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The Association of a Novel Cognitive Frailty Index and Physical Functioning in Older At-Risk Adults

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Abstract

Objectives: Cognitive frailty is a state at the lower end of the continuum of cognitive resilience in which one is at elevated risk for cognitive impairment and dementia. Metrics of a newly developed Cognitive Frailty Index (CFI) were examined for their association with objective functional limitations.

Methods: We used baseline data from 607 participants from the Baltimore Experience Corps Trial with measures on the CFI, a computerized Stroop test, and Short Physical Performance Battery (SPPB) score. Multivariable log-binomial regression models were used to evaluate the associations of CFI metrics (mean reaction time (RT) for total, first-half and second-half trials per condition) with the SPPB. Latent growth models were used to create additional CFI metrics of initial level (intercept) and change (slope) in RT across accurate trials by easy (Color-X) and difficult (Color-Word) conditions. Models were adjusted for race, sex, age, income, major

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morbidities, depressive symptoms, self-reported health, and Stroop interference (for Color-Word condition only).

Results: All CFI RT metrics were associated with SPPB<9, yet latent growth model approaches were most informative. Initial levels of performance on easy (Risk Ratio, [RR]=1.24; 95% Confidence Interval, [CI]: 1.03, 1.49) and difficult conditions (RR=1.22; 95% CI: 1.05, 1.41), not rates of learning (slope) (RR=1.08, 95% CI: 0.81, 1.45 and RR=1.11, 95% CI: 0.96, 1.27 respectively), were associated with worse physical functioning.

Conclusions: The association between the CFI and physical functioning demonstrates the interplay of cognitive frailty and worse objective mobility within a sociodemographic at-risk sample.

Keywords

cognitive frailty; Stroop test; mobility; gait speed; Short Physical Performance Battery

Introduction

Physical frailty is a pathological, reversible aging process where frailty and comorbidity have a bidirectional relationship (Dorner et al., 2013; Fried et al., 2001; Morley et al., 2013; Ruan et al., 2015; Tavassoli et al., 2014). It is characterized by having three or more of the following components: weight loss, exhaustion, slowness, low activity level, and weakness (Fried et al., 2001). Among older adults, the prevalence of physical frailty is 15% in the US (Bandeem-Roche et al., 2015), and incidence of physical frailty is likely to increase with greater age (Fried et al., 2001).

Although much frailty research has focused on physical frailty, research on the parallel concept of cognitive frailty is emerging. The definition of cognitive frailty given by the IANA/IAGG international consensus group is a heterogeneous clinical syndrome characterized by the presence of both physical frailty and cognitive impairment in the absence of concurrent dementia (Kelaiditi et al., 2013). It is a state at the lower end of the continuum of cognitive resilience in which one is at elevated risk for cognitive impairment and dementia. Under this definition, cognitive and physical impairments are presumed to co-occur due to the same underlying processes. However, cognition does not rely directly on structural elements outside of the brain, yet motor components of physical frailty rely on motor control systems both in the brain and other central nervous regions (Buchman & Bennett, 2013). Direct evaluation of cognitive function is not part of the cognitive frailty phenotype (Cesari, Andrieu, Rolland, Nourhashemi, & Vellas, 2013). The pattern of cognitive frailty is not clearly characterized, and the definition is based on a hypothetical condition unsupported by data (Delrieu et al., 2016). Delrieu et al. (2016) then characterized cognitive frailty in older adults as having slower processing speed, poorer selective attention, and poorer mental flexibility, and the authors appeal for adequate cognitive screening tools to diagnosis cognitive frailty in parallel to physical frailty. Measurement of cognitive risk and resilience through a conceptually and operationally distinct frailty tool to predict dementia independent of physical frailty will bridge a gap in understanding of age- and injury- related biological mechanisms that are common and distinct across both systems.

