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The Relationship of Executive Functions and Episodic Memory with Gait Speed Decline in Aging Defined in the Context of Cognitive Reserve

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Abstract

Objectives—The current study was designed to evaluate whether levels of Cognitive Reserve (CR), as measured by WAIS-III Vocabulary test, moderated longitudinal associations between cognitive functions and the decline in gait speed in a community-based cohort of non-demented older adults. Specifically, we hypothesized that the protective effect of Executive Functions (EF) and episodic memory against decline in gait speed would be increased in individuals with higher CR.

Design—Longitudinal study (Median number of repeated annual gait speed measures =3; maximum number of visits=7).

Setting—General community.

Participants—751 community residing non-demented individuals age 70 years and older were followed longitudinally with cognitive and gait evaluations at baseline and at annual visits.

Measures—Decline in gait speed (cm/sec) served as the primary outcome.

The Free and Cued Selective Reminding Test (FCSRT) was used to assess episodic memory. The Digit Symbol Substitution test (DSS) was used to assess attention and EF. The Vocabulary test served as a marker for CR.

Results—Linear mixed effects model showed that gait speed declined over the follow-up period ($p < 0.001$). The significant three-way interactions of time $\times$ DSS $\times$ Vocabulary ($p = 0.015$) and time $\times$ FCSRT $\times$ Vocabulary ($p = 0.021$) revealed that the longitudinal associations of EF and episodic memory with gait speed decline were moderated by levels of CR.

Conclusion—The protective effects of EF and episodic memory against gait speed decline in aging are increased in individuals with higher CR.

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Keywords

Cognitive Reserve; Gait Speed; Executive Functions; Episodic Memory

INTRODUCTION

Identifying early risk factors for and mechanisms of impaired mobility in older adults is critical for developing improved risk assessments and interventions¹. For the purpose of this paper gait speed decline was used to define mobility limitations². Decline in gait speed is common in aging and is associated with increased risk of adverse outcomes including but not limited to cardiovascular disease, disability and mortality²⁻⁴. Recent converging evidence from epidemiologic,⁵ cognitive,⁶ structural imaging,⁷ functional imaging,⁸ and genetic⁹ studies suggests that gait is influenced by higher order cognitive control mechanisms. Of the cognitive functions examined, attention and Executive Functions (EF) have an important, though not exclusive, relationship with walking speed⁶. Episodic memory and verbal IQ are also related to gait speed¹⁰. The associations of gait with EF and episodic memory are explained, in part, by shared brain substrates that underlie complex and distinct cognitive motor circuits. Hippocampal volume and metabolism that are critical for memory function are also related to gait.¹¹ Furthermore, neurologic gait impairments and decline in quantitative measures of gait are evident in amnesic MCI.¹² Recent volumetric⁷ and functional neuroimaging studies⁸ showed that the pre-frontal cortex sub-serves both gait and EF.

Research using measures of cognitive functions at baseline to predict decline in gait, although confirmatory of their association¹³⁻¹⁶, is scarce. Furthermore, previous studies have not evaluated factors that may moderate the relationship between cognitive functions and walking speed. Specifically, whether and how individual differences in Cognitive Reserve (CR) affect longitudinal associations between cognitive functions and age-related decline in gait speed has not been assessed.

CR is conceptualized as an active process that allows the individual to cope with pathology by efficient usage of existing cognitive processes or by recruiting alternative processes to successfully negotiate task demands¹⁷. The CR hypothesis posits that individual differences exist in how people respond to task demands vis-à-vis pathology or brain insults¹⁷. While some controversy exists regarding the measurement of CR there is a consensus that measures of verbal IQ, general fund of knowledge, vocabulary or reading are acceptable markers for this construct¹⁷. We reported that markers for CR including Vocabulary were related to gait speed¹⁰ and to falls history¹ in older adults.

Here we further hypothesized that individual differences exist in how EF and episodic memory resources are utilized in the context of gait performance. Specifically, the current study evaluated the moderating effect of CR, as measured by the Vocabulary test, on the relationships among EF and episodic memory, assessed at baseline, and the decline in gait speed over longitudinal yearly follow-up in non-demented older adults. According to the CR hypothesis individuals with higher levels of reserve utilize cognitive resources more effectively to negotiate task demands. We therefore predicted that the protective effect of EF and episodic memory function against gait speed decline would be greater in individuals with higher CR.

