Polygenic Risk Scores for Clinical ADHD are Associated with Impaired Educational Achievement and Lower IQ in Children and Adults from the General Population

Topic ADHD

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SUBMISSION DETAILS

Background High levels of ADHD symptoms during early childhood carry risk of worse academic performance at age 16 (Washbrook et al. 2013) and can impact on employment and earnings in adulthood (Fletcher 2013). Polygenic score analysis was used to show that common risk alleles for clinical ADHD contribute to the risk of having higher ADHD symptoms in the general population (Martin et al. 2014). We used polygenic risk score analysis to investigate the contribution of common risk variants for clinical ADHD on educational performance and IQ in the general population.

Methods Polygenic risk scores were calculated for Avon Longitudinal Study of Parents and Children (ALSPAC) participants (Boyd et al. 2013, Fraser et al. 2013) (8,365 children and 8,340 mothers) based on the results of a discovery sample, a genome-wide association study of 727 cases with ADHD diagnosis and 5,081 controls from Cardiff University (Stergiakouli et al. 2012) and tested for association with IQ and educational outcomes in adolescence and adulthood. The QC procedures and ascertainment of the target and discovery samples have been described in detail previously (Stergiakouli et al. 2012, Stergiakouli et al. 2014). Educational achievement was assessed using results from Key Stage 3 national tests, externally marked GCSE examinations and the probability of sitting Key Stage 5 examinations in 6,385 children from ALSPAC. Mothers' educational achievement was measured by self-reported highest qualification obtained. We also performed exploratory mediation analysis of the relationship between ADHD polygenic risk scores and ADHD symptoms with educational and cognitive outcomes in ALSPAC children.

Results ADHD polygenic scores on the children were associated with worst educational outcomes at the 3 time points tested; Key stage 3 scores (β=-1.4 (-2 to -0.8), p=2.3 x 10-6), capped GCSE points (β=-4 (-6.1 to -1.9), p=1.8 x 10-4) and reduced probability of sitting Key Stage 5 examinations (OR=0.9 (0.88 to 0.97), p=0.001). They were also associated with lower IQ scores at age 15.5 (β=-0.8 (-1.2 to -0.4), p=2.4x10-4). Maternal ADHD polygenic scores were associated with lower maternal IQ (β=-0.6 (-1.2 to -0.1), p=0.03) and lower maternal educational achievement (β=-0.09 (-0.1 to -0.06), p=0.005). Mediation analysis indicated that the association of ADHD polygenic risk score with educational outcomes was mediated substantially but not entirely by IQ and to a lesser extent by earlier levels of ADHD.

Discussion Using a population-based sample, we demonstrated that genetic risk for clinical disorder is relevant for children and adults from the general population irrespective of whether they reach diagnostic criteria for the disorder. High genetic loading for clinical ADHD is associated with increased risk of educational under-achievement and lower IQ in ALSPAC. Our study highlights the

potential of population samples for investigating the full distribution of psychiatric and cognitive traits in large numbers of individuals without a disorder diagnosis. Further investigation is required to determine if children with subthreshold ADHD symptoms would benefit from appropriate interventions and support to achieve their potential in education.

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