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Longer Fixation Times During Reading Are Correlated With Decreased Connectivity in Cognitive-Control Brain Regions During Rest in Children

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Abstract

Dyslexia, or reading difficulty (RD), is characterized by slow, inaccurate reading and accompanied by deficit in executive functions (EF) and altered functional connectivity (FC) in the related networks (i.e., cingulo-opercular). Individuals with RD also present with altered oculomotor gaze patterns that include longer fixation times. The researchers examined the relationship between fixation times and FC of neural circuits related to EF during rest in children with RD and typical readers. Nineteen children participated in a 10-min resting-state scan. FC analysis was performed with the anterior cingulate cortex (ACC), related to cognitive control, chosen as a seed. Fixation time during word reading was used as a covariate of interest. Results demonstrated that FC between the ACC and the left inferior frontal cortex pars triangularis and left inferior prefrontal cortex during rest were negatively correlated with fixation times during word reading. These exploratory results support the critical role for the cingulo-opercular network, which is related to cognitive control, in the reading process, and likely also in reading impairment.

Dyslexia, or reading difficulty (RD), is characterized by slow and inaccurate reading that persists into adulthood despite remedial interventions and exposure to written language, with a prevalence rate of 5%–20% in school-age children (IDA, 2011; Shaywitz, 2003). Deficits in phonological processing have been shown as the main cause for RD (Scarborough, 1998). However, recent research examining RD-associated reading deficits has also suggested a deficit in executive functions (EF) for individuals with RD (Altemeier, Abbott, & Berninger,

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article. Table S1 Motion parameters for typical readers and children with reading difficulties (independent *t* test results).

2008; Brosnan et al., 2002; Gooch, Snowling, & Hulme, 2011; Helland & Asbjørnsen, 2000; Menghini, Carlesimo, Marotta, Finzi, & Vicari, 2010; Reiter, Tucha, & Lange, 2005; Tiffin-Richards, Hasselhorn, Woerner, Rothenberger, & Banaschewski, 2008). Thus, RD is considered a multifaceted disorder that requires a variety of investigative technologies and methodologies to uncover the various mechanisms driving RD-associated reading impairments.

The term EF encompasses a variety of conscious processes that monitor and optimize performance, which are essential for goal setting, stimuli synthesis, preparatory actions, and execution of behavior (Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986; Luria, 1973). Several studies have determined difficulties in various aspects of EF in children with RD: allocating the attention from one stimulus to the other (or switching) (Facoetti, Paganoni, & Lorusso, 2000; Facoetti, Paganoni, Turatto, Marzola, & Mascetti, 2000; Shaywitz & Shaywitz, 2008), attentional difficulty (i.e., focusing the attention in one stimulus; Facoetti, Paganoni, Turatto, et al., 2000; Shaywitz & Shaywitz, 2008), inhibition (Brosnan et al., 2002), and working memory (Ackerman & Dykman, 1993; Helland & Asbjørnsen, 2000). Importantly, error self-monitoring deficits have also been identified in nonlinguistic and linguistic domains (Horowitz-Kraus & Breznitz, 2008, 2009). Despite the large number of studies that have examined EF impairments in children with RD, a lack of consensus exists as to the involvement of this difficulty in their inability to read effectively (Barkley, Grodzinsky, & DuPaul, 1992; Stoet & Snyder, 2007).

One approach to deepen our understanding of the involvement of impaired EF during the reading process in children with RD is the use of neuroimaging tools to clearly define the involvement of altered neural circuits related to EF in reading among this population. In this approach, cognitive control networks are related to as several regions, functionally connected, that is, with a synchronized time series. The “dual-networks top-down model” is a functional connectivity (FC)-based model for the assessment of cognitive control networks (Power et al., 2011). This model proposes two cognitive-control/EF networks with different neuroanatomical correlates. The first is the frontoparietal network consisting of a rapid adaptive-control network that promotes attention to perceptual cues (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008). The second is the cingulo-opercular network, which is a set-maintenance network responsible for task goals, adjustments of feedback control, and error monitoring (Dosenbach et al., 2008). It is widely accepted that FC within these two networks increases throughout cognitive development (Fair, Dosenbach, Petersen, & Schlaggar, 2012) and, importantly, that both of these networks are engaged during reading (Ihnen, Petersen, & Schlaggar, 2013). Specifically, research has determined that altered EF forms the basis of reading deficits in individuals with RD, such as slower processing speed (Breznitz & Misra, 2003), impaired visual attention (Gabrieli & Norton, 2012), and error monitoring (Horowitz-Kraus & Breznitz, 2008). Relative to these findings, there is an increasing interest in examining FC differences in cognitive-control networks in these individuals. For example, we have demonstrated that children with RD exhibit decreased FC in their cingulo-opercular network (Horowitz-Kraus, Toro-Serey, & DiFrancesco, 2015). Similar work has demonstrated that during error monitoring in individuals with RD, the anterior cingulate cortex (ACC), which is a component of the cingulo-opercular network, exhibited decreased activation compared to typical readers (TRs; Horowitz-Kraus et al.,

