Original Research

The Efficacy of 2 Different Dosages of Methylphenidate in Treating Adults With Attention-Deficit Hyperactivity Disorder

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Objective: To evaluate the efficacy of methylphenidate in treating adults with attention-deficit hyperactivity disorder (ADHD), using subjective (self-report) and objective (computerized test) measures.

Method: This double-blind crossover trial of placebo vs methylphenidate included subjects with childhood and current ADHD symptoms, IQs above 80, no other psychiatric condition explaining their difficulties or requiring other treatment, and no substance abuse in the previous 6 months. We administered 10 mg 3 times daily of medication (that is, placebo or methylphenidate) for 2 weeks. On the final day, subjects completed self-report measures and were tested on computerized tests. We then increased dosage to 15 mg 3 times daily for 2 weeks and administered a complete reassessment on the final day. Following a 1-week washout, we repeated this process on the second medication (that is, placebo or methylphenidate).

Results: Thirty adults with ADHD participated. Self-report measures and computerized tests showed significant improvements in ADHD symptoms on methylphenidate, compared with placebo. Other psychiatric symptoms (notably, anxiety and depression) were alleviated with methylphenidate. There was no significant difference between the 2 dosages of methylphenidate.

Conclusion: Methylphenidate is effective in improving ADHD symptoms in adults with ADHD, is well tolerated, and has minimal side effects.

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Clinical Implications

- Methylphenidate improves symptoms of attention-deficit hyperactivity disorder in adults.
- Methylphenidate is well tolerated in adults and exhibits few side effects.

Limitations

- Higher dosages of methylphenidate than those used may be more beneficial in some cases.
- The sample size was small, and the study period proved to be short when we considered the effectiveness of placebo.

Key Words: *methylphenidate, adults, attention-deficit hyperactivity disorder*

Attention-deficit hyperactivity disorder (ADHD) is a well-established diagnosis in children. However, several studies have indicated that the disorder persists with age: Weiss and others found that disabling symptoms persisted into adulthood in 66% of subjects, and moderate-to-severe symptoms persisted in 51% (1); Gittelman and others found that full diagnostic criteria persisted in 31%, and disabling residual symptoms persisted in a further 5% (2); Mannuzza and

others' reevaluation of Gittelman's group reported 8% with full diagnostic criteria for ADHD and an additional 3% affected by some ADHD symptoms (3). Others have studied the overall incidence of ADHD in adults: in a community sample, Murphy and Barkley found a 1.3% prevalence of ADHD inattentive type, a 2.5% prevalence of ADHD hyperactive-impulsive type, and a 0.9% prevalence of ADHD combined type (4). Murphy and Barkley emphasized in 2 papers (4,5) that the prevalence of ADHD is underestimated in adults because existing diagnostic criteria are developmentally inappropriate. This has produced debate but no resolution, and the matter requires further research (6).

Since symptoms of ADHD are treated successfully with medications in childhood, it seems logical that adults with similar symptoms could also benefit from such treatment. Wilens and others reviewed studies on the effectiveness of medication in adults with ADHD; these authors examined studies that used stimulant (pemoline or methylphenidate) and nonstimulant (tricyclic antidepressants, antihypertensives, and amino acids) medications (7). The response varied across both groups. The medication used in the greatest number of studies was methylphenidate (of these, 6 studies were double-blind, and 1 was an open trial). The variability of response rates (25% to 78%) was attributed to differences in the studies, in diagnostic criteria, and in stimulant dosage, as well as to variations in study population comorbidity and differing outcome measures. The review showed that few studies using stimulants were double-blind crossover studies comparing medication to placebo. No study used objective measures such as the Continuous Performance Test (CPT) to evaluate treatment response.

The 3 double-blind, placebo–methylphenidate crossover studies described below (8–10) involved adults with ADHD and are similar in method, measures of ADHD symptomatology, and experimentation time; they differ mainly in the dosages of methylphenidate given (with some overlap). They show variable results: Mattes and others reported no significant improvement in attention deficit disorder (ADD) symptomatology with "low/moderate" dosages (8). These authors also reported that only 25% of their subjects improved on an average daily dosage of 0.7 mg/kg and a maximum daily dosage of 60 mg, given in divided doses twice daily. Conversely, Wender and others reported significant improvement in 57% of their ADD group with similar "low/moderate" dosages of methylphenidate (9). In their study, the average daily dosage was 0.6 mg/kg and the maximum daily dosage was 80 mg, given in divided doses 3 times daily (9). Spencer and others reported a response rate of 78% with daily dosages of 1 mg/kg of methylphenidate, given in divided doses 3 times daily (10). These researchers reported significant, albeit lesser, improvement in ADHD symptomatology with lower daily dosages of methylphenidate (specifically, 0.5 mg/kg and 0.75 mg/kg).

