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ORIGINAL CONTRIBUTION

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Treatment of attention deficit hyperactivity disorder in children

Predictors of treatment outcome

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Abstract *Objective*: The present study investigated the predictive power of anxiety, IQ, severity of ADHD and parental depression on the outcome of treatment in children with ADHD. *Method*: Fifty children with ADHD (ages 8–12) were randomized to a 10-week treatment of methylphenidate or to a treatment of methylphenidate combined with multimodal behavior therapy. Prior to treatment predictors were assessed. Outcome was assessed separately for parents and teachers on a composite measure of inattentive, hyperactive, oppositional- and conduct disorder symptoms. *Results*: There was neither a significant difference between the two treatments at baseline nor did treatment condition predict outcome. Therefore the data were collapsed across the two treatments. A combination of anxiety and IQ predicted teacher-rated outcome, explaining 18% of the variance. Higher anxiety and higher IQ's indicated better treatment outcome. There were no significant predictors of the parent-rated outcome. *Conclusions*: This study showed a small but significant predictive effect of IQ and anxiety on treatment outcome in children with ADHD. *Clinical implications*: This study supports the idea that for the treatment of ADHD children with comorbid anxiety and higher IQ respond better to the two most used treatments for ADHD.

Key words attention-deficit hyperactivity disorder – children – predictor – anxiety – IQ – methylphenidate – behavior therapy

Introduction

Attention-deficit hyperactivity disorder [ADHD] is a pervasive childhood disorder. The most frequently used treatments for ADHD are stimulant and psychosocial treatments. Especially for psychosocial treatments, however, studies on prediction and moderation of treatment-response are virtually nonexistent [25]. In contrast, in other childhood psychopathological conditions, such as Oppositional Defiant Disorder (ODD) or Conduct Disorder (CD), several studies have been conducted on outcome prediction of psychosocial treatments [8].

The few outcome prediction studies on psychosocial treatments of ADHD available use data from the MTA study [22]. The MTA study is the largest treatment study to date, which compared the outcome of 4 treatment conditions: (1) medication, (2) intense behavior therapy, (3) combined treatment, consisting of medication and intense behavioral therapy treatment, and (4) community care. Results indicated that all 4 conditions showed significant reduction in

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ADHD and related symptoms. However, the medication and the combined treatment showed greater improvements in ADHD and related symptoms compared to the community care and intense behavior therapy alone. Surprisingly, the medication and the combined treatment did not differ significantly on any comparison.

In this study, four predictors for psychosocial treatment outcome are examined: anxiety, intelligence, severity of ADHD and parental depression. Most research to date has been aimed at the predictive value of the child's anxiety for psychosocial treatment outcome in the MTA study [16, 21, 23]. Also, one study examined the predictive value of intelligence, severity of ADHD and parental depression on psychosocial treatment outcome in the MTA study [25].

For all four predictors, anxiety, IQ, parental depression and severity of ADHD, psychosocial and methylphenidate studies are reviewed.

Anxiety

It has been speculated that comorbid anxiety may influence the outcome of treatment for ADHD [16, 23, see for review 12]. Data of the MTA study have shown that comorbid anxiety improved intense behavior therapy outcome [16, 21, 23], meaning that higher anxiety predicted a more positive treatment outcome.

In contrast, however, several methylphenidate studies have shown that comorbid anxiety (i.e. higher anxiety) worsens treatment outcome (e.g., [7, 12, 29, 36]). In the MTA study, however, the presence of anxiety disorders did not predict worse response to methylphenidate [21]. Owens et al. [25] further examined predictors of treatment response in the MTA study, using a categorical measure of "excellent response", rather than a continuous outcome measure, as used in earlier analyses of the MTA data [16, 21]. In that study, anxiety of the child neither predicted response to behavioral treatment nor to methylphenidate treatment. In sum, comorbid anxiety of the child improves behavior therapy outcome (e.g. [16, 21, 23]), but worsens outcome for methylphenidate treatment [7, 12, 29, 36].

