ADHD and Poor Motor Performance From a Family Genetic Perspective

ELLEN FLIERS, M.D., SITA VERMEULEN, IR., FRÜHLING RIJSDIJK, PH.D., MARIEKE ALTINK, M.SC., CATHELIJNE BUSCHGENS, M.SC., NANDA ROMMELSE, PH.D., STEPHEN FARAONE, M.D., PH.D., JOSEPH SERGEANT, PH.D., JAN BUITELAAR, M.D., PH.D., AND BARBARA FRANKE, PH.D.

ABSTRACT

Background: Attention-deficit/hyperactivity disorder (ADHD) is frequently accompanied by motor problems (MPs). We investigated a possible shared etiology between the two traits in the Dutch sample of the International Multicenter ADHD Genetics study comprising 275 children with ADHD and their affected or unaffected sibling and 146 unrelated control children. **Method:** Exploratory data analysis and bivariate structural equation modeling were used to estimate the familiality of MP rated by parents (Developmental Coordination Disorder Questionnaire [DCD-Q]) or teachers (Groningen Motor Observation Scale [GMO]) and to determine the familial and environmental correlation between MP and ADHD. Furthermore, the nature of the familiality was explored by studying the siblings of ADHD-affected children. **Results:** The ADHD-affected children had significantly more MP than their unaffected siblings, who in turn had significantly more MP than the control subjects. The familial component of MP measured by DCD-Q and GMO was 47% and 22%, respectively. The familial correlation between motor performance measures and ADHD was −0.38 for DCD-Q and −0.40 for GMO. Our data suggested that co-occurrence of ADHD and MP possibly marks a distinct subtype of ADHD, rather than signaling increased severity of disease. **Conclusions:** Attention-deficit/hyperactivity disorder and MP have a common basis that may be due to genetic factors and/or shared environmental factors. Attention-deficit/hyperactivity disorder accompanied by MP may behave like a distinct subtype of ADHD, but more research will be needed to support that hypothesis. *J. Am. Acad. Child Adolesc. Psychiatry,* 2009;48(1):25–34. **Key Words:** ADHD, motor performance, dyspraxia, sib pairs, genetics.

Accepted July 24, 2008.

This article was reviewed under and accepted by Ad Hoc Editor Garry Walter, M.D., Ph.D.

Drs. Fliers, Buitelaar, and Franke, and Ms. Vermeulen, Ms. Altink, and Ms. Buschgens are with the Departments of Psychiatry and Human Genetics of the Radboud University Nijmegen Medical Centre. Dr. Fliers is also with the Parnassia Bavo–Europoort Youth Department in Rotterdam. Dr. Rijsdijk is with the Institute of Psychiatry, King's College, University of London. Drs. Rommelse and Sergeant are with the Department of Clinical Neuropsychology of the Vrije Universiteit. Dr. Faraone is with the State University of New York Upstate Medical University.

Dr. Fliers and Ms. Vermeulen contributed equally to the manuscript, and Drs. Buitelaar and Franke shared final responsibility for the work.

This study was partly funded by NIH Grant R01 MH62873-01A1 (to S.V.F.).

The authors thank Annemarie Fibbe and Marleen Bastiaanse for help with data collection.

Correspondence to Ellen Fliers, M.D., Bavo Europoort Youth Department, Twentestraat 52, 3083 BD Rotterdam, The Netherlands; e-mail: e.fliers@psy.umcn.nl.

DOI: 10.1097/CHI.0b013e31818b1ca2

Attention-deficit/hyperactivity disorder (ADHD) is a common and highly heritable neurobehavioral condition that commences in childhood and often persists into adulthood.[1–3] It affects 3% to 5% of children and is characterized by hyperactivity, inattention, and impulsivity. Twin studies have estimated the heritability of ADHD to be approximately 0.80.[4] Three subtypes of ADHD can be distinguished: a mainly inattentive, a mainly hyperactive-impulsive, and a combined subtype. Attention-deficit/hyperactivity disorder is frequently accompanied by psychiatric comorbidity and developmental problems.

