

Sustained Attention and Frailty in the Older Adult Population

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Objectives. We investigated whether sustained attention performance and variability were associated with prefrailty and frailty in the older adult population.

Method. A total of 4,317 participants aged 50 years and over from the Irish Longitudinal Study on Ageing (TILDA) completed a comprehensive health assessment. Frailty was defined by low gait speed, low grip strength, unintentional weight loss, self-reported exhaustion, and low physical activity. Scores of greater than or equal to 3, 1–2, and 0 indicated that participants were frail, prefrail, and nonfrail, respectively. Multinomial logistic regression computed associations between frailty state and measures of performance and variability on the Sustained Attention to Response Task (SART). Cognitive processing speed and executive function were also measured.

Results. Mean reaction time (RT; odds ratio [OR] = 1.13, $p < .05$) and RT variability reflective of the top-down aspect of sustained attention (OR = 1.11, $p < .05$) were associated with prefrailty in the 50–64 age group. Mean RT (OR = 1.72, $p < .05$) was associated with frailty and RT variability (OR = 1.22, $p < .01$) with prefrailty in the 65+ age group. Results remained significant following adjustments for cognitive processing speed, executive function, chronic conditions, medications, age, and gender.

Discussion. Sustained attention performance and variability were associated with prefrailty and frailty in the older adult population and may represent a novel, objective, and modifiable cognitive marker of frailty progression.

Key Words: Frailty—Older adults—Performance—Sustained attention—Variability.

FRAILTY is a multifactorial biological syndrome of decreased reserve and resistance to stressors, leaving one susceptible to adverse outcomes. Although, a recognizable and common phenomenon in ageing, it is difficult to accurately define and diagnose. A number of definitions of frailty have been proposed, with the “frailty phenotype” receiving broad acceptance in the research literature (Fried et al., 2001). It comprises five items: unintended weight loss, muscle weakness, fatigue, low levels of activity, and slow or unsteady gait. Respectively, scores of greater than or equal to 3, 1–2, and 0 indicate whether a person is frail, prefrail, and nonfrail (or robust). Prefrailty is considered an intermediate, preclinical, and reversible state. Frailty has been empirically shown to predict negative outcomes, for example, falls, disability, hospitalization, and death, and impairments of physical function have been widely studied in relation to frailty (Ensrud et al., 2009; Fairhall et al., 2008; Fried, Ferrucci, Darer, Williamson, & Anderson, 2004). However, literature regarding the cognitive dimensions of frailty is comparatively sparse despite evidence suggesting that cognitive deficits may be an important feature of the frailty syndrome (Bergman et al., 2007; Walston et al., 2006).

Frailty has been linked to impaired global cognition and general cognitive decline (Fried et al., 2001; Matusik et al., 2012; Samper-Ternent, Al Snih, Raji, Markides, & Ottenbacher, 2008). However, data identifying the specific cognitive domains affected in frailty are limited. Some studies indicate that frail older people perform poorly on tasks that place higher demands on resources of attention (Harley, Wilkie, & Wann, 2009; Kang et al., 2009; Lundin-Olsson, Nyberg, & Gustafson, 1998; Woollacott & Shumway-Cook, 2002), whereas a recent study showed that frail individuals displayed reduced performance in measures of executive function and processing speed using composite scores from a battery of cognitive tests (Langlois, Vu, Kergoat, et al., 2012).

Sustained attention is a fundamental executive function for achieving complex goals over time. Successful sustained attention performance requires activation of a preferentially right lateralized network of cortical areas, for example, anterior cingulate gyrus, right dorsolateral prefrontal cortex, and inferior parietal lobule. This top-down attentional function (also referred to as vigilance) is supported by the arousal system. Arousal is mediated via a subcortical network involving the thalamus and

noradrenergic brain stem structure, for example, locus coeruleus (LC). Noradrenaline, produced by the LC, modulates sustained attention activation by signaling to areas of the cortex involved in vigilance control (Coull, 1998; Fassbender et al., 2004; O'Connor, Robertson, & Levine, 2011; Sturm et al., 1999). Sustained attention can be assessed using the Sustained Attention to Response Task (SART; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997). Imaging studies of this task confirmed robust activation within the appropriate cortical and subcortical attentional networks (O'Connor et al., 2011). The SART is a continuous performance reaction-time (RT) task. It requires participants to respond to a repeating stream of digits 1–9 (GO trials) and to withhold responding to the digit 3 (NO–GO trials). Commission errors (responding to NO–GO trials) reflect lapses of sustained attention, and omission errors (failure to respond to GO trials) reflect a break from task engagement, also corresponding to lapsing attention. In older adults, fewer SART errors accompanied by slower mean RT represents a speed accuracy trade-off, whereas more SART errors in conjunction with slower mean RT reflects reduced cognitive processing speed and/or lapsing sustained attention (Carriere, Cheyne, Solman, & Smilek, 2010; Greene, Bellgrove, Gill, & Robertson, 2009). Greater RT variability (standard deviation [*SD*] of RT) is associated with attentional problems and correlates with slower mean RT and more SART errors in frail older adults (Bellgrove, Hawi, Kirley, Gill, & Robertson, 2005; O'Halloran, Fan, et al., 2011). The SART provides ample time series data for analysis using the fast Fourier transform (FFT) procedure. This technique distinguishes distinct components of RT variability, namely fast- and slow-frequency variability. The former reflects fluctuations in top-down attentional control and the latter deteriorating brain arousal levels (Johnson, Kelly, et al., 2007; Johnson, Robertson, et al., 2007).

