Decreased functional connectivity of the salience network during narrative comprehension in children with reading difficulties: An fMRI study

Emma Twait[a], Rola Farah[a], Tzipi Horowitz-Kraus[a,b,c,*]

[a] Educational Neuroimaging Center, Faculty of Education in Science and Technology, Technion, Israel
[b] Faculty of Biomedical Engineering, Technion, Israel
[c] Reading and Literacy Discovery Center, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, United States

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ABSTRACT

Dyslexia is a neurobiological learning disability, reflected through deficits in written (i.e. reading) but not in spoken language. Since written and spoken language rely on cognitive control abilities, we aimed to compare functional connectivity of the understudied salience network which is related to cognitive control in children with dyslexia vs. typical readers during a functional MRI narrative comprehension task. Although children with dyslexia showed similar comprehension levels as typical readers, neuroimaging data revealed children with dyslexia showed significantly decreased functional connectivity values of an independent component (IC) related to the salience network. The functional connectivity values in the salience network IC were negatively correlated with behavioral data of working memory in those with dyslexia. These findings further express that dyslexia is manifested through atypical involvement of neural circuits related to EF, specifically the salience network even when attending narratives. Since the salience network is related to switching abilities and error detection, future research should focus on strengthening these abilities early in life for better future reading outcomes.

1. Introduction

Narrative comprehension is an ability we engage in every day, starting from early on in development, when we listen and comprehend oral stimuli (Vannest et al., 2009). A theoretical model that explains the overlapping of narrative comprehension and reading is the simple view of reading model (Gough and Tunmer, 1986). This model proposes two main mechanisms for successful reading: word recognition and comprehension. This model is backed with neural evidence that narrative comprehension and reading have overlapping neural circuits, even though narrative comprehension develops earlier in life (Horowitz-Kraus et al., 2013). Executive functions (EFs), such as working memory and attention, are utilized during narrative comprehension (Schmithorst et al., 2006) and reading (Fitzpatrick and Pagani, 2012). This parallels with the neural circuitry in frontal areas (e.g., activation in BA 40) shared in both reading and narrative comprehension tasks (Horowitz-Kraus et al., 2013; Bach et al., 2010). Therefore, a question arises as to the involvement of neural circuits related to EF during narrative comprehension in children with dyslexia.

Dyslexia is a neurobiological learning disability, defined by word recognition difficulty and poor spelling abilities despite normal intelligence and adequate education and exposure to written material (Shaywitz and Shaywitz, 2008) that affects 5–17% of the population (Gabrieli, 2009). Reading deficits primarily categorize the disorder; however, EF deficits (Brosnan et al., 2002) are also observed in children with dyslexia. Children with dyslexia also perform worse on narrative comprehension tasks, with activation in neural circuits related to EF such as in the right superior frontal gyrus and the left middle frontal gyrus in the reading-impaired group, suggesting a role of EF in narrative comprehension as well as in reading (Horowitz-Kraus et al., 2016). Part of this difficulty is manifested in a deficient error monitoring system, seen as part of cognitive control as it involves behavioral switching and adaptation (Ham et al., 2013).

1.1. EF difficulties in children with dyslexia

Several challenges previously reported in individuals with dyslexia are related to the role of the salience network. One example is error monitoring, correlated to the salience network, composed of the dorsal anterior cingulate cortex and bilateral insula (Ham et al., 2013). Errors result in activation of the salience network (Ham et al., 2013). Similar studies on individuals with dyslexia have explored the error-related

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negativity response (in the anterior cingulate cortex) with electro-encephalogram event-related potential methods (EEG-ERP). The error-related negativity (ERN) response, present after an erroneous response, has been found to have less amplitude in individuals with dyslexia (Horowitz-Kraus and Breznitz, 2008). Several studies related the con-nectivity of this network to the ability to switch attention from basic to higher-order functioning (Ibrahim et al., 2015), an ability which chil-dren with dyslexia have difficulties in, as was found in the Wisconsin task (Horowitz-Kraus, 2014). Further, decreased functional con-nectivity of the cingulo-opercular network, which the anterior cingulate is also a component of, has been found in children with dyslexia and correlated with decreased reading ability (Horowitz-Kraus et al., 2015a; Horowitz-Kraus et al., 2015b; Horowitz-Kraus and Holland, 2015). Despite this evidence, the role of the salience network has yet to be explored in individuals with dyslexia, which is the topic of the current study.

