Shared Genetic Effects Between Clinical ADHD and Smoking, Alcohol and Breastfeeding in Mothers from the General Population

Topic ADHD

Submitter Evie Stergiakouli

SUBMISSION DETAILS

Background Smoking and alcohol consumption during pregnancy have been suggested as possible risk factors for ADHD in children (Huizink and Mulder 2006). However, inferring causality has not been possible because the mother provides both the prenatal environment and genetic risk factors for ADHD. When employing a design that disentangles genetic effects from the prenatal environment, the increased risk for ADHD in children of mothers who smoked during pregnancy was attributed to shared genetic risk factors (Thapar et al. 2009). We investigated if there are shared genetic effects between ADHD and smoking and alcohol consumption during pregnancy, as well as breastfeeding using polygenic risk score analysis in mothers from the general population.

Methods ADHD polygenic risk scores were calculated for Avon Longitudinal Study of Parents and Children (ALSPAC) participants (Boyd et al. 2013, Fraser et al. 2013) (8,340 mothers). The analysis used as 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). Association of scores with smoking status and alcohol consumption before pregnancy and during the first trimester was tested in ALSPAC. Scores were also tested for association with breastfeeding status at 2 months postnatally. 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).

Results Higher genetic risk for ADHD, as indicated by polygenic scores, was associated with higher odds of smoking before pregnancy (OR=1.05 (1.01 to 1.1), p=0.03, N=7,530) and higher odds of continuing to smoke during the first trimester of pregnancy (OR=1.08 (1.03 to 1.15), p=0.002, N=7,543). However, there was no evidence of association with alcohol consumption both before pregnancy (OR=0.99 (0.91 to 1.08), p=0.93, N=7,543) and during the first trimester (OR=0.98 (0.94 to 1.03), p=0.5, N=7,525). Higher ADHD polygenic score was also associated with increased odds of the mother not breastfeeding at 2 months after the birth of the child (OR=1.06 (1.01 to 1.11), p=0.03, N=6,604). Child characteristics could also be influencing a mother in her decision to breastfeed or not. For this reason, the association of maternal ADHD polygenic scores with breastfeeding were adjusted for the ADHD polygenic score of the child. This did not change the association (OR=1.06 (0.99 to 1.13), p=0.09, N=4,619), although the confidence intervals are wider due to the smaller sample size compared to the unadjusted analysis.

Discussion Our results indicate that there are shared genetic effects between ADHD and life style choices, such as smoking during pregnancy and breastfeeding. This is the first time that this has been shown using adults from the general population that do not reach diagnostic criteria for the disorder. In addition, these results raise the possibility of dynastic effects of genetic factors being present. In this case, the mother not only transmits genetic risk for ADHD to her offspring but also

exposes the child to environmental risk factors, both prenatally and postnatally, through her life style choices that are in turn influenced by her genetic risk for ADHD. Importantly, we cannot infer causality from these associations. This should be assessed in a formal causal inference framework using Mendelian Randomization, although the small amount of variance explained by ADHD polygenic scores poses methodological challenges.

Co-Authors

* Presenting Author

First Name	Last Name	Affiliation	E-mail
Evie *	Stergiakouli *	MRC Integrative Epidemiology Unit (IEU) at the University of Bristol, Bristol, UK	e.stergiakouli@bristol.ac.uk
Joanna	Martin	MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK	martinjm1@cardiff.ac.uk
Marian	Hamshere	MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK	hamshereml@cardiff.ac.uk
Beate	St Pourcain	MRC Integrative Epidemiology Unit (IEU) at the University of Bristol, Bristol, UK; School of Oral and Dental Sciences, University of Bristol, Bristol, UK	beate.stpourcain@bristol.ac.uk
Nicholas	Timpson	MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, UK	n.j.timpson@bristol.ac.uk
Anita	Thapar	MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK	thapar@cf.ac.uk

George	Davey Smith	MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, UK	kz.davey-smith@bristol.ac.uk

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Signature Evie Sterg