2014). Smaller event-related potential amplitudes, which were originated from the ACC (i.e., the error-related negativity) during reading, were also found in children with RD and was correlated with their low reading scores (Horowitz-Kraus & Breznitz, 2008, 2014). Hence, these smaller amplitudes reflect decreased activation of the ACC in these readers.

Reading deficits that result from RD are accompanied by altered oculomotor gaze patterns as these readers exhibit longer fixations, shorter saccades, and more regressions compared to their more skilled counterparts (Jainta & Kapoula, 2011; Rayner, 1998). Individuals with RD are also known to exhibit multiple fixations on a greater number of words, with gaze duration (i.e., total fixation time) positively related to word length for both Italian and German readers (Rayner, 1998). It has also been demonstrated that individuals with RD can process only a few letters at each fixation, and that those with reduced visual attention are incapable of increasing the number of letters processed in a reading task (Prado, Dubois, & Valdois, 2007). Initial fixation position during word recognition is also suboptimal in readers with RD, and this leads to a larger number of refixations compared to TRs (Hawelka, Gagl, & Wimmer, 2010). While these types of deficits are consistently demonstrated, it is not yet clear whether fixation performance deficits are related to impaired cognitive control in individuals with RD (Bellocchi, Muneaux, Bastien-Toniazzo, & Ducrot, 2013), which can result in some intervention strategies for this population. Eye-movement patterns have been shown previously to be suitable for observing several key EF involved in reading (planning, working memory, attention to task-relevant and task-irrelevant information, error monitoring, and shifting attention) (Hodgson, Bajwa, Owen, & Kennard, 2000; Mennie, Hayhoe, & Sullivan, 2007; Wass, Porayska-Pomsta, & Johnson, 2011), a connection which was not verified in the RD group yet. However, different eye-movement patterns are likely associated with different types of cognitive processing, and therefore it is difficult to uncover the relationship between oculomotor and specific behavioral deficits (Holmqvist et al., 2011). One method to better understand the cognitive mechanisms underlying these deficits is to examine the relationship between neural FC and fixation performance as negative or reduced FC of cognitive-control regions (or key components of these) in combination with fixation deficits. This method would reveal the critical correspondence between eye-movement patterns and neural circuits related to cognitive control (see also Horowitz-Kraus et al., 2015, for the role of the cognitive-control networks in reading).

As the official definition for RD does not include EF despite the findings pointing at an additional difficulty in EF in this population, the aim of the current study was to strengthen and extend this point even more by connecting physiological data during reading (i.e., eye movement data) to (1) EF and reading ability and (2) neurobiology. We will do that by examining the relationship between fixation times and FC of neural circuits related to EF during rest in both children with RD and TRs. Because we aim to validate the existence of challenges in EF in children with RD, we hypothesized that children with RD will demonstrate lower EF scores than TRs and that longer fixation times during reading would be correlated with decreased (i.e., negative) FC between a key region of the cingulo-opercular network, the ACC, and left-lateralized regions related to cognitive control. Because FC during a resting state data is reflective of an actual task, without being affected from eye movement derived from a specific external stimuli (Tavor et al., 2016), we chose to answer these questions using a resting state data.

METHODS

Participants

Children with RD ($n = 10$; mean age: 9.91 years, $SD = 0.982$, eight males, nine right-handed) and TRs ($n = 9$; mean age: 10.18 years, $SD = 0.714$, five males, all right handed; $t(18) = -1.142$, $p = .2$) participated in the current study. Children were recruited by posted ads in the hospital and clinics, libraries, and schools around the city. The participants in the RD group had been previously diagnosed with RD from external clinics in the community. We also verified the existence of RD using several standardized reading tests: RD was defined as scoring below the 25th percentile on at least two tests from a battery of standardized reading measures (see Behavioral Measures section). All participants were within the normal range of nonverbal intelligence quotient (IQ), and none had a history of neurological or emotional disorders. Children with report of attention deficit hyperactivity disorder (ADHD) as well as those with a moderate and higher probability for attention (as measured by the Conners questionnaires) were excluded from the study (Conners, 1989). No differences were found between the two reading groups in attention ability as measured by the Conners questionnaires (Conners, 1989; $t(18) = 2.267$, ns).