As the salience network has yet to be examined in dyslexia, ex-ploring connectivity differences in these areas during a narrative comprehension task (arising prior to reading) is crucial to fill a gap in the current literature on dyslexia. Such results will allow us to explore the neural correlates behind switching dysfunction in individuals with dyslexia, leading to better intervention and screening techniques.

The aim of the current study was to explore functional connectivity of components related to error monitoring and switching in children with dyslexia during a stories listening task using an independent components (ICs) analysis. We hypothesized a positive correlation be-tween functional connectivity of the salience network with behavioral scores (i.e., reading and EF) based on studies finding an association between decreased functional connectivity of the cingulo-opercular network and lower reading ability. As less amplitude has been seen using the ERN response in individuals with dyslexia, we hypothesized that decreased functional connectivity could be present in dyslexia due to dysfunction in error detection.

2. Methods

2.1. Participants

Children with dyslexia ($N = 31$; mean age = 10.03 years, SD = 1.33 years; 10 females, 25 right-handed) and typical readers ($N = 35$; mean age = 10.27 years, SD = 1.32 years; 18 females, 35 right-handed) participated in the current study. No significant age difference between the two groups was found [$t(64) = 0.75$, $p = .46$]. All participants were monolingual native English speakers. Both groups performed the behavioral and neuroimaging measures. Participants had no history of neurological or psychiatric impairments. Informed consent and assent was given by the parents and participants. The study was reviewed and approved by the Cincinnati Children's Hospital Institutional Review Board.

2.2. Behavioral measures

2.2.1. Executive functioning measures

Executive functioning was assessed using the Behavior Rating Inventory of Executive Function (BRIEF) (Gioia et al., 1996), with the subtests focusing on inhibition, shifting, emotion regulation, behavior regulation, initiative, working memory, planning and organizing, or-ganization of materials, monitoring, metacognition, and an overall global executive composite. The Wechsler Intelligence Scale for Chil-dren (WISC) was also used to assess cognitive ability (specifically the Digit Span Backward subtest) (Wechsler et al., 2012).

2.2.2. Reading measures

Reading abilities were assessed via the Comprehensive Test of Phonological Processing (CTOPP) (specifically the Elision subtest of phoneme manipulation, number naming, and letter naming) (Wagner

et al., 2013) and the Test of Word Reading Efficiency (TOWRE) (spe-cifically the sight word efficiency [SWE] and the phonetic decoding efficiency [PDE] subtests) (Torgesen et al., 1999).

2.3. Neuroimaging data

2.3.1. Narrative-comprehension task

Five stories were presented for a task period of 30-s, with a random noise presented at 200–400 Hz between each story to control for sub-lexical auditory processing. There were 5 blocks per condition (an overall of 10 blocks) (Schmithorst et al., 2006). The stories were be-tween nine to eleven sentences, differing syntax. An example of one of the stories is as follows:

"A frog lived under a flower in the garden.
One day, a little boy picked the pretty flower.
So the frog, who missed his flower, went inside.
"Where could my flower be?" thought the puzzled frog.
A cat sat in the chair above the frog.
The cat blinked his eyes and wiggled his ears.
The frog was scared and hopped in a cup.
The boy saw the frog hiding inside the cup.
He took it outside for the frog's new home" (Schmithorst et al., 2006).

Participants were instructed before the task to attend to the stories and informed that questions will follow the task pertaining to the stories. After all stories were presented, participants were asked to answer ten multiple-choice questions based on the five stories, two questions per story. An example of one of the post-scan questions is:

"Where did the frog live?

  a. under a flower
 b. in the house
 c. in the river
 d. on the roof" (Schmithorst et al., 2006).

2.3.2. MRI acquisition and data preparation

Participants were desensitized prior to the MRI scan, through ex-ploration of the environment with positive reinforcement and practi-cing sitting on the scanner bed "as still as a statue" (Vannest et al., 2014). Motion was controlled for by using elastic straps on either side of the head-coil apparatus, with an additional headband strap across the forehead. After the child was comfortable, a movie began via an MRI-compatible audiovisual system and scanning began. Communica-tion between the child and study coordinator was established through headphones equipped with a built-in microphone. All children were awake during the entire scan.

