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# A Common Cognitive Profile in Elderly Fallers and in Patients with Parkinson's Disease: The Prominence of Impaired Executive Function and Attention

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# Abstract

The present study examined the cognitive profile of fallers relative to healthy controls and patients with Parkinson's disease (PD), a positive control group, using a computerized battery. Fallers performed more poorly than controls on executive function, attention, and motor skills, but performed comparably on memory, information processing and the Mini Mental State Exam. A similar profile was evident for PD patients. However, unlike PD patients, fallers were abnormally inconsistent in their reaction times. These findings indicate that elderly fallers may have a unique cognitive processing deficit (i.e., variability of response timing) and underscore the importance of executive function and attention as potential targets for fall risk screening and interventions.

# Keywords

cognitive function; aging; executive function; falls

# INTRODUCTION

Gait and balance may deteriorate in certain elderly populations when subjects are asked to walk and perform a second task (dual tasking) (Bloem, Valkenburg, Slabbekoorn, & Gert, 2001; Sheridan, Solomont, Kowall, & Hausdorff, 2003;Woollacott & Shumway-Cook, 2002). In particular, an exacerbated dual-task decrement in gait and balance has been observed in elderly fallers (Bloem et al., 2001;Sheridan et al., 2003;Woollacott & Shumway-Cook, 2002). Some investigators have proposed that changes in executive function - a cognitive domain that enables the juggling of multiple tasks and the regulation of complex cognitive responses – are the reason for the dual task decrement observed in patients with Alzheimer's disease (Cocchini et al., 2004;Sheridan et al., 2003), but the explanation for why dual tasking is especially challenging to elderly fallers is largely incomplete. Other than using the popular Mini-Mental

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State Examination (Guideline, 2001), few studies have comprehensively quantified cognitive function in elderly fallers. One recent, prospective study assessed components of a neuropsychological battery and suggested that the ability to pay attention was predictive of falls in older adults (van Schoor, Smit, Pluijm, Jonker, & Lips, 2002). Unfortunately, in that study, executive function and other aspects of cognitive function were not assessed. Thus, despite the evidence for an exaggerated dual-task decrement in elderly fallers and

epidemiological findings indicating that difficulties in cognitive function exacerbate fall risk (Guideline, 2001), relatively little is known about the cognitive function profile of elderly fallers.

The primary goal of the present study was to characterize the cognitive function of elderly, idiopathic fallers. Because of the known dual-task decrement in elderly fallers, we hypothesized that measures of executive function and attention would be decreased in this group of older adults. To test this hypothesis, we compared the cognitive function of elderly fallers to a group of healthy control older adults. Because of the known dual-task decrement in patients with Parkinson's disease (PD) (Hausdorff, Balash, & Giladi, 2003;O'Shea, Morris, & Iansek, 2002) and the observation that deficits in executive function and attention are among the most prominent cognitive changes in PD (Dubois & Pillon, 1997;Uekermann et al., 2004; Zgaljardic, Borod, Foldi, & Mattis, 2003), we also compared the cognitive function of the fallers to that of patients with PD as a "positive control" group with known deficits in domains hypothesized to be impaired in fallers. Comparison of the cognitive profile in fallers with that in PD may help to better characterize features unique to fallers.

# **METHODS**

#### Subjects

Three groups of subjects were studied: elderly fallers (n=18), patients with PD (n=30) and healthy elderly controls (n=25). All subjects walked without ambulatory aids or assistance, and were free from neurological, affective, orthopaedic, acute illness and other co-morbidities (e.g., brain injury, stroke) likely to affect gait or cognitive function other than those presently described. All subjects were non-demented, as per DSM IV criteria, with Mini-Mental State Exam (Folstein, Folstein, & McHugh, 1975) (MMSE) scores  $\geq 24$ . Elderly fallers were older adults (at least 65 yrs old) who fell, due to unknown causes, at least twice in the past year and at least once in the previous 6 months, and did not have a balance or gait impairment that explained their multiple falls, i.e., they were "idiopathic" fallers. All subjects with PD had moderate disease [Hoehn and Yahr stage (Hoehn & Yahr, 1967) 2–3], were taking antiparkinsonian medications, and did not have motor response fluctuations. Subjects with PD, as defined by standard criteria (Gelb, Oliver, & Gilman, 1999), were recruited from an outpatient movement disorders clinic. All of the non-PD older adults were recruited from the community. A motor control study describes a subset of these subjects (Hausdorff, Yogev, Springer, Simon, & Giladi, 2005). They were included as healthy controls if they met the criteria described above and if they reported no falls in the past year. The classification of subjects as PD, idiopathic fallers or healthy (non-faller) controls was confirmed by history and after a general and neurological examination that was designed to identify the cause of any falls including gait, balance, muscular and neurological deficits. The study was approved by the Human Studies Committee of the Tel-Aviv Sourasky Medical Center.

