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# Mini-Mental State Examination performance in frail, pre-frail, and non-frail community dwelling older adults in Ermelino Matarazzo, São Paulo, Brazil

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## ABSTRACT

**Background:** Frailty in older adults is a multifactorial syndrome defined by low metabolic reserve, less resistance to stressors, and difficulty in maintaining organic homeostasis due to cumulative decline of multiple physiological systems. The relationship between frailty and cognition remains unclear and studies about Mini-Mental State Examination (MMSE) performance and frailty are scarce. The objective was to examine the association between frailty and cognitive functioning as assessed by the MMSE and its subdomains.

**Methods:** A cross-sectional population-based study (FIBRA) was carried out in Ermelino Matarazzo, a poor subdistrict of the city of São Paulo, Brazil. Participants were 384 community dwelling older adults, 65 years and older who completed the MMSE and a protocol to assess frailty criteria as described in the Cardiovascular Health Study (CHS).

**Results:** Frail older adults had significantly worse performance on the MMSE ( $p < 0.001$  for total score). Linear regression analyses showed that the MMSE total score was influenced by age ( $p < 0.001$ ), education ( $p < 0.001$ ), family income ( $p < 0.001$ ), and frailty status ( $p < 0.036$ ). Being frail was associated more significantly with worse scores in Time Orientation ( $p < 0.004$ ) and Immediate Memory ( $p < 0.001$ ).

**Conclusions:** Our data suggest that being frail is associated with worse cognitive performance, as assessed by the MMSE. It is recommended that the assessment of frail older adults should include the investigation of their cognitive status.

**Key words:** aging, frailty, cognition, MMSE

## Introduction

Frailty in older adults is defined as a multifactorial syndrome associated with low metabolic reserve, less resistance to stressors, and difficulty to maintain the organic homeostasis due to cumulative decline of multiple physiological systems (Fried *et al.*, 2001; Hogan *et al.*, 2003). There is agreement that it can be considered as a state of vulnerability expressed as an increased risk of accumulating health-related problems, hospitalization, dependency,

institutionalization, and death (Bergman *et al.*, 2007; Rockwood and Mitnitski, 2007; Lang *et al.*, 2009). Identifying frail and pre-frail older adults is a priority in geriatric settings, as these individuals should participate in interventions. There is no consensus about the best definition and criteria to identify the syndrome (Hogan *et al.*, 2003; Walston *et al.*, 2006; Ensrud *et al.*, 2009; Abellan van Kan *et al.*, 2010), and whether cognitive impairment should be added to frailty criteria (Ávila-Funes *et al.*, 2009; Song *et al.*, 2010).

It has been demonstrated that lower cognitive performance is associated with adverse health outcomes such as functional limitations and hospitalization (Raji *et al.*, 2005; Rockwood *et al.*, 2007; Ávila-Funes *et al.*, 2009). Longitudinal studies have reported that physical frailty is associated with lower cognitive performance

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(Samper-Ternent *et al.*, 2008; Ávila-Funes *et al.*, 2009; Auyeung *et al.*, 2011; Jacobs *et al.*, 2011), higher risk for Mild Cognitive Impairment (MCI), and Alzheimer's disease (AD) (Buchman *et al.*, 2007; Boyle *et al.*, 2010).

The study of frailty remains little explored in Latin America. Precise criteria and simple diagnostic tools for the early identification of frail older adults need to be validated for this region of the world, as socioeconomic conditions and access to healthcare may vary. In a previous study which examined the Cardiovascular Health Study (CHS) frailty criteria separately (Yassuda *et al.*, 2012), the percentage of frail older adults who performed below cut-off scores in several cognitive measures was higher than in the other frailty profiles.

