



Network-Level Connectivity Dynamics of Movie Watching in 6-Year-Old Children

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Better understanding of the developing brain's functional mechanisms is critical for improving diagnosis and treatment of different developmental disorders. Particularly, characterizing how the developing brain dynamically reorganizes during different cognitive states may offer novel insight into the neuronal mechanisms of cognitive deficits. Imaging the brain during naturalistic conditions, like movie watching, provides a highly practical way to study young children's developing functional brain systems. In this study we compared the network-level functional organization of 6-year-old children while they were at rest with their functional connectivity as they watched short video clips. We employed both a data-driven independent component analysis (ICA) approach and a hypothesis-driven seed-based analysis to identify changes in network-level functional interactions during the shift from resting to video watching. Our ICA results showed that naturally watching a movie elicits significant changes in the functional connectivity between the visual system and the dorsal attention network when compared to rest ($t_{(32)} = 5.02$, $p = 0.0001$). More interestingly, children showed an immature, but qualitatively adult-like, pattern of reorganization among three of the brain's higher-order networks (frontal control, default-mode and dorsal attention). For both ICA and seed-based approaches, we observed a decrease in the frontal network's correlation with the dorsal attention network (ICA: $t_{(32)} = -2.46$, $p = 0.02$; Seed-based: $t_{(32)} = -1.62$, $p = 0.12$) and an increase in its connectivity with the default mode network (ICA: $t_{(32)} = 2.84$, $p = 0.008$; Seed-based: $t_{(32)} = 2.28$, $p = 0.03$), which is highly consistent with the pattern observed in adults. These results offer improved understanding of the developing brain's dynamic network-level interaction patterns during the transition between different brain states and call for further studies to examine potential alterations to such dynamic patterns in different developmental disorders.

Keywords: resting state functional connectivity, naturalistic stimuli, young children, functional network of the brain, developmental cognitive neuroscience

OPEN ACCESS

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Received: 17 July 2015

Accepted: 05 November 2015

Published: 23 November 2015

Citation:

Emerson RW, Short SJ, Lin W,
Gilmore JH and Gao W (2015)
Network-Level Connectivity
Dynamics of Movie Watching in
6-Year-Old Children.
Front. Hum. Neurosci. 9:631.
doi: 10.3389/fnhum.2015.00631

INTRODUCTION

Early school age is a particularly important developmental phase when complex brain functions are rapidly maturing, concurrent with children beginning their formal education. Studies aiming to unveil the mechanisms underlying normal human functional development are critical for better understanding and treatment of different developmental disorders. Functional connectivity studies based on naturalistic designs, such as movie watching, represent a unique opportunity for delineating functional brain mechanisms during a developmental period when task-based fMRI studies are not a viable option (Bartels and Zeki, 2005; Golland et al., 2007; Hasson et al., 2008, 2010; Emerson and Cantlon, 2012; Cantlon and Li, 2013). These types of studies provide a way to examine how the brain's network-level interactions differ between states, such as being at rest, watching a movie, or performing a task, while offering a feasible method to study functional brain development. Understanding the development of the brain's typical functional interactions represents an emerging emphasis for functional brain imaging research and may aid our understanding of both the brain's intrinsic functional structure and how this structure reorganizes to process various types of information.

In the mature adult brain, three higher-order networks are likely involved in the transition from rest to naturalistic stimuli conditions. First, the default mode network, which is commonly associated with internally directed cognitions (Gusnard et al., 2001; Buckner and Vincent, 2007; Mason et al., 2007; Buckner et al., 2008; Andrews-Hanna et al., 2010) and is reportedly activated during movie watching conditions (Iacoboni et al., 2004; Golland et al., 2007). This network commonly involves regions in parietal cortex (precuneus and posterior cingulate), bilateral inferior-lateral-parietal and ventromedial frontal cortex. Second, the dorsal attention network, which is primarily activated during goal-directed activities that require focused attention (Corbetta and Shulman, 2002; Fox et al., 2005, 2006). This network commonly involves regions in the frontal eye fields, ventral premotor cortex, superior parietal lobule, intraparietal sulcus, and motion-sensitive middle temporal area. These two networks are spatially distinct and likely interact differentially with other higher-order networks during uncontrolled rest vs. movie watching conditions. For example, compared to rest, the visual system is likely to weaken its connection with the dorsal attention network while passively viewing a movie but strengthen its connection to this network if involved in strenuous visual search task. Third, the fronto-parietal control network is spatially interposed between these two previously defined networks and covers regions identified as supporting cognitive control and decision-making processes including lateral prefrontal cortex, anterior cingulate cortex, and inferior parietal lobule (Vincent et al., 2008). The fronto-parietal control network shows enhanced connectivity with the default network but reduced interaction with the dorsal attention network during movie watching compared to resting conditions. Research examining these interactions in adults indicates that the fronto-parietal control network provides a mediating role between the "competing" default and dorsal