Here, we investigated sustained attention and frailty status in a population representative sample of adults aged 50 years and over using the SART. We anticipated that slower mean RT, greater RT variability, and more SART errors would be progressively associated with frailty status. We also predicted that increases in the fast variability measure would be progressively correlated with frailty status to a greater extent than increases in the slow variability measure. This was based on the hypothesis that primary ageing of the frontal cortex coupled with the age-related depletion of noradrenaline would preferentially affect the top-down attentional processes more than the subcortical arousal system (Chan-Palay & Asan, 1989; Greene et al., 2009; Gunning-Dixon & Raz, 2000; Raz et al., 2005; Shibata et al., 2006). In keeping with the proposed precursory nature of prefrailty, we expected that associations with frailty would be stronger than those with prefrailty. We also examined whether the sustained attention measures were more strongly associated with prefrailty and frailty than other commonly used measures of executive function and cognitive processing speed. Finally,

to identify a specific role for sustained attention in the frailty syndrome, we investigated the relationships between the sustained attention measures and the individual components of the frailty phenotype.

METHOD

Sample

The Irish Longitudinal Study on Ageing (TILDA) includes 8,175 participants representative of the community-living population aged 50 and older in Ireland. Households were selected in geographic clusters from a list of all residential addresses in Ireland. Each selected household was visited by an interviewer and residents aged 50 or older, as well as their spouses or partners, were invited to participate. The household response rate was 62.0%. Each participant provided written informed consent. Those with cognitive impairments that prevented meaningful consent being given were not included in the study.

Participants were interviewed in their homes by trained professional interviewers and answered questions on many aspects of health, lifestyle, social interactions, and financial circumstances. Each participant was then invited to travel to one of two health centers for a comprehensive health assessment. The sampling procedure, the home interview, and the health assessment have all been described in detail previously (Kearney et al., 2011). The measures specific to the current analysis are described in detail subsequently.

Ethics

Ethical approval for the study was obtained from the Trinity College Research Ethics committee. All participants provided written informed consent prior to participating in the study.

Frailty Measure

Frailty was operationalized as closely as possible to the phenotypic definition of Fried and colleagues (2001), and their methodology to produce population-specific cut-points rather than to use the absolute values reported was followed. This was done because measures were not directly comparable, owing to differences in the assessments of handgrip strength (using a Baseline dynamometer), physical activity (based on the short form of the International Physical Activity Questionnaire [IPAQ]), and walking speed (using a GAITRite portable walkway instead of a timed walk from a standing start) that made using the absolute cut-points reported by Fried and colleagues inappropriate.

Two measures of handgrip strength were taken from the dominant hand, and the mean of these readings was calculated. The cutoffs applied were 20.5 kg for men with a body mass index (BMI) lesser than 24, 21.5 kg for men with a BMI of 24–26, and 23 kg for men with a BMI greater than 26. For women, the cutoff was 11.5 kg for those with a BMI

lesser than 23 and 13 kg for those with a BMI equal to or greater than 23.

Gait speed was measured using the GAITRite portable electronic walkway system (CIR Systems, Havertown, PA). Participants performed two walks at their usual pace along the 4.88-m (16-ft) walkway. The two walks were combined and average gait speed was calculated. The cutoffs used were 109.7 cm/s for men less than 173 cm in height and 116.7 cm/s for men equal to or taller than 173 cm. For women, the cutoff was 100.7 cm/s for those less than 159 cm in height and 108.4 cm/s for those taller than 159 cm.

Two items from the 20-item Centre for Epidemiological Studies Depression (CES-D) scale (Orme, Reis, & Herz, 1986) were combined to generate a measure of exhaustion, following the approach of Fried and colleagues (2001). Participants were asked how often they feel that "I could not get going" and "I felt that everything I did was an effort" with four possible responses to each question: never, rarely, sometimes, or often. A response of "sometimes" or "often" to either question was considered as "exhaustion."