It is difficult to compare these 3 studies directly. Wender and others focused on studying the efficacy of methylphenidate in adults with ADHD (9); Spencer and others on whether a dosage–response curve existed for methylphenidate (10); and Mattes and others on medication effect in 2 different groups of subjects, based on childhood histories (8).

In summary, available controlled medication studies in adults are few to date and show conflicting results in response rates and optimal dosage (specifically reference 8, compared with references 9 and 10). More controlled studies are required on the treatment of adults with ADHD.

The purpose of the double-blind, placebo-controlled study reported in this paper was twofold: first, to determine the relative efficacy of low and moderate dosages of methylphenidate in treating adults with ADHD; and second, to evaluate changes in symptoms, using both subjective measures of ADHD symptoms (self-report questionnaires) and objective measures of attention and response inhibition (computerized tests). We believe objective-computerized tests have never been used in any adult ADHD study to date. The low dose (0.4 mg/kg) was found beneficial in clinic patients. The moderate dose (0.6 mg/kg) was found beneficial by Wender and others (9). Both doses had few side effects, yielding better compliance. We hypothesized that methylphenidate would be better than placebo in reducing ADHD symptoms under both objective and subjective tests and that a moderate dosage would be better than a low dosage in reducing symptoms.

Method

Screening and Pretrial Evaluation

Subjects were referred by physicians, by other professionals, by family members, and by themselves. Most had read or heard about ADHD and thought they might have this disorder. All desired an evaluation and treatment.

A flow chart (Figure 1) shows the evaluation procedure. We screened subjects in the following 4 steps:

1. Telephone screen

2. Self-report questionnaires (specifically, Wender-Utah [11], Adult ADHD Rating [12] and Adult ADHD Problem Behaviours [13]) mailed, returned, and scored

3. Clinic visits for further testing (that is, computer tests, Symptom Checklist-90-Revised [SCL-90-R] [14], Hamilton Anxiety Rating Scale [HARS] [15]; Beck Depression Inventory [BDI] [16], and IQ estimate using Wechsler Adult Intelligence Scale-Revised [WAIS-R] [17]), after obtaining signed consent

4. Psychiatric evaluation

We administered the following 2 computer tests to obtain objective measures of attention and impulsivity:

1. The CPT (18), a standardized test of attention and response inhibition requiring subjects to press a keyboard space bar whenever a letter other than X appears onscreen and to refrain when X appears. The mean number of omission errors and commission errors during 30 minutes is then calculated.

2. The stop-signal task (19), a test of inhibitory control requiring subjects to press a computer key in response to a stimulus (a forced-choice letter discrimination task) but to inhibit their response when presented with a tone. Inhibition is easiest when the tone immediately follows the stimulus and gets more difficult as it arrives later. Signal reaction time measures inhibitory ability.

Before starting the trial, each subject was seen by a psychiatrist who described the medication trial, reviewed all prior information on the subject, and interviewed the subject about childhood and current ADHD symptoms, current life situation (that is, work or school and family), and medical and psychiatric history (including drug and alcohol use). Each subject then filled out a baseline side effect form (that is, a review of symptoms scale ranging from mild to moderate to severe), and the psychiatrist performed a focused physical exam (measuring weight, heart rate, and blood pressure). Any concerns raised during screening (that is, an elevated BDI score) were carefully reviewed during the interview to determine whether the subject was suffering from a disorder requiring other immediate treatment. Subjects who did not continue in the study were referred to appropriate resources.

