may, therefore, make an important contribution to psychosis risk.

Dopamine Dysfunction, Oxytocin and Psychosis

For the past 40 years, the role of dopamine in the development and maintenance of psychosis-spectrum illnesses has been supported by a large number of biological, neuroimaging and genetic studies (Carlsson, 1977; Howes and Kapur, 2009). Initial evidence linking the effectiveness of antipsychotic medication to changes in dopamine receptors was followed by studies utilizing advances in neurochemical imaging to directly examine dopamine levels among patients suffering from psychosis. These studies consistently report increased presynaptic striatal dopamine levels in psychotic illnesses, particularly during acute phases (Howes and Kapur, 2009). Furthermore, 4 of the 10 candidate genes associated with schizophrenia are directly linked with dopaminergic pathways (Howes et al., 2004; Howes and Kapur, 2009). Advances in research methodologies have led to further investigations in the effects of dopaminergic abnormalities on clinical phenotypic manifestations in psychosis.

Robust evidence indicates that mesolimbic dopamine guides motivational responses by assigning neural significance to external stimuli. Through this process, neutral external information is transformed into engaging or aversive entities on the basis of previous experience and predisposition. It has been consistently shown that in psychosis, dysregulation in dopamine transmission results in stimulus-independent release of dopamine (Kapur, 2003; Kapur et al., 2005). This neurochemical aberration disrupts normal processes of stimuli-based salience, leading to states of heightened awareness ("aberrant salience") with respect to both external and internal stimuli (Kapur, 2003; Howes and Kapur, 2009). According to Kapur (2003), positive psychotic symptoms, particularly delusions and hallucinations, develop over time as personal explanations of the distressing experience associated with aberrant salience.

Recent studies have linked elevated striatal dopamine among CHR individuals, with greater severity of positive symptoms (Howes et al., 2009). Increased dopamine levels in the striatum have also been reported among schizotypal individuals (Soliman et al., 2008) and first-degree relatives of patients with schizophrenia (Huttunen et al., 2008), suggesting that dopaminergic abnormalities could underpin psychosis proneness (Howes and Kapur, 2009).

Pertinently, stress among at-risk individuals has been associated with both psychotic symptom severity and dopamine levels (van Winkel et al., 2008). Data suggest a synergistic relationship between the HPA-axis and the dopaminergic system (Phillips et al., 2006). More specifically, evidence from animal studies indicate that early life adversity within the caregiving environment is linked with chronic dysfunction of the dopaminergic system, particularly in terms of increased rates of dopamine synthesis and release in response to acute stress (Strathearn, 2011). Furthermore, chronic exposure to stress has been shown to decrease tonic activity in the midbrain, normally responsible for regulating dopamine levels in the nucleus accumbens (Phillips et al., 2006). According to neurodevelopmental accounts of psychosis (Keshavan, 1999), dopaminergic disregulation during the premorbid phase of the illness is modulated by a relatively intact PFC, which exerts inhibitory control over subcortical striatal dopamine. In adolescence, however, the derailment of normal maturational processes (i.e., synaptic pruning), as well as a normative increase in basal firing (Luciana et al., 2012), may lead to stress regulatory demands exceeding prefrontal function, and subsequently to the depletion of PFC-based subcortical dopaminergic modulation (Keshavan, 1999).

A complementary account argues that attachment insecurity may worsen dopaminergic dysfunction because of decreased levels of available oxytocin (Brent et al., 2014a). Oxytocin is critical for the regulation of early infant-caregiver relationships (Feldman et al., 2010) and the establishment of later social-affiliative behaviors (Wismer Fries et al., 2005). Oxytocin neurones project to brain structures responsible for the stimulation of maternal behaviors (Strathearn, 2011), and oxytocin facilitates physical proximity and care within mother-infant interactions (Insel, 2010). Evidence from rodent studies suggests that oxytocin administration stimulates a range of maternal behaviors while administration with an oxytocin antagonist inhibits maternal care and induces neglectful maternal attitudes (Pedersen et al., 1994). The prosocial effects of oxytocin have been specifically attributed to its stress regulating properties (Tas et al., 2014). According to Taylor et al. (2006), within stressful interpersonal interactions, hypothalamic oxytocin release modulates stress and rejection-related ideas, allowing individuals to constructively relate to others. Indeed, a number of non-clinical studies have reported that central oxytocin administration improves social cognition and social behavior (Tas et al., 2014). Importantly, although oxytocin facilitates the onset and maintenance of maternal caregiving behavior, the quality of the caregiving environment itself, stimulates the development of the oxytocinergic system in the offspring (Strathearn, 2011). Animal and human studies suggest that non-maternal rearing is linked with decreased levels of cerebrospinal fluid oxytocin during the first years of life (Winslow et al., 2003; Heim et al., 2009) and reports of childhood emotional neglect are negatively correlated with cerebrospinal fluid concentrations (Heim et al., 2009). Thus, adverse experiences within early attachment relationships may exert a prolonged impact on the development and function of the oxytocinergic system.

In schizophrenia, studies have shown associations between reduced serum levels of oxytocin and difficulties in facial emotion identification (Goldman et al., 2008), reduced plasma levels of oxytocin among patients during trust-dependent interactions with others (Kéri et al., 2009), as well as negative associations between oxytocin levels and severity of psychotic psychopathology (Rubin et al., 2010). According to Tas et al. (2014), the oxytocinergic system affects social cognition by acting upon subcortical structures (i.e., amygdala) responsible for basic social cognitive processes (i.e., facial emotion recognition), which in turn affect cortical areas (i.e., PFC), responsible for higher order metacognitive processes such as theory of mind (ToM). While interpersonal arousal in the context of insecure attachment may lead to transient disruptions in cortical brain areas responsible for metacognitive processing (i.e., mPFC, posterior cingulate cortex (PCC)), in healthy subjects the oxytocinergic system modulates amygdala-based stress and promotes mutually beneficial contingent relational responses (Bakermans-Kranenburg and Van IJzendoorn, 2013). The prosocial effects of oxytocin appear to be particularly pertinent through their modulation of avoidant attachment responses.

Data from randomized control trial (RCT) studies in healthy participants suggest that intranasal oxytocin administration enhances the experience of attachment security (Buchheim et al., 2009) and leads to increases in trust and cooperation along with reductions in betrayal aversion (De Dreu, 2012), specifically among those classified as avoidant attached at baseline. The impact of the oxytocinergic system to psychotic psychopathology may thus critically depend on attachment dimensions, and in particular the degree of avoidant attachment displayed by individuals prone to or suffering from a psychotic disorder. In a similar fashion, reduced oxytocin levels may sustain the premorbid social functioning patterns (distrust, social withdrawal and isolation) displayed by children and adolescents who go on to develop psychotic disorders, significantly depriving them of mutually beneficial interpersonal interactions that promote the development of social cognition (Fonagy and Luyten, 2009; Vrtička et al., 2014). Indeed, while trust related interactions are shown to be associated with increased oxytocin levels in healthy controls, the same pattern is absent in patients suffering from schizophrenia (Kéri et al., 2009). In the context of a genetic diathesis for psychosis, attachment insecurity and concomitant depletions of available oxytocin could, therefore, amplify the vulnerability to dopamine dysregulation and heighten the vulnerability to aberrant salience and low-grade psychotic symptoms. It is important to note however that more studies are needed to inform our understanding of the relationship between oxytocin levels and psychotic symptomatology, as well as on the effects of oxytocin on the development of trust in clinical samples. For example, current evidence on the therapeutic effects of oxytocin administration in the treatment of psychotic symptoms are mixed (Feifel et al., 2016; Lee et al., 2016) and although oxytocin administration is shown to facilitate trust and corporation in healthy samples, the opposite effect has been observed in some studies involving patients suffering from BPD (Bartz et al., 2011; Ebert et al., 2013).

