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Effects of Methylphenidate on Complex Cognitive Processing in Attention-Deficit Hyperactivity Disorder

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A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfilment of the requirements of the degree of Doctor of Philosophy.

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Abstract

Three experiments investigated the hypothesis that high doses of methylphenidate (MPH) are particularly effective in enabling boys with Attention-Deficit Hyperactivity Disorder (ADHD) to regulate the allocation of effort and persistence under high information processing demands. In Experiment 1, the performance of boys with ADHD, ages 7 to 13, was investigated on placebo and three dosages of MPH, on a visual - memory search (VMS) task across a wide range of processing loads. Accuracy increased with dosage in a linear fashion. Findings on reaction times (RTs) revealed, however, that MPH dosage had a differential effect depending on processing load. All doses of MPH improved accuracy on low loads without a concomitant increase in processing times. When both processing load and MPH dosage were high, however, the ADHD boys shifted to a more cautious, time consuming strategy, apparently in order to achieve continuing gains in accuracy. Experiment 2 compared the performance of ADHD and control boys on the VMS. It established that the ADHD group had difficulty meeting the processing demands of the VMS across all of the information loads studied, as revealed by higher error rates and slower RTs. The ADHD-control comparison also established that the effects of high doses of MPH at high loads in Experiment 1 constituted a further slowing of the ADHD boys' already slow RTs. A third, normal developmental study of boys ages 7 to 13 showed that both error rates and RTs on the VMS task decreased with age. This study also revealed considerable similarity between the performance patterns of ADHD boys and those of younger control boys on the VMS.

Résumé

Trois expériences ont exploré l'hypothèse que de fortes doses de méthylphénidate (MPH) ont un effet particulièrement facilitant pour permettre aux garçons atteints d'un Trouble Déficit de l'Attention / Hyperactivité (TDAH) d'allouer et de soutenir l'effort dans les situations où la charge de traitement de l'information est élevée. En premier lieu, la performance de garçons entre 7 et 13 ans atteints d'un TDAH fut examinée à l'aide d'une tâche de repérage visuel de cibles mémorisées (RVM) variant la charge d'information à traiter; les garçons étaient répartis en quatre conditions, soit trois doses de MPH et un groupe placebo. La précision des réponses s'avéra augmenter linéairement avec la dose. L'étude du temps de réaction (TR) révéla cependant que la dose de MPH avait un effet différentiel selon la quantité d'information à traiter. Toutes les doses de MPH améliorèrent la précision dans les conditions à charge légère sans que le temps de traitement de l'information augmente. Toutefois, lorsque la charge à traiter et que la dose de MPH étaient toutes deux élevées, les garçons atteints d'un TDAH devenaient plus prudents et ralentissaient leur stratégie, en apparence afin de privilégier la précision. La deuxième étude compara la performance des garçons atteints d'un TDAH avec celle d'un groupe contrôle sur la tâche de RVM. Des taux d'erreur élevés et des TR moindres indiquèrent que le groupe TDAH éprouvait de la difficulté à traiter l'information de la tâche RVM, quelque soit la charge d'information impliquée. La comparaison des groupes TDAH et contrôle révéla également que dans la première expérience, lorsque la charge d'information était lourde, une dose élevée de MPH avait pour effet d'augmenter le TR déjà lent du groupe TDAH. Finalement, une troisième étude se pencha sur le

développement des garçons normaux entre 7 et 13 ans. Les résultats montrèrent d'une part que le taux d'erreur et le TR sur la tâche RVM diminuait avec l'âge. D'autre part, d'importantes données similaires entre la performance des garçons atteints d'un TDAH et celle des garçons les plus jeunes du groupe contrôle furent mises en évidence.

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#### Manuscripts and Authorship\*

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## Statement of Authorship

The three studies reported here have been accepted for publication in <u>The Journal</u> of <u>Abnormal Psychology</u>, with Dr. V. I. Douglas, and Dr. R. G. Barr as co-authors. Dr. Douglas, as my thesis supervisor, maintained an advisory role throughout, providing guidance in the design of the studies, the analysis of the data, and the interpretation of the results. She also provided me with feedback and guidance in the writing of the text. Dr. Barr participated in the clinical aspects of the study, contributing his expertise to our interdisciplinary diagnostic team, prescribing medications, and providing medical supervision and follow up to the children in the studies.

The text also reflects suggestions made by anonymous reviewers for <u>The Journal</u> of <u>Abnormal Psychology</u>.

### Statement of Original Contributions

Experiment 1 was the first study to demonstrate, within the same task and within the same statistical analysis, that the effect of dosage of stimulant medication on the time children with ADHD allocate to cognitive processing depends on information load. This was achieved by restructuring a well known information processing task, the Sternberg (1969) memory search paradigm. Although the memory load remained in the low range traditionally used in studies with the Sternberg task, the visual search component was extended to include extremely heavy loads. Thus, the new visual-memory search (VMS) task made it possible to use a wide range of levels of cognitive load, while maintaining a consistent task format. In addition, since heavy loads were presented in a visual search format, it was possible to explore how children with ADHD dealt with organizing and maintaining attention on a complex task, without overtaxing their memory ability with a large information load.

Experiment 2 made it possible to compare the performance of children with ADHD to that of controls across a wide range of information loads, using the same task as in the medication study. In addition, Experiment 2 provided further context for understanding the pattern of medication effects in Experiment 1. The use of the same task in the comparison study made it possible to demonstrate the unique finding that high MPH doses improved error rates while slowing the performance of children with ADHD on a task on which they were already slower than controls.

Experiment 3 provided a unique contribution in showing the pattern of normal developmental changes on the newly developed VMS task. In addition, the developmental

data showed similarities between the performance of children with ADHD and that of young children on the VMS task, in that both groups showed high error rates and slow and variable RTs on all loads of the task.

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#### Introduction

Attention - deficit / hyperactivity disorder (ADHD) is characterized by poor attentional ability, impulsivity, and high activity level. According to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 1994) it occurs in 3 to 5 % of school aged children, making it the most common behavioral disorder of childhood (Shaywitz & Shaywitz, 1988; Swanson, Shea, McBurnett, Potkin, Fiore & Crinella, 1990). Some epidemiological studies suggest that the prevalence is higher, with rates between 3 and 10 % in the general population (Baumgaertel, Wolraich, & Dietrich, 1995; Leung, Luk, Ho & Taylor, 1996; Wolraich, Hannah, Pinnock, Baumgaertel, & Brown, 1996). Canadian researchers, using data from the Ontario Child Health Study, report a prevalence of 9.0 % in boys and 3.3 % in girls in the general population (Szatmari, Offord & Boyle, 1989). It is estimated that children with ADHD account for half or more of the referrals for children's mental health services (Cantwell, 1996; Popper, 1988; Shaywitz & Shaywitz, 1991).

The most widely used treatment for children with ADHD is stimulant medication (Barkley, 1990). Stimulants have been found to improve performance on many cognitive tasks, and to improve academic functioning and compliance in the classroom (Douglas, Barr, Amin, O'Neill & Britton, 1988; Douglas, Barr, Desilets, & Sherman, 1995; Douglas, Barr, O'Neill & Britton, 1986; DuPaul & Rapport, 1993; Evans, Gualtieri & Amara, 1986; Henker & Whalen, 1989; Michael, Klorman, Salzman, Borgstedt & Danier, 1981; Rapport, Denney, DuPaul, & Gardner, 1994; Rapport & Kelly, 1991; Rapport, Quinn, DuPaul, Quinn & Kelly, 1989; Tannock, Schachar, Carr, Chajzyk & Logan, 1989). The medications have also been found to reduce negative social interactions, and improve peer status (Hinshaw, Henker, Whalen, & Erhardt, 1989; Whalen, Henker, Buhrmester, & Hinshaw, 1989; Whalen, Henker, Swanson, & Granger, 1987). Safer, Zito & Fine (1996) report a 2.5 % increase in methylphenidate use in the U.S. between 1990 and 1995, so that approximately 2.8 % of children, or 1.5 million, between the ages of 5 and 18 were receiving the medication in 1995.

Since the 1970s, research and theory on this group of children has shifted from focusing on high activity levels, to placing at least equal emphasis on cognitive deficits. In 1968, the DSM-II (American Psychiatric Association) listed the disorder as "Hyperkinetic Reaction of Childhood," and emphasized the children's excessive activity level. A number of researchers, however, found that children identified as hyperactive had difficulty with a variety of cognitive tasks. More specifically, they displayed an impulsive cognitive style (Campbell, Douglas, & Morgenstern, 1971; Cohen, Weiss, & Minde, 1972), and had difficulty sustaining attention (Sykes, Douglas, & Morgenstern, 1973; Sykes, Douglas, Weiss, & Minde, 1971). Douglas (1972) theorized that difficulties with attention and impulsivity might be as important as high activity levels in leading to the problems shown by hyperactive children. As a result of this shift in thinking, the American Psychiatric Association changed the diagnostic label to Attention Deficit Disorder (ADD) in the DSM-III (1980), with the diagnostic criteria emphasizing the cognitive symptoms of inattentiveness and impulsivity, as well as hyperactivity.

The DSM-III also recognized the possibility that some children might display only symptoms of poor attention, without showing motor over-activity, by listing two sub-

types of ADD, ADD-H (with hyperactivity) and ADD (without hyperactivity). The DSM-III-Revised (APA, 1987), however, de-emphasized this distinction, since it was judged that there was insufficient research at that time to support the sub-types. Thus, the DSM-III-R included one main category, Attention-Deficit Hyperactivity Disorder, and gave equal emphasis to symptoms of attention, impulsivity and hyperactivity. The DSM-III-R also listed Undifferentiated Attention - Deficit Disorder, a category which the authors suggested might include some of the children who had previously been diagnosed as ADD without hyperactivity, but they cautioned that this category required further study. However, more recent research suggests the validity of somewhat different subtypes of ADHD. The new sub-typing is based mainly on factor analyses of symptom ratings of children with ADHD which yielded two factors, inattention-disorganization and hyperactivity- impulsivity (Lahey, Applegate, McBurnett & Beiderman, 1994; Lahey, Pelham, Schaughency & Atkins, 1988; McBurnett, Lahey, & Pfiffner, 1993). As a result of these developments, the current version of the manual, DSM-IV (APA, 1994) describes a single disorder, ADHD, with three subtypes: predominantly inattentive, predominantly hyperactive - impulsive, and a third, combined category, in which the child has symptoms from both clusters.

Current researchers also recognize that co-morbid diagnoses frequently occur with ADHD. Between 50 % and 80 % of children with ADHD also meet diagnostic criteria for other disorders (Biederman, Newcorn, & Sprich, 1991; Jensen, Martin, & Cantwell, 1997). The most frequent co-morbid diagnoses are the other childhood disruptive behaviour disorders, oppositional defiant disorder and conduct disorder (August, Realmuto, MacDonald & Nugent, 1996; Biederman, Faraone, Milberger, & Jetton, 1996; Newcorn & Halperin, 1994; Jensen et al., 1997). Other commonly reported co-morbid diagnoses include specific learning disabilities, anxiety disorders and mood disorders (August et al., 1996; Biederman et al., 1991; Biederman, Faraone, Mick, & Moore, 1996; Hinshaw, 1992; Jensen et al., 1997; Pliszka, 1992; Russo & Biedel, 1994; Semrud-Clikeman, Biederman, Sprich-Buckminster, & Lehman, 1992). Thus, another task for researchers on ADHD is to distinguish the cognitive effects associated with ADHD from those associated with the presence of co-morbid disorders. In addition, the task of understanding MPH effects on cognitive processing is complicated by evidence that the presence of co - morbid symptoms, such as anxiety, may reduce the efficiency of the medication in ameliorating behavioral and cognitive difficulties (DuPaul, Barkley, & McMurray, 1994; Matier, Halperin, Sharma, Newcorn, & Sathaye, 1992; Tannock, Ickowicz, & Schachar, 1995).

Although deficits in cognitive processing are now considered to be central to the diagnosis of ADHD, debate continues over precisely which underlying cognitive problems are responsible for the pervasive pattern of the difficulties observed in the children. Children with ADHD have been shown to have greater difficulty than controls on a variety of cognitive tasks, including vigilance tasks (Chee, Logan, Schachar & Lindsay, 1989; Corkum & Siegal, 1993; 1995; Losier, McGrath & Klein, 1996; O'Dougherty, Neuchterlein & Drew, 1984; Siedal & Joschko, 1989; Sykes et al., 1973; Sykes et al., 1971), paired associate or word list learning tasks (Borcherding, Thompson, Kruesi, Bartko, Rapoport & Weingartner, 1988; Douglas & Benezra, 1990; O'Neill & Douglas, 1996; Weingartner, Rapoport, Buchsbaum, Bunney, Ebert, Mikkelsen & Caine, 1980), matching to sample tasks (Brown & Wynne, 1984; Campbell et al., 1971; Kuehe, Kehle, & McMahon, 1987; Sonuga-Barke, Houlberg & Hall, 1994), and response inhibition tasks (Jennings, van der Molen, Pelham, Debski, & Hoza, 1997; Oosterlaan & Sergeant, 1996; Pliszka, 1997; Purvis & Tannock, 1997; Schachar & Logan, 1990; Schachar, Tannock, Marriot & Logan, 1995; Tannock, Schachar & Logan, 1993). Methylphenidate (MPH), the medication most widely used to treat ADHD, improves their performance on many of these same tasks (Douglas et al., 1986, 1988, 1995; Evans et al., 1986; Michael et al., 1981; Rapport et al., 1989; Rapport & Kelly, 1991; Tannock et al., 1989).

# Debate Concerning the Core Cognitive Deficits of ADHD

In attempting to understand the wide ranging cognitive difficulties of children with ADHD, investigators have speculated that there may be one or more core, underlying, deficits, which lead to the children's cognitive and behavioral problems. In addition, researchers have theorized that stimulant medication acts to improve these core deficits. Several hypotheses concerning the nature of the most basic cognitive deficits are currently influential in guiding research. Three theories concerning the core cognitive deficits of children with ADHD will be presented. Research concerning the performance deficits of children with ADHD, as it relates to these three theoretical frameworks, will then be reviewed.

# Deficits in Self-Regulatory Processes

Douglas (1983; 1988; in press) has suggested that the wide ranging cognitive

difficulties of children with ADHD stem from deficient self - regulation. Self - regulatory processes, she argues, include the consistent and sustained allocation of attention and effort; inhibition of impulsive responding; preparation to process and respond to task stimuli; and ability to adapt flexibly to changing task demands. Douglas suggests that children with ADHD are likely to have most difficulty when demands for self-regulation are highest. Douglas has also hypothesized that the effects of the stimulant medication, MPH, are most evident when demands for self-regulation are high.

## Inhibitory Difficulties as the Core Deficit

Barkley (1994; 1996; 1997) argues that inhibitory difficulties are the primary cognitive deficit, and that problems with self-regulation and executive functions are secondary to inhibitory problems. Drawing on the theory of Bronowski (1977), Barkley postulates that in order for reflection to take place, there must be a delay between the appearance of a stimulus, and the response. Barkley suggests that this delay requires the ability to inhibit a prepotent response, to stop ongoing responses, and to prevent irrelevant stimuli from interfering with ongoing processing. The delay makes possible what Barkley refers to as the four executive processes: working memory; self-regulation of affect/ motivation/ arousal; internalization of speech; and reconstitution. Barkley traces numerous symptoms of ADHD to deficient inhibitory processes. He suggests that the "apparent" attentional difficulties displayed by children with ADHD actually result from inhibitory difficulties.

Deficits in Activation and Motor Processing as Viewed within the Cognitive Energetic Model

Sergeant, van der Meere, and their colleagues (Sergeant & Scholten, 1983; 1985; van der Meere, Gunning & Stemerdink, 1996; van der Meere & Sergeant, 1987; Sergeant & van der Meere, 1990) have applied a model of cognitive processing introduced by Sanders (1983) in order to understand the cognitive difficulties of children with ADHD. Sanders' model comprises three levels. The first level consists of basic information processing stages, such as feature extraction, response choice, and motor adjustment. Located at the second level are the energetic resources which are needed to carry out the basic processes. Sanders postulates three distinct energy pools. Early stages of processing, such as feature extraction, rely on the arousal pool, while later processing stages, including motor adjustment, rely on the activation pool. A third pool, effort, coordinates, and modulates the activity of the arousal and activation pools, for example by adding energy if the energy pools are under stress. In addition, it supplies energy to the response choice stage. Finally, the third level of Sanders' model consists of an evaluation mechanism, which monitors the energy pools, as well as task output. If the arousal or activation pools become too heavily taxed, for example by prolonged performance, the evaluation mechanism may use the effort pool to supplement the energetic supply. Sergeant and van der Meere (1990) suggested that, within the cognitive - energetic framework, the deficits of children with ADHD seem to be based in the activation pool, which supplies the later stages of processing, including motor response. They also suggested possible deficits in the effort pool.

