Original article

Methylphenidate improves reading performance in children with attention deficit hyperactivity disorder and comorbid dyslexia: An unblinded clinical trial


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ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) and dyslexia are frequently co-occurring disorders. Although methylphenidate (MPH) is the primary treatment for ADHD, the effect on reading in children with these comorbid problems is not yet known. This study was an unblinded clinical trial to evaluate the reading performance before and after treatment with MPH. Reading performance was compared with General Linear Model repeated measures between three groups: (1) an experimental group of children with both ADHD and dyslexia (N = 24), (2) a control group of children with ADHD (N = 9) and (3) a control group of children with dyslexia (N = 10). MPH improved reading performance significantly stronger in the experimental group than in the control groups; the number of correctly read words increased to a larger extent. In conclusion, MPH proved to be an aid in the reading process of children with ADHD and comorbid dyslexia by improving the learning conditions, but MPH cannot cure the reading disorder. Future research should study the effect of MPH on reading in a double-blind clinical trial.

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1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) and dyslexia are both frequently occurring developmental disorders, affecting about 3–10% of the schoolchildren.1–3 These disorders co-occur in both clinical and epidemiological samples more frequently than expected by chance, with estimated rates of overlap varying from 15% to 40%.4–7 Gender differences are noted in this co-occurrence: more boys than girls with dyslexia have behaviour problems and ADHD.8 Both ADHD and dyslexia are associated with multiple cognitive deficits, including abnormalities in executive functions in both disorders.9 The specific cognitive deficits in children with ADHD or children with dyslexia alone are combined in
the comorbid group. Furthermore, children with these comorbid problems have more secondary problems, such as low self-esteem, behavioural problems and dropping out of school, and a worse outcome compared with children diagnosed with solely ADHD or dyslexia. Therefore, early identification and intervention are important. Numerous explanations have been proposed to account for this comorbidity, but the most recent findings support common etiological influences that increase the susceptibility to both disorders. With regard to the causal relations between ADHD en dyslexia, dyslexia neither causes nor exacerbates behaviour problems and ADHD, whereas ADHD stagnates the reading process but only in the group with both ADHD and dyslexia.

Dyslexia is identified if a child has poor reading and/or literacy skills despite adequate intelligence and opportunity to learn. Subsequently, reading achievements are significantly lower than expected for the didactic age of the child, which is the number of months the child has been educated. Children with dyslexia have a core deficit in automatation. More specifically, this automation deficit reveals itself in phonological processing skills, defined as the ability to detect and manipulate individual speech sounds.

Two clusters of symptoms characterize ADHD: attention deficit and hyperactivity/impulsivity. Four subtypes of ADHD can be distinguished: (1) ADHD combined type (ADHD-C), (2) ADHD predominantly inattentive type (ADHD-I), (3) ADHD predominantly hyperactive/impulsive type (ADHD-II), and (4) ADHD not otherwise specified (ADHD-NOS). ADHD is a heterogeneous disorder, characterized by a high rate of comorbidity. The ADHD symptoms are thought to arise from a deficit in inhibitory control implemented in frontostriatal networks. Stimulant medication, especially methylphenidate (MPH), is currently one of the primary treatment approaches for children with ADHD, the effectiveness of which has often been shown empirically. MPH increases the level of dopamine by binding to dopamine transporters (as well as norepinephrine) and in this way blocking the re-uptake, particularly in the striatum. Children with ADHD and comorbid dyslexia responded comparably to MPH with respect to ADHD symptoms compared with children with ADHD only.

Multiple studies have shown robust short-term effects of MPH on the core symptoms of ADHD, cognitive laboratory tasks and academic performance in children with ADHD. However, studies of the effectiveness of MPH beyond 3 months are limited in number. The few long-term effect studies showed that the positive effects of MPH continued during longer-term treatment. However, it is still unclear whether short-term gains of MPH can be translated into long-term improvements in academic achievement. Several explanations for the effect of MPH on academic learning have been proposed: (1) improved ability to selectively attend to relevant stimuli, (2) better efficiency of basic cognitive processes concerned, and (3) improved non-specific cognitive processing mechanisms.