Neuroinflammation, Oxidative Stress and Psychosis

Inflammation refers to one of the organism's first lines of defense against pathogenic infections or injuries and chronic inflammation has been associated with the pathophysiology of various physical and psychiatric illnesses (Kirkpatrick and Miller, 2013). Chronic inflammation in the brain (neuroinflammation), leading to increased microglial activation and inflammatory cytokine release, can disrupt the blood-brain barrier, which normally controls the entry of cytokines and other substances in the brain, causing alterations in brain function (Kirkpatrick and Miller, 2013). A number of studies have reported that individuals suffering from schizophrenia display elevated blood concentrations of inflammatory cytokines compared to healthy controls (Miller et al., 2011). Moreover, blood concentrations of certain inflammatory molecules in psychosis show variations according to clinical status (i.e., higher cytokine blood concentrations than controls during the exacerbation of the illness and no significant differences during periods of clinical remission; Miller et al., 2011). Importantly, neuroinflammatory abnormalities have been found among both FEP subjects and antipsychotic-naïve relatives of patients with schizophrenia, thus independent of antipsychotic medication use (Martínez-Gras et al., 2012). Among patients suffering from schizophrenia, increased blood cytokine levels have been associated with worse cognitive functioning along with measures of regional brain volume and negative psychotic pathology (Kirkpatrick and Miller, 2013). Perkins et al. (2015) reported increased plasma concentration of 15 proinflammatory analytes among CHR subjects that progressed to formal psychosis compared with non-converting CHR subjects and healthy controls, suggesting that inflammation may be a prominent factor in the early stages of psychotic illnesses.

Animal studies suggest that inflammation during critical periods of ND may significantly impact on the "set-point" of the inflammatory system, affecting subsequent inflammatory responses displayed in adulthood (Bilbo and Schwarz, 2009). Indeed, inflammation may mediate various recognized prenatal and perinatal risk factors for schizophrenia such as preterm labor, maternal gestational diabetes, preeclampsia, but also maternal depression and anxiety often associated with insecure attachment (Kirkpatrick and Miller, 2013). For example, (Buka et al., 2001) reported that maternal serum concentrations of specific cytokines (IL-8 and TNF-alpha) during pregnancy were associated with an increased risk of schizophrenia in the offspring.

According to O'Connor et al. (2014) cortisol and other glucocorticoids have clearly demonstrated effects on the immune system, suggesting a bidirectional link between stress and the immune system. Decreased receptor sensitivity to glucocorticoids and increased glucocorticoid exposure resulting from prolonged stress may reduce the anti-inflammatory effect of glucocorticoids, leading to persistent inflammation experienced by stressed individuals and subsequently to the development of various physical and psychological illnesses (O'Connor et al., 2014).

Further, Cannon et al. (2015) longitudinally investigated gray matter changes and plasma based markers of inflammation in a large CHR sample. MRI data indicated that CHR individuals who went on to develop formal psychotic psychopathology showed a steeper rate of gray matter loss in frontal areas and a greater rate of expansion of the third ventricle compared to non-converters and healthy controls. Higher levels of plasma based proinflammatory cytokines at baseline were strongly predictive of the observed steeper rates of gray matter reduction in right PFC areas among CHR converters. Bloomfield et al. (2016) used PET imaging to compare microglial activation between individuals at CHR for psychosis and healthy controls. Data revealed that microglial activation was significantly increased in total, frontal and temporal lobe gray matter in the CHR group compared to healthy controls.

As mentioned above, the PFC modulates the response of subcortical regions to stress and provides inhibitory feedback on the HPA-axis (Teicher et al., 2003). Furthermore, prefrontal regions are essential for the development of multiple processes of social cognition (Lieberman, 2007). It is possible that cortical thickness loss around the onset of psychosis significantly alters the capacity to regulate certain stressors in individuals at CHR, stressors that will inevitably come in the interpersonal domain during adolescence (most notably interpersonal stress, such as bullying; Mackie et al., 2013; Trotta et al., 2013). Additionally, the evidence for increased microglial activation in the frontal and temporal lobes of CHR individuals (Bloomfield et al., 2016) as well as the observed steeper rates of prefrontal gray matter loss, associated with proinflammatory cytokine levels, close to psychosis onset (Cannon et al., 2015), suggest that through their pathogenic effects on prefrontal brain maturation, neuroinflammatory processes may contribute to the alteration of neurodevelopmental mechanisms underpinning self-referential and socio-cognitive processing in adolescence. Along these lines, a recent study by Piskulic et al. (2016) charted the development of different social cognitive domains in a group of 764 CHR participants. Whilst no differences were observed in baseline social cognition between converters and non-converters, the latter were the only group to show significant developmental gain in social cognitive domains over a 1-year interval (Piskulic et al., 2016). The continued improvement in social cognition in non-converters should be further charted along development, as it could critically enable at-risk individuals to regulate the arousal evoked in the context of interpersonal relationships. On the other hand, the levelling-off of social cognitive development around the conversion period to psychosis in converters could mark the attenuation of protective factors opening the gate to psychopathological processes and resulting in severe morbidity in the social domain as observed in chronic schizophrenia.

In addition to inflammation, emerging evidence suggest that the pathophysiology of schizophrenia may be, at least in part, a consequence of oxidative stress due to aberrant reduction-oxidation (redox) control (Bitanihirwe and Woo, 2011). Data from human and animal studies indicate that adverse interpersonal experiences play an important role in sustaining the links between oxidative stress and psychosis (Möller et al., 2011; Aydin et al., 2015). More specifically, according to Do et al. (2009), in psychotic illnesses, genetically based disruptions in antioxidant control (i.e., reductions in glutathione (GSH)) interact with pro-oxidative environmental risk factors (including childhood and adolescent attachment adversity and stress) during critical periods of ND, to significantly disrupt the processes of neural connectivity and synchronization, particularly in relation to prefrontal areas associated with self-referential and socio-cognitive processing (Brent et al., 2014b).

Clinical and preclinical investigations into the mechanisms of antioxidant defenses in the brain suggest multiple pathways through which chronic oxidative stress can affect the development and course of psychotic disorders. Specifically, multiple studies have reported alterations in antioxidant enzymes in schizophrenia (Bitanihirwe and Woo, 2011). Data from a meta-analytic study indicated an increase in the level of lipid peroxidation products and nitric oxide (NO) in schizophrenia along with significantly decreased activity of antioxidant enzymes (Zhang et al., 2010). Moreover, levels of plasma antioxidants are significantly reduced in the illness, independently of other prooxidative factors such as smoking (Yao et al., 2000). Clinical trials provide further support to the association between oxidative stress and schizophrenia. RCT data showed that treatment with the antioxidant N-acetylcysteine significantly reduced psychotic pathological manifestations (Berk et al., 2013). Furthermore, Amminger et al. (2010) found that supplementation with fish oil reduces the progression to FEP in UHR subjects, with baseline levels of specific omega-3 polyunsaturated fatty acids predicting treatment response (Amminger et al., 2015). Additionally, evidence from preclinical studies with rodents show that alterations in antioxidant systems may underlie cognitive impairments and biochemical changes that are relevant to schizophrenia (Cabungcal et al., 2007).