#### Procedures

After providing informed written consent, subjects completed a physical examination. Extrapyramidal and motor signs were quantified using the motor portion (Part III) of the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn, Elton, & Members of the UPDRS development committee, 1987). This test is widely used to quantify parkinsonian and common

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motor signs of aging (e.g., bradykinesia) and predicts gait disability and mortality in nondemented older adults free of PD as well as in PD (Bennett, Shannon, Beckett, & Wilson, 1999;Wilson, Schneider, Beckett, Evans, & Bennett, 2002). Lower scores (out of a possible 108) are better. Average gait speed was also determined by measuring the time to walk 10 meters on level ground at a usual pace. Gait speed is often reduced in fallers and is associated with disability and health outcomes among older adults (Guralnik et al., 2000;Jylha, Guralnik, Balfour, & Fried, 2001).

All participants completed a computerized cognitive test battery designed to evaluate multiple cognitive domains and to detect mild impairment and dementia, Mindstreams<sup>®</sup> (NeuroTrax Corp., NY). Two recent papers describe the validity of the battery compared to traditional measures and the reliability of its summary index scores (Dwolatzky et al., 2003;Schweiger, Doniger, Dwolatzky, Jaffe, & Simon, 2003). Mindstreams is a computerized battery that employs novel adaptations of traditional neuropsychological tests to provide an overall measure of cognitive function as well as evaluation of specific cognitive domains (e.g., memory). Advantages include adaptive testing designs and precise accuracy and reaction time (RT) measurements (millisecond level). All tests were run in the same fixed order and all responses were made with the mouse or with the number pad on the keyboard. Patients were familiarized with these input devices at the beginning of the battery, and practice sessions prior to each test instructed them regarding the particular responses required. Outcome parameters, including accuracy, RT, and standard deviation of RT, varied with each test. Given the speedaccuracy tradeoff (Cauraugh, 1990), a performance index (calculated as [accuracy/RT]\*100) was computed for timed tests to grade performance both in terms of accuracy and RT. Following are brief descriptions of the tests administered: Go-NoGo Response Inhibition test: Timed continuous performance test, adapted from the well established paper-based test, during which responses are made to large colored stimuli that are any color but red. Verbal Memory: Ten pairs of words (the study set) are presented, followed by a recognition test in which one member (the target) of a previously presented pair appears together with a list of four candidates for the other member of the pair. There are four immediate repetitions and one delayed repetition after 10 minutes. Stroop Interference test: Timed test of response inhibition and set shifting adapted from the well established paper-based test (MacLeod, 1991). For example, in the 'No Interference [Meaning]' phase, the task is to choose the color named by a word presented in white letter-color. In the final ('Interference') phase, participants choose the letter-color of a word that names a different color. Non-Verbal Memory: This is similar to the test of verbal memory, except that geometric figures are used instead of words. Finger Tapping: Participants must tap on the mouse button with their dominant hand. Catch Game: A test of motor planning requiring hand-eye coordination and rapid responses. Subjects "catch" a "falling object" by moving a "paddle" horizontally on the computer screen so that it can be positioned directly in the path of the falling object. Staged Information Processing Speed test: This test comprises three levels of information processing load: single digits, twodigit arithmetic problems (e.g., 5-1), and three-digit arithmetic problems (e.g., 3+2-1). For each of the three levels, stimuli are presented at three different fixed rates, incrementally increasing as testing continues. Participants are instructed to respond as quickly as possible by pressing the left mouse button if the digit or result is less than or equal to 4 and the right mouse button if it is greater than 4.

To permit summarizing the performance in each cognitive domain across different types of outcome parameters (e.g., accuracy, RT), each outcome parameter was normalized and fit to an IQ-like scale (mean: 100, SD: 15) in an age- and education-specific fashion. The normative sample consisted of test data for 268 older individuals with an expert diagnosis of cognitively healthy in controlled research studies using Mindstreams. As described previously (Schweiger et al., 2003), normalized subsets of outcome parameters were averaged to produce five summary scores, each indexing a different cognitive domain: memory, executive function,

attention, information processing speed, and motor skills. The information processing index is based on performance on low- and medium-load stages of the Staged Information Processing Speed test. The executive function index score reflects accuracy and overall performance on tasks that maximally tax executive function (e.g., Stroop Interference). In contrast, the attention index score mainly reflects reaction times for tasks that require the patient to focus (e.g., Stroop No Interference [Meaning]) but do not stress executive function per se. These five index scores served as the primary dependent variables for the present analysis. A Global Cognitive Score (GCS) computed as the average of these index scores served as a secondary dependent measure. Raw outcome parameters from tests that contributed to index scores with significant betweengroup differences served as additional dependent measures.

## **Statistical Analyses**

Between-group comparisons of performance on the cognitive function battery were made by univariate analysis of covariance (ANCOVA). Age, education, gender, and computer experience (use computer: yes/no) were potential covariates. Each of these was included as a covariate in a separate analysis when a between-group difference was observed for the potential covariate (p<0.05) along with a within-group correlation between the potential covariate and performance (p<0.10) (or vice versa). An interaction term was included in the ANCOVA when significant at p<0.10 to correct for differential effects of the covariate across study groups and of study group across values of the covariate. Note that a conservative criterion (i.e., p < 0.10) was adopted for inclusion of the interaction term to increase the likelihood that cases of inequality of covariance would be detected and corrected for. If heterogeneity of variance was indicated by a significant Levene's test, homogeneity of variance was achieved via standard transformations (e.g., square, reciprocal). In cases of persistent heterogeneity of variance in the absence of covariates, a non-parametric Mann-Whitney U test was used. Two-tailed statistics were used throughout, and p < 0.05 was considered a significant between-group difference. For faller and PD groups, Spearman's rank-order correlation was computed between each Mindstreams summary measure and number of falls within the previous 6 months. All statistics were computed with SPSS statistical software (SPSS, Chicago, IL).

