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Temporal relationship between handgrip strength and cognitive performance in oldest old people

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Abstract

Background: cognitive decline and muscle weakness are prevalent health conditions in elderly people. We hypothesised that cognitive decline precedes muscle weakness.

Objective: to analyse the temporal relationship between cognitive performance and handgrip strength in oldest old people.

Design: prospective population-based 4-year follow-up study.

Subjects: a total of 555 subjects, all aged 85 years at baseline, were included into the study.

Methods: handgrip strength measured at age 85 and 89 years. Neuropsychological test battery to assess global cognitive performance, attention, processing speed and memory at baseline and repeated at age 89 years. Associations between handgrip strength and cognitive performance were analysed by repeated linear regression analysis adjusted for common confounders.

Results: at age 85 and 89 years, better cognitive performance was associated with higher handgrip strength (all, $P < 0.03$), except for attention. There was no longitudinal association between baseline handgrip strength and cognitive decline (all, $P > 0.10$), except for global cognitive performance ($P = 0.007$). Better cognitive performance at age 85 years was associated with slower decline in handgrip strength (all, $P < 0.01$) after adjustment for common confounders.

Conclusion: baseline cognitive performance was associated with decline in handgrip strength, whereas baseline handgrip strength was not associated with cognitive decline. Our results suggest that cognitive decline precedes the onset of muscle weakness in oldest old people.

Keywords: cognitive performance, brain ageing, handgrip strength, epidemiology, longitudinal cohort study, oldest old, elderly

Introduction

Cognitive decline and muscle weakness are prevalent health conditions in elderly persons. Both predict detrimental outcome in elderly, such as functional impairment and mortality [1–4]. Cognitive decline is among others associated with functional impairment, muscle weakness and sarcopenia [5–9]. Furthermore, handgrip strength is associated with accelerated decline in global cognitive performance [4, 5] and higher risk of Alzheimer's disease and mild cognitive impairment in longitudinal studies [7, 8]. Therefore, handgrip strength is a potential early marker of cognitive decline and incident dementia. It has been proposed to screen older people for signs of functional impairment to identify those elderly at risk of developing cognitive decline in future [4, 7].

The temporal relationship between decline of muscle strength and cognitive performance is still unclear. Longitudinal studies on this topic focused on the relationship between muscle strength and subsequent cognitive decline [4, 5, 7–9]. One other study reported on the relationship between cognitive and functional decline and concluded that cognitive decline preceded functional decline in elderly women [10].

We hypothesised that cognitive decline precedes muscle weakness based on the knowledge that motor skill learning and motor output depend on activity of frontal and parietal brain regions [11–13] and the finding of an interaction and interconnection of the cognitive and motor brain regions with regard to motor output [13].

The aim of this study was to analyse the temporal relationship between handgrip strength and cognitive performance in a prospective population-based cohort of oldest old people, all aged 85 years at baseline.

Method

Subject characteristics

The Leiden 85-plus Study is a population-based prospective follow-up study of inhabitants of the city of Leiden, the Netherlands. All inhabitants who reached the age of 85 years were eligible to participate. There were no selection criteria on health, functioning or demographic characteristics. Enrolment took place between 1997 and 1999. In total 599 persons participated, 87% of all eligible inhabitants. Details are provided in a previous publication [14]. In short, a research nurse visited subjects at their place of

residence. During these visits interviews and performance tests were conducted, blood samples collected and an electrocardiogram recorded. The medical history was obtained from the general practitioner or nursing home physician. Follow-up visits were annually performed.

The study was approved by the Medical Ethical Committee of the Leiden University Medical Center. All subjects gave informed consent or informed consent was given by a guardian.

Handgrip strength

Handgrip strength is a proxy for muscle strength [15–17]. Handgrip strength was measured to the nearest kilogram (kg) with a Jamar hand dynamometer (Sammons Preston, Inc., Bolingbrook, IL, USA). Subjects were allowed to perform one test trial, followed by three trials and the highest value was taken for the analysis. Handgrip strength was measured at age 85 and 89 years.

Cognitive performance

Global cognitive performance was assessed by Mini-Mental State Examination (MMSE). In addition, a dedicated neuropsychological test battery was used to assess specific cognitive performance in subjects with an MMSE score ≥ 19 points for reasons of test validity. Attention and processing speed were assessed with the abbreviated Stroop test trial 3 and the Letter Digit Substitution Task (LDST). Memory function was assessed with the 12-Picture Learning Test (12-PLT).