Despite the frequent co-occurrence of ADHD and dyslexia, few studies have evaluated the effect of MPH on reading performance in these children. A comprehensive literature search in Medline and PsychINFO revealed five relevant studies, of which four were at least 17 years old. Results concerning the effect of MPH on reading performance in children with ADHD and dyslexia were inconsistent. These studies could not be easily compared because of differences in the diagnostic criteria used, period of MPH use, MPH use or not during the test session, and reading tests used. Moreover, these studies contained methodological shortcomings. Therefore, more research on this subject is needed.

The aim of the present study was to evaluate the unblinded effect of MPH on the reading performance in children diagnosed with both ADHD and dyslexia. This study adds value to the existing literature by evaluating the effect of MPH beyond 3 months and assessing a relatively large sample of 43 children, of which 24 were diagnosed with ADHD and dyslexia. Reading performance before the start of medication and after at least 3 months of medication use were compared in the experimental group and a control group of children diagnosed with solely ADHD. Furthermore, a second control group of children diagnosed with only dyslexia was included to compare reading performance over a period of the same length, but without use of MPH.

2. Methods

2.1. Participants

The present study concerned a clinical sample, selected from all consecutive referrals to the specialized multidisciplinary clinic for Learning Disabilities at the Maastricht University Hospital in the period January 2000–January 2006. Participants were included if they met the following criteria: (1) a diagnosis of ADHD and/or a diagnosis of dyslexia depending on the assigned group, (2) start of MPH treatment in children diagnosed with ADHD, (3) a first test administration and a revision test administration at least 3 months afterwards, (4) the examination of at least one reading test, (5) no primary sensory deficits, (6) no neurological or genetic abnormalities, and (7) information processing capacities equal to or higher than 70 and thus not indicative of mental retardation. One experimental and two control groups were included in this study. The experimental group consisted of children diagnosed with both ADHD and dyslexia. The first control group consisted of children diagnosed only with ADHD (ADHD control group) and the second control group contained children diagnosed only with dyslexia (dyslexia control group). The experimental group consisted of 24 children in the age range 6.90–12.82 years at the first assessment (Table 1). Seven children of these had a comorbid diagnosis: developmental coordination disorder (N = 5) and oppositional defiant disorder (N = 2). The ADHD control group consisted of 9 children in the age range 8.32–13.28 years. Two children of these had comorbid developmental coordination disorder. The dyslexia control group included 10 children in the age range 8.24–13.52 years, of which none had a comorbid diagnosis. The three groups did not differ in demographic variables, level of information processing and ADHD subtypes. Furthermore, the groups were comparable regarding the number of months they had been educated (didactic age).
Table 1 – Characteristics of the experimental group, ADHD and dyslexia control groups

<table>
<thead>
<tr>
<th></th>
<th>Experimental group, N = 24, Mean (SD)</th>
<th>ADHD control group, N = 9, Mean (SD)</th>
<th>Dyslexia control group, N = 10, Mean (SD)</th>
<th>Test statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (boys/girls)</td>
<td>17/7</td>
<td>7/2</td>
<td>4/6</td>
<td>3.76*</td>
</tr>
<tr>
<td>Age in years</td>
<td>9.46 (1.39)</td>
<td>9.75 (1.62)</td>
<td>10.07 (1.86)</td>
<td>0.57*</td>
</tr>
<tr>
<td>Didactic age in months</td>
<td>30.29 (13.24)</td>
<td>34.56 (16.51)</td>
<td>38.90 (17.50)</td>
<td>0.31*</td>
</tr>
<tr>
<td>Information processing</td>
<td>97.13 (10.98)</td>
<td>95.78 (6.14)</td>
<td>106.57 (8.54)</td>
<td>2.99*</td>
</tr>
<tr>
<td>MPH dosage (mg/kg)</td>
<td>0.48 (0.13)</td>
<td>0.47 (0.22)</td>
<td>-</td>
<td>0.13*</td>
</tr>
<tr>
<td>ADHD subtype (ADHD-C/ADHD-I)</td>
<td>15/9</td>
<td>6/3</td>
<td>-</td>
<td>0.00*</td>
</tr>
</tbody>
</table>

Note: ADHD = Attention Deficit Hyperactivity Disorder; MPH = methylphenidate; ADHD-C = Attention Deficit Hyperactivity Disorder, combined type; ADHD-I = Attention Deficit Hyperactivity Disorder, predominantly inattentive type.