All participants were scanned using a 3 T Philips Achieva MRI scanner. For presentation of the stimuli (including the movie), an MRI-compatible audio/visual system (Avotec, SS3150/SS7100) was used. A gradient echo planar sequence was used for T2*-weighted BOLD fMRI scans with the following parameters: TR/TE = 2000/38 ms, BW = 125 kHz, FOV = 25.6 × 25.6 cm, matrix = 64 × 64, and slice thickness = 5 mm. Thirty-five slices covered the entire cerebrum. Seventy-eight image volumes were acquired during the fMRI experi-ment consisting of 30 s per condition for a total acquisition time of five minutes and 30 s. For each participant, a 3D T1-weighted inversion recovery gradient echo anatomical whole-brain scan also was acquired for anatomical co-registration and use in spatial normalization of the functional MRI data.

2.3.3. Data pre-processing

Pre-processing of the functional MRI data included slice-time cor-rection, realignment to the first image of the session for motion cor-rection using 3 translational and 3 rotational parameters, coregistration

Table 1
Independent *t*-test analyses of behavioral data between the groups.

Measures	Typical readers (A) M (SD)	Children with dyslexia (B) M (SD)	Contrast	T	P
EF measures					
Parent report					
Inhibition, standard score	45.71(8.87)	54.19(10.59)	B > A	−3.54	0.001
Shifting, standard score	47.71(11.19)	54.39(12.80)	B > A	−2.26	0.03
Emotional, standard score	47.23(9.27)	54.65(10.60)	B > A	−3.03	0.004
Behavior Regulation, standard score	46.14(10.09)	55.16(9.16)	B > A	−3.78	0.00
Initiative, standard score	47.91(10.69)	55.06(10.48)	B > A	−2.74	0.008
Working memory, standard score	45.80(8.93)	56.00(9.93)	B > A	−4.40	0.00
Plan/organize, standard score	44.40(9.27)	57.84(10.55)	B > A	−5.51	0.00
Organization of materials, standard score	48.71(10.26)	55.74(9.89)	B > A	−2.82	0.006
Monitor, standard score	44.49(8.57)	55.68(7.80)	B > A	−5.52	0.00
Metacognition index, standard score	45.23(9.37)	57.35(9.25)	B > A	−5.28	0.00
GEC, standard score	44.60(10.98)	56.94(8.76)	B > A	−5.00	0.00
Performance tasks					
Digit span backward, number of digits recalled *(working memory)*	6.26(1.70)	5.35(1.36)	A > B	16.33	0.00
Letter naming, scaled score *(rapid naming)*	10.17(2.14)	7.81(2.74)	A > B	3.94	0.00
Reading measures					
Elision test, scaled score *(phonological awareness)*	10.66(2.38)	7.55(2.43)	A > B	5.25	0.00
Number naming, scaled score *(rapid naming)*	11.06(2.18)	8.42(2.88)	A > B	4.22	0.00
Sight word efficiency, scaled score	105.89(10.95)	81.84(14.97)	A > B	7.51	0.00
Phonetic decoding efficiency, scaled score	106.17(9.76)	81.74(12.40)	A > B	8.94	0.00

of the anatomical image to the mean aligned functional image, normalization of all images to the Montreal Neurological Institute [MNI] template, suited for children age 5 and above, and spatial smoothing with a 8-mm full width at half-maximum [FWHW] Gaussian kernel. This process was done using SPM12 (Wellcome Department of Cognitive Neurology, London; http://www.fil.ion.ucl.ac.uk/spm/). To assess movement in the scanner, as it is a confounding factor especially in pediatric populations, an average of the framewise displacement was calculated, with a total average of 0.30 mm amongst all participants. An independent *t*-test confirmed no difference in framewise displacement between typical readers ($M = 0.31$, $SD = 0.28$) and children with dyslexia ($M = 0.39$, $SD = 0.30$) ($t(64) = -1.11$, $p = .3$). Following pre-processing, the functional data were fed into the independent component analysis (ICA) pipeline in the functional connectivity (CONN) toolbox Version 17f (Whitfield-Gabrieli and Nieto-Castanon, 2012).

2.3.4. Independent component analysis

The post-processed images were submitted to a subject-wise group ICA implemented in the MATLAB-dependent (The Mathworks, Natick, MA; https://www.mathworks.com/products/matlab.html) functional connectivity (CONN) toolbox Version 17f (Whitfield-Gabrieli and Nieto-Castanon, 2012). Conn includes a pre-defined networks atlas, with the salience network defined as these seven MNI regions-of-interest (ROIs):

Anterior cingulate cortex (0, 22, 35), left anterior insula (−44, 13, 1), right anterior insula (47, 14, 0), left rostral prefrontal cortex (−32, 45, 27), right rostral prefrontal cortex (32, 46, 27), left superior marginal gyrus (−60, −39, 31), and the right superior marginal gyrus (62, −35, 32).