attention networks (Gao and Lin, 2012; Spreng et al., 2013; Elton and Gao, 2014). In other words, the fronto-parietal control network may play a role in guiding how the default and dorsal attention networks interact with each other as well as other functional networks. Taken together, research with adults indicates that the dynamic interaction between these three higher-order networks forms a functional set and that their interactions in the resting brain differ from their interactions during movie watching. However, in order to understand the developing brain's dynamic reorganization mechanisms, these interactions critically need to be investigated in school-aged children.

In this study, we sought to delineate the changing functional connectivity of 6-year-old children's network-level interaction patterns between rest and naturalistic movie watching by conducting functional magnetic resonance imaging (fMRI) scans during each of the two conditions. We tested the differences between these conditions in two steps. First, we performed a data-driven whole brain analysis that identified canonical functional networks and tested the changes between the conditions. Second, we used established regions of interest to perform a seed-based analysis identical to a previous analysis in adults (Gao and Lin, 2012). We predicted that school-age children's pattern of network-level interactions would be similar to adults, but the magnitude of their functional interactions would be immature. Specifically, we predicted that the frontal control network should show an increase in connectivity with the default network but a decrease in connectivity with the dorsal attention network during movie viewing when compared with rest. Because of the increase in the complexity of visual stimulation, we also expected that the visual network would decrease its connectivity with the dorsal attention network and increase its connectivity with the default network during passive viewing.

MATERIALS AND METHODS

Subjects

Thirty-three typically developing 6-year-old children were included in final analysis of this study (17 females and 16 males; mean age = 6.10 ± 0.11 years). All participants were healthy, with no history of neurological impairments or abnormalities and no parental history of major psychiatric illness. Participants were initially recruited for a larger longitudinal study examining brain development from birth through early childhood in typical and high-risk children (Li et al., 2014). Thus, any participants at genetic high-risk for schizophrenia or bipolar disorder, based on maternal diagnosis, were excluded from this study. All guidelines and requirements of the University of North Carolina's Research Subjects Review Board were followed for participant recruitment and experimental procedures.

Stimuli

For the resting state fMRI (rsfMRI) scan, children were instructed to keep their eyes open while a white fixation cross was presented in the middle of a black screen. The

second connectivity scan was acquired while children viewed an age appropriate movie of their choice. Each scan lasted approximately 5 min and the resting state scan was always acquired first at the start of the imaging session.

Image Acquisition

All images were acquired using a 3-T MR scanner (Siemens Medical Systems, Erlangen, Germany) housed in the Biomedical Research Imaging Center (BRIC). All fMRI data was acquired using a T2*-weighted EPI sequence: time repetition (TR) = 2 s, time echo (TE) = 32 ms, 33 slices, voxel size of $4 \times 4 \times 4 \text{ mm}^3$. One hundred and fifty volumes were acquired in 5 min. In order to provide anatomical reference, structural images were acquired using a 3D Magnetization Prepared Rapid Acquisition Gradient-recalled Echo sequence (TR = 1820 ms, TE = 4.38 ms, in-version time = 1100 ms), with a voxel size of $1 \times 1 \times 1 \text{ mm}^3$. To reduce motion children's heads were secured with foam padding.

