ADHD and Poor Motor Performance From a Family Genetic Perspective

ELLEN FLIERS, M.D., SITA VERMEULEN, Ir., FRÜHLING RIJSIDIJK, 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.

Attention-deficit/hyperactivity disorder (ADHD) is a common and highly heritable neurobehavioral condition that commences in childhood and often persists into adulthood.\textsuperscript{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.\textsuperscript{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).\textsuperscript{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
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. The combination of ADHD and MP has a poorer prognosis than ADHD alone in terms of later psychiatric problems and substance abuse. 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 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. 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 and the teacher-rated Groningen Motor Observation Scale (GMO). 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 polygenic 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. 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. 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. Behavior in ADHD-affected children was scored in
medication-free periods, wherever possible. 7 scores of 63 or higher on the Conners ADHD subscales and scores of greater than 90th percentile on the Strengths and Difficulties Questionnaires-Hyperactivity scale were considered as clinical. Children who scored in the clinical range on any of the questionnaires were invited to the hospital, where a semistructured, standardized, investigator-based interview was administered, the Parental Account of Children’s Symptoms.26 A standardized algorithm was applied to the Parental Account of Children’s Symptoms and the teacher-rated Conners ADHD subscales to generate the total number of hyperactive-impulsive and inattentive symptoms of the DSM-IV symptom list.

Motor Measures. Motor symptoms were assessed using the DCD-Q, filled out by parents. The DCD-Q identifies children with MP in daily life. The internal consistency of the questionnaire is high (α = .88).22 In the Netherlands, it was recently translated into Dutch and validated.22 The DCD-Q contains 17 items and 4 subscales: motor control in motion, fine motor control/handwriting, gross motor control/planning, and general coordination. The total score varies from 17 to 85, with low scores representing poor performance. Scores lower than the 10th percentile, between the 10th and the 25th percentile and above the 25th percentile of controls indicate the presence of DCD, suspected DCD, and no DCD, respectively. In this study, the cutoff at the 10th percentile was used to indicate MPs.

Teachers filled out the GMO, developed in the Netherlands.22 It contains 18 items to be scored on a 4-point scale, ranging from “not at all like this child” to “like this child.” The total score varies from 18 to 72. High scores on the GMO indicate poor performance. The cutoff scores to indicate the presence of DCD, suspected DCD, or no DCD are dependent on age and sex. A score below the 15th percentile of an age- and sex-matched control group is considered suspicious for DCD and was used as the cutoff in this study to indicate MP, which is a standard procedure with the GMO.22 The GMO is validated for ages 5 to 11 years; because no validation is available yet for children ages 12 years and older, we used the cutoff points of 11 years. This step in the analysis could underestimate rather than overestimate motor performance as norms become stricter when children get older.

We have shown earlier that the DCD-Q and GMO correlate significantly with each other (r = 0.49, p < .001).8 This correlation suggests that both questionnaires tap into comparable aspects of motor functioning, yet are distinct enough to be valuable as separate measures.

Analyses

We selected for analysis only one sib pair from each family. From families with three (n = 68) or four (n = 9) children, we included a sibling with ADHD, if possible. If not, we chose the sibling in age closest to the proband. We combined the parent and teacher scores on the Conners Rating Scales by adding up the scores on both and dividing by two. To classify a sib pair as ADHD concordant, both children had to score above 62 on the combined scale. A sib pair was classified as discordant if the proband scored above 62 and the sibling scored 56 or lower. All children with Conners scores between 56 and 63 were excluded, ensuring that the pairs were truly concordant or discordant. This procedure reduced the number of participating families from 337 to 275.

For the motor scales (DCD-Q or GMO), prorating using the mean of the list was performed in case a questionnaire had a maximum of five missing items. This was done for 5.4% of children from ADHD families and 3.4% of control children for the DCD-Q and for 11.9% of children from ADHD families and 8.9% of control children for the GMO. Because of non-normality of the GMO data, we applied a Van der Waerden transformation as implemented in SPSS (for Windows, version 14.0),49 which reduced skewness and kurtosis. A similar procedure was used for the DCD-Q. The GMO scores were mirrored, in addition, so that scores on all motor variables would imply the same meaning: a low score was indicative of poor motor performance, and a high score was indicative of good motor performance.