# RESULTS

#### Subject characteristics

As shown in Table 1, the three subjects groups were not different with respect to education, gender, height, weight, handedness, and computer experience (p>0.069). Group mean MMSE scores were similar in the fallers and healthy controls (p=0.178), and were reduced (by 1 point) in the subjects with PD (p=0.013). Healthy controls were comparable to PD participants in age (p=0.520) and were about seven years younger than fallers (p<0.001). The PD group was younger (p=0.006) and consisted of more males (p=0.013) relative to fallers, but was comparable in education, handedness, and computer experience (p>0.140). Statistical analysis of cognitive measures adjusted for potentially confounding differences in age and gender (see above). As expected, falls were most common in the fallers. Gait speed was reduced in the PD and faller groups. Scores on the motor portion of the UPDRS were negligible in the elderly controls, slightly higher in the fallers (p<0.001), and higher still in the subjects with PD (p<0.001).

Significant correlations between number of falls in the previous 6 months and attention ( $r_s$ = -0.59, p=0.017), information processing speed ( $r_s$ =-0.65, p=0.016), and the Global Cognitive Score ( $r_s$ =-0.54, p=0.031) were found in the faller group; correlations with all cognitive summary measures in the PD group were non-significant (p's>0.434)

#### Fallers Compared with Healthy Controls

Fallers performed more poorly than healthy controls in executive function (p=0.047), attention (p=0.012), and motor skills (p=0.013), but performed similarly to controls on memory (p=0.110) and information processing (p=0.606) as well as on the Global Cognitive Score (p=0.236; Figure 1).

To further investigate the observed between-group differences, tests contributing to the executive function, attention, and motor index scores were analyzed. Specifically, outcome parameter performance from the Go-NoGo Responses Inhibition, Stroop Interference, Catch Game, and Finger Tapping were studied (Table 2). On the Go-NoGo test, marked impairment among the fallers was evident for the standard deviation of RT (p=0.002; Figure 2). There were no significant differences for Go-NoGo accuracy, RT, or performance index (p>0.072). For the Stroop non-interference (meaning) condition, robust impairment in the fallers was found for the performance index (p=0.009) and standard deviation of RT (p<0.001; Figure 2). In this condition, significant differences were also found for accuracy and RT (p<0.025). As interactions (p<0.040) were found between group and age for the performance index and RT, it is possible that impairment in fallers on these outcome parameters may be limited to a circumscribed age range. For the Stroop interference condition, a significant difference was found for standard deviation of RT (p=0.035; Figure 2), but not for accuracy, RT, or performance index (p>0.088). On the Catch Game, robust impairment in fallers relative to healthy participants was evident for time to first move (p=0.001), average error for missed catches (p=0.001), and standard deviation of time to first move (p=0.003; Figure 2). A borderline difference was found for weighted accuracy (p=0.055). On the Finger Tapping test, there was no significant difference between fallers and healthy participants on either inter-tap interval or standard deviation of inter-tap interval (p>0.454).

#### Fallers Compared with Parkinson's Disease

Fallers performed similarly to PD participants across all cognitive domains and the GCS (memory: p=0.190; executive function: p=0.957; attention: p=0.626; information processing: p=0.530; motor skills; p=0.211; GCS: p=0.968). This pattern of results was confirmed in a subgroup comparison between PD participants without a history of falls (n=15) and idiopathic fallers; no differences were found in memory, executive function, attention, and information processing (p>0.542).

#### Parkinson's Disease Compared With Healthy Controls

PD participants performed more poorly than controls in executive function (p<0.001), attention (p=0.031), and motor skills (p=0.001) as well as on the GCS (p=0.001; Figure 1). No impairment was found in memory (p=0.251) or information processing (p=0.233). This pattern of results was confirmed in a subgroup comparison between PD participants without a history of falls and controls. As with all PD participants, no impairment was found for this subgroup in memory and information processing (p>0.225), but poorer executive function and attention performance was evident.

To further examine the differences in the summary scores observed between PD participants and controls, tests contributing to executive function, attention, and motor skills index scores were examined for all PD participants relative to controls (Table 2). On the Go-NoGo test, robust impairment in PD was evident for the performance index (p=0.009) and a borderline difference for RT (p=0.054). There were no significant differences for Go-NoGo accuracy or standard deviation of RT (p>0.197; Figure 2). For the Stroop non-interference (meaning) condition, significant differences were found for the performance index and standard deviation of RT (p<0.033; Figure 2) and a borderline difference in RT (p=0.057). There was no difference in accuracy (p=0.500). For the Stroop interference condition, robust impairment in PD was evident for RT (p=0.008). A significant difference was also found for the performance index (p=0.013). No differences were found in accuracy or standard deviation of RT (p>0.129; Figure 2). On the Catch Game, robust impairment in PD was evident for weighted accuracy (p<0.001) and average errors for missed catches (p=0.001). A significant difference was found for time to first move (p=0.046). No difference was found for standard deviation of time to first move (p=0.130; Figure 2). On the Finger Tapping test, robust impairment in PD participants was evident for standard deviation of inter-tap interval (p<0.001). No significant difference was found for inter-tap interval (p<0.001). No significant difference was found for inter-tap interval (p=0.079).

