

Genetic Links between Social-Communication Traits, ADHD Traits and Clinical ADHD During Development

Topic ADHD

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SUBMISSION DETAILS

Background There is high comorbidity between autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD) and population-based studies have shown complex symptom co-occurrence. At least some of these links are due to overlapping genetic influences. While trajectories for ASD symptoms are relatively stable during development however, trajectories for ADHD symptoms are more variable and only sometimes persistent into adulthood. This study was performed to investigate genetic links between ASD traits and ADHD traits in the general population, and ADHD disorder in a clinical sample, from a developmental perspective.

Methods We studied social-communication difficulties (at ages 8, 11, 14 and 17 years; mother-reported Social and Communication Disorders Checklist, SCDC) and combined hyperactive-impulsive/inattentive symptoms (ages 7, 8, 10, 12, 13 and 17 years; mother-reported Strength and Difficulties Questionnaire, SDQ) in $\leq 5,680$ children from a UK population-based birth cohort (Avon Longitudinal Study of Parents and Children, ALSPAC). Traits were rank transformed to normality, and genome-wide analyses carried out using 1000G imputed data in ALSPAC children. Genetic correlations within ALSPAC were assessed with Genome-Wide Complex Trait Analysis (GCTA). Genetic links between these traits and clinical ADHD (2,096 trios, 3,470 cases, 11,494 controls, based on available ADHD PGC GWAS summary statistics) were analysed using LD Score Regression (LDSC).

Results There were genetic links between social-communication difficulties and ADHD traits throughout development, despite considerable variation in GCTA heritability (SCDC GCTA-h²: 0.08 to 0.45; SDQ GCTA-h²: 0.11 to 0.28). Irrespective of when social-communication difficulties were assessed, we observed, on average, smaller genetic correlations between these phenotypes and ADHD traits at 10 to 12 years, ranging between 0.10 to 0.56 ($P_{\min}=0.02$), while ADHD traits before and after this age showed stronger links, ranging between 0.41 to 1 ($P_{\min}=8.0 \times 10^{-5}$).

We also found genetic correlations between clinical ADHD and social-communication difficulties at 8, 11 and 14 years, ranging between 0.33 and 0.75 ($P_{\min}<0.027$), with some attenuation at 17 years ($r=0.22$, $P=0.14$). Findings were confirmed through polygenic score analysis in an ADHD PGC subsample (725 cases, 5081 controls; adjusted-R² $\leq 0.19\%$, $P \geq 0.004$), based on a GWAS of social-communication difficulties in ALSPAC.

As a positive control, we also confirmed genetic correlations between clinical ADHD and SDQ-assessed ADHD traits throughout development, ranging between 0.49 and 0.86 (all $P < 0.05$).

Discussion In summary, our findings support shared common genetic influences between

social-communication difficulties and ADHD traits in the general population, as well as clinically-diagnosed ADHD, but suggest that detectable genetic overlaps may depend on developmental stage.

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Hugh Gurling Award No

DISCLOSURE

Financial Relationships I have no real or apparent conflicts of interest to disclose.

Investigational or off-label use of a product NONE

Research Support The MRC IEU is supported by the Medical Research Council and the University of Bristol (MC_UU_12013/1-9) and the MRC Centre for Neuropsychiatric Genetics and Genomics is supported by the Medical Research Council, the Wellcome Trust and Cardiff University (079711/Z/06/Z). The UK Medical Research Council and the Wellcome Trust (102215/2/13/2) and the University of Bristol provide core support for ALSPAC.

Human or Animal Ethics Board Review Yes

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