The aim of the present study was to assess the association between frailty and performance of 384 older adults on the MMSE total and its subdomain scores. It was hypothesized that cognitive performance would be lower among frail older adults when compared to pre-frail and non-frail. It was also hypothesized that there would be an independent association between frailty and cognitive impairment as assessed by the MMSE and its subdomains. This study was part of a multicenter nationwide effort to collect data on frailty and aging in Brazil, known as the FIBRA network.

## Methods

### Data collection procedures

The district of Ermelino Matarazzo is located in the eastern area of the city of São Paulo and it has a population around 106,000 inhabitants. It is characterized as a region of low socioeconomic status. Older adults ( $\geq 65$  years) represent 4.5% of the residents of the district (SEADE, 2010).

The present study was a population-based survey. Prior to its beginning, the survey was advertised in senior centers and religious groups to enhance participation of older adults. The organization of the sample was based on a multistage procedure that took into account the primary sampling units (PSU) and the households. A PSU is the smallest area considered by the census. The PSU, in turn, may be composed of one single large block that may contain several households or a group of smaller blocks. Sixty-six PSUs were randomly drawn, and a team of trained recruiters identified all households within each PSU. The households were visited to identify seniors 65 years and older, according to inclusion and exclusion criteria, and they were invited to participate in a data collection session at a nearby community

center on a later date. After signing an informed consent form, participants were interviewed by 30 trained Gerontology students, who collected information regarding sociodemographic variables, cognitive status, and CHS frailty criteria. Twelve of those students were involved in cognitive testing. They received four training sessions to make sure that they could apply the MMSE in a standardized way. Procedures lasted from 90 to 120 minutes. After participation, seniors received health counseling based on the information provided. They also received a booklet with health tips and information on healthy lifestyles. This research project was completed in accordance with the Helsinki declaration, and it was approved by the Ethics Committee of the State University of Campinas (UNICAMP), and the University of São Paulo.

In the FIBRA study, for cities with less than one million inhabitants, the minimum sample size was estimated at 385 participants for a sampling error of 5%. Sample size was estimated to guarantee a proportion of 50% for the occurrence of a certain characteristic in the older population.

### Participants

Three hundred and eighty-four older adults participated and were classified as pre-frail if they met one or two of the five CHS frailty criteria and as frail if they met three or more. Frailty criteria were strictly operationalized according to Fried *et al.* (2001) as: (1) weight loss of more than 4.5 kg or 5% of weight loss in the last year; (2) fatigue, assessed by items 7 and 20 from the CES-D (Radloff, 1977); (3) decreased activity level, identified by the lowest 20% in the Minnesota Leisure Time Activities Questionnaire (Ainsworth *et al.*, 2000), adjusted for sex; (4) reduced walking speed, identified by the lowest 20%, assessed by the number of seconds to walk 4.6 m, adjusted for sex and height (Guralnik *et al.*, 1994); (5) reduced grip strength, identified by the lowest 20%, adjusted for sex and body mass index (Rauen *et al.*, 2008).

The sample included elders 65 years and older, who understood instructions, agreed to participate, and were a permanent resident in the household and census tract. Exclusion criteria were: (1) severe cognitive impairment suggestive of dementia, (2) need of a wheelchair, or being bedridden, (3) having sequelae of strokes, with localized loss of strength and/or aphasia, (4) untreated Parkinson's disease, (5) severe deficits in hearing or vision, which greatly hindered communication, and (6) being terminally ill. The inclusion and exclusion criteria were adapted from the Cardiovascular Health Study (CHS), according to Ferrucci *et al.* (2004).

