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The Relationship Between Specific Cognitive Functions and Falls in Aging

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Abstract

The current study examined the relationship between cognitive function and falls in elders who did not meet criteria for dementia or Mild Cognitive Impairment (n=172). To address limitations of previous research, associations between cognitive function and falls controlled for the confounding effects of gait measures and other risk factors. A neuropsychological test battery was submitted to factor analysis yielding three orthogonal factors (verbal IQ, Speed/Executive Attention, Memory). Single and recurrent falls within the last 12 months were evaluated. We hypothesized that Speed/Executive Attention would be associated with falls. Additionally, we assessed whether associations between different cognitive functions and falls varied depending on whether single or recurrent falls were examined. Multivariate logistic regressions showed that worse scores on Speed/Executive Attention were associated with increased single and recurrent falls. Worse scores on Verbal IQ were related only to increased recurrent falls. Memory was not associated with either single or recurrent falls. These findings are relevant to risk assessment and prevention of falls, and point to possible shared neural substrate of cognitive and motor function.

Keywords

cognition; falls; aging

Approximately 30% of community-dwellers and 50% of nursing home residents aged 65 years and older fall each year (Blake, Morgan, & Bendall, 1988). Within the elderly

population falls are a factor in approximately 10% of emergency room visits (Sattin, 1992). Falls have significant negative outcomes on old individuals including physical injury (Bell, Talbot-Stern, & Hennessy, 2000; Tinetti, Speechly, & Ginter, 1988), hospitalization (Lachman, Howland, & Tennstedt, 1998; Runge, 1993), restricted mobility (Kosorok, Omenn, & Diehr, 1992), nursing home admissions (Tinetti & Williams, 1997), and death (Murphy, 2000). The Center for Disease Control and Prevention reported unintentional injuries, with falls as the leading type, as the seventh leading cause of death in the United States in the 65 and over age group. Hence, understanding the causes and risk factors for falls is of significant public health importance.

The risk factors for falls are heterogeneous and include poor balance (Nevitt, Cummings, Kidd, & Black, 1989), impaired gait (Tinetti et al., 1988), musculoskeletal weakness (Prudham & Evans, 1981), use of psychotropic drugs (Cumming, 1998; Thapa, Gideon, & Cost, 1998), impaired visual acuity (Tinetti et al., 1988), and medical conditions such as Parkinson's disease (Jantti, Pykko, & Hervonen, 1993), arthritis (Tinetti, Williams, & Mayewski, 1986), and strokes (Dolinis, Harrison, & Andrews, 1997).

Dementia is a significant risk factor for falls (Buchner & Larson, 1987). However, the relationship between specific cognitive functions and the risk of falls in normal aging or in dementia is poorly understood. Furthermore, whereas multidisciplinary risk assessment and interventions of falls focus on gait, balance and strength (Tinetti, Baker, McAvay, Claus, Garrett, Gottschalk, et al., 1994), neuropsychological assessment, with the exception of gross evaluation of dementia status, is conspicuously absent. Identifying associations between specific cognitive functions and falls in normal aging has significant implications as such findings would suggest that: a) neuropsychological assessment may provide incremental information relevant to risk assessment for falls b) specific cognitive functions may be etiologically related to falls c) shared neural substrate could be implicated in cognitive performance and specific motor outcomes such as falls.

The relationship between attention and falls has been assessed using dual-tasks with simultaneous cognitive and motor demands. This is exemplified by studies that required elder participants to walk and talk at the same time. Such studies revealed that dual-task performance costs, as measured in decrements in walking speed, were related to the risk of falls suggesting that limited attentional resources in older persons were causally related to falls (Camicioli, Howieson, Lehman, & Kaye, 1997; Verghese, Buschke, Viola, Katz, Hall, Kuslansky, et al., 2002). This choice of experimental approach is not surprising given that attentional resources that decline with age (Craig & Byrd, 1982; McDowd & Shaw, 2000) are required for maintaining one's posture and gait, especially in public where the ability to negotiate competing demands from the environment is paramount. Further, dual-task methodology provides a theoretical and empirical basis for evaluating divided attention (see Pashler, 1994; Pashler, 1998, for reviews of theories and empirical findings concerning dual-task paradigms). However, interpreting dual-task costs requires that the single tasks be well characterized and understood in terms of their cognitive demands (Holtzer, Stern, & Rakitin, 2005). More recently we showed that empirically derived cognitive factors were differentially related to gait velocity in single and dual-task conditions in a large non-demented sample of older adults residing in the community (Holtzer, Verghese, Xue, & Lipton, 2006). Specifically, factors that measured verbal IQ, Speed/Executive Attention and Memory were all related to gait velocity when performed as a single task. In contrast, only the Speed/Executive Attention and Memory factors were related to gait velocity in the dual-task (walking while talking). Further, the Speed/Executive Attention factor was the most potent predictor of gait velocity irrespective of gait task condition (Holtzer et al., 2006). Walking and talking dual-task paradigms are useful predictors of falls. However, because gait performance shares variance with cognitive functions and is related to the risk of falls it

is difficult to assess mechanisms using this model. Stated differently, it is difficult to separate cognitive from gait effects on falls using this paradigm. In contrast, independent assessment of cognition and gait affords statistical control of gait performance when evaluating associations between specific cognitive processes and falls.

Our previous findings (Holtzer et al., 2006) characterized the relationship between cognitive functions (Verbal IQ, Executive attention, Memory) and locomotion in aging in single and dual-task conditions. The current study was designed to extend our previous findings and examine whether and how the same cognitive functions were related to falls. Additionally, a number of confounding variables may modulate the association between cognition and falls including demographic characteristics, medical conditions such as arthritis, stroke and Parkinson's disease, and medication use (see Nevitt, 1997, for review of risk factor for falls in aging). Accordingly, we used multivariate models to assess the associations between cognitive functions and falls after adjusting for potential confounders including quantitative and clinical measures of gait performance.

