




Decoupling of the Occipitotemporal Cortex and the Brain's Default-Mode Network in Dyslexia and a Role for the Cingulate Cortex in Good Readers: A Brain Imaging Study of Brazilian Children

Augusto Buchweitz, Adriana Corrêa Costa, Rudineia Toazza, Ana Bassôa de Moraes, Valentina Metsavaht Cara, Nathália Bianchini Esper, Cristiano Aguzzoli, Bruna Gregolim, Luiz Fernando Dresch, Matheus Dorigatti Soldatelli, Jaderson Costa da Costa, Mirna Wetters Portuguez & Alexandre Rosa Franco


To cite this article: Augusto Buchweitz, Adriana Corrêa Costa, Rudineia Toazza, Ana Bassôa de Moraes, Valentina Metsavaht Cara, Nathália Bianchini Esper, Cristiano Aguzzoli, Bruna Gregolim, Luiz Fernando Dresch, Matheus Dorigatti Soldatelli, Jaderson Costa da Costa, Mirna Wetters Portuguez & Alexandre Rosa Franco (2019) Decoupling of the Occipitotemporal Cortex and the Brain's Default-Mode Network in Dyslexia and a Role for the Cingulate Cortex in Good Readers: A Brain Imaging Study of Brazilian Children, *Developmental Neuropsychology*, 44:1, 146-157, DOI: [10.1080/87565641.2017.1292516](https://doi.org/10.1080/87565641.2017.1292516)


To link to this article: <https://doi.org/10.1080/87565641.2017.1292516>

 View supplementary material 

 Published online: 07 Feb 2018.

 Submit your article to this journal 



 Article views: 607

 View related articles 

 View Crossmark data 



Decoupling of the Occipitotemporal Cortex and the Brain's Default-Mode Network in Dyslexia and a Role for the Cingulate Cortex in Good Readers: A Brain Imaging Study of Brazilian Children

Augusto Buchweitz ^a, Adriana Corrêa Costa^a, Rudineia Toazza^b, Ana Bassôa de Moraes^c, Valentina Metsavaht Cara^{c,d}, Nathália Bianchini Esper^{c,e}, Cristiano Aguzzoli^d, Bruna Gregolim^d, Luiz Fernando Dresch^e, Matheus Dorigatti Soldatelli^d, Jaderson Costa da Costa^d, Mirna Wetters Portoguez^d, and Alexandre Rosa Franco ^e

^aSchool of Humanities, Brain Institute of Rio Grande do Sul (BRAINS), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, Brazil; ^bGraduate School of Neurosciences, Basic Health Sciences Institute, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil; ^cGraduate School of Medicine, Brain Institute of Rio Grande do Sul (BRAINS), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, Brazil; ^dSchool of Medicine, Brain Institute of Rio Grande do Sul (BRAINS), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, Brazil; ^eSchool of Engineering, Brain Institute of Rio Grande do Sul (BRAINS), Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, Brazil

ABSTRACT

The goal of the present study was to investigate intrinsic and reading-related brain function associated with dyslexia and typical readers in monolingual Brazilian children. Two fMRI studies were carried out: a resting-state and a word-reading study. The results show (a) underconnectivity between the occipitotemporal region (visual word form area) and the brain's default-mode network in dyslexic readers and (b) more activation of the anterior cingulate cortex for typical readers relative to dyslexic readers. The findings provide evidence for brain connectivity and function differences in an underrepresented population in fMRI studies of dyslexia; the results suggest atypical intrinsic function, and differences in directed attention processes in dyslexia.

Dyslexia is a brain-based learning disorder that affects approximately 5% to 10% of the world's population. It is characterized by a persistent and unexpected difficulty to develop age-appropriate fluent reading by readers who are otherwise motivated, intelligent, and regularly attend school (Lyon, Shaywitz, & Shaywitz, 2003; Pugh et al., 2000; Shaywitz et al., 2002). There are no psychiatric disorders or environmental factors that explain the persistently effortful and inaccurate reading in dyslexia. The disorder is associated with atypical brain structure and function relative to typically-developing readers. In the past 20 years, the evidence for the brain basis of dyslexia has evolved in light of noninvasive brain imaging studies. The present study aims to contribute to the understanding of the brain-behavior relationship in dyslexia.

Dyslexia is associated with atypical function of left-hemisphere posterior brain regions (Paulesu et al., 2001; Shaywitz, 1998; Shaywitz et al., 1998; Shaywitz et al., 2002). The atypical function includes hypoactivation of the left-lateralized, posterior brain systems (occipital, temporal, and

CONTACT Augusto Buchweitz, PhD  augusto.buchweitz@pucrs.br  Instituto do Cérebro do Rio Grande do Sul, Av. Ipiranga, 6690 - Jardim Botânico, Porto Alegre - RS, 91410-000, Brazil.

Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/HDVN.

This article has been republished with minor changes. These changes do not impact the academic content of the article.

 Supplemental data for this article can be accessed on the [publisher's website](#).

parietal) typically activated by children who learn to read fluently and in a timely manner (Devlin, Jamison, Gonnerman, & Matthews, 2006; Horwitz, Rumsey, & Donohue, 1998; Pugh et al., 1996; Shaywitz et al., 1998). There is amassing evidence of a relationship between the difficulty to develop fluent reading and the absence of activation of brain mechanisms associated with learning to read (Hoeft et al., 2011, 2007; Meyler et al., 2007; Shaywitz et al., 1998; Shaywitz et al., 2002, 2004). Typical readers develop a left-lateralized network of posterior brain systems that “grafts” onto the left-lateralized, hardwired language network for spoken language (Buchweitz, Mason, Tomitch, & Just, 2009; Constable et al., 2004; Michael, Keller, Carpenter, & Just, 2001; Pugh et al., 1996; Rueckl et al., 2015).

Dyslexia remains misunderstood in less-than-scientific pedagogical circles. The persistently poor reading performance in dyslexia is at times misrepresented as mere lack of motivation or of opportunity. In some circles it is even argued that there is no such thing as dyslexia; see, for example, the cases narrated in Shaywitz (2008), including schools that refuse to accommodate dyslexic students. Noninvasive brain imaging has contributed, and continues to contribute, to debunking these notions by providing evidence for the neurological basis of dyslexia.