Subjects had to meet the following inclusion-exclusion criteria to participate in the study:

1. DSM-IV criteria for ADHD

2. 1.5 or more on at least 1 ADHD self-report questionnaire (either Conners'Adult ADHD Rating Scale [12] or the Adult ADHD Problem Behaviours [13] scale)

3. Estimated IQ of 80 or above on abbreviated WAIS-R

4. No psychiatric conditions that better accounted for their current symptoms or required other treatment

5. No substance abuse in the preceding 6 months

6. No medical condition contraindicating stimulants (that is, hypertension or cardiac disease)

Medication Trial

The trial was designed as a double-blind crossover comparison of 2 dosages of methylphenidate (10 mg 3 times daily and 15 mg 3 times daily) to each other and to equivalent dosages of placebo. The placebo was a commercially available sugar pill. Each dosage was given for 2 weeks. Subjects were randomly assigned to start either methylphenidate or placebo. We gave the hospital pharmacy a numbered list indicating a randomly chosen (from a hat) order of medication to start first (either methylphenidate or placebo) and assigned each subject a number. Subjects gave their number to the pharmacist when picking up their prescriptions. Medication was started with a 3-day lead-in of increasing dosages, as follows: day 1, 5 mg 3 times daily; day 2, 10 mg 3 times daily; day 3, 15 mg 3 times daily. All subjects were asked to call in or fax a side effect scale for each day of the lead-in. If no prohibitive side effects were found, the subjects resumed the lower dosage (10 mg 3 times daily) and returned to the clinic after 2 weeks for a reevaluation (comprising a psychiatric interview, side effect profile, focused physical exam, self-reported ADHD symptom profile, and objective testing on computers).

We requested subjects to take their medication 1 hour before testing to ensure a satisfactory level of medication during testing. The dosage was increased to 15 mg 3 times daily for 2 subsequent weeks, after which we asked subjects to return for a reevaluation similar to that undertaken after the first 2 weeks. At the end of this 4-week period, each subject had a minimum 5-day washout. The sequence starting with the lead-in was then repeated with the second "medication" (either methylphenidate or placebo).