METHODS

Participants

The current prospective cohort study of non-demented older adults was nested within the Einstein Aging Study (EAS), a longitudinal study of aging and dementia¹⁸. Eligibility criteria required that participants be at least 70 years of age and speak English. Exclusion criteria include severe audiovisual disturbances, inability to ambulate and institutionalization. Individuals diagnosed with dementia were also excluded from this investigation. Diagnoses of dementia were assigned according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV TR, 2000¹⁹) at consensus diagnostic case conferences²⁰. Potential participants were first contacted by letter, then by telephone explaining the nature of the study. The telephone interview consisted of verbal consent, a brief medical history questionnaire, and telephone-based cognitive screening tests that included the Memory Impairment Screen by telephone (MIS-T, a test of semantic memory), the Category Fluency Test (CF-T), and the Telephone Instrument for Cognitive Status (TICS).¹⁸ Discriminative validity for the MIS-T was excellent. Using a cutscore that provided a sensitivity of 78%, specificity was at 93%. Participants who met eligibility criteria over the phone were invited for in-house evaluations. Informed consents were obtained at clinic visits according to study protocols and approved by the local institutional review board. Participants were followed at yearly intervals.

Measures

Gait speed (cm/s) served as the outcome and was measured using an instrumented walkway with embedded pressure sensors (GAITRite, CIR systems, Havertown, PA). The GAITRite system is widely used in clinical and research settings, and has excellent psychometric properties. Gait speed and the mean gait characteristics demonstrated excellent test-retest reliability (ICC 0.80)²¹. Participants were asked to walk on the walkway at their usual pace in a quiet well-lit room wearing comfortable footwear and without any attached monitors. Participants walked for two trials on a walkway with 15 feet (457.2 cm) of recording surface till July 2008. Following which, assessments were done for one trial on a walkway with 20 feet (609.6 cm) of recording surface. The correlation for gait speed measured on the two walkways in 20 participants was excellent (Pearson $r = 0.94$). Reliability between two consecutive walking trials was also excellent (Pearson $r = 0.96$). Start and stop points were marked by white lines, and included three feet (four feet for the longer walkway) from the edge of the recording surface to account for initial acceleration and terminal deceleration.

Neuropsychological predictors

Vocabulary subtest of the Wechsler Adult Intelligence Scale—3rd edition (WAIS-III)²², considered a hold test in that it is not sensitive to the effect of aging and age-related diseases, served as a marker for CR^{1, 10}. The individual is required to provide definitions for a list of words that increase in complexity. Scores range from 0-66 with higher scores indicating better performance. The vocabulary subtest is an objective performance task that correlates highly with other measures of CR.¹⁷

Free and Cued Selective Reminding Test (FCSRT) was used to assess episodic memory²³. The FCSRT is sensitive to age and dementia related memory decline²³. Scores range from 0-48 with higher scores indicating better performance. The FCSRT is a 16-item free and cued recall test that uses category words to present items for learning and then uses the same category words to cue the subject when the item is not freely recalled.

Digit Symbol Substitution subtest (DSS) of the WAIS-III²² is a timed test commonly used to assess speed of processing, visual spatial attention and EF^{1, 10}. The DSS has a key grid of

numbers and matching symbols and a test section that consists of rows containing small blank squares, each paired with a randomly assigned number from 1-9. The participant is required to fill the empty boxes with the symbol that matches each number, as fast and accurately as possible. Scores range from 0-133 with higher scores indicating better performance.

Covariates

Structured clinical interviews were used to identify self-reported medical diagnosis of a range of common health problems. Consistent with our previous studies^{1, 10, 20} dichotomous rating (presence or absence) of diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, Parkinson's disease, chronic obstructive lung disease, angina, and myocardial infarction was used to calculate a disease comorbidity summary score (range 0–10). Usage of medications was also assessed during the structured clinical interview and neurological examination.