IQ

Lower IQ has been suggested to predict worse treatment response to behavioral treatments, because children with lower IQ would be less able to learn new skills and therefore would benefit less from behavioral treatments [17]. To date, only one study has examined the predictive value of childhood intelligence on psychosocial treatment response in ADHD children [25]. Using data of the MTA study, it was shown that IQ in the presence of parental depressive symptoms and severity of childhood ADHD, was a predictor of response in the methylphenidate and combined treatment conditions; a lower IQ predicted worse treatment response. Secondary analyses showed that lower IQ-levels were more strongly related to a worse treatment response in the medication condition than in the conditions including psychosocial treatments.

The effects of IQ in methylphenidate studies have been mixed [7, 12, 36]. Buitelaar et al. [7], for example, found in children with strong methylphenidate response that lower IQ predicted worse response to medication treatment. In children with weaker methylphenidate response, however, IQ was no longer a significant predictor. In an extensive review of methylphenidate prediction studies, Gray and Kagan [12] concluded that intelligence bears little or no relation to methylphenidate responder status.

Severity of ADHD

Regarding psychosocial studies, only one study using MTA data is available on the predictive power of severity of ADHD [25]. In the combined condition of the MTA study, worse outcome has been reported for children displaying high levels of ADHD symptoms at baseline [25]. Studies on methylphenidate treatment have reported severity of the ADHD as predictor of treatment response, with higher levels of baseline ADHD predicting poorer outcome [12, 36].

Parental psychopathology

The influence of parental psychopathology on the outcome of treatment in ADHD has not received much research attention, although parental psychopathology may impact parents' ability to effectively implement behavior management techniques [8]. Owens et al. [25], using the MTA study data, found parental depression to be predictive of worse treatment outcome in the medication condition, but not in the psychosocial condition. Hoza et al. [15], using data of the MTA study, found a relation between maternal self-esteem and treatment outcome in all four MTA treatment conditions. Mothers with higher self-esteem showed better treatment outcome, which supports the idea that parental psychopathology is related to treatment outcome.

The present study examined the predictive power of parental depression, severity of ADHD, IQ and anxiety of the child for treatment outcome in medication naïve children aged 8–12 years old, in two treatments conditions: (1) methylphenidate treatment and (2) combined multimodal behavior therapy and

methylphenidate treatment. For both the methylphenidate and combined treatment, higher severity of ADHD, lower IQ and higher parental depressed mood were expected to worsen treatment outcome. Higher anxiety, however, was expected to worsen treatment outcome with methylphenidate treatment and improve outcome with combined treatment. Since informant agreement in the rating of ADHD has been low (e.g., [1, 33, 39]), parent and teacher ratings were analyzed separately.

Method

Participants

Participants were 50 children between the age of 8 and 12 years (M = 9.9, SD = 1.2). These children also participated in the treatment-outcome study of Van der Oord, Prins, Oosterlaan and Emmelkamp [38]. Children were referred for diagnosis and treatment of ADHD by school psychologists, paediatricians or general practitioners to five different child psychiatric outpatient clinics in the Netherlands. Inclusion criteria for participating in this study were: (1) a DSM-IV diagnosis of ADHD as established with the parent version of the Diagnostic Interview Schedule for Children (DISC-IV) [33] and (2) an estimated full scale IQ of 75 or above, based on a short version of the Wechsler Intelligence Scale for Children-Revised (WISC-R) [40]. In this study, using the short version of the WISC-R, 96% of the children had an IQ of 80 or higher. Exclusion criteria for this study were inadequate mastering of the Dutch language by the child or by both parents, and a history of methylphenidate use.

The ADHD, ODD and CD sections of the DISC-IV parent version [11, 33] were administered by a trained clinical child psychologist. The DISC-IV is a structured diagnostic interview that generates DSM-IV diagnoses. Adequate reliability and validity have been reported for precursors of the DISC-IV [11, 32]. Using the DISC-IV, 31 children met DSM-IV criteria for ADHD combined type, 16 met criteria for ADHD inattentive type and 3 children met criteria for the hyperactive/impulsive type. Twenty-three of these ADHD children showed comorbidity with ODD, and two of these children met criteria for an additional DSM-IV diagnosis of CD.