Brain adaptation and learning to read: The role of the left occipitotemporal region (visual word form area)

Learning to read is a “fragile process” (Shonkoff & Families, 2000) that depends on timely stimulation and systematic instruction. Recently, a brain imaging study of four different languages (Spanish, English, Hebrew, and Chinese) showed evidence of a universal brain signature for listening and reading despite the idiosyncrasies of sounds of the languages, and of the different orthographies. The study showed that the brain signature for reading was similarly constrained by the left-lateralized brain network for spoken language, in all four languages (Rueckl et al., 2015).

Learning to read is associated with systematic adaptation of a brain center in the occipitotemporal region. The center is involved in associative visual processing of faces and objects. As one learns to read, it becomes specialized in the identification of the visual form of words (Cohen et al., 2000; Dehaene, 2009; Dehaene & Cohen, 2011). The region has been coined the visual word form area (VWFA), due to its newly found function (Laurent Cohen et al., 2002; Dehaene, 2009; Dehaene et al., 2010); the process of adaptation, in turn, has been coined “neuronal recycling” (Dehaene, 2009).

The activation of the occipitotemporal region is a brain marker of fluent reading development (Dehaene & Cohen, 2011; Dehaene et al., 2010; McCandliss, Cohen, & Dehaene, 2003). VWFA activation positively correlates with reading fluency, and it is also modulated by the age at which a reader is taught to read: There is more activation of the VWFA in readers who have learned to read as children than adults who learned later in life (Dehaene et al., 2010). It is a marker of the development of automaticity in reading. Visual objects in the shape of words are automatically recognized by the VWFA. The connectivity of the VWFA region was investigated in the present study in its association with dyslexia. We sought to explore evidence of disrupted intrinsic connectivity with the region in dyslexia.

Neural bases of reading in different languages

The investigation of learning disorders with noninvasive brain imaging holds promise for the future of evidence-based education policies. Though research in cognitive neuroscience and education differ in, for example, goals (e.g., understanding mind and brain relationships vs. improving educational material) (Ansari & Coch, 2006), the development of much-needed targeted interventions may benefit from an interaction between neuroscience and education (Stern, 2005).

A challenge faced by cognitive neuroscience is to broaden the research of reading to languages other than English; see, for example, the previously referred multi-language, multi-center study in Rueckl et al. (2015). Reading is nearly universal, and as such needs to be investigated in its different

orthographic forms and demographic settings. The transparency of orthographies is one of the variables across languages.

Orthographic transparency indicates the regularity of the letter-sound (grapheme-phoneme) associations (Seymour, Aro, & Erskine, 2003): the more regular (as in one-to-one) the associations between letters and sounds, the more transparent the orthography. For example, Spanish and Italian orthographies are transparent. In Spanish, there are five vowel sounds, one for each vowel symbol. English and French orthographies, on the other hand, are not transparent. In American English, there are about 16 vowel sounds for the five vowel symbols. Portuguese is relatively more transparent than French and English (Seymour et al., 2003). In a continuum of the transparency of orthographies of European languages, Portuguese is somewhere in the middle between the transparent and opaque (non-transparent) orthographies (Seymour et al., 2003).

This is the first brain imaging study to investigate brain function in Portuguese-speaking dyslexic children relative typical readers (either Continental or Brazilian Portuguese). There are, however, brain imaging studies of Portuguese reading and listening (Buchweitz, Shinkareva, Mason, Mitchell, & Just, 2012; Buchweitz et al., 2009; Castro-Caldas et al., 1999; Castro-Caldas, Petersson, Reis, & Stone-Elander, 1998). The present study aims to contribute to the understanding of atypical brain function that underpins dyslexia and of the disorder in an orthography that is under-represented in brain imaging studies.

The goal of the present study was to investigate brain function and brain functional connectivity in a dyslexic population of children and address the results in the light of brain imaging studies of the disorder. We carried out two functional magnetic resonance imaging (fMRI) studies to investigate brain function in dyslexic children and IQ, socioeconomic status and age-matched typical readers: a task-related study of word reading and a resting-state investigation of brain function.

Methods

Materials

Dyslexic readers were part of a cohort of children evaluated at a reading clinic. The clinic was established as part of an umbrella study of brain markers of reading development and disorders. The following reading tests (validated for Brazilian Portuguese children) were carried out: a word and pseudoword reading task (Salles, Piccolo, Zamo, & Toazza, 2013), a reading (silently and out-loud) fluency test and reading comprehension test (Saraiva, Moojen, & Munarski, 2006). The tests were applied with the reading clinic participants between 2014 and 2015, and typical readers in 2014 at the end of their second year of elementary school. A detailed description of the word and pseudoword reading, reading comprehension and writing evaluations protocols is published elsewhere (Costa, Toazza, Basso, Portuguese, & Buchweitz, 2015).

Participants

The study included 32 children divided into two groups, typical readers (TYP; $n = 16$) and dyslexic readers (DYS; $n = 16$). The participants were all monolingual speakers of Portuguese and right-handed. The two groups were matched for age and sex [age 7–13; mean = 9; $SD = 1.39$; TYP 07 female (mean age = 8.44; $SD = 0.51$); DYS 05 female (mean age = 9.63; $SD = 0.88$)]. All children were participants of a reading disorders and development study but from two different arms of the study: a longitudinal study (public schools) and a cross-sectional study (reading clinic). The 16 typical readers were part of a cohort of students from public schools enrolled in the longitudinal arm of the project; the goal of the study is to investigate the neurological markers of reading development over a 3-year period. For the present study, the school children were evaluated at the end of the 2014 school year, and were scanned during the 2015 school year.

The 16 dyslexic readers were from a pro bono reading clinic supported by the project. The goal of the clinic is to establish a cohort of dyslexic readers of Portuguese and investigate the neurological bases of dyslexia in the language. The clinic offers free psychological and reading and writing skills evaluation to students who present with persistent reading difficulties. It was implemented in 2013 and over 200 children have been evaluated since, out of which 52 dyslexic children have been identified. The 16 dyslexic children are part of this group and were scanned with an MRI between 2014 and 2015.

The reading fluency for the groups was significantly different. The school children showed adequate for age reading speed, and the dyslexic children showed reading performance scores well below what is expected for their age (Costa et al., 2015; Saraiva et al., 2006): TYP average reading speed 84.71 words per minute ($SD = 31.89$); DYS average reading speed 13.07 words per minute ($SD = 7.68$); $t(30) = 7.8$; $p < 0.001$.