The Appendix provides additional details on the between-group analyses of the index scores and the GCS. Note that it was unnecessary to include an interaction term in any of these analyses, reflecting uniform effects of the covariates across groups for all primary study outcomes.

## DISCUSSION

The present, relatively detailed description of the cognitive profile of elderly fallers demonstrates that these older adults have significant cognitive changes. In particular, executive function and attention appear to be impaired, especially the consistency of the response times. In this group of community-living older adults identified based on their fall history, MMSE scores were near perfect, but a closer look with sensitive computerized measures revealed significant cognitive impairment. These findings are consistent with studies demonstrating that older adults at risk for falls do worse on the Trails Making B test (Di Fabio, Kurszewski, Jorgenson, & Kunz, 2004; Lord & Fitzpatrick, 2001) since that test requires scanning as well as executive function (i.e., set shifting, mental flexibility). Moreover, the observed deficits among the elderly fallers may explain why this group has an exacerbated dual tasking decrement (Bloem et al., 2001;Sheridan et al., 2003;Woollacott & Shumway-Cook, 2002). Executive function and attention are needed to appropriately allocate cognitive resources for the optimal performance of simultaneous tasks. Finally, because the present analyses demonstrate that both groups share a similar cognitive profile, our findings also confirm the use of patients with PD as a "positive" control group and agree with a well-established literature characterizing the prominent cognitive changes in patients with PD as alterations in executive function and attention (Dubois & Pillon, 1997;Uekermann et al., 2004;Zgaljardic et al., 2003; Elias & Treland, 1999). Thus, to a large degree, the cognitive profile of fallers is similar to that of patients with PD: deficits in executive function and attention are prominent features (although there are apparently notable differences, as described below).

The present findings also support the idea that the observed deficits in elderly fallers are a manifestation of changes in specific domains and not simply a result of a global decline in cognitive function. In both the fallers and the patients with PD (and the subgroup of PD patients without a fall history), memory and information processing were not markedly different from control values. Moreover, the results suggest that the observed changes in executive function and attention were not simply due to generalized slowed thinking or motor bradykinesia. For example, the inter-tap interval of tapping and the reaction times for the Go-NoGo test were not significantly different from control values, in both the fallers and the patients with PD. As in PD, the prominent attention and executive function deficits observed in the present study may be defining features of the cognitive profile in fallers.

While the overall picture was similar in the fallers and in the patients with PD, we do not wish to imply that the fallers are identical to PD. The medical history, physical and UPDRS scores clearly distinguish between these two groups. In addition, examination of the individual outcome parameters evidencing impairment in the affected cognitive domains points to subtle, but important differences in the cognitive profile of the fallers and the patients with PD. One

of the most intriguing differences concerned the consistency of RTs (i.e., standard deviation of RT). Regularity of RT's was especially poor in the fallers (recall Figure 2). Like other aspects of executive function and attention, recent investigations demonstrate that inconsistency of RTs is a marker for pre-frontal and frontal lobe dysfunction (Stuss, Murphy, Binns, & Alexander, 2003; Bellgrove, Hester, & Garavan, 2004; Stuss et al., 1999). In one study, patients with damage to either the dorsolateral prefrontal cortex or the superior medial frontal, but not the inferior medial frontal cortex, exhibited increased within subject variability on an executive function task (Stuss et al., 2003). Apparently, focal frontal brain damage is a cause for increased inconsistency in RTs. In an fMRI study using a Go-NoGo paradigm similar to the one employed in the present study, Bellgrove et al (Bellgrove et al., 2004) found that brain activation was positively correlated with extent of intra-individual response consistency in a distributed inhibitory network consisting of bilateral middle frontal areas and right inferior parietal and thalamic regions. The fMRI data support the interpretation that those subjects with more inconsistent RTs recruit inhibitory regions to a greater extent, as reflected by heightened activation of this top-down executive/attentional control network (Bellgrove et al., 2004). Taken together, these studies and the results of the present investigation suggest that fallers may have damage to specific neural networks subserving executive function and attention, but further investigation is needed to understand why reaction times are so inconsistent among the fallers.

The MMSE is widely used in geriatric research. Originally designed to quantify the cognitive state of older adults, today the MMSE is frequently used as a screen for dementia and as a cognitive assessment tool. The present findings suggest that the MMSE is not ideal for identifying those changes in cognitive function that are related to fall risk. Mean scores on the MMSE were essentially identical in the elderly fallers and the non-fallers, even though the fallers had measurable declines in certain cognitive domains. Just as the MMSE is not an appropriate tool for evaluating the cognitive changes in patients with subcortical disorders (Elias & Treland, 1999) or for predicting functional status in normal aging (Royall, Palmer, Chiodo, & Polk, 2004), it is not ideal if the objective is to assess fall risk. Apparently, for subcotrical disorders, normal aging and fall risk stratification, tests of executive function may be more appropriate (Elias & Treland, 1999; Royall et al., 2004).