Procedure

Before inclusion in the study, parents gave written informed consent and children gave their verbal consent. A local medical ethics committee approved the study. Participants were randomly assigned to treatment with methylphenidate or combined treatment of methylphenidate and multimodal behavior therapy. The week before the beginning of the treatment, the pre-test was conducted: parents and teachers completed questionnaires and children were assessed at the outpatient clinic. Within a week following the last session of the multimodal behavioral treatment, approximately 11 weeks after the pre-test, participants in both treatment arms received the post-test.

Treatment

Methylphenidate treatment

A four-week, pseudo randomized multiple blind placebo controlled crossover medication design, as described by the MTA [13], was used for individual methylphenidate dose titration. The best dose was evaluated for 5 weeks (4 week titration, 1 week evaluation period), and then the optimal dose was subscribed for 5 weeks. In the titration trial 5, 10 and 20 mg of methylphenidate and placebo were administered in a pseudo random order twice daily at breakfast and at lunch. The highest dose never exceeded 0.9 mg per kg of the body weight. During these four weeks, the effects of methylphenidate and side-effects were monitored daily at school and at home by teachers and parents, respectively, using rating scales, measuring symptoms of ADHD, ODD, impairment and side-effects (see [13]). After these four weeks, five independent clinical raters, using a standardized manual (as described in [31]), blindly reviewed mean dose-response graphs, following which the child was classified as responder, placebo-responder or non-responder to methylphenidate. During this evaluation period of 1 week, children were medication free. By consensus each child's best dose was selected. Following the consensus procedure, a child psychiatrist prescribed the selected best dose (if not placebo) for the child for the remaining five weeks of the study.

Of the 45 titrated children (see Results section for drop-out rates), one child did not complete titration due to side effects, however, post-test scores of this participant were collected. Of the remaining 44 children, 25 (59%) were assigned to an individually, optimally titrated dose of methylphenidate, with an average individual dose of 20.8 mg/day (SD = 10.18). The remaining 19 children were classified as placebo responders. Placebo response may reflect a compression of ratings that is an artefact of rating methodology. Without objective measures, real placebo-responses and rating artefacts are difficult to differentiate (Pelham in [13]). Therefore, manualized instructions for psychiatrists included the option of

prescribing 5 mg twice daily for placebo-responders, in case of recurring ADHD symptoms during the medication-free week. Using this procedure, 8 children were prescribed 5 mg twice a day. During the remaining 5 weeks of methylphenidate treatment subjects were specifically instructed to remain on the assigned dose. However, in case severe symptoms or side effects emerged, the child psychiatrist was consulted and dose adjustments could be made. In 7 of the 44 titrated children (15%) the dose was changed from titration to post-test. In three children the dose was lowered, due to emerging side effects. In four children the dose was raised, because of re-emerging ADHD symptoms.

Combined multimodal behavior therapy and methylphenidate treatment

In addition to the methylphenidate treatment described above, children in the combined treatment condition received a manualized multimodal behavior therapy, which integrated family-based and school-based interventions with cognitive behavior therapy of the child. The multimodal behavior therapy started simultaneously with the methylphenidate treatment.

The parental behavioral therapy module consisted of 10 weekly sessions of 90 min group therapy for 4 or 5 parent couples. This parent training was based on the training developed by Barkley [3]: "Defiant children: a clinicians manual for parent training". The teacher-training module was based on the manual developed by Pelham [27]: "Attention deficit hyperactivity disorder, diagnosis, nature, etiology and treatment" and consisted of a brief two-hour workshop for the teacher of the participating child, in which other teacher-colleagues could participate. Finally, the child cognitive-behavior therapy module consisted of 10 weekly 75 min group sessions in which 4 or 5 children participated. Cognitive-behavioral techniques consisted of the children acquiring problem-solving techniques; the program used was adapted from Kendall and Braswell [18]. More detailed information on these treatment modules has been described in Van der Oord et al. [38].