The MMSE is a screening instrument for dementia and is a measure of global cognitive performance, with lower scores indicating worse performance [18]. The abbreviated Stroop test measures attention, consisting of three trials in which subjects have to name 40 items shown on a card [19, 20]. In trial three, the card contains colour names printed in a different colour than the colour-name and subjects are asked to name the colour of the ink. The score is the time needed to finish trial 3 with higher scores indicating worse performance. The LDST is a modified version of the Symbol Digit Modalities Test, measuring processing speed [21], subjects make as many letter-digit combinations as possible within 60 s, with higher scores indicating better performance. Memory function was assessed with the 12-PLT with immediate recall and delayed recall components [22]. In the immediate recall part of the test, subjects are shown pictures of 12 different objects and then asked three consecutive times to recall as many as possible. The total number of correct answers after the third time is the score. After 20 min subjects are asked again to recall the 12 objects. This number is the score for the delayed recall. Higher scores indicate better performance.

MMSE was measured yearly until end of follow-up. The neuropsychological test battery was assessed yearly until

end of follow-up or until MMSE score was below 19 points. For the present study, cognitive performance scores at age 85 and 89 years were included in the analysis.

Potential confounders

Anthropometric data were collected for all subjects. Net (after-tax) monthly income per household was obtained during face-to-face interviews and dichotomised around the median. Education was rated into two levels: lower education level, including subjects without schooling or primary school only, and higher education level, equivalent to more than 6 years of schooling. Information on chronic somatic diseases was available from the general practitioner, pharmacist's records, electrocardiogram and blood sample analysis. Chronic diseases included myocardial infarction, stroke, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, malignancy, rheumatoid arthritis and osteoarthritis [15]. Comorbidity was defined as the summed score of all chronic diseases. Diseases severity was estimated by the number of prescription medication.

Physical activity was measured with the time spending pattern questionnaire [23]. Four items were selected to constitute physical exercise above routine daily physical activity: (i) walking for fun, (ii) cycling for fun, (iii) exercise alone or in groups or other physical activity and (iv) working in the garden. Each item was scored from 0 (no activity) to 4 (daily participating in activity) and their sum score was used as an indicator for physical activity levels. Depressive symptoms were assessed by the 15-item Geriatric Depression Scale (GDS) [24].

Statistical analysis

All cross-sectional and longitudinal associations between handgrip strength and cognitive performance were analysed by linear regression using three models. In model 1, the analysis was adjusted for gender, height and weight. Model 2 was adjusted as model 1 with further adjustments for income, education, number of medication and GDS. Model 3 was adjusted as model 2 with further adjustment for physical activity. In the longitudinal analysis, the outcome variable was either the decline in handgrip strength or cognitive performance (from age 85 to 89 years), further adjustments were made in model 1 for baseline cognitive performance and handgrip strength, respectively. The use of comorbidity instead of number of prescription medication did not alter the results of the models, therefore only the results for the number of prescription medication are presented in this paper. To visualise the relation between handgrip strength and cognitive performance, handgrip strength was plotted against tertiles of cognitive test scores. SPSS 17.0 for Windows was used for all analyses. *P*-values < 0.05 were considered statistically significant.

Results

Subjects characteristics

At baseline, handgrip strength was measured in 555 subjects (92.7%) of 599 subjects of the Leiden 85-plus Study. Characteristics at ages 85 and 89 years of the study population are shown in Table 1. Supplementary data are available in *Age and Ageing* online, Appendix Figure 1 shows the flow chart of subjects.

Cross-sectional association between handgrip strength and cognitive performance

Figure 1 shows mean handgrip strength in tertiles of cognitive test scores at (A) age 85 years and (B) at 89 years. Supplementary data are available in *Age and Ageing* online, Appendix Table 1 presents the cross-sectional analyses of