Chi-square tests were used to test for differences in frequencies in dichotomous variables between groups. Group differences in continuous motor scores and Conners scores were assessed in univariate analyses of variance in which the study groups (i.e., ADHD concordant pair probands, affected siblings, ADHD discordant pair probands, unaffected siblings, and control children) served as between-subject factors. Sex was introduced into the model as covariate (analysis of covariance). Where appropriate, specific hypotheses about pairwise differences between groups for continuous variables were tested. We used the Bonferroni t test that adjusts the observed significance level for multiple testing. The analyses above were performed using SPSS for Windows, version 14.0.

Polychoric Correlations. We fitted a constrained correlational model to the sib data to get one within-individual cross-trait correlation, one cross-sib cross-trait correlation, and one cross-sib within-motor performance measure. Because the sample had been ascertained for the study of ADHD and we had to take this selection into account, in each correlational model, the ADHD sib correlation was fixed according to the assumed heritability of ADHD, that is 1/2 * 0.80 = 0.40 (see below).

Model-Fitting Analyses. Bivariate genetic model fitting was performed using the Mx program.28 For an extensive description of the method and interpretation, see Neale and Cardon.29 In short, the method allows, using information on the associations within and between different relative pairs (e.g., monozygotic and dizygotic twin pairs), for an estimation of the contribution of genetic factors (A), shared environmental factors (C), and unique environmental factors (E) in the occurrence of a trait or co-occurrence of traits using maximum likelihood techniques. Because our data sample consisted of sib pairs and singletons, we were not able to distinguish between the genetic and shared environmental component. Instead, we used a model in which we estimated the combined effects of A and C, indicated by the familial component (F) and nonshared environment effects (E), the latter also including measurement error. The standardized solution of this model is presented in Figure 1.

Significant cross/sib cross/within-trait covariances imply that common etiological factors between two traits are familial. The analyses yield estimates of a familial (rF) and environmental correlation (rE): the extent to which the same familial or environmental effects have an impact on both ADHD and the motor performance measures. Because the rF and rE do not take into account the familiality of either trait, it is possible for a large genetic correlation to actually explain a small portion of the observed covariation between these two traits. The product of rF and the square root of the standardized F estimates of the two traits constitutes the familial contribution to the total phenotypic correlation (rph,f) between the two traits. In a similar way, we can establish rph,e (Fig. 1).

Because the sample had been selected for ADHD, we corrected for selection. We used a fixed bivariate model described in detail elsewhere.30 This model applies the knowledge that we have of the (genetic) parameters of the disorder (ADHD), which is the selection variable: heritability of 80%, no effects of common environment, and a prevalence of 5%.4 This model assumes a continuum of risk that is normally distributed, with the disorder occurring only when a
certain threshold of liability is exceeded. We used the dichotomous ADHD classification and categorized the motor performance measures into quartiles. To account for the selection on ADHD affection status, we fixed the familial effects to 80% and the threshold on the liability to a \( z \) value of 1.64. Parameters (\( F \), \( E \), and thresholds for the motor performance measures) were free. Precision of free parameters was obtained by maximum likelihood confidence intervals (CIs; 95% CI).

**RESULTS**

Sample Characteristics

Two hundred seventy-five children with ADHD and their affected or unaffected siblings were assessed, as were 146 control children (Table 1 for sample characteristics). The groups did not differ in mean age. Relatively more girls were present in the unaffected sibling and control groups compared with the ADHD groups. The DCD-Q data were available for 556 children; the GMO data for 660 children.