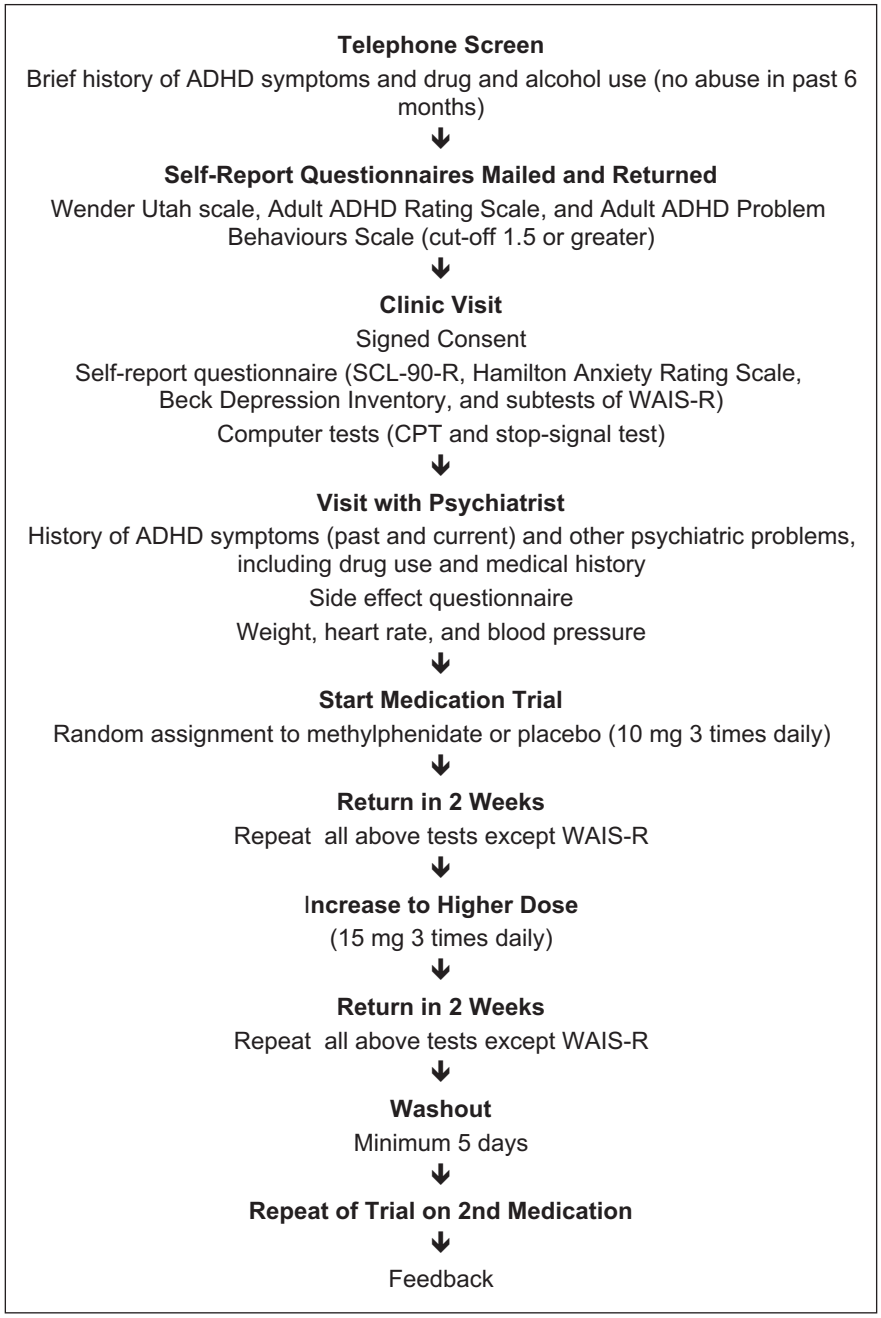
Statistical Analysis

We performed separate 1-way analyses of variance (ANOVAs) to assess the effects of placebo and methylphenidate on the following: ADHD symptoms as measured by 2 self-rating questionnaires (that is, Conners' Adult ADHD Rating Scale and the Adult ADHD Problem Behaviours Scale); ADHD symptoms as measured by the computer tests (that is, the CPT and stop-signal task); other symptoms as measured by the SCL-90, the BDI, and the HARS; and side effects. Neither the dosage level of placebo nor the dosage level of methylphenidate had a significant effect on any measure. Therefore, we combined the 2 dosage levels of both placebo and methylphenidate in the ANOVAs, using contrasts. The exception to this was the analysis of the Global Assessment of Functioning (GAF) and physiological measures, where we used the outcome values at the highest dosage of placebo and methylphenidate. The statistical package used was SYSTAT 6.1 (20).

Results

Of the 93 people (69 men and 24 women) screened for this study, 55 were not enrolled because their scores were too low ($n = 16$), they were already on medication ($n = 11$), they were not interested ($n = 8$), they were not blind to methylphenidate ($n = 5$), or they were not appropriate subjects for other reasons

Figure 1 Flow chart of evaluation process



ADHD = Attention-deficit hyperactivity disorder; CPT = Continuous Performance Test; SCL-90-R = Symptom Checklist-90-Revised; WAIS-R = Wechsler Adult Untelligence Scale-Revised

($n = 15$). A further 8 dropped out after starting because of side effects ($n = 1$), because they were not blind to methylphenidate ($n = 4$), because of "too much going on" ($n = 1$), and for unknown reasons ($n = 2$). A total of 30 adults (24 men and 6 women) completed the study. Their ages ranged from 17 to 51 years (mean 34 years). Their average IQ was 101. They came from a wide range of educational and socioeconomic backgrounds.

Effects on ADHD Symptoms

Table 1 shows the effects of placebo and methylphenidate on the subjects' ADHD symptoms. Methylphenidate reduced ADHD symptoms significantly more than did placebo, as measured by both self-report questionnaires and computer tests. Placebo generated a strong reduction from baseline symptomatology, but medication generated greater reductions than did placebo on all attention and inhibition measures. No measure showed any significant difference between the dosages of methylphenidate or placebo.

Scores on the Adult ADHD Problem Behaviours Scale were significantly lower than baseline for both placebo and methylphenidate; they were significantly lower for methylphenidate than for placebo (mean 0.9 vs mean 1.2, $P < 0.005$).

Similarly, scores on the Conners' Adult ADHD Rating Scale were significantly lower than baseline for both placebo and methylphenidate and significantly lower for methylphenidate than for placebo (mean 1.0 vs mean 1.4, $P < 0.01$).

The CPT commission error rate was lower than baseline for both placebo and methylphenidate and significantly lower for methylphenidate than for placebo (mean 17% vs mean 26%, $P < 0.001$).

The CPT baseline omission error rate in our group (mean 4.3%) was lower than the "norm" (mean 13.8%) for ADHD measured according to Conners' scale (18). For placebo, the CPT omission error rate was not significantly different from baseline; however, the omission error rate was significantly lower than baseline for methylphenidate (mean 4.3% vs mean 1.2%, $P < 0.0001$), and there was a trend toward a significantly lower omission error rate for methylphenidate, compared with placebo (mean 1.2% vs mean 3.8%, $P < 0.1$).