To identify cognitive frailty, a construct hypothesized to mark low cognitive resilience, A Cognitive Frailty Index (CFI), a brief computerized Stroop game, was developed to detect subsequent cognitive impairment independent of components related to physical frailty (Kasper & Freedman, 2014). The CFI is designed to assess trial-based learning under easy (naming color of X's) and more challenging (naming color of color-words) conditions. It assesses processing speed, attention, and a component of executive function (Stroop interference), with millisecond accuracy. Deficits in these cognitive domains in non-demented older adults predict cognitive decline and Alzheimer's disease progression (Albert, Moss, Tanzi, & Jones, 2001; Backman, Jones, Berger, Laukka, & Small, 2005; Bondi, Salmon, Galasko, Thomas, & Thal, 1999; Carlson, Xue, Zhou, & Fried, 2009; Chen et al., 2001; Fine et al., 2008; Lange et al., 2002). The trial-level change in reaction time of the CFI is associated with onset of dementia among older adults who are cognitively healthy and who have Mild Cognitive Impairment (MCI) (Blumberg & Johnson, 2013; Kasper & Freedman, 2014).

Because the CFI is predictive of dementia onset, we hypothesized that the CFI may be also associated with difficulties in physical functioning. Deficits in executive function, a domain targeted by the computerized Stroop test, contribute more to functional decline than global cognition (Atkinson et al., 2007; Fitzpatrick et al., 2007; Johnson, Lui, & Yaffe, 2007; Watson et al., 2010). Areas of executive function targeted by the CFI, processing speed, attention, and inhibition, have been found to be associated with mobility and balance among older adults (Hajjar et al., 2009; Nieto, Albert, Morrow, & Saxton, 2008; Schneider & Lichtenberg, 2011; Studenski et al., 2011; Watson et al., 2010) as well as declines in physical performance (Schneider et al., 2011; Nieto et al., 2008). Particularly, slowed processing speed could be resultant of diffuse cerebral white matter lesions and age-related myelin degeneration, effects from inflammatory processes (Mielke et al., 2012; Palta et al., 2014; Rosano, Newman, Katz, Hirsch, & Kuller, 2008b).

From the CFI and physical functioning measures, we can evaluate external construct validity, the ways in which cognitive frailty, a construct measured by the CFI, is associated with physical functioning, a construct measured by objective measures, such as the Short Physical Performance Battery and gait speed. By relating these two, we can potentially explain the association between cognitive frailty and physical functioning and predict further relationships in older adults, especially since there could be an overlap between cognitive frailty and worse physical functioning. We hypothesize that slower initial performance and lower rate of trial-to-trial learning would be associated with poorer physical functioning in older adults. Additionally, since gait speed has been shown to be a marker of physical decline, we hypothesized that slower initial performance and rate of learning would be associated with slower gait speed.

Methods

Sample

There were 702 participants randomized to the Baltimore Experience Corps Trial (BECT), a sex-stratified, randomized controlled effectiveness trial to examine whether a volunteer program intervention affected the cognitive, physical and psychosocial health of older adults

(Fried et al., 2013). We evaluated participants at baseline prior to randomization. Participants were excluded if they did not perform the CFI and the Short Physical Performance Battery (SPPB), including gait speed at baseline. Of 702 participants, 607 participants had complete measures on the CFI and SPPB at baseline. Also, we included participants with accurate trials of a reaction time (RT) < 300 milliseconds, which is greater than 100 milliseconds, the average threshold for visual processing (Rouder & Morey, 2009), on the CFI. We compared baseline characteristics between those who were included (n=607) and excluded (n=95) from the study to see if there were any differences between included and excluded participants. Details on study design, sampling methodology, recruitment, and enrollment criteria are described elsewhere (Carlson et al., 2015; Fried et al., 2013). The study protocol was approved by the Johns Hopkins School of Medicine Institutional Review Board, and each participant provided written, informed consent. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Cognitive Frailty Index

An automated CFI, administered at the baseline visit, was designed and programmed by Carlson et al. to integrate metrics of cognitive frailty. The computer-based Stroop task was brief and game-like to appeal to a range of cognitive abilities. Participants recorded their responses to individually presented trials using a hand-held wireless keypad with “red”, “green”, and “blue” colored buttons. We measured the participant’s ability to maintain attention under easy and more difficult, executive conditions: naming the color of strings of X’s (Color-X condition), and, naming the color of the ink of a color-word (e.g., “red” printed in green ink; Color-Word condition). Thirty trials for the easy, Color-X condition and 30 trials for the difficult, Color-Word condition were randomly presented. At the end of the automated CFI, performance feedback for the Color-X condition was provided, along with a fireworks display. Accuracy and RT (in milliseconds) of each trial were recorded using E-Prime 2.0 (Schneider, Eschman, & Zuccolotto, 2012). Only accurate trials with RT < 300 milliseconds from Color-X and accurate trials with RT < 300 milliseconds from Color-Word conditions were considered valid.