Preprocessing

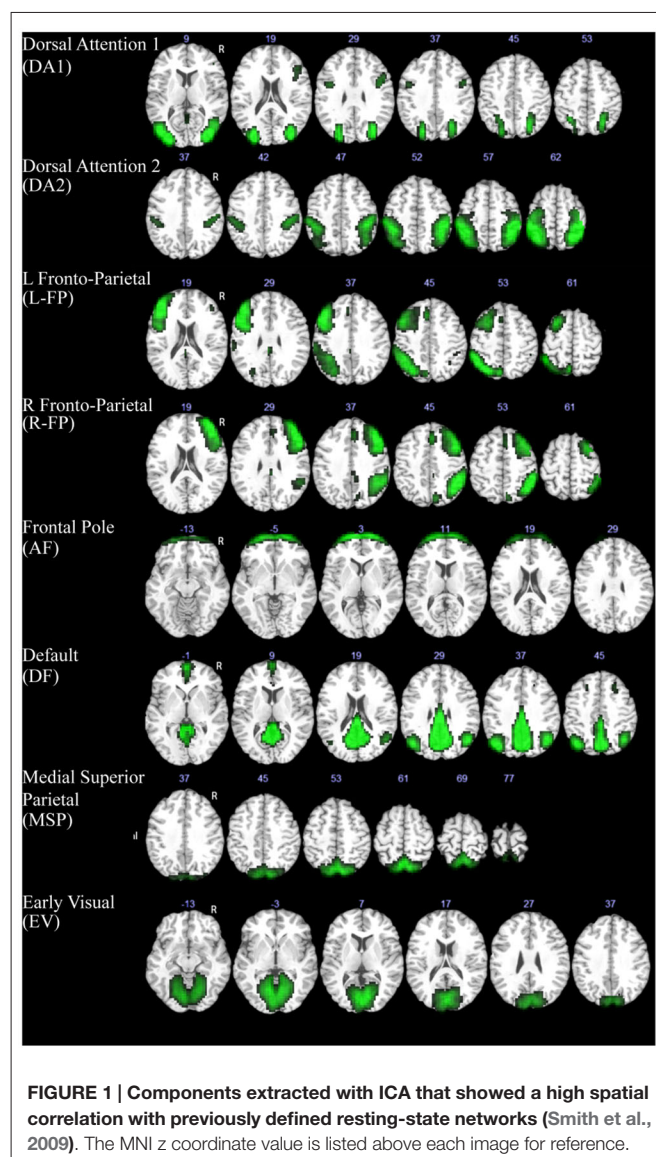
Functional data were preprocessed using FMRIB's Software Libraries (FSL, v 4.1.9; Smith et al., 2004). The preprocessing steps included discarding the first 10 volumes, slice timing correction, motion correction, high-pass ($>0.01 \text{ Hz}$) and low-pass filtering ($<0.08 \text{ Hz}$). Mean signal from white matter, cerebrospinal fluid, whole brain, and six motion parameters were removed using linear regression. Spatial smoothing was applied with a Gaussian kernel of 6 mm full width at half maximum. In order to further reduce the effect of motion on functional connectivity measures, the "scrubbing" approach of controlling the global measure of signal change (0.5%) and frame-wise displacement (0.5 mm) was carried out as proposed by Power et al. (2012). Subjects with more than one-third of volumes (i.e., 50 volumes) removed from the scrubbing procedure were excluded from subsequent analyses. In total, three subjects were removed, leaving the final 33 subjects for further analysis. For each subject and session, after an initial rigid alignment between functional data and the T1 high-resolution structural images, a nonlinear transformation field was obtained from the individual T1 images to the MNI template using FSL. The combined transformation field was used to warp the preprocessed rsfMRI data to the template.

Network Analyses

Group-level independent component analysis (ICA) was performed on all rsfMRI data using GIFT v2.0 toolbox for Matlab (Calhoun et al., 2001). The 20 extracted group-level spatial ICA maps of independent resting-state networks (RSNs) were scaled to z-scores with a threshold of $z > 3$ (corresponding to a significance level of $p < 0.05$). These component maps were then visually inspected and labeled based on the spatial patterns in reference to known anatomical and functional locations (Tzourio-Mazoyer et al., 2002). Components that captured motion artifacts were removed. Subject-specific spatial maps and time courses were estimated for each remaining component and were then back-reconstructed using GIFT

(Calhoun et al., 2001). We further identified a subset of components that matched one of the brain's 10 canonical RSNs (Smith et al., 2009) and subsequent analysis were done on those components that are related to movie watching (i.e., the default mode network, the dorsal attention network, the frontoparietal network, and the visual networks). To ensure a good match, each component was spatially correlated with network templates and a threshold of $r > 0.40$ was used to identify corresponding components. In total there were eight identified components that met these criteria and were used for further analysis (Figure 1).