Animal models provide information into the potential mechanisms linking psychological stress to the pathogenic effects of oxidative stress in the brain. In one rodent study, Wilson et al. (2013) reported that in comparison to control rats, rats in a stress induction condition exhibited slower growth, higher plasma corticosterone levels, greater anxiety-like behavior and a dose response relationship between duration of stress exposure and levels of reactive oxygen species (ROS). Post mortem analysis of brain tissue showed increased levels of oxidative stress parameters in the hippocampus and PFC in the stress-manipulated rats (Wilson et al., 2013). According to Miller and Sadeh (2014), animal models suggest that HPA-axis-based glucocorticoid release under stress is associated with increased ROS and oxidative damage. Additionally, longer duration of glucocorticoid administration has been linked with greater oxidative damage (Costantini et al., 2011) and oxidative stress has been shown to have a mediating role in the effects of glucocorticoids on neurodegeneration (Sato et al., 2010).

Given that early life trauma is a known risk factor for schizophrenia, Möller et al. (2011) examined the association between social isolation rearing (SIR) and oxidative stress in rats. SIR rats displayed profound deficits in social interaction as well as in sensory-motor gating (basic inhibitory process of regulation of sensory input preventing the cognitive fragmentation and sensory overload typical of schizophrenia). SIR led to significantly elevated levels of lipid peroxidation in both the frontal cortex and the striatum of SIR rats, suggesting that both SIR-induced sensory-motor and behavioral changes were associated with increased cortico-striatal oxidative stress (Möller et al., 2011).

In human studies, Aydin et al. (2015) examined the impact of caregiver attachment style and expressed emotion on schizophrenic participant's oxidative stress parameters. Results showed that reduced and oxidized forms of glutathione (GSH and Glutathione disulfide, GSSG), plasma lipid peroxidation and urine malondialdehyde (MDA) levels of patients were higher compared to those reported in the healthy control group. Pertinently, regression analysis revealed that the main significant predictors of patients' GSSG oxidative stress level were their caregivers' emotional over-involvement and anxious-ambivalent attachment style. These data suggest that factors related to interpersonal stress within caregiving relationships may have a significant effect on oxidative stress parameters in psychotic illnesses.

The findings from human and animal studies reviewed above, suggest that traumatic early life stress may promote oxidative damage in the brain, which is shown to both alter processes of ND (Do et al., 2009) and enhance processes of neurodegeneration (Sato et al., 2010). In a pioneering study, Do et al. (2000) reported that GSH levels, which play an important role in protecting against oxidative damage, were reduced by 52% in the mPFC of drug naive patients with psychosis compared to a healthy control group. According to these authors, a deficit in GSH during early development constitutes an important risk factor for psychosis development, as it promotes neurodegenerative processes that lead to a loss of neural connectivity in various brain regions, including the PFC. This observation may relate to Brent et al. (2014b), who underline resting state fMRI studies where greater alterations of mPFC functional connectivity among individuals at genetic high-risk is associated with greater levels of psychotic manifestations. Here, we simply wish to underline that sustained oxidative stress, particularly during early ND, may heighten the risk for psychotic disorders later in life, causing structural and functional brain changes in regions associated with self-processing, a wide-range of cognitive processes (such as spatial learning, spatial memory (Cabungcal et al., 2007)) and sensory-motor gating (Möller et al., 2011). Interestingly, NMDA receptors as well as GABAergic interneurons are also thought to sustain the critical relationship between sensory and metacognitive signaling (Adams et al., 2013), which we will further discuss in the final section.

Overall, our review of the literature highlights that the aberrant neurobiological processes underpinning psychosis proneness and development: (1) are influenced by early adverse, stress-inducing experiences in the context of caregiving attachment relationships, particularly during critical periods of ND; (2) they all, at least in part, exert their pathogenic impact by making the self-processing fronto-tempo-parietal system more vulnerable; and (3) They are associated with sensory and cognitive impairments early, which can critically impact self-processing (**Figure 2**).

MENTALIZING AS A MODERATOR OF PSYCHOSIS VULNERABILITY

In the first section of this article, we reviewed the different strands of evidence underlining the relevance of attachment relationships at each phase of developing psychosis. On the one hand, early attachment insecurity is overrepresented along the continuum of expression of psychosis, from the premorbid manifestations, through the CHR states and into the clinical range of psychosis. On the other hand, attachment security appears to be linked to an increased capacity to engage in psychosocial treatment and to benefit from these interventions, at least in adults diagnosed with a psychotic disorder. In the second section, we presented five neurobiological pathways that fundamental research in neuroscience has revealed to represent possible routes taken by pathogenic processes towards the emergence of psychotic disorders. Importantly, each of these pathways may individually contribute to undermine the regulation of self-experiences, from basic sensory-gating processes to inferential processes about self-generated contents, including bodily experiences, feelings and thoughts; most importantly perhaps, they undermine the very processes that scaffold the illusion of a coherent and stable self, namely mentalizing or social cognition. Indeed, these neurobiological pathways may shed some light into the