All participants were native monolingual English speakers and screened for compatibility for participation in the magnetic resonance imaging (MRI) scan (no dental work or other implants to affect safety or image quality). Participants had no history of neurological or psychiatric impairments. Informed consent and assent were signed by parents and participants, respectively. The study was reviewed and approved by the appropriate institutional review board.

Behavioral Measures

All children were administered the Test of Nonverbal Intelligence (TONI-3; Brown, Sherbenou, & Johnsen, 1997) and the Peabody Picture Vocabulary Test (PPVT-4; Dunn & Dunn, 2007) to verify normal nonverbal IQ and verbal IQ, respectively. Reading ability, fluency and comprehension, and phonological abilities were assessed using the letter-word and word-attack subtests from the Woodcock-Johnson-III (WJ-III; Woodcock & Johnson, 1989), the Test of Silent Reading Efficiency and Comprehension (TOSREC; Wagner, Torgesen, Rashotte, & Pearson, 2010), and the Elision Subtest (from Comprehensive Test of Phonological Processing [CTOPP]; Wagner, Torgesen, & Rashotte, 1999), respectively. We also tested EF in the following domains: shifting (color-word Stroop task; Dellis, Kaplan, & Kramer, 2001), visual attention (i.e., Sky Search task; Manly, Robertson, Anderson, & Nimmo-Smith, 1999), working memory (digit-span subtest; Wechsler, 1999), and learning (Wisconsin test; Nyhus & Barcelo, 2009). Attention difficulties were ruled out by the administration of the Conners child reports (Conners, 1989).

Eye-Movement Data Collection

Lexical Decision Task—Stimuli for the lexical decision task consisted of 80 randomized items, either words or pseudowords (modeled after Van der Mark et al., 2009), and participants indicated whether the stimuli were real words or not through button-pressing. Word stimuli were 40 high-frequency words (four to six letters long) matched for

imageability and concreteness (adapted from Van der Mark et al., 2009). The 40 pseudowords were created by substituting one or two letters in real words. The stimuli were presented horizontally in the center of the screen using Tobii Pro Studio software (Tobii Technologies, Stockholm, Sweden). Following the presentation of each word/pseudoword, participants were provided with a Yes/No screen corresponding to a “thumb up, happy face” and a “thumb down, sad face”, respectively, and were requested to push the “Yes” button for a real word and the “No” button for a nonword. Each stimulus was presented for 800 ms, and subsequently an interstimulus interval of 200 ms followed by a “Yes/No” screen presented for 1,500 ms. Each eye-tracking session started with a practice session of 10 stimuli.

Gaze Data—Gaze data were collected at 60 Hz using a Tobii X2–60 eye tracker (Tobii Technologies, Stockholm, Sweden). The tracker was mounted to the bottom center of a laptop computer that was situated on top of a desk. Participants were instructed to sit upright, approximately 65 cm from the computer, such that the center of the monitor was at eye level. Initially, participants were instructed to follow a moving target using a standardized 5-point calibration. Participants were instructed to restrict their movement as much as possible while performing the reading tasks. If at any point throughout the assessment the participant moved beyond any normal postural sway necessary to maintain an upright seated position (i.e., shifting of weight or an involuntary movement such as coughing or sneezing), the participant was realigned with the screen and recalibrated. Following a practice session of 10 words, data was recorded for analysis purposes. Gaze data were postprocessed and fixations were determined in Tobii Studio using a proprietary algorithm (Olsen, 2012). The processed data were then exported to Matlab (Mathworks, Natick, MA), where reading time and fixation number and duration were parsed from each stimulus presentation. Only data for correct word reading were included in the analysis.