Physical activity was measured using the short form of the International Physical Activity Questionnaire (IPAQ; Hagströmer, Oja, & Sjostrom, 2006). The time spent walking and in vigorous and moderate physical activity was recorded and weighted to provide estimates of energy expenditure in MET-minutes per week. This is equivalent to energy expenditure (kilocalories, kcal) for a 60-kg person, therefore, multiplying by the participant's weight in kg and dividing by 60 leads to an estimate of energy expenditure in kcal/week. The cutoffs used for low physical activity were lesser than 868 kcal/week for men and lesser than 309 kcal/week for women.

Weight loss was ascertained by the question "In the past year have you lost 10 pounds (4.5 kg) or more in weight when you were not trying to." Further details on the operationalization of the Fried's frailty phenotype in the TILDA study have been reported previously (Savva et al., 2012).

Physical and Medical Measures

Disability was determined by scoring greater than or equal to 1 on either the activities of daily living (ADL) scale or the instrumental activities of daily living (IADL) scale. The ADL scale is a measure of functional status and/or disability (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963). The IADL scale is a measure of an individual's ability to live independently in the community (Lawton & Brody, 1969). On both scales, higher scores indicate poorer functional activity with minimum and maximum scores of 0–6. A history of falls was recorded as one or more self-reported falls in the previous 12 months.

The number of chronic diseases was recorded. This included self-reported physician's diagnosis of heart attack, heart failure, angina, hypertension, high cholesterol, stroke, diabetes, lung disease, asthma, arthritis, osteoporosis, cancer,

Parkinson's disease, peptic ulcer, hip fracture, and cataracts. Obesity, categorized as a BMI greater than 30 kg/m², was also included. The number of medications taken regularly, excluding nutritional supplements, was also recorded.

Cognitive Measures

The Color Trails Test (CTT) was used as an alternative to the Trail-Making Task because it removes any cultural or language bias (D'Elia, Satz, Uchiyama, & White, 1996). Color Trail 1 mainly reflects visual scanning and processing speed, and Color Trail 2 requires visual scanning, attention, and mental flexibility, making it an executive functional task. Performance on the CTT was calculated taking the time needed to perform Color Trail 2 minus the time needed for Color Trail 1. This value (Delta CTT) is considered a measure of executive function adjusted for eventual bias due to differences in upper extremity motor speed, simple sequencing, visual scanning, and psychomotor functioning (Ble et al., 2005; Corrigan & Hinkeldey, 1987).

The choice reaction time (CRT) test used a computer-based program and participants were asked to depress a button on a keyboard and wait for a stimulus (yes/no) to appear on screen and then press a corresponding yes/no button on the keyboard in response. There were approximately 100 repetitions. Cognitive RT in milliseconds was the time taken to release a button in response to a stimulus and is an assessment of concentration and cognitive processing speed.

The fixed-SART is a computerized task. Each digit appeared for 300 ms, with an interval of 800 ms between digits. The cycle of digits 1–9 was repeated 23 times, giving a total of 207 trials. The task lasted approximately for 4 min and the following measures were recorded. Mean RT, that is, the mean time (ms) taken for each key press in response to digits 1, 2, and 4–9 across the entire task and the standard deviation of RT (*SD* RT), that is, a simple measure of the overall variability of RT (ms) across the task. The number of commission errors and omission errors was also recorded (Beekman et al., 1997; Manly et al., 2000; Robertson et al., 1997).

In addition to the analysis of the traditional behavioral responses, we also analyzed the RT data of the participants using the FFT procedure described previously (Johnson, Kelly, et al., 2007; Johnson, Robertson, et al., 2007; O'Halloran, Penard, et al., 2011). Briefly, overall variability in RT results from the combination of different sources of variance occurring on different time scales. The slow frequency measure encompassed all sources of variability slower than once per SART cycle and captured any gradual change in variability during the task. The fast frequency measure encompassed all sources of variability faster than once per SART cycle and captured any trial-to-trial variability. We used the FFT procedure to decompose the variance of the RT into these two additive components. The FFT procedure can only be applied to continuous, nonzero

data. Participants with more than six consecutive zero RT responses could not be reliably interpolated using averaging methods and were removed from the analysis.

Analysis

Each frailty component was operationalized as described earlier, and the number of components present was added to create a frailty score from 0 to 5. Those with 0 components present were classified as nonfrail; with 1 or 2 components as prefrail; and with 3, 4, or 5 components as frail. The sample was split into two age groups: 50–64 years and 65+ years. Prevalences were estimated by applying inverse probability weights, corresponding to the probability that a member of the community-living older population of Ireland selected at random underwent the TILDA health assessment. Among those who underwent a health centre assessment, missing data are rare.

Physical, medical, and cognitive variables were summarized by frailty status using means and *SD* for continuous variables, and counts and percentages for categorical variables. Differences in continuous measures between frailty states were determined using regression analyses producing *F* statistics with degrees of freedom and *p* values. *t* tests were used to indicate pairwise differences. Differences in categorical measures were determined using χ^2 tests with degrees of freedom and *p* values.

