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What physical performance measures predict incident cognitive decline among intact older adults? A 4.4 year follow up study

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ABSTRACT

Reductions in physical performance, cognitive impairment (CI) and decline (CD), are common in older age, but few prospective cohort studies have considered the relationship between these domains. In this study we investigated whether reduced physical performance and low handgrip/lower limbs strength, could predict a higher incidence of CI/CD during a 4-year follow-up among a cohort of elderly individuals. From 3099 older community-dwelling individuals initially enrolled in the Progetto Veneto Anziani (PRO.V.A.) study, 1249 participants without CI at the baseline were included (mean age 72.2 years, 59.5% females). Physical performance measures included the Short Physical Performance Battery (SPPB), 4 m gait speed, chair stands time, leg extension and flexion, handgrip strength, and 6-Minute Walking Test (6MWT), categorized in gender-specific tertiles. CI was defined as a Mini-Mental State Examination (MMSE) score below 24; CD a decline of 3 or more points in the MMSE without CI. At baseline, participants developing CI during follow-up scored significantly worse across all physical performance measures compared to those that retained normal cognitive status. After adjusting for potential confounders, a significant trend for MMSE changes was noted for all physical performance tests, except for the SPPB and chair stands time. Multinomial logistic regression revealed that slow gait speed at baseline significantly predicted CD at follow up. Poor SPPB performance and slower gait speed predicted the onset of CI at the follow-up. In conclusion, slow walking speed appears to be the best independent predictor of poor cognitive status over a 4.4-year follow-up, while other items of SPPB were also significantly associated with CI.

1. Introduction

Cognitive impairment (CI) is a common condition in older people, affecting about 20% of individuals over 70 years old, and is associated with increased disability, healthcare utilization and mortality (Plassman et al., 2008). Several risk factors have been elucidated for CI and decline (CD), including aging, low level of formal educational, and several chronic diseases (Alfaro-Acha et al., 2006).

Recently, interest has intensified in understanding modifiable lifestyle factors that might influence the development of CD and CI. Among those that have received considerable attention is physical (in)activity (Norton et al., 2014). Data on physical activity levels are generally collected by means of questionnaires, however, there are inherent difficulties relying purely upon self-report physical activity and function, which are subject to strong recall bias in older people (Schlosser Covell et al., 2015). Data on physical activity whilst useful, indicates how much activity an individual is engaging in and does not reflect an individual's physical performance. Nevertheless, two meta-analyses recently demonstrated that self-reported reduced physical activity level is an independent risk factor for the onset of poor cognitive status (Sofi et al., 2011; Hamer and Chida, 2009). The mechanisms linking declining physical and cognitive performance include lower cognitive reserves, changes in the neurotrophic factors in the hippocampus, and the exacerbation of atherosclerotic processes in the cerebral vessels (Schlosser

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Covell et al., 2015; Blondell et al., 2014; Ahlskog et al., 2011; Buchman et al., 2012; Bennett et al., 2005). Whilst these previous studies have been helpful, assessing actual physical performance and muscle strength with objective measurements might offer a more accurate indicator of actual performance, particularly in older people who might have memory complaints and difficulty accurately recalling activity levels (Mitchell et al., 2014).

To date, a paucity of research has considered objective physical performance as a risk factor for future cognitive status in community dwelling older adults. The research has typically been cross sectional, or prospective with short duration follow up, although walking speed has been the most common physical performance measure considered (Ojagbemi et al., 2015; Mielke et al., 2013). Two prospective studies have found that handgrip strength was associated with a greater decline in memory tests (Alfaro-Acha et al., 2006; Christensen et al., 1994), but another study was unable to confirm these findings (Albert et al., 1995). There is a paucity of lower limb function tests (e.g. Short Physical Performance Battery) considering CD/CI. To our knowledge one cross-sectional study demonstrated that poor lower limb function correlated strongly with poor cognitive status (Rosano et al., 2005), but these results were only partially confirmed by a prospective study (Gallucci et al., 2013). Moreover, no comprehensive prospective representative study has considered the range of physical performance measures (gait speed, handgrip strength, lower limbs strength) in one study over a period of 4 years or more. Therefore, the data regarding physical performance and the prediction of CD/CI is equivocal and it remains unclear which measure might be the optimal predictors and offer most clinical utility.

Given the aforementioned limitations and gaps in the literature, the aim of the present study was to examine which objective physical performance measures provide an optimal predictor of incident CD and CI in a representative cohort of elderly individuals over a follow-up of 4.4 ± 1.2 years.