The current study aimed to identify, cross-sectionally, whether and how specific cognitive functions were related to falls in a large sample of elders who did not meet criteria for dementia or Mild Cognitive Impairments. To accomplish this goal, a comprehensive neuropsychological test battery validated for use with elder adults (Katzman, Aronson, Fuld, Kawas, Brown, Morgenstern, et al., 1989; Masur, Sliwinski, Lipton, Blau, & Crystal, 1994; Sliwinski, Buschke, Stewart, Masur, & Lipton, 1997) was submitted to factor analysis. The resultant orthogonal factors represented separate and empirically defined cognitive domains (Verbal IQ, Speed/Executive Attention and Memory). We used three parameters to evaluate falls within the last year. First, we defined a group of fallers who had one or more fall events in the past year as well as the complimentary group of non-fallers. Second, because recurrent falls are more likely to be indicative of pathology than a single fall, we divided the group of fallers into two sub-groups. Individuals who reported only one fall event comprised the Single Fall subgroup. Individuals who reported two or more fall events comprised the Recurrent Falls subgroup. We hypothesized that Speed/Executive Attention would be associated with falls. However, we also assessed whether associations between different cognitive functions and falls varied depending on whether single or recurrent falls were the outcome variables.

Finally, the current study controlled for the possible confounding effects of clinical gait abnormality and quantitative measures of gait on the associations between cognitive functions and falls.

Method

Participants

Participants were from the Einstein Aging Study (EAS). This population-based longitudinal aging study, which aims to identify the earliest markers that distinguish "normal" aging from dementia, recruited a community-based cohort that has been followed since 1999. Recruitment and study procedures have been detailed previously (Lipton, Katz, Kuslansky, Sliwinski, Stewart, Verghese, et al., 2003). In brief, telephone-based screening interviews were used to enroll and follow the cohort. Inclusion criteria were age 70 and over, English speaking, and residing in the Bronx. Exclusion criteria were institutionalization, and sensory deficits (visual and hearing loss) of sufficient severity to interfere with neuropsychological testing, and pre-existing dementia. EAS participants were randomly recruited from lists of Medicare recipients in the Bronx, and were first contacted by letter, which described the objective of the study, and then by telephone. The telephone interview consisted of a brief medical history questionnaire, obtaining verbal consent, and telephone-based cognitive

screening test (Lipton et al., 2003). Subsequent to the interview, the subjects who met eligibility criteria over the phone were requested to come to the research center for further screening and evaluations. Between 1999-2001 488 subjects were enrolled and informed consents were acquired at clinic visits according to protocols agreed upon by the local institutional review board. Subjects were followed at yearly intervals.

Quantitative gait assessment was introduced to EAS between 2001 and 2004. Of the 488 subjects who were recruited since 1999, 223 (46%) received quantitative gait assessment. For the purpose of this study, we excluded 22 subjects who met criteria for Mild Cognitive Impairment (MCI) (Petersen, Smith, Waring, Ivnik, Tangalos, & Kokmen, 1999; Petersen, Doody, Kurz, Mohs, Morris, Rabins, et al., 2001) and 15 who met criteria for dementia (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984) at the time of their gait evaluation as determined at the EAS consensus diagnostic case conference. Additionally, 14 participants who did not have complete neuropsychological and falls data were also excluded. This study focused on the sub-sample of 172 elderly participants who had complete neuropsychological, quantitative gait and falls data. Of these participants 126 were Caucasians, 39 were African Americans, and 7 were identified with other ethnic groups. This sample was not statistically different ($p > .05$) than the inception cohort at baseline in terms of age, sex, and education.

Measures

Neuropsychological tests—The tests included in this battery have been validated for use in the normal aging population in our and other aging studies (Katzman et al., 1989; Masur et al., 1994; Sliwinski et al., 1997). The goal of the neuropsychological test battery was to assess general level of cognitive status, attention, memory, speed of processing, language, and executive function.

The following test were incorporated into the neuropsychological battery: The Vocabulary (total score), Digit Span (total forward and backward), Digit Symbol (total number correct), and Block Design (total score) sub-tests of the Wechsler Adult Intelligence Scale-revised (WAIS-R, Wechsler, 1981); the Free and Cued Selective Reminding Test [(FCSRT), total free recall; (Grober, Buschke, Crystal, Bang, & Dresner, 1988)]; a 15-item abbreviated version of the Boston Naming Test [(BNT), total correct including semantic cues; (Stern, Andrews, Pittman, Sano, Tatemichi, Lantigua, et al., 1992)]; Letter fluency [(FAS), total number of words; Benton & Hamsher, 1976); Category fluency [animals, fruits and vegetables, using procedures from the Boston Diagnostic Aphasia Examination (BDAE); Goodglass & Kaplan, 1983]; and the Trails Making Test [seconds to completion for Forms A and B, and total errors for form B (Reitan, 1958)].

Falls—Self-reported history of falls within the last year was obtained during a clinical interview that was part of a comprehensive assessment of the subject. Falls were defined using standard criteria as sudden, unintentional, unprovoked changes in body posture resulting in the person being on a lower level, not due to a major intrinsic event (stroke) or overwhelming hazard (Tinetti et al., 1994). We have previously reported a 100% concordance between 6 and 12-month falls data in a smaller sample of non-demented elderly from the EAS cohort (Verghese et al., 2002). Recently, Ganz, Higashi and Rubenstein (2005) reviewed the effect of recall interval on the accuracy of fall reports. Recall of falls in the previous 12 months was specific (specificity 91-95%) but less sensitive (sensitivity 80–89%) than the criterion standard of ongoing prospective collection of fall data using fall calendars or postcards (Ganz et al., 2005). Furthermore, recall bias was related to poorer cognitive function as measured by the MMSE (Folstein, Folstein, & McHugh, 1975). Individuals scoring below 24 were most susceptible to recall bias (Cummings, Nevitt, &

Kidd, 1988). Hence, while a 12-month retrospective self-report of falls has limitations, especially in terms of sensitivity, it appears to have acceptable psychometric properties, at least in non-demented older adults.