The cognitive measures from the SART, CTT, and CRT occur on different scales with varying distributions. Thus, for the purposes of logistic regression analyses, these variables were log transformed and standardized, so that a unit increase in any of these variables represented an increase of 1 *SD* from the mean.

Multinomial logistic regression analyses with frailty as the outcome variable were performed to determine associations between the sustained attention measures and prefrailty or frailty. Binary logistic regression analyses were performed to determine significant associations between the sustained attention measures and the individual frailty components. The regression models included age and gender and were also extended to include additional measures of cognitive processing speed (cognitive RT from CRT), executive function (Delta CTT), number of chronic conditions, and number of medications. We also included the quadratic term age^2 to allow for any potential nonlinear effects of age on frailty in each regression model. For the independent variables in the multinomial logistic regression models, relative risk (RR) ratios with 95% confidence intervals (CIs) were provided. For the independent variables in the binary logistic regression models, OR with 95% CI were provided. Significance at the 5%, 1%, and 0.1% level were indicated as appropriate (* $p \leq .05$, ** $p < .01$, and *** $p < .001$).

All analyses were conducted using Stata (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

RESULTS

Characteristics of the Sample

Of the 8,175 participants aged 50 and older recruited to TILDA, 5,037 underwent the health centre assessment; 52% were women and the median age was 61 (interquartile range [IQR]: 55–68, range: 50–93). Sufficient data were available to calculate frailty scores for 4,858 (96%) participants. In accordance with the exclusion criteria applied by Fried and colleagues (2001), 86 participants with a history of stroke, Parkinson's disease (PD), or a Mini-Mental State Examination (MMSE) score lesser than 18 were excluded from the analysis. This left 4,772 (95%) participants, of whom lesser than 1.0% had MMSE scores lesser than 23 indicating a generally cognitively intact population. The SART was successfully completed by 4,616 (92%) participants. Following the FFT analysis of the SART RT data, 299 participants had more than six consecutive zero responses and were removed from the analysis. This is in accordance with methods described previously (O'Halloran, Penard, et al., 2011) and reduced the number of participants to 4,317 (86%).

Prevalence and Characteristics of Frailty Status

The characteristics of the nonfrail, prefrail, and frail participants are provided in Table 1. The majority were nonfrail (67%), followed by prefrail (31%), and just 86 (2%) participants were frail. None of the participants were frail on all five frailty components. This corresponds to estimated population prevalences of 63%, 34%, and 3%, respectively, in the adult population aged 50 and older. In the younger 50–64 age group, the estimated population prevalence of prefrailty and frailty were 29% and 2%, respectively, lower than that observed for the 65+ age group at 43% and 6%, respectively.

Participants classified as frail by the phenotype model also presented as typically frail (Table 1). They were significantly older, had higher levels of disability, were more likely to have experienced a fall in the past year, had a higher number of chronic conditions, took more medications, and had significantly lower scores on tests of cognitive processing speed and executive function compared with their nonfrail or prefrail counterparts. Prefrail participants were an intermediate group performing significantly worse on these measures compared with the nonfrail group but significantly better than the frail group.

Sustained Attention and Frailty Status

The distributions of the SART measures by frailty status are shown in Figure 1. The association of these measures with prefrailty and frailty in 50–64 and 65+ age groups are summarized in Table 2. When adjusted for age and gender only (Model 1), all seven measures of sustained attention from the SART were significantly correlated with prefrailty

SUSTAINED ATTENTION VARIABILITY AND FRAILITY

Table 1. Characteristics of Nonfrail, Prefrail, and Frail Community-Dwelling Adults Aged 50 and Older

Independent variables, <i>N</i> (%)	Nonfrail, 2,903 (67.2)	Prefrail, 1,328 (30.8)	Frail, 86 (2.0)	Significance test		
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	χ^2	<i>df</i>	<i>p</i> Values
Age group						
50–64 years	2,062 (71.3)	970 (27.3)	39 (1.4)	–	–	–
65+ years	841 (59.0)	538 (37.7)***	47 (3.3)***	73.41	2	<.001
Gender						
Female	1,574 (54.2)	741 (55.8)	52 (60.5)	2.04	2	.360
Disability						
≥1 disability from ADLs or IADLs	113 (3.9)	185 (13.9)***	37 (43.0)***	280.71	2	<.001
Falls						
≥1 fall in the past year	526 (18.1)	286 (21.6)**	30 (34.9)***	20.01	2	<.001
	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	<i>F</i>	<i>df</i>	
Age (years)	60.34 (7.47)	63.08 (8.73)***	67.05 (11.17)***	76.53	2, 4310	<.001
Number of chronic conditions	1.71 (1.37)	2.28 (1.60)***	3.17 (1.85)***	104.81	2, 4317	<.001
Number of medications ^a	1.58 (1.93)	2.65 (2.62)***	4.66 (2.91)***	172.62	2, 4299	<.001
Cognitive processing speed						
Mean RT from CRT (ms)	495 (122)	520 (167)***	573 (179)***	25.10	2, 4278	<.001
Executive function						
Delta CTT (s)	51.31 (24.69)	56.24 (28.04)***	64.03 (34.65)***	23.88	2, 4287	<.001

Notes. ADLs = activities of daily living; CRT = choice reaction time test; CTT = Color Trails Test; IADLs = instrumental activities of daily living; RT = reaction time.

