Neuro-genetics of reading: Initial fMRI findings from readers with and without risk alleles

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Introduction:
Recent studies have shown several genetic factors to be associated with risk of reading disability (dyslexia), while functional neuroimaging has revealed brain regions associated with typical and disordered reading. We are now at the point where these two approaches can begin to directly inform each other. Examining readers with and without known genetic risk factors for reading disability using detailed neuropsychological and functional neuroimaging measures may help identify an endophenotype that would not be evident from using each measure in isolation. Here we report initial results of a study in which participants with or without dyslexia risk alleles read aloud during fMRI words of high or low usage frequency (back vs. gate) and high or low spelling-sound consistency (mill vs. wand), variables studied extensively in brain imaging investigations of reading.

Methods:
94 participants (aged 18-35) underwent neuropsychological testing and DNA typing using TaqMan probes for three single-nucleotide polymorphisms in the KIAA0319/TTRAP/THEM2 region of chromosome 6p: rs9461045, rs2143340, and rs17243157. Neuropsychological tests for this session included a computerized "orthographic choice" test (Olson et al., 1994) and subtests of the Wechsler Abbreviated Scale of Intelligence and the Woodcock-Johnson III.

Based on their risk allele status, participants were selected for a second visit with additional neuropsychological tests and MRI. The tests included the Comprehensive Test of Phonological Processing, the Test of Word Reading Efficiency (TOWRE), and the Test of Irregular Word Reading Efficiency. Analyses reported here involve comparisons of those in the risk allele group who have returned so far for scanning (N = 8; 5 with all 3 risk alleles, 3 with only that for rs9461045) and participants without the risk alleles in question (N = 9). Groups did not differ in gender, age, estimated IQ, or education.
FMRI data were obtained on a 3T GE 750 scanner using a 32-channel head coil. Stimuli were 300 words and 300 pronounceable non-words presented one at a time in a random event-related design for reading aloud. Words consisted of high and low levels of word frequency and spelling-sound consistency, in a crossed 2x2 design. Data were smoothed with a 6 mm FWHM kernel, thresholded at a voxel intensity of p < 0.01, with an extent threshold of 910 mm3, for a mapwise corrected p < 0.05.

Results:
In terms of performance, the groups differed only on a single subtest (the TOWRE phonological decoding efficiency). There were group differences in fMRI activation for high compared to low frequency words, and high compared to low consistency words. For the word frequency contrast, the risk group showed more activation for high than low frequency words in the left supramarginal and middle temporal gyri (SMG and MTG), whereas the non-risk group showed the opposite pattern (Fig. 1). This pattern reflected less deactivation compared to fixation for high than low frequency words in the risk group. For high compared to low spelling-sound consistency words, the risk group showed more activation (less deactivation) for high consistency words in the bilateral rostral cingulate cortex (rCC), whereas the non-risk group showed no differences (Fig. 2).

Conclusions:
The three regions showing group differences in the current study have previously been implicated in aspects of phonological (word sound, SMG) and semantic (word meaning, MTG, rCC) processing. The SMG has also been shown to activate less for dyslexic compared to typical readers in meta-analyses, as has an area adjacent to the current MTG focus (Maisog et al., 2008; Richlan et al., 2009). Although these results are preliminary because of the currently small number of participants in each group, it is plausible to interpret them as reflecting areas carrying out critical aspects of reading. More generally, they support the plausibility of the current approach to the neuro-genetics of reading.

Language:
Reading and Writing
Figure 1: Group differences for the high – low word frequency contrast.
Figure 2: Group differences for the high – low spelling-sound consistency contrast.

Reference