Statistical Analysis

Demographic characteristics, medical history, gait speed, and cognitive test performance were tabulated for the entire sample. Linear mixed effects model was used to examine the effects of the cognitive predictors at baseline on the decline in gait speed. The moderating effects of Vocabulary on the associations between DSS and FCSRT with the decline in gait speed were tested by three-way interactions of 'time × DSS × Vocabulary' and 'time × FCSRT × Vocabulary'. Time in these models represents average rate of change in gait speed over annual follow-ups. Data were inspected descriptively and graphically and model assumptions were formally tested. All analyses reported controlled for gender, age, ethnicity, disease comorbidity, medications and falls history. Statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, N.C.).

RESULTS

Participants

This study included participants enrolled from August 2004 through April 2011. Of the 904 EAS participants seen during this 81-month period, 814 received both gait and cognitive evaluations. Participants were excluded from this analysis if they were diagnosed with dementia at baseline (n=22), had missing neuropsychological tests data (n=30) or missing gait data (n=11). The remaining 751 participants were eligible for this investigation. The number of participants available for follow-up evaluations in years 2, 3, 4, 5, 6 and 7 were 517, 381, 229, 113, 34 and 1, respectively. Median number of repeated annual gait speed measures is 3 (maximum 7) during a median of 1.98 years follow-up (maximum 6.14 years). The excluded participants were older (p= 0.0036) and less educated (p=0.028), but not different in terms of the gender composition (p=0.071). Baseline cohort characteristics are presented in Table 1.

Gait Speed

Mean gait speed at baseline was 93.3 cm/sec. Mean decline in gait speed for the overall cohort was 2.870 cm/sec per year. Linear mixed effects model was used to assess effects of DSS, FCSRT, Vocabulary and their interactions on gait speed decline (Table 2).

Baseline associations between the neuropsychological predictors and gait speed were in the expected direction (Table 2). Gait speed decline over the follow-up period was statistically significant (95% CI=−3.241- −2.495). The two-way interaction of time and Vocabulary was statistically significant (95% CI=−1.165- −0.402) showing that higher Vocabulary scores at baseline were associated with more rapid decline in gait speed among subjects with mean

DSS and FCSRT levels. The two-way interactions of time with DSS and FCSRT were not statistically significant (Table 2). However, the three-ways interactions of time $\times$ DSS $\times$ Vocabulary (95% CI=0.086-0.835) and time $\times$ FCSRT $\times$ Vocabulary (95% CI=0.073-0.915) were significant.

Figure 1 provides a visual depiction of the 3-way interactions of time $\times$ DSS $\times$ Vocabulary and time $\times$ FCSRT $\times$ Vocabulary on gait speed decline. The DSS, FCSRT and Vocabulary were each dichotomized into quartile 4 (best) versus the remaining 3 quartiles. The protective effects of high DSS scores (4 quartile) vs. lower DSS scores (quartiles 1-3) are contrasted in the low (figure 1 panel a) and high (Figure 1 panel b) Vocabulary groups. The protective effects of high FCSRT scores (4 quartile) vs. lower FCSRT scores (quartiles 1-3) are contrasted in the low (Figure 1 panel c) and high (Figure 1 panel d) Vocabulary groups. Consistent with the mixed linear effects model, the figure shows protective effects for higher scores (quartile 4) compared to low scores (quartiles 1-3) on the FCSRT and DSST only in the high Vocabulary groups (panels b and d).

Sensitivity analysis restricting the duration of follow-up to three years (Table 2 model 2) showed that the interaction of time $\times$ DSS $\times$ Vocabulary (95% CI=0.051-1.259) remained significant. However, the interaction of time $\times$ FCSRT $\times$ Vocabulary (95% CI=-0.042-0.811) was not significant.

DISCUSSION

The protective effects of EF and possibly episodic memory against decline in gait speed were stronger in participants with high CR than those with lower CR. For instance, the protective effect of one standard deviation increase in DSS scores against gait speed decline is significantly increased by 0.46 cm/sec per year as Vocabulary score is increased by one standard deviation.