Predictors

IQ: Revised Wechsler Intelligence Scale for Children (WISC-R)

Four subtests of the WISC-R were administered to assess intelligence. Subtests of this short version were: Vocabulary, Arithmetic, Block Design, and Picture Arrangement. The estimation of the IQ as obtained by these four subtests correlates between $r = .93$ and $r = .95$ with Full Scale IQ [14].

ADHD symptom severity: Disruptive Behavior Disorder Rating Scale (DBDRS)

The DBDRS [24, 26] was developed to obtain parent and teacher ratings of disruptive behavior disorder symptoms, based on the DSM-IV criteria. The DBDRS consists of 42 items and contains four subscales: Inattention, Hyperactivity/Impulsivity, ODD and CD. Parents and teachers rate the behavior of the child on a 4-point Likert scale ranging from 0 (not at all) to 3 (very much). The Dutch translation of the DBDRS has adequate reliability (Cronbach's alpha range = .88–.94) [24]. Two subscales were used for assessment of ADHD symptoms severity: Inattention (9 items) and Hyperactivity/Impulsivity (9 items). The Inattention and Hyperactivity/Impulsivity pre-test subscale scores were summed into one ADHD score. Higher scores on the DBDRS indicate more severe symptoms.

Trait anxiety: State Trait Anxiety Inventory for Children (STAIC)

For assessment of anxiety, the trait anxiety scale of the Dutch version of the State- Trait Anxiety Inventory for Children (STAIC) [2, 35] was used. This trait anxiety scale consists of 20 items. Items of the STAIC are rated by the child on a 3-point Likert scale ranging from 1 (almost never) to 2 (often). Reliability of this scale is high in a Dutch sample (Cronbach's alpha = .80) [2]. Higher scores indicate more severe anxiety symptoms.

Parental depression: Center for Epidemiologic Studies Depression Rating Scale (CES-D)

The CES-D was developed to assess depressive symptoms in the past week. The primary care-taker of the child rated their depressive symptoms on the CES-D. The CES-D consists of 20 items rated on a 4-point Likert scale ranging from 0 (*almost never*) to 3 (*most of the time or always*). Internal consistency (Cronbach's alpha .92) of the Dutch version of the CES-D is high [6]. Higher scores indicate more depressive symptoms.

Criterion

Following Sonuga-barke, Daley and Thompson [34], treatment outcome was measured using a composite score of disruptive symptoms. All four post-test subscale (Inattention, Hyperactivity/Impulsivity, ODD and CD) scores of the DBDRS (described above) were used for computation of this composite score. First, the four scale scores were z-transformed (based on data from the present sample) and then scores were averaged for parents and teachers separately.

This composite reduces multiple testing and increases the reliability of the outcome estimate. Cronbach's alpha for this composite score was high for both teacher (.83) and parent ratings (.80).

Statistical analyses

First, we tested the effectiveness of the two treatments with repeated measures ANOVAs. In these repeated measures ANOVAs the treatment outcome was the dependent variable, and the treatment condition (methylphenidate or combined treatment) was the between treatment variable (see also Van der Oord, Prins, Oosterlaan and Emmelkamp [38]). Further, to assess potential differential treatment response, on our newly constructed parent and teacher composite scores (the criterion), two separate linear regression analyses were conducted with the treatment condition as predictor and the composite score as the criterion. To assess associations between predictors and composite scores, Pearson correlations were computed.

To assess the predictive effect of anxiety, IQ, severity of ADHD, and parental depression on treatment outcome, two separate stepwise multiple linear regression analyses were performed. The first had the parental composite score as criterion and the second regression analyses had the teacher composite score as criterion. In both analyses, baseline trait anxiety, IQ, parent-or teacher rated ADHD symptom severity and parental depressed mood were entered as predictors. Since previous research is scarce and no specific predictions could be made about order of entry of the predictors, predictors were entered simultaneously in the regression model.