^aNumber of medications excluding nutritional supplements.

Significant differences between the prefrail and nonfrail or frail and nonfrail participants are indicated at the level ***p* < .01 and ****p* < .001.

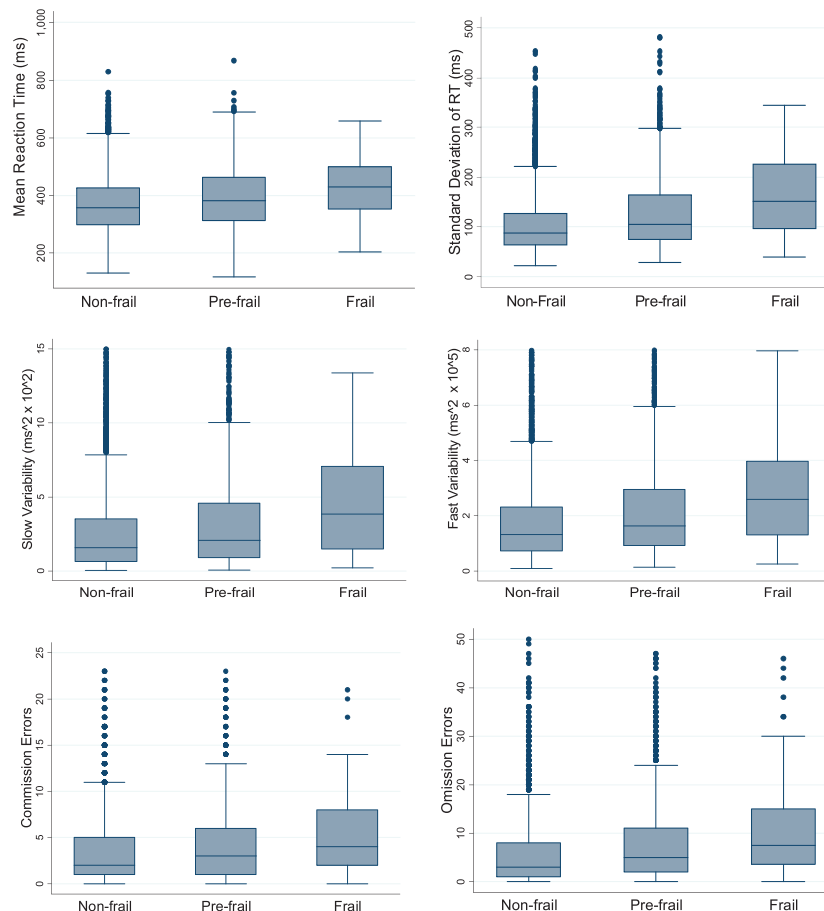


Figure 1. Distribution of the sustained attention measures grouped by frailty category in the population aged 50 years and older. Error bars represent 95% confidence intervals.

in both age groups. Cognitive processing speed and executive function were associated with prefrailty in both age groups also. When processing speed, executive function, number of chronic conditions, and number of medications were added to the regression models between the sustained attention measures and prefrailty (Model 2), commission errors were no longer correlated with prefrailty in the 65+ age group.

SD RT and the slow and fast variability measures of sustained attention were associated with frailty in both age groups when adjusted for age and gender, as was cognitive processing speed. Mean RT and omission errors were only correlated with frailty in the 65+ age group, as was executive function (Model 1). When processing speed, executive function, number of chronic conditions, and number of

medications were added to the regression models between the sustained attention measures and frailty (Model 2), Mean RT, *SD* RT, slow, and fast variability measures were correlated with frailty in the 65+ age group. None of the sustained attention measures remained significantly correlated with frailty in the younger 50–64 age group.

