Published in final edited form as:
*J Am Geriatr Soc*. 2008 April ; 56(4): 695–700.

# Can methylphenidate reduce fall risk in community living older adults? A double blind, single-dose cross-over study

**Ron Ben-Itzhak, MD**[1,4], **Nir Giladi, MD**[1,2,3], **Leor Gruendlinger, MS**[1], and **Jeffrey M Hausdorff, PhD**[1,2,5]

1 *Movement Disorders Unit, Tel-Aviv Sourasky Medical Center; Tel-Aviv, Israel*

2 *Departments of Physical Therapy, Tel-Aviv University, Tel-Aviv, Israel*

3 *Neurology, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel*

4 *Department of Geriatrics, Reuth Medical Center, Tel-Aviv, Israel*

5 *Division on Aging, Harvard Medical School, Boston, MA USA*

## Abstract

**Objectives—**Among older adults, falls are a major health concern. A decrease in executive function (EF), common with aging, has been associated with gait instability, reduced mobility and other markers of fall risk. It is not known, however, whether augmenting EF affects gait and fall risk. We tested the hypothesis that methylphenidate modifies markers of fall risk in older adults.

**Design—**Randomized, double-blind, placebo-controlled, single dose crossover study

Address for Correspondence and Proofs: Jeffrey M. Hausdorff, PhD, Laboratory for Gait Analysis & Neurodynamics, Movement Disorders Unit, Tel Aviv Sourasky Medical Center, 6 Weizman Street, Tel Aviv 64239, Israel, fax: +972-3-697-4911, e-mail: jhausdor@tasmc.health.gov.il.

This work was presented in part at the 59th Annual Meeting of the American Academy of Neurology, Boston, May, 2007 and at the American Geriatrics Society meeting, Seattle, May, 2007.

**Author Contributions:** Indicate authors' role in study concept and design, acquisition of subjects and/or data, analysis and interpretation of data, and preparation of manuscript. (See section on "Authorship and Duplicate Publication").

RBY contributed to the study design, data collection, interpretation of the results, and wrote the first draft of the manuscript. NG contributed to the study design, data collection, interpretation of the results and revisions of the manuscript. LG contributed to data analysis, interpretation of the results, and revisions of the manuscript. JMH contributed to the study design, data collection, interpretation of the results, and revisions of the manuscript. All authors have seen and approved of the final version of the manuscript.

**Sponsor's Role:** Indicate sponsor's role in the design, methods, subject recruitment, data collections, analysis and preparation of paper.

**Conflict of Interest Disclosures:** Below is a checklist for all authors to complete and attach to their papers during submission.

| Elements of Financial/Personal Conflicts | * Author 1 RBY | | Author 2 NG | | Author 3 LG | | Author 4 JMH | |
|---|---|---|---|---|---|---|---|---|
| | Yes | No | Yes | No | Yes | No | Yes | No |
| Employment or Affiliation | | x | | x | | x | | x |
| Grants/Funds | | x | | x | | x | | x |
| Honoraria | | x | | x | | x | | x |
| Speaker Forum | | x | | x | | x | | x |
| Consultant | | x | | x | | x | | x |
| Stocks | | x | | x | | x | | x |
| Royalties | | x | | x | | x | | x |
| Expert Testimony | | x | | x | | x | | x |
| Board Member | | x | | x | | x | | x |
| Patents | | x | | x | | x | | x |
| Personal Relationship | | x | | x | | x | | x |

* Authors can be listed by abbreviations of their names.

For "yes" x mark(s): give brief explanation below:

**Setting—**Outpatient movement disorders clinic.

**Participants—**Twenty-six non-demented, community-living older adults (mean age: 73.8 years) with subjective complaints of "memory problems."

**Interventions—**The study examined the effects of a single dose of 20 mg of methylphenidate (MPH) on cognitive function and gait. Participants were evaluated before and two hours after taking MPH or a placebo in sessions separated by 1–2 weeks.

