Association of Genetic Risk Variants With Attention-Deficit/Hyperactivity Disorder Trajectories in the General Population.


Abstract

IMPORTANCE:
Attention-deficit/hyperactivity disorder (ADHD) is a heritable neurodevelopmental disorder that shows clinical and genetic overlap with other childhood neurodevelopmental disorders. Levels of ADHD symptoms typically decline across childhood and adolescence, although they remain elevated for some individuals. The determinants of symptom persistence and decline are not yet fully understood.

OBJECTIVES:
To test the hypothesis that genetic risk variant load for ADHD (indexed by polygenic risk scores [PRS]), but not for other psychiatric disorders, is associated with population-based ADHD symptom trajectories across childhood and adolescence, and to examine whether higher genetic liability for ADHD is correlated with total number of additional neurodevelopmental disorders (multimorbidity) in childhood.

DESIGN, SETTING, AND PARTICIPANTS:
The Avon Longitudinal Study of Parents and Children, an ongoing prospective population-based cohort study, has been collecting data on 14,701 children, including 9,757 with data on symptoms of ADHD at multiple time points, since September 6, 1990. The primary exposure variables, PRS, were generated using results of a genome-wide association study from the Psychiatric Genomics Consortium. Childhood multimorbidity scores (ages 7-9 years) were measured by total impairments in 4 domains known to share genetic liability with ADHD: IQ, social communication, pragmatic language, and conduct. Data analysis was conducted from March 1 to September 8, 2016.

MAIN OUTCOMES AND MEASURES:
Attention-deficit/hyperactivity disorder symptom trajectories from ages 4 to 17 years (7 time points).

RESULTS:
Among 9,757 children with data on symptoms of ADHD at multiple time points (age range, 4-17 years; 4,968 boys and 4,789 girls), 4 ADHD symptom trajectories were identified: low (82.6%), intermediate (7.7%), childhood-limited (5.8%), and persistent (3.9%). Mean (SE) PRS for ADHD were higher in children in the persistent trajectory (0.254 [0.069]) compared with each of the other 3 trajectories (low, -0.018 [0.014], \( \chi^2_{11} = 14.67, P < .001, \) odds ratio, 1.31; intermediate, 0.054 [0.055], \( \chi^2_{11} = 4.70, P = .03, \) odds ratio, 1.22; and childhood-limited, 0.017 [0.060], \( \chi^2_{11} = 6.50, P = .01, \) odds ratio, 1.27). Findings were specific to PRS for ADHD; PRS for other psychiatric conditions did not differ across trajectories. The proportion of children with multimorbidity was also highest in those in the persistent trajectory (42.5%; 95% CI, 33.9%-51.1%; \( P < .001 \)) and was associated with persistence of ADHD symptoms independent of PRS.

CONCLUSIONS AND RELEVANCE:
Persistence of ADHD symptoms across childhood and adolescence in the general population is associated with higher PRS for ADHD. Childhood multimorbidity was also associated with persistence of ADHD symptoms and may help to identify children with ADHD whose symptoms are most likely to continue into adolescence.