Besides deriving the mean RT for each condition, we created two other cognitive frailty metrics under the Color-X and Color-Word conditions. These were the first-half mean RT to measure the rate of task learning from trial to trial during the first half of the task (15 trials) and the second-half mean RT to measure task-related fatigue during the latter 15 trials. Other CFI metrics were derived from latent growth models, which are described in more detail below.

Performance-Based Lower Extremity Function

The Short Physical Performance Battery (SPPB) assesses lower extremity function using tests of 4-meter walk, side-by-side stand, semi-tandem stand, tandem stand, and five chair stands (Guralnik, Ferrucci, Simonsick, Salive, & Wallace, 1995). For each test, participants received a score ranging from zero to four, with zero indicating inability to complete the test and four indicating the highest level of performance (Supplemental Table 1). Scores from each test were summed to create a total score ranging from zero to 12, with higher scores indicating better lower-extremity function. A cutoff of 9 was used to discriminate good

physical functioning from poor physical functioning (Guralnik et al., 1995). We assessed each SPPB component as either having functional limitation (scores from 0 to 3) or normal function (score of 4) (Supplemental Table 1). Additionally, we used a cut-off of 0.8 m/s for four meters, since 0.8 m/s has been found to have clinical utility in predicting adverse outcomes (Abellan van Kan et al., 2009; Studenski et al., 2011).

Adjustment Covariates

Adjustment covariates included demographic characteristics (age, sex, race, education, and income), depressive symptoms, major morbidities, self-reported health status, and baseline Mini Mental State Examination (MMSE) score. Self-reported health status (n=43) and was imputed, based on individual-based imputation from months 12 and 24 visits. Six missing observations for income were imputed, using regression-based missing data imputation from age, sex, race, education, physical activity (inactive, moderately active, very active), self-reported health, mobility, depressive symptoms, and MMSE. Age was measured at baseline and centered on its mean. Sex was coded either female or male. Race was white or non-white. Income was categorized as <\$15,000, \$15,000–<\$35,000, and \$35,000 (Gruenewald et al., 2016). Self-reported health was categorized as excellent, very good, good, fair, and poor from the Late Life Function and Disability Scale (Jette et al., 2002). Depressive symptoms were measured by the Geriatric Depression Scale (Marc, Raue, & Bruce, 2008; Sheikh & Yesavage, 1986). Major morbidities (hypertension, cardiovascular disease conditions [myocardial infarction, intermittent claudication, angina, congestive heart failure], stroke, and diabetes) were the number of major morbid conditions participants reported as diagnosed by a doctor (Gruenewald et al., 2016). Education was either high school graduate or less than high school. The MMSE score was the overall continuous score (Folstein, Folstein, & McHugh, 1975).

Statistical Analysis

Latent growth models (LGMs) were used to characterize the changes in RTs across correctly completed Stroop trials by both easy and difficult conditions on the computerized Stroop test (Gross et al., 2013; Jones, Rosenberg, Morris, & Allaire, 2005). LGM is flexible in terms of the shape of the modeled developmental trajectory (Gross et al., 2013; Jones et al., 2005). Our LGM has a latent variable to capture initial status, i.e., random intercept, and additional variables to describe change over time, where time trend is modeled as random coefficients acting as latent variables. Characterization of the time trend is a process of curve fitting to evaluate linear, quadratic, and logarithmic growth trends (Gross et al., 2013; Jones et al., 2005). The functional form of the rate of learning, or trial-to-trial change in RTs was determined by comparing plots of fitted and observed means and comparing statistics, including Bayesian Information Criterion, Akaike Information Criterion, root mean squared error of approximation, comparative fit index, and Tucker Lewis Index (Tanaka, 1987). RTs were divided by 500, so RTs could be interpreted as half-seconds. Analyses were conducted with Mplus software package using limited information maximum likelihood estimator (Muthén & Muthén, 1998–2012).