**TABLE 1**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ADHD Concordant Sib Pairs</th>
<th>ADHD Discordant Sib Pairs</th>
<th>Control Children (( n = 146 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Probands (( n = 94 ))</td>
<td>Affected Siblings (( n = 94 ))</td>
<td>Nonaffected Siblings (( n = 181 ))</td>
</tr>
<tr>
<td>Age, y</td>
<td>11.4 (2.9)</td>
<td>10.9 (3.2)</td>
<td>11.2 (2.6)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>78 (83%)</td>
<td>58 (61%)</td>
<td>157 (87%)</td>
</tr>
<tr>
<td>Conners mean inattentiveness</td>
<td>70.2 (6.9)</td>
<td>68.0 (6.4)</td>
<td>67.8 (6.4)</td>
</tr>
<tr>
<td>Conners mean hyperactivity-impulsiveness</td>
<td>75.9 (7.2)</td>
<td>70.1 (8.2)</td>
<td>74.0 (8.2)</td>
</tr>
<tr>
<td>DCD-Q mean total score</td>
<td>74.9 (7.0)</td>
<td>70.9 (6.0)</td>
<td>72.7 (6.8)</td>
</tr>
<tr>
<td>GMO mean total score</td>
<td>53.6 (11.8)</td>
<td>55.0 (11.9)</td>
<td>54.4 (11.2)</td>
</tr>
</tbody>
</table>

Note: ADHD = attention-deficit/hyperactivity disorder; DCD-Q = Developmental Coordination Disorder Questionnaire; GMO = Groningen Motor Observation Scale.

Comparison of Motor Scores and Frequencies of MPs in the Sampled Groups

As shown in Figures 2A and B, we found MPs as measured by the DCD-Q more often in sib pairs concordant for ADHD (35% for probands and 33% for sibs) and affected probands of discordant pairs (34%) compared with the unaffected siblings (8%; all \( p < .001 \)). Classification based on the GMO showed 38% motor disorders in probands and 32% in ADHD concordant sibs versus 38% and 10% in discordant pairs (comparisons, all \( p < .001 \)). In the control children, the results were as expected: 5% motor-affected children according to the DCD-Q and 7% according to the GMO. These percentages were significantly lower than those for the ADHD probands and the ADHD-affected siblings (\( p < .001 \)).

The sibling pairs and the controls also differed significantly on continuous motor performance scores according to DCD-Q (\( F_{4,550} = 37.82, p < .001; \) Fig. 3A) and GMO (\( F_{4,654} = 36.60, p < .001; \) Fig. 3B). Post hoc analysis showed significant differences for the ADHD-affected sibs versus the unaffected sibs and
controls (both DCD-Q and GMO, \( p < .001 \)), and for the unaffected siblings compared with the control children (DCD-Q: \( p = .001 \); GMO: \( p = .01 \)). The ADHD-affected children scored lower than the unaffected siblings, who in turn scored lower than the control subjects. Introducing sex as covariate did not change these results.

Model Fitting Results

Table 2 shows the polychoric correlation estimates for ADHD and motor performance as measured by the GMO (\( r = -0.59; 95\% \text{ CI } -0.64 \) to \(-0.52 \)) and the DCD-Q (\( r = -0.55; 95\% \text{ CI } -0.58 \) to \(-0.48 \)). The correlations between ADHD and the DCD-Q subscales varied from \(-0.28 \) for gross motor/planning to \(-0.62 \) for fine motor/handwriting. Cross-member within-trait correlation was markedly higher for the DCD-Q (0.43; 95% CI 0.30–0.55) than the GMO (0.16; 95% CI 0.02–0.29), indicating a smaller familial component for the latter. Cross-member cross-trait correlations were statistically significant at the \( p < .05 \) level and suggested that at least a part of the correlation between ADHD and MPs is due to familial effects that the two traits have in common.

Table 3 contains the results of the bivariate model-fitting procedure. The estimated contribution of familial effects to the observed variation in GMO and DCD-Q

![Fig. 2](image1.png)

**Fig. 2** A, Percentage of motor-affected children according to parents (DCD-Q) in ADHD probands and their ADHD-affected or unaffected siblings and controls. The percentages were significantly lower in unaffected siblings and controls \(( p < .001 )\). B, Percentage of motor-affected children according to teachers (GMO) in ADHD probands and their ADHD-affected or unaffected siblings and controls. The percentages were significantly lower in unaffected siblings and controls \(( p < .001 )\). ADHD = attention-deficit/hyperactivity disorder; DCD-Q = Developmental Coordination Disorder Questionnaire; GMO = Groningen Motor Observation Scale.