# Research Demonstrating Cognitive Deficits in Children with ADHD

# Allocation of Attention

Attention is one of the aspects of self-regulation identified by Douglas (1983; 1988; in press) as an area of difficulty for children with ADHD. One widely used measure of the ability to display consistent, adequate attention is the Continuous Performance Task, or CPT. The CPT (Rosvold, Mirsky, Sarason, Bransome & Beck, 1956) has traditionally been considered to be a test of vigilance or sustained attention. On the CPT, subjects watch a screen on which stimuli, usually letters or numbers, appear one at a time. The subject has to press a button whenever a target item appears. There are several versions, such as the X-only paradigm, in which the subject presses the button whenever he sees a specific target (eg. the letter X), or the A-X paradigm, in which the subject presses whenever he sees a particular two target sequence (eg. an A followed by an X).

Measures to assess performance on the CPT include omission errors (failing to press the button when the target is present, thought to measure attention or vigilance) and commission errors (pressing the button when the target is not present, thought to reflect inhibition or impulsivity). In recent studies using the task, reaction times have also been measured. Many researchers also apply signal detection theory analysis to their results. This analysis yields two measures: perceptual sensitivity (or d') and response criterion (or  $\beta$ ), (Davies & Parasuraman, 1981). The d' measure reflects the ease with which the subject is able to distinguish a target from a non-target item.  $\beta$  refers to the subject's response criterion, or the degree of certainty the subject requires before he will classify a stimulus as a target. More recently, Halperin and his colleagues (Halperin, Sharma, Greenblatt, & Shwartz, 1991; Halperin, Wolf, Greenblatt, & Young, 1991) have suggested using three somewhat different measures; inattention (composed of omission errors plus very slow correct responses), plus two categories of commission errors, impulsivity and dyscontrol errors. They argue that the three new measures may have more reliability than traditional measures.

The results of studies comparing the performance of children with ADHD to that of controls on the CPT have been summarized in several recent reviews. Corkum and Siegal (1993) concluded that approximately 50 % of the studies they reviewed found that children with ADHD made more omission errors, and approximately the same proportion found differences in commission errors. These authors found a similar pattern in an updated review (Corkum & Siegal, 1995), carried out to address criticisms by Keolega (1995). A meta-analysis of ADHD versus control studies using the CPT carried out by Loisier et al. (1996), which used strict inclusion criteria for studies, reported an even stronger pattern of deficits. They concluded that 82 % of the studies reviewed found significantly more errors in the ADHD than the control groups. For studies using signal detection analyses, Corkum and Siegal (1993) found that four out of five showed that children with ADHD had poorer perceptual sensitivity, though there was little evidence for a difference in response bias. Losier et al. (1996) also concluded that children with ADHD show evidence of a deficit in perceptual sensitivity. They agreed with Corkum and Siegal that there was little evidence of a difference on the response bias measure. In addition, a number of researchers have shown that children with ADHD have slower and more variable RTs than controls on the task (Klorman et al., 1979; van der Meere,

Shalev, Borger & Gross-Tsur, 1995; Strangburg, Marsh, Brown, & Asarnow, 1996; Teicher, Ito, Glod & Barber, 1996).

A more controversial issue has been the question of whether children with ADHD have difficulty maintaining their performance over time, the most stringent definition of sustained attention. Sykes et al. (1973) generated interest in this issue with their finding that hyperactive children's performance deteriorated to a greater extent than that of normal controls, over the course of their 15 minute CPT. They suggested that the hyperactives had more difficulty maintaining their attention over time. However, a number of researchers have failed to replicate this finding, showing instead that the performance of children with ADHD and that of controls deteriorate at about the same rate (Nuechterlein, 1983; O'Dougherty et al, 1984; Schachar, Logan, Wachsmuth & Chajczyk, 1988; van der Meere & Sergeant, 1988). Moreover, Sergeant and van der Meere (1990; van der Meere and Sergeant, 1988) pointed out that, while the hyperactive children's performance deteriorated over time in the Sykes et al. study, the normal control group's performance actually improved slightly over time, reflecting a practice effect on the task. They suggested that any task that shows practice effects has failed as a test of sustained attention, since the attentional factor is confounded with the practice effect.

More recently, three studies (Hooks, Milich and Lorch, 1994; Siedal and Joschko, 1990; van der Meere et al., 1995) have replicated the earlier finding showing that the performance of children with ADHD deteriorated over time. In addition, the studies showed no practice effects, with the performance of normal control children remaining constant over time. Task factors may play a role in explaining the discrepant findings on the CPT. The CPT can be made more or less difficult by varying factors such as rate of stimulus presentation, and duration of stimulus displays. Van der Meere and his colleagues (van der Meere et al., 1995) attributed their finding of a steeper decrement in performance over time to their use of a very slow presentation rate (inter-trial intervals of 10 to 35 seconds). They also found that the time on task effect in their study was maximized when the experimenter was not present during task performance.

# Allocation of Effort

Several investigators have shown that children with ADHD have particular difficulty with tasks that require the deployment of high levels of effort (August & Garfinkel, 1990; Borcherding et al. 1988). For example, several studies have shown intact performance on relatively simple memory tasks, such as recognition or cued recall, but deficits in performance on more effortful free recall tasks (Borcherding et al., 1988; Weingartner et al., 1980). Similarly, Douglas and Benezra (1990) found that children with ADHD did not differ from normal controls when they were asked to memorize lists of related word pairs, whereas deficits appeared on pairs of unrelated words, which require more organized effort to learn. In addition, the group differences appeared on later learning trials, where organized rehearsal strategies become more important. Several studies have also shown that children with ADHD are less likely than other children to use effortful task strategies. They tend to allocate less time and effort to both learning material and attempting to recall it (O'Neill & Douglas, 1991; 1996). They are also less likely to group words strategically, when learning word lists (August, 1987; O'Neill & Douglas, 1996; Voelker, Carter, Sprague, Gdowski, & Lachar, 1989), and tend to use less

effortful strategies to categorize items in stimulus classification tasks (Amin, Douglas, Mendelson & Dufresne, 1993; Hamlett, Pellegrini, & Conners, 1987). Children with ADHD are also more likely than other children to give up when attempting to solve difficult puzzles, particularly following failure experiences (Milich & Okazaki, 1991). Inhibition of Impulsive Responding

The evidence that children with ADHD have difficulty with impulsive responding is of interest for a number of reasons. Inhibition constitutes another of the self-regulatory processes which Douglas (1983; 1988; in press) identifies as being problematic for ADHD. In addition, Barkley (1994; 1996; 1997) identified inhibitory deficits as the most basic cognitive problem in ADHD.

There is considerable evidence that children with ADHD have difficulty with inhibition. One of the earlier tasks used to identify this difficulty is the Matching Familiar Figures Task (MFFT). The MFFT (Kagan, Rosman, Day, Albert & Phillips, 1964) was designed to measure the degree of reflectiveness or impulsivity of a child's cognitive style. The task consists of sets of drawings of familiar objects and animals. The child is shown a model picture, and then asked to choose which of a set of six alternatives is identical to the model. If the child makes an error, he or she is told to look again. The variables scored are usually latency to first response, and number of errors. Kagan (1965) obtained a negative relationship between response speed and accuracy, with fast responses being less accurate. He defined a reflective child as one whose response style is characterized by long latencies and few errors, while an impulsive child shows short reaction times, and a large number of errors. Children with ADHD tend to show an impulsive pattern on the MFFT. In a review of six studies using the MFFT, Pennington and Ozonoff (1996) found that children with ADHD showed higher error rates in all the studies, and faster RTs in four of the six studies. Similar results showing high error rates and fast RTs have been found in several other studies using the MFFT which were not included in the Pennington and Ozonoff review (Brown, 1983; Brown & Quay, 1977; Brown & Wynne, 1984; Campbell et al., 1971; Conte, 1986; Firestone & Martin, 1979; Fuhrman & Kendall, 1986; Juliano, 1974; Kuehne et al., 1987; Rosenbaum & Baker, 1984; Sonuga-Barke, 1995; Sonuga-Barke et al., 1994).

In addition to a general impulsive cognitive style, children with ADHD appear to have difficulty interrupting or inhibiting a response once it has been set in motion. The Stop Task has been used to examine this type of momentary inhibition. On the Stop Task, participants carry out a primary task, usually a choice reaction time task. Periodically a stop signal is presented, which requires the child to inhibit the response to the primary task. Stop signals are presented at varied intervals after the primary task stimulus. Longer intervals make response inhibition more difficult, presumably because the response process has progressed further before the stop signal appears. Children with ADHD have been repeatedly shown to have slower response inhibition than control children on the Stop task (Daugherty, Quay, & Ramos, 1993; Jennings et al., 1997; Oosterlaan & Sergeant, 1996; Pliszka, Borcherding, Spratley, Leon, & Irick, 1997; Purvis & Tannock, 1997; Schachar & Logan, 1990).

A number of studies have also explored whether the Stop task can distinguish

between children with ADHD and other clinical groups. To address this question, Oosterlaan (1996) carried out a meta-analysis of eight studies published since 1990 using the stop or change tasks with children with either ADHD, conduct disorder or anxiety disorders. He concluded that both children with ADHD and children with conduct disorder showed inhibitory difficulties. Children with anxiety, however, performed similarly to control children on the task. Thus, while the Stop task may have utility in distinguishing children with disruptive behaviour disorders from other clinical groups, it may not be effective in distinguishing between ADHD and CD.

Children with ADHD have also shown difficulty with inhibition on the Stroop task (Stroop, 1935). The interference condition of the Stroop task consists of a series of colour names printed in a conflicting ink colour (eg. the word "RED" in blue ink). The subject is asked to name the colour of the ink, rather than to read the word. Since reading is a highly automatized response, subjects have difficulty inhibiting the more automatized, reading response. Consequently, responses in the interference condition typically take longer than responses in the colour naming control condition, in which the subject is asked to name the colour of Xs.

Three recent papers have reviewed the performance of children with ADHD on the Stroop task. Barkley, Grodzinsky and DuPaul (1992) found that five of the six studies they located showed that children with ADHD had more difficulty than controls on the interference condition of the Stroop. Barkley (1997) updated the earlier review, and found four further studies with similar results. Pennington and Ozonoff (1996) noted that four of the five studies they reviewed found that children with ADHD had difficulty with the interference condition. Barkley et al. noted that the one published study which failed to show a difference between ADHDs and controls (Cohen et al., 1972) used adolescents who had been diagnosed with ADHD five years earlier, as opposed to younger children who had been diagnosed recently.

Grodzinsky and Diamond (1992) pointed out, however, that in some of studies that reported that children with ADHD had greater difficulty than controls on the interference condition of the Stroop, the researchers did not control for differences in the basic colour naming condition . In their study, Grodzinsky and Diamond found that children with ADHD performed poorly on all of the conditions of the Stroop. In addition, they failed to find a group by condition interaction. Thus their findings suggested the presence of broader deficits, for example in rapid naming, rather than specific difficulty with the interference condition. It should be noted, however, that a few studies that controlled for differences in colour naming ability still found that children with ADHD had greater difficulty than other children on the interference condition (eg. Berman, Douglas, & Dunbar, 1994; Gorenstein, Mammato, & Sandy, 1989).

Despite this abundant evidence that children with ADHD have difficulty with inhibitory tasks, there is debate over whether inhibition constitutes the primary deficit in ADHD, as Barkley (1994; 1996; 1997) has suggested, with difficulties in attention and effort occurring only as secondary problems. Douglas (in press) points out that there is evidence to support both activating and inhibitory problems in ADHD. In addition, there is physiological evidence that attention may be involved in ADHD performance deficits. For example, studies measuring event related potentials have repeatedly found that children with ADHD have smaller P3 amplitudes than control children (see Jonkman, 1997; Klorman, 1991, for reviews). P3 amplitude is considered to reflect allocation of attention to a task. Thus, the smaller evoked potential amplitudes suggest that children with ADHD allocate less attention to tasks than other children.

Douglas (in press) also points out the difficulty of determining whether attentional or inhibitory deficits are primary. She notes that while some theorists argue that attentional problems result from inability to inhibit responding to extraneous stimuli. others argue that processing of irrelevant stimuli results from a failure to allocate adequate attention to essential task demands. For example, some researchers have questioned the interpretation of the Stroop task as a measure of inhibitory ability. One team has presented a parallel distributed processing model of the Stroop, focusing on the attentional allocation requirements of the task (Cohen, Dunbar, & McClelland, 1990; Dunbar & Sussman, 1995; Macleod, 1991). They suggested that the processing pathways for the highly practiced word reading activity are likely to be stronger than pathways for the less practiced activity, colour naming. In their model, the allocation of attention to either word reading or colour naming sensitizes the units in the corresponding processing pathway. Thus, difficulties in task performance are seen as stemming from difficulties in allocating sufficient attention to the colour naming pathway to allow it to override the stronger, word reading pathway.

## Preparation and Flexible Adaptation to Task Demands

Children with ADHD have difficulty maintaining preparation to respond, for example on a warned reaction time (WRT) task. The WRT task consists of a series of trials in which a warning signal is followed by a signal to respond. The warning signal and the response signal are separated by a preparatory interval. Children with ADHD have slower and more variable RTs than controls on this task (Cohen & Douglas, 1972; Elbaz & Douglas, 1998; Firestone & Martin, 1979; Zahn, Kruesi, & Rapoport, 1991). Recent studies have shown that children with ADHD have particular difficulty when the preparatory interval is consistently long (for example, 8 rather than 2 seconds), which further taxes the children's ability to maintain preparation (Elbaz & Douglas, 1998; Zahn et al., 1991). Sonuga-Barke and Taylor (1992) found similar results on a RT task where children had to respond by pressing a button at the offset of a light. They found that the RTs of the ADHD group, unlike those of controls, were slower when they had to wait longer periods (up to 30 seconds) for the light to extinguish. Sonuga-Barke and his colleagues have noted that children with ADHD appear to be "delay averse" (Sonuga-Barke et al., Hall, 1994; Sonuga-Barke, Taylor, Sembi, & Smith, 1992). Children with ADHD have also shown poorer performance with slow event rates on the CPT (Chee et al., 1989; van der Meere et al., 1995) and the Sternberg task (van der Meere, Vreeling, & Sergeant, 1992).

Children with ADHD also appear to have difficult with another component of selfregulation, cognitive flexibility, which includes the ability to change cognitive set, or to flexibly switch the focus of attention. Berman et al., (1994) used two computer presented variations of the Stroop task to assess the children's ability to deal with unpredictable task demands. The "predictable" version resembled the traditional Stroop task; prior to a block of trials, the children were told either to name the colour or to read the word for all trials in that block. In the "unpredictable" version, they were cued by a high or low tone prior to each stimulus either to name the colour or to read the word on that trial. The children with ADHD had particular difficulty in the unpredictable condition. They showed high error rates on the colour naming trials, due to a tendency to make the more automatic word reading response. Similar problems with unpredictable conditions appeared on a four choice stimulus-response compatibility task (Elbaz & Douglas, 1998). In this task, children with ADHD had particular difficulty in a mixed condition, where compatible and incompatible trials were mixed within one block, and the child was cued how to respond prior to each trial.

Children with ADHD have also shown difficulty rapidly switching attention on the Change task, a variation of the Stop task. On the Change task, after stopping the primary task, participants are required to rapidly switch to a second task. Thus, the Change task measures both response inhibition and response re-engagement. Schachar and his colleagues have reported that children with ADHD have difficulty with both the inhibition and re-engagement requirements of the task (Schachar & Tannock, 1995; Schachar et al., 1995).

There is also some evidence that children with ADHD show impaired cognitive flexibility on problem solving tasks, such as the Wisconsin Card Sorting Test (WCST), although the findings are more equivocal. On the WCST, the subject is presented with stimulus cards, with designs that vary in colour, shape, and number of elements. The subject's task is to sort the cards into piles. During the task, the correct sorting principle changes, for example from colour to form, without warning. Thus, the subject must display flexibility by being able to shift to the new sorting principle.

In a review of studies using the WCST, Barkley et al. (1992) found that eight of the thirteen studies reviewed showed that children with ADHD had greater difficulty with the task than controls. They noted that studies using young, pre-adolescent subjects were more likely to show differences between ADHD and control groups than studies using adolescent subjects. An updated review (Barkley, 1997) identified six further studies, four of which reported differences between children with ADHD and controls, while two did not. A review by Pennington and Ozonoff (1996), however, found less consistent evidence of ADHD- control differences. Unlike the Barkley reviews, the Pennington and Ozonoff review was restricted to published articles, excluding abstracts, unpublished dissertations, and conference presentations. Only four of the ten studies in this review showed that children with ADHD performed poorly on the WCST. In addition, three of the studies using elementary school age subjects failed to show ADHD deficits (Grodzinsky & Diamond, 1992; Pennington, Grossier, & Welsh, 1993; Weyandt & Willis, 1994). Thus, it appears that evidence for perseveration on the WCST for children with ADHD is highly variable, even for the school age population.