Among the limitations of the present study are the sample size and the relatively older age of the fallers. Age was, nonetheless, taken into account in all of the analyses (recall the Appendix). Notwithstanding, a study of a larger cohort is needed to confirm these findings and evaluate possible additional, more subtle group differences. With the current sample size, we may not have had sufficient power to detect certain group differences. The present findings should set the stage for such follow-up studies. A prospective study designed to examine the degree to which specific cognitive deficits lie in the causal pathway of falls and how they modify dual tasking abilities and fall risk would be especially informative. During the past three decades, great advances have been made toward understanding and reducing fall risk in older adults, but there is still a need to examine potential contributory factors for fall risk that have received limited consideration (Guideline, 2001;Lavery & Studenski, 2003). The present findings support the idea that when evaluating and attempting to reduce fall risk, emphasis should be placed not only on traditional fall risk factors like muscle strength and motor function, but also on executive function and attention.

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## References

- American Geriatrics Society; British Geriatrics Society; American Academy of Orthopaedic Surgeons Panel on Falls Prevention. Guideline for the prevention of falls in older persons. Journal of the American Geriatrics Society 2001;49:664–672. [PubMed: 11380764]
- Bellgrove MA, Hester R, Garavan H. The functional neuroanatomical correlates of response variability: evidence from a response inhibition task. Neuropsychologia 2004;42:1910–1916. [PubMed: 15381021]
- Bennett DA, Shannon KM, Beckett LA, Wilson RS. Dimensionality of parkinsonian signs in aging and Alzheimer's disease. Journals of Gerontology Series A: Biological and Medical Sciences 1999;54:M191–M196.
- Bloem BR, Valkenburg VV, Slabbekoorn M, Gert vD. The multiple tasks test. Strategies in Parkinson's disease. Experimental Brain Research 2001;137:478–486.
- Cauraugh JH. Speed-accuracy tradeoff during response preparation. Research Quarterly for Exercise and Sport 1990;61:331–337. [PubMed: 2132891]
- Cocchini G, Della SS, Logie RH, Pagani R, Sacco L, Spinnler H. Dual task effects of walking when talking in Alzheimer's disease. Revue Neurologique (Paris) 2004;160:74–80.
- Di Fabio RP, Kurszewski WM, Jorgenson EE, Kunz RC. Footlift asymmetry during obstacle avoidance in high-risk elderly. Journal of the American Geriatrics Society 2004;52:2088–2093. [PubMed: 15571548]
- Dubois B, Pillon B. Cognitive deficits in Parkinson's disease. Journal of Neurology 1997;244:2–8. [PubMed: 9007738]
- Dwolatzky T, Whitehead V, Doniger GM, Simon ES, Schweiger A, Jaffe D, et al. Validity of a novel computerized cognitive battery for mild cognitive impairment. BMC Geriatrics 2003;3:4. [PubMed: 14594456]
- Elias JW, Treland JE. Executive function in Parkinson's disease and subcortical disorders. *Seminars in Clinical*. Neuropsychiatry 1999;4:34–40.
- Fahn, S., Elton, R., & Members of the UPDRS development committee (1987). Unified Parkinson's disease rating scale. In S. Fahn, C. D. Marsden, D. Calne, & M. Goldstein (Eds.), *Recent developments in Parkinson's disease* (pp. 153–163). Florham Park, NJ: Macmillan Healthcare Information.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician". Journal of Psychiatric Research 1975;12:189–198. [PubMed: 1202204]
- Gelb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson disease. Archives of Neurology 1999;56:33–39. [PubMed: 9923759]
- Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. Journals of Gerontology Series A: Biological and Medical Sciences 2000;55:M221–M231.
- Hausdorff JM, Balash J, Giladi N. Effects of cognitive challenge on gait variability in patients with Parkinson's disease. Journal of Geriatric Psychiatry and Neurology 2003;16:53–58. [PubMed: 12641374]
- Hausdorff, J. M., Yogev, G., Springer, S., Simon, E. S., & Giladi, N. Walking is more like catching than tapping: gait in the elderly as a complex cognitive task. *Experimental Brain Research*, (in press).
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967;17:427–442. [PubMed: 6067254]
- Jylha M, Guralnik JM, Balfour J, Fried LP. Walking difficulty, walking speed, and age as predictors of self-rated health: the women's health and aging study. Journals of Gerontology Series A: Biological and Medical Sciences 2001;56:M609–M617.
- Lavery LL, Studenski SA. Tai chi, falls, and the heritage of JAGS. Journal of the American Geriatrics Society 2003;51:1804–1805. [PubMed: 14687361]
- Lord SR, Fitzpatrick RC. Choice stepping reaction time: a composite measure of falls risk in older people. Journals of Gerontology Series A: Biological and Medical Sciences 2001;56:M627–M632.