Correlation Analysis of Behavioral Reading Measures and Fixation Duration

Before determining the relations between eye-movement patterns and neuroimaging data, we calculated the relationship between reading ability, EF, and eye-movement patterns on the behavioral level using a Pearson correlation. To determine the relations between eye-movement patterns and reading ability we used the word and non-word reading (Woodcock & Johnson, 1989), phonological awareness (Wagner et al., 1999), fluency, and comprehension (Torgesen, Wagner, & Rashotte, 1999). To examine the relations between the eye-movement patterns and EF we used attention shifting (Dellis et al., 2001), visual attention (Manly et al., 1999), working memory (Wechsler, 1999), and learning (Nyhus & Barcelo, 2009), and fixation duration was performed. Data was corrected using Bonferroni correction.

Neuroimaging Procedure

A resting-state condition was administered using a Philips Achieva 3 T MRI scanner (Philips Medical Systems, Best, The Netherlands). Participants were asked to look at a gray cross in the center of a projector screen for 10 min and avoid sleeping or closing their eyes other than blinking during the scan. A T2-weighted, gradient echo, echo planar imaging or EPI sequence was used with functional MRI (fMRI) parameters: time repetition/time echo =

2000/38 ms, matrix size = 64×64 , and slice thickness = 5 mm, resulting in a voxel size = $4 \times 4 \times 5 \text{ mm}^3$. During the resting-state scan, 300 whole-brain volumes were acquired for a total imaging time of 10 min. The initial 10 time points acquired were discarded to allow for T1 relaxation equilibrium. In addition, a high-resolution T1-weighted three-dimensional anatomical scan was acquired using an inversion recovery or inversion recovery-prepared turbo gradient-echo acquisition protocol with a spatial resolution of $1 \times 1 \times 1 \text{ mm}^3$.

Participants were acclimated and desensitized to the scanner to condition them for comfort during imaging (see Byars et al., 2002, for details). Head motions were controlled using elastic straps that were attached to either side of the head-coil apparatus.

MRI Data Analysis

During image reconstruction, a multi-echo reference scan was initially used to correct for Nyquist ghosts and geometric distortion due to B0 field inhomogeneity. Reconstructed fMRI data were then spatially preprocessed using SPM8 software (www.fil.ion.ucl.ac.uk/spm/), including slice-timing correction, realignment for motion correction, coregistration of the anatomical image to the mean aligned functional image, segmentation by gray matter, white matter, and cerebrospinal fluid tissue classes, normalization of all images to the Montreal Neurological Institute or MNI space, and spatial smoothing with an 8-mm full width at half-maximum or FWHM Gaussian kernel. Motion was corrected using pyramid coregistration (Thevenaz, Ruttimann, & Unser, 1998) in SPM12. Using the ART toolbox for motion correction implemented in the CONN toolbox, we performed three-dimensional affine transformation to align the volumes, which resulted in six motion parameters (three translational and three rotational). Time points with excessive motion were rejected from the postprocessing pipeline ($>0.02 \text{ mm}$). Data was visually inspected for artifacts such as missing voxels, stripes, ghosting, or intensity differences. All data frames survived these criteria and are included in the analysis. All data met the criterion of median voxel displacement $<0.02 \text{ mm}$ in the center of the brain. See online Supporting Information for the nascent of differences in motion between the two groups.

Following the spatial preprocessing described, the neuroimaging data were fed into a FC toolbox for Matlab (CONN) (Whitfield-Gabrieli & Nieto-Castanon, 2012). Additional preprocessing under the anatomical component-based noise-correction framework or aComp-Cor (Behzadi, Restom, Liau, & Liu, 2007) was performed and included extraction of the first five principle eigenvariates of the BOLD time-courses from white-matter and cerebral spinal fluid regions for use as regressors in the analysis to remove signal variation associated with these noncortical regions. In addition, the six motion parameters for each session, together with their first derivatives, were regressed out of the voxel time series. Finally, the voxel time-series data were band-pass filtered between 0.008 and 0.2 Hz, as recommended by Baria, Baliki, Parrish, and Apkarian (2011).

FC Analysis

FC between the chosen cognitive control region (the left and right ACC [Brodmann area (BA) 24]), and the regions in the entire brain (left and right) as target regions of interest (ROI) was calculated as the correlation coefficient for the average voxel signal for each ROI pair.

Correlation of Reading and EF Behavioral Measures

To determine the relationship between EF and reading measures, Pearson correlation was conducted. Data were corrected for multiple comparisons.