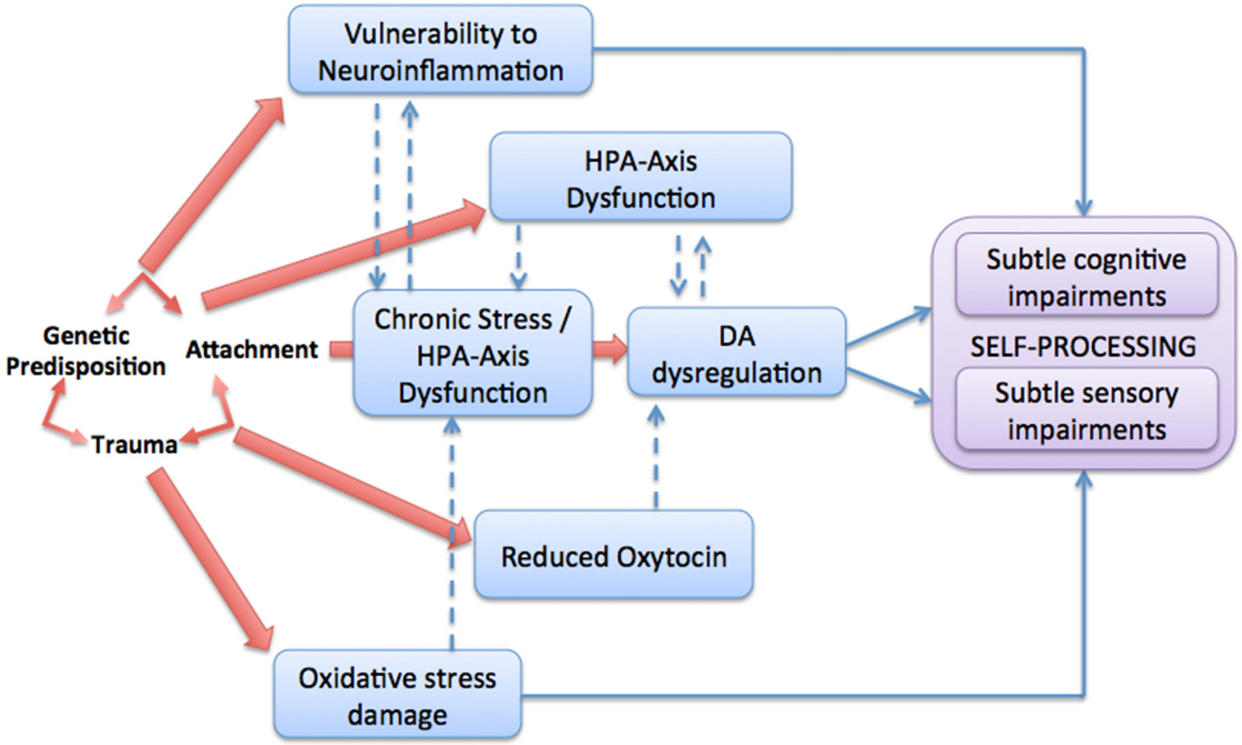

FIGURE 2 | Illustration of the five neurobiological pathways (red arrows) through which attachment adversity (both during childhood and adolescence) may augment risk for psychosis. Dotted arrows represent potential interactions between pathways.

mechanisms underlying disturbed self-experiences (Brent et al., 2014a,b).

In this third and final section, we will explore the hypothesis that the suite of processes falling under the umbrella term of *mentalizing* may act as moderators of risk for transitioning to psychosis. We will build our case on evidence suggesting that early impairments in mentalizing, caused either by environmental factors (e.g., trauma), biological factors or a combination of both, are associated with sub-clinical manifestations of psychosis at the trait and state levels of expression. Second, we review evidence suggesting that robust mentalizing during adolescence is associated with the natural resolution and the disappearance of hallucination and delusion-like phenomena. Finally, we propose a bridge with the computational psychiatry account of psychosis to reduce the divide between social cognitive state manifestations of psychosis and sensory-based, trait markers of risk for psychosis. We argue that processes falling under the rubric of *embodied mentalizing*, the capacity to experience the body as the seat of emotional responses and to reflect on the relationship between bodily states and mental representations (Luyten et al., 2012) may enhance our understanding of the potential aberrations in the relationship between sensory-affective experience and metacognitive certainty.

Evidence of Early Impairments in Mentalizing Along the Psychosis Continuum

Mentalizing is a multidimensional construct that signifies attempts to understand oneself and others as driven by intentional mental states, such as beliefs, desires, emotions or intentions (Fonagy and Luyten, 2009; Bateman and Fonagy, 2012). A number of phenomena related to psychosis entail aberrant mentalizing. At the most concrete level, individuals with psychosis may develop rigid convictions about others' intentions based solely on their physical observable behavior, while losing the capacity to consider alternative perspectives on the basis of internal mental states (teleological mentalizing; Fonagy and Bateman, 2006), such as in cases where others' behavior gives rise to paranoid delusions. For example, a patient describing random eye contact with a stranger on the bus may say "*He turned around and looked at me, clearly wanting to hurt me*". They may also experience their thoughts about themselves or others as isomorphic to reality (psychic equivalence; Fonagy and Target, 1996). Ideas of reference constitute a good example of mentalizing in psychic equivalence, because the individual denies the opacity of others' states of mind (i.e., an idea of reference held in psychic equivalence: "*I feel that the news broadcaster is hinting a message specifically addressed to me*"). Finally, phenomena such as hyper-reflexivity characterize a type of mentalizing activity that has dissociated from present perceptual, sensory and affective content (mentalizing in pretend mode; Fonagy and Target, 1996). For example, psychotic patients in psychotherapy often develop a hyper-reflexive mode of discourse characterized by intricate and convoluted explanations of self and others' mental states, a discourse that will typically be detached from the patient's current emotional arousal (for example, immediate feelings vis-à-vis the relationship to therapist). In such instances, the therapist will often experience feeling lost or confused by the patient's discourse held in pretend mode mentalizing (Debbané et al., 2016).

Developmentally, mentalization is fostered by secure attachment. A number of studies have shown that secure attachment is positively associated with the normative development of emotion recognition, ToM, and mind-mindedness (Fonagy et al., 2002). The caregiver's contingent and *marked mirroring* (attuned yet slightly distorted reflection) of the infant's emotional communication is hypothesized to provide a mentalizing playground where second-order representations about self-experience can be elaborated in safe and playful interactions (Gergely and Watson, 1996). Later on, mature mentalization builds on the linking of specialized social cognitive functions, which necessarily interact in the adult's mind to construe accurate interpretations of complex social behaviors as motivated by underlying intentional mental states of self and others. In essence, the articulation and binding of processes giving rise to mentalization represent a developmental achievement that critically depends on interacting systems, or in neuroscientific terms, on multi-layered connectivity within and between systems that sustain self and other monitoring, and more broadly, social cognitive functions. It may thus not appear entirely surprising that psychotic symptoms, most consistently characterized as coming from "dysconnectivity" (Friston, 1999; McGlashan and Hoffman, 2000), present themselves in forms of aberrant mentalizing of self and others.

Previously, Brent and Fonagy (2014) have proposed that among genetically predisposed individuals, mentalizing deficits particularly in the context of stress-inducing experiences associated with early attachment disturbances, may interact with dopaminergic dysfunction to facilitate the breakdown of reality testing and the development of psychosis. To date however, mentalizing deficits in psychosis have been primarily investigated through the use of ToM tasks, which overlap only with the cognitive, other-oriented portion of mentalization. Meta-analytic data from ToM studies have confirmed the presence of stable mentalizing deficits in the course of psychotic illnesses, independent of IQ, age and gender (Harrington et al., 2005; Sprong et al., 2007). Moreover, ToM disturbances have been associated with positive psychotic symptoms (paranoid delusions in particular; Harrington et al., 2005), poor illness insight (Bora et al., 2007) and increased social functioning difficulties (Fett et al., 2011).

Self-monitoring deficits have also been consistently reported along the psychotic continuum of expression (Franck et al., 2001; Brunelin et al., 2007; Lagioia et al., 2011). These studies would be considered to overlap with the cognitive, self-oriented portion of mentalization. Despite these findings, the specific mentalization impairments characterizing psychotic illnesses remain empirically unexplored (Brent et al., 2014a). We will review the developmental evidence suggesting that aberrant mentalization in clinical psychosis is preceded by more subtle alterations during childhood and adolescence, related to distal (schizotypy) and proximal (CHR) manifestations of risk for psychosis. We will further highlight the studies suggesting that those youths with better mentalization skills resolve early sub-clinical psychotic manifestations on their own, possibly through the protective effect of solid developing mentalizing skills.

Indirect Evidence in Childhood for an Early Association Between Mentalizing Impairments and Vulnerability to Psychosis

Mentalizing deficits have been characterized as trans-diagnostic (Fonagy et al., 2011), yet it remains unclear whether specific mentalizing deficits can be identified along the different stages of psychotic expression. In this regard, early schizotypal expressions such as odd beliefs and ideas of reference may represent the more specific manifestations of early mentalizing aberrations, indicating an increased risk for psychosis. According to Schiffman et al. (2004), the observed premorbid ToM deficits may reflect a general underlying vulnerability for the development of psychopathology (similar to the case of childhood trauma). Another possibility is that intact mentalizing may constitute a resilience factor, protecting against the development of psychotic-spectrum illnesses in individuals who are otherwise at increased risk due to genetic, interpersonal or social influences.