The stop-signal task reaction time was lower than baseline for both placebo and methylphenidate but did not differ significantly for methylphenidate, compared with placebo.

For this study, we only considered medication responses greater than the relatively high placebo response. We calculated the response rate as follows:

Table 1 Means (SDs) on ADHD measures and computer tests across baseline, placebo, and medication with ANOVA results across the conditions

Measure	Baseline Mean (SD)	Placebo 1[a] Mean (SD)	Placebo 2[b] Mean (SD)	Medication 1[c] Mean (SD)	Medication 2[d] Mean (SD)	Baseline vs placebo	Baseline vs medication	Placebo vs medication
Adult problem behaviours[e]	1.9 (0.4)	1.2 (0.5)	1.2 (0.5)	0.9 (0.5)	0.9 (0.5)	$F_{1,29} = 102.99$ $P < 0.0001$	$F_{1,29} = 125.59$ $P < 0.0001$	$F_{1,29} = 9.63$ $P < 0.005$
Conners' Rating Scale[e]	1.9 (0.4)	1.4 (0.6)	1.4 (0.6)	1.1 (0.5)	1.0 (0.6)	$F_{1,29} = 43.89$ $P < 0.0001$	$F_{1,29} = 89.25$ $P < 0.0001$	$F_{1,29} = 8.16$ $P < 0.01$
Continuous Performance Test % commission error	35.5 (14.7)	26.4 (13.2)	25.0 (14.1)	18.4 (14.1)	16.1 (14.3)	$F_{1,29} = 17.65$ $P = 0.0001$	$F_{1,29} = 43.42$ $P = 0.0001$	$F_{1,29} = 13.75$ $P < 0.001$
Continuous Performance Test % omission error	4.3 (4.3)	3.9 (7.6)	3.7 (8.5)	1.3 (2.1)	1.0 (1.7)	ns	$F_{1,29} = 16.78$ $P < 0.0001$	$F_{1,29} = 3.75$ $P < 0.1$
Stop-signal task All blocks combined[f]	236.8 (54)	200.5 (54)	215.0 (52)	201.0 (53)	189.8 (39)	$F_{1,27} = 7.03$ $P < 0.05$	$F_{1,27} = 16.90$ $P < 0.0001$	ns

[a]Placebo 1 = 10 mg placebo 3 times daily
[b]Placebo 2 = 15 mg placebo 3 times daily
[c]Medication 1 = 10 mg methylphenidate 3 times daily
[d]Medication 2 = 15 mg methylphenidate 3 times daily
[e]Scale: 0 = none; 3 = very much
[f]Milliseconds
ANOVA = analysis of variance

1. We recorded a subject's score on each self-report questionnaire.

2. We calculated a mean of the score on the high and low dosage of medication for each questionnaire.

3. The fraction of all subjects who both improved beyond placebo and scored below 1.5 on at least 1 self-report questionnaire was then expressed as a percentage.

This calculation yielded a response rate (based on improvement on self-report questionnaires scores) of 63%. Overall, 73% of the subjects made fewer commission errors on methylphenidate than on placebo. Therefore response rate was between 63% and 73%.

Overall, methylphenidate appears to be significantly superior to placebo in reducing ADHD symptoms on both self-report questionnaires and on computer tests.

Effects on Other Measures

Table 2 shows the effects of placebo and methylphenidate on non-ADHD symptoms. There was a reduction in anxiety (HARS) and depression (BDI) scores with both placebo and methylphenidate. However, methylphenidate was significantly superior to placebo in reducing anxiety scores ($P < 0.05$), and there was a trend for it to be superior in reducing depression scores. Although there was no significant improvement with methylphenidate on the overall SCL-90-R T-score, methylphenidate was associated with significantly lower scores on 2 scales: obsessive–compulsive and hostility. There was no significant difference between the 2 dosages of methylphenidate on any measure.

We compared GAF scores in a subsample of 13 subjects (chosen because a single rater gathered all data). The mean GAF scores were 68.5 at baseline, 69.9 on the highest dosage of placebo, and 75.3 on the highest dosage of methylphenidate. There was no significant difference between baseline and placebo, but there was a highly significant difference between baseline and methylphenidate ($P < 0.0001$) and a further significant improvement in methylphenidate, compared with placebo ($P < 0.01$).