**Table 1.** Sociodemographic characteristics and cognitive status of non-frail, pre-frail, and frail participants, in percentages, Ermelino Matarazzo, São Paulo, 2009

FACTOR	TOTAL ( <i>n</i> = 384)	NON-FRAIL ( <i>n</i> = 142)	PRE-FRAIL ( <i>n</i> = 211)	FRAIL ( <i>n</i> = 31)	<i>p</i> -VALUE*
Sex					<i>p</i> = 0.927
Female	67.19	68.31	66.35	67.74	
Male	32.81	31.69	33.65	32.26	
Age					<i>p</i> < 0.001
65–69	38.02	50.00	33.18	16.13	
70–74	31.51	28.87	33.65	29.03	
75–79	16.93	16.20	17.54	16.13	
≥ 80	13.54	4.93	15.64	38.71	
Education (years)					<i>p</i> = 0.002
0	18.02	12.06	18.96	38.71	
1–4	61.62	71.63	58.29	38.71	
≥ 5	20.36	16.31	22.75	22.58	
Family income <sup>a</sup>					<i>p</i> = 0.472
≤ 1	8.75	8.55	8.47	11.54	
1,1–3	53.75	52.99	54.80	50.00	
3,1–5	23.75	19.66	25.42	30.77	
> 5	13.76	18.80	11.30	7.69	
MMSE					<i>p</i> = 0.014
Impairment	21.15	15.60	22.27	38.71	
No impairment	78.85	84.40	77.73	61.29	
Mean (SD)	23.72 (3.77)	24.56(2.92)	23.63(3.72)	20.52(5.54)	

\**p* value for chi square or Fisher test.

Note: MMSE: Mini-Mental State Examination. SD: Standard deviation.

<sup>a</sup>Monthly family income in minimum wages.

## Instruments

Sociodemographic data were gathered by means of a structured protocol. Cognitive performance was assessed by the MMSE and its subdomains (Folstein *et al.*, 1975). To identify participants with possible cognitive impairment in the descriptive analyses, education adjusted cut-off scores were used, suggested by a previous study (Brucki *et al.*, 2003). The sample was stratified into cognitively impaired and unimpaired only for descriptive purposes (see Table 1).

## Statistical analysis

The chi square and Fisher exact tests were used to compare the distribution between the categorical variables. The Mann–Whitney test was used to compare numerical variables between two groups, and the Kruskal–Wallis test was used to compare numerical variables between three or more groups, as variables did not follow normal distribution. Spearman's correlation was used to assess the association between the numerical variables. These variables were transformed into ranks due to the absence of normal distribution. To study the relationship between the independent variables (age, sex, education, family income, and frailty profile) and the MMSE total and subdomain

scores, univariate and multivariate linear regression analyses with stepwise criteria for variable selection were used. Statistical analyses used SAS System for Windows, version 8.02 (SAS Institute Inc, 1999–2001, Cary, NC, USA). Descriptive statistics were presented to characterize the sample. Significance level was set at *p* < 0.05. In the description of the sample, some of the percentages reported are slightly different from the ones presented in Yassuda *et al.* (2012) due to the fact that in the present analyses statistical software did not incorporate weight factors based on census data, as the focus of the current analyses was not epidemiological.

## Results

The sample (*N* = 384) was composed mostly of older adults, i.e., individuals aged 65–69 years (38%, *M* = 72.3, *SD* = 5.8), with a higher presence of females (67.2%). Most of the sample had between one to four years of education (60.2%, *M* = 3.4, *SD* = 2.8) and family income from 1.1 to three minimum wages (53.8%, *M* = 3.4, *SD* = 3.1). In the study, 8% of the older adults were classified as frail and 54.2% were classified as pre-frail. Regarding cognitive screening, 21.2% of them were identified as having cognitive impairment

**Table 2.** Means and standard deviation (in parentheses) for the MMSE total score and subdomains for non-frail, pre-frail, and frail, Ermelino Matarazzo, São Paulo, 2009