Bartels-Velthuis et al. (2011) examined the moderating role of mentalizing in the development of delusional ideation secondary to abnormal perceptual experiences (AVH) during childhood. They used the ToM Storybook Frank (Blijd-Hoogewys et al., 2008), in which children are tested on their ability to understand first and second-order false beliefs, white lies, irony, deception, double bluffs and faux pas, while being presented with pictures and listening to the story read aloud. Among children experiencing auditory hallucinations at age 7–8 and/or 12–13 years, as measured by the auditory vocal hallucinations scale (AVHRS, Jenner and Van de Willige, 2002), the risk for the development of secondary delusional ideation was significantly higher in those with lower ToM task scores, suggesting that better mentalizing capacities may provide a protective barrier against the development of delusional explanations of unusual perceptual experiences (Bartels-Velthuis et al., 2011).

In another study, Clemmensen et al. (2014) examined ToM using the Danish version of the ToM Storybook Frank, in a sample of 1630 children (11–12 years old) from the general population (study I) and in a case-control based sample of 259 children aged 12–13 years, half of whom reported AVH at age 7–8 years (study II). It was hypothesized that PE measured by the K-SADS-PL (Kaufman et al., 1997) would be specifically associated with a selective mentalizing pattern of hyper-ToM (over-attribution of intentions). In sample I, children with low ToM scores (below the median) were at an elevated risk of experiencing PE compared to children with higher ToM scores. However, this effect was not found in sample II. Pertinently, children who displayed a hypermentalizing style were significantly more likely to experience PE (sample I OR = 2, sample II OR = 1.6) compared to non-hypermentalizing children, and this effect was particularly pronounced for experiences of paranoid/persecutory ideation. According to Clemmensen et al. (2014), the observed hyper-ToM pattern may be stress-induced as studies have shown that increased cortisol production is linked to a hypermentalizing pattern of social cognition (Smeets et al., 2009). In another targeted study, Clemmensen et al. (2016) examined the specificity of the association between hypermentalizing (measured by the Danish version of the ToM Storybook Frank) and PE compared to other known risk factors (i.e., family illness, gender, bullying, changes in family income, etc.), in a sample of 1630 children (11–12 years) from the general population. Analyses revealed that hypermentalizing along with a concurrent psychiatric diagnosis, involvement in bullying and low family income were all associated with PE. Importantly, however, hypermentalizing was the only factor independently associated with PE in the absence of concurrent illness. Moreover, involvement in bullying was associated with an increased risk for PE but was also associated with an elevated risk for the development of general psychopathology without PE. Thus, while most factors associated with PE (like bullying) appear to be linked with a non-specific risk for the development of psychopathology, in this study, hypermentalizing alone appears to be specifically associated with the emergence of psychotic-like experiences (Clemmensen et al., 2016).

These studies are suggestive of a relationship, quite early in development, between mentalization and the first sub-clinical signs of psychosis. Studies involving older adolescents and young adults, which we will review below, further strengthen the case of a developmental interaction between mentalization and risk for psychosis.

Mentalization During Adolescence and Psychosis High-Risk States

To our knowledge, very little research has focused on metacognitive reasoning about the self in adolescents along the continuum of psychotic expression. Our group has carried out two investigations examining the relationship between self-monitoring difficulties and schizotypy during adolescence (Debbané et al., 2008, 2009). In both studies, we observed a significant association between increased self-reported schizotypy and self-monitoring impairments, suggesting that metacognitive difficulties related to the self may underpin the early expression of risk for psychosis in adolescence. We also found that self-reported schizotypy during adolescence correlated with atypical brain activation patterns in the medial and lateral prefrontal cortices during reality monitoring and self-other trait adjective attribution tasks (Lagioia et al., 2011; Debbané et al., 2014). In studies with older adolescents and adults, self-monitoring deficits have also been identified in the prodromal phase of psychosis (Johns et al., 2001, 2010), indicating that self-monitoring impairments precede the full expression of psychotic psychopathology.

The associations between mentalizing deficits and positive psychotic manifestations in adolescence reported by Barragan et al. (2011) are in line with studies of adult psychometric risk samples. Langdon and Coltheart (1999) found selective ToM deficits among high schizotypal (on the basis of SPQ scores) non-clinical individuals, which were independent of executive planning or inhibitory control deficits. Additionally, Pickup (2006) found that higher positive schizotypy scores predicted subtle ToM deficits in a healthy population sample. No significant associations were found between ToM scores and total or negative schizotypy, suggesting that the relationship between ToM and negative psychotic manifestations may only emerge following the transition to psychosis (Pickup, 2006).

A relatively small amount of research has examined the role of ToM deficits in the transition from the psychosis risk state to the psychiatric form of the illness. Evidence suggests that deficits in social cognition are present in the prodromal phase of psychosis (Thompson et al., 2012) and are often similar to those found among formal psychosis samples (Thompson et al., 2011). Meta-analytic data have shown that similarly to unaffected relatives of patients with psychosis, CHR individuals have significantly impaired ToM compared to healthy controls, but significantly better ToM compared to first episode sufferers (Bora and Pantelis, 2013). Chung et al. (2008) reported significantly worse ToM performance (measured by the False Belief, the Strange Story and a Cartoon tasks) in a CHR sample of young adults (mean age = 20.88) compared to an age and IQ matched healthy control sample, with intermediate effect size levels (0.64–0.68). These findings suggest that ToM deficits may constitute important vulnerability factors underpinning the development of psychosis and highlight the need for prospective studies examining the specific effects of mentalization on the developmental unfolding of psychotic disorders.

In a longitudinal study investigating ToM in a group of 49 subjects at CHR for psychosis, Kim et al. (2011) observed that CHR individuals who transitioned to psychosis over a 5.2 year-period displayed worse baseline scores on False Belief, Strange Story and cartoon ToM tasks, as well as on a number of neurocognitive assessments, compared with non-converters. Moreover, the authors reported that a model combining both ToM and neurocognitive scores significantly predicted the time of transition to formal psychosis. Contrary to the data reported by Kim et al. (2011), recent longitudinal evidence in CHR from the large NAPLS-2 cohort (Piskulic et al., 2016) indicates that differences in social cognition alone, may not be sufficient to predict the transition from prodromal psychotic manifestations to the clinical form of the illness. Although the CHR group ($n = 764$) as a whole displayed significantly worse performance in various domains of social cognition (ToM, social perception, facial emotion perception) compared to healthy controls ($n = 280$), no significant group differences emerged in any of the social cognitive domains between CHR individuals who transitioned to psychosis and their non-converting counterparts (Piskulic et al., 2016). Importantly, however, improvements in social cognition over time (one year follow-up) were more prominent in CHR non-converters and healthy controls compared to CHR converters.

