Critical Review:

Does pharmacological treatment have an effect on language performance in school-aged children with ADHD?

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This critical review examines the effect of pharmacological treatment on the language performance of school-aged children with attention deficit hyperactivity disorder (ADHD) in six studies. Study designs included: three non-randomized clinical trials, two within-groups clinical trials and one within-groups crossover study. Overall, the research provides equivocal evidence that pharmacological treatment has an effect on language performance of school-aged children with ADHD.

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that is characterized by inattentive and/or hyperactive/impulsive behaviour, with impairment that is observed across at least two settings (American Psychiatric Association, 2000). According to previous epidemiological studies, prevalence rates of ADHD in Canada, the United States, and the United Kingdom are 3-9%, 6-16%, and 2-5%, respectively (Breton et al., 1999; Froehlich et al., 2007; Ford, Goodman, & Meltzer, 2003). It has been well established that school-aged children with a diagnosis of ADHD endure significant academic challenges that are difficult to overcome (Loe and Feldman, 2007; Rapport, Scanlan, & Denney, 1999). In particular, some of the core deficits that have been suggested to be associated with ADHD include difficulties with planning, organization, self-regulation, monitoring, and higher-order processing skills, all of which may lead to an increased risk for language impairment in this population (Lorch, Berthiaume, Milich, & van den Broek, 2007; Francis, Fine, & Tannock, 2001).

Historically, stimulant medication has been reported to be effective in improving attention, reducing classroom disruptions, increasing on-task behaviour and improving basic academic performance (DuPaul & Eckert, 1997; Loe & Feldman, 2007). However, few studies exist that explore the effect of pharmacological intervention on language performance in school-aged children with ADHD, and even fewer still explore the effect of medication on children with ADHD and comorbid language impairment (LI). The following review will appraise the current research pertaining to the effect of medication on language performance in children with ADHD and attempt to determine the impact of pharmacological intervention on language performance in those children with ADHD who have also been identified as having a language impairment.

Objectives

The objective of this article is to critically evaluate existing literature regarding the use of pharmacological intervention in children with ADHD, and specifically, its effect on language performance.

Methods

Search Strategy

Computerized databases, including PubMed, CINAHL, and PsycINFO were searched using the following search strategy:

> ((adhd) OR (attention deficit hyperactivity disorder) AND (medication OR pharmacolog*) AND (language OR story OR retell OR lexical OR grammar OR morpholog* OR synta*) AND (treatment OR intervention) AND (children)).

Selection Criteria

Studies that were selected for inclusion in this critical evaluation were required to investigate the effect of any type of pharmacological intervention on language performance in children with ADHD between the ages of 5 and 15 years. Outcome measures were limited only by their ability to measure skills associated with language use or comprehension.

Data Collection

Results of the literature search based on the selection criteria yielded the following types of articles: within-groups crossover trial (1), non-randomized clinical trial (3), and within-groups clinical trial (2).

Results

Within-groups crossover trial # 1. A study by Francis, Fine, and Tannock (2001) examined the effects of stimulant medication on story grammar, comprehension, and errors in the narratives of 7-12 year old children with ADHD who either had (ADHD; n=27) or did not have comorbid LI (ADHD+LI; n=23). In order to investigate an effect of dosage, as well as overall drug effect, the children within the two groups received two different doses (10 mg and 20 mg) of methylphenidate (MPH) and placebo over 4 testing sessions (1st session was a practice session). Each child was randomly assigned to the order of administration of medication or placebo.

During the experimental task, children were aurally presented an audio taped story while they viewed a wordless picture book. After the audio presentation, children were asked to retell the story and answer comprehension questions; their responses were recorded by an experimenter who was blinded to the medication conditions and coded in terms of story grammar (*structural and content relationships that exist within stories that give them narrative shape)*, length (*assessed using communication units*), retelling errors, and story comprehension (*assessed by five factual and five inferential questions based on the story*) (Francis et al., 2001).