SUBDOMAINS (MAXIMUM SCORE)	NON-FRAIL (N = 142)	PRE-FRAIL (N = 211)	FRAIL (N = 31)	P-VALUE*
MMSE total score (30)	25.56 (2.92)	23.63 (3.72)	20.52 (5.54)	<0.001 <sup>a</sup>
Time Orientation (5)	4.80 (0.51)	4.58 (0.82)	3.97 (1.43)	<0.001 <sup>a</sup>
Spatial Orientation (5)	4.89 (0.36)	4.86 (0.43)	4.61 (0.92)	0.261
Attention/ Calculation (5)	2.54 (1.71)	2.30 (1.79)	1.65 (1.72)	0.027
Immediate Memory (3)	2.90 (0.30)	2.77 (0.49)	2.39 (0.84)	<0.001 <sup>a</sup>
Delayed Memory (3)	1.68 (0.99)	1.68 (1.02)	1.16 (1.13)	0.046
Naming (2)	2.00 (0.00)	2.00 (0.07)	1.97 (0.18)	0.077
Repetition (1)	0.93 (0.26)	0.90 (0.30)	0.77 (0.43)	0.032
Commands (3)	2.74 (0.49)	2.77 (0.48)	2.42 (0.76)	0.006 <sup>a</sup>
Reading** (1)	0.88 (0.33) <sup>d</sup>	0.79 (0.41) <sup>c</sup>	0.84 (0.37) <sup>b</sup>	0.133
Writing** (1)	0.82 (0.38) <sup>d</sup>	0.70 (0.46) <sup>c</sup>	0.68 (0.48) <sup>b</sup>	0.051
Constructional Praxis (1)	0.52 (0.50)	0.43 (0.50)	0.29 (0.46)	0.038

\**p*-value refers to the Kruskal–Wallis test. Significant differences: *p* < 0.01. \*\*for Reading and Writing, illiterate participants were not included in the analyses.

Note: MMSE: Mini-Mental State Examination.

<sup>a</sup>Non-frail ≠ Frail, Pre-frail ≠ Frail.

<sup>b</sup>*n* = 19.

<sup>c</sup>*n* = 170.

<sup>d</sup>*n* = 123.

according to the MMSE education-adjusted cut-off points. Among non-frail participants (*n* = 141), 15.6% had cognitive impairment, among the pre-frail (*n* = 211), 22.3% were impaired, and 38.7% of frail older adults (*n* = 31) had cognitive impairment. Frail participants were significantly older, less educated, and more impaired in the MMSE, as detailed in Table 1.

To control for the possibility of finding random significant results due to multiple comparisons involving the MMSE subdomains, for these analyses, results were considered significant if *p* < 0.01. Frail participants were significantly different from pre-frail and non-frail older adults in the MMSE total score and in Time Orientation, Immediate Memory and Commands (Table 2).

As can be seen in Table 3, the MMSE total score and subdomain scores were influenced by sex, age, education, family income, and frailty. Results indicated that women, those who are older, with lower education and income, and those who meet CHS criteria for frailty tend to score lower in the MMSE total and subdomain scores. Age and education displayed the strongest influence on cognition as assessed by the MMSE.

## Discussion

The present study compared MMSE performance among 384 frail, pre-frail, and non-frail older community dwellers in Ermelino Matarazzo, a poor subdistrict of the city of São Paulo, Brazil.

Prevalence of frailty was similar to previous studies (Fried *et al.*, 2001; Ávila-Funes *et al.*, 2008; Ottenbacher *et al.*, 2009). However, we should point out that frailty prevalence may be different in other regions of Brazil, as there was a higher presence of younger older adults in the studied sample. In agreement with previous findings (Ávila-Funes *et al.*, 2008), frail older adults were significantly older, more likely to be female, less educated, and report lower income, in comparison to non-frail participants.