Results

Of the 50 children included in the study, 23 children were randomized to the methylphenidate treatment and 27 to the combined treatment condition. Five children dropped out, due to various reasons. One child refused to participate after randomization to the methylphenidate treatment condition. Further, one child did not show up at post-test and two parent couples dropped out, because of marital problems and inconvenient time of treatment, respectively. Criterion for treatment attendance in the combined treatment condition was attending at least 75% of all treatment sessions. One child was omitted from the analyses because this criterion was not met.

Differences between treatments

The repeated measure ANOVAs for treatment outcome differences showed a consistent pattern. On all measures significant improvements were found from pre-to post-test. Further, there were no significant time by treatment condition interactions. These analyses showed that both treatment conditions did not differ in their improvement from pre-to post-test. Also, all time by treatment condition effect sizes were small and there were no treatment differences in post-test doses of methylphenidate (see [38]).

Descriptives of the two composite scores and the four predictors are shown in Table 1. Univariate ANOVAs showed no significant differences between the two treatment conditions on any of the predictors or criterion variables (Table 1). Additionally, two linear regression analyses were conducted with treatment condition as predictor and the parent- and teacher composite scores, respectively, as criterion variables. In both analyses, treatment condition was no significant predictor of outcome. Since there were no treatment differences on any of the analyses, data were collapsed across the two treatments. Pearson correlations between baseline and dependent variables are displayed in Table 2.

The stepwise multiple regression analysis of the parent rated composite score revealed no significant

Table 1 Means (*M*), Standard Deviations (*SD*), and *F* statistics (*F*) for predictor and criterion variables

	Methylphenidate treatment (n = 21)		Methylphenidate + Multimodal behavioral treatment (n = 24)		
	M	*SD*	*M*	*SD*	*F*
IQ (WISC-R)	96.81	12.10	100.04	17.26	.51
Anxiety (STAIC)	33.19	5.70	32.87	6.77	.03
ADHD parent (DBDRS)	30.50	9.50	27.91	8.51	.91
ADHD teacher (DBDRS)	27.43	11.62	26.52	7.93	.09
Depressed mood (CES-D)	6.81	4.57	6.94	8.14	.00
Parent: disruptive symptoms composite	−.06	.83	−.03	.72	2.32
Teacher: disruptive symptoms composite	.19	.92	−.17	.63	.02

Note: WISC-R = Wechsler Intelligence scale for Children-Revised, STAIC = State Trait Anxiety Inventory for Children, DBDRS = Disruptive Behavior Disorder Rating Scale, CES-D = Center for Epidemiologic Studies-Depression
*$P \leq .05$, **$P \leq .01$

Table 2 Pearson correlations between predictor and criterion variables

	2. Anxiety	3. ADHD-Parent	4. ADHD-Teacher	5. Depressed mood	6. Parent: disruptive symptoms composite	7. Teacher: disruptive symptoms composite
1. IQ (WISC-R)	.02	−.19	−.09	.05	.01	−.30*
2. Anxiety (STAIC)		37*	−.34*	.14	.13	−.31*
3. ADHD-parent (DBDRS)			−.28	.33*	.18	−.16
4. ADHD-Teacher (DBDRS)				−.13	−.36*	.23
5. Depressed mood (CES-D)					.20	−.10
6. Parent: disruptive symptoms composite						−.19
7. Teacher: disruptive symptoms composite						

Note: WISC-R = Wechsler Intelligence scale for Children-Revised, STAIC = State Trait Anxiety Inventory for Children, DBDRS = Disruptive Behavior Disorder Rating Scale, CES-D = Center for Epidemiologic Studies-Depression
*$P \leq .05$, **$P \leq .01$

predictors. Both anxiety and IQ significantly predicted the teacher rated composite score and explained 18% of the variance ($R^2 = .18$, adjusted $R^2 = .14$, F (2, 39) = 4.22, $P = .02$). Anxiety alone accounted for 9.4% of the variance ($R^2 = .09$, adjusted $R^2 = .07$, F (1, 40) = 4.19, $P = .05$) and IQ for an additional 8.4% of the variance ($\Delta R^2 = .08$, F (1, 39) = 3.97, $P = .05$).

