



**Karolinska
Institutet**

Institutionen för Medicinsk Epidemiologi och Biostatistik

The Origins and Consequences of Attention Deficit Hyperactivity Disorder

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska
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ABSTRACT

Attention deficit hyperactivity disorder (ADHD) is characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity, and is the most common neurodevelopmental disorder of childhood. This highly prevalent disorder is estimated to affect about 5% of school-age children worldwide, with a substantial degree of persistence over time. Although the specific cause of ADHD is still largely unknown, despite a long history of research, it is believed to involve multiple genetic and environmental factors. ADHD is also associated with considerable comorbidities and functional impairments, which place a substantial burden on affected individuals, their families and society. Stimulant medication is considered as one of the most important treatments for ADHD, but the increased use over the years has also raised numerous public concerns. Therefore, the general aim of this thesis was to investigate how genetic and environmental factors contribute to the development of ADHD, as well as to investigate the consequences of ADHD and potential effects of ADHD medication.

Study I explored the relative contribution of genetic and environmental influences of ADHD from childhood through early adulthood. The study found that the shared view of self- and informant-rated ADHD is highly heritable in childhood, adolescence, and early adulthood. It also found evidence of both stable and dynamic genetic influences on ADHD over the course of the development.

Study II examined the association between young maternal age at childbearing and subsequent risk for ADHD in offspring, using a genetically-informative design. The study found that maternal age at first birth, not maternal age at the current birth, predicted offspring ADHD. Thus, all offspring born to teenage mothers were at increased risk of ADHD. The association was mainly explained by passive gene-environment correlations. That is, genetic factors transmitted from mothers to children contribute to both mothers' age at childbearing and ADHD in offspring.

Study III investigated how the two symptom dimensions of ADHD (hyperactivity-impulsivity and inattention) are associated with early-onset substance use. The study found that that hyperactivity-impulsivity, but not inattention, independently predicted early-onset tobacco use, even after controlling for conduct problems. Twin analyses showed that the association between hyperactivity-impulsivity and early-onset substance use were mainly influenced by genetic factors.

Study IV estimated the association between ADHD and the risk of serious transport accidents, and explored the extent to which ADHD medication influenced this risk among ADHD patients. The study found that ADHD patients were at increased risk for serious transport accidents, and that ADHD medication was associated with a significant reduction of accidents, among males patients, even when using within-individual analyses to control for confounding.

Study V explored whether stimulant ADHD medication is associated with risk for long-term substance abuse. The study found no indication of increased substance abuse at follow-up. Rather, the results suggested there was a decrease in substance abuse for up to four years after taking ADHD medications, and that patients who took ADHD medication for longer durations had lower rates of substance abuse.

In conclusion, ADHD is a prevalent, persistent and impairing disorder. Genetic factors play an important role in the development of the disorder from childhood to adulthood. ADHD predicts poor developmental and health outcomes, and ADHD medications appear to be useful in reducing some serious adverse outcomes, such as transport accidents and substance abuse. The findings in this thesis highlight the importance of using quasi-experimental designs, including genetically-informative studies, when exploring how risk factors and adverse consequences are associated with ADHD.