The present results revealed lower MMSE performance for frail participants, in agreement with earlier studies (Samper-Ternent *et al.*, 2008; Ávila-Funes *et al.*, 2009). In the sample, 38.7% of frail older adults scored below education-adjusted cut-off scores for the MMSE. Similarly, in a sample of older adults, i.e., 85 years and older followed up in Jerusalem, 53% of frail seniors scored below 24 points in the MMSE (Jacobs *et al.*, 2011). These findings may imply that, in part, frailty may be related to neurodegenerative disorders, such as Alzheimer's disease (AD). AD pathology may be present in the brain at least a decade before clinical symptoms emerge (Sperling *et al.*, 2011), therefore, it is plausible that the frailty syndrome may be explained by these brain changes. Epidemiological studies have suggested that frailty may indeed be a precocious marker of mild cognitive impairment and AD (Buchman *et al.*, 2007; Boyle *et al.*, 2010).

In the present analyses, the full range of MMSE scores was included as participants with scores below education-adjusted cut-off scores were not

**Table 3.** Multivariate linear regression analyses for the MMSE total score and subdomains, Ermelino Matarazzo, São Paulo, 2009

VARIABLES	CATEGORIES	BETA (SE)*	P-VALUE	R <sup>2</sup> PARTIAL
Time Orientation				
1. Education	Continuous Variable (years)	0.18(0.04)	<0.001	0.0831
2. Age	Continuous Variable (years)	-0.12(0.04)	0.005	0.0388
3. Frailty	Non-frail (ref.)	-		
	Pre-frail	-12.89(9.45)	0.174	
	Frail	-50.80(17.55)	0.004	0.0230
Spatial Orientation				
1. Education	Continuous Variable (years)	0.12(0.03)	<0.001	0.0465
Immediate Memory				
1. Frailty	Non-frail (ref.)	-		
	Pre-frail	-9.62(8.39)	0.252	
	Frail	-56.02(15.58)	<0.001	0.0559
2. Age	Continuous Variable (years)	-0.08(0.04)	0.030	0.0140
Delayed Memory				
1. Age	Continuous Variable (years)	-0.27(0.05)	<0.001	0.0765
Attention/Calculation				
1. Sex	Male (ref.)	-		
	Female	-74.01(11.58)	<0.001	0.1300
2. Education	Continuous Variable (years)	0.21(0.05)	<0.001	0.0738
3. Age	Continuous Variable (years)	-0.14(0.05)	0.005	0.0209
4. Family income	Continuous Variable (MW)	0.15(0.06)	0.012	0.0154
Naming				
1. Frailty	Non-frail (ref.)	-		
	Pre-frail	-1.00(1.79)	0.575	
	Frail	-7.48(3, 25)	0.022	0.0159
2. Sex	Male (ref.)	-		
	Female	3.56(1.77)	0.045	0.0125
Repetition				
1. Frailty	Non-frail (ref.)	-		
	Pre-frail	-2.06(6.34)	0.746	
	Frail	-23.79(11.55)	0.040	0.0137
Commands				
1. Age	Continuous Variable (years)	-0.12(0.04)	0.004	0.0259
Reading				
1. Frailty	Non-frail (ref.)	-		
	Pre-frail	-16.62(7.71)	0.032	
	Frail	-8.10(15.96)	0.612	0.0196
2. Family income	Continuous Variable (MW)	0.08(0.04)	0.048	0.0151
Writing				
1. Education	Continuous Variable (years)	0.15(0.05)	0.002	0.0492
2. Age	Continuous Variable (years)	-0.12(0.04)	0.003	0.0333
Constructional Praxis				
1. Education	Continuous Variable (years)	0.34(0.05)	<0.001	0.1539

**Table 3.** Continued

VARIABLES	CATEGORIES	BETA (SE)*	P-VALUE	R <sup>2</sup> PARTIAL
MMSE total score				
1. Education	Continuous Variable (years)	0.30(0.05)	<0.001	0.1772
2. Age	Continuous Variable (years)	-0.24(0.05)	<0.001	0.0629
3. Sex	Male (ref.)	-		
4. Family income	Female	-42.78(11.01)	<0.001	0.0429
5. Frailty	Continuous Variable (MW)	0.18(0.06)	0.002	0.0222
	Non-frail (ref.)	-		
	Pre-frail	-2.88(11.17)	0.797	
	Frail	-43.69(20.76)	0.036	0.0103

\*Beta: estimated value or slope on the regression line.