**Measurements—**The Timed Up and Go and gait variability quantified mobility and fall risk. A computerized neuropsychology battery quantified memory and EF.

**Results—**Compared to baseline, Timed Up and Go times, stride time variability, and measures of EF significantly improved in response to MPH, but not in response to the placebo. In contrast, memory and finger tapping abilities were not significantly affected by MPH.

**Conclusions—**In older adults, MPH appears to improve certain aspects of EF, mobility and gait stability. Although additional studies are required to assess clinical utility and efficacy, the present findings suggest that methylphenidate and other drugs that are designed to enhance attention may have a role as a therapeutic option for reducing fall risk in older adults.

### Keywords

methylphenidate; gait variability; falls; cognitive function; aging

## INTRODUCTION

Gait disturbances and falls are a leading cause of morbidity and mortality among older adults. In 2003, 13,700 elderly 65 years of age or older died from falls, and 1.8 million were treated in emergency departments for nonfatal injuries from falls in the United States alone[1]. Among older adults hospitalized as a result of a fall, only 50% survive one year later[2]. While much is known about the multi-factorial nature of falls, the number of falls and fall-related injuries among older adults continues to increase[3]. Alternative treatment options are needed for optimal reduction of fall risk. The present study was designed to begin assessing the potential benefits of a cognitive intervention using methyphenidate (MPH) to reduce fall risk in community-living elderly.

The rational for using MPH to treat fall risk is based in part on the fact that executive function (EF) generally declines with aging[4]. EF refers to higher cognitive processes that use and modify information from posterior cortical sensory systems to modulate behavior, to allocate attention among tasks that are performed simultaneously, and to regulate response inhibition[5]. Recent reports also demonstrate that these cognitive changes have ramifications for mobility since in older adults, gait apparently utilizes EF. For example, time to complete an obstacle course was shorter, indicative of better performance, among community-living older adults who did better on a test of EF[6]. These reports indicate that there is a range of EF abilities among older adults, that those with better EF tend to perform better on tests of gait and mobility, and that gait among older adults should be considered a complex task that makes use of EF[6–12]. Further, diminished EF apparently leads to an increased fall risk[6,7,10,11]. EF was also associated with falls in a study of 172 older people who did not meet criteria for dementia or mild cognitive impairment[13].

These findings raise the question: if age-associated reductions in EF abilities contribute to gait instability and fall risk in older adults, can an intervention that enhances EF reverse this trend to improve gait and reduce the risk of falls? To address this question, we tested the hypothesis that a single dose of methylphenidate (MPH) modifies known markers of fall risk in

community-living older adults. The Timed Up and Go, a well established screening test for fall risk, was chosen as the primary outcome[14,15] and stride time variability, a measure of instability[10,16,17], was the secondary outcome. Other measures were assessed to help explain any observed effects. MPH was chosen for several reasons: 1) its ability to achieve a short-term effect, 2) drug "washout" can be assumed two days after exposure, 3) pilot work demonstrating safety and short-term efficacy in patients with Parkinson's disease[18,19] as well as reports of safe use of MPH for treatment of depression and apathy in the elderly[20,21], and 4) the well-studied effects of MPH on EF and attention in children and adults with ADHD.

## METHODS

### Study Design and Protocol

A randomized, double, placebo-controlled, cross-over, study design was used to evaluate the effects of a single dose of MPH on markers of fall risk. During the course of a two week period, there was an initial visit for baseline assessment and two more evaluations, each two hours after subjects took 20 mg of MPH (Ritalin®) or placebo in a randomized fashion. A single dose of MPH was used to demonstrate the short-term potential of a drug to act on surrogates of fall risk in older adults; we chose a dose that was likely to show an effect, that has a convenient form of delivery, that could potentially be used in clinical trials and ultimately perhaps, in clinical practice, and that appears to be safe and tolerable, based in part on a pilot study in Parkinson's disease[18]. Testing was performed blindly, by the first author, two hours after administration of the study drug because the maximum clinical effects of MPH occurs at this time when plasma concentrations peak[22]. Blood pressure and heart rate were recorded every half hour before and after the administration of the study drugs to monitor the cardiovascular response.