Upon determination of the shape of the growth function of the rate of learning for each condition, we modeled the association of the growth function with physical functioning

measures, i.e., SPPB and its components and gait speed, by using multivariable log-binomial regression models jointly. The main exposures were the initial level (intercept) and rate of learning from the trial-to-trial change in RTs (slope), two other CFI metrics under evaluation. Additionally, we used log-binomial regression models to examine the effects of the other CFI metrics, which were mean-centered overall mean RT, first-half mean RT (learning), and second-half mean RT (fatigue) on physical functioning measures. All models were adjusted for either demographic characteristics only or demographic characteristics, self-reported health, depressive symptoms, and major morbidities. When evaluating the difficult, Color-Word condition, we further adjusted by Stroop interference. Stroop interference is the difference between the average reaction times of the difficult, Color-Word and easy, Color-X conditions divided by the average reaction time of the easy, Color-X condition.

Results

Study Sample

Characteristics of the study sample at baseline are presented in Table 1. Those with a SPPB score ≥ 9 were more likely to be older, earn $< \$35,000$, have diabetes, have a stroke, have hypertension, have arthritis, have slower gait speed, and have more major morbidities (Table 1). The two groups also differed in self-reported health. The two groups were similar in terms of depressive symptoms, sex, race, education, cancer, and MMSE. Those who were included in the sample were more likely to report better self-reported health and have less major morbidities than those excluded from the sample, but the two groups were similar on age, race, sex, income, gait speed, depressive symptoms, and SPPB score ≥ 9 (Supplemental Table 2).

Determination of Growth Function for Trial Change in Reaction Time

Supplemental Table 3 summarizes the results of model fitting for determining the growth function (i.e., linear, quadratic, logarithmic) that best characterized the trial change in RTs. It includes Akaike Information Criterion, Bayesian Information Criterion, root mean squared error of approximation, comparative fit index, Tucker Lewis Index, and estimated mean and variance parameters for the growth model. The logarithmic growth curve model for both the easy, Color-X and difficult, Color-Word conditions had the best model fit, as compared to the model fit of the linear and quadratic growth curve models (Figure 1).

The mean of the initial level of performance was 2.26 half-seconds for the easy condition and 3.18 half-seconds for the difficult, executive condition (Supplemental Table 3). At the start of each condition, it took 2.26 half-seconds to perform the easy condition accurately and 2.18 half-seconds to perform the difficult condition accurately. The mean of the trial-to-trial rate of learning was -0.40 half-seconds for the easy condition and -0.96 half-seconds for the difficult condition.

Associations of CFI Metrics and Physical Functioning by Condition

Table 2 shows the results of the multivariable log-binomial regression models used to examine the association between CFI metrics and SPPB by condition. After adjusting for

race, sex, age, and income, a one half-second increase in mean RT of the easy condition increased the risk of having a SPPB score ≥ 9 by 29% (RR=1.29, 95% CI: 1.08, 1.55). A one half-second increase in the first-half mean RT of the easy condition increased the risk of having a SPPB score ≥ 9 by 26% (RR=1.26, 95% CI: 1.06, 1.49), which was similar to results for a one half-second increase in second-half mean RT after covariate adjustment (RR=1.26, 95% CI: 1.06, 1.49) (Table 2). The level (RR=1.26, 95% CI: 1.05, 1.52), not the slope (RR=1.05, 95% CI: 0.83, 1.31), of the easy condition was associated with a SPPB score ≥ 9 after adjusting for age, sex, race, and income, suggesting that higher RT was associated with worse physical functioning. When the models are further adjusted by self-reported health, geriatric depressive symptoms, and major morbidities, the effects of RTs from the easy condition on the risk of having a SPPB score ≥ 9 slightly changed (Table 2).

A similar trend was seen for the difficult executive condition. When adjusting for demographic characteristics and Stroop interference, a one half-second increase in the mean RT of the difficult condition increased the risk of having a SPPB score ≥ 9 by 23% (RR=1.23, 95% CI: 1.06, 1.42). Similar increases were seen for the first-half mean RT (RR=1.17, 95% CI: 1.02, 1.32) and the second-half mean RT (RR=1.22, 95% CI: 1.06, 1.40). The level (RR=1.23, 95% CI: 1.07, 1.43), not the slope (RR=1.11, 95% CI: 0.96, 1.27) of the difficult condition, was statistically associated with a SPPB score ≥ 9 . When adding self-reported health, geriatric depressive symptoms, and major morbidities to the model, the risk ratios did not change substantially (Table 2).