Inspection of Pearson correlation coefficients showed a negative association between anxiety and the teacher rated composite score, indicating that high anxiety was associated with low teacher composite scores, that is a better treatment outcome. Moreover, IQ showed a negative association, with high IQ being related to low teacher composite scores (i.e., better treatment outcome).

Additionally, it was examined whether the significant predictors interacted with treatment condition. None of the significant predictors showed a significant interaction with treatment condition. This supports the idea that predictors are identical for both treatments. Finally, it was examined whether the significant predictors interacted with baseline levels of ADHD symptoms. Both IQ and anxiety showed no significant interaction with baseline levels of ADHD symptoms. This supports the idea that both IQ and anxiety are associated with treatment outcome, regardless of baseline levels of ADHD.

Discussion

Especially for psychosocial treatment in children with ADHD, studies on the prediction of treatment outcome are virtually non-existent [25]. However, re-analyses of the MTA-study results have assessed predictors of psychosocial treatment outcome [16, 21, 23, 25]. The present study examined the predictive power of anxiety, IQ, severity of ADHD and parental depression for the outcome in children with ADHD of the two most widely used treatments for childhood ADHD: methylphenidate and a combination of methylphenidate and multimodal behavioral treatment. This study showed a small, but significant predictive effect of IQ and anxiety on treatment outcome in childhood ADHD. For both the methylphenidate and combined treatment predictors were identical. Baseline ADHD symptoms could not account for the predictive effect of IQ and anxiety for outcome. IQ and anxiety were unrelated, which underlines that both had a unique influence. Children with higher anxiety had a better treatment outcome, as was the case for children with higher IQ scores. Severity of the baseline ADHD symptoms and parental depressed mood were of no influence on treatment outcome.

Contrary to most methylphenidate studies, no adverse effect was found for comorbid anxiety on outcome as measured both in methylphenidate and combined treatment [12]. In contrast, the present study showed higher levels of IQ to be predictive of better treatment outcome. Most methylphenidate studies reporting the effects of anxiety, have used short term, fixed dosing procedures (e.g. [10, 29]), often using prediction models in which "change models" are used: the differential predictive effect of methylphenidate versus placebo. Our study, however, focused on the predictions of response to long-term optimally dosed methylphenidate treatment and did not employ a change models approach (e.g. [9, 36]). Similarly, in the MTA study, also long-term optimally dosed methylphenidate treatment was used, and no predictive effect of anxiety was reported for the medication only condition [16, 21]. However, in the MTA study, children with a comorbid diagnosis of anxiety responded better to the combined treatment of medication and behavior therapy [21, 23], and to behavior therapy alone.

In line with the MTA study, we found comorbid anxiety to improve treatment outcome, however, this improvement was found for both the methylphenidate and the combined treatment conditions. Differences between parents of anxious children with ADHD and parents of non-anxious children with ADHD may

have mediated or moderated treatment outcome. For example, several studies have shown more anxiety symptoms in the mothers of children with ADHD and comorbid anxiety compared to mothers of children with ADHD without comorbid anxiety [5, 28]. Also, parental over protectiveness was found to be related to comorbid child anxiety in children with ADHD [28]. It may be speculated that these anxious, over-protective parents of anxious children with ADHD were more inclined to comply to treatments and may have been better able to follow the treatment regimen than the parents of the non-anxious children with ADHD, resulting in better treatment outcome for the anxious children with ADHD for both the methylphenidate and combined treatment. As we, in our study, have not assessed parental anxiety symptoms and over protectiveness, this needs to be tested in future research.

Previous research has found anxiety to be a predictor of parent-rated treatment outcomes [21, 23], while other researchers [25] have reported no predictive effect of anxiety on parent- and teacher rated ADHD and ODD outcomes. In the present study, significant predictors were found for teachers' but not for parent rated outcome. Some suggest teacher's ratings to be the most accurate, but research is inconclusive [4, 20, 30].