### Participants

Older adults were recruited from several sources in the community, e.g., local senior centers. Subjects were invited to participate if they were between 65 and 90 years of age, were able to ambulate independently and did not use a walking aid. To help identify subjects who might be more likely to respond favorably to a cognition-enhancing drug, we included only subjects who complained about memory decline. We excluded people with dementia [as determined by DSM IV and ICD 10 criteria and scores < 24 on the Mini Mental State Exam (MMSE) [23]]. Subjects were also excluded if they had clinically significant musculo-skeletal, cardiovascular or respiratory diseases, clinically significant vestibular disorder, history of significant head trauma, Parkinson's disease, or other neurodegenerative diseases, major depression (using DSM IV criteria) or uncorrected visual disturbances. Subjects with glaucoma, uncontrolled high blood pressure, heart failure or a cardiac arrhythmia, a history of epilepsy and subjects taking mono-amine oxidase inhibitors or tricyclic anti-depressants were excluded due to the side effect profile of MPH. Routine medications were not altered. The study was approved by local human studies committee and informed written consent was obtained prior to enrollment.

To characterize the study population, medical and fall history (not specifically an eligibility requirement) were reviewed and the following tests were administered during the first visit. The Charlson Comorbidity Index was used to quantify disease burden (higher scores indicate greater co-morbidities)[24]. The Geriatric Depression Scale (GDS, original 30 item version) was used to evaluate depressive symptoms and emotional well-being[25]. The Clock Drawing Test was used as another measure of cognitive function and quantified as described by Watson et al.[26]. The MMSE was used as a screen for dementia and as part of the cognitive assessment[23]. The Barthel Activities of Daily Living Index and the Frenchay Activities Index were used to characterize disability[27] and lifestyle and functional independence[28]. Higher

scores on both of these tests reflect better function. The Activities-specific Balance Confidence Scale was administered to assess fear of falling (higher scores indicate greater confidence) [29].

## Drug Administration

Each drug sample was prepared in the pharmacy before the start of the study. MPH and the placebo pills (sacchrine) were inserted into empty capsules. There were no specific instructions regarding fasting. Volunteers were given half a glass of water with capsule administration. The sessions generally took place during the morning. Before the start of the study, a randomization table was prepared. This table was available only to a person who was not involved with testing and had no contact with the study participants. None of the authors was involved in this selection process or knew of the contents of the pill until after all data analyses were completed and a third party broke the blinding.

## Assessment of Gait and Mobility

The Timed Up and Go (TUG) test was used to assess functional mobility and fall risk. Subjects were asked to stand up from a standard chair, walk at their normal pace for 3 meters, turn around, and return to a seated position. As per standard procedures, the second of two trials was used (minimizing practice effects). Higher values on the TUG test indicate an increased risk of falls[14,15]. To evaluate stride time variability, subjects walked at their normal pace on level ground for two minutes while wearing pressure-sensitive insoles. Previously established methods[10,30] were used to quantify gait speed, stride time, and the variability of stride time (using the coefficient of variation, CV). Stride time variability quantifies the automaticity of gait. Higher CV values reflect decreased rhythmicity and reduced automaticity and are associated with elevated fall risk[10,16,30,31].

## Cognitive Assessment

Mindstreams® (NeuroTrax Corp., NJ) computerized neuropsychological tests were used to measure cognitive function as well as tapping and "catching" performance[32,33]. The Go-NoGo test and a test of non-verbal memory were administered. The Go-NoGo is a well-established cognitive test of EF that measures the facility with which an individual is able to inhibit a response and to continue with an activity in the face of competing stimuli[34]. To quantify EF, we evaluated Go-NoGo accuracy. Go-NoGo reaction time was also measured to evaluate stimulant effects. The computerized version used has been described elsewhere in detail; outcome measures have been associated with continuous performance based measures of attention[33]. Because non-verbal memory generally does not require EF[5], non-verbal memory was assessed as a "control" to see if any observed EF effects were specific to this cognitive domain. Test details have been described previously[7,32,33].