Typically, CR has been studied in the context of age-related decline in cognitive function and risk of dementia²⁴. Applying the concept of CR to the study of gait speed is novel but theoretically and empirically-driven given that the latter is subject to higher order cognitive control⁸. CR can be used to account for differences among individuals in how they negotiate task demands as well as in their age-related or disease-related trajectories of decline¹⁷. Specifically, whereas neural reserve suggests that individual differences exists in task processing among persons without pathology, neural compensation proposes that in the face of pathology individuals may recruited alternative task-related brain networks to support successful task performance¹⁷. An alternative proposal is that CR is not task-specific but rather generalizes to multiple tasks²⁵, which is consistent with our findings. We suggest that individuals with higher CR may use brain systems that sub-serve EF and memory to protect against decline in gait speed more effectively than those with lower CR. This interpretation, which is consistent with Stern's notion of neural reserve, requires further evaluation in future neuroimaging studies. Interestingly, prefrontal cortex activation during walking increased when attention demands were experimentally increased⁸. By extension, the results reported here suggest that individual differences in CR may underlie differential recruitment of networks that sub-serve both EF and gait speed in older adults.

Higher CR at baseline was associated with increased risk of gait speed decline during the follow-up period. This result is consistent with previous research showing that higher CR was associated with more rapid cognitive decline²⁶. This counter intuitive relationship between CR and gait speed decline may be attributed, in part, to regression to the mean as higher levels of CR were associated with faster gait speed at baseline. This finding, however, should be interpreted with caution given that the literature concerning the relationship

between CR and clinically relevant outcomes such as cognitive decline and dementia has been equivocal and possibly dependent on the markers used to measure CR.²⁷ While speculative it is possible that the more rapid decline in gait speed among those with higher CR has been delayed until a critical change point has occurred as previously reported for dementia.²⁸

The strengths of this study include the detailed characterization of the cohort and longitudinal objective cognitive and gait assessments. The large sample, although representative in terms of key demographic characteristics of the Bronx population, age 70 years and over, comprised non-demented older adults who reside in the community.

Study limitations: gait is impaired in MCI compared to normal aging¹² and decline in gait speed predicts incident MCI²⁹. The generalizability of our findings to MCI and to dementia remains to be evaluated. Due to loss of participants during the follow-up sensitivity analysis (Table 2, model II) was conducted replicating the moderating effect of CR on the relationship between EF and gait speed decline. In this analysis CR did not moderate the relationship between episodic memory and gait speed decline. Whether or not the moderating effect of CR on the relationship between EF and gait speed decline can be generalized to other cognitive functions remains to be evaluated. We used the Vocabulary test as a marker for CR. In Separate analysis (Table 2, model III) the moderating effect of education on the relationship between EF, episodic memory and gait speed decline was similar but with borderline statistical significance. This slight difference is likely attributed to increased measurement error in self-report compared to objective performance-based measures of CR. Replicating the effects of CR with different markers should be evaluated in future studies. Finally, whether changes in cognitive functions predict gait decline should be determined in future research.

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REFERENCES

1. Holtzer R, Friedman R, Lipton RB, et al. The relationship between specific cognitive functions and falls in aging. *Neuropsychology*. 2007; 21:540–548. [PubMed: 17784802]
2. Verghese J, Wang C, Holtzer R. Relationship of clinic-based gait speed measurement to limitations in community-based activities in older adults. *Arch Phys Med Rehabil*. 2011; 92:844–846. [PubMed: 21530734]
3. Newman AB, Simonsick EM, Naydeck BL, et al. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. *JAMA*. 2006; 295:2018–2026. [PubMed: 16670410]
4. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA*. 2011; 305:50–58. [PubMed: 21205966]
5. Verghese J, Lipton RB, Hall CB, et al. Abnormality of gait as a predictor of non-Alzheimer's dementia. *N Engl J Med*. 2002; 347:1761–1768. [PubMed: 12456852]
6. Holtzer R, Wang C, Verghese J. The relationship between attention and gait in aging: Facts and fallacies. *Motor Control*. Jan. 2012 :16–64.
7. Rosano C, Studenski SA, Aizenstein HJ, et al. Slower gait, slower information processing and smaller prefrontal area in older adults. *Age Ageing*. 2011; 41:58–64. [PubMed: 21965414]