Using appropriate repeated measures analysis of variance for each story grammar element, each type of story error, and the comprehension questions with between subjects variables, Francis et al. found that when both ADHD and ADHD + LI groups were analyzed together, MPH had an overall effect on children's recall of characters' internal responses ($n2$ = 0.09) and attempts ($n2$ = 0.07), which are said to tap internal emotional states and actions taken by characters in the stories. No interaction of drug treatment was found between ADHD and ADHD + LI groups. No significant difference was found between the effect of low and high doses for internal responses. However, only high dose MPH was found to have a significant positive effect on performance for attempts when compared to placebo, while low dose was not significantly different than either placebo or high dose MPH.

Overall, this study was well-designed and appropriate to the question being addressed. This study provides compelling evidence that MPH treatment increases the ability of children with ADHD to recognize and/or express explicitly internal responses and attempts during story recall regardless of whether they have a comorbid language impairment.

Non-randomized clinical trial # 1. In 2008, Semrud-Clikeman, Pliszka and Liotti examined the effects of stimulant medication history in children (9-15 years old) with ADHD on a variety of tasks including verbal working memory. For the purposes of the present review, the verbal working memory tasks employed were two subtests from the *Clinical Evaluation of Language Fundamentals 3 (CELF-3)* (Semel, Wiig, & Secord, 1995) commonly used to assess expressive and receptive language (formulated sentences; concepts and following directions). Four different groups were evaluated while unmedicated: children with ADHD who have a history of medication treatment (ADHD/Rx), children with ADHD who are treatment naïve (ADHD/TN), children with learning disabilities (LD) and a normal control group. All children were diagnosed with ADHD prior to the study, and children in the ADHD/Rx group were required to have previously been on stimulant medication (amphetamine or methylphenidate prescribed by their physician) for at least one year. Each child was withdrawn from their medication treatment at least 24 hours before testing, which was completed within a single session.

Results of the appropriate statistical multivariate analysis of variance (MANOVA) tests found that children with a treatment history of stimulant medication performed significantly better than the ADHD/TN and LD groups, while the ADHD/Rx and control groups did not differ on the two language subtests from the CELF-3. The researchers argue that stimulant medication treatment has a positive effect on language tasks involving verbal working memory and these gains persist even after the medication has been discontinued. Although the measures employed are not commonly used to assess working memory, the results do suggest that children with ADHD without a history of medication may perform more poorly on standard language measures. Nevertheless, only two subtests of language were employed, which may be insufficient to correctly estimate language abilities.

Overall, the current study was well designed, appropriate to the current question, and the results of the two subtests provide fairly compelling evidence that stimulant medication treatment has a positive effect on the language abilities of children with ADHD even after the medication has been discontinued.

Non-randomized clinical trial # 2. In 2009, DeJong et al. investigated atomoxetine, a non-stimulant alternative treatment to MPH, and its effects on lexical decision in children with ADHD aged 8-12 years. While not specific to the question addressed by the current review, the study also measured executive functioning. The study included 4 groups: children with ADHD, children

with reading disorder (RD), children with ADHD and RD, and normal controls. Children in the ADHD, ADHD + RD and RD groups were randomized as to whether they received either atomoxetine treatment or placebo first and each treatment lasted 28 days and was followed by a washout period of 14 days.

The lexical decision task required children to discriminate between valid words and pseudowords that were presented on a computer screen and their performance was measured by accuracy and mean reaction time (MRT). Appropriate statistical analyses (ANOVAs) failed to find any significant effects of atomoxetine treatment relative to that of the placebo condition on lexical decision, indicating that accuracy and speed of lexical decision were not influenced by atomoxetine.

One limitation to the current study is that the measures employed were necessarily influenced by the children's reading ability, as participants were required to make decisions based on visually-presented words. Another limitation is that lexical decision is not a commonly used measure of language performance in the school-aged population. Based on the above limitations, the current study provides equivocal evidence on the impact of non non-stimulant medication (specifically atomoxetine) on language performance in children with ADHD.