To evaluate whether any of the observed motor effects were specific to gait, we also assessed catching and finger tapping abilities[7,32]. In the catch game[32], participants must "catch" an object falling vertically from the top of the computer screen. The test requires hand-eye coordination and scanning and its outcome measures have been associated with higher-level cognitive function and EF[7]. Finger tapping may be considered a less cognitively demanding task[7]. The cognitive battery includes a practice component before each test.

## Statistical Analysis

Descriptive statistics are reported as mean ± SE. We used the Wilcoxon Signed Rank test to evaluate the response of the different dependent variables (e.g., TUG times) to the different medication states (e.g., baseline vs. MPH). This non-parametric equivalent of the paired t-test is less sensitive to outliers and does not assume that the data are normally distributed. P-values

reported are based on two-sided comparisons. A p-value ≤ 0.05 was considered statistically significant. Statistical analyses were performed using SPSS.

# RESULTS

## Subject Characteristics

Twenty-six subjects (17 women) with a mean age of 73.8±1.2 years were studied. Average scores on the MMSE and the GDS were 27.8±1.4 and 8.2±5.6, respectively. Participants had 13.2±0.6 years of formal education. Mean scores on the Barthel ADL Index and the Frenchay Activities Index were 98.5±4.4 and 30.3±7.8, respectively. The Charlson Comorbidity Index was 1.0±0.2. Average score on the Clock Drawing Test was 2.9±2.2. Mean Activities-specific Balance Confidence score was 80.9±4.2. Table 1 shows the average values of gait and mobility at baseline.

## Effects of MPH and the Placebo on Mobility and Gait

In spite of generally normal performance at baseline, 20 mg MPH significantly decreased (improved) TUG times, compared to baseline, and compared to the effect seen with placebo (Table 1). MPH significantly improved stride time variability, while the placebo did not. MPH and the placebo had similar effects on gait speed and on average stride time (Table 1).

## Effects of MPH on Cognitive Function

MPH significantly improved Go-NoGo accuracy, above the placebo effect (Table 2). MPH also significantly improved catch game time to first move and catch game accuracy, while the placebo did not. Both MPH and the placebo had similar effects on Go-NoGo reaction time. MPH and the placebo did not significantly affect memory, tapping rate or tapping variability.

## Other Secondary Analyses

At the conclusion of each testing session, participants and the administering physician each wrote down whether they thought that the pill received was MPH (or placebo) in order to assess subjective perceptions. Thirty-one percent of the subjects guessed that they had been given a placebo, when in fact they were given MPH. The physician guessed placebo 27% of the times that MPH was administered. In almost half of the cases (46%), the subject and the administering physician either guessed incorrectly about MPH or did not agree.

To gain insight into the factors that may have explained the observed MPH effects on the mobility, we explored potential covariates. The change in TUG times (delta between baseline and MPH values) and the change in stride time variability in response to MPH were not significantly different in subjects who reported a fall in the previous year (n=9) and were not significantly related to age, gender, years of education, MMSE score, GDS score, Activities-specific Balance Confidence, Charlson Comorbidity index, most of the cognitive function measures, or other subject characteristics (in univariate correlation analysis). There were two exceptions to this rule: 1) improvement in TUG times after MPH treatment was greater in subjects who had higher (poorer) TUG times at baseline ($r=0.59$; $p=0.002$) and in subjects with lower Barthel scores ($r=-0.57$; $p=0.002$), and 2) subjects who showed greater improvement in stride time variability tended to have increased variability at baseline ($r=0.70$; $p<0.001$) and lower Barthel scores ($r=-0.49$; $p=0.01$). The improvements in TUG times in response to MPH tended to be associated with improvements in Go-NoGo accuracy ($r=0.29$; $p=0.14$) and stride time variability improvements in response to MPH tended to be associated with improvements in catch game accuracy ($r=0.30$; $p=0.15$). Two subjects had relatively high Geriatric Depression Scores (> 20), but most (n=19) scored less than 10 on this scale. The effects of MPH on the

TUG, gait speed and stride time variability seen in the group as a whole were also observed in the sub-groups whose mood was rated as normal.