Socioeconomic status (SES) and IQ were determined for the two population samples. SES was determined using the ABIPEME criteria for classification in Brazil (ABEP, 2008), which provides a score based on schooling and possession of consumer goods. These scores were available for 11 of the 16 participants in each group. The dyslexic and the typical readers were classified, on average, as level B2 SES in Brazil (DYS $M = 24.1$; $SD = 4.9$; TYP $M = 26.4$; $SD = 6.5$); there were no significant SES differences between the groups. The IQ was determined for all participants in the two groups (Wechsler Abbreviated Scale of Intelligence). There were no significant IQ differences between the groups (DYS $M = 108.3$, $SD = 15.5$, range 88–144; TYP $M = 102.7$, $SD = 15.3$, range 86–127).

Children and their guardians voluntarily enrolled in the clinic by e-mail. The first screening was carried out by phone, after which children who fit the study criteria were asked to participate in psychological and reading evaluations (Costa et al., 2015). The schools, in turn, were part of a larger longitudinal study of reading. The participants were selected based on reading scores carried out in the schools. The 16 children had the top reading scores among those who agreed to participate in the reading evaluations and the brain imaging parts of the longitudinal study, and were the better matches for age, IQ and SES with the 16 dyslexic participants. There was no penalty for choosing not to participate at all in the study or participating only in the reading evaluations stage of the study; the longitudinal and cross-sectional studies were approved by the Pontifical Catholic University of Rio Grande do Sul Research Ethics Committee.

Experimental design

A task-related and a resting-state paradigm were administered. The order of administration of the task and the resting state paradigms was randomized between participants (see [Supplementary Figure 1](#) for an illustration of the design matrix).

Resting-state

Participants were asked to keep their eyes open and stare at a fixation crosshair for 7 min. They were asked to clear their minds and try not to think of anything in particular for the duration of the experiment.

Word-reading task

A mixed event-related experiment was conducted using a word and pseudoword reading test validated for Brazilian children (Salles et al., 2013). The test stimuli are controlled for regularity of letter-sound association, word length and frequency in Portuguese. The task consists of 20 regular words, 20 irregular words, and 20 pseudowords. The 60 stimuli were divided into two 30-item runs to give participants a break halfway into the task. Words and pseudowords were presented on the screen one at a time, for 7 sec each. The duration of 7 sec was established in a behavioral pilot study (unpublished) with dyslexic children (average word reading time was approximately 4 1/2 sec, with a 2-sec standard deviation). A question was presented to participants together with each word (does the word exist?), to which participants had to select “Yes” or “No” by pressing response buttons. The

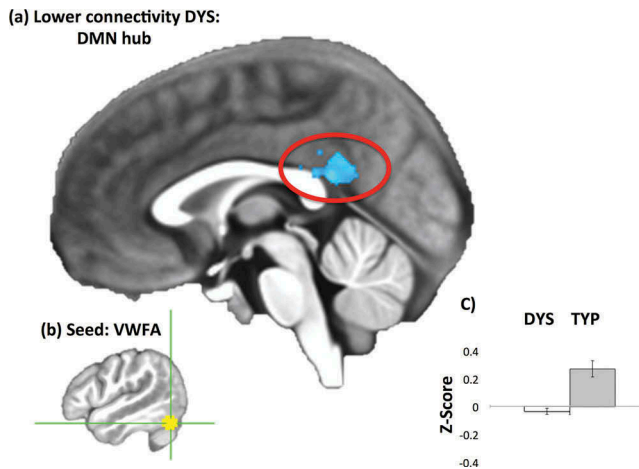


Figure 1. Lower connectivity between the VWFA and the posterior cingulate cortex for dyslexic readers relative to typical readers: (a) clusters significant at $p < 0.05$, corrected for multiple comparisons; MNI coordinates for posterior cingulate cluster: $x = -2.3$; $y = -41.0$; $z = 28.0$; 107 voxels. (b) VWFA seed located at MNI coordinates $x = -44$, $y = -58$, $z = -15$ (Dehaene & Cohen, 2011; Vigneau et al., 2005); the seed had an 8.0 mm radius. (c) Z-score difference between groups for the cluster shown in (a). The red ellipse highlights the cluster in the posterior cingulate cortex.

left-hand button was set for “Yes,” and right-hand button, for “No;” the configuration matched the left-right presentation of “Yes” and “No” on the screen. Response times and accuracy were recorded and computed for all trials. Prior to the scanning session, participants were given an out-of-scanner practice in an MRI simulator (Psychology Software Tools, Pittsburgh, PA) to become acclimated with the scanner environment and noise. The practice session included a shorter version of the word and pseudoword reading task that used different stimuli.

Stimulus presentation was offset by jittered intervals. The jittered intervals between word presentations ranged from 1 to 3 sec (in 1 sec intervals) and were randomly inserted after each trial. After 10 trials (10 words) either a baseline condition or rest period was inserted in the study. The baseline condition consisted of presentation of a crosshair in the middle of the screen for 30 sec. During the presentation of the crosshair, participants were instructed to relax and clear their minds. There were two 30-sec baseline conditions, one in each run. The rest periods also consisted of presentation of a crosshair, for 7 sec. Rest periods were not explicitly modeled in the analysis. A 6-sec dummy scan was inserted at the beginning of each 30-word set of tasks to ensure T1 magnetization reaches an equilibrium state. After the last presentation of stimuli, an additional 10-sec rest was inserted in each run. One subject from each group had to be excluded due to excessive head motion (see fMRI analyses in the following section).

Data collection

fMRI parameters

Data was collected on a GE HDxT 3.0 T MRI scanner with an 8-channel head coil. The following MRI sequences were acquired: a T1 structural scan (TR/TE = 6.16/2.18 ms, isotropic 1mm^3 voxels); two task-related 5-min 26-sec functional fMRI EPI sequences; and a 7-min resting state sequence. The task and the resting-state EPI sequences used the following parameters: TR = 2000 ms, TE = 30 ms, 29 interleaved slices, slice thickness = 3.5 mm; slice gap = 0.1 mm; matrix size = 64 x 64, FOV = 220 x 220 mm, voxel size = 3.44 x 3.44 x 3.60 mm.