The group ICA was performed with twenty factors and a dimensionality reduction of sixty-four. Out of all the twenty ICs, only one IC corresponded with the salience network and was selected for further analyses: the IC related to the salience network, determined via a correlational spatial match-to-template using the pre-defined networks created by Conn. The connectivity values for each cluster in the salience IC were exported from CONN and imported into the Statistical Package for Social Sciences, v.24 (SPSS, Chicago, IL). Then, for each participant, the cluster values were averaged for one IC value per participant. Results were corrected for multiple comparison in Conn with a p-FDR corrected value of < 0.05.

2.4. Statistical analysis for the behavioral data

In order to find differences between children with dyslexia and typical readers, in executive functioning and reading measures, independent two-sample *t*-tests were performed on the behavioral data comparing the two groups.

2.5. Statistical analysis for the neuroimaging data

Independent two-sample t-tests were performed on the connectivity values of the salience network between groups.

2.6. Correlation between neuroimaging and behavioral data

To find the relations between functional connectivity of the salience network and reading and EF ability, Pearson's correlations were performed between the functional connectivity values of the salience network and the behavioral measures for reading and EFs.

3. Results

3.1. Behavioral measures

Independent *t*-test analyses suggested that individuals with dyslexia show higher scores for BRIEF sub-tests (i.e., lower EF abilities), as well as worse performance on working memory (digit span) and phonological (Elision, phonetic decoding, sight word efficiency) tasks. Lower scores on all reading measures were also observed. See Table 1 for these results.

3.2. Neuroimaging data

3.2.1. Narrative comprehension ability

Independent *t*-test analyses were performed on the percent correct responses of a post-test questionnaire on the comprehension of the story presented during the MRI scan. No significant difference was found (t (64) = 0.32, p = .75).

3.2.2. Functional connectivity for the salience network

An independent t-test suggests that both children with dyslexia and typical readers display different connectivity values for the IC related to
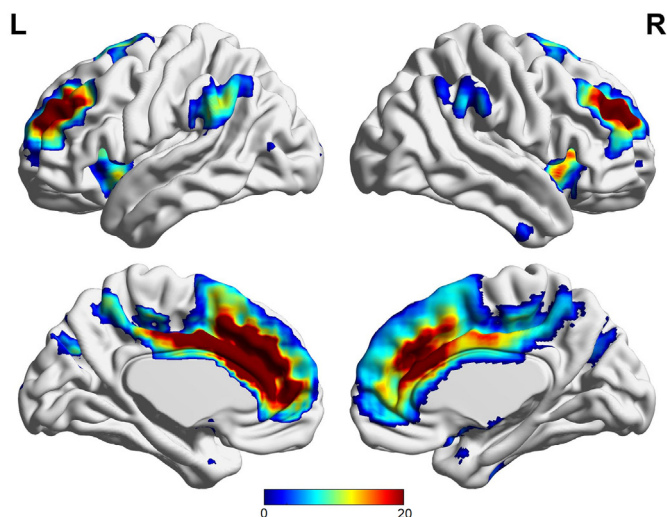
Fig. 1. The salience network IC in all subjects.
Left and right sagittal views of ICs for all subjects. Hot color stands for a higher functional connectivity whereas the cool color stands for decreased functional connectivity. The intensities for all participants were 0 to 20.
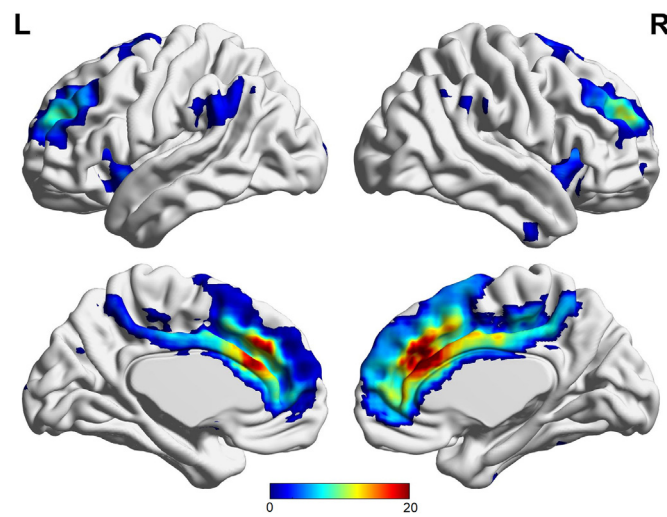