Note: ref. = reference level; MW = minimum wages; SE: standard error. *R*<sup>2</sup>: determination coefficient. Stepwise criteria to select variables. *R*<sup>2</sup> Total Time orientation: 0.1449. Intercept (SE): 190.75 (13.84); *P* < 0.001. *R*<sup>2</sup> Total Spatial Orientation: 0.0465. Intercept (SE): 169.83 (6.74); *P* < 0.001. *R*<sup>2</sup> Total Immediate Memory: 0.0699. Intercept (SE): 221.00 (8.63); *P* < 0.001. *R*<sup>2</sup> Total Delayed Memory (11): 0.0765. Intercept (SE): 243.30 (11.59); *P* < 0.001. *R*<sup>2</sup> Total Attention/Calculation: 0.2401. Intercept (SE): 204.03 (20.84); *P* < 0.001. *R*<sup>2</sup> Total Naming: 0.0284. Intercept (SE): 191.13 (1.82); *P* < 0.001. *R*<sup>2</sup> Total Repetition: 0.0137. Intercept (SE): 198.37 (4.92); *P* < 0.001. *R*<sup>2</sup> Total Commands: 0.0259. Intercept (SE): 216.31 (8.99); *P* < 0.001. *R*<sup>2</sup> Total Reading: 0.0347. Intercept (SE): 152.26 (9.22); *P* < 0.001. *R*<sup>2</sup> Total Writing: 0.0825. Intercept (SE): 144.19 (14.42); *P* < 0.001. *R*<sup>2</sup> Total MMSE total: 0.3155. Intercept (SE): 184.35 (20.57); *P* < 0.001.

excluded from the analyses. This fact may have magnified the relationship between frailty and cognition. Ottenbacher *et al.* (2009) and Ávila-Funes *et al.* (2009) adopted the same procedure as they justified their interest in predicting adverse health outcomes and strengthening the predictive validity of the frailty syndrome. Including participants with different cognitive profiles may help capture, in a more precise way, the shared vulnerability of those who decline simultaneously in the physical and cognitive domains. In addition, exclusion criteria in the FIBRA may have limited the participation of older adults with acute cognitive and physical limitations, therefore, we felt including in the analyses only cognitively unimpaired participants who would, in turn, further select the sample toward non-frailty.

Current findings suggest that being frail is associated with worse performance in several aspects of cognition, such as time orientation, immediate memory, and following commands. The fact that frailty is associated with lower performance in several domains is consistent with the hypothesis that frailty and cognitive decline could be caused by physiological changes related to aging (Alfaro-Acha *et al.*, 2006; Buchman *et al.*, 2007; Samper-Ternent *et al.*, 2008; Ávila-Funes *et al.*, 2009; Boyle *et al.*, 2010).

Among the limitations of the study, besides the strict exclusion criteria, one could cite the significant number of young older adults present in the sample. Another limitation refers to its cross-sectional nature and current absence of follow-up data from this cohort. On the other hand, the criteria and procedures used were similar to those adopted by international studies on frailty, which may facilitate cross-cultural comparisons.

To conclude, the results bear important implications for the comprehensive care of the older adults. In clinical settings, when patients meet frailty criteria they should be seen as patients at risk for cognitive decline. MMSE scores, in particular, some of its domains such as time orientation and immediate memory may help identify patients with physical and cognitive vulnerabilities.

### Conflict of interest

None.

### Descriptions of authors' roles

C. Macuco designed the study and wrote the paper. D. Falcão, S. Batistoni, A. Lopes, and M. Cachioni collected the data and supervised the data collection and revised the paper. A. Neri designed the study and revised the final version of the paper. M. Yassuda designed the study, collected the data, supervised the data collection, assisted with writing the paper, and revised the final version of the paper.

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