These prospective longitudinal studies are essential to further our understanding of early social cognitive development that precedes the emergence of psychotic disorders. It appears that impairments in mentalization are not consistent “predictors” of transition, but may signal a breakdown in resilience factors protecting against the emergence of psychosis. Still, many of the studies reviewed in this section focus on state manifestations of psychosis risk (positive psychotic-like symptoms), which are not as enduring as trait risk factors represented by endophenotypes (such as sensory gating abnormalities, neurological soft signs, social and physical anhedonia) that are evidenced in individuals at genetic risk for psychosis (Gottesman and Gould, 2003). According to a recent model (Debbané et al., 2015), state-risk manifestations may reflect a series of developmental interactions or exacerbation of an underlying schizotypal trait-liability (Rado, 1953; Meehl, 1962) that is dimensionally distributed in the general population at different degrees (from complete absence and schizotypal personality characteristics to the extreme of clinical psychotic symptomatology). It is thus conceivable that sub-optimal mentalization capacities, often found in the context of insecure attachment, may combine with the underlying schizotypal “seed” or liability, to undermine resilience processes protecting against the transition to clinical psychosis. In this way the degree of psychosis expression and the derailment of social-cognitive processes would be conceptualized as a developmental transaction, converging towards a clinical psychosis outcome. Below, we further consider how computational psychiatry may contribute in bridging the divide between cognitive impairments and sensory-based endophenotypes along the trajectory of risk for psychosis.

A Computational Framework for Integrating Attachment, Neurobiology and Mentalization

In this final section, we will propose that insecure attachment may be connected to disturbed and potentially psychotic experience of oneself through mechanisms subsumed under the umbrella term of *embodied mentalizing*, an expression that translates the processes needed to *detect*, *identify* and *regulate* signals coming from one’s body to harness them with one’s mind. The concept of embodied mentalizing translates early insights from the field of psychoanalytic psychosomatics suggesting that mentalization represents a suite of processes responsible for the regulation and transformation of physiological activation through higher-order psychological processes (Marty, 1991; Lecours and Bouchard, 1997). Recent conceptualizations have emphasized the role played by embodied mentalizing in the development and treatment of functional somatic disorders

(Luyten et al., 2012; Luyten and Fonagy, 2016) and depression (Luyten et al., 2013). We argue that the concept of embodied mentalizing may help bridge the gap to understand how early signs of risk for psychosis may link to later emerging psychotic states during the CHR and psychosis onset, and most importantly, to severely impaired social cognition.

As in high-risk psychosis research, studies in clinical developmental neuroscience distinguish two levels of psychotic impairment that may be usefully articulated in the context the embodied mentalizing hypothesis. First, at the "trait" level of liability to psychosis, processes of neuromotor integration ("neurological soft signs"; Compton et al., 2007) and sensory gating, represent well-known endophenotypes of psychosis, which are observable in first-degree relatives and along the continuum of severity in psychotic disorders (Braff et al., 2001). These endophenotypes are linked to both genetic vulnerability as well as to developmental oxidative stress for which, as reviewed above, attachment adversity may act as one factor promoting early impairment. At the second level, sub-clinical to clinical "state" symptoms, encompassing subclinical psychotic-like phenomena, CHR manifestations, and frank hallucinatory or delusional states, may be best characterized as false inferences emerging from a failure to regulate the relationship between certainty about *prior belief* and certainty about sensory experience (Adams et al., 2013). We would like to underline here that we will employ the expression "*sensory-affective*" experiences to account for the lived experience pertaining to fear, hostility and anguish underpinning PE; importantly, sensory-affective experiences permeating psychotic manifestations are often triggered in the context of intimate relationships, such as closeness, attraction, and sexual arousal which are most often difficult to tolerate and subject to avoidance in people suffering from psychosis, because these experiences typically carry the disorganizing effect of blurring self-other boundaries (Fonagy, 2008).

Sensory-affective experience is key to a contemporary, developmental, and psychodynamically-oriented understanding of the emergence of psychosis. In this framework, mentalization constitutes an interesting construct by virtue of the fact that it seeks to account for the dynamic connectivity between systems sustaining low-level embodied experience and systems sustaining superior cognitive inferential processes, which constantly interact to shape one's understanding of self and others' behaviors. As we will argue on the basis of contemporary neuroscience (Palaniyappan et al., 2012; Seth, 2013), different forms of **imbalance** between certainty about sensory-affective experience and certainty about prior beliefs in oneself may help explain aberrant *embodied mentalizing* along the psychosis continuum, where too little or too much weight to either prior beliefs or sensory-affective evidence could sustain both trait and state expression of psychosis from sub-clinical to clinical manifestations.

Another important issue from our perspective relates to psychosexual development from adolescence to adulthood, in parallel to the neural maturation and specialization of cerebral networks. On the basis of clinical conceptualizations (Fonagy and Luyten, 2016), we suggest that among individuals at-risk for psychosis and in the context of early attachment adversity, difficulties in embodied mentalizing may become particularly relevant during adolescent development, which is characterized by the initiation of intimacy in interpersonal relationships, together with psychophysiological changes which profoundly modify the youth's position in two domains: sexuality and aggression (Laufer and Laufer, 1995). Whereas before puberty the domains of sexuality and aggression were less integrated in the agentive sphere of the individual, their potentiation through pubertal development gradually brings novel possibilities: procreation and potentially causing enduring harm through one's aggression. This poses an inherent challenge for mentalizing during adolescence, as body-states associated with new experiences of sexual and aggressive arousal remain without fully regulatory second-order representations, unlike other forms of affective arousal stemming from basic emotions which have been mirrored throughout childhood and internalized in the self-regulatory repertoire (Target, 2007; Fonagy, 2008; Fonagy and Allison, 2016; Fonagy and Luyten, 2016). This makes new arousal states in adolescence prone to poorly regulated thought and behavior, especially in situations of stress (Fonagy and Luyten, 2016). Under favorable circumstances, adolescents with relatively stable mentalizing capacities, manage to utilize the widening of interpersonal relationships (peer, romantic) during adolescence, to further elaborate their ability to form representations of their own and other people's mental states, and to integrate their sexual and aggressive states in their developing identities.

Importantly however, children who have experienced sexual or physical abuse in the context of early attachment relationships, enter adolescence with a severely undermined mentalizing capacity (Cicchetti et al., 2003; Ensink et al., 2015). For these youths, adolescent-specific confrontations with unmentalized feelings of aggression and sexuality, and more importantly, with the bodily-states that accompany them, may produce severe distress, leading to further disruptions of mentalizing and the re-emergence of prementalizing modes of psychic reality as a means of coping with painful interpersonal experiences.

In order to develop the hypothesis that embodied mentalizing constitutes an important moderator of the relationship between attachment adversity and psychosis, we will further specify the computational psychiatric framework of psychosis as critically involving the relationship between certainty of the sensory (sensory-affective states) and belief (cognitive states) systems, and conclude by presenting a heuristic model of embodied mentalizing as a moderator of psychotic manifestations along their continuum of severity.