Total disease score—Dichotomous rating (present or absent) of diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, Parkinson's disease, chronic obstructive lung disease, angina, and myocardial infarction, was used when calculating a summary score of disease comorbidity (range 0-10). Medical history was obtained from multiple sources. Subjects were asked to bring written documents concerning their medical history, hospitalization records and list of current medications. Trained research assistants used structured clinical interview and the study physician obtained medical history during the neurological examination independently of the structured clinical interview. Significant others and family physicians were contacted when available to corroborate subjects' reports. Finally, information gathered from all the above sources was carefully examined prior to data entry.

Clinical Gait Assessment—Structured clinical evaluations were done at each visit by study clinicians who determined whether gaits were normal or abnormal (Verghese et al., 2002; Verghese Katz, Kuslansky, Hall, Derby, & Lipton, 2004). Abnormal gaits were classified as either non-neurological (due to causes such as arthritis or cardiac disease) or neurological (unsteady, ataxic, frontal, parkinsonian, neuropathic, hemiparetic, and spastic) using previously described methods (Verghese et al., 2002). We reported 89 percent agreement (kappa 0.6) on gait evaluations done a year apart by multiple study clinicians in 189 subjects in our previous cohort (Verghese et al., 2002). We also prospectively compared gait assessments done by junior and senior clinicians in 30 participants from the current cohort, and showed high inter-rater reliability (kappa 0.8; Verghese et al., 2004).

Quantitative gait assessment – Gait Velocity—Details regarding the quantitative gait assessment and walking protocol were reported in our previous study (Holtzer et al., 2006). In brief, research assistants conducted quantitative gait evaluations independent of the clinical evaluation. Quantitative gait parameters were collected using a 12-foot computerized gait mat (180 × 35.5 × 0.25 inches) with embedded pressure sensors (GAITRite, CIR systems, NJ). Participants were asked to walk on the mat in a well-lit hallway at their 'normal walking speed' for three trials. Start and stop points were marked by white lines on the floor, and included three feet each for initial acceleration and terminal deceleration. Monitoring devices were not attached to the participants during the test. Gait velocity (cm/second) was computed by the software as dividing the distance covered on two trials by the ambulation time. Excellent reliability and validity for GAITRite assessments were reported in previous research in our center (Verghese et al., 2002) and in other studies (Bilney, Morris, & Webster, 2003).

Statistical Analyses

Demographic variables were tabulated for the entire sample and then further subdivided for fallers and non-fallers. For descriptive purposes, group comparisons (faller vs. non-fallers) on demographic characteristics and individual neuropsychological tests were examined using t-tests for independent samples for continuous variables and Chi-Square analyses for categorical variables.

The raw neuropsychological test scores were submitted to Principal Components Factor Analysis to reduce the number of measures and to derive empirical factors that represented separate cognitive functions (Bryant & Yarnold, 1995). Because the principal-components analysis was run on the correlation matrix, the raw scores were normalized on the basis of

the distribution of the entire sample. Varimax rotation was used to derive orthogonal factor scores ($M=0$, $SD=1$) and the minimum eigenvalue for extraction was set at 1. Each factor was defined as a linear combination of all the neuropsychological tests. However, statistical significance for the factor loadings was set at 0.5 to simplify the interpretation of the factor analysis and because loadings of 0.5 or greater are also considered to be practically significant (Hair, Anderson, & Tatham, 1998). The resultant neuropsychological factors served as independent variables in regression analyses that aimed to predict falls. This analytic approach offers several advantages. First, the reduction of a large number of individual neuropsychological tests that are often correlated into cognitive domains is empirically based. Second, the resultant neuropsychological factors are orthogonal and hence can be used as independent variables in the same regression analyses without the risk of collinearity. Third, the factors can provide direction to future hypothesis testing of how specific cognitive functions within a general domain are related to falls. Additionally, the same analytic approach was used in our previous paper examining the relationship between cognitive functions and gait in aging (Holtzer et al., 2006). Replicating this methodology allowed us to extend our previous findings and examine whether and how the same cognitive functions were related to falls.

Three separate multivariate logistic regressions examined the relationship between specific cognitive functions and falls. The orthogonal neuropsychological factors served as independent variables. Any, single and recurrent falls served as the dichotomous dependent variables in three separate regressions. That is, non-fallers were compared to individuals with a history of a) any falls b) single falls c) recurrent falls. All regression analyses controlled for age, sex, education, ethnicity, total disease comorbidity status, clinical gait abnormality, gait velocity, and medications. Medication use was examined both as the sum of individual medications (irrespective of class) as well as classes of medications (any use within a class even if more than once) per subject. The latter was restricted to antipsychotics, antidepressants, and benzodiazepines as these three classes of medications have been reported to show the strongest association with falls (Nevitt, 1997). The final results were not materially different using both approaches. Hence, we report only the analyses using the latter approach that is considered more stringent. All analyses were done with SPSS version 12 (2003). Internal validity of the logistic regressions was examined using the Hosmer and Lemeshow Goodness-of-Fit Test (Hosmer & Lemeshow, 1989), which divides subjects into deciles based on predicted probabilities, and then computes a chi-square from observed and expected frequencies. If the Hosmer and Lemeshow Goodness-of-Fit test statistic is .05 or less the null hypothesis that there is no difference between the observed and predicted values of the dependent measure is rejected implying that the model is not valid. Non significant chi-square indicates failure to reject the null hypothesis implying that the model's estimates fit the data at an acceptable level.

Results

Sample characteristics

Demographic characteristics and neuropsychological tests for the sample are summarized in Table 1.

Table 1 reveals balanced gender distribution and mean education level that exceed high-school diploma. The participants were relatively healthy, as indicated by their low disease score and number of medications used. The prevalence of medications that previously were associated with falls was low and comparable in the non-fallers (7%) and fallers (10%) samples. This low prevalence is not surprising given that subjects in this study were healthy and functionally independent community residents. Only one participant scored below an established empirical cutoff on the Free and Cued Selective Reminding Test that has been

associated with increased risk of incident dementia (score < 24; Grober et al., 1988). Fallers comprised 23% of the sample. Group comparisons between fallers (n=40) and non-fallers (n=132) revealed that fallers were somewhat older and had worse scores on the Trails B and Digit Symbol tests. Of the 40 participants who fell 25 reported single falls and 15 reported recurrent falls (14 had two falls and one had three falls).