No adverse events were observed in response to MPH (or the placebo). Systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate did not significantly increase in response to the placebo or MPH (Table 3).

## DISCUSSION

The present findings are similar to the results of a previous report in patients with Parkinson's disease. In that study, a single dose of MPH improved gait speed, decreased TUG times, and reduced stride time variability[18], effects that were also seen in the present study. In that study, MPH also improved EF, but did not affect memory or finger tapping performance; effects that were also very similar to those seen in the present study. The present study extends those previous findings in two critical ways: 1) the MPH effect is shown in generally healthy older adults, and 2) the MPH effect is demonstrated in a placebo-controlled trial. MPH significantly improved TUG times, stride time variability, and EF (e.g., Go-NoGo accuracy), effects that were not seen after treatment with the placebo.

The observed findings could be interpreted in several ways. One interpretation is that cognitive therapy helps to improve mobility in the elderly. This explanation is consistent with the recent reports that have found that older adults who perform better on tests of EF tend to have better mobility and lower fall rates and the idea that mobility in older adults relies upon cognitive function[6–12]. This intriguing possibility would suggest that MPH and perhaps other cognition-enhancing therapies may have a role in reducing fall risk among older adults who are likely to suffer from age-associated declines in EF[4]. Support for this explanation comes from the specific effects of MPH on TUG, stride time variability and Go-NoGo accuracy (recall Tables 1 and 2).

Another explanation of the observed results is that MPH elicited an amphetamine-like effect that improved performance. Similarly, MPH also has known effects on dopamine uptake[35], a neurotransmitter that plays a key role in motor function. One could argue, therefore, that the observed MPH effects are not due to its modulation of cognitive function, but arise from a more direct influence on motor function or the result of the stimulant effects. These possibilities cannot be completely ruled out; however, examination of Tables 1 and 2 suggest that these are not the most likely explanation. Compared to baseline values, gait speed increased similarly in response to MPH and in response to the placebo. Gait speed is a measure that is likely to be especially sensitive to dopamine uptake and stimulant effects, and perhaps also to the expectations of the participants. One could argue that the placebo and MPH evoked similar stimulant effects while the changes in EF, TUG and stride time variability in response to MPH were in fact a specific, cognitive-related response. Compared to steady-state walking, the TUG is a much more complex procedure that includes planning, potentially explaining the difference between its results and those for average gait speed.

Participants in the present study were community-living older adults. Average scores on the MMSE and the Clock Drawing test are consistent with an absence of dementia and only mild or no cognitive decline. Scores on the GDS indicate none-to-mild depressive symptoms, except for the two participants who had more severe complaints about mood, and scores on the Barthel ADL Index and the Frenchay Activities Index indicate that subjects were free of major deficits, consistent with the low (good) scores on the comorbidity index. Nonetheless, self-confidence regarding balance tended to be slightly below normal[29] and all subjects complained about their memory. Among older adults, complaints about memory are associated with a wide array of mental health and physical disturbances, including impaired EF, depression and frailty[36,37].

Memory, EF, TUG times, average gait speed, and stride time variability were normal or slightly worse than that seen in "healthy" older adults[15,17,30,36]. Thus, the participants can be described as generally healthy, functionally independent community-living older adults with normal to mild decline in cognitive function and mobility.