- MacLeod CM. Half a century of research on the Stroop effect: an integrative review. Psychological Bulletin 1991;109:163–203. [PubMed: 2034749]
- O'Shea S, Morris ME, Iansek R. Dual task interference during gait in people with Parkinson disease: effects of motor versus cognitive secondary tasks. Physical Therapy 2002;82:888–897. [PubMed: 12201803]
- Royall DR, Palmer R, Chiodo LK, Polk MJ. Declining executive control in normal aging predicts change in functional status: the Freedom House Study. Journal of the American Geriatrics Society 2004;52:346–352. [PubMed: 14962147]
- Schweiger A, Doniger GM, Dwolatzky T, Jaffe D, Simon ES. Reliability of a novel computerized neuropsychological battery for mild cognitive impairment. Acta Neuropsychologica 2003;1:407–413.
- Sheridan PL, Solomont J, Kowall N, Hausdorff JM. Influence of executive function on locomotor function: divided attention increases gait variability in Alzheimer's disease. Journal of the American Geriatrics Society 2003;51:1633–1637. [PubMed: 14687395]
- Stuss DT, Murphy KJ, Binns MA, Alexander MP. Staying on the job: the frontal lobes control individual performance variability. Brain 2003;126:2363–2380. [PubMed: 12876148]
- Stuss DT, Toth JP, Franchi D, Alexander MP, Tipper S, Craik FI. Dissociation of attentional processes in patients with focal frontal and posterior lesions. Neuropsychologia 1999;37:1005–1027. [PubMed: 10468365]
- Uekermann J, Daum I, Bielawski M, Muhlack S, Peters S, Przuntek H, et al. Differential executive control impairments in early Parkinson's disease. J Neural Transmission Supplement 2004:39–51.
- van Schoor NM, Smit JH, Pluijm SM, Jonker C, Lips P. Different cognitive functions in relation to falls among older persons. Immediate memory as an independent risk factor for falls. Journal of Clinical Epidemiology 2002;55:855–862. [PubMed: 12393072]
- Wilson RS, Schneider JA, Beckett LA, Evans DA, Bennett DA. Progression of gait disorder and rigidity and risk of death in older persons. Neurology 2002;58:1815–1819. [PubMed: 12084882]
- Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: a review of an emerging area of research. Gait and Posture 2002;16:1–14. [PubMed: 12127181]
- Zgaljardic DJ, Borod JC, Foldi NS, Mattis P. A review of the cognitive and behavioral sequelae of Parkinson's disease: relationship to frontostriatal circuitry. Cognitive and Behavioral Neurology 2003;16:193–210. [PubMed: 14665819]

# APPENDIX

See Table 3, Table 4, and Table 5 in the Figures and Tables section.



#### Figure 1.

Index scores and Global Cognitive Score performance (mean+standard error) for the healthy controls and for the Parkinson's disease and faller groups. Data is normalized and fit to an IQ-style scale (mean: 100, SD: 15) in an age- and education-specific fashion. \* indicates p<0.05 versus healthy controls by analysis of covariance (ANCOVA).

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#### Figure 2.

Consistency of reaction times in the three study groups. Standard deviation of reaction time for Go-NoGo and Stroop tests and standard deviation of time to first move for the Catch Game was significantly larger in the faller group compared to the healthy controls. \* indicates p<0.05 versus healthy controls by analysis of covariance (ANCOVA). See the text for additional details.

#### Table 1

Demographic and Clinical Characteristics of Fallers, Parkinson's Disease, and Healthy Control Groups (Entries are mean±SD or %, as indicated).

	Healthy Controls (N=25)	Fallers (N=18)	Parkinson's Disease (N=30)
Age (years)	70.0±6.1	77.1±4.9 <sup>*</sup>	71.3±7.8
Education (years)	13.6±2.1	13.4±2.3	14.1±3.7
Height (meters)	1.69±0.08	$1.65 \pm 0.08$	$1.69 \pm 0.11$
Weight (kg)	73.3±12.5	70.6±9.9	74.5 ±15.8
Gender, % female	44 %	67 %	30 %
% right-handed	96 %	100 %	93 %
Computer Experience (% no)	64 %	83 %	63 %
Mini Mental State Exam	29±1.1	29.0±1.5	28.1+1.7*
Falls Within Last 6 months (% yes)	0 %	$100\%^{*}$	50 %
# of Falls Within Last 6 Months	0±0	$2.6 \pm 1.5^{*}$	0.9+1.0*
Gait Speed (m/sec)	1.31±0.19	$0.98\pm25^{*}$	1.05±0.23*
Motor Signs (Part III of the UPDRS)	0.5±0.9	$2.9{\pm}1.8^{*}$	$18.1{\pm}8.0^{*}$

\* indicates p<0.05 compared to healthy controls. See the Results for further details.

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# Table 2

Raw outcome parameter performance from tests contributing to executive function, attention, and motor skills index scores in Healthy Control, Faller, and Parkinson's Disease Groups (Entries are mean±SD).

