Complex effects of dyslexia risk factors account for ADHD traits: evidence from two independent samples.


doi: 10.1111/jcpp.12612. [Epub ahead of print]

Abstract

BACKGROUND:
Developmental dyslexia (DD) and attention deficit/hyperactivity disorder (ADHD) are among the most common neurodevelopmental disorders, whose etiology involves multiple risk factors. DD and ADHD co-occur in the same individuals much more often than would be expected by chance. Several studies have found significant bivariate heritability, and specific genes associated with either DD or ADHD have been investigated for association in the other disorder. Moreover, there are likely to be gene-by-gene and gene-by-environment interaction effects (G × G and G × E, respectively) underlying the comorbidity between DD and ADHD. We investigated the pleiotropic effects of 19 SNPs spanning five DD genes (DYX1C1, DCDC2, KIAA0319, ROBO1, and GRIN2B) and seven DD environmental factors (smoke, miscarriage, birth weight, breastfeeding, parental age, socioeconomic status, and parental education) for main, either (a) genetic or (b) environmental, (c) G × G, and (d) G × E upon inattention and hyperactivity/impulsivity. We then attempted replication of these findings in an independent twin cohort.

METHODS:
Marker-trait association was analyzed by implementing the Quantitative Transmission Disequilibrium Test (QTDT). Environmental associations were tested by partial correlations. G × G were investigated by a general linear model equation and a family-based association test. G × E were analyzed through a general test for G × E in sib pair-based association analysis of quantitative traits.

RESULTS:
DCDC2-rs793862 was associated with hyperactivity/impulsivity via G × G (KIAA0319) and G × E (miscarriage). Smoke was significantly correlated with hyperactivity/impulsivity. We replicated the DCDC2 × KIAA0319 interaction upon hyperactivity/impulsivity in the twin cohort.

CONCLUSIONS:
DD genetic (DCDC2) and environmental factors (smoke and miscarriage) underlie ADHD traits supporting a potential pleiotropic effect.