Individual whole brain spatial maps for each subject were compared between resting and movie watching using paired *t*-tests for each included component. Using each subjects' back-reconstructed component time course, pairwise correlations were calculated between each component to assess network-level functional connectivity. Paired *t*-tests were then performed



between resting and movie watching data for each of the network-level connections. Within-network connectivity was evaluated based on the back-reconstructed spatial map of each ICA network for each subject. Specifically, voxel-wise comparisons were done using paired *t*-test based on the individual spatial maps to test whether there were any significant differences in within-network connectivity. The false discovery rate (FDR; Benjamini and Yekutieli, 2001) method was used to correct for multiple comparisons and significant connections were defined at $q < 0.05$ after FDR correction.

A seed-based analysis was also performed with network seeds that were previously tested in adults during a similar task (Gao and Lin, 2012). These network seeds are shown in **Figure 2** and **Table 1**. Specifically, we tested the interconnectivity of the visual, dorsal attention, default mode, and fronto-parietal networks. A 5 mm sphere was created around each of the 32 coordinates and the average time course was extracted for each subject. For each individual, time courses were correlated between each network seed. After Fisher's *z* transform and averaging across all subjects, group mean matrices were obtained for each pair of seeds during resting and movie watching states and then used to test the differences between both states. Each network's connectivity was tested using a one sample *t*-test from 0 to identify significant positive/negative interactions. For between-network comparison, the interactions between two networks were averaged for each subject and then compared between movie watching and resting states using paired *t*-tests. Similarly, for within-network comparisons, the correlation between all nodes of a network were averaged for each subject and compared across states using paired *t*-tests. $P < 0.05$ after FDR correction was considered significant.

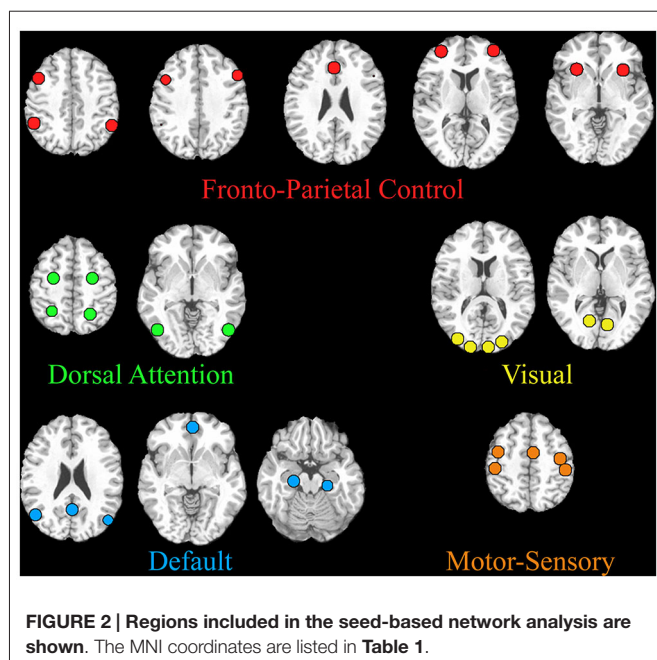


TABLE 1 | MNI coordinates for the regions of interest within the five predefined networks in adults.

Dorsal attention	lMTp: (−45, −69, −2) rMTp: (50, −69, −3) lIPS: (−27, −52, 57) rIPS: (24, −56, 55) lFEF: (−25, −8, 50) rFEF: (27, −8, 50)
Fronto-parietal control	laPFC: (−36, 57, 9) raPFC: (34, 52, 10) ACC: (3, 31, 27) laIPL: (−52, −49, 47) raIPL: (52, −46, 46) ldlPFC: (−50, 20, 34) rdlPFC: (46, 14, 43) lINS: (−31, 21, −1) rINS: (31, 22, −2)
Default mode	lHF: (−21, −15, −14) rHF: (24, −19, −21) vmPFC: (0, 51, −7) PCC: (1, −55, 17) lpIPL: (−47, −71, 29) rpIPL: (50, −64, 27)
Visual	lCal: (−8, −72, 4) rCal: (16, −67, 5) lCS: (−5, −96, 12) rCS: (18, −96, 1) lLO: (−23, −89, 12) rLO: (37, −85, 13)

