Increased risk of diseases of the basal ganglia and cerebellum in patients with a history of attention-deficit/hyperactivity disorder

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) is marked by an ongoing pattern of inattention and/or hyperactivity and involves dysregulated dopaminergic pathways. Dopaminergic agents (i.e., amphetamine and methylphenidate) are thus prescribed to treat ADHD. As little is known regarding long-term consequences of either ADHD or its treatment, the objective of this study was to determine if either alters the risk of diseases of the basal ganglia and cerebellum, including Parkinson's disease. Statewide medical records from 1996 to 2016 were retrieved from the Utah Population Database to conduct a retrospective cohort study. Participants included ADHD patients (International Classification of Diseases, 9th version (ICD-9) diagnosis codes 314.0-314.2, 314.8, 314.9) and 5:1 random sex-matched and age-matched subjects with no ADHD diagnosis history. Both patients and non-ADHD subjects met the following eligibility criteria: (1) no prior diagnosis of Parkinson's disease, secondary parkinsonism, basal ganglia disease, or essential tremor (ICD-9 codes 332.0, 332.1, 333.0, 333.1), (2) born in 1950 or later and age ≥20 years at last follow-up, and (3) no history of substance abuse (illicit drugs or alcohol). Outcomes were measured as time to diagnosis of diseases of the basal ganglia and cerebellum, death, or study-end. A Cox model incorporating a competing risk of death was used to provide hazard ratio estimates. Patients with ADHD (N = 31,769) had a 2.4-fold increased risk of basal ganglia and cerebellum diseases (95% confidence interval (CI): 2.0-3.0; P < 0.0001) compared with 158,790 non-ADHD persons, after controlling for sex and age and adjusting for tobacco use and psychotic conditions. In 4960 ADHD patients prescribed psychostimulants, risk of basal ganglia and cerebellum diseases between ages 21 and 49 years was especially pronounced, at 8.6-fold (95% CI: 4.8-15.6; P < 0001). The association of ADHD patients prescribed psychostimulants with higher risk of diseases of the basal ganglia and cerebellum may reflect a more severe ADHD phenotype rather than a direct association between prescribed stimulant use and basal ganglia or cerebellum disorders. Future studies to assess and stratify patient risk so as to inform treatment are warranted.