To establish which measures were driving the relationship between sustained attention and prefrailty or frailty, we entered all six measures of sustained attention into the models for prefrailty and frailty, along with age, gender, and the measures for cognitive processing speed, executive function, number of chronic conditions, and number of medications (Table 3). Only the mean RT and fast variability measures remained significantly associated with prefrailty and frailty. A 1 *SD* increase in mean RT increased the

Table 2. Summary of Associations Between Prefrailty or Frailty and Individual Measures of Sustained Attention, Executive Function, and Cognitive Processing Speed in Community-Dwelling Adults Aged 50–64 and 65+ Years

Independent variables	Model	50–64 years				65+ years			
		Prefrail vs nonfrail		Frail vs nonfrail		Prefrail vs nonfrail		Frail vs nonfrail	
		RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Mean RT	Model 1	1.15***	1.06–1.25	1.22	0.89–1.68	1.21***	1.08–1.35	1.81***	1.31–2.50
	Model 2	1.13**	1.04–1.23	1.03	0.73–1.44	1.15*	1.02–1.29	1.80***	1.23–2.63
<i>SD</i> RT	Model 1	1.23***	1.13–1.34	1.38*	1.00–1.91	1.28***	1.15–1.43	1.84***	1.35–1.250
	Model 2	1.18***	1.07–1.29	1.12	0.78–1.61	1.19**	1.05–1.34	1.62*	1.11–2.35
Slow-frequency variability	Model 1	1.15**	1.05–1.25	1.42*	1.02–1.98	1.22***	1.09–1.38	1.80***	1.26–2.57
	Model 2	1.11*	1.01–1.21	1.21	0.84–1.74	1.14*	1.00–1.30	1.55*	1.04–1.29
Fast-frequency variability	Model 1	1.20***	1.10–1.31	1.53*	1.09–2.14	1.34***	1.19–1.51	2.03***	1.42–2.90
	Model 2	1.16**	1.05–1.27	1.32	0.91–1.93	1.25***	1.09–1.42	1.78**	1.17–1.70
Commission errors	Model 1	1.16**	1.06–1.27	1.15	0.82–1.61	1.17**	1.05–1.31	1.22	0.91–1.64
	Model 2	1.11*	1.01–1.23	0.90	0.62–1.31	1.11	0.95–1.25	1.06	0.76–1.49
Omission errors	Model 1	1.22***	1.11–1.35	1.35	0.96–1.90	1.27***	1.13–1.42	1.44*	1.05–1.96
	Model 2	1.18***	1.06–1.30	1.13	0.78–1.64	1.18*	1.04–1.34	1.17	0.82–1.68
Cognitive RT from CRT	Model 1	1.11*	1.01–1.22	1.41*	1.07–1.84	1.24***	1.11–1.39	1.55***	1.24–1.94
Delta CTT	Model 1	1.11*	1.01–1.21	1.35	0.94–1.96	1.13*	1.02–1.27	1.37*	1.00–1.92

Notes. CI = confidence interval; CRT = choice reaction time test; CTT = Color Trails Test; RR = relative risk; RT = reaction time; *SD* = standard deviation.

Model 1—Adjusted for age and gender. Model 2—Model 1, also adjusted for cognitive processing speed, executive function, number of chronic conditions, and number of medications excluding supplements.

RR ratios and 95% CI are provided with significance at the following levels: * $p \leq .05$. ** $p < .01$. *** $p < .001$.

Table 3. Summary of Associations Between Prefrailty or Frailty and All Measures of Sustained Attention in Community-Dwelling Adults Aged 50–64 and 65+ Years

Independent variables	50–64 years		65+ years	
	Prefrail vs nonfrail		Frail vs nonfrail	
	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
SART Measures				
Mean RT	1.16 (1.02–1.33)*	1.06 (0.65–1.72)	1.16 (0.98–1.37)	1.72 (1.03–2.86)*
Fast-frequency variability	0.99 (0.80–1.33)	1.25 (0.54–2.88)	1.43 (1.07–1.91)*	1.70 (0.69–4.24)
Processing speed				
Cognitive RT from CRT	1.07 (0.95–1.20)	1.06 (0.70–1.62)	1.04 (0.90–1.20)	1.10 (0.78–1.56)
Executive function				
Delta CTT	1.01 (0.91–1.12)	0.97 (0.64–1.45)	1.04 (0.91–1.20)	1.13 (0.74–1.73)

Notes. CI = confidence interval; CRT = choice reaction time test; CTT = Color Trials Test; RR = relative risk; RT = reaction time; SART = Sustained Attention to Response Task; *SD* = standard deviation.

All sustained attention measure were included in a single model of prefrailty or frailty for each age group, that is, mean RT, *SD* RT, slow-frequency variability, fast-frequency variability, commission errors, and omission errors. Models were also adjusted for age, gender, cognitive processing speed, executive function, number of chronic conditions, and number of medications excluding supplements.

RR ratios and 95% CI are provided with significance at the following level: * $p \leq .05$.

likelihood of being prefrail by 16% in the 50–64 age group and increased the likelihood of being frail by 72% in the 65+ age group. A 1 *SD* increase in the fast variability measure was associated with a 42% increased likelihood of being prefrail in the 65+ age group. Cognitive processing speed and executive function measures were not independently associated with prefrailty or frailty in these models. The number of medications and number of chronic conditions were significantly associated with prefrailty and frailty but age and gender were not (data not shown).