Table 3 shows the results of the log-binomial regression models and latent growth models of RT of the CFI and gait speed by condition. After adjusting by demographic characteristics, half-second increases in mean RT (RR=1.79, 95% CI: 1.33, 2.41), first-half mean RT (RR=1.80, 95% CI: 1.36, 2.38), second-half mean RT (RR=1.58, 95% CI: 1.17, 2.13), and the level (RR=1.70, 95% CI: 1.24, 2.32) of the logarithmic function showed higher odds of gait speed ≥ 0.8 m/s. The slope (RR=0.95, 95% CI: 0.60, 1.51) was not significant. Estimates were similar when self-reported health, geriatric depressive symptoms, and major morbidities were added to the models (Table 3).

For the difficult condition, after adjusting for Stroop interference, race, sex, age, and income, half-second increases in mean RT (RR=1.52, 95% CI: 1.18, 1.94), first-half mean RT (RR=1.43, 95% CI: 1.13, 1.82), second-half mean RT (RR=1.46, 95% CI: 1.14, 1.87), and the level (RR=1.57, 95% CI: 1.20, 2.40) of the logarithmic function showed higher risk of gait speed ≥ 0.8 m/s. The slope of the logarithmic function (RR=1.08, 95% CI: 0.81, 1.45) was not significant. The results were the same after adding self-reported health, depressive symptoms, and major morbidities to the models (Table 3).

Table 4 shows the results from multivariable log-binomial regression models for each SPPB component. The results were similar to those observed for the overall SPPB test. Level, not the slope, was significant for each SPPB component, i.e., walk, balance, and chair stands, for models with all covariates. Slopes, or rates of learning, during the difficult condition from the Stroop game were associated with worse balance (RR=1.33, 95% CI: 1.06, 1.67) and worse chair stand performance (RR=1.14, 95% CI: 1.05, 1.25) after covariate adjustment.

Discussion

In this study of sociodemographic at-risk older adults, we extend the utility of the CFI by showing that CFI metrics of initial level of performance, but not the rate of learning (slope) on both easy, Color-X and difficult, Color-Word conditions was associated with worse objective physical functioning. Those who were slower at the beginning of both easy and difficult conditions, on average, had a higher risk of worse physical functioning. Rate of learning was not associated with worse physical functioning, suggesting that those with poor physical function did not improve considerably over trials. The latent growth model approach provided additional information about the association of the CFI to physical impairment from its utilization of all available information from all trials of the CFI. Results using total, first-half, and second-half metrics mirrored those for the initial level of the logarithmic RT function, showing that metrics for the easy condition were as or more predictive than the those for the more difficult executive condition. In summary, these findings collectively indicate that those with worse physical function were slower on the CFI and did not improve much from trial to trial, suggesting that only a few trials on the easy condition are necessary to observe this association.

When we evaluated the CFI metrics with overall physical performance, gait speed, and SPPB components (walking, balance, chair stands), we found a similar pattern across the outcomes with the exception of the CFI metrics from the Color-Word condition. Growth in rates of change of the CFI meant worse performance on balance and chair stands. Also, the CFI best predicted poorer gait speed, in addition to worse physical performance on the SPPB. Results for chair stands were most reflective of the overall results from presence or absence of physical functional difficulty on SPPB.

These results are consistent with previous findings that show an association between cognition and mobility in older adults. Buchman, Boyle, Leurgans, Barnes, and Bennett (2011) found that baseline global cognition was associated with incident mobility impairment in older adults. However, the cognitive domain is questionable. Rosano, Newman, Katz, Hirsch, and Kuller (2008a) found that decreases in processing speed and slower gait, alone or combined, were risk factors for disability and mortality among community-dwelling older adults. In contrast, Ble et al. (2005) found that declines in executive function were associated in slower walking speed. Executive function might not be a key driver of the association of the CFI metrics with functional limitations, since we did not observe stronger associations for the difficult Stroop Color-Word condition and further adjusted for Stroop interference. Findings from the CFI easy condition, summarized above, suggest that slower processing speed could be driving the association between the CFI metrics and functional limitations.