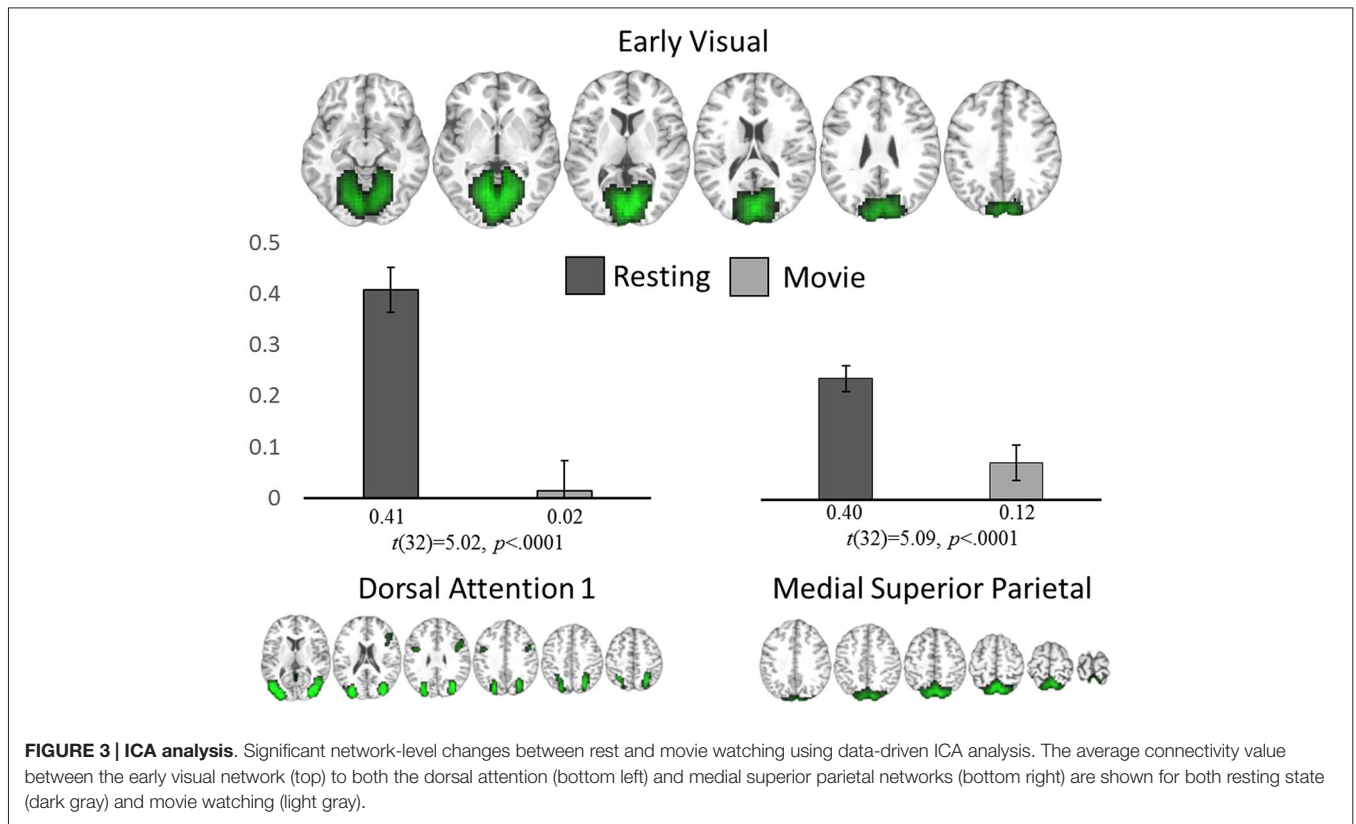
These coordinates define the center of a 5 mm sphere used in the seed-based analysis. aPFC, anterior prefrontal cortex; dlPFC, dorsal lateral prefrontal cortex; ACC, anterior cingulate cortex; INS, insula; aIPL, anterior inferior parietal lobule; IPS, bilateral intra-parietal sulcus; FEF, frontal eye field; MTp, middle temporal area; PCC, posterior cingulate cortex; MPFC, medial prefrontal cortex; pIPL, bilateral posterior inferior parietal lobule; HF, hippocampus formation; Cal, bilateral calcarine; CS, cuneus; LO, lateral occipital.