Factor analysis – neuropsychological tests

PCA of the neuropsychological test scores yielded exactly three significant orthogonal factors that accounted for 61 percent of the variance in neuropsychological test scores. Results of the PCA (summarized in Table 2) replicated the factor structure obtained in our prior study (Holtzer et al., 2006) with a similar sample of older adults who did not meet criteria for dementia or for MCI.

The first factor, Verbal IQ, encapsulated a broad range of verbal capabilities that vary in terms of their sensitivity to detect age-related cognitive decline. Tests with coefficient loading at or above .5 on this factor included the Vocabulary, Information, FAS, BNT, and Digit Span. The Speed/Executive Attention factor captured facets of higher order cognitive abilities that are typically considered representative of attention and executive processes. It is important to note that the tests with coefficient loadings at or above .5 on this factor were all timed: Trail A (time), Trail B (time, errors), Digit Symbol, and Block Design. The loading coefficients of individual neuropsychological tests on the Speed/Executive Attention factor (see Table 2) point to the directionality of relationship between scores on individual tests and the factor scores. The negative loadings of Trails A and B (time to completion and errors) indicate that higher factor scores are associated with less time to complete the tasks and with fewer errors. The positive loadings of digit symbol and block design indicate that higher scores on these two tests are associated with higher factor scores. Stated differently, better performance on individual neuropsychological tests is expressed in terms of higher normalized factor scores and vice versa. The Memory factor represented aspects of episodic and semantic verbal memory. Tests with coefficients loading at or above .5 included the FCSRT, and the Category Fluency test.

Relation of cognitive functions to falls

Summary of the multivariate analyses examining the relation of cognitive functions to any, single and recurrent falls is presented in Table 3.

The Hosmer-Lemeshow goodness-of-fit test and showed adequate internal validity for the multivariate logistic models predicting any falls χ^2 (8, N=172) = 4.073, $p=0.850$, single falls χ^2 (8, N=157) = 4.548, $p=0.805$, and recurrent falls χ^2 (8, N=147) = 12.422, $p=0.133$. Only the Speed/Executive Attention was significantly related to any falls, $OR=.495$, 95%CI =.314-.779, $p=.002$, and to single falls $OR=.518$, 95%CI =.304-.884, $p=.016$ (see Table 3). The Speed/Executive Attention, $OR=.339$, 95%CI=.148-.774; $p=.010$, Verbal IQ $OR=.213$, 95%CI=.081-.562, $p=.002$, and disease comorbidity, $OR=2.698$, 95%CI=1.271-5.724, $p=.010$ were significantly related to recurrent falls (see Table 3).

To further illustrate the important association between executive attention and falls, scores on the Speed/Executive Attention factor were divided into three percentile groups. Fallers comprised 12.3%, 22.4%, and 35.1% of the high, intermediate and low scoring groups, respectively. Moreover, logistic regression using the three level Speed/Executive Attention factor as a predictor and falls as the outcome showed that individuals in the low scoring group were almost four times more likely to fall than individuals in the high scoring group, $OR=3.861$, 95%CI=1.478-10.083, $p=.006$.

To examine the overlap between cognition and motor function the three cognitive factors were correlated with gait velocity adjusting for age, sex, and education. The correlations were statistically significant for Speed/Executive Attention $r=.298$, $p<.001$, Memory $r=.165$, $p=.028$, and Verbal IQ $r=.200$, $p=.011$.

Estimates of effect sizes for the logistic regressions: effect sizes for the cognitive factors in the logistic regressions can be estimated using a previously described method (Breslow & Day, 1987). In brief, the log of the odds ratio associated with each factor score is approximately equivalent to the effect size comparing non-fallers to fallers assuming a common variance in the factor score. For instance, the estimated effect size for the odds ratio of the Speed/Executive attention factor in the logistic regression predicting any falls (.495) is 0.70.

Discussion

The current study showed that of the cognitive functions we examined Speed/Executive Attention had the most potent and consistent associations with falls in healthy elders who reside in the community. A one-point increase (i.e., one standard deviation) on the Speed/Executive Attention factor scores in this sample was associated with approximately 50% reduction in the risk of falls. Whereas previous research failed to control for the confounding effect of clinical and quantitative gait abnormalities on the relationship between attention and falls the current study addressed this limitation because cognitive function and gait performance were assessed independently. Furthermore, the correlations between the cognitive factors and gait were significant but relatively small suggesting that the variance in the cognitive and gait measures we examined was to a large degree non-overlapping. The implications of these findings with respect to the role neuropsychology may have in assessment and intervention procedures for falls are discussed under “future implications”.

The relationship between cognitive functions and falls varied depending on whether single or recurrent falls were evaluated. Whereas only Speed/Executive Attention function was related to single falls, Verbal IQ and disease comorbidity explained incremental portion of the variance when recurrent falls were assessed. Verbal IQ is conceptualized as a proxy of cognitive reserve (Stern, 2002) and has been related to functional outcomes (Scarmeas & Stern, 2003). The results of this study suggest that cognitive reserve is also related to the risk of falls, at least when falls are repeated and likely represent increased pathology. However, these findings should be interpreted with some caution because the recurrent falls group was comprised of 15 individuals and analyses that are based on small samples may be unreliable. These findings will have to be replicated in future prospective studies with larger samples.