Behavioral data analysis

Participants responded to the task using mice buttons. The response and response times were recorded using E-Prime (Psychology Software Tools, Pittsburgh, PA) for all trials. Behavioral data were analyzed for significant differences between TYP and DYS response times and accuracy for the lexical decision task.

fMRI analyses

Word reading task

Functional data were preprocessed using AFNI's (<http://afni.nimh.nih.gov/>) *afni_proc.py* program (Cox, 1996). Preprocessing included slice-time and motion correction, smoothing with a 6-mm FWHM Gaussian kernel, and a nonlinear spatial normalization to 3.0 x 3.0 x 3.0 mm voxel template (HaskinsPedsNL template). TR's with motion outliers (>0.9 mm) were censored from the data. The criteria for exclusion due to head motion were: excessive motion in 20% of the TRs. The average head motion for each group for the participants included in the study, in the word-reading paradigm, was: DYS $M = 0.16$ ($SD = 0.08$), TYP $M = 0.18$ ($SD = 0.15$). One participant from each group was excluded due to excessive head motion.

First level analysis included modeling regressors for the conditions for each of the three types of word (regular words, irregular words and pseudowords), and for the fixation condition, convolved with the canonical hemodynamic response function as implemented in AFNI (Cox, 1996). The 7-sec rest periods were not explicitly modeled. T-test analyses were carried out to compare the distribution of activation between the two groups (*3dttest++*) using a random-effects model and the contrast images for all word types versus fixation. To correct for multiple comparisons, the *3dClustSim* program was used to calculate a corrected p-score of <0.05: following the calculation, the analyses were carried out for a cluster of $p < 0.005$ with a minimum cluster size = 62 voxels (1674 μ l). Participant age was entered as a covariate in the analyses between groups to control for any effects due to the average one-year difference in age between the groups.

Resting-state

Preprocessing for the resting-state data was equivalent to the word reading task. Additional preprocessing for the resting-state data included a nuisance regression of the six estimated motion parameters (x, y, z roll, pitch, yaw) and time-series of the average signal of the white matter and cerebral spinal fluid, as well as signal detrending using a third order polynomial fit and a bandpass temporal filter (0.01 and 0.1 Hz) (Weissenbacher et al., 2009). TR's with motion outliers (>0.9 mm) were censored from the data. Participants with more than 20% of the TRs exceeding the limit were excluded. The average head motion for the participants included in resting state study was: DYS $M = 0.10$ ($SD = 0.05$), TYP $M = 0.15$ ($SD = 0.10$). The average number of TRs censored for the Dyslexic Group was 9.0 (± 9.2) and 12.8 (± 14.0) for the typically developing group for the resting task. Independent sample t-tests between groups for each task showed a t-score of -0.886 ($p = 0.383$). For additional verification of the effects of head-motion on resting-state results (e.g. Satterthwaite et al., 2012), we carried out a more conservative analysis of the data: participants with motion outliers >0.3 mm in 20% of the TRs were excluded. The reanalysis eliminated five participants (4 typical, 1 dyslexic). Nonetheless, the seed-based connectivity result reported in the results section remained significant. We thus report the result for the analysis of resting-state data including all 32 participants. The average number of TRs censored for the Dyslexic Group was 11.5 (± 18.1) and 11.5 (± 11.1) for the typically developing group for the reading task. Independent sample t-tests between groups for each task showed a t-score of 0.12 ($p = 0.990$).

In the present study, functional connectivity refers to correlations of resting-state BOLD signal for specific language-related regions of the brain and the default mode network, within subjects

in the two groups. Seed-based analysis of connectivity was performed. A spherical seed was drawn to investigate the connectivity between reading-related regions of the left-hemisphere and the remainder of the brain. The following areas of the brain were investigated: (all radii 8.0 mm; all coordinates Montreal Neurological Institute, MNI) left fusiform gyrus/visual word form area ($x = -44$, $y = -58$, $z = -15$); left angular gyrus ($x = -45$, $y = -64$, $z = 33$); left inferior frontal gyrus ($x = -44$, $y = 24$, $z = 2$); left middle temporal gyrus ($x = -52$, $y = -19$, $z = 7$); left superior temporal gyrus ($x = -51$, $y = -17$, $z = 0$). For each subject, the average time course of the voxels within the seed was extracted and then a Pearson's correlation was calculated of this time-series against all the voxels of the brain. The resulting r -score was then converted to z using Fisher's method. An independent sample t -test analysis was performed between groups, where age was included as a covariate. Statistical group differences were corrected for multiple comparison as previously described.

Results

Resting-state: Intrinsic connectivity of the VWFA and the posterior cingulate cortex in dyslexia

The results for the resting state experiment show lower connectivity for the DYS group between the VWFA seed and the posterior cingulate cortex (107 voxels, 2.8 ml, peak coordinate: $x = 1.5$, $y = -44.5$, $z = 21.5$) (Figure 1). The other language-related seeds investigated did not show a significant difference between dyslexic and typical readers in the analyses of resting-state data. The decoupling of the VWFA and the posterior cingulate cortex (PCC) was also found using the stricter threshold for head motion (head motion TR >0.03 mm; 145 voxels; 3.9 ml, $p < 0.05$ corrected for multiple comparisons).

Word-reading task: More activation of the anterior cingulate cortex for good readers

The results show more activation of the dorsal portion of the Anterior Cingulate Cortex (ACC) in typical readers, relative to dyslexic readers (Figure 2). The dorsal portion is part of the subdivision of the ACC associated with cognitive control (Bush, Luu, & Posner, 2000; Devinsky, Morrell, & Vogt, 1995; Vogt, Finch, & Olson, 1991). The comparison of activation for reading regular, irregular, and pseudo-words for typical readers relative to dyslexic readers also showed more activation of the ACC in each of the three conditions; these results are shown in Supplementary Figure 2. Additionally, a plot of the impulse response for the reading tasks separated by word-type condition and collapsed across all words is shown in Supplementary Figure 3. The impulse response is shown for the VWFA, it shows under-activation of the posterior region in dyslexia, relative to typical readers. Combined, the results for the resting-state experiment and the word-reading experiment suggest differences in typical readers and dyslexic readers in intrinsic connectivity and in task-related VWFA function.