Sustained Attention Measures and Individual Frailty Components

Having identified that mean RT and the fast variability measure were driving the relationship between sustained attention and both prefrailty and frailty, we then sought to establish which of the five frailty components were specifically related to the SART measures (Table 4). Among the younger 50–64 age group, a 1 *SD* increase in mean RT was correlated with a 16% increased odds of being frail on the low-physical activity component, and a 1 *SD* increase in the fast variability measure was correlated with a 39% increased odds of being frail on the low-gait speed component. Among the older 65+ age group, a 1 *SD* increase in mean RT was correlated with a 38% increased odds of being frail on the weight loss component, and a 1 *SD* increase in the fast variability measure was correlated with 31% and 38% increased odds of being frail on the low-gait speed and low-grip strength components, respectively. All associations were adjusted for cognitive processing speed, executive function, age, gender, number of chronic conditions, and number of medications.

DISCUSSION

We explored the relationship between sustained attention and the frailty phenotype as defined by Fried and colleagues (2001) in a large sample representative of the community-dwelling population aged 50 years and older in Ireland. We illustrated that the prevalence of frailty was

lower than previously reported in other European and North American populations at 3%, although remarkable variation between countries has been shown (Cigolle, Ofstedal, Tian, & Blaum, 2009; Fried et al., 2001; Santos-Eggimann, Cuénoud, Spagnoli, & Junod, 2009; Santos-Eggimann et al., 2009). However, international comparability is limited by the subjective nature of parts of the frailty assessment and the use of sample-specific cut-points for some components, a problem that highlights the need for objective comparable frailty measures. Despite this, individuals categorized as frail using the phenotype model were typical of frail individuals in other cohorts. The prevalence of prefrailty was similar to previous studies and consistent with prefrailty being an intermediate state and a precursor of frailty, we also found that prefrail individuals performed worse than those who were nonfrail and better than those who were frail on all physical, medical, and cognitive measures.

We found a strong association between prefrailty and declining sustained attention as indexed by slower mean RT, greater RT variability, and more SART errors in both age groups. Similarly, there was a strong association between frailty and declining sustained attention as indexed by slower mean RT and greater RT variability in the older age group. There was an unexpected lack of association between frailty and mean and variability of RT in the younger age group (and SART errors in both age groups). A likely explanation may be a loss of power to detect such associations due to the relatively small numbers of frail compared with prefrail participants. Alternatively, chronic illness and medications may have a greater impact on frailty in younger individuals. When all measures of sustained attention, executive function, and cognitive processing speed are regressed against prefrailty or frailty, the data indicate that the relationships between executive function or cognitive processing speed and prefrailty or frailty, are mediated by sustained attention as measured by the SART.

Female gender was significantly associated with prefrailty and weakly correlated with frailty in the older 65+ age group only. Female gender was also associated with all measures of sustained attention and cognitive processing

Table 4. Summary of Associations Between Prefrailty or Frailty and Significant Measures of Sustained Attention in Community-Dwelling Adults Aged 50–64 and 65+ Years

	Exhaustion OR (95% CI)	Weight loss OR (95% CI)	Low physical activity OR (95% CI)	Low gait speed OR (95% CI)	Low grip strength OR (95% CI)
Adults aged 50–64 years					
Mean RT	1.07 (0.92–1.25)	1.09 (0.91–1.31)	1.16 (1.02–1.32)*	1.01 (0.81–1.27)	1.14 (0.94–1.37)
Fast-frequency variability	1.04 (0.89–1.22)	1.12 (0.93–1.35)	1.02 (0.90–1.17)	1.39 (1.10–1.76)**	1.15 (0.95–1.38)
Adults aged 65 and older					
Mean RT	1.10 (0.85–1.42)	1.38 (1.04–1.84)*	1.07 (0.90–1.28)	1.04 (0.85–1.26)	1.07 (0.88–1.29)
Fast-frequency variability	0.93 (0.73–1.20)	0.97 (0.73–1.28)	1.15 (0.96–1.36)	1.31 (1.08–1.59)**	1.38 (1.13–1.68)**

Notes. CI = confidence interval; OR = odds ratios; RT = reaction time.

Mean RT and fast-frequency variability, adjusted for age, gender, cognitive processing speed, executive function, number of chronic conditions, and number of medications excluding supplements.

OR and 95% CI are provided with significance at the following levels: * $p < 0.05$. ** $p < .01$. *** $p < .001$.

speed in both age groups. Executive function was associated with female gender in the younger 50–64 age group only (data not shown).

Next, we established which measures were driving the relationship between sustained attention and prefrailty or frailty. This revealed that sustained attention performance, as indexed by mean RT, was modestly associated with prefrailty in both age groups and strongly associated with frailty in the older age group. Sustained attention variability, as indexed by the fast variability measure, was strongly correlated with prefrailty and less so with frailty in the older age group. Once again these measures mediated the link between cognitive processing speed, executive function, and prefrailty or frailty.