We recently showed that Speed/Executive Attention, Memory and Verbal IQ were related to gait velocity in normal aging (Holtzer et al., 2006). The current study revealed that of these three cognitive domains only Speed/Executive Attention was consistently related to falls. Hence, although gait and falls are related, their association with cognitive function differs. Informative associations between measures of attention and executive function and mobility in the elderly have been reported by others as well (Giordani, & Persad, 2005; Persad, Giordani, Chen, Ashton-Miller, Alexander, Wilson, et al., 1995). These findings also have important implications with respect to neural networks that are possibly shared by motor and cognitive function. Cortical control mechanisms of gait and balance are not well established but appear to extend over large cortical and subcortical regions and include the frontal (Guo, Steen, Matousek, Anderson, Larsson, Palsson, et al., 2001) and temporal (Kerber, Enrietto, Jacobson, & Baloh, 1998) lobes. White matter irregularities reduce processing speed (Dow, Seidenberg, & Hermann, 2004) and are related to mobility impairments (Benson, Guttmann, Wei, Warfield, Hall, Schmidt, et al., 2002; Whitman, Tang, Lin, & Baloh, 2001; Whitman,

DiPatre, Lopez, Liu, Noori, Vinters, et al., 1999). The association between gait and multiple cognitive functions is consistent with the extended cortical and sub-cortical correlates of gait. In contrast, the potent association between Speed/Executive Attention and falls suggests that frontal basal ganglia circuitry, specifically the prefrontal dorsolateral circuit, which mediates executive control processes (D'Esposito & Postle, 2002; Curtis & D'Esposito, 2003; Middleton & Strick, 2001) may have an important causative relation to the risk of falls in cognitively normal elders. In this context it is of interest to note that memory function was not related to either single or to recurrent falls. The differential relation of distinct cognitive functions to falls argues against the notion that any cognitive function sensitive to the aging process would be related to the risk of falls.

Our findings also raise important questions that will have to be addressed in future research. The Speed/Executive Attention factor encapsulated cognitive functions that depend on speed of processing and visual-spatial abilities. Future studies should decipher the possible contribution of specific components of attention and executive function (e.g., Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991; Holtzer, Burright, & Donovanick, 2004; Holtzer, Rakitin, & Stern, 2004) to the prediction of falls. Moreover, in the context of prospective research, it will be of interest to examine whether baseline performance and or changes over time on measures of attention and executive functions predict falls. Additionally, the association between Verbal IQ and recurrent falls requires further elucidation as this factor captured a broad base of verbal ability with tests that vary in terms of their sensitivity to age-related decline in cognitive function.

The limitations of the present study should be considered. Cross-sectional associations between cognitive processes and falls can not be used to infer causality. Our findings need to be replicated in prospective studies with larger samples with different demographic characteristics and a wider spectrum of cognitive performance. Specifically, it is of interest to evaluate whether the unique association between executive attention and falls can be generalized to patients with dementia and MCI. Another limitation is concerned with the method used to collect falls data. Reliance on self-report and the long recall interval are threats to both reliability and validity. However, Ganz et al. (2005) found that 12-month self reported falls had high specificity but somewhat reduced sensitivity when compared to the gold standard of prospective falls assessment. The lower sensitivity for the 12-month retrospective recall of falls would have resulted in reduced power to demonstrate significant effects. Nonetheless, the relationship between Speed/Executive Attention and falls remained significant even with stringent control of confounding variables including clinical and quantitative measures of gait. These findings should be replicated in prospective research using more sensitive and frequent assessments of falls. It is important to note that the factor analysis was intended to achieve a meaningful data reduction of neuropsychological tests data in non-demented EAS subjects. We have replicated the three factor structure in non-demented EAS samples and showed that the cognitive factors were differentially related to outcomes of interest. However, establishing construct validity for the factors across samples that vary in terms of demographic characteristics and cognitive function was not our intent and is well beyond the scope of the present study. Strengths of our study include the systematic clinical and quantitative gait evaluations, comprehensive study of cognitive function, and the large sample which was representative of individuals 70 and older in the Bronx catchment area.

Future implications

Falls present a major public health concern in the aging population. However, risk assessment and prevention programs have had limited success (Tinetti et al., 1994). At the present adequate cognitive evaluation is conspicuously absent from standard risk assessment for falls. This may be attributed in part to limited knowledge of whether and how specific

cognitive functions are related to falls. This study suggests that measures of attention and executive function, which rely on speed and visual processing, were most strongly related to falls at cross-section. Accordingly, performance on such measures may provide incremental information relevant for risk assessment of falls. However, to establish causality these associations have to be demonstrated prospectively.

Future research should examine how individual neuropsychological tests and cognitive neuroscience paradigms dissecting visual attention and executive function into specific processes are related to falls. For instance, the alerting, orienting and executive attention components of the Attention Networks Test [(ANT); Fan, McCandliss, Sommer, Raz & Posner, 2002] are related to separate brain networks (Corbetta, Kincade, Ollinger, McAvoy & Shukman, 2000; Posner & Peterson, 1990) and to genetic polymorphisms (Fossella, Sommer, Fan, Wu, et al., 2002). Identifying whether and how these specific aspects of visual attention and executive function are related to falls will further advance research toward identifying mechanism as opposed to correlates of falls in aging. Such research may possibly lead to more effective fall prevention programs in the elderly as well. For example, identifying deficits in specific aspects of attention and executive function (e.g., alertness, selective or divided attention) may point to pharmacological and cognitive interventions that are tailored to rehabilitate specific deficits (Manly & Robertson, 2003; Sturm, Willmes, Orgass, & Hartje, 1997; Zimmermann, North, & Finn, 1993). Further, interventions may also aim to identify conditions under which attention to safe walking or to the maintenance of secure posture may become compromised.

