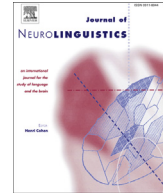




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Gene–environment interaction on neural mechanisms of orthographic processing in Chinese children



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ABSTRACT

The ability to process and identify visual words requires efficient orthographic processing of print, consisting of letters in alphabetic languages or characters in Chinese. The N170 is a robust neural marker for orthographic processes. Both genetic and environmental factors, such as home literacy, have been shown to influence orthographic processing at the behavioral level, but their relative contributions and interactions are not well understood. The present study aimed to reveal possible gene-by-environment interactions on orthographic processing at the behavioral and neural level in a normal children sample. Sixty 12 year old Chinese children from a 10-year longitudinal sample underwent an implicit visual-word color decision task on real words and stroke combinations. The ERP analysis focused on the increase of the occipito-temporal N170 to words compared to stroke combinations. The genetic analysis focused on two SNPs (rs1419228, rs1091047) in the gene *DCDC2* based on previous findings linking these 2 SNPs to

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orthographic coding. Home literacy was measured previously as the number of children's books at home, when the children were at the age of 3. Relative to stroke combinations, real words evoked greater N170 in bilateral posterior brain regions. A significant interaction between rs1091047 and home literacy was observed on the changes of N170 comparing real words to stroke combinations in the left hemisphere. Particularly, children carrying the major allele "G" showed a similar N170 effect irrespective of their environment, while children carrying the minor allele "C" showed a smaller N170 effect in low home-literacy environment than those in good environment.

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1. Introduction

Developmental dyslexia is a genetically complex, neurodevelopmental disorder, which affects about 5–12% of school age children who experience severe difficulties in acquiring reading (Bates et al., 2009; Katusic, Colligan, Barbaresi, Schaid, & Jacobsen, 2001). Heritability estimates for dyslexia range between moderate and high (Fisher & DeFries, 2002; Francks, MacPhie, & Monaco, 2002; Olson, 2002). This variation in heritability estimates may reflect the multigenetic nature of the disorder and the environmental influence during reading acquisition, given that dyslexia is a learning disorder. One way to address the question of how environment and genes interact during the development of dyslexia is to use specific measures of brain activation as endophenotypes that potentially indicate particular genes more clearly while still being sensitive to environmental influences during learning (Galaburda, LoTurco, Ramus, Fitch, & Rosen, 2006). Given that learning to read is best addressed in a longitudinal study design, we made use of a 10-year longitudinal study (Lei et al., 2011) with children in order to investigate how genes and environment influence brain functions that are related to dyslexia.

Several genes have been proposed as susceptibility candidates for either dyslexia or the basic reading-related phenotypes (Bates et al., 2009; Cope et al., 2005; Lind et al., 2010; Luciano et al., 2007; Meng, 2005; Taipale et al., 2003). Among all of them, the *DCDC2* gene received relatively more consistent observations (Brkanac et al., 2007; Lind et al., 2010; Meng, 2005; Schumacher et al., 2006; Wilcke et al., 2009). In general, the *DCDC2* gene was not only associated with dyslexia (Deffenbacher et al., 2004; Meng, 2005; Schumacher et al., 2006; Wilcke et al., 2009), but also played an essential role for reading in the normal population (Lind et al., 2010). Using twenty-nine intensively distributed SNPs across the 211.5-kb *DCDC2* locus in a large Australian general population, Lind et al. (2010) detected 2 SNPs, rs1419228 (with risk allele "C", $P = 0.0038$) and rs1091047 (with risk allele "G", $P = 0.0034$), that were significantly associated with reading irregular words, a task that is thought to indicate orthographic coding ability in alphabetic languages (Lind et al., 2010). In Chinese, however, the orthographic rules are different. Unlike in alphabetic writing systems, Chinese orthography requires the reader to encode characters in terms of units representing major character components and to subtly process the internal content of the components (Anderson et al., 2013). Moreover, previous genetic studies on dyslexia used samples from Caucasian populations which may have different genetic distributions from Han populations in China. Therefore, whether the association between these two SNPs (rs1419228 and rs1091047) and orthographic coding can be replicated in Han population, a non-alphabetic language sample, was a first interest of our study.

With the development of imaging genomics, increasing researchers tended to focus on the associations between genes and the brain. The brain became a bridge connecting genes and behavior. Recently, the *DCDC2* gene was detected to be associated with gray matter volume and white matter volume (Darki, Matsson, Kere, & Klingberg, 2012; Meda et al., 2007). RNA interference experiments in rats indicated that dyslexia candidate genes appear to regulate neuronal migration, and thus influencing the neocortical development (Meng, 2005; Paracchini, 2006; Rosen et al., 2007). In other words,

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