Table 1. Characteristics of subjects at ages 85 and 89 years

	85 years (n = 555)	89 years (n = 307)
Men, n (%)	194 (35.0)	90 (29.3)
Height (SD), m	1.60 (0.1)	1.58 (0.1) ^a
Weight (SD), kg	69.9 (12.8)	67.3 (12.6)
High income, n (%)	456 (82.2)	255 (83.1)
Lower education, n (%)	353 (63.6)	186 (60.6)
Living arrangements		
Independent, n (%)	319 (57.5)	119 (38.8)
Sheltered, n (%)	156 (28.1)	87 (28.3)
Institutionalised, n (%)	80 (14.4)	101 (32.9)
Health characteristics		
Mean handgrip strength, mean (SD), kg		
Men	30.6 (8.2)	25.4 (8.1)
Women	18.7 (5.5)	16.3 (5.1)
≥ 3 Chronic diseases	186 (33.5)	84 (27.4)
Prescription medication, median (IQR), n	3 (1–5)	3 (2–5)
Physical activity score, mean (SD), points	7.2 (2.4)	5.5 (2.0)
Depressive symptoms ^b , median (IQR), points	2 (1–3)	2 (0.25–4)
Cognitive performance		
MMSE ^c , median (IQR), points	26 (23–28)	25 (19–28)
Stroop test ^d , trial 3, median (IQR), s	75.1 (59.6–97.6)	77.5 (63.4–95.5)
LDST ^e , mean (SD), correct answers	17.1 (7.1)	16.6 (6.3)
12-PLT ^f , immediate recall, mean (SD), pictures	24.0 (5.8)	21.8 (6.5)
12-PLT ^f , delayed recall, mean (SD), pictures	8.7 (2.7)	7.8 (3.1)

n, number; kg, kilogram; SD, standard deviation; IQR, inter-quartile range; MMSE, Mini-Mental State Examination; LDST, Letter Digit Substitution Task; 12-PLT, 12-Picture Learning Test.

^aHeight at age 89 years was not measured. Given value is height at age 88 years.

^bGDS-15, Geriatric Depression Scale 15 items, score ≥4 points. GDS was restricted to subjects with MMSE >18.

^cn = 555 at age 85 years and n = 307 at 89 years.

^dn = 444 at age 85 years and n = 211 at 89 years.

^en = 437 at age 85 years and n = 207 at 89 years.

^fn = 458 at age 85 years and n = 229 at 89 years.

the association between handgrip strength and cognitive performance at age 85 and 89 years. Better cognitive test scores were significantly associated with higher handgrip strength after adjustment for sex, height and weight ($P < 0.001$), except for the Stroop test. Adjustment for socio-economic status, number of prescription medication and depressive symptoms weakened the relationship (model 2). At age 85 years significance for most of the cognitive performance tests, except processing speed and handgrip strength was attenuated after further adjustment for physical activity (model 3). At age 89 years the positive relationship between cognitive performance and handgrip strength remained significant after full adjustment ($P \leq 0.01$, model 3), except for the Stroop test.

Longitudinal association between baseline handgrip strength and decline in cognitive performance

Table 2 in the left panel shows the results of the longitudinal analysis of the association between baseline handgrip strength and decline in cognitive performance. Baseline handgrip strength was not associated with a decline in cognitive performance (all, $P > 0.05$), except for MMSE ($P = 0.007$).

Longitudinal association between baseline cognitive performance and decline in handgrip strength

Figure 1C shows the mean decline in handgrip strength from age 85 to 89 years in tertiles of cognitive performance. A better cognitive performance at baseline was associated with slower decline in handgrip strength between ages 85 and 89 years. Table 2 presents the results of the longitudinal analysis of this association in the right panel. Better performance on all cognitive tests at 85 years was associated with slower decline in handgrip strength over time (all, $P < 0.001$). Handgrip strength decline over time was slower by 0.25 kg per point (MMSE), 0.03 kg per s (Stroop), 0.16 kg per correct answer (LDST), 0.18 and 0.38 kg per recalled picture (12-PLT, immediate and delayed). Adjustment for possible confounders did not change the results (all, $P < 0.02$, model 3).

Discussion

The aim of this study was to analyse the temporal relationship between handgrip strength and cognitive performance in a population-based cohort of oldest old people. Handgrip strength and cognitive performance were significantly correlated in the cross-sectional analysis. In the longitudinal analysis, better baseline cognitive performance, in particular attention, processing speed and memory function, was associated with slower decline in handgrip strength, whereas low baseline handgrip strength was not associated with an accelerated decline in cognitive