8. Holtzer R, Mahoney JR, Izzetoglu M, et al. fNIRS Study of Walking and Walking While Talking in Young and Old Individuals. *J Gerontol A Biol Sci Med Sci*. 2011; 66:879–887. [PubMed: 21593013]
9. Holtzer R, Ozelius L, Xue X, et al. Differential effects of COMT on gait and executive control in aging. *Neurobiol Aging*. 2010; 31:523–531. [PubMed: 18547681]
10. Holtzer R, Verghese J, Xue X, et al. Cognitive processes related to gait velocity: results from the Einstein Aging Study. *Neuropsychology*. 2006; 20:215–223. [PubMed: 16594782]
11. Zimmerman ME, Lipton RB, Pan JW, et al. MRI- and MRS-derived hippocampal correlates of quantitative locomotor function in older adults. *Brain Res*. 2009; 1291:73–81. [PubMed: 19631621]
12. Verghese J, Robbins M, Holtzer R, et al. Gait dysfunction in mild cognitive impairment syndromes. *J Am Geriatr Soc*. 2008; 56:1244–1251. [PubMed: 18482293]
13. Buchman AS, Boyle PA, Leurgans SE, et al. Cognitive function is associated with the development of mobility impairments in community-dwelling elders. *Am J Geriatr Psychiatry*. 2011; 19:571–580. [PubMed: 21606900]
14. Atkinson HH, Rosano C, Simonsick EM, et al. Cognitive function, gait speed decline, and comorbidities: The health, aging and body composition study. *J Gerontol A Biol Sci Med Sci*. 2007; 62:844–850. [PubMed: 17702875]
15. Atkinson HH, Rapp SR, Williamson JD, et al. The relationship between cognitive function and physical performance in older women: Results from the women's health initiative memory study. *J Gerontol A Biol Sci Med Sci*. 2010; 65:300–306. [PubMed: 19789197]
16. Watson NL, Rosano C, Boudreau RM, et al. Executive function, memory, and gait speed decline in well-functioning older adults. *J Gerontol A Biol Sci Med Sci*. 2010; 65:1093–100. [PubMed: 20581339]
17. Stern Y. Cognitive reserve. *Neuropsychologia*. 2009; 47:2015–2028. [PubMed: 19467352]
18. Lipton RB, Katz MJ, Kuslansky G, et al. Screening for dementia by telephone using the memory impairment screen. *J Am Geriatr Soc*. 2003; 51:1382–1390. [PubMed: 14511157]
19. Association, AP. Diagnostic and Statistical Manual of Mental Disorders. text revision ed. Author; Washington, DC: 2000.
20. Holtzer R, Verghese J, Wang C, et al. Within-person across-neuropsychological test variability and incident dementia. *JAMA*. 2008; 300:823–830. [PubMed: 18714062]
21. Brach JS, Perera S, Studenski S, et al. The reliability and validity of measures of gait variability in community-dwelling older adults. *Arch Phys Med Rehabil*. 2008; 89:2293–2296. [PubMed: 19061741]
22. Wechsler, D. Wechsler Adult Intelligence Scale. 3rd edition. The Psychological Corporation; New York: 1997.
23. Grober E, Sanders AE, Hall C, et al. Free and cued selective reminding identifies very mild dementia in primary care. *Alzheimer Dis Assoc Disord*. 2010; 24:284–290. [PubMed: 20683186]
24. Hall CB, Lipton RB, Sliwinski M, et al. Cognitive activities delay onset of memory decline in persons who develop dementia. *Neurology*. 2009; 73:356–361. [PubMed: 19652139]
25. Stern Y, Zarahn E, Habeck C, et al. A common neural network for cognitive reserve in verbal and object working memory in young but not old. *Cereb Cortex*. Apr.2008 18:959–967. [PubMed: 17675368]
26. Singh-Manoux A, Marmot MG, Glymour M, et al. Does cognitive reserve shape cognitive decline? *Ann Neurol*. 2011; 70:296–304. [PubMed: 21563209]
27. Muniz-Terrera G, Matthews F, Denning T, et al. Education and trajectories of cognitive decline over 9 years in very old people: methods and risk analysis. *Age Ageing*. 2009; 38:277–282. [PubMed: 19252209]
28. Hall CB, Lipton RB, Sliwinski M, et al. A change point model for estimating the onset of cognitive decline in preclinical Alzheimer's disease. *Stat Med*. 2000; 19:1555–1566. [PubMed: 10844718]
29. Buracchio T, Dodge HH, Howieson D, et al. The trajectory of gait speed preceding mild cognitive impairment. *Arch Neurol*. 2010; 67:980–986. [PubMed: 20697049]

30. Verghese J, Mahoney J, Ambrose AF, et al. Effect of cognitive remediation on gait in sedentary seniors. *J Gerontol A Biol Sci Med Sci*. 2010; 65:1338–1343. [PubMed: 20643703]

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Clinical implications

Cognitive remediation of attention and EF resulted in improved gait speed after 12 weeks of training in community residing older adults³⁰. Improving CR levels through recreational activities and enhancing EF and memory with cognitive remediation may have synergistic effects on mobility outcomes in aging.