* Chi-square test.

† One-way ANOVA F-test, 40.

‡ Independent two-samples t-test.

The diagnostic process included a neurological examination, inspection of general health and psychological data based on recommendations by Goldman et al. 39,40 Psychological data were obtained from multiple information sources in a standardized fashion by senior clinical child neuropsychologists: (1) information about development, school and current functioning of the child by means of a clinical interview with parents, (2) a battery of neuropsychological tests, and (3) behaviour questionnaires completed by parents and teachers. Diagnoses were established by a multidisciplinary team consisting of child neuropsychologists, a child neurologist, a youth health care physician and a linguist based on the above-mentioned information sources combined with a clinical judgment.41 ADHD was diagnosed based on the diagnostic criteria of the DSM-IV.16 Dyslexia was diagnosed based on the diagnostic criteria of the Reading Disorder in the DSM-IV combined with a criterion for didactical resistance.16,42 Didactical resistance refers to the persistence of reading problems despite adequate, remedial instruction and practice for at least 6 months.42,43

2.2 Procedure

Participants were selected for an unblinded clinical medication assessment. In order to evaluate the effect of MPH, the tests were administered according to a pretest and posttest design. At the pretest session all participants were thoroughly tested according to a neuropsychological standardized test protocol that assessed cognitive functions such as information processing, language skills, memory, attention, visual motor integration, and academic skills.44 Administration of this test battery required on average 2h. A well-trained neuropsychologist tested the participants individually. All children were medication free and no one had used MPH before the pretest session. The posttest session occurred at least 3 months after the start of MPH use and the same standardized test protocol was used. Whenever possible, parallel versions of a test were used to minimize the effect of repeated measures. Test situation concerning test room, time of testing and experimenter remained stable between both test sessions. The neuropsychologist, who executed the neuropsychological testing, was not blind for the medication condition. MPH was prescribed by the child neurologist of the multidisciplinary team, to ensure that participants received the medication according to a standard procedure. For each child who started with MPH treatment, 5 mg MPH was prescribed twice a day. The beneficial and possible side effects of MPH were evaluated telephonically after 2 weeks. In an outpatients’ appointment 4 weeks after the start of MPH treatment, the effect of MPH and the biometrics were assessed. If necessary the MPH dosage was adjusted, followed with another evaluation 4 weeks later. Children who received MPH treatment remained under medical supervision by the neuropsychologist for the complete time medication was used. This follow-up system intends to monitor medication adherence and to detect possible changes in medication effectiveness and side effects. In the present sample medication adherence was 100%. MPH was prescribed on a well-tolerated dose, varying form 0.18 to 0.79 mg/kg body weight during 24 h (mean = 0.48; SD = 0.16). The dosage of MPH did not differ between the experimental and ADHD control group (Table 1). The length of the interval between the test sessions varied from 0.29 to 1.44 years (mean = 0.81; SD = 0.33) for the experimental group and from 0.34 to 1.17 years (mean = 0.59; SD = 0.26) for the ADHD control group. For the dyslexia control group, the length of the test interval varied from 0.49 to 0.99 years (mean = 0.76; SD = 0.17). The three groups did not differ in terms of the length of the test interval (F(2,40) = 1.86; p = 0.168).

2.3 Instruments

Reading was the main function of importance in the present study. Two other relevant neuropsychological tests on sustained attention and automation were also evaluated. Furthermore, the screening instruments used in the diagnostic process will be discussed.