![Fig. 3](image2.png)

**Fig. 3** A, Mean of raw scores on DCD-Q motor scale, normalized, in different groups. B, Mean of raw scores on GMO motor scale, normalized and mirrored, in different groups. DCD-Q = Developmental Coordination Disorder Questionnaire; GMO = Groningen Observation Scale.
scores was 0.22 and 0.47, respectively (both estimates significant at \(p \leq 0.001\)). The estimates of the familial component of the DCD-Q subscales varied slightly (0.33–0.41). The results were statistically significant at the \(p \leq 0.05\) level. The phenotypic correlation between ADHD and motor performance was comparable for DCD-Q and GMO and strongest for fine motor/handwriting and general coordination. Overall, these results suggested that, for all measurement scales, approximately two thirds of the phenotypic correlation is due to shared familial factors; and one third, to shared environmental factors. Because we observed an association between GMO scores and sex, we also fitted a sex-specific bivariate model; no sex differences in familial effects were detected (\(p = .948\)).

### Exploration of the Relation Between ADHD and MP

To find indications for ADHD+MP being a distinct subtype of ADHD, prevalence of MP in the siblings was calculated according to the motor status of the proband. Indeed, for the DCD-Q, 11 (15.5%) of 71 siblings of probands with ADHD+MP also had the combination of ADHD+MP, whereas only 13 (6.4%) of 204 siblings of probands with ADHD-only had this combination (\(p = .013\)), which would suggest a distinct subtype. However, for the GMO, this was 11 (11.0%)

### TABLE 2

Polychoric Correlations for ADHD (95% Confidence Interval) and Motor Performance Measures

<table>
<thead>
<tr>
<th>Scale</th>
<th>Within-Member Cross-Trait (ADHD(<em>{sib1}) − MP(</em>{sib1}) = ADHD(<em>{sib2}) − MP(</em>{sib2}))</th>
<th>Cross-Member Within-Trait (MP(<em>{sib1}) − MP(</em>{sib2}))</th>
<th>Cross-Member Cross-Trait (ADHD(<em>{sib1}) − MP(</em>{sib2}) = ADHD(<em>{sib2}) − MP(</em>{sib1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMO</td>
<td>−0.59 (−0.64 to −0.52)</td>
<td>0.16 (0.02−0.29)</td>
<td>−0.20 (−0.28 to −0.12)</td>
</tr>
<tr>
<td>DCD-Q</td>
<td>−0.55 (−0.58 to −0.48)</td>
<td>0.43 (0.30–0.55)</td>
<td>−0.25 (−0.33 to −0.16)</td>
</tr>
<tr>
<td>Control during movement</td>
<td>−0.29 (−0.38 to −0.20)</td>
<td>0.35 (0.19–0.48)</td>
<td>−0.17 (−0.26 to −0.08)</td>
</tr>
<tr>
<td>Fine motor/handwriting</td>
<td>−0.62 (−0.68 to −0.55)</td>
<td>0.35 (0.21–0.47)</td>
<td>−0.24 (−0.32 to −0.16)</td>
</tr>
<tr>
<td>Gross motor/planning</td>
<td>−0.28 (−0.36 to −0.19)</td>
<td>0.33 (0.17–0.47)</td>
<td>−0.10 (−0.18 to −0.01)</td>
</tr>
<tr>
<td>General coordination</td>
<td>−0.60 (−0.66 to −0.52)</td>
<td>0.37 (0.23–0.49)</td>
<td>−0.28 (−0.33 to −0.19)</td>
</tr>
</tbody>
</table>

*Note:* Cross-member ADHD correlation (ADHD\(_{sib1}\) − ADHD\(_{sib2}\)) is fixed to 0.40 based on the applied genetic model for ADHD (\(f^2 = 0.80\), prevalence 5%). ADHD = attention-deficit/hyperactivity disorder; DCD-Q = Developmental Coordination Disorder Questionnaire; GMO = Groningen Motor Observation Scale; MP = motor problems.