#### Activation and Motor Processing

Using Sanders (1983) model of cognitive processing, Sergeant, van der Meere, and their colleagues (Sergeant & Scholten, 1983; 1985; van der Meere, Gunning & Stemerdink, 1996; van der Meere & Sergeant, 1987; Sergeant & van der Meere, 1990) have postulated that children with ADHD have deficits in motor processing. Consequently, they postulated deficits in the activation pool, and possibly at the effort level of the model. They based their theory on a series of studies using Sternberg's (1969) memory search task (Sergeant & Scholten, 1983; 1985; Van der Meere & Sergeant, 1987; Sergeant & van der Meere, 1990). The Sternberg task is particularly relevant to the studies reported in this dissertation, since the task used in the studies employed the same basic format, with some important modifications. Sternberg theorized that cognitive processing on his task involved four stages; encoding, memory search, decision, and motor response. Subjects begin by memorizing a set of items, the memory set. Memory set sizes typically remain within the span of working memory, ranging from one to eight items. Subjects are then presented with a probe item, and must indicate whether or not it matches any of the items in the memory set. The encoding stage consists of the time taken to process the probe item. In the memory search stage the subjects then compare the probe item to each of the items stored in memory. In the decision stage, they choose either a yes or a no response. Finally, in the response stage they initiate and carry out the motor movements necessary to make the response, by pressing one of two buttons.

Sergeant and his colleagues compared the performance of children with ADHD and controls in a series of studies using the Sternberg task. They found that children with ADHD had slower and more variable RTs and lower accuracy levels than controls over all loads of the task (Sergeant & Scholten, 1983; 1985; Van der Meere et al., 1996; Van der Meere & Sergeant, 1987; Sergeant & van der Meere, 1990). They ruled out difficulties with encoding by presenting stimuli in two conditions, intact, and degraded (Sergeant & Scholten, 1985). They found that children with ADHD and controls showed similar slowing on the degraded stimuli. They also failed to find an interaction between diagnosis and memory load in their studies. That is, as memory load increased, both groups showed a similar pattern of slowing RTs, and increasing error rates. Thus, Sergeant and his colleagues concluded that children with ADHD do not have specific difficulties with either encoding or memory search.

Sergeant and his colleagues concluded that the information processing deficiencies of children with ADHD are restricted to the motor response stage of the Sternberg task. since motor processing is not affected by cognitive load. This position was strengthened by findings from two further studies which showed that children with ADHD had particular difficulty under complex motor response conditions (van der Meere, van Baal & Sergeant, 1989; van der Meere et al., 1992). In the first study (van der Meere et al., 1989), children had to respond under either compatible (responding with the hand on the same side as the target) or incompatible (responding with the hand on the opposite side) motor response conditions. They found that children with ADHD had difficulty under incompatible motor response demands. In a further study (van der Meere, Vreeling & Sergeant, 1992), they attempted to replicate this apparent difficulty with incompatible motor response. In addition, they manipulated event rate, which is considered to affect motor preparation within Sanders' model. In this experiment, they failed to replicate their earlier finding with respect to compatible versus incompatible motor conditions. They found, instead, that the ADHD group had more difficulty than controls with the medium and slow event rates. These findings lead them to suggest that motor preparation is the aspect of motor processing which poses the greatest challenge for children with ADHD.

Sergeant and van der Meere (1990) suggested that, within the cognitive - energetic

framework, the deficits observed in children with ADHD seem to be based in the activation pool, since it supplies motor processes. They postulated difficulties with the effort pool as well, since a slow event rate, in addition to affecting activation, places high demands on effort (van der Meere et al., 1992). They pointed out that in an earlier study using the CPT, children with ADHD showed particular vulnerability to a slow event rate, in that they showed a greater decrement in performance over time in a slow event rate condition (van der Meere et al., 1995). Thus, they concluded that both studies pointed to deficits in the activation and effort pools for children with ADHD.

#### Effects of Stimulant Medication on Cognitive Processing

### Stimulant Effects on Self - Regulation

Douglas and her colleagues have suggested that stimulant medications act on regulatory processes (Douglas, 1988; in press; Douglas et al., 1988; 1995). In addition, some investigators have argued that MPH is likely to have its strongest effects on tasks where demands for regulatory processes are high, such as complex tasks, or tasks which require maintaining attention or effort over a long period (Douglas, 1988; in press; Douglas et al., 1988; 1995; Rapport & Kelly, 1991). In addition, there is evidence that higher MPH doses produce greater improvement in performance than lower doses. In an extensive review of the literature on MPH dosage effects, Rapport & Kelly (1991) observed that significant improvement with increased dosage occurred most often in studies which involved high task difficulty and complexity. They suggested that low doses may lead to optimal performance on relatively simple tasks, such as those requiring attention and vigilance, while higher doses lead to optimal performance on tasks requiring
greater effort and organization.

Researchers have suggested a number of different mechanisms for stimulant mediated improvements in the performance of ADHD children. Douglas (1988; in press; Douglas et al., 1988) argues that MPH allows children with ADHD to allocate their cognitive resources at closer to their optimal level. She notes that while normal individuals also seldom perform at their optimal level, the gap between typical performance and optimal performance may be greater for children with ADHD. Hicks, Mayo, and Clayton (1989) argued that children with ADHD are characterized by excessive variability in their levels of arousal, as demonstrated by their highly variable reaction times and activity levels. They suggested that these problems result from deficiencies in frontal lobe function. They further argued that MPH acts to canalize arousal and reactivity, by increasing low arousal "troughs" and decreasing "peaks" of over-arousal.

However, a number of researchers have argued against the idea that MPH improves processing on complex tasks. They have suggested that, while lower MPH doses have a general positive effect on performance, higher doses may interfere with more complex processing. Some investigators have hypothesized that MPH doses show an "inverted U-shaped" effect on cognitive performance on demanding tasks, with low doses improving performance, and higher doses interfering with performance (Sprague & Sleator, 1977; Swanson & Cantwell, 1989; Swanson, Cantwell, Lerner, McBurnett & Hanna, 1991). These investigators suggest that children with ADHD sometimes are prescribed doses which interfere with cognitive performance on more demanding tasks, since the optimal dose to improve behavioral manageability may be higher than the optimal dose to improve cognitive processing, at least in some sub-groups of children (Cantwell, 1996; Cantwell & Swanson, 1992; 1997). They further suggest that high MPH doses cause a deterioration in cognitive performance by interfering with the learning of new material (Sprague and Sleator, 1977; Swanson et al., 1991), or by reducing cognitive flexibility (Flintoff, Barron, Swanson, Ledlow & Kinsbourne, 1982; Tannock & Schachar, 1992).

The next section will review evidence of stimulant medication effects on cognitive tasks. Information on general medication effects, as well as studies of the effects of higher versus lower doses, will be reviewed. In addition, any evidence for negative medication effects on complex tasks will be included.

# Research Demonstrating Stimulant Medication Effects on Cognitive Processing Stimulant Effects on Allocation of Attention

There is evidence that MPH is particulary helpful on tasks requiring sustained attention. On the CPT, MPH reduces error rates (Losier et al., 1996; Rapport & Kelly, 1991), speeds RT and reduces RT variability (Coons, Klorman, & Borgstedt, 1987; Fitzpatrick, Klorman, Brumaghim, & Borgstedt, 1992; Klorman, Brumaghim, Fitzpatrick, & Borgstedt, 1991; Klorman, Brumaghim, Salzman, Strauss, Borgstedt, McBride, & Loeb, 1988; Klorman, Salzman, Bauer, Coons, Borgstedt, & Halperin, 1983; Klorman, Salzman, Pass, Borgstedt, & Dainer, 1979; Peloquin & Klorman, 1986; Strongburg et al., 1996; Teicher et al., 1996; van der Meere et al., 1995; Werry, Aman, & Diamond, 1980). There is also evidence that MPH reduces deterioration in performance over time on task on the CPT (de Sonneville, Njiokiktjien & Hilhorst, 1991; Sykes, Douglas & Morgenstern, 1972, van der Meere et al., 1995).

Rapport and Kelly (1991) note that relatively simple tasks, such as the CPT, are less likely than more complex tasks to show dosage effects, which would be reflected in linear dosage effects or significant between dose differences. None of the CPT studies included in their review on MPH dosage effects reported significant between dose differences on the CPT. Several additional studies of MPH dosage effects on the CPT have been reported since Rapport and Kelly's review. Some confirm that, while MPH reduces errors on the CPT, lower doses are as effective as higher doses in improving performance (O'Toole, Abramowitz, Morris, & Dulcan, 1997; Rapport, Carlson, Kelly, & Pataki, 1993). Two studies, however, have shown some evidence of greater improvements with higher doses. Nigg, Hinshaw, and Halperin (1996) found linear dosage effects on CPT errors, and Barkley, DuPaul, and McMurray (1991) found significant between dose differences on the error measure.

# Stimulant Effects on Allocation of Effort

MPH also appears to be helpful in maintaining effort and motivation on more complex tasks. Using the alternate uses task, a test of divergent thinking, Solanto & Wender (1989) found that, without medication, performance deteriorated over the course of several administrations of the task, while with MPH, performance level was better maintained. They suggested that MPH countered the loss of motivation that otherwise occurred over successive test days. MPH also appears to improve the ability of children with ADHD to sustain effort under challenging circumstances. For example, several studies have shown that MPH helps children with ADHD persist following a failure experience, such as following an attempt to solve an insolvable word puzzle task (Carlson, Pelham, Milich & Hoza, 1993; Milich, Carlson, Pelham & Licht, 1991; Pelham, Kipp, Gnagy & Hoza, 1997).

There is also evidence suggesting that higher MPH dosages may have a stronger impact when demands on attention and effort are high. Douglas, Barr, O'Neill, and Desilets (1998) showed that performance on later trials of a paired associate task is particularly enhanced under some conditions by higher dosages of MPH. They argued that later trials make higher demands for persistent, organized effort than early trials. They found a similar result on an overt rehearsal, word list recall task; higher doses had most impact on later trials. Solanto & Wender (1989) also found that higher doses of MPH were more effective than lower doses in maintaining the performance of children with ADHD over repeated administrations of their divergent thinking task. O'Toole et al. (1997) found that while low and high doses were equally effective in improving performance on a simple shape-learning task, higher doses were more effective in improving recall on a more difficult version of the task. Thus, there is evidence suggesting that higher doses of MPH are particularly effective in improving task performance under conditions which tax effort.

However, investigators who argue that higher doses of MPH have negative effects on effortful tasks point to results from other studies in which complex or high load tasks were used. Sprague & Sleator (1977) reported that higher doses (1.0 mg/kg) of MPH increased error rates and slowed RTs of children with ADHD on the more complex conditions of a high load memory search task, which contained up to 15 items. Swanson et al. (1991) also argued that negative effects of higher MPH doses are likely to occur on high load search tasks. In addition, although some studies using paired associate learning tasks have shown a linear effect of dosage on number of pairs learned (Douglas et al., 1998; Rapport et al., 1989; Rapport, Loo & Denney, 1995), others have shown a levelling off, or even a slight drop, as dosages reached levels above 0.5 mg/kg (Douglas et al., 1988; Gan & Cantwell, 1982; Swanson et al., 1991). Some of the reports of negative effects, however, are not strongly substantiated. For example, Sprague and Sleator (1977) did not carry out statistical comparisons between the high and low load conditions of their memory task. Other reports of levelling off, or slight decreases in performance on high dosages, such as those on paired associate tasks, may reflect ceiling effects, resulting from little room for further improvement at the highest doses (Douglas et al., 1988; Rapport & Kelly, 1991).

# Stimulant Effects on Inhibition

A number of studies have examined the effects of stimulant medication on the performance of children with ADHD on the MFFT. Campbell et al. (1971) showed that MPH made hyperactive children's response style less impulsive, reducing error rates and slowing reaction times. The finding that MPH reduces error rate and increases latency on the MFFT has been replicated a number of times (Rapport & Kelly, 1991). There is also evidence that higher MPH dosages may be more effective than lower doses in improving performance on the MFFT. Douglas et al. (1988) found a linear, dose response relationship between dosage and both response latency and accuracy. As doses increased, up to 0.6 mg / kg, the children's error rates decreased, and their responses slowed. Rapport, Stoner, DuPaul, Kelly, Tucker & Schoeler (1988) explored dosage effects up to 20 mg. They also found linear dosage effects, with higher doses significantly more effective than lower doses, for both error rate and latency. Several other researchers have found results which partially replicate these. For example, Rapport, DuPaul, Stoner, Birmingham & Masse (1985) found a similar linear relationship for dosage and accuracy, though they did not find a significant relationship between dosage and RT. Tannock et al. (1989) found that MPH increased latency linearly, with higher doses significantly more effective than lower doses, but they did not obtain significant medication effects on error rate.

Stimulant medication has also been shown to improve the performance of children with ADHD on other inhibition tasks. For example, MPH improves performance on the Stop Task (Tannock et al., 1989; Tannock, Schachar, & Logan, 1995). In one study, Tannock et al. (1989) found that a high dose of 1.0 mg/kg improved inhibition significantly more than a low dose of 0.3 mg/kg. In a second study, however, they found that inhibition processes were best at a medium dose of 0.6 mg/kg (Tannock et al., 1995). MPH has also been shown to improve error rate on the interference condition of the Stroop task, described earlier. Berman et al. (1994) found a linear dosage effect on error rate up to 0.9 mg/kg.

# Stimulant Effects on Preparation and Flexible Adaptation to Task Demands

Stimulant medication appears to decrease the difficulties shown by children with ADHD in regulating their attention in order to maintain preparation to respond.

Stimulants have been shown to reduce errors, speed RT, and reduce RT variability on the WRT task (Cohen, Douglas, & Morgenstern, 1971; Douglas et al., 1988; Zahn, Rapoport, & Thoman, 1980). There is also preliminary evidence that MPH improves the specific vulnerability shown by children with ADHD to long preparatory intervals on the WRT task (Douglas, in press). In addition, the medication may help children with ADHD to respond flexibly. For example, Douglas (in press) reported preliminary findings in which MPH improved the children's performance on the mixed condition of the stimulus-response compatibility task, where compatible and incompatible trials were mixed within one block.

Although there have been reports that MPH decreases cognitive flexibility, for example, by interfering with performance on the WCST (Dyme, Sahakian, Golinko, & Rabe, 1982; Tannock & Schachar, 1992), these results are inconclusive. In their report of negative effects on the WCST, Dyme et al. (1982) used a very small sample (5 subjects) in their study. Thus, their findings may be unreliable. Tannock and Schachar (1992) found conflicting evidence. The first time their subjects took the WCST, they found a nonsignificant tendency for perseverative errors to increase on medication, while the second time the subjects took the task there was a significant decrease in perseverative errors. In a study designed to address the hypothesis that high doses impair cognitive flexibility, Douglas et al., (1995) found no adverse medication effects, and some evidence of linear improvement with increasing MPH doses up to 0.9 mg / kg on tasks measuring divergent thinking and ability to shift mental set. These included the WCST, Trailmaking, the Instances test, the Alternate Uses test, and the Contingency naming task.

# Stimulant Effects on Activation and Motor Processing

Klorman and his colleagues carried out a series of studies examining stimulant medication effects on the performance of children with ADHD on the Sternberg task. They interpreted their findings within Sanders' (1983) cognitive energetic model. Klorman and his colleagues concluded that the effects of MPH were not dependent upon load (Brumaghim, Klorman, Strauss, Levine, & Goldstein, 1987; Fitzpatrick, Klorman, Brumaghim, & Keefover, 1988; Klorman, Brumaghim, Fitzpatrick, & Borgstedt, 1992). Instead, they suggested that MPH acted largely by facilitating motor response (Brumaghim et al., 1987; Fitzpatrick et al., 1988; Klorman et al., 1992). Fitzpatrick et al. (1988) found that MPH speeded RTs in a "rotated mapping" response condition, similar to the incompatible motor response condition used by van der Meere et al. (1989) in their study comparing children with ADHD to controls. Within Sanders' cognitive energetic framework, the motor response stage is supplied by the activation energy pool (Sergeant & van der Meere, 1990). Since the rotated mapping condition was highly effortful, Fitzpatrick et al. (1988) suggested that MPH might also influence effort. The finding that MPH improved motor response appeared to coincide with van der Meere et al.'s (1989; 1992) speculation that motor processes were the locus of ADHD cognitive deficits.

However, recent findings by Klorman and his colleagues have lead to a shift in their thinking. Several of their recent studies suggest that both ADHD - control differences and MPH effects can be demonstrated at earlier stages of processing. In a study measuring event related potentials, Klorman et al. (1992) showed that adolescents with ADHD failed to show the usual pattern of faster P3B latencies to targets than to nontargets. Since the P3B is considered to reflect the end of stimulus evaluation (which occurs before the motor processing stage), this suggests that the slower overall RTs of children with ADHD are at least partially caused by slower processing at stages prior to motor processing. Klorman and his colleagues (Klorman et al., 1992; Klorman, Brumaghim, Fitzpatrick, Borgstedt, & Strauss, 1994) also found that MPH speeded P3B latency to target items. These findings lead them to conclude that children with ADHD have a deficit in stimulus evaluation processes preceding motor processing, and that MPH ameliorates this deficit.

