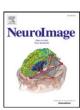
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Temporo-parietal connectivity uniquely predicts reading change from childhood to adolescence



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ARTICLE INFO

Article history: Received 3 November 2015 Accepted 30 June 2016 Available online 2 July 2016

Keywords: Semantic Association strength fMRI Longitudinal Connectivity

ABSTRACT

Previous research has shown that left posterior middle temporal gyrus (pMTG) is a core node in the semantic network, and cross-sectional studies have shown that activation in this region changes developmentally and is related to skill measured concurrently. However, it is not known how functional connectivity with this region changes developmentally, and whether functional connectivity is related to future gains in reading. We conducted a longitudinal functional magnetic resonance imaging (fMRI) study in 30 typically developing children (aged 8–15) to examine whether initial brain measures, including activation and connectivity, can predict future behavioral improvement in a semantic judgment task. Participants were scanned on entering the study (time 1, T1) and a follow-up period of 2 years (time 2, T2). Character pairs were arranged in a continuous variable according to association strength (i.e. strong versus weak), and participants were asked to determine if these visually presented pairs were related in meaning. Our results demonstrated greater developmental changes from time 1 to time 2 for weaker association pairs in the left pMTG for the children (aged 8-11) as compared to the adolescents (aged 12-15). Moreover, the results showed greater developmental changes from time 1 to time 2 for weaker association pairs in connectivity between the pMTG and inferior parietal lobule (IPL) for the children as compared to the adolescents, Furthermore, a hierarchical stepwise regression model revealed that connectivity between the pMTG and IPL in weak association pairs was uniquely predictive of behavioral improvement from time 1 to time 2 for the children, but not the adolescents. Taken together, the activation results suggest relatively rapid development before adolescence of semantic representations in the pMTG. Moreover, the connectivity results of pMTG with IPL tentatively suggest that early development of semantic representations may be facilitated by enhanced engagement of phonological short-term memory.

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Introduction

Reading ability is associated with maturational changes in the brain, which in turn is essential for functioning in our daily life (Friederici, 2006; Johnson, 2011; Schlaggar and Church, 2009). Reading involves a rapid mapping between orthography and semantic representations in printed words. In neuroimaging studies, various regions (i.e. inferior frontal gyrus, angular gyrus, and middle temporal gyrus) have been indicated to be supportive to semantic processing (Booth et al., 2002;

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Chou et al., 2009; Wu et al., 2012). A longitudinal study using functional magnetic resonance imaging (fMRI) followed two developmental cohorts (children: age 8–11 and adolescents: age 12–15) during a semantic judgment task in Chinese. Using two cohorts allowed us to determine whether longitudinal changes differed between younger and older participants (McNorgan et al., 2011). Ours is the first study to determine the relationship of initial brain measures (i.e. brain activity, functional connectivity) to changes in skill of reading Chinese characters.

Chinese is different from alphabetical languages in the nature of the mapping between orthography and semantics at a mono-morphemic level. About 80% of Chinese characters are phonetic compounds (phonograms) that consist of a semantic radical and a phonetic radical (Zhou, 1978). The semantic radicals may provide a cue to the semantic category of the character (Ho et al., 2000). Thus, it is important to explore whether the unique linguistic features of

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Chinese influence developmental changes in the neural substrate for semantic processing.

Integration mechanisms have been investigated by examining the brain activation due to stronger versus weaker semantic association (Chou et al., 2009; Fletcher et al., 2000; Raposo et al., 2006). Previous fMRI studies in English have shown that stronger association results in greater activation in the left angular gyrus (AG, BA 39) (Chou et al., 2006a, 2006b; Raposo et al., 2006). In addition, greater activation was observed in the left AG when participants were cued to be aware of the semantic features of the incoming word target (Cristescua et al., 2006). Several studies have proposed that the activation in the AG is related to the integration of multiple shared features between word pairs (Grossman et al., 2003; Koenig et al., 2005; Lee et al., 2015).

In contrast to greater activation in AG for stronger semantic association, processing weaker association has elicited greater activation in the left posterior middle temporal gyrus (pMTG, BA 21) and the ventral regions of left inferior frontal gyrus (IFG, BA 45/47). Several studies in English have shown that word pairs with weaker association strength result in greater activation in the left pMTG (Chou et al., 2006a, 2006b; Wible et al., 2006). This region is often considered as a repository site for semantic knowledge (Binder et al., 2009). Greater activation in this region for low association may result from a more extensive access to semantic representations in order to identify the distant relationships between words (Booth et al., 2007; Chou et al., 2009). Word pairs with weaker association strength also elicited greater activation in the left IFG. Greater activation in this region is likely related to difficulty of selecting relevant semantic features, as word pairs with weaker association share few semantic features (Fletcher et al., 2000). For weaker association pairs, in order to make appropriate semantic decisions, participants may engage greater activation in both pMTG and IFG.