Behavioral results: Lower accuracy and slower response in dyslexia

The accuracy and response times for the task in the scanner show that DYS were significantly less accurate and slower than typical readers to make the lexical decisions: DYS accuracy = 0.62 ($SE = 0.06$); TYP accuracy = 0.91 ($SE = 0.02$); $t(30) = -4.30$, $p < 0.001$. DYS RT = 3858 ms ($SE = 268$); TYP RT = 2138 ms ($SE = 116$); $t(30) = 5.87$; $p < 0.001$. The results corroborate our previous reading tests carried out in the schools and reading clinic, and the existing literature, which show that dyslexic readers are characteristically slower and less accurate than appropriate for reading age.

TYP > DYS

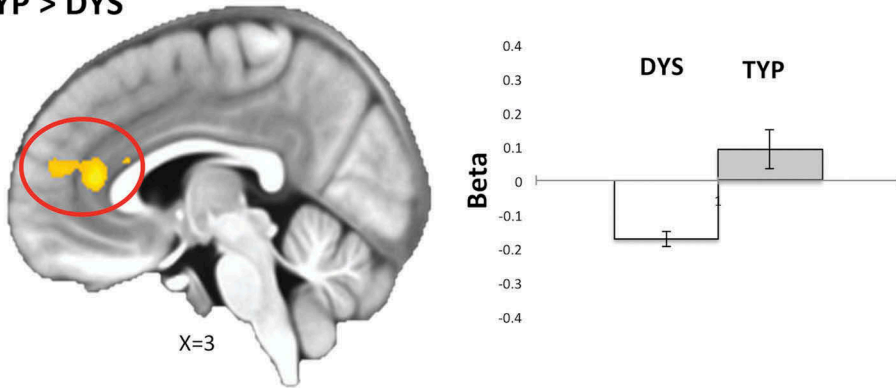


Figure 2. More activation of the anterior cingulate gyrus for typical readers relative to dyslexic readers during reading. Clusters significant at $p < 0.05$, corrected for multiple comparisons (165 voxels, 4.455ml; MNI coordinates $x = 1.5$; $y = 33.5$; $z = 12.5$). The bar graphs show the beta values for both groups for activation in the anterior cingulate region highlighted with the red ellipse. Standard error bars are shown for the beta values.

Discussion

The present study shows evidence of brain-behavior relationship for the anterior and posterior regions of the cingulate cortex in typical reading and in dyslexia. The resting-state study showed that there is a disruption in the connectivity between the PCC and a key area for reading, in dyslexia. In the word reading task, the ACC was more active in typical readers. More activation of this portion of the ACC suggests executive function processes associated with achieving fluent reading in the early stages of typical reading.

VWFA and the default mode network: The functional architecture of the reading brain at rest

An increasing number of studies have used resting-state to investigate the intrinsic functional connectivity of the brain in clinical populations (Binder et al., 1999; Damoiseaux & Greicius, 2009; Mannell et al., 2010; Supekar et al., 2010). One of the reasons for the increasing number of resting-state studies is the reproducibility across studies and sites (Franco, Mannell, Calhoun, & Mayer, 2013): for example, the multi-site consortium of autism brain imaging data (Nielsen et al., 2013).

Resting-state brain imaging studies have helped unveil neuromarkers associated with the brain function of clinical conditions, such as social anxiety (Geiger et al., 2015; Toazza et al., 2016), stutter (Xuan et al., 2012), autism (Nielsen et al., 2013), and dyslexia (Koyama et al., 2010; Schurz et al., 2015; Wei, Zhichao, Yanchao, & Hua, 2015). The technique shows promise for the understanding of the brain architecture of clinical populations, and for predicting brain-behavior relationships based on patterns of intrinsic brain connectivity. The question, in relation to dyslexia, lies in understanding the patterns of brain function at rest associated with key centers for reading.

The present study shows evidence of disrupted connectivity between the visual word form area and the PCC in a resting-state paradigm (there was a negative correlation between VWFA and PCC function). For typical readers, in turn, there was a positive correlation between the two centers. The result converges with other resting-state studies that suggest that the coupling between occipitotemporal regions of the brain and the brain's default mode network is disrupted in dyslexia. In a study of three dyslexic groups (no remediation, partial remediation, and full remediation), an increase in resting-state functional connectivity was identified between the visual word form area and medial prefrontal cortex in full remediation participants (Koyama et al., 2013). In another study, reading performance positively correlated with stronger connectivity between the visual word form

area and anterior and posterior regions of the brain associated with phonological processing (Koyama et al., 2011). A study of correspondence between brain function in tasks and at rest showed the occipitotemporal region integrated a frontal-posterior network of brain regions that were strongly left-lateralized and associated with language paradigms (Smith et al., 2009). The present study corroborates the evidence that the coupling of the occipitotemporal region with other centers in the brain is associated with reading performance.

We postulate that the coupling of the VWFA in typical reading, and decoupling in dyslexia, may be evidence that as a child learns to read an “open channel” of communication is setup between the default mode network and the visual word form area. At rest, the brain of a typical reader would sync up with the VWFA; it may evidence of a state of readiness for reading. At rest, the brain of a dyslexic reader, in turn, is decoupled from the VWFA.

Role for the anterior cingulate in early reading development

The ACC is associated with emotional processes, as part of the limbic system, but is also implicated in executive functions and the ability to focus attention (Bush et al., 2000; Vogt et al., 1991). According to more fine-grained investigations of ACC function, cognitive and emotional processes are subserved by different sections of the ACC: the dorsal cognitive division, and the rostral emotional division, respectively (Bush et al., 2000; Devinsky et al., 1995; Vogt et al., 1991). In the present study, the region of the ACC more active for typical readers was the dorsal cognitive division described in previous studies.

Activation of the ACC has been identified in investigations of typical, nonimpaired readers relative to dyslexic readers (Shaywitz et al., 2002; Shaywitz & Shaywitz, 2005). The study showed more activation for the ACC, relative to baseline, for nonimpaired readers than poor readers while they performed a rhyme task in the scanner (in the study, the ACC activation for the nonimpaired readers in the rhyme task did not survive the direct comparison with the dyslexic readers). Additionally, in the same study, activation of the ACC was negatively correlated with performance. The latter result was interpreted as an indication of poorer reading being associated with the need to put forth a greater deal of mental effort (Shaywitz et al., 2002). A role for the ACC activation for nonimpaired readers remains to be better understood.