Correlation of Neuroimaging Data and Eye-Movement Measures

In order to have a full array of the shortest and longest fixation times in the analysis, the calculated FC was correlated with the fixation time during correct word reading (in milliseconds) for each child, the entire study cohort (both children with RD and TRs), and each group separately. Threshold was set to $p < .005$ (uncorrected).

RESULTS

Behavioral Measures

Verbal and nonverbal general ability and attention performance were within the average range for all participants. Children with RD showed nonverbal ability and attention scores similar to those for TRs, but demonstrated significantly lower reading scores in all reading domains measured (word and nonword reading, phonological awareness, fluency, and reading comprehension), as well as in verbal ability. Children with RD also showed lower scores than TRs in all EF measured, but were significantly lower only in shifting, working memory, and learning (see Table 1).

Eye-Movement Patterns

Longer fixation times were observed for children with RD ($X = 128.0$ ms, $SD = 100.0$) compared to TRs ($X = 56.19$ ms, $SD = 17.95$); $t(17) = -2.04$, $p < .05$, $d = 0.646$, mean difference = -71.857 , standard error difference = 37.073 . The average fixation time was 90.23 ms ($SD = 82.99$) during correct word reading for the lexical decision task. Children with RD and TRs did not differ in their reaction time (RD: $X = 810.88$ ms, $SD = 12.3$; TR: $X = 804.82$ ms, $SD = 5.42$, $t(17) = -1.417$, ns, $d = 0.447$, mean difference = -6.065 , standard error difference = 4.28) and accuracy rate (RD: $X = 86.43\%$, $SD = 10.42$; TR: $X = 89.61\%$, $SD = 10.99$, $t(17) = 0.644$, ns, $d = 0.2$, mean difference = 3.173 , standard error difference = 4.93) for correct word reading.

Correlational Analyses

The Correlation of Reading and EF Measures—To verify the relations between cognitive control (or EF) and reading measures, Pearson correlation analysis was conducted. Significant correlation between reading and EF in both groups (contextual fluency and word reading with working memory; $r(19) = 0.507$, $p < .05$; $r(19) = 0.625$, $p < .01$, respectively) and between phonological processing and working memory, attention shifting, visual attention, and learning abilities, $r(19) = 0.552$, $p < .05$; $r(19) = 0.494$, $p < .05$; $r(19) = 0.494$, $p < .05$; $r(19) = -0.457$, $p < .05$, was found. Greater fluency, word reading, and phonological processing were correlated with higher EF scores.

The Correlation of Behavioral Measures and Eye-Movement Measures

Eye-movement data was found to be related to the behavioral data. Significant negative correlation between fixation time and letter word reading or attention shifting was found, $r(19) = 0.788, p < .05$ and $r(19) = -0.421, p < .05$, respectively, and longer fixation times were correlated with lower word-reading and attention-shifting scores.

Correlation of FC and Eye-Movement Measures

Children with RD—Significant correlation occurred between the cognitive control region (ACC) and the left inferior frontal cortex pars triangularis (BA 45; $t(9) = -5.17, p < .005$ uncorrected) in children with RD, and fixation times during word reading were observed (Figure 1). Results suggest that lower negative FC between these regions was correlated with longer fixation times during reading.

Typical Readers—Significant correlation occurred between the cognitive control region (ACC) and the left posterior entorhinal cortex (BA28; $t(7) = -5.89, p < .005$ uncorrected) and left superior temporal gyrus (BA22; $t(7) = -4.14, p < .005$ uncorrected) in TRs, and fixation times during word reading were observed (Figure 2). Results suggest that lower negative FC between these regions was correlated with longer fixation times during reading.

Both Reading Groups—Significant correlation occurred between the cognitive control region (ACC) and the left inferior frontal cortex pars triangularis (BA 45; $t(17) = -3.25, p < .005$ uncorrected) and left inferior prefrontal cortex (BA10; $t(17) = -3.03, p < .005$ uncorrected) in all study participants, and fixation times during word reading were observed (Figure 3). Results suggest that lower negative FC between these regions was correlated with longer fixation times during reading.