Finally, we investigated the relationships between the specific frailty components and the significant sustained attention measures. Mean RT was correlated with the self-reported components of frailty, that is, low physical activity and weight loss in the younger and older age groups, respectively. The fast variability measure was strongly correlated with the objectively measured components of frailty, that is, low grip strength and low gait speed in both age groups. Neither the cognitive processing speed nor executive function measures were associated with any of the frailty components in these models. Female gender was negatively associated with the low-physical activity and low-gait speed components in the younger age group and positively associated with unintended weight loss and exhaustion in both age groups (data not shown).

It is worth noting that the phenotypic concept of frailty defined by [Fried and colleagues \(2001\)](#) omits any direct measurement of cognition. This was done to ameliorate the inflated impact of dementia and generalized, age-related, cognitive declines on frailty. However, the data presented here support a relationship between sustained attention and frailty in a cognitively intact sample. It suggests that sustained attention, as measured by the SART, may capture fundamental cognitive characteristics of the frailty phenotype, beyond that captured by other measures of executive function and processing speed. This highlights how domain-specific changes in cognitive function may make important contributions to the frailty phenotype.

The main strengths of this study are its large population representative sample and comprehensive health assessment. TILDA is one of the largest population-based studies including a health assessment from which a definition of phenotypic frailty, close to that described by [Fried and colleagues \(2001\)](#), can be operationalized. The main limitation of our analysis is the lack of a gold standard for frailty. We determined the ability of the SART to identify differences between nonfrail, prefrail, and frail members of the population using the phenotypic definition of frailty as a gold standard and assuming that each frailty component was measured without error. Measurement error in our frailty assessment will have had the effect of reducing the apparent

power of the SART to identify significant differences in sustained attention. This coupled with the relatively small number of frail participants means that our estimates are likely to be conservative.

The results presented here are consistent with those reported previously by us in a separate convenience sample of adults aged 60 and older ([O'Halloran, Fan, et al., 2011](#)). Our data expand on the recent work by [Langlois, Vu, Kergoat, and colleagues \(2012\)](#) and indicate that associations between executive function, processing speed, and frailty, are mediated by sustained attention. Progressively slower mean RT and particularly greater fast-frequency variability may reflect reduced control of the cortical-sustained attention system in prefrail and frail older adults ([Bellgrove et al., 2005](#); [Johnson, Kelly, et al., 2007](#); [Johnson, Robertson, et al., 2007](#)). Primary ageing of the frontal cortex, for example, white matter loss and alterations, leading to a decline in top-down functioning and processing speed may be a contributing factor to this observation ([Gunning-Dixon & Raz, 2000](#); [Raz et al., 2005](#)). This effect may also be compounded by changes in subcortical noradrenergic brainstem structures, for example, LC as we age. The LC is the major source of noradrenaline in the brain and projects synaptically and extrasynaptically to the entire cerebral cortex, including the attentional networks, and to the thalamus ([Nieuwenhuis, Aston-Jones, & Cohen, 2005](#)). Degeneration of the LC is observed in patients with mild cognitive impairment and Alzheimer's disease and the reduction in noradrenaline levels in such patients is closely linked to the progression and extent of cognitive impairment ([Grudzien et al., 2007](#)). Furthermore epidemiological research shows that the dopamine β -hydroxylase-1021C/T polymorphism, which influences noradrenaline availability in the brain, is associated with lapses in sustained attention ([Greene et al., 2009](#)). The decrease in noradrenaline occasioned by the T allele may impair sustained attention by reducing participants' ability to remain alert throughout the task and by increasing their susceptibility to distracters. Finally, noradrenaline has been shown to have a neuroprotective role in the brain through anti-inflammatory, neurogenesis-inducing, amyloid toxicity-reducing, dopamine- and cholinergic-cell-rescuing, and dopamine- and glutamate-stimulating mechanisms ([Robertson, 2013](#)). This myriad of processes mediated by noradrenaline may underpin the association of sustained attention with prefrailty and frailty.

In conclusion, sustained attention may be a novel, objective, and modifiable cognitive marker of progression into frailty. The task is brief and not physically demanding and can be comfortably performed by older adults. Physical exercise training has been shown to cognitively benefit frail older adults by improving processing speed and executive function ([Langlois, Vu, Chasse, et al., 2012](#)). Many aspects of attention are also amenable to interventions such as meditation techniques or attention and alertness training

(MacLean et al., 2010; O'Connell et al., 2008). In light of the findings presented here, tests of frailty interventions that measure sustained attention as an outcome, and incorporate an attentional training component, may prove of additional clinical significance in the progression of frailty. The ability of the SART to detect sustained attention differences between nonfrail and prefrail individuals may be of particular relevance, as prefrailty is considered to be an intermediate and reversible state. Interventions at the prefrail stage are likely to accrue more successful and long-term benefits.

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