This study has a number of limitations. For example, the sample size and the specific subject characteristics raise questions regarding the generalizability of the findings. Although the mobility outcomes measured have been associated with fall risk, we did not evaluate whether chronic administration of MPH succeeds in lowering fall rates, whether potential benefits outweigh possible risks, or whether the administered dose is optimal. Further investigations are needed to address these issues and to assess more fully the effects of long-term MPH administration and other cognitive-enhancing drugs or therapeutic options on gait, cognitive function, fall risk and their interplay among different older adult populations. Adverse events were not observed in the present study, consistent with previous reports in older patients[18–21], but issues regarding safe administration of MPH in older adults need to be studied further. Still, the findings of the present investigation suggest that such future studies are warranted, highlight the connection between fall risk and cognitive function, and demonstrate the potential of using pharmacologic agents that augment cognitive function as an alternative, complementary therapy for reducing fall risk in older adults.

**Acknowledgements**

We thank the participants for their time and effort and Talia Herman for invaluable assistance.

Funding was provided in part by the NIH (AG14100).

This study was not supported by any industry grant.

## References

1. Fatalities and injuries from falls among older adults--United States, 1993–2003 and 2001–2005. MMWR Morb Mortal Wkly Rep 2006;55:1221–1224. [PubMed: 17108890]
2. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. Age Ageing 2006;35(Suppl 2):ii37–ii41. [PubMed: 16926202]
3. Kannus P, Palvanen M, Niemi S, et al. Alarming rise in the number and incidence of fall-induced cervical spine injuries among older adults. J Gerontol A Biol Sci Med Sci 2007;62:180–183. [PubMed: 17339643]
4. Verhaeghen P, Cerella J. Aging, executive control, and attention: a review of meta-analyses. Neurosci Biobehav Rev 2002;26:849–857. [PubMed: 12470697]
5. Lezak, MD. Neuropsychological assessment. New York: Oxford University Press, Inc; 1995.
6. Ble A, Volpato S, Zuliani G, et al. Executive function correlates with walking speed in older persons: The InCHIANTI study. J Am Geriatr Soc 2005;53:410–415. [PubMed: 15743282]
7. Hausdorff JM, Yogev G, Springer S, et al. Walking is more like catching than tapping: gait in the elderly as a complex cognitive task. Exp Brain Res 2005;164:541–548. [PubMed: 15864565]
8. Alexander NB, shton-Miller JA, Giordani B, et al. Age differences in timed accurate stepping with increasing cognitive and visual demand: a walking trail making test. J Gerontol A Biol Sci Med Sci 2005;60:1558–1562. [PubMed: 16424288]
9. Coppin AK, Shumway-Cook A, Saczynski JS, et al. Association of executive function and performance of dual-task physical tests among older adults: analyses from the InChianti study. Age Ageing 2006;35:619–624. [PubMed: 17047008]
10. Springer S, Giladi N, Peretz C, et al. Dual-tasking effects on gait variability: the role of aging, falls, and executive function. Mov Disord 2006;21:950–957. [PubMed: 16541455]
11. Verghese J, Buschke H, Viola L, et al. Validity of divided attention tasks in predicting falls in older individuals: a preliminary study. J Am Geriatr Soc 2002;50:1572–1576. [PubMed: 12383157]