Evidence from cross-sectional studies shows that developmental changes in semantic processing continue into early adulthood and it is associated with changes in the left IFG and MTG. Previous studies using a semantic association task have identified age-related changes in these two regions (Chou et al., 2009; Lee et al., 2011; Lee et al., 2015). Left IFG is proposed to be specialized for selecting relevant semantic features (Fletcher et al., 2000). Consistent with this notion, age-related increases in this region, particularly for the adolescents, may imply greater executive control needed to select relevant features. In addition, developmental changes in the MTG may reflect the elaboration of semantic knowledge with increasing numbers of semantic representations and stronger interconnections between these representations. Consistent with this argument, behavioral studies demonstrate that as vocabulary knowledge increases, the child's semantic system gradually matures due to a greater number of conceptual links (McGregor and Appel, 2002; McGregor et al., 2002). Although there is extensive support for the core role in the left MTG in developmental changes in semantic processing, a larger left-lateralized network for comprehension is also found to support age-related changes. An agerelated increase in functional connectivity was found among the bilateral temporal regions, left IFG, and left AG in children using a narrative comprehension task (Karunanayaka et al., 2007; Schmithorst et al., 2007). These inter-connections in the semantic network may enable appropriate semantic representations to be accessed and integrated (Bokde et al., 2001; Turken and Dronkers, 2011). Taken together, previous work suggests that as children age they are more capable of maintaining conceptual knowledge in an organized state, using a flexible mechanism to retrieve/select relevant information and integrating relationships between these concepts (Blakemore and Choudhury, 2006; Crone et al., 2009).

In the current study, we were interested in developmental changes in the relationship between brain activation, connectivity, and behavioral improvement. Previous work shows that individual differences in reading performance are related to amount of activation in the pMTG, IFG, and AG. Previous studies have shown that better behavioral performance correlates with greater activation in the temporoparietal region,

whereas lower behavioral performance correlates with greater activation in the IFG in semantic tasks, including category judgment (Shaywitz et al., 2002), and semantic judgment (Blumenfeld et al., 2006; Chee et al., 2001). In addition, the strength of structural connectivity of temporal-parietal regions correlates with the reading performance (Beaulieu et al., 2005; Klingberg et al., 2000). To our knowledge, no imaging study has tested for a link between functional connectivity in temporo-parietal cortex with behavioral performance in the semantic task.

Previous studies showing developmental changes in semantic processing have relied on cross-sectional samples (Blumenfeld et al., 2006; Chou et al., 2009; Lee et al., 2011). The current study is the first in Chinese to examine developmental changes in the neural correlates of semantic processing by using a longitudinal design. Longitudinal studies allow investigators to determine whether developmental changes are larger in certain age groups, and it allows investigators to predict changes over time (Gabrieli et al., 2015; Hoeft et al., 2007). In this study, we select two age cohorts because cross-sectional fMRI studies during semantic judgments in Chinese have shown that adolescents aged 12-15 might have better ability in selecting and retrieving semantic representations than children aged 8-11 (Lee et al., 2011; Lee et al., 2015). Several behavioral studies have also proposed the importance of forming and organizing links for semantic representations from childhood into early adolescence (Chan and Poon, 1999; Kav'e, 2006; Matute et al., 2004; Sauzeon et al., 2004). By examining the functional recruitment and connectivity in children (aged 8-11) and adolescents (aged 12-15) longitudinally, we aimed to determine whether there would be greater transition during semantic processing from childhood to early adolescence, as compared to the transition from early adolescence to late adolescence. In the present study, we also aimed to examine whether the initial brain activity and/or connectivity would be predictive of the future behavioral improvements. We expected that the initial brain activity in the pMTG and/or the initial connectivity of the pMTG with other regions may be predictive of the behavioral improvements for the transition from childhood to early adolescence, as compared for the transition from early adolescence to late adolescence.

Methods

Participants

In the semantic judgment task, a group of 30 native monolingual Chinese children (mean age = 11.8, standard deviation = 1.94, 14 girls) participated. To examine the developmental changes of conceptual knowledge (Lee et al., 2015), we divided participants into two age groups: children (8- to 11-year-old, n = 15, 8 girls) and adolescents (12- to 15-year-old, n = 15, 6 girls) (Table 1). The children participated in the experiment twice, with a two-year interval between scans. All 30 children were recruited from the Taipei city metropolitan area. The parents were given an informal interview to ensure that their children met the following inclusionary criteria: (1) right-handedness, (2) normal hearing (3) normal or correctedto-normal vision, (4) free of neurological disease or psychiatric disorders, (5) no history of intelligence, reading, or oral-language deficits, and (6) no learning disability or attention deficit hyperactivity disorder (ADHD). After the administration of the informal interview, informed consent was obtained. The informed consent procedures

Table 1Means (SDs) for subject characteristics for children and adolescents in the experiment.

	Children ($n = 15$)	Adolescents ($n = 15$)
Age at Time 1 (years)	10.1 (0.9)	13.5 (0.8)
Age at Time 2 (years)	12.0 (0.6)	15.5 (0.9)
Follow-up intervals (months)	26.1 (0.7)	25.8 (0.4)

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