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References

- Bell A, Talbot-Stern J, Hennessy A. Characteristics and outcomes of older patients presenting to the emergency department after a fall: a retrospective analysis. *Medical Journal of Australia*. 2000; 173:176–177. [PubMed: 11008588]
- Benson RR, Guttmann CRG, Wei X, Warfield SK, Hall C, Schmidt JA, et al. Older people with impaired mobility have specific loci of periventricular abnormality on MRI. *Neurology*. 2002; 58:48–55. [PubMed: 11781405]
- Benton, A.; Hamsher, K. Multilingual aphasia examination. University of Iowa; Iowa City: 1976.
- Bilney B, Morris M, Webster K. Concurrent related validity of the GAITRite walkway system for quantification of the spatial and temporal parameters of gait. *Gait Posture*. 2003; 17(1):68–74. [PubMed: 12535728]
- Blake A, Morgan K, Bendall M. Falls by elderly people at home: prevalence and associated factors. *Age & Ageing*. 1988; 17:365–372. [PubMed: 3266440]
- Breslow, NE.; Day, NE. Statistical methods in cancer research. Volume II--The design and analysis of cohort studies. IARC Scientific Publications; Lyon, France: 1987.
- Bryant, FB.; Yarnold, PR. Principal-components analysis and exploratory and confirmatory factor analysis. In: Grimm, LG.; Yarnold, PR., editors. *Reading and understanding multivariate statistics*. First ed.. American Psychological Association; Washington DC: 1995. p. 99-136.
- Buchner D, Larson E. Falls and fractures in patients with Alzheimer-type dementia. *JAMA*. 1987; 257:1492–1495. [PubMed: 3820464]

- Camicioli R, Howieson D, Lehman S, Kaye J. Talking while walking: The effect of a dual task in aging and Alzheimer's disease. *Neurology*. 1997; 48:955–958. [PubMed: 9109884]
- Corbetta M, Miezin FM, Dobmeyer S, Shulman GL, Petersen SE. Selective and divided attention during visual discrimination of shape, color and speed: functional anatomy by positron emission tomography. *Journal of Neuroscience*. 1991; 11:2383–2402. [PubMed: 1869921]
- Cumming R. Epidemiology of medication-related falls and fractures in the elderly. *Drugs and Aging*. 1998; 12:43–53. [PubMed: 9467686]
- Cummings SR, Nevitt MC, Kidd S. Forgetting falls: The limited accuracy of recall of falls in the elderly. *Journal of the American Geriatric Society*. 1988; 36:613–616.
- Curtis CE, D'Esposito M. Persistent activity in the prefrontal cortex during working memory. *Trends Cognitive Science*. 2003; 7(9):415–423.
- D'Esposito, M.; Postle, BR. The neural basis of working memory, storage, rehearsal and control processes: Evidence from patient and functional magnetic resonance imaging studies. In: Squire, LR.; Schacter, D., editors. *Neuropsychology of Memory*. The Guilford Press; New York: 2002. p. 215-224.
- Dolinis J, Harrison JE, Andrews GR. Factors associated with falling in older Adelaide residents. *Australian and New Zealand Journal of Public Health*. 1997; 21:462–468. [PubMed: 9343889]
- Dow C, Seidenberg M, Hermann B. Relationship between information processing speed in temporal lobe epilepsy and white matter volume. *Epilepsy and Behavior*. 2004; 5(6):919–925. [PubMed: 15582841]
- Craik, FIM.; Byrd, M. Aging and cognitive deficits: The role of attentional resources. In: Craik, FIM.; Trehub, S., editors. *Aging and cognitive processes*. Plenum Press; New York: 1982. p. 191-211.
- Fan J, McCandliss B, Sommer T, Raz A. Testing the efficacy and independence of attentional networks. *Journal Cognitive Neuroscience*. 2002; 14(3):340–347.
- 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]
- Fossella J, Sommer T, Fan J, Wu Y, Swanson JM, Pfaff DW, et al. Assessing the molecular genetics of attention networks. *BMC Neuroscience*. 2002; 4:3–14.
- Giordani, B.; Persad, CC. Neuropsychological influences on gait in the elderly. In: Hausdorff, J.; Alexander, N., editors. *Gait disorder – evaluation and management*. Taylor & Francis Group; Tampa, Florida: 2005. p. 117-142.
- Goodglass, H.; Kaplan, E. *The assessment of aphasia and related disorders*. 2nd ed.. Lea & Febiger; Philadelphia: 1983.
- Grober E, Buschke H, Crystal HA, Bang S, Dresner R. Screening for dementia by memory testing. *Neurology*. 1988; 38:900–903. [PubMed: 3368071]
- Guo X, Steen B, Matousek M, Anderson LA, Larsson L, Palsson S, et al. A population-based study on brain atrophy and motor performance in elderly women. *Journal of Gerontology Medical Sciences*. 2001; 56(10):633–637.
- Hair, JE., Jr.; Anderson, RE.; Tatham, RL.; Black, WC. *Multivariate data analysis*. 5th ed.. Prentice Hall; Upper Saddle River, NJ: 1998.
- Holtzer R, Burright RG, Donovan PJ. The Sensitivity of Dual-task Performance to Cognitive Status in Aging. *Journal of the International Neuropsychological Society*. 2004; 10(2):230–238. [PubMed: 15012843]
- Holtzer R, Rakitin CB, Stern Y. Age-related differences in executive control of working memory. *Memory & Cognition*. 2004; 32(8):1333–1345.
- Holtzer R, Stern Y, Rakitin BC. Predicting age-related dual-task effects with individual differences on neuropsychological tests. *Neuropsychology*. 2005; 19(1):18–27. [PubMed: 15656759]
- Holtzer R, Verghese J, Xue X, Lipton R. Cognitive processes related to gait velocity: Results from the Einstein Aging Study. *Neuropsychology*. 2006; 20(2):215–223. [PubMed: 16594782]
- Hosmer, DW.; Lemeshow, S. *Applied Logistic Regression*. Wiley; New York: 1989.
- Jantti PO, Pykko VI, Hervonen AL. Falls among elderly nursing home residents. *Public Health*. 1993; 107:89–96. [PubMed: 8480017]