Fig. 3. The salience network IC in controls.
Left and right sagittal views of ICs for controls. Hot color stands for a higher functional connectivity whereas the cool color stands for decreased functional connectivity. The intensities for both typical readers were 0 to 20.
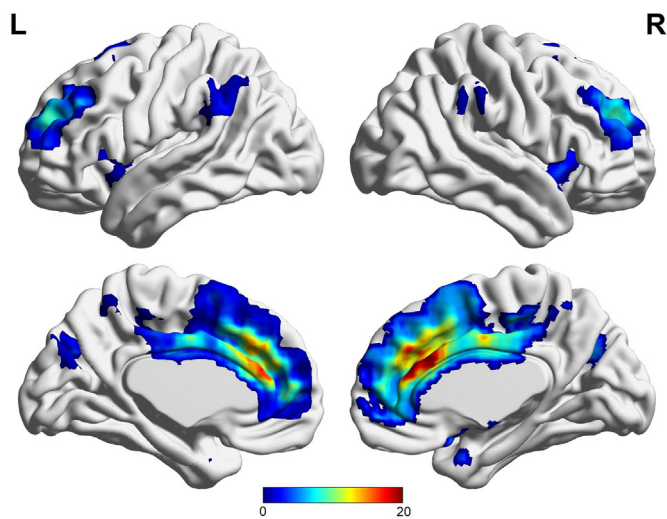

Fig. 2. The salience network IC in dyslexics.
Left and right sagittal views of ICs for dyslexics. Hot color stands for a higher functional connectivity whereas the cool color stands for decreased functional connectivity. The intensities for children with dyslexia were 0 to 20.
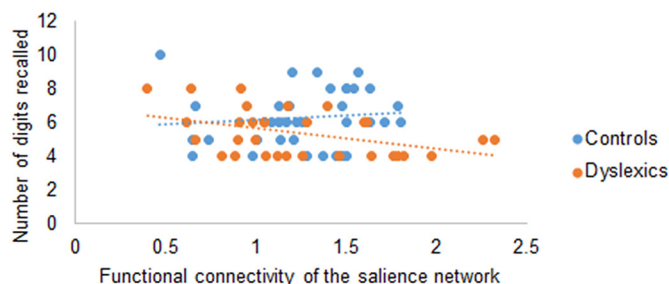

Fig. 4. Correlation between the functional connectivity of the salience network and working memory.
Scatter plot for the correlation between the functional connectivity of the salience network and working memory, as assessed by the WISC digit span backward. The X axis represents the functional connectivity of the salience network in all participants, and the Y axis represents the number of digits recalled via the digit span backward. Orange color represents children with dyslexia and blue color represents typical readers.

the salience network (t(64) = 0.24, $p < .05$, $\eta^2 = 0.0009$). Children with dyslexia demonstrated lower functional connectivity of the salience network, compared to typical readers (children with dyslexia: M = 1.24, SD = 0.48, typical readers: M = 1.27, SD = 0.34). The intensities for all participants were 0 to 20. See Fig. 1 for a visualization of the salience network IC averaged in all participants and Figs. 2 and 3 for a visualization of the salience network in each group.

3.2.3. Correlation between neuroimaging and behavioral data
A Pearson correlation revealed a significant negative correlation between the functional connectivity of the salience network and working memory abilities in dyslexics (i.e. digit span backward of the WISC) ($r = -0.43$, $p = .02$), signifying increased functional connectivity in the salience network correlates with decreased working memory ability (see Fig. 4).

4. Discussion

The aim of the current study was to explore the involvement of the salience network in narrative comprehension in children with dyslexia by exploring the functional connectivity of the salience network during a narrative comprehension task compared to typical readers. To our hypotheses, we found decreased functional connectivity in the salience network during the narrative comprehension task and decreased EF and reading abilities via the behavioral measures in children with dyslexia. A negative correlation was found between the functional connectivity of the salience network and working memory.