# Rationale and Objectives of the Studies to be Reported

This literature review focused on evidence that ADHD children have difficulty with self - regulation, which includes problems allocating adequate attention and effort, inhibiting inappropriate responding, and maintaining flexible readiness to respond. Douglas (1983; 1988; in press) has pointed out that the next step in testing the theory that self - regulation is central to ADHD is to make predictions based on the model, and then to test them. Douglas (1983; 1988) laid the groundwork, by operationally defining factors which she predicted would affect task demands for self-regulation. These factors included degree of information processing demands, such as number of stimuli, or task complexity; availability of external regulation, such as the use of rewards, or the presence of an adult during testing; and distracting factors, such as novelty or salience of distractors. Douglas suggested that current research on ADHD should systematically manipulate factors which would be expected to tax control processes, in order to test the prediction that processing deficits will be more likely to occur, and MPH will be most likely to improve performance, when demands for regulation are high. In their review of MPH dosage effects, Rapport and Kelly (1991) made a similar suggestion. They recommended using tasks which varied in difficulty and complexity, in order to test the prediction that the effects of different stimulant medication dosages depend on task demands.

The studies to be reported focused on one of the factors which Douglas identified as determining the demand for self-regulation; the number of stimuli to be processed, or cognitive load. The structure of the task used was based on Sternberg's (1969) memory search task. However, in order to explore the effects of a wide range of cognitive loads, we modified the Sternberg task by extending the visual search component to include extremely heavy loads. It was expected that the high cognitive loads in the combined visual - memory search (VMS) task would place high demands on attentive, controlled, effortful processing. Experiment 1 explored the effects of MPH dosage on the VMS. using a range of cognitive loads. The objective of the experiment was to test the prediction that MPH would be most helpful at high cognitive loads. By including a range of MPH doses, the experiment also made it possible to test Rapport and Kelly's (1991) prediction that further improvements with higher MPH doses would be most likely to occur on more complex tasks. Experiment 2 compared the performance of children with ADHD and controls on the VMS. This experiment tested the prediction that children with ADHD would be particularly challenged under high load conditions. The ADHD-control comparison was also carried out in order to provide a context for understanding the effects of MPH on performance, by clarifying the pattern of difficulties which children with ADHD displayed on the task. Finally, Experiment 3 explored the effects of age on

performance on the VMS. The developmental study was carried out in order to provide normal developmental data on the task. The results also helped to determine whether children with ADHD showed a unique pattern of processing deficits on the VMS, or whether their performance resembled that of younger children.

# Running head: EFFECTS OF METHYLPHENIDATE

Effects of Methylphenidate on Complex Cognitive

Processing in Attention-Deficit Hyperactivity Disorder

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### Abstract

Three experiments were conducted to explore the effects of methylphenidate (MPH), ADHD diagnosis, and age, on performance on a complex visual - memory search task. Results showed that the effects of MPH varied with information load. On low processing loads, all doses of MPH helped children with ADHD improve accuracy with no cost to RT, while on high loads, higher MPH doses improved error rates while slowing RT. Without medication, children with ADHD showed high error rates and slow RTs across both low and high loads, as did younger normal control children. Since MPH slowed performance only on the most difficult, high load conditions, it is argued that the drug improves self-regulatory ability, enabling children with ADHD to adapt differentially to high and low loads.

Attention - Deficit Hyperactivity Disorder (ADHD) is the most frequently diagnosed psychiatric disorder of childhood (Shaywitz & Shaywitz, 1988; Swanson, Shea, McBurnett, Potkin, Fiore, & Crinella, 1990). There is continuing debate, however, about the nature of the cognitive deficits shown by children with ADHD, and the actions of stimulant medication, the most frequently used method of treating ADHD, on cognitive processes (Barkley, 1994; 1997; Douglas, Barr, Amin, O'Neill, & Britton, 1988; Douglas, Barr, Desilets, & Sherman, 1995; Douglas, Barr, O'Neill, & Britton, 1986; Hicks, Mayo,

Douglas (in press; Douglas et al., 1986; 1988; 1995) suggested that methylphenidate (MPH) is particularly effective in helping children with ADHD perform tasks which place high demands on self - regulation. Self - regulatory processes, she argues, include the deployment of attention and effort, the inhibition of impulsive responding, the ability to maintain or change cognitive set to meet task demands, and planning and organization.

& Clayton, 1989; Rapport & Kelly, 1991; Sergeant & van der Meere, 1990).

There is evidence that MPH is particulary helpful on tasks requiring high levels of sustained attention or effort, one component of self - regulation. For example, on laboratory measures of sustained attention, such as the continuous performance task (CPT), MPH reduces deterioration in performance over time (de Sonneville, Njiokiktjien, & Hilhorst, 1991; Sykes, Douglas, & Morgenstern, 1972; van der Meere, Shalev, Borger, & Gross - Tsur, 1995). Similar results have been reported on more complex tasks. Using the alternate uses task, a test of divergent thinking, Solanto & Wender (1989) found that MPH reduced the deterioration in performance of children with ADHD over the course of

several administrations of the task, which they had observed when the children were not medicated. They suggested that MPH countered the loss of motivation which otherwise occurred over successive test days. MPH also appears to improve the ability of children with ADHD to sustain effort under challenging circumstances. For example, several studies have shown that MPH helps children with ADHD persist following a failure experience, such as attempting an insolvable word puzzle task (Carlson, Pelham, Milich, & Hoza, 1993; Milich, Carlson, Pelham, & Licht, 1991; Pelham, Kipp, Gnagy, & Hoza, 1997). In addition, MPH has been shown to increase the degree to which children with ADHD slow down following an error on the Sternberg task (Krusch et al., 1996). This suggests that the medication increases the children's ability to allocate additional effort and care when they are uncertain about their performance.

Other researchers, however, have suggested that while lower MPH doses have a generally positive effect on performance, higher doses may interfere with processing at high information loads. Some have hypothesized that MPH doses have an "inverted U-shaped" effect on cognitive performance on high load tasks, with low doses improving performance, and higher doses interfering with performance (Sprague & Sleator, 1977; Swanson & Cantwell, 1989; Swanson, Cantwell, Lerner, McBurnett, & Hanna, 1991). These investigators suggest that children with ADHD are sometimes prescribed doses which interfere with performance on more demanding tasks, since the optimal dose to improve behavioral manageability may be higher than the optimal dose to improve cognitive processing (Cantwell, 1996; Cantwell & Swanson, 1997). Sprague & Sleator (1977) reported that higher doses (1.0 mg/kg) of MPH had a negative effect on the

performance of children with ADHD on a high load memory search task, which contained up to 15 items. Swanson et al. (1991) also argued that negative effects of higher MPH doses are likely to occur on high load search tasks. In addition, although some studies using paired associate learning tasks have shown a linear effect with dosage (Douglas, Barr, O'Neill, & Desilets, in preparation; Rapport, Quinn, DuPaul, Quinn, & Kelly, 1989; Rapport, Loo, & Denney, 1995), others have shown a levelling off, or even a slight drop, as dosages reached levels above 0.5 mg/kg (Douglas et al., 1988; Gan & Cantwell, 1982; Swanson et al., 1991). Some investigators have suggested that high MPH doses cause a deterioration in cognitive performance by interfering with the learning of new material (Sprague and Sleator, 1977; Swanson et al., 1991), or by reducing cognitive flexibility (Flintoff, Barron, Swanson, Ledlow, & Kinsbourne, 1982; Tannock & Schachar, 1992).

In a study designed to address the hypothesis that high doses impair cognitive flexibility, however, Douglas et al., (1995) found no adverse effects, and some evidence of linear improvement with increasing MPH doses up to 0.9 mg / kg on tasks measuring perseveration, divergent thinking and ability to shift mental set. In addition, in an extensive review of the available literature on MPH dosage effects, Rapport & Kelly (1991) concluded that, in all studies where differences were found between higher and lower dosages, performance was most improved in the high dose condition. They also observed that significant improvement with increased dosage appeared to occur most often in studies using complex, effortful tasks.

In Experiment 1, we explored the effects of MPH dosage on a search task that included varying degrees of complexity. This made it possible to investigate whether

higher doses of MPH were most effective when demands for self - regulation were greatest, or conversely, whether higher doses interfered with more complex processing. The structure of the task used was based on Sternberg's (1969) memory search task. In the Sternberg task, participants are presented with one or more items to learn, called the memory set. They are then presented with one or more search items, and are asked to determine whether there is a match with any of the memory set items. Klorman and his colleagues carried out a series of studies investigating the effects of MPH on performance on the Sternberg task. Using memory loads or visual search loads of up to 5 items, Klorman and his colleagues showed that MPH improved accuracy and either did not change, or speeded RTs on the Sternberg task (Brumaghim, Klorman, Strauss, Levine, & Goldstein, 1987; Coons, Klorman, & Borgstedt, 1987; Fitzpatrick, Klorman, Brumaghim, & Keefover, 1988; Klorman, Brumaghim, Fitzpatrick, & Borgstedt, 1992; Klorman, Brumaghim, Fitzpatrick, Borgstedt, & Strauss, 1994; Krusch, Klorman, Brumaghim, Fitzpatrick, Borgstedt, & Strauss, 1996; Peloquin & Klorman, 1986).

Because we were interested in investigating MPH effects on more complex, effortful processing, we modified the Sternberg task. Although the memory load remained in the range used by Klorman and his colleagues, the visual search component was extended to include extremely heavy loads. It was expected that the high cognitive loads in the combined visual - memory search (VMS) task would place high demands on attentive, controlled, effortful processing (Shiffrin, 1988). In addition, since the task included both a memory search and a visual search component, the child was required to alternate searches between the visual search and memory sets in order to locate a match,

thus requiring the ability to switch attentional focus. The new task also placed heavy demands on working memory, since the memory load items had to be retained while the child conducted a visual search of the display set. To further increase self - regulatory demands, the task included a varied set procedure. In this procedure, the participant must learn a new set of target items before each trial, as opposed to the less demanding fixed set procedure, where the target items remain the same throughout a block of trials.

In Experiment 1 we used the VMS to investigate the effects of MPH dosage on a range of processing loads, in order to determine whether higher MPH doses had positive or deleterious effects when demands for self - regulation were high. Experiment 2 compared the performance of children with ADHD to that of controls on the same loads of the VMS, to determine whether high loads were particularly challenging for children with ADHD. Information on ADHD children's cognitive difficulties is important in understanding the effects of MPH on their performance. Finally, in order to determine whether children with ADHD show a unique pattern of processing deficits, or whether their performance resembles that of younger children, Experiment 3 explored the effects of age on performance on the VMS.

# **EXPERIMENT 1**

In Experiment 1 we investigated the relationship between the effects of cognitive load and dosage level of MPH on the performance of children with ADHD on the VMS task. Four dosage levels: placebo, 0.3, 0.6 and 0.9 mg/kg, were used in an acute dosage MPH trial with a group of boys with ADHD. Dosage effects were studied using three memory loads, (1, 2 or 4 items), and three visual search loads, (4, 9 or 16 items).

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If higher MPH dosages reduced accuracy on our higher loads, this would provide support for the suggestion that MPH interferes with performance on highly complex tasks. However, if higher MPH doses improved accuracy on high loads, it would support the hypothesis that MPH is helpful when demands for self - regulation are high. Investigators have reported a linear relationship between MPH dosage and improved performance on a variety of cognitive tasks, using doses up to 0.6, or 0.9 mg/kg (Douglas et al., 1988; Douglas et al., in preparation; Douglas et al., 1995; Evans, Gualtieri, & Amara, 1986; Pelham, Bender, Cadell, Booth, & Moorer, 1985; Rapport & Kelly, 1991; Rapport, Loo, & Denney, 1995; Rapport, Stoner, DuPaul, Kelly, Tucker, & Schoeler, 1988; Rapport et al., 1989; Vyse & Rapport, 1989). There is also evidence suggesting that higher MPH dosages may have a stronger impact when demands on attention and effort are high. Douglas et al. (in preparation) showed that performance on later trials of a paired associate task was particularly enhanced by higher dosages of MPH. They argued that later trials make higher demands for persistent, organized effort than early trials. They found a similar result on an overt rehearsal, word list recall task; higher doses had most impact on later trials. Solanto & Wender (1989) also found that higher doses of MPH were more effective than lower doses in maintaining the performance of children with ADHD over repeated administrations of their divergent thinking task. O'Toole, Abramowitz, Morris, and Dulcan (1997) showed that higher doses were more effective than lower doses in improving performance on a difficult non-verbal learning task. Thus, there is evidence suggesting that higher doses of MPH are particularly effective in improving task performance under conditions which tax effort and persistence, as the

higher loads of the VMS task were designed to do.

With respect to dosage effects on RT, we expected that MPH would have a more complex effect, depending on both load and dosage. On relatively fast paced tasks, with typical RTs in the order of milliseconds, MPH often speeds responding, while improving error rates. For example, on relatively fast paced Warned Reaction Time (WRT) Tasks, on which children with ADHD make more errors and respond more slowly than controls (Cohen & Douglas, 1972; Firestone & Martin, 1979; Zahn, Kruesi, & Rapoport, 1991), MPH improves error rates, speeds RT, and reduces RT variability (Sykes et al., 1972; Douglas et al., 1988). Similarly, on vigilance tasks such as the CPT, on which children with ADHD typically have slow RTs and high error rates (Chee, Logan, Schachar, & Lindsay, 1989; Corkum & Siegal, 1993; Klorman, Salzman, Pass, Borgstedt, & Dainer, 1979; Losier, McGrath, & Klein, 1996; Siedal & Joschko, 1990; Sykes et al, 1972; Sykes, Douglas, & Morgenstern, 1973), MPH reduces errors, speeds RT and reduces RT variability (Coons, Klorman, & Borgstedt, 1987; Klorman et al., 1979; Losier et al., 1996; Peloquin & Klorman, 1986). On standard, lower load versions of the Sternberg task, on which children with ADHD show slow and variable RTs and high error rates (Sergeant & Scholten, 1983; 1985; van der Meere & Sergeant, 1987; Sergeant & van der Meere, 1990), MPH also reduces errors, and sometimes speeds RTs and reduces RT variability (Brumaghim et al., 1987; Fitzpatrick et al., 1988; Klorman et al., 1992; 1994).

In contrast to these effects on relatively fast paced tasks, there is evidence that MPH slows RTs on slower paced tasks. The Matching Familiar Figures Task (MFFT), for example, is a complex visual search task, with typical response latencies in the range of

several seconds. Correct responding on the MFFT places high demands on slow, careful, deliberate processing. Several investigators have reported that children with ADHD typically respond quickly and impulsively on the MFFT (Brown, 1983; Campbell, Douglas, & Morgenstern, 1971; Cohen, Weiss, & Minde, 1972; Pennington & Ozonoff, 1996; Sonuga - Barke, Houlberg, & Hall, 1994). On this task, there is evidence that MPH reduces their impulsivity, slowing RTs, while reducing errors (Campbell et al., 1971; Douglas et al., 1988; Rapport et al., 1988). In addition, dosage studies have shown that the slowing effects are more pronounced at higher MPH doses (Douglas et al., 1988; Rapport et al., 1988).

The findings suggesting that MPH speeds RT on relatively fast paced tasks, but slows responding on slower paced tasks, are consistent with the argument that the effects of MPH result, at least in part, from an improvement in the ability of children with ADHD to regulate attention, inhibition and effort (Douglas, 1983; 1988; Douglas et al., 1988; Hicks et al., 1989; Rapport & Kelly, 1991). That is, rather than simply speeding, or slowing performance, MPH appears to enable the children to change their response rate in order to meet the specific requirements of a given task.

These findings suggested that we would find that dosage effects on RT differed for the lower and higher cognitive loads. We anticipated that, on low cognitive loads, MPH would either not change or speed responding, as previously found on fast paced cognitive tasks such as the WRT, the CPT or the Sternberg (Coons et al., 1987; Douglas et al., 1988; Klorman et al., 1979; Peloquin & Klorman, 1986; Sykes et al., 1972). On high loads, we anticipated that higher doses would slow responding, as previously found on the MFFT (Douglas et al., 1988; Rapport et al., 1988).

# Method

# **Participants**

Seventeen boys between the ages of 7 and 13, who met DSM-III-R (American Psychiatric Association, 1987) criteria for ADHD, participated in the study. The boys were recruited from the McGill University-Montreal Children's Hospital Hyperactivity Project. Referrals to the project are made by parents, teachers, physicians and school psychologists. Because ADHD is considerably more common in males than in females (American Psychiatric Association, 1994), only boys were included. Boys were accepted into the study only if ADHD was judged by an interprofessional diagnostic team to be the primary diagnosis. Onset of inattentive, impulsive and / or hyperactive symptoms had to occur before age 6. The symptoms had to appear before the onset of any additional disorder (Swanson et al., 1990). The symptoms had to be judged to be severely disabling, chronic and pervasive. Exclusionary criteria included serious visual, auditory or speech deficits, and known neurological damage. In addition, there had to be no indication of serious emotional or behavior problems, or stressful events in the boy's life which could explain the symptoms.