Side Effects

Table 3 shows the physiological side effects. There was a nonsignificant increase in heart rate with methylphenidate (baseline mean, 71 beats per minute, placebo mean 72 beats per minute, methylphenidate mean 76 beats per minute). There was no significant increase of either systolic or diastolic blood pressure between baseline and placebo and no significant increase of diastolic blood pressure between baseline and methylphenidate. However, there was a significant increase of systolic blood pressure with methylphenidate, compared

Table 2 Means (SDs) on non-ADHD measures across baseline, placebo, and medication with ANOVA results across the conditions

Measure	Baseline Mean (SD)	Placebo 1[a] Mean (SD)	Placebo 2[b] Mean (SD)	Medication 1[c] Mean (SD)	Medication 2[d] Mean (SD)	Baseline vs placebo	Baseline vs medication	Placebo vs medication
Hamilton Anxiety Rating Scale[e]	0.8 (0.4)	0.4 (0.3)	0.5 (0.4)	0.4 (0.3)	0.3 (0.3)	$F_{1,29} = 58.10$ $P < 0.0001$	$F_{1,29} = 87.37$ $P < 0.0001$	$F_{1,29} = 5.49$ $P < 0.05$
Beck Depression Inventory[f]	11.5 (8.1)	7.7 (7.0)	8.2 (7.7)	6.0 (6.4)	6.0 (7.4)	$F_{1,29} = 13.11$ $P < 0.001$	$F_{1,29} = 20.64$ $P < 0.0001$	$F_{1,29} = 4.06$ $P < 0.1$
SCL-90-R[g]	67.8 (9)	60.7 (10)	60.0 (13)	58.0 (11)	56.8 (13)	$F_{1,23} = 14.41$ $P < 0.001$	$F_{1,23} = 43.91$ $P < 0.0001$	ns
Obsessive–Compulsive Scale[g]	73.0 (9)	66.0 (11)	65.0 (12)	61.0 (10)	60.0 (11)	$F_{1,23} = 12.09$ $P < 0.05$	$F_{1,23} = 34.32$ $P < 0.0001$	$F_{1,23} = 4.81$ $P < 0.05$
Hostility Scale[g]	60.1 (9)	56.0 (11)	57.2 (12)	54.1 (11)	53.3 (11)	$F_{1,23} = 2.61$ ns	$F_{1,23} = 11.20$ $P < 0.005$	$F_{1,23} = 3.33$ $P < 0.1$

[a]Placebo 1 = 10 mg placebo 3 times daily
[b]Placebo 2 = 15 mg placebo 3 times daily
[c]Medication 1 = 10 mg methylphenidate 3 times daily
[d]Medication 2 = 15 mg methylphenidate 3 times daily
[e]Scale: 0 = none; 4 = very severe
[f]Scale: 0–9 = minimal; 10–16 = mild; 17–29 = moderate
[g]*T*-score
ANOVA = analysis of variance; SCL-90-R = Symptom Checklist-90-Revised

with baseline (mean 124 vs mean 128, $P < 0.01$) and with methylphenidate, compared with placebo (mean 123 vs mean 128, $P < 0.05$).

Table 4 shows other reported symptoms. Generally, there were no significant differences in other reported symptoms among baseline, placebo, and methylphenidate. On average, over one-quarter of the sample had some physical complaint before starting methylphenidate. The principal complaint with methylphenidate was decreased appetite. Mild-to-moderate appetite decrease was found in 41% of subjects with the higher dosage of methylphenidate, compared with 23% at baseline and 19% with placebo. Despite this, there was no significant weight loss (mean weights were 75.8 kg at baseline, 78 kg with placebo, and 76.4 kg with methylphenidate). Insomnia was a common complaint at baseline (41% of subjects experienced mild-to-moderate insomnia). This improved on placebo (25% of subjects reported mild-to-moderate insomnia) and on methylphenidate (26% of subjects reported mild-to-moderate insomnia). Headache was also a common complaint: at baseline, 25% of subjects complained of headache, compared with 35% on placebo and 21% on methylphenidate. A small proportion of subjects cited irritability, light-headedness, and motor ticks as symptoms, but these symptoms seemed unrelated to any study condition.

Discussion

Implications

Well-controlled studies on the efficacy of methylphenidate in adults with ADHD are few and show conflicting results. This study evaluated the efficacy of low or moderate dosages of methylphenidate on adults with ADHD. These dosages appeared to have positive effects in clinical practice and to be easy to use. Although self-report questionnaires have been used to evaluate the effect of medication on ADHD symptoms, this is the first study to use objective measures (computer tests) to evaluate methylphenidate's efficacy on symptoms of ADHD in adults.