12. Yogev-Seligman, G.; Hausdorff, JM.; Giladi, N. Mov Disord. 2007. The role of executive function and attention in gait. in press
13. Holtzer R, Friedman R, Lipton RB, et al. The relationship between specific cognitive functions and falls in aging. Neuropsychology 2007;21:540–548. [PubMed: 17784802]
14. Kristensen MT, Foss NB, Kehlet H. Timed “up & go” test as a predictor of falls within 6 months after hip fracture surgery. Phys Ther 2007;87:24–30. [PubMed: 17142643]
15. AGS Guidelines. Guideline for the prevention of falls in older persons. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. J Am Geriatr Soc 2001;49:664–672. [PubMed: 11380764]
16. Hausdorff JM, Rios D, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. Arch Phys Med Rehabil 2001;82:1050–1056. [PubMed: 11494184]
17. Hausdorff JM, Edelberg HK, Mitchell SL, et al. Increased gait unsteadiness in community-dwelling elderly fallers. Arch Phys Med Rehabil 1997;78:278–283. [PubMed: 9084350]
18. Auriel E, Hausdorff JM, Herman T, et al. Effects of methylphenidate on cognitive function and gait in patients with Parkinson’s disease: a pilot study. Clin Neuropharmacol 2006;29:15–17. [PubMed: 16518128]
19. Devos D, Krystkowiak P, Clement F, et al. Improvement of gait by chronic, high doses of methylphenidate in patients with advanced Parkinson’s disease. J Neurol Neurosurg Psychiatry 2007;78:470–475. [PubMed: 17098845]
20. Galynker I, Ieronimo C, Miner C, et al. Methylphenidate treatment of negative symptoms in patients with dementia. J Neuropsychiatry Clin Neurosci 1997;9:231–239. [PubMed: 9144102]
21. Emptage RE, Semla TP. Depression in the medically ill elderly: a focus on methylphenidate. Ann Pharmacother 1996;30:151–157. [PubMed: 8835049]
22. Wilens TE, Spencer TJ, Biederman J. A review of the pharmacotherapy of adults with attention-deficit/hyperactivity disorder. J Atten Disord 2002;5:189–202. [PubMed: 11967475]
23. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state” A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198. [PubMed: 1202204]
24. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–383. [PubMed: 3558716]
25. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17:37–49. [PubMed: 7183759]
26. Watson YI, Arfken CL, Birge SJ. Clock completion: an objective screening test for dementia. J Am Geriatr Soc 1993;41:1235–1240. [PubMed: 8227899]
27. Wade DT, Collin C. The Barthel ADL Index: a standard measure of physical disability? Int Disabil Stud 1988;10:64–67. [PubMed: 3042746]
28. Turnbull JC, Kersten P, Habib M, et al. Validation of the Frenchay Activities Index in a general population aged 16 years and older. Arch Phys Med Rehabil 2000;81:1034–1038. [PubMed: 10943751]
29. Powell LE, Myers AM. The Activities-specific Balance Confidence (ABC) Scale. J Gerontol A Biol Sci Med Sci 1995;50A:M28–M34. [PubMed: 7814786]
30. Yogev G, Giladi N, Peretz C, et al. Dual tasking, gait rhythmicity, and Parkinson’s disease: Which aspects of gait are attention demanding? Eur J Neurosci 2005;22:1248–1256. [PubMed: 16176368]
31. Barak Y, Wagenaar RC, Holt KG. Gait characteristics of elderly people with a history of falls: a dynamic approach. Phys Ther 2006;86:1501–1510. [PubMed: 17079750]
32. Dwolatzky T, Whitehead V, Doniger GM, et al. Validity of a novel computerized cognitive battery for mild cognitive impairment. BMC Geriatr 2003;3:4. [PubMed: 14594456]
33. Schweiger A, Abramovitch A, Doniger GM, et al. A clinical construct validity study of a novel computerized battery for the diagnosis of ADHD in young adults. J Clin Exp Neuropsychol 2007;29:100–111. [PubMed: 17162726]
34. Riccio CA, Reynolds CR. Continuous performance tests are sensitive to ADHD in adults but lack specificity. A review and critique for differential diagnosis. Ann N Y Acad Sci 2001;931:113–139. [PubMed: 11462737]

35. Volkow ND, Wang GJ, Fowler JS, et al. Dopamine transporter occupancies in the human brain induced by therapeutic doses of oral methylphenidate. Am J Psychiatry 1998;155:1325–1331. [PubMed: 9766762]

36. Giladi N, Mordechovich M, Gruendlinger L, et al. Brain Screen": A self-referral, screening program for strokes, falls and dementia risk factors. J Neurol 2006;253:307–315. [PubMed: 16208527]

37. Comijs HC, Deeg DJ, Dik MG, et al. Memory complaints; the association with psycho-affective and health problems and the role of personality characteristics. A 6-year follow-up study. J Affect Disord 2002;72:157–165. [PubMed: 12200206]