A structured interview based on DSM-III-R criteria (Swanson & Taylor, 1990) was carried out with parents. For inclusion, children had to meet the criteria for ADHD. In addition, parents completed the Abbreviated Conners Rating Scale (Goyette, Conners, & Ulrich, 1978) and the IOWA Conners Parent Rating Scale (Loney & Milich, 1982). Parents were also asked to supply copies of all available report cards, and any previous

psychological, educational and psychiatric assessments. Teachers completed the Teacher versions of the Abbreviated Conners Rating Scale and the IOWA Conners Rating Scale. They also completed the SNAP Rating Scale based on DSM criteria (Swanson, Nolan, & Pelham, 1982). In order to establish that the ADHD symptoms were pervasive, participants had to receive a minimum rating of 1.5 from both parents and teachers on the Hyperactivity Index of the Conners Rating Scale, as well as scores above the established cut-offs for Inattention and Impulsivity on teachers' ratings on the SNAP. In addition, they met a minimum rating of 1.5 on the IOWA Conners Inattentive / Overactive scale.

The DSM-III-R parent interview (Swanson & Taylor, 1990) also enquired about symptoms of two disorders that are often co-morbid with ADHD; oppositional defiant disorder (ODD) and conduct disorder (CD). Eleven boys (64.7 % of the sample) met the criteria for a diagnosis of ODD. Although two of the boys (11.8 %) met the minimal criteria for CD, these symptoms were not considered severe enough to require exclusion from the study. In addition, the Revised Behavior Problem Checklist (Quay & Peterson, 1983; 1987), was used to check for the presence of symptoms of anxiety. Five boys (29.4 %) had ratings on the Anxiety-Withdrawal scale of the Revised Behavior Problem Checklist that were above the criterion score (more than two standard deviations above the mean). However, interviews with parents and teachers, and the other available evidence, including age of onset, suggested that these symptoms were secondary to ADHD.

Intellectual and academic assessments were also conducted. IQ was assessed using an abbreviated version of the WISC-R, consisting of four subtests, Block Design,

Picture Completion, Similarities and Vocabulary, which comprise a reliable short form (Sattler, 1990). All boys had IQs over 85. In addition, the Word Identification and Passage Comprehension subtests of the Woodcock Reading Mastery Tests - Revised (Woodcock, 1987) were used to assess the presence of reading difficulties. Four boys (23.5 %) were two or more grade levels behind expected grade level on both subtests, and an additional two boys (11.8 %) were two or more grades behind on Passage Comprehension only.

The boys had a mean age of 128.0 months, <u>SD</u> of 9.9, a mean IQ of 103.4, <u>SD</u> of 8.49, and a mean Hollingshead (1975) SES rating of 4.3, <u>SD</u> of .96, (scores on the Hollingshead run from 1, low SES to 5, high SES). Four boys who were taking MPH at the beginning of the study were required to be free of medication for a minimum of 48 hours prior to testing.

#### Apparatus

The VMS task was programmed with Micro Experimental Laboratory (MEL, Schneider, 1990) software on an IBM compatible computer. The computer presented and timed the stimuli, and collected RT and accuracy data. Stimuli were presented in the middle of the screen. The "Z" and "/" keys on the keyboard were covered with white stickers, indicating which keys were to be used for "Yes" and "No" responses.

# <u>Task</u>

On each trial of the VMS children were required to learn a set of letters, the memory set, and then search for them in a visual display, the visual search set. The memory set consisted of one, two or four letters presented on the computer screen.

Display time depended on the number of letters in the set: one letter remained on the screen for one second, two letters for two seconds, and four letters for four seconds. Only consonants were used. After the display time elapsed, the memory set was replaced by the word "READY", which remained on the screen for one second. This was followed by the visual search set, consisting of 4, 9 or 16 letters, arranged in a matrix. The child searched through the display items for any one of the letters that had appeared in the memory set. The search set remained on the screen until the child pressed either the yes or the no key, indicating whether or not he thought there was a match. A correct response was followed by the word "Correct," accompanied by a high tone lasting 500 msec, while an incorrect response was followed by the word "Incorrect," accompanied by a 500 msec low tone. The next trial immediately followed the tone.

Both the choice of target letters and the position of targets within the visual search matrices were randomized. The non-target letters were also generated randomly. The positions of the "Yes" and "No" keys on the left and right were counterbalanced across subjects.

#### Procedure

Both parents and children were asked to sign a consent form outlining details of the experiment. The boys came to the lab for a morning or afternoon session, during which they were assessed on a varied battery of tasks including the VMS, a tracing task, an arithmetic task, and a paired associate learning task. The order of the tasks was fixed, with each of the three blocks of the VMS separated by another task. Each boy was tested individually, in a quiet room with one experimenter. To introduce the VMS task, two

examples of the stimuli appeared on the computer screen as the boy received verbal instructions. He was told that a group of letters would appear, and that his job was to remember them. The letters would then disappear, and would be replaced by a new group of letters. He was told to search through the new group of letters, to see if any of them matched any of the letters in the first group. It was emphasized that he only needed to find one letter from the memory set for a match. He was then instructed to press either the "Yes" or "No" key, to indicate if he found a match. Speed and accuracy were equally emphasized. Following the instructions, a practice block was administered, consisting of 12 trials of the task using a four letter visual search set. The 12 trials consisted of two target present ("Yes") trials and two target absent ("No") trials at each of the three memory loads.

The task was divided into three blocks, one for each of the three visual search loads. Each block consisted of 48 trials, eight target present and eight target absent trials for each of the three memory loads. Trials with each of the memory load sizes were presented in random order. The order of the three blocks was counterbalanced across participants. Each block took about 15 minutes.

The boys received feedback after each trial, but no rewards were given for their performance on the task.

# **Medication**

The boys came to the lab on nine days, including a first baseline day, on which they carried out all of the tasks in the testing battery with no medication, followed by eight days of medication and placebo trials. To improve reliability of the drug trial, they were

tested on placebo and each medication dose on two different days (first and second dose administration). The statistical analyses reported in this study are based on data from the eight medication days. Data from the baseline day is presented in Experiment 2. To ensure compliance, medication was administered in the laboratory. The child was given gelatin capsules containing either placebo (100 mg lactose), or one of three doses of methylphenidate HCL (Ritalin), 0.3, 0.6, and 0.9 mg/kg. After a one hour delay, the testing session began.

Medications were prepared in opaque gelatin capsules and administered in a double-blind manner. Capsules containing the three MPH doses were prepared individually for each boy, based on body weight. The mean dose at the 0.3 mg / kg level was 11.4 mg, SD = 4.0, at the 0.6 level, M = 22.8, SD = 8.0, and at the 0.9 level, M = 34.2, SD = 11.9. The drug order was determined by consecutive assignment to a randomly ordered list of 24 possible combinations of placebo and the three medication levels.

#### Behavior and Side Effect Ratings

Two types of behavior rating scales were completed by the examiner on each testing day. The first consisted of the Hyperactivity Index of the Abbreviated Conners Rating Scale (Goyette et al., 1978). The second consisted of effort ratings of the boy's performance on each task. Effort was rated on a 7-point (0 - 6) scale in which 0 indicated no effort, 3 indicated reasonable effort, and 6 indicated excellent effort (Douglas et al., 1988).

Barkley's (1981) side effects rating scale was also completed for each boy. The

scale included 17 commonly reported symptoms such as decreased appetite, stomachaches and tics. Each item was rated on a 10 point scale from 0 (none) to 9 (serious).

# **Results**

A 4 (dose) X 2 (first or second dose administration) X 2 (target condition) X 3 (visual search load) X 3 (memory load) within subjects analysis of variance was performed for each of the variables; error rate, RT, and standard deviation of RT. In order to determine whether the medication effects were influenced by whether it was the first or second time the child received that dose, the effects of first and second dose administration were examined. Neither the main effect for first versus second administration nor any of the interactions involving dose administration proved to be significant for error rate or RT. Although, in the standard deviation analysis, first versus second dose administration interacted with memory load size and search load size, the patterns for the first and second administrations were very similar. Therefore, data for the two administrations of each dose for each of the three dependent variables was averaged for the further analyses.

Only data for correct responses were included in the RT analyses. Full degrees of freedom are reported, but for within subjects effects, the reported significance levels reflect the Greenhouse-Geisser correction. For pairwise comparisons, Tukey's HSD tests were used ( $\alpha = .05$ ). For significant effects involving dose,  $\eta^2$  was used as a measure of effect size (Tabachnick & Fidell, 1989).

Errors: A main effect for dosage showed that error rates decreased with increasing

doses of MPH, E (3, 48) = 18.01, p < .001,  $\eta^2 = .53$ . Trend analysis confirmed a linear effect of dose in reducing error rate, E (1, 48) = 47.47, p < .01, which accounted for 87.7 % of the variance, as well as a smaller significant quadratic trend, E (1, 48) = 6.13, p < .05, accounting for only 11.35 % of the variance. The small quadratic effect reflects the fact that although the beneficial effects of the medication on accuracy were evident up to the highest dose, the slope of improvement became less steep with increased doses. Post hoc tests on the dose main effect found that the children were more accurate on each of the three medication doses than they were on placebo, with no significant between dosage differences. The mean percentage of errors (with standard deviations in parentheses) at each of placebo, 0.3, 0.6, and 0.9 mg / kg were 15.8 % (11.7), 10.3 % (9.4), 8.3 % (6.5) and 7.3 % (6.3), respectively. There were no other significant effects involving dosage on error rate.

The remaining results for error rate showed that the experimental manipulations were effective. As expected, main effects showed that the children became less accurate as both memory load,  $\mathbf{E}(2,32) = 47.69$ ,  $\mathbf{p} < .001$ , and visual search load,  $\mathbf{E}(2, 32) =$ 23.91,  $\mathbf{p} < .001$ , increased. A significant interaction between the two load variables showed that the children made the most errors when both types of load were high,  $\mathbf{E}(4,$ 64) = 6.88,  $\mathbf{p} < .001$ . A main effect for target condition showed that they made more errors on target present than on target absent trials,  $\mathbf{E}(1, 16) = 47.87$ ,  $\mathbf{p} < .001$ . Target condition also interacted with memory load,  $\mathbf{E}(2, 32) = 12.15$ ,  $\mathbf{p} < .001$ . Post hocs demonstrated that the increased error rate for the target present condition was significant only for the two larger memory loads. Thus the children were more likely to miss a target when they were dealing with larger loads.

Mean Reaction Time: A dose main effect indicated that RT slowed as dose increased, E(3, 48) = 5.14, p < .007,  $\eta^2 = .24$ . As expected, RT was also slowed at larger loads, with significant main effects for both memory load, E(2, 32) = 169.87, p < .001, and visual search load, E(2, 32) = 86.51, p < .001. As well, a main effect for target condition showed that the children responded more slowly in the target absent than the target present condition, E(1, 16) = 80.56, p < .001. This is a common finding on search tasks because, unlike target present trials, where the participant stops searching upon finding the target, target absent trials require the child to search to the end of the set.

Each of these main effects, however, was modified by a series of two-way interactions. An interaction between dose and target condition showed that the medication had a more pronounced slowing effect in the target absent condition than in the target present condition,  $\mathbf{F}(3, 48) = 8.19$ ,  $\mathbf{p} < .001$ ,  $\eta^2 = .34$ . An interaction between memory load and visual search load showed that RT was slowed still further when both types of load were high,  $\mathbf{F}(4, 64) = 40.79$ ,  $\mathbf{p} < .001$ . In addition, target condition interacted with each of the two load variables; both higher memory loads,  $\mathbf{F}(2, 32) = 52.98$ ,  $\mathbf{p} < .001$ , and higher visual search loads,  $\mathbf{F}(2, 32) = 51.65$ ,  $\mathbf{p} < .001$  slowed RTs more in the target absent condition.

There were also three three-way interactions. Two of these involved the dosage manipulation; the first between dose, target condition and visual search load size, E (6, 96) = 5.00, p < .002,  $\eta^2 = .24$ , and the second between dose, memory load size and visual search load size, E (12, 192) = 2.91, p < .017,  $\eta^2 = .15$ . The third three-way interaction

occurred between target condition, memory load, and visual search load, E(4, 64) = 5.65, g < .006. Tukey HSD post hoc tests were carried out to further explore each of the threeway interactions. Because our major interest was in medication effects, only results involving dose will be discussed in detail. Post hocs on the dose by target condition by visual search load interaction (see Figure 1) showed that higher doses slowed response significantly only in the target absent condition. Also, within this condition, the slowing was significant only for the two larger visual search loads. More specifically, on the 9 item visual search load, subjects responded more slowly on the 0.9 mg/kg dose than on placebo or the 0.3 mg/kg dose. In the case of the largest, 16 item, visual search load, responses slowed as dosage increased across all four dose levels, with only the difference between placebo and 0.3 mg/kg failing to reach significance. These results suggest that MPH slowed responses most dramatically under very demanding conditions, in which high load and the target absent condition were combined.

Post hoc tests to explore the dose by visual search load size by memory load size interaction (see Figure 2) revealed that medication slowed responding when the children were dealing with the two larger visual search loads (9 and 16 items), when these high search loads were combined with the two higher memory loads (2 and 4 items). On the largest, 16 item, visual search load, the medication slowed responding on the two larger memory loads; on the two item memory load, the children responded more slowly on the 0.9 mg/kg dose than on any of the other dosage levels; on the four item memory load they responded more slowly when receiving 0.6 and 0.9 mg/kg than when receiving placebo or 0.3 mg/ kg. In the case of the 9 item visual search load, MPH slowed subjects' responses

only on the largest, 4 item memory load; responses on the 0.9 mg/kg dose were significantly slower than on placebo or 0.3 mg/kg. Thus, again, higher dosages of the medication slowed response only in the most difficult, highest load conditions. <u>Variability</u>: Dosage had only minor effects on RT variability. Although there was a significant interaction for intra-subject standard deviation (SD) between dose and memory load size, E(6, 96) = 2.83, g < .03, post hocs on the interaction showed that dosage affected RT significantly only at the two item memory load, where responses were less variable on the 0.6 mg/kg dosage than on placebo. In addition, there were slight differences in the degree to which memory load increased variability at different medication doses; SD was significantly higher on the four item memory load than on the one item load at all dosages, but differences between each of these loads and the medium sized, two item load, were not consistent.

The variability of the children's responses increased as both memory load, E(2, 32) = 64.00, g < .001, and visual search load, E(2, 32) = 44.37, g < .001, increased. An interaction between memory load and search load showed that variability increased further when both loads were high, E(4, 64) = 13.68, g < .001.

### **Behavior and Side Effect Ratings**

Anovas were performed to examine the effects of dosage on Conners Hyperactivity Index scores and effort ratings. On the Conners, there was a significant main effect for dosage, E(3, 48) = 20.134, p < .001. A significant linear trend, E(1, 16)= 25.142, p < .001, accounted for 81.21 % of the variation due to dosage, with a significant quadratic trend, E(1, 16) = 20.99, p < .001, accounting for a further 18.78 %. The linear trend reflected the overall tendency for Conners scores to improve with dosage, while the quadratic trend reflected that the scores reached their minimum at 0.6 mg / kg, with a slight, non-significant increase at 0.9 mg / kg. The mean Conners scores for each of the four dosages, from placebo to 0.9, were 0.79 (SD = 0.58), 0.39 (SD = 0.41), 0.19 (SD = 0.21) and 0.21 (SD = 0.22).

For the effort ratings, there was also a significant main effect for dosage, E(3, 48) = 18.50, g < .001. Trend analyses revealed a significant linear trend, E(1, 16) = 25.33, g < .001, accounting for 85.19 % of the variation due to dose, and a significant quadratic trend, E(1, 16) = 10.85, g < .005, accounting for a further 14.52 %. The linear trend reflected the increase in effort with increased dosage. The quadratic trend showed that the improvements tended to level off at the higher dosage levels, possibly because examiners were already rating children very near the top of the 0 - 6 point effort scale on the 0.6 mg /kg dose. The mean effort scores for each dosage were 4.09 (SD = 1.33), 5.00 (SD = 0.90), 5.40 (SD = 0.41) and 5.47 (SD = 0.52).

Side effects were not a major problem in this acute dosage study. Severity ratings were generally low across all of the symptoms surveyed. Most side effects reported were intermittent, and mild in severity, with ratings of four or less out of a possible nine. Three boys received one or two scores in the 5 - 6 range, one boy for headache, one for dizziness and one for anxiety. Each of these symptoms occurred when medication dosage was 0.6 or 0.9 mg / kg.

