Neuroscience 298 (2015) 318–328

REGIONAL AMPLITUDE OF THE LOW-FREQUENCY FLUCTUATIONS AT REST PREDICTS WORD-READING SKILL

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Abstract—Individuals' reading skills are critical for their educational development, but variation in reading skills is known to be large. The present study used functional magnetic resonance imaging (fMRI) to examine the role of spontaneous brain activity at rest in individual differences in reading skills in a large sample of participants ($N = 263$). Specifically, we correlated individuals' word-reading skill with their fractional amplitude of low-frequency fluctuation (fALFF) of the whole brain at rest and found that the fALFFs of both the bilateral precentral gyrus (PCG) and superior temporal plane (STP) were positively associated with reading skills. The fALFF–reading association observed in these two regions remained after controlling for general cognitive abilities and in-scanner head motion. A cross-validation confirmed that the individual differences in word-reading skills were reliably correlated with the fALFF values of the bilateral PCG and STP. A follow-up task-based fMRI experiment revealed that the reading-related regions overlapped with regions showing a higher response to sentences than to pseudo-sentences (strings of pseudo-words), suggesting the resting-state brain activity partly captures the characteristics of task-based brain activity. In short, our study provides one of the first pieces of evidence that links spontaneous brain activity to reading behavior and offers an easy-to-access neural marker for evaluating reading skill.

Key words: fractional amplitude of low-frequency fluctuations, resting state fMRI, word reading, precentral gyrus, superior temporal plane.

INTRODUCTION

Reading is an essential part of educational development and a critical skill required for success in our increasingly literate society. However, there are substantial individual differences in reading skills among individuals. Some can finish the bestseller "The Lord of The Rings" in just one day, whereas others cannot manage to read movie subtitles before they disappear from the screen. Previous task-based functional magnetic resonance imaging (fMRI) studies have identified multiple regions in the temporal, frontal, and parietal cortex that are associated with individual differences in reading skills (e.g., Blau et al., 2010; Ben-Shachar et al., 2011; Jobard et al., 2011). However, for some special groups (e.g., children, especially those with neurodevelopmental disorders, or patients with acquired brain deficits), performing a task in scanner may be difficult; therefore, an easy-to-access neural marker of reading without the demand of performing a task can be helpful for evaluation or diagnosis. To this end, here we explored whether the spontaneous brain activity during resting can be used to predict behavioral performance in reading with resting-state fMRI (rs-fMRI).

The spontaneous brain activity is measured by rs-fMRI that demands no particular cognitive task or instructions (e.g. Raichle, 2010). Previous rs-fMRI studies have found that some characteristics of the spontaneous brain activity are associated with various cognitive processing, such as conceptual processing (Wei et al., 2012; Wang et al., 2013), working memory (Zou et al., 2013), cognitive control and response inhibition (Mennes et al., 2011). Besides, the spontaneous brain activity could predict the task-evoked brain activity during different cognitive tasks (Fox et al., 2006; Fox and Raichle, 2007; Mennes et al., 2010, 2011; Liu et al., 2011; Zou et al., 2013). Therefore, the task-free spontaneous brain activity is likely an ideal candidate for the easy-to-access neural marker for reading. We hypothesized that the spontaneous activity in brain regions belonging to the fronto-temporal language system (Vigneau et al., 2006, 2011; Fedorenko et al., 2010, 2011; Price, 2012) may be particularly related to behavioral performance in reading.

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Abbreviations: ALFF, amplitude of low-frequency fluctuation; APM, Advanced Progressive Matrices; BOLD, blood oxygen level-dependent; EPI, echo-planar imaging; fALFF, fractional amplitude of low-frequency fluctuation; FLIRT, FMRIB's Linear Image Registration Tool; fMRI, functional magnetic resonance imaging; FSL, FMRIB Software Library; PAC, primary auditor cortex; PCG, precentral gyrus; PT, planum temporale; rs-fMRI, resting-state fMRI; SCLC, supracalcarine cortex; STP, superior temporal plane.

