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Resting state functional connectivity of the anterior striatum and prefrontal cortex predicts reading performance in school-age children

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ABSTRACT

The current study investigated the neural basis of reading performance in 60 school-age Spanish-speaking children, aged 6 to 9 years. By using a data-driven approach and an automated matching procedure, we identified a left-lateralized resting state network that included typical language regions (Wernicke's and Broca's regions), prefrontal cortex, pre- and post-central gyri, superior and middle temporal gyri, cerebellum, and subcortical regions, and explored its relevance for reading performance (accuracy, comprehension and speed). Functional connectivity of the left frontal and temporal cortices and subcortical regions predicted reading speed. These results extend previous findings on the relationship between functional connectivity and reading competence in children, providing new evidence about such relationships in previously unexplored regions in the resting brain, including the left caudate, putamen and thalamus. This work highlights the relevance of a broad network, functionally synchronized in the resting state, for the acquisition and perfecting of reading abilities in young children.

1. Introduction

Learning to read requires intensive practice and refinement during childhood and adolescence. During this process, several brain regions are recruited and start to specialize and integrate into an extensive network that is generally left lateralized (Houdé, Rossi, Lubin, & Joliot, 2010; Martin, Schurz, Kronbichler, & Richlan, 2015). This network includes, among others, three main functionally specialized regions described in a classical model for reading (Pugh et al., 2000): the temporo-parietal cortex, the ventral occipito-temporal region and the inferior frontal cortex. The temporo-parietal cortex, including the superior temporal, supramarginal and angular gyri is associated with grapho-phonological conversion and thus, with phonology-based reading. The occipito-temporal region includes the fusiform and inferior temporal regions, and has been termed as the visual word form area, associated with visual-orthographic word recognition (Cohen et al., 2000). Finally, the inferior frontal cortex, including the inferior frontal and precentral gyri, has been attributed with linking phonemic sequences with motor gestures. Developmentally, this model assumes that beginning readers mainly use a phonology-based strategy, while skilled readers rely on a visual-orthographic strategy for word recognition (Pugh et al., 2000). Recent meta-analyses of task-based functional magnetic resonance imaging studies (fMRI) have contributed to better describe such network and its developmental properties (Houdé et al., 2010; Martin et al., 2015). However, meta-analyses of task-based fMRI studies may struggle to capture the functional specialization and integration of a broader brain network for reading across development. For example, the striatum has been associated with semantic, phonological, and articulatory processes while reading (Binder, Medler, Westbury, Liebenthal, & Buchanan, 2006; Bitan et al., 2007; Brem et al., 2009; Xu, Kemeny, Park, Frattali, & Braun, 2005); nonetheless, the meta-analyses of task-based studies in children fail to identify consistent activation of such structures (Houdé et al., 2010; Martin et al., 2015).

The use of functional magnetic resonance imaging (fMRI) to explore the resting brain has proven to be a valuable tool to provide complementary information about its functional architecture (Biswal, Yetkin, Haughton, & Hyde, 1995). The resting state data can be explored in terms of functional connectivity, that is, the inter-regional correlation of low-frequency (<0.1 Hz) fluctuations of BOLD signal. This technique has been valuable in exploring the maturation of brain functional organization in children and infants as young as 2 weeks of age (Gao, Alcauter, Smith, Gilmore, & Lin, 2015; Gao et al., 2015; Muetzel et al., 2016; Power, Fair, Schlaggar, & Petersen, 2010), and has identified the relevance of such functional architecture for cognitive performance (Alcauter et al., 2015; Gordon, Devaney, Bean, & Vaidya,

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2015; van den Heuvel, Stam, Kahn, & Hulshoff Pol, 2009; Xu et al., 2014). In particular, recent studies have explored the relationship between reading performance and the functional connectivity of sets of regions previously identified as relevant for reading (Hampson et al., 2006; Koyama et al., 2010). Some of these studies have already focused on the study of the reading-related networks in children, showing interesting developmental differences from adults (Koyama et al., 2011; Vogel et al., 2013). Although results of the above studies have been valuable, most of them focused on exploring a limited set of regions mainly dictated by meta-analyses of task-based studies, probably hindering the description of a wider network and its relevance for the early acquisition and further refinement of reading abilities.

Here, we applied a data-driven approach to identify a set of resting state networks in a sample of school-age children (6 to 9 years old). Then, we tested if any of these networks showed a similar configuration as the set of regions previously reported in the meta-analyses of reading-related studies in children (Houdé et al., 2010; Martin et al., 2015). Finally, we examined whether the intrinsic functional connectivity of such a network (if identified) showed any correlation with reading performance. We made use of independent component analysis (ICA) as the data-driven approach, which aims to decompose the resting state fMRI (rsfMRI) data into a set of time-courses and associated maps (Beckmann, DeLuca, Devlin, & Smith, 2005). This procedure has already revealed several brain networks highly similar to the networks identified in a variety of tasks (Beckmann et al., 2005; Smith et al., 2009). Then we obtained a matching score with previously identified reading-related regions in children to test if we could identify a “reading-related” network. We hypothesized that ICA would reveal a resting state network containing the relevant regions for reading in children, as reported in a recent meta-analysis (Martin et al., 2015) and that intrinsic functional connectivity of this network would correlate with reading performance.