A Computational Framework for the Psychosis Continuum

The clinical developmental course of psychotic disorders, illustrated earlier in **Figure 1**, delineates periods characterized by sub-clinical and clinical manifestations associated with risk and onset of psychosis. At a descriptive level, these manifestations can be differentiated into relatively stable, *trait* abnormalities (such as the psychophysiological endophenotypes evidenced in both people with schizophrenia and their non-affected family members), and more transient state manifestations (such as thought disturbances and cognitive-perceptual abnormalities). In linking the descriptive and developmental perspectives, two important observations may be underlined. First, trait abnormalities involve a range of subtle impairments acting upon normative psychophysiological, sensorimotor and basic affective drive functions which presumably all reach maturity before puberty (Debbané and Barrantes-Vidal, 2015). For example, the schizophrenia endophenotype known as prepulse inhihibition characterizes abnormal sensory gating function, and is thought to reach adult-like levels around 8 years of age (Braff et al., 2001). Endophenotypes typically do not correlate with state manifestations of psychosis (Gottesman and Gould, 2003); they more likely influence the developmental cascade of higher order cognition, such as metacognition or mentalization, whose failures are apparent in the cardinal symptoms of psychosis. Second, these endophenotypes typically act as stable procedural regulation mechanisms for low-level processing. This would suggest that children at high-risk for psychosis (i.e., CHR or genetic high-risk individuals) develop higher cognitive functions (executive and social cognition) in the context of these subtle dysfunctions. It further suggests that at-risk individuals may need to compensate for slight abnormalities in the earliest stages of information processing, through higher-order cognition such as mentalization, appraisal, and/or metacognitive mechanisms (Debbané et al., 2016).

From a computational perspective, trait abnormalities along the continuum of psychosis have been framed as the brain's impairment in consistently predicting sensory input (Adams et al., 2013). With regards to sensory gating impairments, larger P50 responses confront the psychosis-prone individual with experiences of "surprise" in the context of closely contingent stimuli presentations. Later, along the information processing trajectory, reduced discriminatory responses evidenced by mismatch negativity or oddball paradigms speak to increased difficulty in discarding irrelevant information. Critically, such subtle impairments in early processing may significantly challenge higher cognitive functioning downstream in the information processing pathway. Following this hypothetical proposition, Kantrowitz et al. (2014) provide an empirical illustration of how early sensory processing impairments in patients with schizophrenia-spectrum disorders disturb higher order cognition, using the case of perception of sarcasm (Kantrowitz et al., 2014). The authors employ an experimental auditory functional neuroimaging task to measure sarcasm processing, in relation to two important sub-processing, namely pitch processing and emotion recognition. They find that early auditory processing impairments significantly contribute to decreased sarcasm perception in the patient group, independent of general cognitive impairment. Functional connectivity within the patient group's auditory processing network, but not within the core mentalizing network, correlated significantly with impaired sarcasm perception. This study nicely illustrates how subtle impairments in early sensory processing may, alter downstream, the deployment of accurate mentalizing. In control participants, functional connectivity between mentalizing core regions, including areas dedicated to embodied mentalizing (i.e., insular cortices) were engaged in sarcasm perception, suggesting the importance of assessing the cross-talk between the sensory-affective and cognitive processing regions when examining accurate mentalizing.

At the computational level, the relationship between the sensory and cognitive signals can be studied using a normative (Bayes-optimal) account of cerebral functioning. Adams et al. (2013) propose a computational account of the anatomy of psychosis, articulated within a hierarchical predictive coding model that may contribute, in part, to further examine the nature of trait and state manifestations of psychosis (Adams et al., 2013). Predictive coding assumes that the brain is an inference machine seeking to reduce its prediction error (Friston, 2010). From this perspective, the brain encodes a number of *priors* (e.g., prior beliefs, mentalizing working models about self and other, and/or metacognitive beliefs) on the basis of experience, and hierarchically construes a virtual interpretative algorithm, which continues to refine itself when it comes in contact with information that signals significant error of prediction. In technical terms, refinement of priors augment their *precision*, and putatively, the experience of certainty. Sensory-affective perception is characteristically precise and interpreted as "real" with an important degree of certainty, because it is easily accessible and can be reliably predicted. In our general experience, the brain encodes that our sensory experience is real (our senses do not lie), their signals are highly reliable. However, prior beliefs attenuate the experience of sensory precision, as for example, our cultural belief that the senses should not be fully trusted, emanating from Cartesian philosophy. The prediction algorithm's goal is to minimize surprise (error), and pursue its hierarchical elaboration to accurately compute increasing complexity that may be used to navigate within the world and interpret new information accurately.

In this account, (**Figure 3**) trait manifestations of psychosis risk, represented by endophenotypes, are conceptualized as the result of failures of top-down priors to attenuate the sensory-affective precision. As mentioned earlier, basic psychophysiological function such as sensory gating regulate the novelty or oddness of predictable (most often sensory) information. In computational terms, basic sensory gating mechanisms regulate the precision (certainty) of the sensory signal. In cases of subtle failures of these low-level regulatory mechanisms, sensory experience is attributed more precision (increased surprise, stronger certainty) and requires a top-down mechanism to attenuate certainty. In cases of weak prior beliefs (in other words, in cases of sub-optimal mentalization and/or metacognitive function—such as in children, or in at-risk individuals), even predictable sensory signals may be

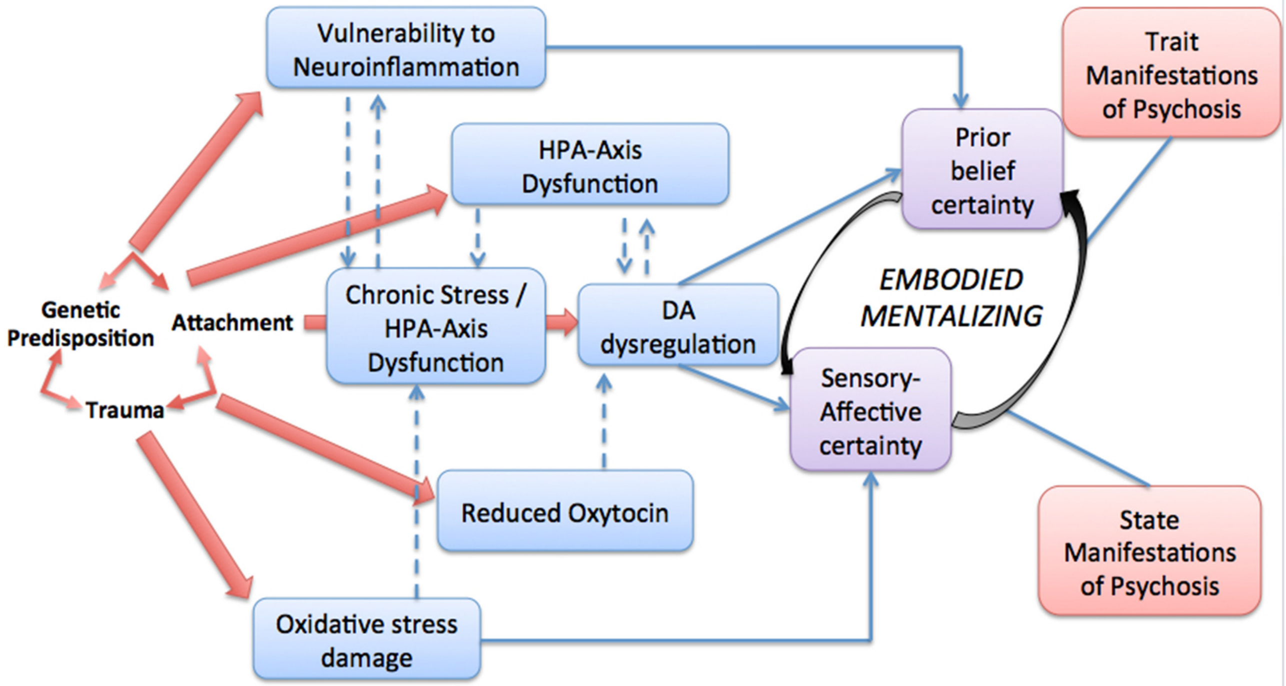

FIGURE 3 | Illustration adapting Figure 2 to account for the interaction between sensory and beliefs priors influencing each other's precision (certainty); at different levels of analysis, this relationship is foundational to embodied mentalizing, and may differentially sustain early trait vulnerability, and later state manifestations of psychosis.

experienced as somewhat newer, more surprising, and perhaps with a stronger sense of realness. Typical development of metacognitive skills, including mentalization, diminish the propensity to experience self-generated content as surprising or magical (Bartels-Velthuis et al., 2011; Debbané et al., 2013). The role of embodied mentalizing in regards to trait manifestations of psychosis would be to attenuate the sensory precision emanating from subtle impairments in low-level sensory gating regulation.