DISCUSSION

The aim of the current study was to strengthen the existence of an EF difficulty in children with RD and to define the neural circuits underpinning altered eye-movement patterns related to reading and EF during rest in children with RD. Resting-state data was acquired from children with RD and TRs, and data were correlated with fixation times during word reading. In support of our hypotheses, children with RD demonstrated lower reading and EF abilities than TRs. Lower word-reading scores were positively related to lower shifting abilities. In addition, children with RD showed longer fixation times during word reading compared to TRs. Overall, longer fixation time was negatively correlated with reading ability, attention shifting, and decreased FC between the ACC and cognitive-control-related regions (inferior frontal gyrus and inferior prefrontal cortex). Specifically, children with RD showed negative FC between the cognitive control region (ACC) and additional cognitive control-related regions (inferior frontal gyrus), whereas the negative FC also involved language regions in TRs (superior temporal gyrus and entorhinal cortex). These results are discussed in the context of the involvement of EF and EF-related neural circuits for both typical and atypical reading.

Longer Fixation Associated with Impaired Reading—Why?

The results of the negative correlations between fixation duration and word-reading ability and attention shifting and the significant differences in fixation times between children with RD and TRs confirm that impaired reading is associated with longer fixation times. As Rayner has suggested, the reader obtains new visual information during fixations in the written text (Rayner, 1998). Hutzler and Wimmer compared fixation duration in children with RD in German versus Italian and demonstrated longer fixations in German, which shares similarities to English syllables (Hutzler & Wimmer, 2004). English and German languages contain initial and/or final consonant clusters, which makes it more challenging to assemble the syllables in reading in these languages. Due to the well-described phonological deficit in individuals with RD, the letter-sound correspondence does not come as natural for the RD reader as it does for TRs. Therefore, longer fixations are needed to match the correct sound to the letter, especially when the word involves complex syllables (Hutzler & Wimmer, 2004).

Is There an Association Between Cognitive Control and Longer Fixations?

Rayner and colleagues outline the cognitive processes involved in the decision-making process that underlies eye movements during reading (Rayner, 1998; Rayner & Pollatsek, 1989; Rayner, Schotter, Masson, Potter, & Treiman, 2016). The authors suggest that eye movements are basically motor responses that require time to plan and execute and describe several processes that are all happening simultaneously: The reader processes the fixated word, plans to move the eyes forward, and processes the upcoming word using parafoveal information. This concept has been recently supported by Luthi and colleagues, who report that eye-movement patterns involve key EF and that a agnetic stimulation of key neural circuits related to EF (i.e., dorsolateral prefrontal cortex) affects EF (Luthi et al., 2014). We suggest that the reading process specifically involves several key EF that can be reflected in eye-movement patterns: visual attention (the ability to ignore irrelevant visual information), working memory that enables the update of new information to that previously read, planning of the next step in the process (i.e., should the reader gaze forward or backward?), and decision making. Therefore, it is not surprising that key regions involved in the described abilities show decreased FC in relationship to altered eye movements during reading (i.e., longer fixation times). In the current study, we observed a decreased FC between the ACC (decision making and planning as part of the cingulo-opercular network; Dosenbach et al., 2008), inferior prefrontal cortex (working memory and visual attention; Burgess, Dumontheil, & Gilbert, 2007; Gilbert et al., 2006), and inferior frontal gyrus (interference and response selection, part of working memory abilities; see Badre, Poldrack, Pare-Blagoev, Insler, & Wagner, 2005; Jonides & Nee, 2006; see Nee et al., 2013, for review).

The link between low FC (i.e., decreased cognitive control) and longer fixation time indicates that the fixation behavior, which was previously reported for readers with RD, is potentially due to underdeveloped or maladaptive cognitive-control processes. Importantly, different fixation behaviors are associated with different types of cognitive processes (Holmqvist et al., 2011). During reading, for example, initial-word fixations are linked to lexical activation, while later fixations are associated with discourse integrative processes

(Rayner, 1998). It has been suggested that the duration of fixations can differentiate between these different processes, and fixations shorter than 140 ms are associated with lexical properties (McConkie, Reddix, & Zola, 1992). In the current study, the average fixation time was 90.23 ms—a time duration under the 140 ms threshold, which suggests that lexical processes did occur. However, longer fixation time at the word level may suggest an impaired and nonautomatic process of attention shifting of perceiving the word and then looking for a semantic meaning in working memory, as has been previously suggested (Rayner, 1998) and which is also reflected by a reduced FC of neural circuits related to cognitive control. These findings are in line with previous studies suggesting an overall altered eye-movement patterns in readers with RD (Bednarek, Tarnowski, & Grabowska, 2006; Prado et al., 2007). Based on the current study's results, if there are significant relations between altered eye-movement patterns and EF and neural circuits supporting it, it is not surprising that the altered eye movement characteristics extend beyond the linguistic domain. An additional study should examine if the same neural circuits support this eye movement alteration.