- Katzman R, Ronson M, Fuld P, Kawas C, Brown T, Morgenstern H, et al. Development of dementing illnesses in an 80-year-old volunteer cohort. *Ann Neurology*. 1989; 25(4):317–24.
- Kerber K, Enrietto JA, Jacobson KM, Baloh RW. Disequilibrium in older people: A prospective study. *Neurology*. 1998; 51(2):574–580. [PubMed: 9710038]
- Kosorok M, Omenn G, Diehr P. Restricted activity days among older adults. *American Journal of Public Health*. 1992; 82:1263–1267. [PubMed: 1503169]
- Lachman M, Howland J, Tennstedt S. Fear of falling and activity restriction: The survey of activity and fear of falling in the elderly (SAFE). *Journal of Gerontology*. 1998; 53:43–50.
- Lipton RB, Katz MJ, Kuslansky G, Sliwinski MJ, Stewart WF, Verghese, et al. Screening for dementia by telephone using the memory impairment screen. *Journal of the American Geriatric Society*. 2003; 51:1382–1390.
- Manly, T.; Robertson, IH. The rehabilitation of attentional deficits. In: Halligan, PW.; Kischka, U.; Marshall, JC., editors. *Handbook of clinical neuropsychology*. Oxford University Press; New York, NY: 2003. p. 89-109.
- Masur DM, Sliwinski M, Lipton RB, Blau AD, Crystal HA. Neuropsychological prediction of dementia and the absence of dementia in healthy elderly persons. *Neurology*. 1994; 44(8):1427–32. [PubMed: 8058143]
- McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan E. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology*. 1984; 34:939–944. [PubMed: 6610841]
- McDwoud, JM.; Shaw, RJ. Attention. In: Craik, FIM.; Salthouse, TA., editors. *Handbook of aging and cognition*. 2nd ed.. Erlbaum; Mahwah, NJ: 2000. p. 221-292.
- Middleton F, Strick P. Cerebellar projections to the prefrontal cortex in the primate. *Journal of Neuroscience*. 2001; 21(2):700–712. [PubMed: 11160449]
- Murphy SL. Deaths: Final data for 1998. *National Vital Statistics Reports*. 2000; 48(11):1–105. [PubMed: 10934859]
- Nevitt, M. Falls in the elderly: risk factors and prevention. In: Masdue, JC.; Sudarsky, L.; Wolfson, L., editors. *Gait disorders of aging falls and therapeutic strategies*. Lippincott – Raven publishers; New York, NY: 1997. p. 13-36.
- Nevitt MC, Cummings S, Kidd S, Black D. Risk Factors for recurrent nonsyncopal falls: a prospective study. *JAMA*. 1989; 261:2663–2668. [PubMed: 2709546]
- Pashler HE. Dual-task interference in simple tasks: Data and theory. *Psychological Bulletin*. 1994; 116:220–224. [PubMed: 7972591]
- Pashler, HE. *The psychology of attention*. MIT Press; Cambridge, MA: 1998.
- Persad CC, Giordani B, Chen H, Ashton-Miller JA, Alexander N, Wilson CS, et al. Neuropsychological predictors of complex obstacle avoidance in healthy older adults. *Journal of Gerontology: Psychological Sciences*. 1995; 50B(5):272–277.
- Petersen RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV, et al. Current concepts in Mild Cognitive Impairment. *Archives of Neurology*. 2001; 58:1985–1992. [PubMed: 11735772]
- Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: Clinical characterization and outcome. *Archives Neurology*. 1999; 56:303–308.
- Posner MI, Petersen SE. The attention system of the human brain. *Annual Review Neuroscience*. 1990; 13:25–42.
- Prudham D, Evans J. Factors associated with falls in the elderly: A community study. *Age and Ageing*. 1981; 10:141–146. [PubMed: 7270321]
- Reitan RM. Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual & Motor Skills*. 1958; 8:271–276.
- Runge J. The cost of injury. *Emerg med clin North America*. 1993; 11:241–253.
- Sattin R. Falls among older persons: A public health perspective. *Annual Review of Public Health*. 1992; 13:489–508.
- Scarmeas N, Stern Y. Cognitive reserve and lifestyle. *Journal of Clinical and Experimental Neuropsychology*. 2003; 5:625–633. [PubMed: 12815500]

- Sliwinski M, Buschke H, Stewart WF, Masur D, Lipton RB. The effect of dementia risk factors on comparative and diagnostic selective reminding norms. *J. International Neuropsychological Society*. 1997; 3:317–326.
- Spss for Windows, Release 12. SPSS Inc; Chicago: 2003.
- Stern Y. What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society*. 2002; 8:448–460. [PubMed: 11939702]
- Stern Y, Andrews H, Pittman J, Sano M, Tatemichi T, Lantigua, et al. Diagnosis of dementia in a heterogeneous population. Development of a neuropsychological paradigm-based diagnosis of dementia and quantified correction for the effects of education. *Archives of Neurology*. 1992; 49:453–460. [PubMed: 1580806]
- Sturm W, Willmes K, Orgass B, Hartje W. Do specific attention deficits need specific training? *Neuropsychological Rehabilitation*. 1997; 7(2):81–103.
- Thapa P, Gideon P, Cost T. Antidepressants and the risk of falls among nursing home residents. *New England Journal of Medicine*. 1998; 339:875–882. [PubMed: 9744971]
- Tinetti M, Williams CS. Falls, Injuries Due to Falls, and the Risk of Admission to a Nursing Home. *New England Journal of Medicine*. 1997; 337:1279–1284. [PubMed: 9345078]
- Tinetti M, Speechly M, Ginter S. Risk factors for falls among elderly persons living in the community. *New England Journal of Medicine*. 1988; 319:1701–1707. [PubMed: 3205267]
- Tinetti M, Williams F, Mayewski R. A fall risk index for elderly patients based on number of chronic disabilities. *American Journal of Medicine*. 1986; 80:429–434. [PubMed: 3953620]
- Tinetti ME, Baker DI, McAvay G, Claus EB, Garrett P, Gottschalk M, Koch ML, Trainor K, Horwitz RI. A multifactorial intervention to reduce the risk of falling among elderly people living in the community. *New England Journal of Medicine*. 1994; 331:821–827. [PubMed: 8078528]
- Verghese J, Buschke H, Viola L, Katz M, Hall C, Kuslansky G, et al. Validity of divided attention tasks in predicting falls in older individuals: a preliminary study. *Journal of the American Geriatric Society*. 2002; 50:1572–1576.
- Verghese J, Katz M, Kuslansky G, Hall C, Derby C, Lipton RB. Reliability and validity of a telephone base mobility assessment questionnaire. *Age and Ageing*. 2004; 33(6):628–632. [PubMed: 15501841]
- Verghese J, Lipton RB, Hall CB, Kuslansky G, Katz MJ, Buschke H. Abnormality of gait as a predictor of non-Alzheimer's dementia. *New England Journal of Medicine*. 2002b; 347(22):1761–1768. [PubMed: 12456852]
- Wechsler, D. Wechsler Adult Intelligence Scale-Revised. The Psychological Corporation; New York, NY: 1981.
- Whitman GT, DiPatre PL, Lopez IA, Liu F, Noori NE, Vinters HV, et al. Neuropathology in older people with disequilibrium of unknown cause. *Neurology*. 1999; 53:375–382. [PubMed: 10430429]
- Whitman GT, Tang T, Lin A, Baloh RW. A prospective study of cerebral white matter abnormalities in older people with gait dysfunction. *Neurology*. 2001; 57:990–994. [PubMed: 11571322]
- Zimmermann, P.; North, P.; Flimm, B. Diagnosis of attentional deficits: theoretical considerations and presentation of a test battery. In: Stachowiak, F., editor. *developments in the assessment and rehabilitation of brain damaged patients*. G. Narr-Verlag; Tübingen: 1993.