Test	Outcome Parameter	Healthy Controls (N=25)	Fallers (N=18)	Parkinson's Disease (N=30)
бо- коссо везночая вышегом	Accuracy, % correct Average RT, msec Performance Index, (accuracy/RT)100*	$\begin{array}{c} 93.4 \pm 5.87 \\ 473.08 \pm 81.07 \\ 20.24 \pm 3.32 \end{array}$	$\begin{array}{c} 86.78 \pm 16.60 \\ 646.78 \pm 209.71 \\ 15.23 \pm 5.65 \end{array}$	$90.47 \pm 9.82$ $545.01 \pm 137.17$ $17.51 \pm 4.03^{*}$
	Standard Deviation of RT, msec No Interference: Word Meaning Accuracy & correct	$137.36 \pm 108.56$ $97.6 \pm 7.11$	$319.13 \pm 226.58^{*}$	170.93 ±101.81 96.40 +6.0
	Average RT, msec	$647.08 \pm 206.30$	$944.44 \pm 340.99$	$790.33 \pm 316.48$
STROOP INTERFERENCE	Performance Index, (accuracy/RT)100 Standard Deviation of RT, msec	$16.40 \pm 4.46$ $167.24 \pm 152.41$	$10.52 \pm 3.07$ 479.39 $\pm 281.32^{*}$	$13.74 \pm 4.50$ $475.33 \pm 290.19$ *
	Interforence: Letter Cotor vs. Word Meaning Accuracy, % correct Average RT, msec	$\begin{array}{c} 78.04 \pm 34.29 \\ 720.81 \pm 320.93 \end{array}$	$58.31 \pm 35.96$ $1076.67 \pm 490.27$	$65.28 \pm 28.93$ $1010.85 \pm 478.29$ *
	Performance Index, (accuracy/RT)100 <sup>*</sup> Standard Deviation of RT, msec Time to Mate 1 et Monte meec	$12.97 \pm 7.22$ $318.13 \pm 319.17$ $768  67 \pm 213  87$	$6.66 \pm 5.12$ $549.36 \pm 384.01^{*}$	$8.35 \pm 5.85$ $475.33 \pm 287.29$
CATCH GAME	time to make as thore, insec Standard Deviation of Time to 1st Move, msec Weighted Accuracy (max. 1000) Average Error For Missed Catches	$223.49 \pm 109.43$ $274.52 \pm 212.49$ $0.56 \pm 0.35$	$1105.09 \pm 255.98$ $434.70 \pm 139.32$ $280.08 \pm 183.46$ 1.27 + 0.57	$902.16 \pm 2.59.44$ $276.40 \pm 138.88$ $375.64 \pm 171.02^{*}$ $0.94 \pm 0.47^{*}$
<b>FINGER TAPPING</b>	Inter-Tap Interval, msec Standard Deviation of Tap Interval, msec	$226.0 \pm 52.28$ $37.8 \pm 16.18$	$262.71 \pm 50.45$ $59.11 \pm 75.97$	$259.34 \pm 79.48$ $80.23 \pm 55.51$
RT=reaction time				
mean-millicannde				

Average RTs are given for correct responses only.

\* p<0.05 relative to controls (after covarying for age, education, gender, or computer experience, as appropriate; see Methods)

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Fallers Compared with Healthy Controls. Adjusted summary measures, co-variates and transformations used. Unadjusted measures are reported in Figure 1. Table 3

Mindstreams Summary Measure	Covariation Necessary? <sup>a</sup>	Covariate Included	Correlation in Fallers (r)	Correlation in Controls (r)	Interaction Term? <sup>b</sup>	Transformation? <sup>c</sup>	Transformation Used	F	đf	d	Fallers: (Adjusted) Mean ± SD	Controls: (Adjusted) Mean ±SD
Memory Executive	no yes	 Age	 -0.19	 -0.47	01	no	1 1	2.67 4.22	$1,41 \\ 1,40$	$0.110 \\ 0.047$	$89.83 \pm 13.10$ $94.89 \pm 9.78$	$96.99 \pm 14.91$ $101.51 \pm 9.51$
Function	Ю	1	1	1	1	yes	x <sup>4</sup>	6.91	1,41	0.012	$78.30*10^6 \pm 28.01*10^6$	$105.67*10^{6} \pm 20.22*10^{6}$
Information	Ю	I	1	1	ł	no	1	0.27	1,37	0.606	$94.55 \pm 9.68$	$96.61 \pm 12.89$
rucessing Motor Skills GLOBAL COGNITIVE	no yes	 Age	 -0.34	 -0.43	ou	no	11	6.83 1.45	1,40 1,40	0.013 0.236	$93.84 \pm 12.63$ $94.68 \pm 8.71$	$101.79 \pm 7.05$ 98.14 $\pm$ 8.47
SCORE												

 $a^{0}$  Determined by a significant between-groups difference at p<0.05 and a significant within-group correlation with performance at p<0.1 (or vice versa; see Methods)

 $b_{\text{If significant at }p<0.1}$  (see Methods).