The associations between the CFI and physical functioning measures further show utility of the CFI to assess cognitive vulnerability among those at risk of worse outcomes, such as physical frailty and cognitive impairment. Cognitive frailty could be related to functional limitations, especially since there have been findings to suggest association between cognition and mobility (Rosso et al., 2013; Varma et al., 2016; Wang, Luo, Barnes, Sano, & Yaffe, 2014). Cognition and mobility may share common underlying pathophysiology

(Hausdorff & Buchman, 2013). For example, slower gait in older adults leads to slower information processing through volumetric declines of structures in the prefrontal cortex (Rosano et al., 2012). Previous findings have suggested that cognitive decline could be reversible, since physical activity interventions can improve processing speed in late life (Rosano et al., 2010) and may delay dementia onset (Barnes, Whitmer, & Yaffe, 2007).

The study offers several strengths. First, we standardized administration of the CFI and the lower-extremity physical function measures. Second, the CFI offers greater precision relative to the traditional administration of the Stroop test in the measurement of participant response, thus reducing the number of trials needed to assess cognitive ability (Blumberg & Johnson, 2013). Third, the BECT itself attracted older adults with a history of low physical activity from communities with lower access to health promotion and higher level of morbidity (Tan et al., 2009). Fourth, this study adds to findings from previous studies on the association between executive function and physical functioning among African Americans (Krall, Carlson, Fried, & Xue, 2014; Nieto et al., 2008; Schneider & Lichtenberg, 2011).

This study has limitations. This cross-sectional analysis is designed to identify cognitive frailty from the CFI and its association with lower-extremity physical function independent of intervention effects. Therefore, we cannot assess the causal direction of whether CFI performance affects physical functioning or physical functioning affects CFI performance over time. Another limitation is that the sample itself had better physical performance at baseline (Tan et al., 2009). Also, those who were excluded from the study reported worse health outcomes and had more major morbidities than those included in the study. This may lead to an underestimation of the association between CFI and physical functioning, but we still found strong associations between the CFI and measures of physical functioning, including gait speed.

We found that baseline level increases for both conditions of the CFI were related to worse physical functioning. We identified that the initial performance, not the rate of learning, was associated with worse physical functioning, as opposed to the unclear distinction in using the other CFI metrics (mean slope, mean first-half RT, and mean second-half RT). Since mobility and cognition contribute to reduced quality of life, there is a need for population-based strategies to reduce burden (Varma et al., 2016). Future directions include examining the CFI in other cohort studies and evaluating its utility longitudinally in other outcomes, i.e., all-cause mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Fit of trial-to-trail change in reaction time by condition of the Cognitive Frailty Index 245×163 mm (96 $\times$ 96 DPI)

Table 1.

Baseline sample characteristics of the Baltimore Experience Corps Trial (N=607)

	SPPB > 9	SPPB = 9	p-value for difference[†]
	N=289	N=318	
Age, in years, mean (SD)	65.9 (5.0)	68.5 (6.2)	<0.01
Female, n(%)	235 (81.3)	278 (87.4)	0.04
African American, n(%)	270 (93.4)	291 (91.5)	0.37
Less than high school, n(%)	171 (59.2)	170 (53.5)	0.16
Income, n(%)			0.04
<\$15,000	75 (26.0)	104 (32.7)	
\$15,000–<\$35,000	96 (33.2)	115 (36.2)	
\$35,000	118 (40.8)	99 (31.1)	
Self-reported Health, n(%)			<0.01
Excellent	38 (13.1)	23 (6.1)	
Very good	136 (47.1)	130 (40.9)	
Good	90 (31.1)	123 (38.7)	
Fair	23 (8.0)	44 (13.8)	
Poor	2 (0.7)	1 (0.3)	
GDS, mean (SD)	1.1 (1.7)	1.2 (1.7)	0.24
Diabetes, n(%)	71 (25.5)	105 (33.5)	0.03
CVD, n(%)	21 (7.6)	57 (18.2)	<0.01
Stroke, n(%)	14 (5.0)	30 (9.6)	0.04
Hypertension, n(%)	187 (67.5)	250 (79.9)	<0.01
Cancer, n(%)	24 (8.7)	25 (8.1)	0.78
Arthritis, n(%)	150 (54.0)	200 (63.9)	0.01
Major morbidities, mean (SD)	1.7 (1.1)	2.1 (1.1)	<0.01
Gait Speed, mean (SD)	1.1 (0.3)	0.8 (0.2)	<0.01
Normal Walk [*] , n (%)	276 (96.5)	147 (46.8)	<0.01
Normal Balance [*] , n(%)	266 (93.3)	161 (51.9)	<0.01
Normal Chair Stands [*] , n(%)	125 (43.6)	42 (13.9)	<0.01
MMSE, mean (SD)	28.3 (1.5)	28.1 (1.6)	0.13