This double-blind crossover study found that, compared with placebo, low or medium dosages of methylphenidate reduced the symptomatology of ADHD in adults, as measured by both subjective and objective tests. This finding supports the efficacy of methylphenidate for ADHD symptoms in adults and indicates that low and moderate dosages are effective. It does not resolve whether higher dosages of methylphenidate further reduce ADHD symptoms but suggests that some subjects may not require high dosages.

Methylphenidate and placebo were tried for 1 month each. We chose this short period because stimulants can be adequately evaluated within a month in children and to encourage greater participation and compliance. The significant placebo response may last as long as 4 weeks. This underlines the importance of using a double-blind placebo trial in evaluating the response to ADHD medication. Longer trials may be

Table 3 Means (SDs) on physiological measures across baseline, placebo, and medication with ANOVA results across the conditions

Measure	Baseline Mean (SD)	Placebo 2[a] Mean (SD)	Medication 2[b] Mean (SD)	Baseline vs placebo 2	Baseline vs medication 2	Placebo 2 vs medication 2
Heart rate, beats per minute	71.0 (12)	72.0 (10)	76.0 (10)	ns	ns	ns
Systolic blood pressure, mm Hg	123.0 (11)	123.0 (11)	128.0 (12)	ns	$F_{1,23} = 8.25$ $P < 0.01$	$F_{1,23} = 7.59$ $P < 0.05$
Diastolic blood pressure, mm Hg	79.0 (8)	81.0 (8)	81.0 (9)	ns	ns	ns
Weight, kgs	75.8 (16.2)	78.0 (15)	76.4 (6)	ns	ns	ns

[a]Placebo 2 = 15 mg placebo 3 times daily
[b]Medication 2 = 15 mg methylphenidate 3 times daily

Table 4 Percentages of subjects reporting symptoms across baseline, placebo, and medication with ANOVA results across the conditions

Symptoms	Baseline % reported	Placebo 2[a] % reported	Medication 2[b] % reported	Baseline vs placebo 2	Baseline vs medication 2	Placebo 2 vs medication 2
Appetite Loss						
Mild	9	14	32	ns	ns	ns
Moderate	14	5	9	ns	ns	ns
Severe	0	0	0	ns	ns	ns
Trouble sleeping						
Mild	24	17	22	ns	ns	ns
Moderate	17	8	4	ns	ns	ns
Severe	4	4	0	ns	ns	ns
Headache						
Mild	21	26	17	ns	ns	ns
Moderate	4	9	4	ns	ns	ns
Severe	0	0	4	ns	ns	ns

[a]Placebo 2 = 15 mg placebo 3 times daily
[b]Medication 2 = 15 mg methylphenidate 3 times daily

required to adequately assess methylphenidate's efficacy on global function and to decrease the placebo effect.

The subjects in this study were neither comorbid for other psychiatric illnesses nor did they have pure ADHD. Overall, ADHD symptomatology was in the moderate range; few were severely affected. This may explain the greater placebo response found in this study, compared with Spencer and others' study (10), where subjects may have had more severe ADHD symptoms or more comorbidity.

The greatest effect of methylphenidate on computerized tests was to lower the commission error score of the CPT (73% of the group showed an improvement with methylphenidate over placebo). This confirms that methylphenidate reduces ADHD symptoms. This positive effect on attention and response inhibition suggests that methylphenidate may also improve work performance in adults with ADHD. The stop-signal task is relatively new and not discriminatory in this treatment study with methylphenidate. Perhaps a higher dosage of methylphenidate would be required to get a significant improvement on this test.

Non-ADHD symptoms improved with methylphenidate: it reduced symptoms of anxiety and showed a trend toward reducing depressive symptoms, compared with placebo. There was also more improvement with methylphenidate than with placebo on obsessive–compulsive scores and a trend toward improvement on SCL-90-R hostility scores.

Overall, rating scale scores of anxiety and depression in subjects were low. Methylphenidate may directly relieve non-ADHD symptoms, but it seems more plausible that this improvement resulted from increased general well-being secondary to reduced ADHD symptoms. Anxiety may decrease if a subject's performance at work improves.

The study population was varied, with a 4:1 preponderance of male subjects over female subjects—a ratio similar to that

reported for children but different from other adult studies with a higher proportion of women. There is no clear explanation for this. It may be a close approximation to the true ratio or a chance sampling within a small population. Our referral sources may have tended to refer men with ADHD symptoms while categorizing women in more depressive diagnoses. One expects more women to be referred in future, as community referral sources become more aware of adults with ADHD.