RESULTS

ICA Analysis

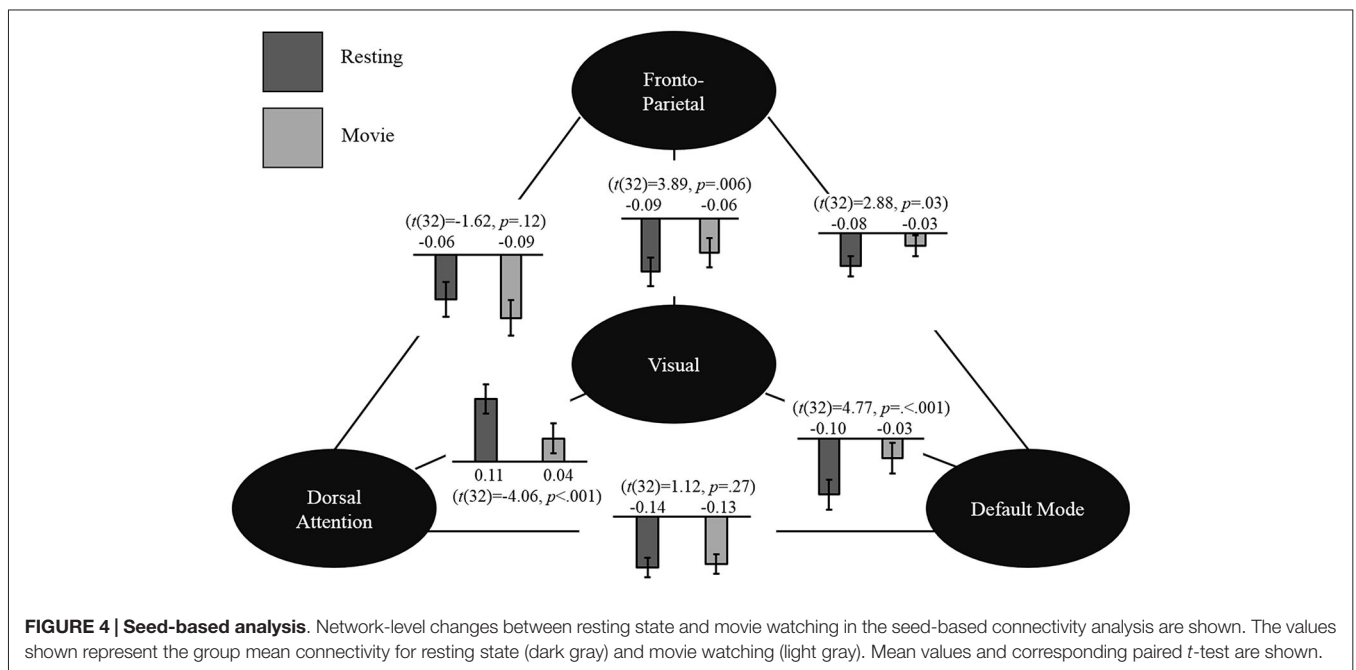
The ICA analysis produced a total of eight components that met the specified criterion and were included in further analyses. These networks included two dorsal attention components (DA1, DA2), bilateral frontal-parietal components (L-FP, R-FP), a default-mode network component (DMN), an anterior frontal control component (AF), a medial superior parietal component (MSP), and an early visual component (EV; **Figure 1**).

Whole brain comparisons of the component spatial maps revealed no significant differences in within-network connectivity between rest and movie watching. However, two inter-network connections showed a significant difference; EV significantly reduced its connectivity with DA1 ($t_{(32)} = -5.02$, $p = 0.0001$) and MSP ($t_{(32)} = -5.09$, $p = 0.0001$) during movie watching (**Figure 3**) when compared with rest. At rest, the EV component was significantly positively correlated with both DA1 ($r = 0.41$, $p = 0.01$) and MSP ($r = 0.40$, $p = 0.01$) while during movie watching, it desynchronized with DA1 ($r = 0.01$, $p = 0.83$ in a one-sample *t*-test from 0) and maintained a reduced positive connectivity with MSP ($r = 0.12$, $p = 0.03$).



Post hoc analyses (described above) were carried out to test our hypothesis regarding the three higher order networks (i.e., DA1, DA2, DM, L-FP, R-FP and AF, **Figure 4**). While none of the differences in inter-network connections between rest and movie

watching reached significance after FDR correction, there were some interesting trends. Specifically, AF decreased its correlation with DA1 ($t_{(32)} = -2.46, p = 0.02$) and increased its connectivity with DMN ($t_{(32)} = 2.84, p = 0.008$), which is highly consistent



with the trend observed in adults. Additionally, AF also increased its connectivity with EV ($t_{(32)} = 2.81, p = 0.008$), and L-FP ($t_{(32)} = 2.74, p = 0.009$). Other state-related changes in connections between these networks did not show any uncorrected trends in significance (all $p > 0.05$). These results suggest that children share a similar but immature pattern of network-level functional reorganization during the transition from movie watching to rest when compared with adults.