SD=standard deviation, SPPB=Short Physical Performance Battery Score, MMSE=Mini Mental State Examination, GDS=Geriatric Depression Scale, CVD=cardiovascular disease

^{*} Components of the SPPB with scores ranging from 0 to 4. Normal meant a score of 4 for best possible functioning for each SPPB component.

[†] Chi-squared tests were used for categorical variables. Two-sample t-tests were used for continuous variables.

Table 2.

Log-binomial regression models and latent growth models of the reaction time (in half-seconds) of the Cognitive Frailty Index comparing SPPB > 9 and SPPB ≤ 9 by condition after covariate adjustment (N=607)

	Easy, Color-X Condition			Difficult, Color-Word Condition		
	Model 1*	Model 2**		Model 3*	Model 4**	
Cognitive Frailty Index Metrics	RR	95% CI	RR	95% CI	RR	95% CI
Total Mean RT	1.29	(1.08, 1.55)	1.26	(1.05, 1.52)	1.23	(1.06, 1.42)
First-half Mean RT (learning)	1.26	(1.06, 1.49)	1.23	(1.04, 1.46)	1.17	(1.02, 1.35)
Second-half Mean RT (fatigue)	1.26	(1.06, 1.49)	1.24	(1.04, 1.48)	1.22	(1.06, 1.40)
Logarithmic RT Function						
Intercept (initial level)	1.26	(1.05, 1.52)	1.24	(1.03, 1.49)	1.23	(1.07, 1.43)
Slope (rate of learning)	1.05	(0.83, 1.31)	1.05	(0.84, 1.32)	1.11	(0.96, 1.27)

RT = reaction time; RR = Risk Ratio, CI: Confidence Interval, Bolded numbers indicate significance < 0.05.

* Models 1 and 3 were adjusted by race, sex, age, income, and Stroop interference (Model 3 only).

** Models 2 and 4 were adjusted by race, sex, age, income, self-reported health, depressive symptoms, major morbidities, and Stroop interference (Model 4 only).

Table 3.

Log-binomial regression models and latent growth models of the reaction time (in half-seconds) of the Cognitive Frailty Index and gait speed (0.8 m/s vs. >0.8 m/s) by condition after covariate adjustment (N=607)

	<u>Easy, Color-X Condition</u>			<u>Difficult, Color-Word Condition</u>		
	Model 1 *	Model 2 **	Model 3 *	Model 4 **	Model 3 *	Model 4 **
Cognitive Frailty Index Metrics	RR	95% CI	RR	95% CI	RR	95% CI
Total Mean Reaction Time	1.79	(1.33, 2.41)	1.68	(1.24, 2.27)	1.52	(1.18, 1.94)
First-half Mean Reaction Time (learning)	1.80	(1.36, 2.38)	1.67	(1.25, 2.23)	1.43	(1.13, 1.82)
Second-half Mean Reaction Time (fatigue)	1.58	(1.17, 2.13)	1.52	(1.13, 2.05)	1.46	(1.14, 1.87)
Logarithmic Reaction Time Function						
Intercept (initial level)	1.70	(1.24, 2.32)	1.60	(1.16, 2.21)	1.57	(1.20, 2.40)
Slope (rate of learning)	0.95	(0.60, 1.51)	0.99	(0.62, 1.58)	1.08	(0.81, 1.45)

RR = Risk Ratio, CI: Confidence Interval. Bolded numbers indicate significance < 0.05.

* Models 1 and 3 were adjusted by race, sex, age, income, and Stroop interference (Model 3 only).

** Models 2 and 4 were adjusted by race, sex, age, income, self-reported health, depressive symptoms, major morbidities, and Stroop interference (Model 4 only).