The results of the current study support the critical role for cognitive control, and specifically of the cingulo-opercular network in both the reading process and reading impairment. These results echo our previous findings of the overall lower FC (i.e., global efficiency) of this network in children with RD during rest (Horowitz-Kraus et al., 2015). The cingulo-opercular network is related to a set-maintenance that maintains task goals, sustains adjustments for feedback control, and monitors errors, all of which are critical for reading (Horowitz-Kraus et al., 2015). Since the described cognitive abilities are all part of the reading process, it is only natural that the critical role of this network was also evident in reading remediation, as was previously observed (Horowitz-Kraus et al., 2015). In that study, an EF-based reading remediation program resulted in increased FC of the cingulo-opercular network in children with RD (Horowitz-Kraus et al., 2015). Future studies should examine whether the change in FC in this network among children with RD following training may also be reflected in eye-movement patterns, specifically with shorter fixation times. In support of these suggestions, an Italian study demonstrated how repetitive exposure to video games resulted in better reading in adults with RD (Franceschini et al., 2013). The authors suggested that the positive effect on reading ability was mediated through the effect of the exposure to the video games on attention and reaction times, which was “leaking” to the reading. Future studies should also examine the effect of cognitive-control training on both reading ability and the relationship between eye movements and neural circuits related to reading and cognitive control.

Interestingly, differences between the regions involved in FC and the cognitive control region (ACC) were found between children with RD and TRs. Whereas TRs showed a relationship between longer fixations and decreased FC between the ACC and language (superior temporal gyrus) and cognitive-abilities (entorhinal cortex) regions, children with RD showed a relationship between the ACC and only cognitive regions (inferior frontal gyrus). The literature suggests a critical role of the entorhinal cortex as a hub in a widespread network for memory and navigation (Moscovitch et al., 2005). The entorhinal cortex interacts with the hippocampus, which is critical for semantic and spatial memory, both of which are critical for reading (Moscovitch et al., 2005), and also controls the

association of impulses from the eye and the ear (Freeman, 2004). The reading process involves synchronized visual and auditory information (Breznitz, 2006). Therefore, it may be that in TRs longer fixations are due to a synchronization failure, whereas longer fixations in children with RD are mainly due to a failure in the executive system. Further studies should be performed to map the association of different eye-movement measures (e.g., dilation, regressions, saccades) with neural circuits related to reading ability (i.e., cognitive control, language, and visual processing) (see Horowitz-Kraus et al., 2014, for ROI related to these abilities). This approach would potentially reveal the underlying neural circuits for reading challenges in both children with RD and TRs and the eye-movement patterns reflecting the activation and FC of these brain regions.

Limitations of the Study

The results of the current study should be considered taking into account the following limitations. First, despite the relatively high threshold used in this analysis ($p < .005$), the number of participants in this study was relatively small and therefore the results did not survive multiple comparisons when including all ROI in the brain (right and left BAs) and the repressors of interest (eye-movement measures) and no interest (six motion parameters) included in the analysis. Therefore these results should be considered exploratory and an additional study should employ a larger number of participants. Second, the analysis for the study was based on an a priori chosen ROI as a seed reflecting a key region related to cognitive control (i.e., the ACC), which therefore limited the results to regions correlated with this specific ROI. Future study should examine the FC with both the whole brain and the various cognitive-control networks (cingulo-opercular, frontoparietal, and default-mode networks). Third, we used single-word reading and not sentences reading, preventing the interpretation of our results at the contextual level, which is a more natural way to evaluate reading ability. Future study should compare eye-movement patterns and the FC related to these measures for both word reading and contextual reading in both children with RD and TRs.