It is possible that in earlier stages of reading, a greater deal of directed attention is a marker of more fluent reading. The present study shows that typical readers activated the ACC more than dyslexic readers in the word reading task. The difference resulted from significant deactivation of the ACC in dyslexic readers in the task, relative to baseline (as the Beta values show) versus activation of the ACC in typical readers, relative to baseline. The ACC is remarkably disengaged in dyslexic readers.

ACC dysfunction has been associated with inattention and impulsivity in attention-deficit/hyperactivity disorder (Bush et al., 1999). The ACC has also been implicated in a study of reading compensation in young adults. The accuracy-improved (compensated) poor readers, relative to persistently poor readers, showed more activation of the ACC (Shaywitz et al., 2003). It is possible that typical readers engage the ACC as a function of focusing attention and the effort associated with reading in early stages. Their average reading speed, for example, was 84 words per minute; reading at this speed reflects effortful reading at the word level (though it is an adequate speed for the age of the typical readers). The ability to read more fluently and accurately at this age may require more attention at the word level than at later, more mature stages of reading as some adult fluent readers surpass the 180 words per minute mark.

The increased activation of the ACC may be associated with psychological processes of strategic control that are part of learning of a novel process (Chein & Schneider, 2005). In sum, the present study provides evidence of the functional organization of dyslexia and typical reading, suggesting differences in the configuration of the brain at rest and during word reading. The findings extend previous studies and suggest a mechanism of coupling/decoupling between the VWFA and the brain's DMN associated with dyslexia.

Funding

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001

ORCID

Augusto Buchweitz  <http://orcid.org/0000-0003-3791-7472>

Alexandre Rosa Franco  <http://orcid.org/0000-0002-1552-1090>

References

- Associação Nacional de Empresas e Pesquisas (ABEP). (2008). *Critério de classificação econômica Brasil* [Brazilian Association of Market Research Institutes Criterion]. São Paulo, Brazil: ABEP.
- Ansari, D., & Coch, D. (2006). Bridges over troubled waters: Education and cognitive neuroscience. *Trends in Cognitive Sciences*, 10(4), 146–151. doi:10.1016/j.tics.2006.02.007
- Binder, J. R., Frost, J. A., Hammeke, T. A., Bellgowan, P. S. F., Rao, S. M., & Cox, R. W. (1999). Conceptual processing during the conscious resting state: A functional MRI study. *Journal of Cognitive Neuroscience*, 11(1), 80–93. doi:10.1162/089892999563265
- Buchweitz, A., Mason, R., Tomitch, L., & Just, M. (2009). Brain activation for reading and listening comprehension: An fMRI study of modality effects and individual differences in language comprehension. *Psychology and Neuroscience*, 2(2), 111–123. doi:10.3922/j.psns.2009.2.003
- Buchweitz, A., Shinkareva, S. V., Mason, R. A., Mitchell, T. M., & Just, M. A. (2012). Identifying bilingual semantic neural representations across languages. *Brain and Language*, 120(3), 282–289. doi:10.1016/j.bandl.2011.09.003
- Bush, G., Frazier, J. A., Rauch, S. L., Seidman, L. J., Whalen, P. J., Jenike, M. A., ... Biederman, J. (1999). Anterior cingulate cortex dysfunction in attention-deficit/hyperactivity disorder revealed by fMRI and the counting Stroop. *Biological Psychiatry*, 45(12), 1542–1552. doi:10.1016/S0006-3223(99)00083-9
- Bush, G., Luu, P., & Posner, M. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, 4(6), 215–222. doi:10.1016/S1364-6613(00)01483-2
- Castro-Caldas, A., Miranda, P. C., Carmo, I., Reis, A., Leote, F., Ribeiro, C., & Ducla-Soares, E. (1999). Influence of learning to read and write on the morphology of the corpus callosum. *European Journal of Neurology: the Official Journal of the European Federation of Neurological Societies*, 6, 23–28. doi:10.1046/j.1468-1331.1999.610023.x
- Castro-Caldas, A., Petersson, K. M., Reis, A., & Stone-Elander, S. (1998). The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. *Brain*, 121, 1053–1063. doi:10.1093/brain/121.6.1053
- Chein, J. M., & Schneider, W. (2005). Neuroimaging studies of practice-related change: FMRI and meta-analytic evidence of a domain-general control network for learning. *Brain Research. Cognitive Brain Research*, 25(3), 607–623. doi:10.1016/j.cogbrainres.2005.08.013
- Cohen, L., Dehaene, S., Naccache, L., Lehéricy, S., Dehaene-Lambertz, G., Hénaff, M. A., & Michel, F. (2000). The visual word form area: Spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain: A Journal of Neurology*, 123(Pt 2), 291–307. doi:10.1093/brain/123.2.291
- Cohen, L., Lehéricy, S., Chochon, F., Lemer, C., Rivaud, S., & Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the visual word form area. *Brain: A Journal of Neurology*, 125(Pt 5), 1054–1069. doi:10.1093/brain/awf094
- Constable, R. T., Pugh, K. R., Berroya, E., Mencl, W. E., Westerveld, M., Ni, W., & Shankweiler, D. (2004). Sentence complexity and input modality effects in sentence comprehension: An fMRI study. *NeuroImage*, 22(1), 11–21. doi:10.1016/j.neuroimage.2004.01.001
- Costa, A. C., Toazza, R., Bassoa, A., Portuguese, M. W., & Buchweitz, A. (2015). Ambulatório de Aprendizagem do Projeto ACERTA (Avaliação de Crianças Em Risco de Transtorno de Aprendizagem): Métodos e resultados em dois anos [Clinic for learning, Project ACERTA (evaluation of children at risk for learning disorders): Methods and results over the course of two years]. In J. F. Salles, V. G. Haase, & L. Malloy-Diniz (Eds.), *Neuropsicologia do Desenvolvimento: Infância e adolescência* (pp. 151–158). Porto Alegre, Brazil: Artmed.
- Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal*, 29(3), 162–173. doi:10.1006/cbmr.1996.0014
- Damoiseaux, J. S., & Greicius, M. D. (2009). Greater than the sum of its parts: A review of studies combining structural connectivity and resting-state functional connectivity. *Brain Structure & Function*, 213(6), 525–533. doi:10.1007/s00429-009-0208-6
- Dehaene, S. (2009). *Reading in the brain: The new science of how we read*. New York, NY: Penguin Books.