Seed-Based Analysis

To further validate the observed pattern, we conducted seed-based analyses using previously defined network seeds in adults (Gao and Lin, 2012). As expected, the fronto-parietal network showed a trend of decreased connectivity with the dorsal attention network ($t_{(32)} = -1.62, p = 0.12$) and increased connectivity with the default mode network ($t_{(32)} = 2.28, p = 0.03$). Moreover, highly consistent with the ICA results reported above, the visual network significantly increased its connectivity with the default mode ($t_{(32)} = 4.77, p < 0.001$) and fronto-parietal networks ($t_{(32)} = 3.89, p = 0.006$), while significantly decreasing its connectivity with the dorsal attention network ($t_{(32)} = -4.06, p = 0.001$) during moving watching. Finally, the dorsal attention and default mode network were found to be anticorrelated during both rest ($r = -0.14, p = 0.02$) and movie viewing ($r = -0.13, p = 0.03$) and no significant difference was detected for this network-level interaction ($t_{(32)} = 1.12, p = 0.27$). The general pattern of results is displayed in **Figure 4**.

DISCUSSION

In this study, we aimed to delineate the dynamic reorganization pattern of the brain's functional networks during the transition from rest to naturalistic movie watching in a cohort of healthy 6-year-old children. Our results revealed that movie watching in children elicits significant uncoupling between the visual input network and dorsal attention network, which is accompanied by an adult-like, but immature, reorganization pattern of the network-level interactions among three higher order networks: the dorsal attention, the default-mode, and the frontal control network. Characterizing typical functional connectivity dynamics in young children can provide insight into how the brain supports their growing set of cognitive skills and behaviors, and eventually may allow for objective identification of cognitive or functional delays and developmental abnormalities.

Many studies have found a relationship between disruptions of intrinsic functional networks (i.e., measured at rest) and atypical cognitive development in different neurodevelopmental disorders (Cao et al., 2009; Church et al., 2009; Vogel et al., 2010; Bray et al., 2011; Elton et al., 2014). However, to further extend our understanding of the neurobiological basis of developmental disorders with specific cognitive deficits, it is beneficial to examine the brain's dynamic functional organization during the transition from resting to corresponding task states (Gao and Lin, 2012; Gao et al., 2013; Spreng et al., 2013; Elton and Gao, 2014, 2015). Presently, one of the biggest challenges in studying younger children's functional development in the context of cognitive tasks is the fact that traditional task-based

fMRI experimental designs often fail to engage young children, leading to a very low success rate. Collecting data during natural viewing conditions has the potential to usurp these challenges, representing a realistic and practical method to study the developing brain. Specifically, by experimentally controlling the content of the movies, researchers will be able to determine how the brain accesses particular types of information while under conditions that mirror those found in everyday experience, making it feasible to explore the functional organization of children's minds before they enter school. Neuroimaging data from this critical time in development is currently extremely limited. Dynamic network-level functional connectivity analyses in young children using naturalistic stimuli, as done in this study, will benefit further research that aims to explore how individual differences in functional brain networks are related to different domains of cognitive functions.

Overall, our results suggest that the dynamic reorganization patterns of the brain's major functional networks in early school-age children feature large changes related to the visual input network and an immature, but similar interaction pattern among three higher order cognitive networks. Specifically, we detected a significant reduction in functional connectivity between the visual input network and the dorsal attention network during movie watching. This pattern could reflect a shift in children's visual processing away from the goal-directed focus of attention that is typically associated with the dorsal attention network when they watch movies. The dorsal attention network has been hypothesized to generate and maintain a goal-directed, top-down signal to selectively bias visual cortical activity (Gitelman et al., 1999; Hopfinger et al., 2000; Corbetta and Shulman, 2002) and is typically active during visual search, visuospatial cuing, and other goal-directed tasks that involve spatial attention. It's possible that the movie watching state may incur substantial internally driven cognitive processes so the visual input network may become more coupled with the default-mode network. Indeed, a significant enhancement of the functional connectivity between the visual network and the default-mode network during movie watching was observed in our subsequent seed-based analyses. Therefore, our results indicated that there is likely a rebalancing of top-down control of the primary visual network during the transition from resting to movie watching, potentially reflecting a shift away from external, goal-directed search to internally driven processing.