In the present study, higher IQ-levels were a significant predictor of better treatment response. Other researchers have reported higher IQ-levels to be associated with better methylphenidate response (e.g., 7]), but only in strong methylphenidate responders. Owens et al. [25] also reported IQ to be a predictor of treatment response in both the methylphenidate as well as the methylphenidate and behavioral treatment conditions, but only in the presence of high baseline ADHD and parental depressive symptoms. In samples of antisocial children, low IQ has been suggested to worsen psychosocial treatment response, because children with lower IQs would be less able to learn new skills and therefore would benefit less from behavioral treatment [17]. Our supplementary analyses did not support the idea that the effect of IQ was related to the ability to learn new skills, as in both the methylphenidate and combined condition IQ was a significant predictor, and no significant interaction was found between treatment outcome and IQ. Due to our small sample size, possibly we were not able to detect differences. Alternatively, a third not measured variable related to IQ, for example compliance or social economical status, was related to the predictive effect of IQ.

Contrary to Owens et al. [25], we did not find parental depression and severity of ADHD symptoms to be predictive of treatment outcome. Possibly this was caused by the higher rate of parents with depressed mood in the sample studied by Owens et al. [25]. Inspection of the sample's mean depression score, however, shows that similar to our study, mothers of children in the Owens et al. study were not severely depressed. Similarly, with regard to severity of the disorder, children in our sample may have displayed less severe levels of ADHD than the children participating in the MTA study. However, the children participating in this study displayed severe baseline levels of ADHD symptoms (see [38]) and all children fulfilled DSM-IV criteria for ADHD. Further, the MTA study included the combined subtype of ADHD only, while our study also included children of the ADHD-inattentive subtype. Buitelaar et al. [7], however, consistent with our study, also did not find severity of the disorder, as rated by parents and teachers, to be predictive of methylphenidate treatment outcome. In that study, severity of the disorder was only found to be predictive of treatment outcome as measured by an independent observer's rating during a lab test.

Limitations

We acknowledge that our study incorporated a limited set of predictors. Examination of other predictors, such as parenting style, comorbid ODD/CD, compliance and receiving public assistance, would also be important. Others have found high levels of maternal ADHD to be a predictor of worse response to psychosocial treatment in preschoolers with ADHD [34]. It is suggested that parental ADHD interferes with the treatment of the child's ADHD, as parents may have difficulty adhering to a treatment plan [41], which may apply to both psychosocial and methylphenidate treatment. Due to power limitations, however, we limited our analyses to a selection of the most important and empirically based predictors. Further, the amount of variance accounted for by IQ and anxiety was small, never exceeding 10%. It is therefore unlikely that any single variable will be an effective predictor of a child's individual treatment outcome [12]. A further limitation of the present study is the small sample size. Due to the small sample size, we possibly did not find a treatment condition effect for the predictors, as for the inclusion of an interaction term in a regression analyses often a larger sample is needed. Another limitation of our study is the open label nature of the study. Participants and researchers were not blind to the treatment condition the child was given, possibly influencing post-test outcome scores. However, regardless of the open-label nature of the study no treatment differences were found. Our study focused on predictors for treatment outcome, regardless of how they might have been related to outcome. Future research should explore mechanisms

by which predictors exert their influence on treatment outcome [19].

Finally, a non-measured variable may be related to both anxiety and intelligence. For example, comorbid ODD/CD may be related to both anxiety and intelligence. Jensen et al. [16], however, found anxiety to improve treatment outcome of behavioral treatments regardless of the presence of ODD/CD. Also, compliance to treatment may be an underlying variable causing both children with higher intelligence and higher levels of anxiety to respond better to treatment. Children with higher intelligence more easily may understand the necessity to comply with the medication and behavioral treatment. Moreover, due to their anxious symptoms, children with higher levels of anxiety may be more inclined to comply with treatment. Thiruchelvam, Charach and Schachar [37], however, did not find an association between IQ, anxiety and long-term compliance to stimulant medication. Clearly, more research on the interrelations of these variables is warranted.

All in all, this study shows that children with higher IQ and higher levels of anxiety are more likely to respond better to methylphenidate and to multimodal behavioral treatment combined with methylphenidate treatment as rated by teachers, but not by parents.

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