Reading performance was measured using standardized Dutch reading tests: One-Minute-Test (Een-Minuut-Test EMT45,46), Three-Minutes-Test (Drie-Minuten-Test DMT47) and the Klepel48. Parallel versions of these tests have high test-retest reliability coefficients (r = 0.91).48 The EMT and DMT are
comparable technical reading tests, which measure lexical decoding skills. The child is asked to correctly read aloud as many words as possible. The DMT consists of 3 reading cards of 1 min each, whereas the EMT consists of one reading card of 1 min. Dependent measures of the DMT were averaged over the three reading cards and can therefore be considered comparable to the EMT variables. Dependent measures are the raw score and the reading quotient (RQ). The raw score is the total number of read words minus the number of errors, so that both reading accuracy and reading speed were considered. The reading quotient is the reading age divided by didactic age multiplied with 100 (100% is in accordance with age; below 70% is indicative of serious reading problems). The Klepel is a test for non-existing (nonsense) word reading skills, which measures reading by phonological decoding. In this test, the child is asked to correctly read as many words as possible for 2 min. Dependent measures are the total number of read words minus errors (raw score) and the standard score (mean = 10; SD = 3).

The Bourdon-Vos test (BV) is a Dutch test commonly used to measure visual sustained attention. The BV is a paper-and-pencil cancellation test that consists of 33 lines, each containing 24 figures made up of dots. The child is asked to mark all figures with 4 dots as fast and as accurately as possible. Outcome measures are the speed (mean line time) and accuracy (total number of omissions, commissions and corrections) (mean = 0; SD = 1). Test-retest reliability is high for speed ($r = 0.84$), but relatively small for accuracy ($r = 0.35$).

The validity of the BV is confirmed in lower speed and accuracy scores for children with attention problems compared with a control group.

The symbol-digit task is a subtest of the Wechsler Intelligence Scale for Children – Revised (WISC-R) used to measure automation in the visual channel. The child is asked to fill in symbols corresponding to certain forms or digits (mean = 10; SD = 3).

Three behavioural questionnaires were used in the diagnostic process: the Dutch versions of the Child Behaviour Checklist (CBCL) and Teacher Report Form (TRF) and the Disruptive Behaviour Disorders (DBD) rating scale. The CBCL and TRF measure general pathology and have demonstrated to be useful in detecting children with and without behaviour problems. With regard to ADHD, these questionnaires are excellent as screening instruments for the absence of ADHD. Broadband scales and subsequently nine narrow-band scales can be derived based on 113 ordinal-scaled items ($0$ = not true, $1$ = somewhat or sometimes true, and $2$ = very true or often true). Furthermore, the Dutch version of the DBD was completed by parents, which contained 42 items ($0$ = not true, $1$ = little true, $2$ = fairly true, and $3$ = very true). The DBD consists of four subscales, which obtain ratings of, respectively inattention, hyperactivity–impulsivity, oppositional defiant disorder and conduct disorder according to the DSM-VI criteria. The validity of the DBD is confirmed in positive correlations with externalizing subscales ($r = 0.47$) and negative correlations with internalizing subscales ($r = -0.34$) of the CBCL and TRF.

The clinical interview with parents is used to obtain information in a standardized way on the following domains: referral course, course of development, school, academic and present functioning. The diagnostic criteria of developmental disorders according to the DSM-IV are inquire, including ADHD and dyslexia.

2.4. Data analysis

One-way analysis of variance with post hoc Tukey tests for honestly significant differences (HSD) was used to compare the three groups in regard to reading measures at the pretest session. A General Linear Model (GLM) repeated measures with group (3 levels) as the between subject variable and time of measurement (2 levels) as the within-subject variable was used with separate runs for each dependent reading variable, attention, and automation measures. Task performance was analysed separately for reading, attention and automation measures because attention and automation variables were only available for the experimental and ADHD control group. GLM was performed for each reading variable to differentiate between the different aspects of reading. If statistical significant effects were found, post hoc comparisons were performed. Effect sizes were calculated using partial eta square ($\eta_{p}^{2}$), which estimates the degree of association in the sample.