**Table 1**

Effects of MPH and placebo on mobility and gait*

| | | | | P-values | | |
|---|---|---|---|---|---|---|
| | **Baseline/Unmedicated** | **Placebo** | **MPH** | **Baseline vs. Placebo** | **Baseline vs. MPH** | **MPH vs. Placebo** |
| **Timed Up & Go (sec)** | 10.3 ± 0.6 | 9.9 ± 0.6 | 9.4 ± 0.5 | 0.206 | **0.004** | **0.030** |
| **Gait speed (m/sec)** | 1.12 ± 0.05 | 1.19 ± 0.05 | 1.20 ± 0.05 | **0.003** | **0.001** | 0.354 |
| **Stride Time (sec)** | 1.09 ± 0.02 | 1.07 ± 0.02 | 1.06 ± 0.02 | **0.006** | **0.025** | 0.517 |
| **Stride Time Variability (%)** | 3.52 ± 0.44 | 3.08 ± 0.32 | 2.72 ± 0.24 | 0.395 | **0.028** | 0.551 |

*Entries are mean±SE. P-values < 0.05 are in bold.

**Table 2**

Effects of MPH and placebo on cognitive function*

| | | | | P-values | | |
|---|---|---|---|---|---|---|
| | **Baseline/Unmedicated** | **Placebo** | **MPH** | **Baseline vs. Placebo** | **Baseline vs. MPH** | **MPH vs. Placebo** |
| **Memory Accuracy (average during learning phase) (%)** | 51.0 ± 4.8 | 49.8 ± 4.7 | 49.6 ± 4.9 | 0.726 | 0.599 | 0.932 |
| **Delayed Memory Accuracy (%)** | 50.7 ± 5.0 | 49.6 ± 5.8 | 53.5 ± 5.7 | 0.795 | 0.441 | 0.861 |
| **Go-NoGo Accuracy (%)** | 88.8 ± 2.8 | 90.0 ± 2.6 | 94.5 ± 1.5 | 0.962 | **0.030** | **0.027** |
| **Go-NoGo Response Time (msec)** | 601.9 ± 44.9 | 492.6 ± 26.7 | 489.3 ± 24.5 | **0.015** | **0.005** | 0.282 |
| **Catch Game Time to First Move (msec)** | 901.8 ± 46.0 | 902.4 ± 44.5 | 850.4 ± 49.4 | 0.339 | **0.034** | 0.204 |
| **Catch Game Accuracy (total score)** | 443.8 ± 39.2 | 485.1 ± 50.9 | 494.1 ± 43.4 | 0.192 | **0.044** | 0.681 |
| **Tapping Interval (msec)** | 257.1 ± 15.7 | 229.8 ± 8.7 | 246.3 ± 14.1 | 0.366 | 0.559 | 0.543 |
| **Tapping Variability (msec)** | 34.7 ± 4.8 | 43.5 ± 6.1 | 37.0 ± 5.3 | 0.414 | 0.681 | 0.513 |

* Entries are mean±SE. P-values < 0.05 are in bold.

## Table 3

Effects of MPH and placebo on cardiovascular function*

| | MPH | | Placebo | |
|---|---|---|---|---|
| | Pre | 2 Hours After | Pre | 2 Hours After |
| **Systolic Blood Pressure (mm Hg)** | 123.9 ± 3.5 | 129.2 ± 3.6 | 126.5 ± 3.8 | 131.9 ± 3.5 |
| **Diastolic Blood Pressure (mm Hg)** | 71.1 ± 1.6 | 71.9 ± 1.7 | 73.1 ± 1.7 | 73.5 ± 1.5 |
| **Heart Rate (bpm)** | 76.9 ± 2.0 | 76.7 ± 2.3 | 74.5 ± 2.1 | 70.8 ± 2.0 |

*None of the pre vs. post comparisons (2 hours after taking MPH or placebo) were significantly different, except that there was a small, but significant drop in heart rate 2 hours after the subjects took the placebo (p=0.030).