### TABLE 3

Results of the Bivariate Genetic Models for ADHD and Motor Performance Measures Fitting Familial (Genetic + Common Environment) and Nonshared Environmental Effects

<table>
<thead>
<tr>
<th>Scale</th>
<th>(f^2)</th>
<th>(e^2)</th>
<th>(r_{ph,f})</th>
<th>(r_{ph,e})</th>
<th>(r_{ph})</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMO</td>
<td>0.22 (0.11–0.35)</td>
<td>0.78 (0.65–0.89)</td>
<td>−0.38 (−0.46 to −0.29)</td>
<td>−0.23 (−0.27 to −0.18)</td>
<td>−0.60 (−0.67 to −0.53)</td>
</tr>
<tr>
<td>DCD-Q</td>
<td>0.47 (0.34–0.58)</td>
<td>0.53 (0.42–0.66)</td>
<td>−0.40 (−0.48 to −0.31)</td>
<td>−0.18 (−0.22 to −0.14)</td>
<td>−0.58 (−0.65 to −0.49)</td>
</tr>
<tr>
<td>Control during movement</td>
<td>0.35 (0.20–0.49)</td>
<td>0.65 (0.51–0.80)</td>
<td>−0.24 (−0.34 to −0.14)</td>
<td>−0.07 (−0.13 to −0.02)</td>
<td>−0.32 (−0.41 to −0.22)</td>
</tr>
<tr>
<td>Fine motor/handwriting</td>
<td>0.40 (0.26–0.52)</td>
<td>0.60 (0.48–0.74)</td>
<td>−0.41 (−0.49 to −0.32)</td>
<td>−0.22 (−0.27 to −0.18)</td>
<td>−0.63 (−0.70 to −0.55)</td>
</tr>
<tr>
<td>Gross motor/planning</td>
<td>0.33 (0.18–0.48)</td>
<td>0.67 (0.52–0.82)</td>
<td>−0.17 (−0.27 to −0.07)</td>
<td>−0.11 (−0.16 to −0.05)</td>
<td>−0.28 (−0.38 to −0.18)</td>
</tr>
<tr>
<td>General coordination</td>
<td>0.41 (0.28–0.53)</td>
<td>0.59 (0.47–0.72)</td>
<td>−0.44 (−0.52 to −0.35)</td>
<td>−0.19 (−0.23 to −0.14)</td>
<td>−0.63 (−0.69 to −0.55)</td>
</tr>
</tbody>
</table>

*Note:* \(f^2\): familial component of motor performance measurement scale; \(e^2\): environmental component of motor performance measurement scale; \(r_{ph}\): total phenotypic correlation; \(r_{ph,f}\), \(r_{ph,e}\): part of the phenotypic correlation due to familial and environmental effects, respectively. Fixed genetic model for ADHD used: \(f^2 = 0.80\), prevalence 5%. ADHD = attention-deficit/hyperactivity disorder; DCD-Q = Developmental Coordination Disorder Questionnaire; GMO = Groningen Motor Observation Scale.
of 100 versus 17 (9.7%) of 175, which did not reach significance ($p = .580$; Table 4).

When comparing the frequency of ADHD in siblings of ADHD+MP and ADHD-only probands to determine whether MPs were related to severity of ADHD, we found that probands with ADHD+MP had a sibling with ADHD equally often as probands with ADHD-only: 35.3% of ADHD+MP probands had a sibling with ADHD, and 33.8% of probands with ADHD-only had a sibling with ADHD ($p = .885$) according to the DCD-Q; the GMO gave comparable results (33.0% versus 34.9% [$p = .793$]). Conners scores were also comparable in probands with and without MP (Table 5), as were the scores of siblings of ADHD+MP probands and siblings of ADHD-only probands ($F_{1,273} = 0.468$, $p = .494$ for DCD-Q; $F_{1,273} = 0.565$, $p = .453$ for GMO). This suggests that the presence of MP is not a sign of increased severity of ADHD.

Because we had selected only one sibling from families that consisted of more than one sibling pair, we evaluated whether the distribution of families with one or more sibling pairs was similar for the probands with and without MP to ensure that the sibling selection on ADHD status had not impaired the analyses previously described. We could confirm this: the groups showed no difference (DCD-Q: $p = .675$; GMO: $p = .270$).