# Discussion

The results of Experiment 1 showed that reductions in error rates continued up to

the highest dose of MPH. These findings are consistent with those in a number of dosage studies which found a linear relationship between dose and improvement in task performance (Douglas et al., 1988; Douglas et al., 1995; Evans et al., 1986; Pelham et al., 1985; Rapport & Kelly, 1991; Rapport et al., 1989; Solanto & Conners, 1982).

Although we did not find an interaction between dose and load on the error measure, the effects of MPH on RT were dependent on both load and dosage. The two three - way interactions showed that slowing occurred with higher MPH doses when task demands were high. The first interaction showed that the slowing at the higher doses (0.6 and 0.9 mg/kg) occurred particularly when high visual search loads were combined with the target absent condition, which required the children to continue the search through to the end of the display in order to determine that the target was not present. The slowing seems to reflect increased deployment of effort and the ability to persevere longer with a difficult search. The second three - way interaction showed that the higher doses of MPH also slowed processing particularly when a high memory load was combined with a high visual search load. This combination of conditions required the children to switch attention between memory and search items.

Although several earlier studies using the lower load Sternberg task found speeding with MPH (Brumaghim et al., 1987; Fitzpatrick et al, 1988; Klorman et al, 1992; 1994), we found no evidence that MPH speeded RT, even at the lowest loads included in the VMS task. However, we did find that MPH improved error rates at the lower loads without any concomitant cost in RTs at any dosage. When our results demonstrating slowing effects at higher loads, and those of Klorman and his colleagues, showing

speeding effects on smaller Sternberg task loads, are considered together, they confirm that MPH can speed responding on more automatic, faster paced tasks, while slowing responding on more highly controlled, effortful tasks.

The degree of slowing observed on high loads with high MPH doses was noteworthy. For example, in the highest load, target absent, condition, the overall mean RT slowed to 12229.59 msec at the 0.9 mg/kg dosage, compared with a mean of 8380.90 on placebo. This degree of slowing suggests that higher medication doses caused the children to change the strategy they used to deal with high loads of the task. Although the task instructions placed equal emphasis on speed and accuracy, the fact that improved error rates were accompanied by a dramatic slowing in RTs suggests that the boys were adopting a strategy that favored accuracy over speed on the high loads of the task when they were on higher dosages. This strategy requires considerable effort because it involves persisting with the search until the child feels relatively confident about his response.

It could be argued that the slower RTs show that the higher doses had an adverse effect on cognitive processing. This interpretation would be consistent with previous reports that higher MPH dosages have a negative effect on performance on high load tasks (Sprague & Sleator, 1977; Swanson & Cantwell., 1989; Swanson et al., 1991). However, Sprague and Sleator's findings differed from ours in that they reported both an increase in error rates and an increase in RT at their highest MPH dosage on the high loads of their memory search task. In contrast, we found that error rates continued to decrease up to the highest MPH dose, with a significant linear effect accounting for 87.7% of the

variance. It may be that Sprague and Sleator's procedure, which placed high loads of up to 15 items in the memory set, taxed the limits of the memory ability of the children in their study. In addition, Douglas et al. (1995) pointed out that some studies reporting negative cognitive effects at higher MPH doses used a procedure in which children received two or more medication doses per day. They argue that this procedure may result in medication levels which are higher than intended, due to carry over effects from one dose to the next. Nonetheless, the slowing of RT on the VMS suggests that the children had become extremely cautious. Under circumstances where an error would be very costly, the slowing could be appropriate, while under other circumstances, faster performance might be more desirable.

In addition, we found a close correspondence between the dose - response curves for the behavior ratings and for accuracy. For the error rate, the Conners ratings, and the effort ratings, the linear trend accounted for 80 to 90 % of the variance of the drug effect. Each analysis also showed a small quadratic effect, reflecting that the improvements began to level off, or decrease very slightly, between 0.6 and 0.9 mg/kg. Thus, it appears that selecting medication dosage based on improvements in behavior ratings would also optimize medication effects on cognitive processing on our task. This argues against the suggestion (Cantwell, 1996; Cantwell & Swanson, 1997; Sprague and Sleator, 1977; Swanson et al., 1991) that basing dosage on behavioral effects leads to the prescribing of excessively high MPH doses.

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# **EXPERIMENT 2**

The results of Experiment 1 showed that higher doses of MPH greatly slowed the RTs of boys with ADHD when they were required to process high cognitive loads. This slowing effect appeared to be restricted to task conditions where loads were high. In Experiment 2, we compared the performance of boys with ADHD to control boys on the VMS task. We were interested in determining whether children with ADHD had particular difficulty processing high loads. If this were so, it would suggest that they required the extra time expenditure on high MPH doses in order to improve their performance.

There are several previous studies in which the performance of children with ADHD was compared with that of controls on the lower load Sternberg (1969) memory search task (Sergeant & Scholten, 1983; 1985; Sergeant & van der Meere, 1990; Van der Meere, Gunning, & Stemerdink, 1996; Van der Meere & Sergeant, 1987; van der Meere, van Baal, & Sergeant, 1989). Sergeant and his colleagues found that children with ADHD had slower and more variable RTs and lower accuracy levels than controls. They did not, however, find an interaction between diagnosis and memory load; both groups showed a similar pattern of slowing RTs and increasing error rates, as memory load increased. Thus, children with ADHD did not have differential difficulty processing high loads.

The memory loads used by Sergeant and his colleagues, however, were relatively low (memory or visual search loads of up to 4 items) (Sergeant & Scholten, 1983; 1985; van der Meere & Sergeant, 1987; van der Meere et al., 1989; 1996). In addition, several of the studies used a fixed memory set procedure, rather than a more demanding varied set

(Sergeant & Scholten, 1983; 1985; van der Meere et al., 1989). Several investigators have shown that children with ADHD are more likely to have relative difficulty with tasks that require highly effortful processing. For example, several studies have shown intact performance on relatively simple memory tasks, such as recognition or cued recall, while deficits appear on more effortful free recall (Borcherding, Thompson, Kruesi, Bartko, Rapoport, & Weingartner, 1988; Weingartner, Rapoport, Buchsbaum, Bunney, Ebert, Mikkelsen, & Caine, 1980). Similarly, Douglas and Benezra (1990) found that children with ADHD did not differ from normal controls when they were asked to memorize lists of related word pairs, whereas deficits appeared on pairs of unrelated words, which require more organized effort to learn. In addition, the group differences appeared on later learning trials, where organized rehearsal strategies and persistence become more important.

Several studies have also shown that children with ADHD are less likely than other children to use effortful task strategies. They tend to allocate less time and effort to learning material and attempting to recall it (O'Neill & Douglas, 1991; 1996). They are less likely to use the more active, effortful strategy of grouping words, when learning word lists (August, 1987; O'Neill & Douglas, 1996). They also tend to use less effortful strategies to categorize items in stimulus classification tasks (Amin, Douglas, Mendelson, & Dufresne, 1993). These findings suggested that our ADHD group would have relatively more difficulty than controls on the high load conditions of the VMS, since to deal with the higher loads it is necessary to make an organized, effortful search through the large number of items in the search and memory sets, and to coordinate the two searches.

Although we predicted that boys with ADHD would have relatively higher error rates than controls on high loads of the VMS, we considered two possible ways in which difficulties on high loads might affect RT when the boys were not receiving MPH. First, it was possible that the boys with ADHD would respond more quickly and impulsively than controls when dealing with high loads. Impulsive responding has been reported in children with ADHD on the Matching Familiar Figures Task (MFFT), which requires careful, organized search (Brown, 1983; Campbell et al., 1971; Cohen et al., 1972; Conte, 1986; White & Sprague, 1992). If the RTs of the boys in the ADHD group were faster than those of the boys in the control group under high load conditions, it could be argued that the higher doses of MPH brought less effortful, impulsive responding under control. Alternatively, the ADHD group might show slower RTs, as well as higher error rates, than the control group, as found by Sergeant and his colleagues on the lower load Sternberg task (Sergeant & Scholten, 1983; 1985; Sergeant & van der Meere, 1990; van der Meere & Sergeant, 1987). In this case, it would be necessary to conclude that the effect of MPH on high loads was to make their already slow RTs even slower.

# Method

# **Participants**

Forty boys participated in the study. Twenty met the criteria for a DSM-III-R diagnosis of ADHD and twenty were controls. The boys' ages ranged from 7 to 13 years. As in Experiment 1, all boys had IQs over 85. All of the boys spoke English as their first language.

Boys with ADHD were recruited from the McGill University-Montreal Children's Hospital Hyperactivity Project, using the same criteria as in Experiment 1. Since twelve of the boys also participated in Experiment 1, it was possible to use the data collected on their medication-free, baseline day in this study. Data for the remaining eight boys was also collected during medication- free baseline days before they participated in another medication trial in our laboratory. As in Experiment 1, the boys were screened for a number of co-morbid disorders. Twelve (60 % of the sample) met DSM-III-R criteria for ODD, and three (15%) met minimal criteria for CD, but these symptoms were not considered serious enough to require exclusion from the study. Five (25 %) had ratings above the criterion score for anxiety on the Revised Behavior Problem Checklist (Quay & Peterson, 1983, 1987). However, the other available evidence, such as age of onset, suggested that these symptoms were secondary to ADHD. Three (15%) of the boys scored two or more years below grade level on both the Word Identification and Passage Comprehension subtests of the Woodcock Reading Mastery Tests - Revised (Woodcock, 1987), and another two (10%) scored two years behind on Passage Comprehension only. The boys were required to be free of medication for a minimum of 48 hours prior to testing.

Boys in the control group were recruited through a newspaper advertisement. Parents had to report that the children were not experiencing behavioral problems at home or at school, and the boys had to receive ratings of less than 1.5 on the Hyperactivity index of the parent version of the Revised Conners Rating Scale (Goyette et al., 1978). Boys were excluded from the study if they met DSM-III-R criteria for ADHD, ODD or

CD. The boys were also screened for anxiety problems using the Revised Behavior Problem Checklist (Quay & Peterson, 1983; 1987), and for reading problems using the Word Identification subtest of the Woodcock (Woodcock, 1987). None of the boys included in the study met criteria for either problem.

Data on age, IQ, SES, and Conners scores for the ADHD and control groups appears in Table 1. The two groups did not differ significantly on age, IQ or SES (ps >.05). As expected, the Conners scores for the ADHD group were significantly higher than those of the controls, t(38) = 13.09, p < .001.

#### <u>Task</u>

The same version of the VMS task used in Experiment 1, with memory loads of one, two and four items, and visual search loads of 4, 9 and 16, was used in this study.

### **Results**

A 2 (diagnosis) X 2 (target condition) X 3 (visual search load) X 3 (memory load) analysis of variance was conducted for each of the three variables; error rate, RT, and SD. Full degrees of freedom are reported, but for within subjects effects, the significance levels reported reflect the Greenhouse-Geisser correction. For pairwise comparisons, Tukey's HSD tests were used ( $\alpha = .05$ ). Only data for correct responses were included in the RT analyses. For significant effects involving diagnosis,  $\eta^2$  was used as a measure of effect size.

<u>Errors</u>: Table 2 displays means for percentage of errors as a function of diagnosis, visual search and memory load. The most important finding for the error data was a main effect for diagnosis, showing that boys with ADHD made more errors than control boys across

all conditions,  $\mathbf{E}(1, 38) = 11.07$ ,  $\mathbf{g} < .002$ ,  $\eta^2 = .23$ . Boys with ADHD had a mean error rate of 21.88 % (SD = 8.1) and controls had a mean error rate of 14.93 % (SD = 4.6). Contrary to our expectations, none of the interactions between diagnosis and the three task variables reached significance. Thus, although the boys with ADHD made more errors overall, the two groups of boys were affected similarly by the load variables and the target conditions.

As expected, main effects showed that the combined subject groups made more errors as either memory load,  $\mathbf{E}(2, 76) = 55.60$ ,  $\mathbf{g} < .001$ , or visual search load,  $\mathbf{E}(2, 76)$ = 14.93,  $\mathbf{g} < .001$ , increased. Post hoc comparisons on the search load main effect showed that subjects made more errors on the 16 item matrix than on the two smaller matrices. A main effect for target condition indicated that they also made more errors on target present than on target absent trials,  $\mathbf{E}(1, 38) = 59.98$ ,  $\mathbf{g} < .001$ . There was an interaction between memory load size and target condition,  $\mathbf{E}(2, 76) = 15.31$ ,  $\mathbf{g} < .001$ . Post hoc tests showed that the size of the memory load affected errors only on target present trials, with the children making more errors on the highest memory load than on either of the two smaller memory loads. As in Experiment 1, post hocs showed that the finding of more errors on target present than target absent trials was significant only for the two larger memory loads. Thus, in both experiments the children were more likely to miss a target when they were dealing with higher loads.

<u>Mean Reaction Time</u>: Table 2 displays means for RT as a function of diagnosis, visual search and memory load. There was one significant effect involving diagnosis: a main effect showing that ADHD children responded more slowly than normal controls, E(1, 1)

38) = 5.89, p < .02,  $\eta^2 = .13$ . The mean RT of the ADHD group was 3233.70 msec (SD = 826.3), compared to a mean RT for the control group of 2643.70 msec (SD = 706.9). As with the error scores, there were no interactions involving diagnosis, indicating again that, although the boys with ADHD had higher overall error rates and slower RTs, both groups were affected similarly by the task manipulations.

As expected, main effects indicated that both groups of boys responded more slowly as memory load, E(2, 76) = 138.91, p < .001, and visual search load, E(2, 76) =97.03, p < .001, increased. In addition, an interaction between the two load variables showed that a combination of high loads on both of these factors caused the most slowing, F(4, 152) = 10.65, p < .001. Also as expected, a target condition main effect showed that the combined groups were slower on target absent than on target present trials, F(1, 38)= 119.74,  $\underline{p} < .001$ . Target condition also interacted with both memory load, <u>F</u> (2, 76) = 23.83, p < .001, and visual search load, F(2, 76) = 43.57, p < .001. In addition, the three way interaction between memory load, visual search load and target condition, was significant, F(4, 152) = 4.84, p < .003. Pairwise comparisons on this interaction showed that, in most cases, an increase in either of the load variables resulted in a significant increase in RT, with the few exceptions occurring when both loads were small, such as when the memory load increased from one to two items on the smallest search set. The pairwise comparisons also showed that the slowing effect of the target absent condition, as opposed to the target present condition, reached significance only for the two larger search set sizes. Both groups of boys required more time to make a negative decision only when they were required to search a large number of items.

<u>Variability</u>: A main effect for diagnosis showed that the RTs of the boys in the ADHD group were significantly more variable than those of the controls, E(1, 38) = 10.52, p < .002. Main effects also showed that the RTs of both groups became more variable as memory load, E(2, 76) = 37.72, p < .001, and search load, E(2, 76) = 38.67, p < .001, increased. An interaction indicated that both groups showed still greater variability when both the memory load and the visual search load were high, E(4, 152) = 3.45, p < .02. A target condition main effect showed that the children's RTs were also more variable on target absent than on target present trials, E(1, 38) = 13.96, p < .001.

# Discussion

The results of Experiment 2 showed that, while both groups of boys had more difficulty as memory and search loads increased, the boys with ADHD made more errors than controls, and had slower and more variable RTs, across all loads of the VMS task. However, the results did not support our prediction that boys with ADHD would have relatively greater difficulty than control boys with higher loads.

The failure to find an interaction between diagnosis and load on both the RT and error measures is consistent with results from earlier studies comparing the performance of ADHD and control groups on the lower load Sternberg task. As in our experiment, while both groups showed greater difficulty as loads increased, the performance of children with ADHD was less accurate, slower, and more variable than that of controls across loads, and there was no interaction between load and diagnosis (Sergeant & Scholten, 1983; 1985; Sergeant & van der Meere, 1990; van der Meere et al., 1996; van der Meere & Sergeant, 1987). Thus, it appears that children with ADHD have difficulty maintaining speed and accuracy on search tasks across the wide range of processing loads used in our study.

The likelihood of showing an interaction indicating that the ADHD group was having particular difficulty on high loads may have been reduced by the fact that the boys with ADHD were clearly having difficulty even on the lowest loads. Although previous studies also showed that children with ADHD had more difficulty than controls with visual and memory search tasks even at relatively low loads (Sergeant & Scholten, 1983; 1985; Sergeant & van der Meere, 1990; van der Meere & Sergeant, 1987), the degree of difficulty that our ADHD group showed on the smallest VMS loads was surprising. On our smallest load condition, consisting of one memory item, and four visual search items. the mean RT for the ADHD group in the target present condition was 1713.82 msec. compared with 1232.52 msec for the control group. In addition, their mean error rate was 15.0 %, compared with 9.4 % for the control group. In the studies by Sergeant and his colleagues, although children with ADHD had more difficulty than controls, their mean RTs for comparable load conditions generally remained below 1400 msec, and their error rates were usually below 10 %. Thus, even with VMS loads that were as small as those used in the earlier studies, the boys in our study responded more slowly and made more errors.