2. Material and methods

2.1. Subjects

The participants were part of a larger study exploring the relationship between brain connectivity and cognitive performance in school-age children (Moreno, Concha, González-Santos, Ortiz, & Barrios, 2014). A general invitation explaining the characteristics and inclusion criteria of the study was made through local schools in the metropolitan area of Queretaro, Mexico; parents were asked to talk with their children about whether they wanted to participate in interviews and MRI sessions. Inclusion criteria consisted of full-term gestation (at least 37 weeks) and being enrolled in elementary school. Exclusion criteria included any neurological, psychiatric, neurodevelopmental, learning and/or language impairment as well as repetition of a prior school year. Informed written consent was obtained from the parents of every participant that decided to take part in the study. The methods for this research project followed the principles of the Declaration of Helsinki and were approved by the Bioethics Committee of the Neurobiology Institute (Comité de Bioética del Instituto de Neurobiología).

The sample of this study was retrospectively identified, based on availability of a resting state functional MRI and high resolution T1 images (see below for details), resulting in a dataset of 66 participants (30 boys, 36 girls), aged 6.7–9.8 years, native Spanish speakers (no multilingual subjects included). The protocol included the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID), a short structured diagnostic interview for psychiatric disorders in children and adolescents (Sheehan et al., 2000, 2010), a general medical examination, MR imaging (see Moreno et al. (2014)), and an extensive neuropsychological exploration (ENI, from the Spanish “Evaluación Neuropsicológica Infantil”, which can be translated as Neuropsychological Assessment for Children) (Matute, Rosselli, Ardila, & Ostrosky-Solís, 2007).

The data from six subjects (5 boys, 1 girl) had to be excluded due to excessive motion artifacts in the fMRI data (see below). Thus, from the original 66 fMRI datasets, only 60 (25 boys, 35 girls, mean age: 8.46 ± 0.77 years) were suitable for the subsequent analyses.

2.2. Neuropsychological assessment

An integrated battery of tests was applied as an initial exclusion evaluation in the original sample, including the MINI-KID for children and adolescents (Sheehan et al., 2000), which allows the identification of psychiatric disorders of infancy based on the DSM − IV and CIE-10. Only those participants with typical development were tested with the ENI, which evaluates diverse cognitive abilities grouped into three categories: executive functions, cognitive functions, and academic performance. In particular, this neuropsychological battery can be used to assess reading abilities in Spanish-speaking school-age children from ages 5–16 (Matute, Inozemtseva, González Reyes, & Chamorro, 2014; Matute et al., 2007). Reading domains evaluated by the ENI include accuracy, comprehension, and speed. Briefly, the subject is presented with syllables, words, sentences (instructions) and short stories to read, one item at a time. Reading accuracy is based in the number of correct items read; reading comprehension is based on the number of correct execution of instructions and correct answers to questions related to the short stories read (2 aloud, 1 in silence); reading speed is based on the correct number of words read normalized to words per minute, estimated when reading the short stories (more characteristics of items detailed in Supplementary Table I). For each participant and domain, the resulting scores were combined and converted to standard scores (percentiles, i.e., from 1 to 100) according to a Spanish-speaking Latin-American reference sample (Matute et al., 2007, 2014). Pearson correlation tests were performed to identify possible sex or age effects. In addition, a linear regression analysis was performed for each reading domain, with the model including age, sex, and age∗sex interaction.

2.3. Imaging

Brain imaging was performed with a 3T MR scanner (General Electric, Waukesha, WI), using a 16-channel-array head coil. Whole brain resting state functional images were acquired using a gradient recalled echo T2∗ echo-planar imaging sequence (TR = 2000 ms, TE = 40 ms, final voxel size $4 \times 4 \times 4\ \text{mm}^3$), while participants were lying in the scanner with their eyes closed. In total, 150 volumes were obtained with an acquisition time of 5 min. For anatomical reference, high resolution structural T1-weighted images were acquired using a 3D spoiled gradient recalled (SPGR) acquisition with a $1 \times 1 \times 1\ \text{mm}^3$ spatial resolution (TR = 8.1 ms, TE = 3.2 ms, flip angle = 12.0°).

2.4. Data analysis

Image analysis was performed by using FMRIB's Software Libraries (FSL v.5.1.9). Preprocessing included slice timing correction, head motion correction, brain extraction, spatial smoothing by use of a Gaussian kernel (FWHM of 6 mm), high-pass temporal filtering to remove slow drift (cutoff frequency = 0.01 Hz) and registration of each rsfMRI dataset with its corresponding structural image, followed by a spatial normalization to Montreal Neurological Institute (MNI) standard space by using rigid body and non-lineal transformations, respectively. For each volume within the rsfMRI datasets, the root mean squares (rms) of estimated motion parameters were obtained. Subjects with more than 30 volumes with rms > 0.25 mm were discarded (Satterthwaite et al., 2013; Van Dijk et al., 2010). Based on this criteria, 6 subjects (5 male) were discarded from further analyses.

To explore the functional network architecture at the ages here explored, probabilistic ICA was performed for the whole sample. Specifically, after preprocessing, a temporal-concatenation group independent component analysis (TC-GICA) was performed on the rsfMRI