LETTER TO THE EDITOR

Cortical differences in preliterate children at familiar risk of dyslexia are similar to those observed in dyslexic readers

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Sir,

In their recent report in *Brain*, Clark *et al.* (2014) presented cortical thickness data obtained from a cohort of 27 children that were compared longitudinally at three time points (first grade: ages 6–7, third grade: ages 8–9, sixth grade: ages 11–12) categorized as either dyslexic or not according to their reading outcome in sixth grade. Based on their observations, the authors conclude that the neuroanatomical precursors of developmental dyslexia are found predominantly in primary sensory cortices and that structural abnormalities in the reading network only emerge after children have learned how to read and write. This study is indeed invaluable as it follows preliterate children longitudinally until the disorder is diagnosed, providing a unique picture of structural cortical changes in dyslexic and non-dyslexic children during this time. However, there are a number of discrepancies between the presented findings and results from other groups including our own. These differences might be explained by the relatively low statistical power of the analyses carried out by Clark and colleagues. Moreover, because genetic and environmental factors are not included in their analyses, it remains unclear how the data can be integrated into a comprehensive account of developmental dyslexia.

The first limitation is based on the experimental design of the study. Although the subsamples compared by Clark *et al.* (2014) are small for a neuroimaging study [MRI time point 1: children who later were identified as dyslexic (*n* = 7) and those who were not (*n* = 10); MRI time point 3: children who were identified as having dyslexia (*n* = 11) and those who were not (*n* = 13), male dyslexic children (*n* = 5) and male control children (*n* = 8), female dyslexic children (*n* = 6) and female control children (*n* = 5)], the authors do not report results from a pretest power analysis. Hence, it is hard to determine whether the observations are truly significant or whether the effects were randomly detected and might not be reproducible in larger samples. The chosen whole-brain significance threshold of *P* < 0.05 (cluster size corrected to *P* < 0.05) is the most liberal confidence level possible in a neuroimaging study. The consequences of a potential power problem may be aggravated by substantial subsample size variations across measurement points. In particular, at MRI time point 1, < 64%
of the data about the children with dyslexia and <77% of the control data were available compared to MRI time point 3. We understand that such variations are almost unpreventable as they primarily emerge from the complex logistics of longitudinal surveys enrolling children in the given age range. Nevertheless, these variations compromise the longitudinal comparability of the data, even given very good scan-rescan reliability, and would therefore have deserved more detailed discussion.

The second limitation relates to the conceptual framework for interpreting the results. Developmental dyslexia is moderately to highly heritable with rates of inheritance ranging from 30% in families with low levels of parental education to 70% in families with high levels of parental education (Scerri and Schulte-Körne, 2010). Unfortunately, the authors accounted for neither the impact of genetic nor environmental variance, particularly parental education, in their analyses. This is limiting because previous imaging genetics studies indicate that the direct effect of dyslexia susceptibility genes on cortical thickness phenotypes is stronger than on behavioural phenotypes such as reading and spelling (Peterson and Pennington, 2012). This supports the assumption that genetic factors but not parental education and profession are an important source of variance for explaining the observed cortical differences.

The anatomical confinement of these effects to temporo-parietal and occipito-temporal cortices is not only in line with the adult literature (Peterson and Pennington, 2012) but also supports all other comparably powered studies investigating brain structure and function in preliterate children at risk of dyslexia. Both regions were identified cross-sectionally with respect to familial risk in a functional MRI study on phonological processing at a pre-reading age (Raschle et al., 2012). Additionally, the arcuate fasciculus as the long-distance white matter fibre tract connecting temporo-parietal cortical areas with temporal and frontal areas was not only shown cross-sectionally to be related to phonological awareness (Saygin et al., 2013) but was also shown to predict reading outcome at third grade (Myers et al., 2014).

In conclusion, the current literature and our own results obtained in larger samples suggest an endophenotypic developmental continuum of genetic risk factors affecting
temporo-parietal and occipito-temporal cortical maturation. This is assumed to be present in pre-reading children as well as in young and adult readers, which is in contrast to the results reported by Clark and colleagues. Given the relatively small sample size and longitudinal group variations in this study, it cannot be excluded that the absence of differences in several cortical areas, which form the later reading network, might be obscured by limited statistical power to detect such effects, whereas effects in other areas might be overestimated. Crucially, Clark and colleagues had only 57% power in their sample at MRI time point 1 to detect the clusters in the left supramarginal gyrus and the left occipito-temporal cortex identified in our analyses (effect size = 0.93; effect size in Clark et al. = 0.53; effect size is defined as the mean difference divided by common standard deviation). Despite the significant value of the longitudinal study by Clark and colleagues for the field, larger and statistically more powerful studies may be required to reveal ultimately which of the contrary hypotheses best approximates reality. This could comprise international collaborations to investigate larger samples collected from populations being comparable with respect to orthographic regularity and genetic background.

References