3. Results

Table 2 shows test performances for the three groups at the pretest and posttest sessions. The experimental group and the two control groups differed with regard to all reading variables at the pretest session. The ADHD control group had average scores corresponding to their level of information processing and scored significantly higher than both the experimental and dyslexia control group on technical reading quotient ($F_{2,39} = 13.49; p < 0.000; \eta_{p}^{2} = 0.40$), non-existing word reading raw score ($F_{2,37} = 10.14; p < 0.000; \eta_{p}^{2} = 0.35$), and standard score ($F_{2,37} = 16.32; p < 0.000; \eta_{p}^{2} = 0.47$). The technical reading raw score of both control groups were higher than the experimental group ($F_{2,37} = 14.59; p < 0.000; \eta_{p}^{2} = 0.42$). According to the classification of Cohen (1988), we found medium to high effect sizes ($f$) for the reading differences between groups at the pretest session.

With regard to the technical reading test, for the raw score a significant group $\times$ time interaction effect, main effect for group and main effect for time were revealed (Table 2). Post hoc comparisons showed that MPH produced a larger improvement in reading in the experimental group than in the ADHD control group ($p = 0.046$) and also a trend for larger improvement than in the dyslexia group over time ($p = 0.057$). The control groups did not differ from each other. For the reading quotient, no difference was found between the pretest and posttest, but the experimental and dyslexia control group had a significant lower mean score over the pre and posttest session than the ADHD control group.

For non-existing word reading skills, a significant group $\times$ time interaction effect, a main effect for group and for time was shown for the raw score (Table 2). The experimental group showed more improvement than the ADHD control group ($p = 0.003$) and a trend for greater improvement compared with the dyslexia control group ($p = 0.094$). A main
effect for group was shown for the standard score, in which the experimental and dyslexia control group performed worse than the ADHD control group. We found generally medium effect sizes ($f^2$) for the group × time interaction effect on reading variables.\textsuperscript{41}

However, at the posttest session the experimental group still scored very low on technical as well as non-existing word reading tests.

The GLM repeated measures showed a significant main effect for time of measurement for the attention accuracy ($F_{(1,31)} = 37.50; p<0.000; \eta^2_g = 0.56$) as well as for the attention speed ($F_{(1,31)} = 22.82; p<0.000; \eta^2_g = 0.43$). MPH increased the performance on the sustained attention variables in both the experimental and ADHD control group. The effect sizes for MPH on attention were large.

The GLM repeated measures for automation in the visual channel revealed a main effect for time ($F_{(1,25)} = 25.90; p<0.000; \eta^2_g = 0.52$), with a large effect size.

### 4. Discussion

The present study evaluated the unblinded effect of MPH and showed an improvement in raw reading scores, which was significantly stronger in children with combined ADHD and dyslexia compared with ADHD control and dyslexia control groups. For both technical and non-existing word reading, more words were correctly read in a restricted time period. In contrast, the standardized scores of the technical (RQ) and non-existing word (SS) reading tests were unaffected by MPH.

Both standard scores were unable to differentiate between very low raw scores in children with dyslexia and may have masked an advance in reading. Thus, the standardized variables of the reading tests did not detect small improvements in children with reading problems due to a floor effect. In conclusion, MPH improved the number of correctly read words in children with ADHD and dyslexia. MPH may prevent further stagnation of the reading process, but cannot solve the reading problems. These present results are promising, because significant interaction effects of medium effect sizes were found despite a small power of 0.55 ($N = 43, f^2 = 0.15, \alpha = 0.05$). Therefore, future similar research with larger samples is very interesting and may show even larger effect sizes of MPH on reading in children with ADHD and comorbid dyslexia.

Reading performance in children with dyslexia did not improve automatically over time as was shown by the dyslexia control group. Therefore, MPH treatment had supplemental value in improving the reading performances in children with ADHD and dyslexia. However, MPH only seemed to improve reading if a child had problems with this skill. The ADHD control group, which had average reading scores at pretest and posttest sessions, almost did not show improvement by MPH compared with the experimental group.

MPH is supposed to improve the attention capacity of children with ADHD, as was confirmed in both the experimental group and the ADHD control group\textsuperscript{22,62} Therefore, reading improvement in the experimental group could not solely be attributed to an improved attention capacity as assumed by Balthazor et al.,\textsuperscript{26} since reading improvement in
the ADHD control group was significantly smaller than in the experimental group.