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Figure 1.

Visual depiction of the 3-way interactions of time $\times$ Digit Symbol Substitution Test $\times$ Vocabulary and time $\times$ Free and Cued Selective Reminding Test $\times$ Vocabulary on gait speed decline. The Digit Symbol Substitution Test, Free and Cued Selective Reminding Test and Vocabulary were each dichotomized into quartile 4 (best) versus the remaining 3 quartiles. The protective effects of high Digit Symbol Substitution Test scores (4 quartile) vs. lower Digit Symbol Substitution Test scores (quartiles 1-3) are contrasted in low (figure 1 panel a) and high (Figure 1 panel b) Vocabulary groups.

The protective effects of high Free and Cued Selective Reminding Test scores (4 quartile) vs. lower Free and Cued Selective Reminding Test scores (quartiles 1-3) are contrasted in low (Figure 1 panel c) and high (Figure 1 panel d) Vocabulary groups.

Table 1

Summary of sample characteristics, cognitive functions and gait velocity at baseline

Total sample (n)	751		
Women: Number, (%)	467, (62.2)		
Caucasian: Number, (%)	512, (68.2)		
	Mean(SD)	Median	Range
Age years:	80.035(±5.433).	79.42	69.62-100.43
Education years:	14.067(±3.393)	14.00	3.00-22.00
Disease Comorbidity Index:	1.292(±1.046)	1.00	0.00-7.00
Medication count	3.5(±2.6)	3.00	0.00-10.00
Vocabulary (total score):	44.577(±12.573)	46.00	5.00-66.00
DSS (total score):	45.277(±14.239)	45.00	0.00-85.00
FCSRT (total score):	30.831(±6.311)	32.00	1.00-45.00
Gait Velocity (cm/sec):	93.307(±23.607)	94.80	11.80-173.90

Note: FCSRT=Free and Cued Selective Reminding Test – free recall condition; DSS=Digit Symbol Substitution total score

Table 2

Linear mixed effect model: cognitive predictors of gait speed decline

Variable	Estimate	t	95%CI	P
Model I: Primary Analysis				
DSS	3.385	3.53	1.505-5.264	0.0004
FCSRT	1.6007	1.81	−0.0878-3.2894	0.069
Vocabulary	2.3882	2.58	0.5781-4.1983	0.009
Time	−2.871	−15.09	−3.2419- −2.4956	<0.0001
Time × DSS	−0.06609	−0.32	−0.4716-0.3394	0.747
Time × FCSRT	−0.04326	−0.20	−0.4683-0.3818	0.839
Time × Vocabulary	−0.7838	−4.02	−1.1651- −0.4025	<0.0001
DSS × Vocabulary	0.3313	0.38	−1.3206-1.9831	0.701
FCSRT × Vocabulary	−0.01035	−0.05	−1.4875-1.4668	0.959
Time × Vocabulary × DSS	0.4609	2.42	0.08636-0.8354	0.015
Time × Vocabulary × FCSRT	0.4941	2.30	0.07309-0.9151	0.021
Model II: Sensitivity analysis: follow-up reduced to 3 years				
Time × Vocabulary × DSS	0.655	2.13	0.0514-1.2596	0.033
Time × Vocabulary × FCSRT	0.1938	0.62	−0.0421-0.8118	0.538
Model III: Analysis using years of educations as a marker for cognitive reserve				
Time × education × DSS	0.095	1.90	−0.0031-0.194	0.057
Time × education × FCSRT	0.110	1.72	−0.0153-0.2354	0.085

Models I II and III adjusted for age, gender, ethnicity, medical illness index, and medications. FCSRT=Free and Cued Selective Reminding Test – free recall condition; DSS=Digit Symbol Substitution total score.