- Dehaene, S., & Cohen, L. (2011, June). The unique role of the visual word form area in reading. *Trends in Cognitive Sciences*, 15, 254–262. doi:10.1016/j.tics.2011.04.003
- Dehaene, S., Pegado, F., Braga, L. W., Ventura, P., Nunes Filho, G., Jobert, A., ... Cohen, L. (2010). How learning to read changes the cortical networks for vision and language. *Science (New York, N.Y.)*, 330(6009), 1359–1364. doi:10.1126/science.1194140
- Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain: A Journal of Neurology*, 118(Pt 1(August)), 279–306. doi:10.1093/brain/118.1.279
- Devlin, J. T., Jamison, H. L., Gonnerman, L. M., & Matthews, P. M. (2006). The role of the posterior fusiform gyrus in reading. *Journal of Cognitive Neuroscience*, 18(6), 911–922. doi:10.1162/jocn.2006.18.6.911
- Franco, A. R., Mannell, M. V., Calhoun, V. D., & Mayer, A. R. (2013). Impact of analysis methods on the reproducibility and reliability of resting-state networks. *Brain Connectivity*, 3(4), 363–374. doi:10.1089/brain.2012.0134
- Geiger, M. J., Domschke, K., Ipser, J., Hattingh, C., Baldwin, D. S., Lochner, C., & Stein, D. J. (2015). Altered executive control network resting-state connectivity in social anxiety disorder. *The World Journal of Biological Psychiatry: The Official Journal of the World Federation of Societies of Biological Psychiatry*, 17(1), 47–57. doi:10.3109/15622975.2015.1083613
- Hoefl, F., McCandliss, B. D., Black, J. M., Gantman, A., Zakerani, N., Hulme, C., ... Gabrieli, J. D. E. (2011). Neural systems predicting long-term outcome in dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 108(1), 361–366. doi:10.1073/pnas.1008950108
- Hoefl, F., Ueno, T., Reiss, A. L., Meyler, A., Whitfield-Gabrieli, S., Glover, G. H., ... Gabrieli, J. D. E. (2007). Prediction of children's reading skills using behavioral, functional, and structural neuroimaging measures. *Behavioral Neuroscience*, 121(3), 602–613. doi:10.1037/0735-7044.121.3.602
- Horwitz, B., Rumsey, J. M., & Donohue, B. C. (1998). Functional connectivity of the angular gyrus in normal reading and dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 95(15), 8939–8944. doi:10.1073/pnas.95.15.8939
- Koyama, M. S., Di Martino, A., Kelly, C., Jutagir, D. R., Sunshine, J., Schwartz, S. J., ... Milham, M. P. (2013). Cortical signatures of dyslexia and remediation: An intrinsic functional connectivity approach. *Plos One*, 8(2), e55454. doi:10.1371/journal.pone.0055454
- Koyama, M. S., Di Martino, A., Zuo, X.-N., Kelly, C., Mennes, M., Jutagir, D. R., ... Milham, M. P. (2011). Resting-state functional connectivity indexes reading competence in children and adults. *The Journal of Neuroscience: the Official Journal of the Society for Neuroscience*, 31(23), 8617–8624. doi:10.1523/JNEUROSCI.4865-10.2011
- Koyama, M. S., Kelly, C., Shehzad, Z., Penesetti, D., Castellanos, F. X., & Milham, M. P. (2010). Reading networks at rest. *Cerebral Cortex (New York, N.Y. : 1991)*, 20(11), 2549–2559. doi:10.1093/cercor/bhq005
- Lyon, G. R., Shaywitz, S. E., & Shaywitz, B. A. (2003). A definition of dyslexia. *Annals of Dyslexia*, 53(1), 1–14. doi:10.1007/s11881-003-0001-9
- Mannell, M. V., Franco, A. R., Calhoun, V. D., Cañive, J. M., Thoma, R. J., & Mayer, A. R. (2010). Resting state and task-induced deactivation: A methodological comparison in patients with schizophrenia and healthy controls. *Human Brain Mapping*, 31(3), 424–437. doi:10.1002/hbm.20876
- McCandliss, B. D., Cohen, L., & Dehaene, S. (2003, July). The visual word form area: Expertise for reading in the fusiform gyrus. *Trends in Cognitive Sciences*, 7, 293–299. doi:10.1016/S1364-6613(03)00134-7
- Meyler, A., Keller, T. A., Cherkassky, V. L., Lee, D., Hoefl, F., Whitfield-Gabrieli, S., ... Just, M. A. (2007). Brain activation during sentence comprehension among good and poor readers. *Cerebral Cortex (New York, N.Y. : 1991)*, 17(12), 2780–2787. doi:10.1093/cercor/bhm006
- Michael, E. B., Keller, T. A., Carpenter, P. A., & Just, M. A. (2001). fMRI investigation of sentence comprehension by eye and by ear: Modality fingerprints on cognitive processes. *Human Brain Mapping*, 13(4), 239–252. doi:10.1002/(ISSN)1097-0193
- Nielsen, J. A., Zielinski, B. A., Fletcher, P. T., Alexander, A. L., Lange, N., Bigler, E. D., ... Anderson, J. S. (2013). Multisite functional connectivity MRI classification of autism: ABIDE results. *Frontiers in Human Neuroscience*, 7 (September), 599. doi:10.3389/fnhum.2013.00599
- Paulesu, E., Démonet, J. F., Fazio, F., McCrory, E., Chanoine, V., Brunswick, N., ... Frith, U. (2001). Dyslexia: Cultural diversity and biological unity. *Science*, 291(5511), 2165–2167. doi:10.1126/science.1057179
- Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Jun Ren Lee, S. J., ... Shaywitz, B. A. (2000). Functional neuroimaging studies of reading and reading disability (developmental dyslexia). *Mental Retardation & Developmental Disabilities Research Reviews*, 6(3), 207–213. doi:10.1002/1098-2779(2000)6
- Pugh, K. R., Shaywitz, B. A., Shaywitz, S. E., Constable, R. T., Skudlarski, P., Fulbright, R. K., ... Gore, J. C. (1996). Cerebral organization of component processes in reading. *Brain*, 119(6), 1221–1238. doi:10.1093/brain/119.4.1221
- Rueckl, J. G., Paz-Alonso, P. M., Molfese, P. J., Kuo, W.-J., Bick, A., Frost, S. J., ... Frost, R. (2015). Universal brain signature of proficient reading: Evidence from four contrasting languages. *Proceedings of the National Academy of Sciences of the United States of America*, 112(50), 15510–15515. doi:10.1073/pnas.1509321112
- Salles, J., Piccolo, L. R., Zamo, R. S., & Toazza, R. (2013). Normas de desempenho em tarefa de leitura de palavras/pseudopalavras isoladas (LPI) para crianças de 1º ano a 7º ano [Developmental Standards in a Word/Pseudoword