http://dx.doi.org/10.1016/j.neuroscience.2015.04.025
0306-4522/

In this study, we focused on the low-frequency (0.01–0.1 Hz) fluctuations in the blood oxygen level-dependent (BOLD) signal at rest, which are related to spontaneous brain activity (Biswal et al., 1995; Logothetis et al., 2001; Raichle, 2006). Specifically, we employed fractional amplitude of low-frequency fluctuations (fALFFs, Zou et al., 2008), which represents a normalized index of the amplitude of low-frequency fluctuations (ALFFs). The fALFF refers to the total power within the frequency range bound by 0.01 and 0.1 Hz relative to the total power across all measurable frequencies. In healthy individuals, fALFF/ALFF is found to be associated with individual differences in object color knowledge (Wang et al., 2013), conceptual processing (Wei et al., 2012), working memory (Zou et al., 2013), cognitive control and response inhibition (Mennes et al., 2011), empathy (Cox et al., 2012), and personality traits (Wei et al., 2012; Kong et al., 2014, 2015), whereas individuals with cognitive–affective brain disorders exhibit abnormal fALFF in the regions involved in cognitive–affective processes (Hoptman et al., 2010; Han et al., 2011; Liu et al., 2013). These known associations indicate that fALFF can effectively reflect the neural basis underlying a variety of cognitive abilities.

To investigate the extent to which fALFF predicts individual differences in reading, we performed the following analyses. First, the participants' reading skills were measured. Because reading is a complex cognitive process from decoding symbols to constructing or deriving meaning; therefore, it consists of both modality-specific components (e.g., visually analyzing the shape of words or orthographic processing) and high-level amodal components (e.g., deriving meaning of words or semantic processing). Here we measured the efficiency of mapping orthography to semantics (i.e., semantic processing), a core component of reading (Harley, 2014), with an animal-word cancelation test (Zou et al., 2012). A previous study has shown that the score of this test was highly correlated with that of a homophone cancelation test where participants crossed out words with an onset of /b/ among words with other onsets, and a sentence test where participants were instructed to judge whether the meaning of a sentences was ambiguous (Zou et al., 2012), suggesting the validity of using the semantic test to index participants' reading skills. Then, a correlational analysis was performed to search for brain regions in which regional fALFF was associated with individual differences in reading. Finally, a task-based fMRI experiment was conducted to examine whether the regions showing the association between reading and fALFF at rest were also functionally involved in a reading task.

EXPERIMENTAL PROCEDURES

Participants

Two hundred and sixty-three college students (159 females; mean age = 22.05, SD = 0.82; 244 right-handed; 14 left-handed, three without handedness information) from Beijing Normal University (BNU), Beijing, China, participated in our study. All participants were native Chinese speakers with no history of neurological or psychiatric disorders. The study was approved by the Institutional Review Board of BNU. Informed written consent was obtained from all participants before starting the experiment.

General procedure

To assess reading skills, the current study focused on word-level reading. One's ability to read individual words constitutes a key component of a wider range of reading skills (Wandell et al., 2012). A word cancelation test was employed to assess word-reading skills of all of the participants (Zou et al., 2012). In addition, a symbol cancelation test was administered to all participants. The symbol cancelation test assesses one's general cognitive ability of analyzing the shape of objects and, as such, served as a control so that the measure of the word cancelation test mainly reflects high-level amodal language-processing mechanisms. In addition, Raven's Advanced Progressive Matrices (Raven's APM; Raven et al., 1998) were employed to assess participants' high-level general cognitive ability; therefore, after it was controlled for, the measure of the word cancelation test mainly reflects reading-specific processing. Finally, all participants were subjected to: (1) a rs-fMRI scan used to measure spontaneous brain activity, and (2) a T1-weighted anatomic scan that enabled the spatial registration of rs-fMRI images. To characterize the regions activated by reading, 21 participants (10 females) were randomly chosen from all participants to perform a language localizer task (Fedorenko et al., 2011; for an introduction to this particular task, see below).

Word cancelation test

Participants' reading skill was assessed using a word cancelation test. The test consisted of 220 two- or three-character words with an average frequency of occurrence of approximately 16 times per million words. Among these words, 74 referred to animals (e.g., "小猫", /xiao3mao1/, kitten) and were designated as target words. The other 146 words were distracters, referring to anything but animals (e.g., "南瓜", /nan2gua1/, pumpkin). The animal and non-animal words were randomly intermixed and printed on a piece of paper, line-by-line. In total, 22 lines were presented, each of which consisted of 10 words separated by blanks (Fig. 1A). Participants were instructed to differentiate animal words from non-animal words by canceling the animal words with a slash ["/"] while leaving the non-animal words untouched (Fig. 1B). Participants were instructed to cancel the animal words as quickly as possible. The maximum time provided was 50 s, a period of time that was insufficient for *all* participants to process all of the words included in the test. Due to the severe time restriction, a higher count of canceled animal words indicates a higher test performance and thus better reading skills.

Before the formal test a practice test consisting of ten words (i.e., three animal words and seven non-animal