REVIEW

Genetic and Environmental Stability in Attention Problems Across the Lifespan: Evidence From the Netherlands Twin Register

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Objective: To review findings on attention-deficit/hyperactivity disorder and attention problems (AP) in children, adolescents, and adults, as established in the database of the Netherlands Twin Register and increase the understanding of stability in AP across the lifespan as a function of genetic and environmental influences. **Method:** A longitudinal model was fitted on Netherlands Twin Register AP scores from 44,607 child (<12-year-old), adolescent (12- to 18-year-old), and adult (>18-year-old) twins. **Results:** Mean AP showed a downward trend with age. Age-to-age correlations ranged from 0.33 (50–≥60 years old) to 0.73 (10–12 years old). Stability in individual differences in AP was due to genetic and environmental factors, and change was due primarily to environmental factors. Nonadditive genetic influences were present from childhood to adulthood. Total genetic variance decreased slightly throughout aging, whereas environmental variance increased substantially with the switch from maternal to self-ratings at 12 years of age. As a result, heritability coefficients decreased from 0.70 to 0.74 in childhood (maternal ratings) to 0.51 to 0.56 in adolescence (self-ratings), and 0.40 to 0.54 in adulthood (self-ratings). In childhood, male subjects scored higher than female subjects. After the rater switch at 12 years of age, female subjects tended to score higher than male subjects. **Conclusions:** Stability of AP is the result of genetic and environmental stability. The decrease in estimated heritability at 12 years of age is due to an increase in occasion-specific environmental variance and likely reflects a methodologic effect. Because environmental influences have lasting effects on AP, their early detection is crucial. J. Am. Acad. Child Adolesc. Psychiatry; 2012;52(1):12–25.
Key Words: attention problems, attention-deficit/hyperactivity disorder, heritability, genetic stability, rater effects

Attention-deficit/hyperactivity disorder (ADHD) is a developmental disorder characterized by symptoms of inattention, hyperactivity, and impulsivity.[1] The prevalence of ADHD is highest in childhood, after which the number and the severity of its symptoms tend to decrease.[2] However, of the children who are diagnosed with ADHD, 15% retain this diagnosis by 25 years of age, whereas 50% are characterized by partial remission.[3] Notably, the decrease in ADHD symptoms tends to be more pronounced in hyperactivity and impulsivity than in inattention.[4] Taken together, these findings show that throughout development, ADHD and its symptoms demonstrate change, but also stability. Further support for stability in ADHD and ADHD symptoms can be found when considering individual differences in ADHD-related traits. Individual differences in attention problems (AP), for example, are moderately to highly stable over time.[5]

The aim of the present study was to increase the understanding of individual differences in AP and ADHD as a function of genetic and environmental effects and age. To this end, the authors summarize how the longitudinal database of the Netherlands Twin Register (NTR) has furthered the current understanding. Next, the authors elaborate on this line of research and investigate genetic and environmental stability and change in AP across the lifespan by fitting a longitudinal behavior genetic model to data from the NTR

This article is discussed in an editorial by Drs. James J. Hudziak and Douglas K. Novins on page 6.

database. These data were collected in 44,607 preadolescent (<12-year-old), adolescent (12- to 18-year-old), and adult (>18-year-old) twins over a period longer than two decades.

THE NTR: A LONGITUDINAL DATABASE

Recruitment and Data Collection

Previous NTR studies have been devoted to the description of the participants' recruitment, response rates, demography, and data collection.[6,7] Here, the authors provide a brief summary, followed by a review of the findings on the etiology of ADHD and AP, as established in the NTR database.

The NTR (http://www.tweelingenregister.org) has recruited newborn twins since 1987. Since then, about 40% of all Dutch newborn twins (and higher-order multiples) have been registered by their parents. These parents constitute the most important source of information during their children's early development (at 1, 2, 3, 5, 7, 10, and 12 years of age). When the twins turn 7, 10, and 12 years old, the parents are asked for permission to approach their children's teachers. At 14 and 16 years of age, the twins are asked to provide self-ratings. At this point, the siblings of the twins, if present, are invited to participate. Once the twins turn 18 years old, they, their siblings, and their parents enroll into the adult register and are invited to take part in ongoing studies.

In 1990, the NTR recruited, through city councils in the Netherlands, a large additional sample of adolescent and adult twins and their family members (parents, siblings, and spouses). Registration is ongoing. As of 2012, more than 35,000 twin pairs are enlisted with the NTR. Cross-sectional and longitudinal data have been collected by mailed surveys every 2 to 3 years, starting in 1991 (~22,000 participants from 5,546 families have taken part). Ongoing surveys 8 and 9 were initiated in 2009 and 2011, respectively. The registered twins are born in all strata of society, and the NTR participants are representative of the general population.[8] The NTR does not have exclusion criteria, mainly because the inclusion of special groups allows research in possible risk groups (such as children who are born at low birth weight or who are conceived with in vitro fertilization). Hence, all multiples and their family members are welcome to participate.

The data collected concern growth, health, cognition, and emotional and behavioral problems. Longitudinal measurements include variables relating to life events, demographics, lifestyle (exercise behavior, smoking, drinking, and other substance use), major medical illnesses, medication use, body mass index, personality, depression and anxiety, and variables related to ADHD. Subgroups of participants take part in projects that involve brain (EEG and magnetic resonance imaging) research, neuropsychological testing, psychiatric interviews, and cardiovascular studies. A large part of the adult participants has taken part in the NTR Biobank study.[9] Biological samples, which include DNA, RNA for expression profiling, cell lines, and multiple serum and plasma samples for biomarker studies, have been collected from about 10,000 adult subjects. DNA samples of children are also available. As part of the Genome of the Netherlands project, DNA sequence data have been assessed in 110 trios (parents and offspring) in 20 families consisting of parents and two twin offspring. Some individuals have provided multiple biological samples, which have been used to explore the longitudinal stability of DNA methylation.[10]

RESULTS CONCERNING ADHD AND AP

The NTR database has furthered the understanding of many aspects of various human biological and psychological traits, including healthy and pathologic outcomes of development. Table 1 presents the results of the NTR research into ADHD and AP.[11–32]

The findings most relevant to this study are the following. ADHD is more appropriately conceptualized as the extreme end of a continuum (or set of continuums) rather than a discrete category (or multiple discrete categories),[11] which is important theoretically. Although ADHD, ADHD symptoms, and AP are different phenotypes, their heritability estimates are of about the same magnitude. Moreover, ADHD, ADHD symptoms, and AP are, at least in childhood, affected by largely the same sets of genes.[12] However, the actual genes underlying these phenotypes remain unidentified.[13]

Heritability estimates of individual differences in ADHD symptoms and AP depend to some extent on rater and (to a lesser extent) on instrument. According to mother ratings on the Child Behavior Checklist (CBCL), AP are about 75% heritable,[14] whether AP are measured at 7, 10, or 12 years of age. Mother ratings on the Conners