Automation, which is assumed to be a core deficit in children with dyslexia, was lower than average in both the experimental and ADHD control groups. Thus, the automation deficit was not specific to dyslexia. MPH improved automation in both groups. Therefore, the improvement in automation could not explain the reading advance in children with ADHD and dyslexia.

Alternative explanations for the reading advance, such as improved specific and/or general cognitive abilities due to MPH were supported in this study. MPH did not have a direct effect on the reading deficit, but an indirect effect by improving the limiting conditions of reading, and learning in general. This explanation is consistent with the present finding that reading performance is improved by MPH, but remained problematic. Other influences on reading improvement, such as school instruction, were considered to be minimal. Reading instruction in class as measured with the number of months children had been educated (didactic age), did not differ between the groups. However, the influence of additional tutoring intervention could not be excluded. Tutoring intervention for reading was absent in the ADHD control group, because this group had no reading problems. In the experimental and dyslexia control groups, tutoring intervention was considered to be a steady variable. Tutoring interventions had to be present for at least 6 months before diagnosing dyslexia as well as afterwards, according to the didactical resistance criteria for diagnosing dyslexia and the treatment plan for dyslexia. However, it is possible that the children in the experimental group were more susceptible to tutoring interventions due to the influence of MPH. Therefore, additional tutoring interventions need to be controlled in future research.

Several limitations of the present study need to be considered. First, children diagnosed with ADHD were only included if they had started with MPH treatment. This selection bias possibly limits the generalization of the present findings to the total population of children with ADHD and comorbid dyslexia. The present sample of children with ADHD and dyslexia may differ from the total population in the degree of experienced problems and the attitude of their parents towards MPH treatment. Nevertheless, the majority (66%) of children with ADHD and dyslexia in our clinic starts with MPH treatment and can therefore be considered typical of the total population. Second, the experimental and ADHD control group included different subtypes of ADHD. However, Barkley et al. indicated no differences in the effect of MPH in different ADHD subtypes and therefore this heterogeneity probably has not influenced the present results. The third possible limitation concerns the small number of participants in both control groups, which may have influenced the significance of the results. Nevertheless, an improvement of attention by MPH could be shown in spite of the small ADHD control group. Therefore, the failure of detecting reading improvement in both control groups is improbable primary due to the small samples. Future similar research should include larger control groups and include the theoretically best control group of children with ADHD and dyslexia without MPH treatment. However, this group of children is almost impossible to find. Fourth, the test interval length varied over subjects from 0.29 to 1.44 years due to practical limitations in the clinical field, but did not differ between the three groups. The present findings did not change by repeating the statistical analyses with test interval as a covariate. The group × time interaction effects on the raw reading scores remained significant and the effects were still of medium size. That implies that the variability in test intervals did not influence the present results. Furthermore, in the present study both the experimenter and participants were not blind for the medication condition, because the participants were selected from a clinical sample in which the patients’ care was the primary responsibility. This may have introduced subjective bias (placebo effect, observer bias, and experimenter’s bias) and therefore, future research should be double blind for the medication condition to prevent these biases.

A useful result for clinical practice is that in children with the frequently occurring combination of ADHD and dyslexia, MPH has a supplemental positive effect on reading performance in addition to improvement already shown in attention capacities. The present study showed that during the period that MPH is taken, reading performance improved. However, the reading level remained problematic and below average. Therefore, MPH is an aid to children with ADHD and dyslexia in the reading process and may prevent further stagnation in reading, but cannot cure the reading disorder. It can be expected that long-term effects may be extended by the combination of MPH with tutoring intervention. Future research comparing different interventions (none, MPH, tutoring intervention, MPH+tutoring intervention) will give a definite answer. Finally, the present findings indicate that the co-occurrence of ADHD and dyslexia is an indication for treatment with MPH as suggested by others.

References

60. Hendriksen JGM, Feron FJM, Vles JSH. Klinisch Ontwikkeling Interview [Clinical development interview]. Department of Psychiatry and Neuropsychology, Internal publication University Hospital Maastricht, 2000.