The low and moderate dosages used in this study are well tolerated, seem equally effective, and are comparable with those given to children. Side effects were minimal, and some symptoms were common in many individuals before the study. Adults with ADHD may suffer from greater somatic complaints or be more aware of their physical malaise. Although the increase in systolic blood pressure measured with methylphenidate does not seem clinically significant, it indicates methylphenidate's effect on the cardiovascular system. This suggests that blood pressure should be monitored with the administration of methylphenidate.

Study Limitations and Future Directions

We tested only 2 relatively low dosages of methylphenidate. A higher dosage of methylphenidate might have benefited some subjects, and further improvements might have been observed, as suggested by Spencer (10).

Subject evaluation did not include reports on symptomatology from spouses, friends, coworkers, or employers. This information is harder to obtain for adults than for children. Such reports could have further confirmed our data. However, computer test results confirmed subjective data measured by self-report, suggesting that our data are valid.

The sample size (30 subjects) was relatively small. A larger sample would clarify the effects of methylphenidate on comorbid symptoms and establish whether methylphenidate has a differential response on attention, impulsivity, and hyperactivity. Our sample was not large enough to identify an order effect.

Improvement of ADHD symptoms seems to be a clear response to methylphenidate. Although encouraging, this finding is difficult to extrapolate to individuals with ADHD and comorbid psychiatric symptoms. The efficacy of methylphenidate on populations with comorbidity needs more research and was not addressed.

This study was short-term, which stands out most clearly in the placebo-response finding. It would be worthwhile to determine the duration of placebo response and to determine whether the beneficial effects of methylphenidate continue over time in adults, as in children.

Summary

Methylphenidate was superior to placebo in alleviating ADHD symptomatology (using both subjective and objective measures) in 30 adults diagnosed with ADHD. Methylphenidate was better than placebo at alleviating symptoms of anxiety and showed a trend toward significance in alleviating depressive symptoms. There was no significant difference between the 2 dosages (10 mg 3 times daily and 15 mg 3 times daily) of methylphenidate. Methylphenidate was well tolerated, with no significant clinical effect on physiological measures (that is, blood pressure, pulse, and weight) and minimal self-reported side effects.

Many questions remain to be investigated in the medication treatment of adults with ADHD. Further studies should address dosage response, medication treatment effects over a longer term, populations with comorbidity, and functional impairment of work performance and personal relationships.

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Résumé : L'efficacité de 2 différents dosages de méthylphénidate dans le traitement d'adultes souffrant du trouble d'hyperactivité avec déficit de l'attention

Objectif : Évaluer l'efficacité du méthylphénidate pour traiter les adultes souffrant du trouble d'hyperactivité avec déficit de l'attention (THADA), à l'aide de mesures subjectives (auto-déclaration) et objectives (test informatique).

Méthode : Cet essai croisé à double insu d'un placebo contre le méthylphénidate comprenait des sujets présentant une symptomatologie actuelle et dans l'enfance du THADA, des quotients intellectuels supérieurs à 80, aucune autre affection psychiatrique expliquant leurs difficultés ou exigeant un autre traitement, et aucun abus de substance dans les 6 mois précédents. Nous avons administré 10 mg 3 fois par jour de « médicament » (c'est-à-dire, le placebo ou le méthylphénidate) pendant 2 semaines. Le dernier jour, les sujets ont répondu à des mesures auto-déclarées et à des tests informatiques. Nous avons ensuite augmenté le dosage à 15 mg 3 fois par jour pendant 2 semaines et administré une réévaluation complète, le dernier jour. Après une élimination d'une semaine, nous avons répété le processus avec le deuxième « médicament » (c'est-à-dire, le placebo ou le méthylphénidate).

Résultats : Trente adultes souffrant du THADA ont participé. Les mesures auto-déclarées et les tests informatiques ont indiqué des améliorations significatives des symptômes du THADA par le méthylphénidate, comparativement au placebo. D'autres symptômes psychiatriques, notamment l'anxiété et la dépression, ont été soulagés par le méthylphénidate. Il n'y avait pas de différence significative entre les 2 dosages de méthylphénidate.

Conclusion : Le méthylphénidate est efficace pour soulager les symptômes du THADA chez les adultes souffrant de ce trouble, est bien toléré et comporte des effets secondaires minimes.