2. Materials and methods

2.1. Data source and subjects

The data included participants from the *Progetto Veneto Anziani* (PRO.V.A.), observational cohort study among community-dwelling Italian older adults aged ≥65 years. The study population included 3099 age- and sex-stratified Caucasian participants (1854 women and 1245 men) randomly selected between 1995 and 1997 using a multistage stratification method. Sampling procedures and data collection methods have been described elsewhere. (Corti et al., 2002) The only follow-up evaluation was scheduled to occur at 4 years after baseline.

The ethical committees of Padova University and the Local Health Units (USSL) n. 15 and n. 18 of the Veneto Region approved the study protocol, and participants gave their written informed consent.

2.2. Clinical data

Participants were examined at city hospitals by trained physicians and nurses. Information was collected during a face-to-face interview. Regular physical activity was defined as ≥4 h/week in the previous month of at least moderate physical activity (brisk walking, cycling, gardening, dancing, or physical exercising), being 4 h/week the median value of the PRO.V.A. sample. Monthly income was categorized as ≥500 vs. <500 €, being 500 € the median value of the sample as whole. Smoking status was classified as "current" vs. "never"/"previous" (for at least 1 year in the past). Educational level was categorized as ≥5 vs. <5 years of schooling (which corresponds to the years of compulsory education in Italy when our participants were of school age). Body weight and height were measured by trained physicians, and body mass index (BMI) (kg/m^2) was calculated. Functional status was assessed using the ADL (activities of daily living) and IADL (instrumental activities of daily living) scores. Any depressive symptoms were assessed with the Geriatric Depression Scale (GDS), a 30-item self-reporting tool for identifying depression that has been validated for use in the elderly (Yesavage et al., 1982).

The presence of diabetes, cardiovascular diseases (CVD), osteoarthritis, fractures, chronic obstructive pulmonary disease (COPD), hypertension or cancer was ascertained by board-certified physicians involved in the study, who examined all of the clinical information collected for each participant. Additional information collected included disease history, symptoms self-reported using standardized questionnaires, medical and hospital records, blood tests, and a physical examination (Ojagbemi et al., 2015). We considered CVD as the presence of one of the following: congestive heart failure, angina requiring a stent or angioplasty or hospitalization, myocardial infarction, stroke, atrial fibrillation, or peripheral artery disease. Diabetes was defined as fasting plasma glucose levels ≥ 7.0 nmol/L, HbA1c ≥ 6.5%, the use of glucose-lowering drugs, or a history of a 2 h post-load glucose ≥ 11.1 mmol/L. (American Diabetes Association, 2013).

2.3. Definition of exposure and outcome

2.3.1. Physical performance tests

Physical performance, handgrip strength and lower limbs strength measures were assessed using standardized objective performance tests. Since a significant difference existed between genders for all the parameters investigated ($p < 0.001$), the tertiles for each test were calculated using gender-specific cut-offs. In all the analyses, the cut-off value was included in the lowest tertile, i.e. the first cut-off in the first and the second in the second tertile.

➢ Short Physical Performance Battery (SPPB) (Guralnik et al., 1994) scores were derived from three objective physical function tests. Each test was scored from 0 (inability to complete the test) to 4 (highest level of performance). The scores for all three tests were pooled to obtain a composite score of 0 to 12, higher scores reflecting a better physical function. The cutoffs for dividing the sample into tertiles were 10 and 11 points in men, and 9 and 10 points in women.
✓ Tandem test: participants were asked to maintain their balance in side-by-side, semi-tandem, and full-tandem positions.
✓ 4 m walking speed: the best performance achieved in two walks at participants' usual pace along a 4-m corridor was recorded in meters per second. Participants were allowed to use canes or walkers.
✓ Chair stands time: participants were asked to stand up and sit down 5 times as quickly as possible, with their hands folded across their chest. The time taken to complete the test, in seconds was recorded.

Since the 4 m walking speed and chair stands time are independent predictors of several negative outcomes in older people (Veronese et al., 2014a), these parameters were also considered as separate items in this analysis. The cutoffs used for the 4 m walking speed were 0.82 and 0.95 m/s in males, and 0.71 and 0.83 m/s in females; for the chair stands time, the corresponding cutoffs were 11.3 and 9.2 in males, and 10.3 and 13.0 s in females.

➢ Leg extension and flexion: knee extensor (quadriceps) and hip flexor (iliopsoas) strength was ascertained using a Nicholas Manual dynamometer (BK-7454, Fred Sammons, Inc.). The highest value recorded between the two legs for quadriceps strength was used in this analysis (Bandinelli et al., 1999). The cutoffs for leg extension were 22.1 and 33.3 kg in men, and 16.3 and 23.2 kg in women; for leg flexion, they were 23.4 and 31.0 kg in men, and 15.5 and 21.4 kg in women.
➢ Handgrip strength: this was measured in kg using a JAMAR hand-held dynamometer (BK-7498, Fred Sammons, Inc.). The best result obtained at three attempts with each hand was used for our