There are several possible reasons why even the low loads of the VMS task presented difficulty for the ADHD group. The use of a varied memory set, in which the boys had to learn a new set of target items before each trial, increased the difficulty level of the task, and thus the requirement for effortful processing (Shiffrin, 1988). Even more

importantly, although the visual search loads were presented in blocks of the same load, the three memory load sizes were randomly mixed for presentation. Thus, the children had to deal with memory load sizes which changed from one trial to the next. The presence of the higher loads within each block may have established an overall "set" to respond slowly. Leung & Connolly (1996) reported that the presence of difficult items within a block of trials slowed performance of children with ADHD, even on trials which did not contain the difficult stimuli. In addition, there is accumulating evidence that children with ADHD have particular difficulty when they must respond flexibly to changing task conditions. They have been shown to have difficulty with unpredictable preparation intervals on warned RT tasks (Elbaz & Douglas, 1998; Zahn, Kruesi, & Rapoport, 1991), and with unpredictable response requirements on a version of the Stroop task in which a tone was used on each trial to signal to the child whether to read the item, or name its colour (Berman, Douglas, & Dunbar, 1994).

It is interesting to note that two studies have reported an interaction between diagnosis and load indicating that children or adolescents with ADHD had relatively greater difficulty than controls on high loads as compared to low loads on the Sternberg task (Klorman et al., 1992; Leung and Connolly, 1994). In both studies, the smallest cognitive load consisted of one memory item and one search item. Klorman et al. reported, however, that the group by load interaction no longer reached significance when they excluded the load consisting of 1 item in each set from their analysis. They point out that processing of single items does not require serial scanning. Thus, although the performance of children with ADHD is relatively unimpaired when only simple

comparisons are required, difficulties become apparent when even very limited search is required.

It should be noted that the data from Experiments 1 and 2 cannot be compared directly, since in Experiment 2 the boys carried out the task only once, while in the medication study they carried out the task repeatedly (eight times), and thus were more highly practiced. Nonetheless, the results of Experiment 2 provide a context for understanding the comparisons between performance on placebo and the different dosages of MPH in Experiment 1. Experiment 2 showed that the RTs of boys with ADHD were slower than those of controls. Thus, MPH further slowed their already slow RTs. This finding supports the interpretation that higher doses of MPH brought about a change in strategy on the higher loads, in which the boys with ADHD emphasized accuracy over speed.

# **EXPERIMENT 3**

In Experiment 3 we examined the effect of age on the performance of normal boys across the range of processing loads assessed by the VMS task. We were surprised, in Experiment 2, by the high degree of difficulty boys with ADHD had even on low loads of the task. We suggested that this might be attributable to task characteristics of the VMS, including the use of varied memory sets, and the mixing of memory loads. We wondered whether young children would also have difficulty with low loads under these conditions, or whether this vulnerability to varying task parameters was specific to ADHD.

A number of investigators have examined age effects on other visual or memory search tasks in normal samples. Typically, they found that RTs became faster and error

rates decreased with age (Bisanz & Resnick, 1978; Harris & Fleer, 1974; Herrmann & Landis, 1977; Kail, 1988; Keating & Bobbitt, 1978; Keating, Keniston, Manis, & Bobbitt, 1980; van der Meere et al., 1996). Findings with respect to age by load interactions have been inconsistent. Some studies covering a wide age range, comparing the performance of young children with adolescents and adults, reported an age by load interaction for RT, indicating that young children had relatively greater difficulty with high loads than adolescents or adults (Bisanz & Resnick, 1978; Herrmann & Landis, 1977; Kail, 1988; Keating et al., 1980). Other investigators failed to find an interaction between age and load either between pre-adolescents of different ages, or between young children and adults (Harris & Fleer, 1974; Klorman et al., 1994; van der Meere et al., 1996).

#### Method

#### **Participants**

As described in Experiment 2, normal boys aged 7 to 13 years were recruited through a newspaper advertisement. Forty-one boys participated in Experiment 3. These included the twenty boys tested in Experiment 2, and an additional twenty-one others who were recruited using the same criteria. The parents had to report that the children were not experiencing behavior problems at home or at school. In addition, the children had to receive ratings of less than 1.5 on the Hyperactivity index of the parent version of the Revised Conners Rating Scale (Goyette, Conners, & Ulrich, 1978), and could not meet the criteria for a DSM-III-R diagnosis of ADHD, oppositional defiant disorder (ODD) or conduct disorder (CD). The boys were also screened for reading difficulties and anxiety symptoms. Four boys (9.8 % of the sample) had scores slightly above the criterion level for anxiety-withdrawal on the Revised Behavior Problem Checklist. However, interviews with parents, as well as other available information, suggested that these symptoms were not serious enough to require exclusion from the study. In addition, one boy (2.4 % of the sample) had a score two or more grades behind his own grade on the Woodcock Word Identification subtest. The boys had a mean age of 126.3 months, SD = 22.9, a mean IQ score of 117.5, SD = 12.8, a mean Hollingshead SES score of 4.2, SD = 0.9, and a mean Conners rating of 0.42, SD = .37.

The boys were divided into three age groups, young (9 years and under,  $\underline{n} = 14$ ,  $\underline{M} = 99.9$  months,  $\underline{SD} = 12.34$ ), medium (10 to 11 years,  $\underline{n} = 17$ ,  $\underline{M} = 132.1$  months,  $\underline{SD} = 7.4$ ) and older (12 years and over,  $\underline{n} = 10$ ,  $\underline{M} = 153.3$  months,  $\underline{SD} = 7.6$ ). The three groups did not differ significantly on IQ,  $\underline{F}(2, 38) = .32$ ,  $\underline{p} > .05$ ; means for the young, medium and older groups were 115.3,  $\underline{SD} = 13.7$ , 118.6,  $\underline{SD} = 13.6$ , and 118.8,  $\underline{SD} = 10.8$ , respectively. The mean SES for the youngest group was significantly, but only slightly, lower than those of the two older groups,  $\underline{F}(2, 38) = 6.80$ ,  $\underline{p} < .01$ ; means were 3.57,  $\underline{SD} = 0.76$ , 4.41,  $\underline{SD} = 0.80$ , and 4.60,  $\underline{SD} = 0.70$ , respectively.

# <u>Task</u>

The VMS task and testing procedure were identical to those of the two previous studies.

### Results

A 3 (age group) X 2 (target condition) X 3 (memory load) X 3 (visual search load) analysis of variance was conducted for each of the three variables, error rate, RT, and variability of RT. As in the previous studies, full degrees of freedom are reported, but for

within subjects effects, the significance levels reported reflect the Greenhouse-Geisser correction. For pairwise comparisons, Tukey's HSD tests were used ( $\alpha = .05$ ), and only data for correct responses were included in the RT analyses. For significant effects involving age,  $\eta^2$  was used as a measure of effect size.

Errors: Table 3 displays means for percentage of errors as a function of age, visual search and memory load. A main effect for age showed that error rates decreased with age, E (2, 38) = 4.96, p < .01,  $\eta^2 = .21$ . A main effect for target condition, E (1, 38) = 115.92, p <.001, showed, as expected, that the boys made more errors in the target present than in the target absent condition. There was also a main effect for memory load, E (2, 76) = 59.71, p < .001, showing that error rates increased with size of memory load.

These effects were modified by two two-way interactions, one between age and target condition,  $\mathbf{E}(2, 38) = 3.68$ ,  $\mathbf{p} < .05$ ,  $\eta^2 = .16$ , and one between memory load and target condition,  $\mathbf{E}(2, 76) = 17.52$ ,  $\mathbf{p} < .001$ . In addition, there was a three way interaction between age, target condition and memory load size  $\mathbf{E}(4, 76) = 3.82$ ,  $\mathbf{p} < .01$ ,  $\eta^2 = .17$ . Post hoc testing on the three way interaction showed that the youngest group of boys made significantly more errors than each of the older groups on the highest, four item memory load, in the target absent condition. Thus the younger boys had a significantly higher error rate than the older boys only at the highest memory load, in the target absent condition. In addition, the post hocs showed that, for the youngest group of boys, increasing memory loads lead to higher error rates in both the target present and target absent conditions, while for the two older groups of boys, higher memory loads resulted in high error rates only in the target present condition.

A main effect for visual search load showed that error rates also increased with search set size, E(2, 62) = 8.54, p < .001. Post hocs showed that the children made more errors on the 16 item search load than on either of the two smaller search loads. Visual search load did not interact with age, or with any of the other variables.

Mean Reaction Time: Table 3 displays means for RTs as a function of age, visual search load and memory load. There was only one significant effect involving age, a main effect showing that older children responded faster overall, E(2, 38) = 5.65, p < .007,  $\eta^2 = .23$ . Pairwise comparisons between the age groups showed that the oldest group responded significantly faster than both the younger groups. The mean RTs for each of the three age groups from youngest to oldest (with SD's in parentheses) were 3060.66 (882.68), 2905.29 (611.39), and 2165.70 (360.97) msec.

The remaining results did not differentiate among the three age groups. As would be expected, larger loads were associated with longer RTs, as shown by main effects for both memory load,  $\mathbf{E}(2, 76) = 127.9$ ,  $\mathbf{p} < .001$ , and for visual search load,  $\mathbf{E}(2, 76) =$ 156.76,  $\mathbf{p} < .001$ . In addition, there was an interaction between the two load variables,  $\mathbf{E}(4, 152) = 13.85$ ,  $\mathbf{p} < .001$ , with responses slowing still further when both types of load were high. A main effect for target condition showed that the children responded more slowly in the target absent than in the target present condition,  $\mathbf{E}(1, 38) = 150.56$ ,  $\mathbf{p} <$ .001. Target condition also interacted with both memory load,  $\mathbf{E}(2, 76) = 25.3$ ,  $\mathbf{p} < .001$ , and visual search load,  $\mathbf{E}(2, 76) = 58.53$ ,  $\mathbf{p} < .001$ . There was also a three way interaction between memory load, visual search load and target condition,  $\mathbf{E}(4, 152) = 3.68$ ,  $\mathbf{p} <$ .007, showing that responses were slowed still further when both types of load were high, particularly in the target absent condition.

<u>Variability</u>: A main effect for age group showed that variability of RT decreased with age, E(2, 38) = 5.57, g < .008. Post hoc tests showed that the youngest children were more variable in their responding than the oldest group. Mean intra-subject standard deviations for each group, from youngest to oldest, were 1011.84, 838.21, and 620.30 msec.

There were also significant main effects for memory load size,  $\mathbf{E}(2, 76) = 29.27$ ,  $\mathbf{p} < .001$ , and for search load size,  $\mathbf{E}(2, 76) = 53.68$ ,  $\mathbf{p} < .001$ , showing that the children responded more variably on higher loads. In addition, the two types of load interacted,  $\mathbf{E}(4, 152) = 7.45$ ,  $\mathbf{p} < .001$ . Post hocs on the interaction showed that variability was increased further when both types of load were high. Finally, there was a main effect for target condition,  $\mathbf{E}(1, 38) = 4.11$ ,  $\mathbf{p} < .05$ , showing that responses were more variable in the target absent than the target present condition.

#### Discussion

Consistent with earlier studies using visual and memory search tasks, error rates decreased with age, and older children responded faster overall than younger children (Bisanz & Resnick, 1978; Harris & Fleer, 1974; Herrmann & Landis, 1977; Kail, 1988; Keating & Bobbitt, 1978; Keating et al., 1980). We did not find a significant interaction between age and load on the RT measure, indicating that the responses of children in the different age groups were slowed to a similar degree by increasing loads.

The RT measure revealed similarities between the ways the youngest group and children with ADHD carried out the task. Both groups showed a pattern of slow responses at all task loads, including the lowest load conditions. The RTs of the youngest group on low loads closely resembled those of the ADHD group in Experiment 2, despite the fact that the mean age of the ADHD group was considerably higher (mean ages of the ADHD group and the youngest group were 128.9 and 99.9 months respectively). For example, in the lowest load condition, for target present trials, the mean RT of the ADHD group, 1713.82 msec, resembled that of the youngest group, 1738.44 msec. The fact that the youngest group, like the ADHD group, had difficulty with both low and high load conditions supports the conclusion that even the low VMS loads were demanding, perhaps due to the unpredictable presentation conditions in which high and low memory loads were mixed together. The similarities between the performance of children with ADHD and younger controls also suggests cognitive immaturity in the ADHD group.

The youngest group differed from the children with ADHD in only one way. The youngest group of children had relatively greater error rates than the two older groups on the highest memory load, target absent, condition. This finding indicates that the accuracy level of the youngest group was particularly affected by the high memory loads. It may be that the young children had difficulty remembering all of the items in the highest load. Children with ADHD did not encounter this particular difficulty with high memory loads.

# **General Discussion**

We hypothesized that higher doses of MPH would be particularly effective in enabling boys with ADHD to allocate the necessary effort and persistence to improve their performance under complex, high load conditions. Although we did not obtain a significant interaction between dose and load on the error measure, the results from Experiment 1 demonstrated that MPH enabled the ADHD group to show improvement in their error rates across all loads. Moreover, MPH effects on RT were load-dependent. At low loads, the improvement in accuracy occurred with no cost in RT at all doses of MPH, while at the higher loads, higher doses slowed RTs considerably. Although the VMS was particularly designed to include heavy processing loads, Experiment 2 showed that children with ADHD showed surprising difficulty even at the lowest loads. The developmental data confirmed that the low loads of the VMS task were also difficult for young children.

The findings on the RT measure in Experiment 1 suggest that, while MPH reduced errors to a similar degree at all loads, the drug acted differentially at low and high loads of the VMS task. The improvement in performance on lower loads resembled previous MPH findings from lower load tasks, including the Sternberg (Brumaghim et al., 1987; Coons et al., 1987; Fitzpatrick et al., 1988; Klorman et al., 1992; Klorman et al., 1994; Peloquin & Klorman, 1986), as well as other tasks such as the CPT (Coons et al, 1987; Klorman et al, 1979; Losier et al., 1996; Peloquin & Klorman, 1986) and warned RT tasks (Sykes et al., 1972; Douglas et al., 1988). The effects of MPH on these relatively fast-paced tasks appears to involve an increase in processing efficiency, since errors decreased with either no cost, or a speeding, in RT. As Klorman (Klorman et al., 1994) pointed out, this result is analogous to the effects of maturity on cognitive processing, since children show both improved accuracy and faster RTs with increasing age. This pattern was observed in Experiment 3, where both errors and RT decreased with age.

The MPH-induced improvements in processing efficiency at low loads may reflect an increase in allocation of attentional capacity. Several investigators have used the

amplitude of the P300 component of EEG event related potentials during task performance to assess the amount of processing capacity allocated to a task. Smaller P300 amplitudes have been observed in children with ADHD (Holcomb, Ackerman, & Dykman, 1985; Klorman et al., 1979; Loiselle, Stamm, Maitinsky, & Whipple, 1980; Michael, Klorman, Salzman, Borgstedt, & Dainer, 1981). In addition, Klorman et al. (1994) found that MPH increased the amplitude of P300 during performance on the Sternberg task, suggesting that MPH acted to increase the allocation of attention. There have been similar reports showing that MPH increases P300 amplitude on the CPT (Coons et al., 1987; Klorman, 1991; Peloquin & Klorman, 1986).

The results on higher loads of the VMS, however, were very different. While higher MPH doses produced continued improvement in accuracy, the improvement was accompanied by an increase in RT. This pattern partially resembles previous findings with the MFFT, where MPH has been found to slow RTs (Campbell et al., 1971; Douglas et al., 1988; Rapport et al., 1988). However, on the MFFT, the medication acts to reduce fast and careless responding. On the VMS, the slow RTs of the ADHD group before they received medication suggest that MPH helped them to slow down even further to compensate for their difficulty performing the task.

The fact that MPH slowed performance only on the most difficult, high load conditions supports Douglas' hypothesis that the drug improves regulatory ability (Douglas et al., 1986; 1988; 1995). Rather than slowing RT at all loads of the task, MPH enabled the children to devote more processing time under the most challenging conditions. Moreover, since higher and lower memory loads were presented in

randomized order within each block, the medication appears to have allowed the boys to slow down on difficult trials, while maintaining speed on easier trials within the same block. The results are also consistent with the observations of dosage effects made by Rapport and Kelly (1991) in their literature review. They noted that, across a wide variety of tasks, carried out by many different researchers, higher dosages appeared to be most effective on complex, effortful tasks. The medication study succeeded in demonstrating this effect by contrasting more and less complex conditions within the same task. The slowing effects of higher doses of MPH on RT appeared only under the more complex task conditions.