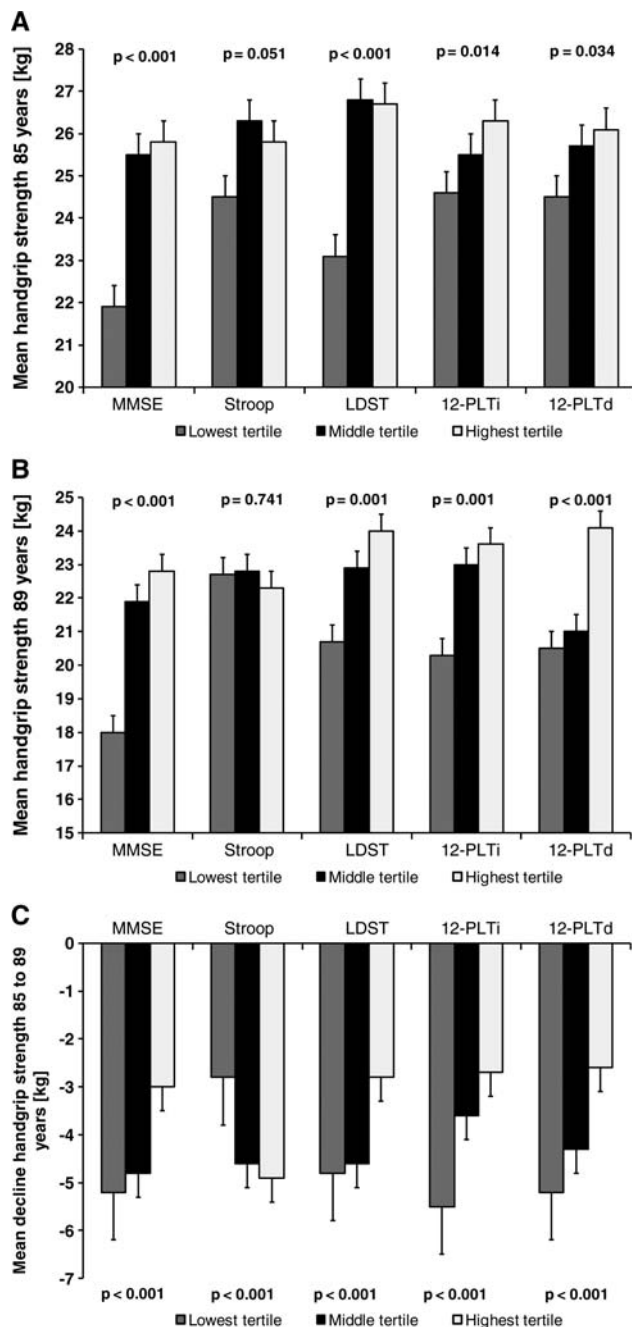


Figure 1. Mean handgrip strength at (A) age 85 and (B) 89 years in tertiles of baseline cognitive performance and (C) decline in handgrip strength from age 85 to 89 years in tertiles of baseline cognitive performance (MMSE, Stroop, Letter Digit Substitution Task (LDST) and 12-Picture Learning Test (12-PLT immediate (i) and delayed recall (d)). Error bars indicate standard error (SE). *P* value indicates *p* for trend of mean handgrip strength in tertiles of test scores (linear regression analysis adjusted for sex, height and weight). Take note that lower Stroop scores indicate better performance.

performance. Based on these findings, we conclude that cognitive decline precedes the onset of muscle weakness.

In humans motor function depends on frontal cognitive functions, such as attention, processing speed and working

memory [13]. Skilled hand movement and grip force control involve not only cortical motor areas, but also higher cognitive performance, reflected by activity in frontal and parietal cortical regions [12]. Functional neuroimaging has been used to study age-associated changes in brain activity patterns during hand movement. A study comparing brain activity in young and older subjects when performing isolated simple hand movement showed that in the elderly motor performance was associated with higher activity in more cortical areas [11]. Increased complexity of movement and coordination tasks was associated with increased cognitive control, reflected by more activity in the frontal lobe areas in healthy elderly [11]. Our finding that in healthy oldest old subjects, better attention, processing speed and memory were all significantly associated with slower handgrip strength decline over time could thus be explained by a sustained cognitive ability to control hand movement and grip force.

We are the first to report on the temporal association between executive function and memory with handgrip strength decline in a well functioning cohort of oldest old people. Others have found attention and processing speed to be associated with impairment in activities of daily living (ADL) [25] and lower extremity function in elderly subjects [26–29]. ADL ability and walking ability demand complex coordinated movements and are possibly even more dependent on cognitive function than the relatively simple measurement of handgrip strength [11].