Turning now to CHR state symptoms, such as subclinical hallucinations, the computational framework argues that they may result from an increase in prior belief precision, such that they remain impervious to contrary (imprecise) sensory-affective evidence (Adams et al., 2013). Again, the focus is on the relationship of priors relative to sensory-affective precision that is key. Note that hallucinations could also result from a failure of the corollary discharge to attenuate the sensory precision of self-generated acts, such as inner speech (Fletcher and Frith, 2009). The case of delusions may be compensatory in nature, as a way for the system to discard overwhelming "surprise", i.e., sensory-affective precision of disturbing nature. Delusional explanations secondary to perceptual aberrations could fall under this explicative model. In essence, state symptoms of psychosis more directly involve the top-down component, which recruits a form of dis-embodied mentalizing where the sensory-affective signal is discarded to regulate its disturbing effects through extreme certainty in prior beliefs. This contemporary account resonates with the concept of "splitting" as a psychological defense mechanism put forward by psychoanalysis to account for psychotic functioning (Freud, 1911; Klein, 1946; Bion, 1957). The computational approach to splitting may enable direct and fine-grain hypothesis testing of different psychotic phenomena.

To summarize, the concept of embodied mentalizing provides a bridge to the theoretical propositions put forward by computational psychiatry, as it represents the integration of sensory-affective and metacognitive signals to modulate certainty of each, ensuring updating of beliefs and guidance of behavior. Further research is required to determine the mechanisms by which the interplay between the sensory-affective and metacognitive signals occur at different levels of analysis (cellular, network, systems and psychological levels).

CONCLUSION

This article provides a comprehensive review of the literature linking attachment, neurobiology and mentalizing along the continuum of psychosis expression, from the premorbid subclinical manifestations to full-blown psychotic disorder. This review has led us to propose an integrative model of psychosis based on three key assumptions: (1) attachment security constitutes a non-specific protective factor in individuals at increased risk for psychosis.; (2) Disturbed attachment can impact on at least five different neurobiological pathways implicated in sustaining self and other mentalizing; and

(3) Embodied mentalizing may serve as a moderating factor in the expression of psychosis.

At the interpersonal level, attachment security is associated with help-seeking behavior and with more favorable outcomes in individuals suffering from psychosis. In the preclinical stages of individuals at risk for psychosis, attachment security is associated with less severe manifestations of early trait signs (schizotypy). At the psychological level, attachment security provides a key developmental context to acquire the building blocks for robust social cognition and mentalizing. Disruptions in attachment are often linked to early trauma as well as bullying during adolescence. In some individuals, developmental adversity may promote the use of anxious, avoidant, or even disorganized attachment strategies. While these strategies may constitute adaptation attempts to adverse and hostile environments, they tend to undermine the development of the capacity to attend to one and others' minds (mentalizing), and they affect the unfolding of social cognitive skills. We suggest that the oft-cited relationship between insecure attachment, trauma and psychosis does not represent a causal, etiological chain towards psychotic disorders, but rather, a transactional process taking place during development, which increases the risk of transitioning to psychosis in at-risk individuals, by virtue of detrimental effects on self and other mentalizing during childhood and adolescence, particularly in relation to embodied mentalizing.

Second, the proposed integrative model suggests five developmental pathways through which disturbed attachment may affect the neurological integrity of key networks sustaining self and other mentalizing in individuals at risk for psychosis. Specifically, impairments in the HPA-axis, dopamine dysfunction, reduced oxytocin levels, neuroinflamation and oxidative stress all may constitute potential pathways through which genetic, interpersonal and environmental risk may impinge on otherwise vulnerable individuals. At the same time, adversity in early attachment has been shown to impact the severity of neuroinflammation, oxidative stress and HPA-axis dysfunction. These impairments may further interact with the dopaminergic and oxytonergic systems, known to be involved in regulating the reward and the salience of relationships in particular. Most importantly perhaps, these five neurobiological pathways are further involved in developmental alterations of sensory-affective processes (basic sensory-gating and affect regulation processes) as well as higher-order cognitive processes (reality monitoring and metacognitive reasoning) underpinning trait and state symptoms of psychosis.

Finally, we have pointed to the potential moderating role of embodied mentalizing in the expression of psychosis. Embodied mentalizing refers to the capacity of experiencing the body as the seat of emotional responses; as an active process it aims to reflectively detect, identify and regulate signals coming from one's body to harness them with one's mind. Recent advances in computational psychiatry have revived the interest in the relationship between sensory-affective experience and belief-reasoning (cognitive) processes. Normative functioning involves co-regulation between sensory-affective and cognitive processes to sustain the development of complex cognition, and also to prevent aberrant interpretations of experience. In the case where sensory-affective experience fails to be harnessed by regulatory or compensatory cognitive mechanisms, it can come to dominate subjective experience as expressed in trait symptoms of psychosis (from endophenotypes to negative symptoms). In cases where cognitive priors dominate and fail to be modulated by sensory-affective experience, state manifestations of psychosis are more likely to dominate the experience of the individual (from magical thinking to frank delusional ideation). The co-regulation between sensory-affective and cognitive, which can be subsumed under the notion of embodied mentalizing, may thus constitute a moderating set of processes along the continuum of psychosis expression.

The present model may assist in hypothesis building for neuroscientific research purposes, and also further inform the development of preventive treatment methods that target mentalizing as a protective factor, or psychotherapeutic methods focussing on mechanisms of change (Brent and Fonagy, 2014; Debbané et al., 2016; Weijers et al., 2016). Most importantly perhaps, treatment schemes such as mentalization-based treatment (MBT) may integrate a more pragmatic treatment paradigm in the early phases of an emerging psychosis promoted by the stage-sensitive conceptualization for treatment (McGorry et al., 2007). In its current form, the "clinical staging approach", which is extensively used for other progressive medical diseases, leaves many questions open, especially with regards to the active ingredients, also known as *mechanisms of change*, at every treatment stage of emerging psychotic disorders. Working from the bottom-up, the staging approach may benefit from therapeutic models that are developmental in nature, in order to achieve the kind of personalized-medicine it seeks to promote (McGorry, 2013). It may be that psycho-therapeutic care targeting mentalizing or social cognition may be superior to the general psychosocial care currently proposed for the early stages corresponding to CHR for psychosis. The latter remains an empirical question that will have to be examined as we enter a new stage of developing preventive treatments for psychosis.

AUTHOR CONTRIBUTIONS

All authors contributed to the conceptualization of the review. Each author worked specifically on a sub-section of the review, contributing literature review and writing. MD as well as GS merged the sub-sections and wrote the draft. All authors contributed in refining the final draft and approved of its contents.

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