Table 1

Descriptive statistics of demographic variables, neuropsychological raw tests scores, clinical gait abnormality, and gait velocity for the entire sample and per falls status

Variable	Entire Sample (n=172)		Non-Fallers (n=132)		Fallers (n=40)	
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>
Education: (years)	14.37±3.3		14.26±3.24		14.74±3.59	
Age: (years) *	77.69±4.38		77.28±3.90		79.09±5.51	
% Female	54.7		54.5		55	
Total Disease	1.86±1.19		1.78±1.13		2.15±1.35	
% Gait Abnormality ^a	39.5		36		50	
Medications	2.9±2.2		2.8±2.1		3.1±2.3	
Gait Velocity (cm/sec)	97.84±23.42		99.46±21.95		92.49±27.34	
Vocabulary	50.08±12.18		50.35±12.18		49.20±12.55	
BNT	12.33±2.39		12.47±2.22		11.87±2.85	
Information	22.76±5.71		22.77±5.60		22.72±6.02	
Letter Fluency	38.41±12.24		39.11±12.21		36.10±12.17	
Digit Span	13.70±3.83		13.84±3.80		13.327±3.96	
Block Design	19.16±8.87		20.18±8.48		17.72±9.92	
Digit Symbol *	38.90±10.80		39.94±11.03		35.47±9.30	
TrailA (Sec)	55.44±21.57		53.93±20.75		60.42±23.68	
TrailB (Sec) *	131.12±59.43		124.63±58.00		152.52±59.78	
TrailB (errors) *	1.49±2.24		1.10±1.56		2.78±3.43	
FCSRT-FR	33.97±4.39		33.79±4.68		34.58±3.261	
Category Fluency	39.48±8.86		39.57±8.69		39.20±9.50	

FCSRT-FR=Free Recall from Free and Cued Selective Reminding Test; BNT=Boston Naming Test. Independent samples t-tests (df = 170) were used to examine group differences (fallers vs. non-fallers) on all continuous measures. Chi Square analyses examined group differences in gender distribution and classification of clinical gait abnormality.

* p<.05

^aClinical diagnosis of gait abnormality was determined by according to standardized published criteria and independent of the neuropsychological tests scores and quantitative gait assessment

Table 2

Results of the principal components factor analysis

Variable	Verbal IQ	<i>Speed/Executive Attention</i>	Memory
% of variance	25.66	22.74	12.91
Eigenvalues	3.08	2.73	1.55
Tests			
Information	.819	.146	.056
Vocabulary	.799	.173	.172
BNT	.689	.223	.122
Letter Fluency	.610	.144	.437
Digit Span	.527	.267	-.014
Trails: A (time)	-.043	-.823	-.222
Trails: B (time)	-.189	-.828	-.212
Trails: B (errors)	-.195	-.613	-.021
Digit Symbol	.409	.611	.338
Block Design	.400	.614	-.059
FCSRT	-.041	.159	.847
Category Fluency	.492	.137	.638

Note: bold print indicates loading coefficients above .5

Italics indicates significant group differences (fallers vs. non-fallers) on mean factor scores FCSRT-FR=Free Recall from Free and Cued Selective Reminding Test; BNT=Boston Naming Test. Errors on Trails Form A were not included in the PCA due to a ceiling effect.

Table 3

Multiple logistic regressions predicting any, single and multiple falls.

Factor/ Variable	Any falls (n fallers=40) Multivariate		Single falls (n fallers=25) Multivariate		Recurrent falls (n fallers=15) Multivariate	
	OR	95% CI	OR	95% CI	OR	95% CI
Verbal IQ	.635	.386-1.044	1.020	.543-1.915	.213	.081-.562
Executive attention	.495**	.314-779	.518*	.308-.884	.339**	.148-.774
Memory	1.243	.807-1.916	1.518	.934-2.469	1.037	.511-2.103
Age	1.055	.962-1.157	1.049	.937-1.175	1.061	.908-1.239
Education	1.115	.976-1.273	1.104	.945-1.290	1.101	.895-1.356
Sex	.801	.324-1.981	.802	.283-2.271	.888	.166-4.748
Disease index (1-10)	1.263	.897-1.781	1.056	.700-1.593	2.698*	1.271-5.724
Gait Velocity	1.007	.986-1.028	1.004	.979-1.029	.999	.961-1.038
Gait abnormality	.725	.294-1.788	.921	.301-2.821	.931	.228-3.798
Medications	1.064	.252-4.491	1.013	.169-6.077	.424	.040-4.443

Note: Analyses controlled for ethnicity. Caucasians served as the reference group against which African Americans and others were compared. General effect of ethnicity was not significant in the multivariate analyses predicting any falls (Wald=2.56, p=.633), single falls (Wald=1.066, p=.587) and recurrent falls (Wald=2.723; p=.256). Specific comparisons between the reference and other two groups were not significant.

* p<.05

** p<.01