- Reading Task for Children in Elementary School]. *Estudos E Pesquisas Em Psicologia*, 13(2), 397–419. doi:10.12957/ep.2013.8416
- Saraiva, R., Moojen, S., & Munarski, R. (2006). *Avaliação da compreensão leitora de textos expositivos* [Evaluation of reading comprehension of expository texts]. São Paulo, Brazil: Casa Do Psicólogo.
- Satterthwaite, T. D., Wolf, D. H., Loughhead, J., Ruparel, K., Elliott, M. A., Hakonarson, H., ... Gur, R. E. (2012). Impact of in-scanner head motion on multiple measures of functional connectivity: Relevance for studies of neurodevelopment in youth. *NeuroImage*, 60(1), 623–632. doi:10.1016/j.neuroimage.2011.12.063
- Schurz, M., Wimmer, H., Richlan, F., Ludersdorfer, P., Klackl, J., & Kronbichler, M. (2015). Resting-state and task-based functional brain connectivity in developmental dyslexia. *Cerebral Cortex*, 25(10), 3502–3514. doi:10.1093/cercor/bhu184
- Seymour, P. H. K., Aro, M., & Erskine, J. M. (2003). Foundation literacy acquisition in European orthographies. *British Journal of Psychology* (London, England: 1953), 94(Pt 2), 143–174. doi:10.1348/000712603321661859
- Shaywitz, S. E. (1998). Dyslexia. *New England Journal of Medicine*, 338, 307–312. doi:10.1056/NEJM199801293380507
- Shaywitz, S. E. (2008). *Overcoming dyslexia: A new and complete science-based program for reading problems at any level* (Vintage). New York, NY: Vintage.
- Shaywitz, B. A., Shaywitz, S. E., Blachman, B. A., Pugh, K. R., Fulbright, R. K., Skudlarski, P., ... Gore, J. C. (2004). Development of left occipitotemporal systems for skilled reading in children after a phonologically-based intervention. *Biological Psychiatry*, 55(9), 926–933. doi:10.1016/j.biopsych.2003.12.019
- Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, P., ... Gore, J. C. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. *Society of Biological Psychiatry*, 3223(2), 101–110. doi:10.1016/S0006-3223(02)01365-3
- Shaywitz, S. E., & Shaywitz, B. A. (2005). Dyslexia (specific reading disability). *Biological Psychiatry*, 57(11), 1301–1309. doi:10.1016/j.biopsych.2005.01.043
- Shaywitz, S. E., Shaywitz, B. A., Fulbright, R. K., Skudlarski, P., Mencl, W. E., Constable, R. T., ... Gore, J. C. (2003). Neural systems for compensation and persistence: Young adult outcome of childhood reading disability. *Biological Psychiatry*, 54(1), 25–33. doi:10.1016/S0006-3223(02)01836-X
- Shaywitz, S. E., Shaywitz, B. A., Pugh, K. R., Fulbright, R. K., Constable, R. T., Mencl, W. E., ... Gore, J. C. (1998). Functional disruption in the organization of the brain for reading in dyslexia. *Proceedings of the National Academy of Sciences*, 95(5), 2636–2641. doi:10.1073/pnas.95.5.2636
- Shonkoff, J. P., & Families, B. on C. Y. (2000). *From neurons to neighborhoods: The science of early childhood development*. Washington, DC: National Academies Press.
- Smith, S. M., Fox, P. T., Miller, K. L., Glahn, D. C., Fox, P. M., Mackay, C. E., ... Beckmann, C. F. (2009). Correspondence of the brain's functional architecture during activation and rest. *Proceedings of the National Academy of Sciences of the United States of America*, 106(31), 13040–13045. doi:10.1073/pnas.0905267106
- Stern, E. (2005). Pedagogy meets neuroscience. *Science*, 310(5749), 745. doi:10.1126/science.1121139
- Supekar, K., Uddin, L. Q., Prater, K., Amin, H., Greicius, M. D., & Menon, V. (2010). Development of functional and structural connectivity within the default mode network in young children. *NeuroImage*, 52(1), 290–301. doi:10.1016/j.neuroimage.2010.04.009
- Toazza, R., Franco, A. R., Buchweitz, A., Molle, R. D., Rodrigues, D. M., Reis, R. S., ... Manfro, G. G. (2016). Amygdala-based intrinsic functional connectivity and anxiety disorders in adolescents and young adults. *Psychiatry Research: Neuroimaging*, 257, 11–16. doi:10.1016/j.psychres.2016.09.010
- Vogt, B. A., Finch, D. M., & Olson, C. R. (1991). Functional heterogeneity in cingulate cortex: The anterior executive and posterior evaluative regions. *Cerebral Cortex* (New York, N.Y.: 1991), 2(6), 435–443.
- Wei, Z., Zhichao, X., Yanchao, B., & Hua, S. (2015). Altered connectivity of the dorsal and ventral visual regions in dyslexic children: A resting-state fMRI study. *Frontiers in Human Neuroscience*, 9(September), 1. doi:10.3389/fnhum.2015.00495
- Weissenbacher, A., Kasess, C., Gerstl, F., Lanzenberger, R., Moser, E., & Windischberger, C. (2009). Correlations and anticorrelations in resting-state functional connectivity MRI: A quantitative comparison of preprocessing strategies. *NeuroImage*, 47(4), 1408–1416. doi:10.1016/j.neuroimage.2009.05.005
- Xuan, Y., Meng, C., Yang, Y., Zhu, C., Wang, L., Yan, Q., ... Yu, C. (2012). Resting-state brain activity in adult males who stutter. *Plos One*, 7(1), e30570. doi:10.1371/journal.pone.0030570