Non-randomized clinical trial # 3. Zoega et al. (2012) evaluated the effect of starting times of stimulant medication treatment on academic performance in children with ADHD. This retrospective cohort study compared children's performance on nationally coordinated standardized assessments of mathematics and language arts taken in grade four (9-year-olds) and in grade seven (12-year-olds) by linking data from the Icelandic Medicines Registry and the Database of National Scholastic Examinations. The difference in performance on the language arts assessment was the measure of interest for the purposes of the current review. Children with ADHD were investigated based on the length of time between their fourth grade assessment and the beginning of stimulant medication treatment and the changes in their performance on the standardized tests. The authors assessed this difference by grouping the children as follows: children with ADHD beginning stimulant medication ≤12 months (n=130), 13-24 months (n=106), and 25-36 (n=81) months after fourth-grade testing, and these groups were compared to the nonmedicated children (n=12588), resulting in four overall groups.

Drugs that were investigated in the study consisted of amphetamine, methylphenidate and atomoxetine, each of which included ADHD as their main indication. However, since the Icelandic Medicines Registry does not hold information on the indication for drug treatment, it was "assumed" by the investigators that "essentially all medicated children fulfilled the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for ADHD" (Zoega et al., 2012). This assumption was deemed by the authors to be reasonable based on the fact that in Iceland, a diagnosis of ADHD must be verified by a pediatric, psychiatric or neurologic specialist for reimbursement (Zoega et al., 2012).

The study conducted (statistically appropriate) analyses using risk ratios (RR), which are commonly used in cohort studies (Viera, 2008), in order to assess the probability of decline in test performance based on the timing of treatment start between examinations. Results found that the estimated effect of later treatment start (>12 months following fourth-grade testing) on decline in language arts was elevated slightly for boys, but showed a slight inverse effect in girls. However, The authors conceded that adjusted effect estimates did not differ much from crude estimates and indicated weak associations. Another limitation to the current study is that the measures employed cannot be sufficiently verified on their appropriateness to the question being addressed by the current review, as no detail was given on the content of the standardized language arts assessment.

Overall, this study presents equivocal evidence of the impact of stimulant medication treatment starting times on language performance in children with ADHD.

Within-groups clinical trial # 1. Derefinko, Bailey, Milich, Lorch, and Riley (2009) investigated the effects of stimulant drug treatment in children with ADHD compared to placebo during an online narrative story telling task. The study took place over two sessions and included two groups of children between 9 and 14 years of age: those who had a diagnosis of ADHD and were currently being treated with psychostimulant medication (n=17), and a comparison group (n=25) that consisted of children who did not have a diagnosis of ADHD. The psychostimulant medications included in the study were methylphenidate hydrochloride, amphetamine/ dextroamphetamine, methylphenidate transdermal system, and dexmethylphenidate hydrochloride. The groups did not differ significantly on variables such as age, gender, race and parental education level. The children in the ADHD group were randomly assigned as to whether they received the placebo on the first or second testing day, as testing was completed over two sessions that occurred at least one week apart. During placebo sessions, children were

required to have been off their regular medication for 24 hours before testing, as a result, neither the parent or child were blinded as to when the placebo was administered. Nevertheless, the children were told that the placebo pill was being studied for research purposes. Children in each treatment condition were asked to narrate a different wordless picture book for each session and were assessed on story structure based on goal-attempt-outcome sequences.

Although no omnibus MANOVA was reported, t-tests revealed that the control group produced significantly more instances of the positive outcome of the story, completion of the characters' overall goal, and specific attempts linked to the goal than the children with ADHD while on placebo. When compared to placebo, children with ADHD included more clauses in their narrations while on medication. However, no significant effect was found for stimulant medication on outcomes related to comprehension, including goal-based story events.

The authors argue that the results of this study provide evidence that stimulant medication alone is not adequate in reducing deficits of story comprehension in children with ADHD. However, based on the previous experiment, it may be that the 24-hour washout period in the present study was insufficient to negate effects of the regular medication. In addition, inappropriate statistical analyses (t-tests) were used to report effects of three conditions on several different measures. Overall, the current study provides suggestive evidence that stimulant medication alone is not adequate to improve story comprehension in children with ADHD.