CONCLUSIONS AND FUTURE STUDY

The current study is one of the first studies to associate FC during rest with eye-movement patterns in reading. In line with Pennington's studies looking at profiles of children with RD with ADHD (Pennington, 2006; Pennington, Groisser, & Welsh, 1993; Welsh, Pennington, & Groisser, 1991; Willcutt et al., 2001; Willcutt et al., 2010), the population of children with RD might be subgrouped also into profiles of children suffering from challenges in different types of EF, which can be characterized by different profiles of eye-movement patterns and may require different clinical approach. This point should be examined in depth. Our results strengthen previous behavioral studies connecting eye-movement patterns with EF and provide neurobiological support for this connection in children. Additional research mapping the neural correlates for additional eye-movement measures may allow the use of fixation time as a biomarker for difficulties with reading in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Correlation coefficient matrices for decreased functional connectivity in children with reading difficulty (RD). (a) The anterior cingulate cortex (BA24) (in green) is negatively correlated with the left inferior frontal gyrus (BA45, in blue), presented in sagittal axis. Connectivity strength is reflected in the line thickness. (b) Anterior cingulate cortex (black circle) and regions related to cognitive control (left inferior frontal gyrus) (blue circle) and longer fixation time during reading in children with RDs ($n = 10$), $p < .005$, uncorrected. Figures are presented in an axial display. (c) Effect size of the functional connectivity analysis (effect size is noted in the y -axis).

Fig. 2. Correlation coefficient matrices for decreased functional connectivity in typical readers. (a) The anterior cingulate cortex (BA24) (in green) is negatively correlated with the left superior temporal gyrus (BA 22) and left posterior entorhinal cortex (BA 28), both in blue, presented in sagittal axis. Connectivity strength is reflected in the line thickness. (b) Anterior cingulate cortex (black circle) and regions related to language processing (left superior temporal gyrus) and cognitive control (left posterior entorhinal cortex) (blue circles) and longer fixation time during reading in typical readers ($n = 9$), $p < .005$, uncorrected. Figures are presented in an axial display. (c) Effect size of the functional connectivity analysis (effect size is noted in the y-axis).

Fig. 3.

Correlation coefficient matrices for decreased functional connectivity in both groups. (a) The anterior cingulate cortex (BA24) (in green) and the left inferior frontal gyrus (BA45) and the inferior prefrontal cortex (BA 47), both in blue, presented in sagittal axis. Connectivity strength is reflected in the line thickness. (b) Anterior cingulate cortex (black circle) and regions related to cognitive control (left inferior frontal gyrus and inferior prefrontal cortex) (blue circles) and longer fixation time during reading in the entire study sample ($n = 19$), $p < .005$, uncorrected. Figures are presented in an axial display. (c) Effect size of the functional connectivity analysis (effect size is noted in the y-axis).

Table 1
Behavioral Measures for Children With Reading Difficulties (RDs) and Typical Readers (TRs)

Ability	Measure	RD, mean (SD) (A)	TR, mean (SD) (B)	Contrast, t (17), p	Mean difference	Standard error difference	Effect size (d)
Nonverbal ability	TONI (scaled score)	104.20 (6.52)	105.22 (8.467)	A < B, -0.296 ns	-1.022	3.448	0.09
Verbal ability	PPVT (scaled score)	99.1 (7.53)	114.55 (10.8)	A < B, -3.648 **	-15.455	4.236	1.15
Attention	Conner's Child (percent)	52.70 (27.79)	32.89 (8)	A > B, 2.146 ns	-2.756	1.135	0.67
Reading fluency and comprehension	TOSREC (index)	85.33 (6.12)	112.77 (16.63)	A < B, -4.645 **	-27.444	5.9	1.46
Phonological awareness	CTOPP, Elision (scaled score)	7.80 (2.15)	13.56(1.74)	A < B, -6.366 ***	-5.756	-7.663	2.01
Word reading	Woodcock Johnson Letter-Word (scaled score)	94.70 (6.881)	108.78 (8.074)	A < B, -4.104 **	-25.889	3.292	1.29
Decoding	Woodcock Johnson Word-Attack (scaled score)	91.00 (6.11)	116.89 (8.192)	A < B, -7.863 ***	-14.078	3.43	2.48
Attention shifting (switching)	Stroop Color-Word, (scaled score)	9.8 (3.04)	12.56 (1.59)	A < B, -2.427 *	19.811	9.231	0.76
Visual attention	Sky Search (standard score)	6.6 (3.06)	9 (3.24)	A < B, -1.654, ns	-2.4	1.446	0.52
Working memory	Digit Span (standard score)	7.8 (2.89)	10.56 (1.13)	A < B, -2.781 *	-2.756	.991	0.87
Learning	Wisconsin (total errors, percent)	23.25 (12.49)	14.33 (6.2)	A > B, 1.898 *	8.917	4.697	0.59

Note. CTOPP, Comprehensive Test of Phonological Processing; SD, standard deviation.

* $p < .05$.

** $p < .01$.

*** $p < .001$. ns, not significant.