Table 4.

Log-binomial regression models and latent growth models of the reaction time (in half-seconds) of the Cognitive Frailty Index by SPPB components and condition after covariate adjustment (N=607)

A. Walking									
Easy, Color-X Condition				Difficult, Color-Word Condition					
Model 1 *		Model 2 **		Model 3 *		Model 4 **			
Cognitive Frailty Index Metrics	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	
Mean RT	1.58	(1.21, 2.06)	1.50	(1.15, 1.96)	1.40	(1.12, 1.75)	1.36	(1.15, 1.96)	
First-half Mean RT (learning)	1.55	(1.21, 2.00)	1.47	(1.14, 1.89)	1.30	(1.05, 1.62)	1.26	(1.14, 1.89)	
Second-half Mean RT (fatigue)	1.46	(1.11, 1.91)	1.42	(1.09, 1.85)	1.41	(1.14, 1.75)	1.39	(1.09, 1.85)	
Logarithmic RT Function									
Intercept (initial level)	1.54	(1.17, 2.02)	1.48	(1.12, 1.94)	1.43	(1.13, 1.81)	1.48	(1.12, 1.94)	
Slope (rate of learning)	1.06	(0.72, 1.57)	1.09	(0.74, 1.62)	1.12	(0.88, 1.43)	1.09	(0.74, 1.62)	
B. Balance									
Easy, Color-X Condition				Difficult, Color-Word Condition					
Model 1 *		Model 2 **		Model 3 *		Model 4 **			
Cognitive Frailty Index Metrics	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	
Mean RT	1.66	(1.28, 2.16)	1.57	(1.19, 2.07)	1.50	(1.21, 1.85)	1.44	(1.15, 1.80)	
First-half Mean RT (learning)	1.60	(1.25, 2.06)	1.50	(1.15, 1.96)	1.42	(1.15, 1.76)	1.38	(1.11, 1.72)	
Second-half Mean RT (fatigue)	1.57	(1.23, 2.00)	1.51	(1.17, 1.95)	1.46	(1.20, 1.79)	1.41	(1.14, 1.75)	
Logarithmic RT Function									
Intercept (initial level)	1.65	(1.25, 2.17)	1.55	(1.16, 2.08)	1.50	(1.20, 1.88)	1.44	(1.14, 1.82)	
Slope (rate of learning)	1.27	(0.87, 1.86)	1.23	(0.82, 1.83)	1.33	(1.06, 1.67)	1.30	(1.04, 1.62)	
C. Chair Stands									
Easy, Color-X Condition				Difficult, Color-Word Condition					
Model 1 *		Model 2 **		Model 3 *		Model 4 **			
Cognitive Frailty Index Metrics	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	
Mean RT	1.27	(1.12, 1.43)	1.23	(1.09, 1.39)	1.19	(1.07, 1.31)	1.16	(1.04, 1.29)	

A. Walking	Easy, Color-X Condition				Difficult, Color-Word Condition			
	Model 1 *		Model 2 **		Model 3 *		Model 4 **	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Cognitive Frailty Index Metrics								
First-half Mean RT (learning)	1.25	(1.11, 1.40)	1.21	(1.07, 1.36)	1.15	(1.04, 1.27)	1.12	(1.01, 1.24)
Second-half Mean RT (fatigue)	1.23	(1.10, 1.38)	1.20	(1.07, 1.36)	1.17	(1.07, 1.29)	1.15	(1.04, 1.27)
Logarithmic RT Function								
Intercept (initial level)	1.25	(1.11, 1.41)	1.22	(1.08, 1.39)	1.17	(1.06, 1.29)	1.15	(1.03, 1.28)
Slope (rate of learning)	1.13	(0.98, 1.29)	1.12	(0.97, 1.30)	1.14	(1.05, 1.25)	1.13	(1.02, 1.24)

RR = Risk Ratio, CI: Confidence Interval, RT: reaction time, Bolded numbers indicate significance < 0.05.

* Models 1 and 3 were adjusted by race, sex, age, income, and Stroop interference (Model 3 only).

** Models 2 and 4 were adjusted by race, sex, age, income, self-reported health, depressive symptoms, major morbidities, and Stroop interference (Model 4 only).