### DISCUSSION

Up to now, there are only two studies (including ours) that have examined a possible shared etiological back-
sensitivity, specificity, and classification accuracy. These findings stress the importance of using multiple informants to obtain a full picture of a child’s functioning. In addition, in our study of sib pairs, the DCD-Q was filled out by the same parent for a sib pair, whereas two different teachers per sib pair filled out the GMO. This may have inflated the environmental contribution in the analysis of the GMO. Interestingly, Figures 2A and B show the same pattern for parents’ and teachers’ ratings in the prevalence of MP in concordant and discordant sib pairs, although the GMO and DCD-Q do not perfectly correlate.

Because both our study and the study by Martin and coworkers suggest a common (at least partly familial) background of ADHD and MP, we asked the question of how this common etiology may express itself. We found some evidence suggesting that the co-occurrence of ADHD and MP represents a distinct subtype of ADHD, but cautious interpretation of these findings is required. First, the analyzed subgroups contained small numbers of observations. In addition, although the results for DCD-Q and GMO showed the same pattern, only the results for the DCD-Q reached statistical significance. The fact that 11.9% of the GMO questionnaires contained missing items (1–5 items) that were prorated using the mean of the list compared with 5.4% of the DCD-Q questionnaires may have contributed to this apparent inconsistency between raters.

One may speculate which pathophysiological mechanisms play a role in the co-occurrence of ADHD and MP. Neuroimaging studies have demonstrated structural and functional abnormalities of neural circuits in ADHD. In particular, dysfunction of the cingulate area and of fronto-striatal circuits; reduced volumes of the whole brain, nucleus caudatus, frontal areas, and cerebellar regions; smaller size of the corpus callosum; reduced thickness of the cingulate cortex; and delayed cortical maturation have been established. The biological substrate of MP is far from clear, although most researchers agree that the cerebellum and the basal ganglia also play an important role. In the combination of ADHD and MP, a dopamine-induced dysbalance of the basal ganglia neurocircuits may be pivotal. The role of the dopamine system is well established in ADHD, and genetic variation in dopaminergic genes contributes to ADHD risk. Different lines of evidence indicate that the dopaminergic system also plays an important role in motor control. Interestingly, polymorphisms in the dopamine-carboxylase gene (DCD), whose product catalyzes the final step in the synthesis of serotonin and dopamine, were found to be associated with locomotor behavior in animal studies. All in all, dopamine pathway genes deserve further investigation in the search for a common background of ADHD and MP.

Our results should be interpreted in the context of the strengths and limitations of the study. Possible limitations concerning the motor screening are the use of questionnaire data only and the absence of objective motor tests (e.g., the Movement Assessment Battery for Children or assessments of motor functioning by experienced clinicians). These procedures, however, are rather time consuming and expensive and less compatible with testing large samples of children as was done in our study. We compensated for this potential weakness by using parent and teacher ratings of motor development, allowing us to assess the influence of the measurement scales on the estimate of the familial component. However, given the strong dependence of our results and those of Martin and coworkers on the measurement scales, more research will be necessary to arrive at a reliable estimate of the contribution of familial and heritable factors to the shared etiology of ADHD and MP and to determine the distinct value of the various measurement scales. The strengths of our study are the large sample size, the strict DSM-IV–based algorithm used to diagnose ADHD, and the use of only extremely concordant and discordant sib pairs, ensuring exclusion of subclinical ADHD cases.

This study confirms the presence of an underlying shared etiology for ADHD and MP. It also gives, although speculatively at this time, a first indication that ADHD with MP marks a distinct subtype of ADHD. This finding paves the way for further studies into the molecular genetics, where dopamine-related or other specific genes may play a role in the common background of ADHD and MP.
ADHD MOTOR PROBLEMS SHARED BACKGROUND

Eli Lilly, Janssen-Cilag BV, and Shire Laboratories. Dr. Buitelaar has been a consultant to, member of the advisory board of, and/or a speaker for Janssen-Cilag BV, Eli Lilly, Bristol-Myers Squibb, UBC, Shire Laboratories, and Medic. The other authors report no conflicts of interest.

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