For the dynamic interaction patterns among the dorsal attention, frontal control, and default-mode networks, our *post hoc* analyses revealed a qualitatively adult-like pattern. Specifically, the frontal control network shows up-regulated connectivity with the default mode network and down-regulated connectivity with the dorsal attention network (DA1) which is highly consistent with patterns observed in adults during similar movie watching state (Gao and Lin, 2012). This ICA-derived pattern is further confirmed with our seed-based hypothesis-driven analysis, supporting the robustness of this finding. However, the children's network-level interactions among these three higher-order cognitive networks only show marginally significant changes between resting state and movie watching. With the bigger sample size employed in this study compared

with other adult studies it is not likely that these statistically weaker changes are driven by a lack of power. Rather, these results suggest that the network-level dynamic interaction patterns observed in adults are immature in children.

In contrast to the immature connections observed in our ICA analysis, we consistently found a relatively adult-like anticorrelation pattern between the default-mode network and dorsal attention network in children during both rest and movie watching. This anticorrelated relationship represents a mechanism that is postulated to mediate the switch between internal and external processes (Corbetta and Shulman, 2002; Fox et al., 2005, 2006). One of our previous studies suggests that this relationship emerges during infancy (Gao et al., 2009, 2013) so it would likely be already established by 6 years of age. Given this adult-like interaction pattern between the default mode and dorsal attention networks, the immature reorganization pattern among the three higher-order networks observed in this study is likely driven by the protracted development of the frontal control network. By 6 years of age, the brain volume is already approximately 95% of the adult size. However, at this period in development the brain is undergoing a critical fine-tuning process along with forms of cellular maturation, such as myelination and synaptic pruning, allowing for further cognitive development, particularly in the frontal lobe (Rakic et al., 1994; Huttenlocher and Dabholkar, 1997; Amso and Casey, 2006; Petanjek et al., 2008). Behaviorally, higher-order executive control functions such as planning, cognitive flexibility, inhibitory control, and attention change dramatically from early childhood to young adulthood (Luna et al., 2004). Resting state fMRI studies have demonstrated a shift from diffuse to focal activation patterns and simultaneous pruning of local connectivity paired with strengthening of long-range connectivity from later childhood to late adolescence (Fair et al., 2009; Power et al., 2010; Uddin et al., 2010). Therefore, it is likely that the maturation of the functional connections of the frontal network underlies the continued development of children's executive functions, particularly with their ability to regulate the processes governed by the dorsal attention and default networks. Further research linking individual differences in functional network organization to cognitive function is needed to support this hypothesis.

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One limitation of the current study is that our subjects are watching different movies of their own choice, which limits specific interpretations of the observed functional connectivity changes. Future studies that utilize the same movie stimuli across subjects are warranted to validate the current findings. Further research is also needed to determine the effects that the immature relationship between the frontal control network and the dorsal attention and default networks have on children's individual cognitive and behavioral profiles. Eventually such knowledge might allow researchers to assess children's risk for various disorders, like ADHD, from a very young age.

CONCLUSION

In the current study, we identified differences in the network-level functional connectivity during the naturalistic condition of movie watching compared to resting in a cohort of healthy 6-year-old children. Our results from both the data-driven ICA and hypothesis-driven seed-based analyses show that changes in children's functional interactions during naturalistic movie watching are supported primarily by their visual system in tandem with their developing higher-order cognitive networks. Specifically, significant changes in connectivity between the visual and attention-related networks are observed which are accompanied by a maturing tri-network interaction patterns among the default-mode, dorsal attention, and frontal pole networks. By examining the dynamic functional connectivity changes between resting state and naturalistic movie watching in young children, this study provides novel insights into our understanding of how children process complex stimuli, revealing a developmental immaturity in the frontal lobe's contribution to the interactions between three of the brain's higher-order functional networks. Future studies using a similar design could provide a more advanced insight into how the brain's functional networks, in the early years of life, are related to typical cognitive development and developmental disorders.

ACKNOWLEDGMENTS

This work was supported in part by NIH funding to JHG (MH070890), SJS (1K01MH099411) and UNC start-up fund to WG R21 grant (1R21NS088975-01A1).

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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