Approximately 30% to 50% of children with ADHD also have motor problems (MP), currently referred to as developmental coordination disorder (DCD).[5–8] Developmental coordination disorder describes a marked impairment in the performance of motor skills that is found in 5% to 7% of school-age children in the general

population.[9] The condition is not due to medical problems like cerebral palsy, and the diagnosis should not be given to children with an IQ below 70.[9–16] The combination of ADHD and MP has a poorer prognosis than ADHD alone in terms of later psychiatric problems and substance abuse.[17] Therefore, the coexistence of ADHD and MP has important clinical consequences.

The increased prevalence of MP in ADHD-affected children compared with the general population suggests a shared etiology for both disorders because of genetic and/or environmental factors underlying both traits. So far, only one study has investigated the determinants of a shared etiology. In 2006, Martin and coworkers[18] showed a high heritable component of 0.69 for MP in a population-based twin sample; the shared heritability for ADHD and MP ranged between 0.29 and 0.51 for ADHD combined type, depending on the rating scale. The available information on the subtype of ADHD and the subscales of the Developmental Coordination Disorder Questionnaire (DCD-Q) allowed a genetic analysis on several levels. However, the ADHD diagnosis was based on questionnaires only, the number of ADHD combined type–affected children was rather limited, and no motor performance scale other than the DCD-Q was used.

Here, we report a second study on the overlap of ADHD and MP etiologies. We investigated a large clinical group of children with ADHD combined type that participated in the International Multicenter ADHD Genetics study, a program investigating the genetics of ADHD.[19,20] We examined the relation between ADHD and MP from a family-genetic perspective using a sample of ADHD concordant and discordant sibling pairs and control children in which motor performance had been measured by the parent-rated DCD-Q[21,22] and the teacher-rated Groningen Motor Observation Scale (GMO).[23] More precisely, we compared the frequency of MP and continuous motor scores between five distinct groups: ADHD-affected probands having ADHD-affected sibs, these ADHD-affected sibs, ADHD-affected probands having unaffected sibs, these ADHD-unaffected sibs, and controls. We argued that if ADHD and MP indeed share a common familial etiology, ADHD concordant pairs would show more MP in both siblings compared with ADHD discordant pairs. Also, the ADHD-unaffected siblings would show more MP than control children.

In a second part of the study, we calculated polychoric correlations and fitted bivariate genetic models to quantify the familial component of MP (which indicates the combined effects of genes and shared environment) and the extent to which the overlap between ADHD and MP is due to familial effects, while taking the selected nature of the sample into account.

Furthermore, we explored the relation of ADHD and MP in more detail by comparing the frequencies of presence of ADHD and/or MP in siblings of probands with ADHD only versus siblings of probands with ADHD and MP. Also, we compared the ADHD scores of probands with ADHD only and probands with ADHD and MP. These results would be expected to give information about the possibility of ADHD plus MP being a distinct subtype of ADHD or just an expression of increased severity of the disorder.

METHOD

Participants

Children with ADHD and their siblings were recruited for the collaborative International Multicenter ADHD Genetics study, which aims to identify genes that increase the risk for ADHD using quantitative trait loci linkage and association strategies.[19] In the Netherlands, 365 families of Dutch white descent participated; data on children's motor development were gathered in 337 of these families. Families were recruited from pediatric and child psychiatric services and through advertisements in the magazine and Web site of the Dutch organization for parents of children with ADHD. Elaborate description of the subjects and methods is given elsewhere.[20] Probands had to fulfill a clinical diagnosis of *DSM-IV* combined-subtype ADHD. Probands and siblings were 5 to 19 years old, lived at home, and attended primary or high school. Exclusion criteria applying to both included an IQ of less than 70, known genetic syndromes (Down, Turner, and fragile X), neurological disorders, autism, or epilepsy now or in the past.

Control children were recruited from elementary and high schools in the Netherlands. Parents received questionnaires by mail. Both parents and teachers completed the Conners rating scales (long versions, see below). Control children had to obtain nonclinical scores on both the parent and teacher version (Conners-N-scale: T score ≤ 62) to rule out ADHD among them. Regional ethics review boards in the Netherlands approved the study, which was performed in accordance with the Helsinki Declaration. Parents provided written informed consent for their children younger than 12 years; children ages 12 years and older gave written informed consent themselves in addition to their parents.

Instruments

ADHD Measures. Screening questionnaires (Conners Rating Scales, long version, and Strengths and Difficulties Questionnaires) for parents and teachers were used to identify children with ADHD symptoms.[24,25] Behavior in ADHD-affected children was scored in