4.1. Salience network in narrative comprehension

The salience network, comprised of the anterior cingulate cortex and the insula, is involved in narrative comprehension abilities (Ibrahim et al., 2015; Uddin et al., 2013). The insula also has a role in attentional capture and in facilitating working memory abilities (Sridharan et al., 2008), supporting the correlation found in the current

study between the salience network and working memory abilities. Both attention and working memory are crucial to stay attended to the narrative and to recall previous memories in the narratives for accurate comprehension (Mar, 2004). The other portion of the salience network, the anterior cingulate cortex, supports narrative comprehension (Mar, 2004; Yarkoni et al., 2008), attentional control and switching (Van Veen and Carter, 2002). In healthy adults, the right anterior cingulate is active during stories involving mental inference (Vogeley et al., 2001). Brain network dynamics implicate the salience network (Sridharan et al., 2008). Specifically, the right insula acts as an "on" and "off" switch between central executive and default mode networks (Sridharan et al., 2008). A stable switching mechanism of the external (i.e., central executive) and internal (i.e., default mode) networks could be crucial for successful narrative comprehension. This ability is especially important for childhood development as the functional coupling between the salience, default mode, and central executive network nodes is stronger in adults than in children, expressing a developmental trend (Uddin et al., 2011). Due to this, exploring its role in neurodevelopmental disorders (e.g., dyslexia) is crucial.

4.2. Salience network in narrative comprehension in children with dyslexia

Our current findings suggest that the salience network shows decreased within network functional connectivity in children with dyslexia during narrative comprehension. This finding is consistent with previous research on the level of activation and functional connectivity in key-regions within the salience network, through decreased ERN amplitude during errors made in a reading (Horowitz-Kraus, 2011; Horowitz-Kraus, 2012; Horowitz-Kraus, 2013; Horowitz-Kraus and Breznitz, 2013) and non-reading (Horowitz-Kraus, 2014) tasks in children with dyslexia compared to controls on a portion of the salience network using EEG (Horowitz-Kraus and Breznitz, 2008). Moreover, decreased functional connectivity within the cingulo-opercular network was observed in children with dyslexia and was related to decreased reading ability in this population (Horowitz-Kraus et al., 2015a; Horowitz-Kraus et al., 2015b; Horowitz-Kraus and Holland, 2015). As the anterior cingulate cortex is a key region in both the generation of the ERN and within the cingulo-opercular network, as well as the salience network, the findings of the current study may extend these previous findings to the salience network in children with dyslexia.

The functional connectivity of the salience network was also negatively correlated with skills in working memory, which can contribute to impaired switching found in children with dyslexia (Horowitz-Kraus, 2014; Poljac et al., 2010). Individuals with dyslexia may have a neural switching problem between networks, which may explain the switching disability on a neurological level. The left insula (Paulesu et al., 1996) and the anterior cingulate (Shaywitz and Shaywitz, 2005) are under activated in dyslexia, strengthening our results of overall dysfunction in the salience network in dyslexia. These findings show a clear role of dysfunction in a region implicated in successful network dynamics, representing failed network dynamic capabilities in dyslexia. Dysfunction in network dynamics may explain the nuances and conflicts in prior research about functional connectivity in dyslexia. Further research should explore the developmental dysfunction of the salience network in individuals with dyslexia over their lifetime for a more accurate understanding.

4.3. Limitations

However, the current study had the following limitation. Even though the IC analysis was more data-driven than other approaches, the "extra" areas not involved in the salience network that we selected during the analysis could have acted as confounders. To check for this, the study used the networks implemented in the CONN toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012) for an ICA-match-to-template to ensure that the IC selected represented the defined salience network. Future studies should explore parcellation approaches that include many sub-components of the salience network for a more detailed analysis (Craddock et al., 2012).

4.4. Future directions

The findings from this first study of the salience network in children with dyslexia emphasize the dysfunction of the salience network in these children. The findings point to new investigations of interventions to strengthen the error monitoring system and to add knowledge of the neural correlates behind reading disability. Further, switching between the central executive and default mode networks occurs in the right insula of the salience network. As other studies show impaired EF networks in dyslexia, future research should explore the default mode network as well as the salience network in dyslexia to understand more network dynamics in dyslexia. Future interventions to ensure better academic outcomes in at-risk individuals with dyslexia should focus primarily on executive functioning, especially error monitoring and switching behavior. Activities for children with dyslexia, in addition to reading acceleration programs that have already demonstrated success (Horowitz-Kraus et al., 2015a), could include getting immediate confirmation of errors to strengthen their salience network and adding exercises to acknowledge errors.

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