The present study has several strengths for studying the relationship between cognitive performance and muscle strength in oldest old subjects. The Leiden 85-plus Study is a longitudinal population-based cohort study with extensive measures for health and functioning and allowed us to demonstrate a temporal association. There was substantial attrition due to death. However, this will inevitably affect all studies of very old people and should not necessarily be seen as a weakness. It does, however, limit generalisation to the population of successfully aged oldest old. Also, However, it should be noted that people with moderate to severe impairment of cognitive functioning (MMSE <19 points) were not included in the analyses and therefore the findings cannot be generalised to that group.

In conclusion, we found that better cognitive performance was associated with better muscle strength and a slower decline in muscle strength. This suggests that cognitive decline precedes muscle weakness in oldest old people. It seems likely that in elderly subjects impaired cognitive control of movement affects muscle function and strength. These findings emphasise the need for increased awareness in clinical practice that current cognitive impairment is associated with future muscle weakness in elderly people, but also that current muscle weakness is a possible marker of as yet asymptomatic cognitive impairment. However, further clinical research is needed to assess suitable diagnostic and therapeutic interventions.

Table 2. Temporal association between cognitive performance and handgrip strength (kg) between age 85 years and 89 years ($n = 307$)

	Decline in cognitive performance according to handgrip strength at age 85 years		Decline in handgrip strength according to cognitive performance at age 85 years	
	β (SE)	P-value	β (SE)	P-value
MMSE (points)				
Model 1: adj. for sex, height, weight, baseline score ^a	-0.11 (0.05)	0.018	-0.25 (0.06)	<0.001
Model 2: as 1 and income, education, prescription medication and baseline GDS	-0.14 (0.05)	0.004	-0.30 (0.10)	0.012
Model 3: as 2 and physical activity score	-0.13 (0.05)	0.007	-0.27 (0.06)	0.015
Stroop, trial 3 (s)				
Model 1: adj. for sex, height, weight, baseline score ^a	-0.43 (0.29)	0.151	0.03 (0.01)	0.001
Model 2: as 1 and income, education, prescription medication and baseline GDS	-0.51 (0.31)	0.099	0.03 (0.01)	0.006
Model 3: as 2 and physical activity score	-0.53 (0.31)	0.092	0.02 (0.01)	0.009
LDST (correct answers)				
Model 1: adj. for sex, height, weight, baseline score ^a	-0.05 (0.05)	0.280	-0.16 (0.04)	<0.001
Model 2: as 1 and income, education, prescription medication and baseline GDS	-0.04 (0.05)	0.384	-0.16 (0.04)	<0.001
Model 3: as 2 and activity score	-0.04 (0.05)	0.400	-0.16 (0.04)	<0.001
12-PLT, immediate recall (pictures)				
Model 1: adj. for sex, height, weight, baseline score ^a	-0.08 (0.06)	0.224	-0.18 (0.05)	<0.001
Model 2: as 1 and income, education, prescription medication and baseline GDS	-0.09 (0.06)	0.174	-0.17 (0.05)	<0.001
Model 3: as 2 and physical activity score	-0.09 (0.06)	0.158	-0.17 (0.05)	<0.001
12-PLT, delayed recall (pictures)				
Model 1: adj. for sex, height, weight, baseline score ^a	-0.02 (0.03)	0.454	-0.38 (0.10)	<0.001
Model 2: as 1 and income, education, prescription medication and baseline GDS	-0.03 (0.03)	0.305	-0.35 (0.10)	0.001
Model 3: as 2 and physical activity score	-0.03 (0.03)	0.371	-0.35 (0.10)	0.001

kg, kilogram; β , estimate; SE, standard error; MMSE, Mini-Mental State Examination; GDS, Geriatric Depression Score, 15 items; LDST, Letter Digit Substitution Task; 12-PLT, 12-Picture Learning Test.

^aBaseline score refers to handgrip strength at age 85 years in the analysis of handgrip strength decline and baseline cognitive performance score at age 85 years in the analysis of decline in cognitive performance.

Key points

- Better cognitive performance is associated with slower decline in muscle strength in oldest old people.
- Cognitive impairment in oldest old people is associated with future muscle weakness.
- Muscle weakness is a possible marker of asymptomatic cognitive impairment.

Conflicts of interest

None declared.

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Quality of life outcomes for residents and quality ratings of care homes: is there a relationship?

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