Since gains in accuracy were levelling off at the higher MPH doses, there is some indication that the slowing of RT at the highest doses constituted a heavy time expenditure to achieve relatively minor further improvement. Thus, in selecting appropriate clinical dosages for children with ADHD, it may be important to consider whether the child's response style becomes excessively slow and cautious under higher dose conditions. This is particularly true since stimulant dose response curves for children with ADHD are highly individual, meaning that the appropriate dosage for each child must be titrated independently (Rapport et al., 1988; Vyse & Rapport, 1989). Moreover, in clinical practice, children with ADHD are typically given two or more doses per day. This may result in dosage levels which are higher than intended, due to carryover effects (Douglas et al., 1995).

In summary, although children with ADHD had more difficulty than controls across all loads of the VMS task, stimulant medication effects differed on low versus high

loads. On lower processing loads, MPH allowed boys with ADHD to improve their accuracy, without significant cost in RT. On higher loads, higher medication doses allowed further improvement in accuracy, but with an apparent strategic change involving substantial slowing in RTs. These results demonstrate that MPH did not slow responding indiscriminately, but enabled children with ADHD to respond differentially to high versus low loads.

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# Table 1

# Demographic and Clinical Characteristics of the ADHD and Control Groups

| Measure      | ADHD Group |       | Control Group |           |
|--------------|------------|-------|---------------|-----------|
|              | М          | SD    | М             | <u>SD</u> |
| Age (months) | 128.85     | 19.12 | 127.80        | 23.14     |
| IQ           | 106.83     | 9.39  | 114.08        | 11.04     |
| SES          | 3.84       | 1.01  | 4.10          | 0.85      |
| Conners      |            |       |               |           |
| Parent       | 2.16       | 0.40  | 0.45          | 0.42      |
| Teacher      | 1.99       | 0.45  |               |           |
Table 2

# Experiment 2 - Mean Error Rates and Reaction Times for ADHD and Control Groups

| visual Search Load 4 | Mean (SD) |                         |                  |                         |  |  |
|----------------------|-----------|-------------------------|------------------|-------------------------|--|--|
|                      | AI        | OHD                     | Control          |                         |  |  |
| Memory Load 1        |           |                         |                  |                         |  |  |
| Percent Error        | 15.31     | (10.44)                 | 7.19             | (6.50)                  |  |  |
| Reaction Time (msec) | 1781.51   | (476.49)                | 1320.44          | (351.73)                |  |  |
| Memory Load 2        |           |                         |                  |                         |  |  |
| Percent Error        | 14.38     | (8.86)                  | 10.00            | (11.18)                 |  |  |
| Reaction Time (msec) | 2260.38   | (544.43)                | 1735.00          | (495.75)                |  |  |
| Memory Load 4        |           |                         |                  |                         |  |  |
| Percent Error        | 22.50     | (11.36)                 | 17.81            | <b>(</b> 9. <b>58</b> ) |  |  |
| Reaction Time (msec) | 2795.00   | (883.01)                | 2247.42          | (611.44)                |  |  |
| isual Search Load 9  | Mean (SD) |                         |                  |                         |  |  |
|                      | ADHD      |                         | Control          |                         |  |  |
| Memory Load 1        |           |                         |                  |                         |  |  |
| Percent Error        | 13.13     | <b>(</b> 11. <b>98)</b> | 9.69             | <b>(8</b> .71)          |  |  |
| Reaction Time (msec) | 2185.48   | (594.90)                | 1 <b>796</b> .01 | (622.55)                |  |  |
| Memory Load 2        |           |                         |                  |                         |  |  |
| Percent Error        | 16.88     | (14.91)                 | 10.94            | (9.91)                  |  |  |
| Reaction Time (msec) | 2992.47   | <b>(1150.98)</b>        | 2421.06          | (699.49)                |  |  |
| Memory Load 4        |           |                         |                  |                         |  |  |
| Percent Error        | 30.00     | (11.93)                 | 23.44            | (12.96)                 |  |  |
| Reaction Time (msec) | 3818.60   | (1234.00)               | 3315.28          | (1129.32                |  |  |

| Visual Search Load 16 | Mean (SD) |           |         |           |  |  |
|-----------------------|-----------|-----------|---------|-----------|--|--|
|                       | AI        | OHD       | Control |           |  |  |
| Memory Load 1         |           |           |         |           |  |  |
| Percent Error         | 24.06     | (13.65)   | 10.00   | (8.46)    |  |  |
| Reaction Time (msec)  | 3273.93   | (940.28)  | 2662.72 | (857.11)  |  |  |
| Memory Load 2         |           |           |         |           |  |  |
| Percent Error         | 26.88     | (15.33)   | 17.19   | (8.81)    |  |  |
| Reaction Time (msec)  | 4421.57   | (1492.77) | 3532.81 | (985.93)  |  |  |
| Memory Load 4         |           |           |         |           |  |  |
| Percent Error         | 33.75     | (16.40)   | 28.13   | (15.38)   |  |  |
| Reaction Time (msec)  | 5574.34   | (2243.50) | 4762.56 | (1884.60) |  |  |

## Table 3

RT (msec)

3828.50

(1688.16)

3659.30

(913.87)

2694.60

(818.72)

| Visual Search Load 4 | Mean (SD) |                 |                 |          |         |          |  |
|----------------------|-----------|-----------------|-----------------|----------|---------|----------|--|
|                      | Younger   |                 | Middle          |          | Oldest  |          |  |
| Memory Load 1        |           |                 |                 |          |         |          |  |
| Percent Error        | 12.05     | (13.08)         | 5.51            | (6.20)   | 7.50    | (3.95)   |  |
| RT (msec)            | 1718.78   | (464.56)        | 1288.31         | (175.02) | 1047.54 | (219.69) |  |
| Memory Load 2        |           |                 |                 |          |         |          |  |
| Percent Error        | 10.26     | (7.99)          | 8.09            | (6.90)   | 6.25    | (13.50)  |  |
| RT (msec)            | 2148.72   | (535.93)        | 1757.19         | (352.44) | 1300.34 | (158.17) |  |
| Memory Load 4        |           |                 |                 |          |         |          |  |
| Percent Error        | 21.88     | (12.91)         | 13.60           | (9.69)   | 15.63   | (8.96)   |  |
| RT (msec)            | 2646.65   | (703.37)        | 2300.54         | (511.70) | 1741.68 | (225.30) |  |
| Visual Search Load 9 | Mean (SD) |                 |                 |          |         |          |  |
|                      | Younger   |                 | Middle          |          | Oldest  |          |  |
| Memory Load 1        |           |                 |                 |          |         |          |  |
| Percent Error        | 12.05     | (6.70)          | 6.99            | (7.61)   | 4.37    | (6.63)   |  |
| RT (msec)            | 2256.35   | (686.57)        | 1859.95         | (422.14) | 1375.91 | (220.06) |  |
| Memory Load 2        |           |                 |                 |          |         |          |  |
| Percent Error        | 12.50     | (12.98)         | 9.56            | (7.03)   | 8.75    | (5.28)   |  |
| RT (msec)            | 2931.44   | <b>(910.98)</b> | 2605.9 <b>8</b> | (763.81) | 1968.43 | (326.93) |  |
| Memory Load 4        |           |                 |                 |          |         |          |  |
| Percent Error        | 20.99     | (13.34)         | 19. <b>8</b> 6  | (11.95)  | 19.38   | (14.63)  |  |

# Experiment 3 - Mean Error Rates and Reaction Times by Age Group

| Visual Search Load 16 | Mean (SD) |           |         |                         |                |                         |  |
|-----------------------|-----------|-----------|---------|-------------------------|----------------|-------------------------|--|
|                       | Younger   |           | Middle  |                         | Oldest         |                         |  |
| Memory Load 1         |           |           |         |                         |                |                         |  |
| Percent Error         | 12.50     | (10.96)   | 9.56    | (9.14)                  | 7.50           | (6.45)                  |  |
| RT (msec)             | 3086.81   | (926.33)  | 2943.73 | <b>(688</b> .10)        | 2197.53        | (338.31)                |  |
| Memory Load 2         |           |           |         |                         |                |                         |  |
| Percent Error         | 22.33     | (10.60)   | 12.86   | (6.43)                  | 11.88          | <b>(</b> 9.9 <b>8</b> ) |  |
| RT (msec)             | 3993.05   | (1182.87) | 4029.91 | (931.72)                | <b>3010.92</b> | (584.68)                |  |
| Memory Load 4         |           |           |         |                         |                |                         |  |
| Percent Error         | 34.83     | (19.73)   | 26.10   | <b>(</b> 10. <b>89)</b> | 21.25          | (12.23)                 |  |
| RT (msec)             | 4935.66   | (2293.67) | 5702.69 | (1854.92)               | 4154.40        | (1284.99)               |  |

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## **Figure Captions**

Figure 1. The effect of dosage on RT at three visual search loads for the target present and target absent conditions.

Figure 2. The effect of dosage on RT at three visual search loads, for the three memory loads.





#### General Conclusions

The three studies presented in this dissertation focused on the role of information processing load in a complex search task as a determinant of regulatory demands in boys with ADHD. The studies investigated the role of information load in determining: the effects of the stimulant medication, MPH, on performance; differences between children with ADHD and control boys; and normal developmental changes in performance. Since the three experiments have been accepted as an integrated paper for publication in The Journal of Abnormal Psychology, the manuscript of the paper includes a General Discussion, in which the results of the three studies are discussed together (pages 75 to 79 of the thesis). Consequently, this integrative discussion will not be repeated in the General Conclusions section. Instead, this section will provide suggestions for future research, and will discuss possible clinical implications of the studies.

### **Directions for Future Research**

The study of the effects of MPH on children with ADHD leaves unanswered the question of how the medication would affect the performance of normal individuals on the VMS task. Douglas (in press; Douglas et al., 1988) has suggested that since MPH improves allocation of attention and effort, it would also be expected to improve the performance of normal controls on many tasks, though to a lesser extent than that of ADHD children. She noted that, like children with ADHD, normal individuals do not always perform at their optimal level, though the gap between "typical" and "optimal" performance would be smaller for the normal group. Several studies have explored the effects of MPH on the performance of normal children or adults on the Sternberg task

(Brumaghim et al., 1987; Fitzpatrick et al., 1988; Peloquin & Klorman, 1986). These investigators found that MPH reduced error rates, while either leaving RTs unchanged or speeding them. As Douglas' theory would predict, these results are similar to those obtained with children with ADHD on the low loads typically used with the Sternberg task (Coons et al., 1987; Klorman et al., 1992; 1994).

Although ethical considerations might limit the feasibility of carrying out a study using MPH with control children, it would be possible to undertake a study of the effects of MPH on the VMS performance of normal adult subjects. The hypothesis that MPH improves regulatory ability in children with ADHD leads to the prediction that MPH would have different effects on normal adults than on ADHD children on higher loads of the VMS. In Experiment 1, we argued that, since high VMS loads were so challenging for them, it was necessary for ADHD children to slow performance in order to achieve high accuracy. Presumably normal adults would not find the high loads of the VMS to be as challenging as the ADHD boys did. Consequently, they might not need extra time to improve accuracy. That is, adults would be expected to improve accuracy either without slowing their performance, or by slowing their performance only slightly at the highest information loads. It is also possible that speeding of performance would be observed at the lower loads. These results would support the interpretation that MPH improves regulatory ability, since performance would not be slowed to the same extent in a group that did not "need" the extra time.

It is also important to further define the circumstances under which MPH improves regulatory ability. In the three studies reported here, the boys received feedback about their response accuracy following each trial. It is not known whether such immediate, accurate feedback is a necessary condition for the regulatory effects of the medication to appear. It is possible, for example, that in the absence of feedback, MPH would not improve accuracy to the same degree. It is also possible that the increased RT at high loads observed in Experiment 1 was mediated, at least partially, by feedback. If this were true, it would suggest that children with ADHD need both stimulant medication and feedback in order to achieve their maximum regulatory potential. A study is currently underway at the McGill University-Montreal Children's Hospital Hyperactivity Project to determine the effects of feedback in mediating MPH effects on the VMS performance of children with ADHD.

Also unresolved is the question of whether tasks involving high information processing loads present particular difficulty for children with ADHD. In Experiment 2 children with ADHD had more difficulty than controls at all loads of the task, including the lowest loads. We argued that their poor performance, even at the low loads, resulted from the mixing of higher and lower loads within each block. This hypothesis is based on previous evidence showing that children with ADHD have particular difficulty under unpredictable conditions (Berman et al., 1994; Elbaz & Douglas, 1998; Leung & Connolly, 1996; Zahn et al., 1991). Thus, it is possible that our design, which mixed high and low loads, masked an interaction between load and diagnosis, and may therefore have obscured a particular vulnerability of children with ADHD to high load tasks. The hypothesis that children with ADHD have particular difficulty with high loads on the VMS could be tested by administering separate blocks of low memory load items and high memory load items, rather than presenting them in randomized order. A design with both memory loads and search loads blocked would be more likely to reveal an interaction between diagnosis and load, if it, in fact, exists.

Using the VMS with blocked versus randomized memory loads would also add to the existing literature on the effects of unpredictable task demands on children with ADHD and controls. Based on previous research showing that children with ADHD have more difficulty under unpredictable conditions, children with ADHD would be expected to be particularly vulnerable to the randomized presentation. This finding would support the view that children with ADHD have difficulty with flexible response demands, which Douglas hypothesizes to be another important aspect of self-regulation. If the prediction that children with ADHD have particular difficulty with randomized presentation is supported, it would also be interesting to use this manipulation in a medication study, to determine whether MPH helps children with ADHD deal more successfully with unpredictable task demands.

Experiment 2 was limited to a comparison of the performance of children with ADHD and normal controls. There is, however, increasing recognition of the importance of differentiating the pattern of cognitive deficits associated with ADHD from those found in other clinical groups, such as aggressive children, or children with learning disabilities (Hall, Halperin, Schwartz, & Newcorn, 1997; Oosterlaan, 1996; McGee, Williams, Moffit, & Anderson, 1989; Pennington, Groisser, & Welsh, 1993). It would be useful, in a future study, to compare the performance of children with ADHD to that of other clinical groups on the VMS, to determine whether they show different patterns of performance. For example, there is evidence suggesting that children with learning disabilities have difficulty with high loads on the Sternberg task (van der Meere et al., 1989). In addition, it would be interesting to compare the performance of children with ADHD to that of other clinical groups on the alternate versions of the VMS proposed above, the version manipulating use of feedback, or the version comparing blocked versus randomized presentation. Children with ADHD would be predicted to be more affected by these manipulations than other clinical groups, since both the manipulations affect task demands for self-regulation. Clinical Implications

The present series of studies suggested that, even when stimulant medication improved their accuracy, children with ADHD did not approach the high load, complex VMS task in the same manner as the comparison children. When receiving stimulants, particularly at higher doses, they became extremely careful and methodical. It was argued that they may have needed this extra time to continue to improve under the difficult task conditions. These results suggest that even when children with ADHD are receiving stimulant medication, they may require extra time to complete challenging work, at least initially. It is possible that ADHD children tend not to receive adequate practice in carrying out complex tasks, since, without medication, they may avoid them. Thus, it might become possible for them to perform such tasks more quickly after they have received the necessary practice while on medication.

The VMS task, since it allows a wide range of information processing loads to be used within a consistent format, may also make a valuable addition to the task batteries currently being used to titrate appropriate medication dosages for children with ADHD. A

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number of researchers have noted the advantages of using individual cognitive testing, in addition to behavior ratings, to determine the most appropriate medication dosage for a particular child (Barkley, McMurray, Edelbrock, & Robbins, 1989; Pelham et al., 1985; Rapport et al., 1988; Swanson, 1989; Swanson et al., 1991; Swanson, McBurnett, Christian, & Wigal, 1995; Vyse & Rapport, 1989). Tasks that have been used for this purpose include paired associate learning (Swanson, 1989; Swanson et al., 1991; 1995), academic analogue tasks (Douglas et al., 1986; 1988; Pelham et al., 1985), lower load Sternberg-like memory scanning tasks (Swanson et al., 1991; 1995), as well as direct measures of classroom productivity (Douglas et al., 1986; DuPaul & Rapport, 1993; Rapport, Denney, DuPaul, & Gardner, 1994; Rapport, Stoner, DuPaul, Birmingham, & Tucker, 1985). The addition of the VMS could provide information concerning stimulant medication effects on effort and persistence on complex, high-information-load tasks. In addition, since higher medication doses appear to lead to a strategy of slowing down to improve accuracy at high loads of the VMS, the task could assess whether a particular child becomes excessively slow and cautious at higher dosages.

To summarize, the present series of studies suggests that MPH helps children with ADHD regulate attention and effort on cognitive tasks. On lower processing loads, MPH allowed boys with ADHD to improve their accuracy, without significant cost in RT. On higher loads, higher medication doses allowed further improvement in accuracy, but with an apparent strategic change involving substantial slowing of RTs. Further research might clarify whether children with ADHD have greater difficulty than controls with the VMS and other high load tasks, when high and low loads are presented separately. Additional studies could also clarify whether these children require consistent feedback, in addition to stimulant medication, in order to achieve optimal improvement in their self-regulatory ability.

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