Within-groups clinical trial # 2. Subsequent to the above study, Bailey, Derefinko, Milich, Lorch, and Metze (2011) investigated whether stimulant medication improved the story recall of children with ADHD relative to placebo. The study included the same participants that were involved in the Derefinko et al. (2009) study, followed the same study design and investigated the same psychostimulant medications. Bailey et al. (2011) measured which group showed better recall as story events increased in thematic importance, and when events are part of the causal chain involved in tying events together. In addition, Bailey et al. (2011) examined the coherence of the children's free recalls. All measures were coded by experimenters who were blinded to group status and study hypothesis, and inter-rater reliability between coders was determined as kappa = 0.93.

Children in each condition were assessed on their story recall over two sessions where a different story was used for each session. Appropriate statistical analyses (ANOVAs) using the mean differences of testing sessions revealed that the overall number of story events recalled was higher for the stimulant medication condition, however, stimulant medication did not significantly interact with importance level, or causal chain status, and did not influence coherence ratings. Based on these results, the authors assert that although children with ADHD who received stimulant medication produced more overall story events than their placebo peers, but they did not perform better in recalling information that was central to the stories.

A relative strength for the current study was that the authors averaged the children's performance over two separate testing sessions (and on two different stories), using the means in the analyses, which may increase the reliability of the results of the experiment. Overall, the study was well-designed and appropriate for the objectives of the current review and provides compelling evidence that stimulant medication alone will not eliminate deficits of story comprehension in children with ADHD.

Discussion

This review examined studies related to the use of pharmacological intervention and its effects on the language performance of children with ADHD. Overall, there was equivocal evidence indicating that further investigation is required in order to disambiguate the current state of the literature.

There are several challenges that are inherent in studying the effects of medication treatment. One such challenge is determining the appropriate length of time required for proper washout of medication to ensure that residual effects of prior pharmacological treatment do not carry-over into non-medicated or placebo testing sessions in within-groups designs. For example, the study by DeJong et al. (2009) included a 14-day washout period, whereas the Derefinko et al. (2009) study employed a 24-hour washout period. Based on the results of the Semrud-Clikeman et al. study (2008), who found that stimulant medication has a positive effect on several measures (including language measures) after children have been withdrawn from their medication for at least 24 hours, the 24-hour washout period in the Derefinko et al. (2009) study may not have been sufficient to negate the effect of prior medication treatment. Therefore, caution must be made while interpreting the differences in performance between medicated and unmedicated sessions in within-groups study designs, as the appropriateness of washout period length must be considered.

Another potential challenge in this type of study is that since a specific population is being evaluated (children with ADHD), it is not possible to conduct a fully-randomized control trial. Despite this apparent limitation, some of the studies in the current review employed a within-groups control trial design and although the children in these studies were not randomly selected in order to make up the ADHD groups, children within the ADHD groups were randomized as to which treatment condition they were tested on first. It can be argued that this type of study design would allow for the highest level of evidence possible for investigating differences in such a specific population *and* allow comparisons to be made to typically developing children, and may be the most appropriate design for the current review.

Based on the state of the current literature, there is no strong evidence that medication has an impact on the language performance of children with ADHD, although, there is some suggestive evidence that pharmacological intervention may have a positive effect which raises the need for further research. In addition to the need for further studies, the evidence in the current review must be interpreted with caution as there are limitations that should be considered. For example, it has been established that stimulant medication is effective in improving attention, reducing classroom disruptions, increasing on-task behaviour and improving basic academic performance (DuPaul & Eckert, 1997; Loe & Feldman, 2007), therefore, any effect on language performance could be the result of a more domain-general improvement such as an increase in attention or on-task behaviour. Another limitation is the fact that language was not comprehensively sampled in any of the studies included in this review, which makes it difficult to confidently evaluate changes in the language abilities of these children.

Conclusion

Based on the research evaluated within this critical review, the evidence concerning the impact of pharmacological treatment on language performance in school-aged children with ADHD is equivocal, indicating a need for further research.

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