 $^{c}\mathrm{Determined}$  by significant Levene's test at  $p{<}0.05.$ 

SD: Standard Deviation

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Fallers Compared with Parkinson's Disease (PD). Adjusted summary measures, co-variates and transformations used. Unadjusted measures are reported in Figure 1. Table 4

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$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	mory scutive	yes no	gender 	0.08	0.44 	ou 	ou	11	1.77 0.00	1,45 1,46	0.190 0.957	$87.63 \pm 14.58$ 92.31 $\pm 8.91$	$\begin{array}{c} 93.56 \pm 14.33 \\ 92.46 \pm 9.55 \end{array}$
cessing       yes       gender $-0.37$ $-0.32$ no       no $$ $1.61$ $1,43$ $0.211$ $95.93 \pm 12.30$ $91.03 \pm 12.08$ tor Skills       yes       gender $-0.37$ $-0.32$ no $$ $1.61$ $1,43$ $0.211$ $95.93 \pm 12.30$ $91.03 \pm 12.08$ tor NBAL       no $$ $$ $0.00$ $1,46$ $0.968$ $92.29 \pm 8.94$ $92.19 \pm 7.77$	iction ention ormation	no	1 1			1 1	no	11	0.24 0.40	1,46 1,33	0.626 0.530	$91.71 \pm 12.79$ $94.55 \pm 9.68$	$\begin{array}{c} 93.65 \pm 13.53 \\ 91.87 \pm 13.61 \end{array}$
	cessing tor Skills OBAL GNITIVE	yes no	gender 	-0.37	-0.32	ou	ои	11	$1.61 \\ 0.00$	1,43 1,46	0.211 0.968	$95.93 \pm 12.30$ $92.29 \pm 8.94$	$91.03 \pm 12.08$ $92.19 \pm 7.77$

aDetermined by a significant between-groups difference at p<0.05 and a significant within-group correlation with performance at p<0.1 (or vice versa; see Methods)

b If significant at p < 0.1 (see Methods).

 $^{\mathcal{C}}$  Determined by significant Levene's test at  $p{<}0.05.$ 

SD: Standard Deviation

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Parkinson's Disease (PD) Compared With Healthy Controls. Adjusted summary measures, co-variates and transformations used. Unadjusted measures are reported in Figure 1. Table 5

Memory         no             no          1.35         1.53         0.251         92.24±15.30         96.99±14.9           Executive         no            no          17.61         1.53         <0.051	Mindstreams Summary Measure	Covariation Necessary? <sup>a</sup>	<b>Covariate</b> Included	Correlation in Fallers (r)	Correlation in Controls (r)	Interaction Term? $^{b}$	Transformation? <sup>c</sup>	Transformation Used	H	đf	d	PD: (Adjusted) Mean ±SD	Controls: (Adjusted) Mean ± SD
Function Attentionnoyes $x^2$ 4.911.530.03189.47*10^2 \pm 101.66*10^2Attentionno1.461.440.23391.87 ± 13.6196.61 ± 12.88Processingno1.461.440.23391.87 ± 13.6196.61 ± 12.88Processingnoyes $x^2$ 12.241,520.00186.54*10^2 ± 104.10*10^2 ± 13.610*2010^2 ± 13.60*10^2 ± 13	Aemory Accutive	ou	11	11	11	11	оп	11	1.35 17.61	$1,53 \\ 1,53$	0.251 <0.001	$\begin{array}{c} 92.24 \pm 15.30 \\ 92.46 \pm 9.55 \end{array}$	$96.99 \pm 14.91$ $103.36 \pm 9.64$
Information no 1.46 1,44 0.233 91.87 ± 13.61 96.61 ± 12.8 Processing $x^2$ 10 1.46 1,44 0.233 91.87 ± 13.61 96.61 ± 12.8 Processing no yes $x^2$ 12.24 1,52 0.001 $86.54^{*}10^2 \pm 104.10^{*}10^{2}$ 13.99 $x10^2$ 13.96 $x17$ 93.86 ± 7.95 COGNITIVE	<sup>T</sup> unction Attention	no	-		I		yes	x <sup>2</sup>	4.91	1,53	0.031	$89.47*10^2 \pm 2000$	$101.66*10^2 \pm$
Processing     Processing       Motor Skills     no         104.10 <sup>2</sup> ±     104.10 <sup>2</sup> ±       Motor Skills     no         104.10 <sup>2</sup> ±     104.10 <sup>2</sup> ±       GLOBAL     no         13.90 <sup>*10<sup>2</sup></sup> ±     104.10 <sup>2</sup> ±       GLOBAL     no        no     21.50 <sup>*10<sup>2</sup></sup> ±     104.10 <sup>2</sup> ±       COGNITIVE     no        no      13.90 <sup>*10<sup>2</sup></sup> ±	nformation	ои	ł		-		по	1	1.46	1,44	0.233	$23.50^{\circ}10^{-}$ 91.87 ± 13.61	$96.61 \pm 12.89$
GLOBAL no $12.90  ext{ 1.53 } 0.001  ext{ 92.19} \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 99.86} \pm 7.95  ext{ 0.001 } 92.19 \pm 7.77  ext{ 0.001 } 92.1$	rocessing Aotor Skills	ои	ł		-	I	yes	x <sup>2</sup>	12.24	1,52	0.001	$86.54*10^2 \pm 0.0000$	$104.10*10^{2} \pm$
	SLOBAL YOGNITIVE	no			I		ио	1	12.99	1,53	0.001	$22.19 \pm 7.77$	$15.90 \times 10^{-10}$

aDetermined by a significant between-groups difference at p<0.05 and a significant within-group correlation with performance at p<0.1 (or vice versa; see Methods)

 $b_{\text{If significant at }p<0.1}$  (see Methods).

 $^{\mathcal{C}}$  Determined by significant Levene's test at  $p{<}0.05.$ 

SD: Standard Deviation