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ORIGINAL REPORT

SELF-REPORTED FATIGUE AND PHYSICAL FUNCTION IN LATE MID-LIFE

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Objective: **To determine the association between the 5 subscales of the Multidimensional Fatigue Inventory (MFI-20) and physical function in late mid-life.**
Design: **Cross-sectional study.**
Subjects: **A population-based sample of adults who participated in the Copenhagen Aging and Midlife Biobank population cohort (*n*=4,964; age 49–63 years).**
Methods: **Self-reported fatigue was measured using the MFI-20 comprising: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. Handgrip strength and chair rise tests were used as measures of physical function. Multiple logistic regression analyses were used to determine the associations between handgrip strength and the chair rise test with the MFI-20 subscales, adjusted for potential confounders.**
Results: **After adjustments for potential confounders, handgrip strength was associated with physical fatigue (adjusted odds ratio (OR) 0.75 (95% confidence interval (CI) 0.66–0.86); $p \leq 0.001$) and reduced motivation (adjusted OR 0.85 (95% CI 0.75–0.96); $p \leq 0.05$), but not with the other subscales. After these adjustments, the chair rise test was associated with physical fatigue (adjusted OR 0.61 (0.53–0.69); $p \leq 0.001$), general fatigue (adjusted OR 0.72 (0.62–0.84); $p \leq 0.001$), reduced activity (adjusted OR 0.79 (0.70–0.90); $p \leq 0.001$) and reduced motivation (adjusted OR 0.84 (0.74–0.95); $p \leq 0.01$), but not with mental fatigue. Subgroup analyses for sex did not show statistically significant different associations between physical function and fatigue.**
Conclusion: **The present study supports the physiological basis of 4 subscales of the MFI-20. The association between fatigue and function was independent of gender.**

Key words: hand strength; fatigue; questionnaires; cross-sectional studies; self-reported fatigue; chair rise test.

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INTRODUCTION

Fatigue can compromise quality of life. In population studies up to 46% of individuals reported fatigue and, in cancer, multiple sclerosis, and stroke patients, the incidence of fatigue can reach 92% (1–4). After adjustments for confounding factors, such as age, sex, weight, chronic diseases, and depressive symptoms, longitudinal primary care and population studies showed that fatigue predicts outcomes such as poor self-rated health (5); use of home help (6); hospitalization (6); angina pectoris (7); non-fatal myocardial infarction (7); up to 15-year mortality (5, 8); mobility disability (8–10); and disability with regard to activities of daily living (5, 10). These poor health outcomes associated with fatigue and its disabling nature underline the importance of preventing and treating fatigue.

However, fatigue is an ambiguous concept. It is a summed reaction to biological processes after intensive or prolonged work because metabolic demands exceed energy resources. In addition, fatigued individuals report low energy, vitality, cognitive slowness, depression, anxiety and a strong desire to sleep (3). Population studies show that middle-aged and old individuals report fatigue at a significantly higher rate than young individuals (11, 12). Yet, most fatigue measures are designed to quantify fatigue in patients who have a specific condition such as cancer or stroke. However, when measuring fatigue in the general population, as in the present study, the idea is to measure critical aspects of fatigue relevant to each individual, regardless of whether a specific disease, medication or a psychological problem is the cause of fatigue.

To assess fatigue both unidimensional and multidimensional self-report instruments have been developed that include disease-specific tools. Examples of unidimensional fatigue measures are the Fatigue Severity Scale (13) and the Mobility-Tiredness Scale (6); examples of multidimensional instruments are the Fatigue Scale (14) and the Multidimensional Fatigue Inventory (MFI-20) (15). Unlike unidimensional measures, multidimensional scales of fatigue facilitate the characterization of subjects with respect to the nature of their fatigue, and thus support condition-specific interventions. Of the self-reported multidimensional fatigue

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measures, the MFI-20 is probably the one most frequently used in Europe, especially in cancer patients (12).

The objective of the present study was to determine the association between MFI-20 subscales and physical function in a subset of 4,964 late mid-life participants in the Copenhagen Aging and Midlife Biobank (CAMB) cohort. An examination of the associations between the MFI-20 subscales and grip strength and chair rise performance at an early stage, such as late mid-life, is a logical strategy for the development and prescription of (cost-) effective preventive programmes to decrease fatigue and other poor outcomes in high-risk individuals.

METHODS

Study sample and procedure

The CAMB cohort has been described previously (16). Briefly, it comprises late mid-life participants from 3 cohorts: (*i*) the Metropolit Study; 7,750 men born in Copenhagen in 1953 (17); (*ii*) The Copenhagen Perinatal Cohort; 5,282 men and women born in the National University Hospital in Copenhagen in 1959–1961 (18); and (*iii*) The Danish Longitudinal Study on Work, Unemployment and Health; a random sample of 4,906 men and women born in 1949 and in 1959 (19). Subjects living outside Eastern Denmark were excluded. For safety reasons participants with high blood pressure (BP) (i.e. diastolic blood pressure > 100 mmHg or systolic blood pressure > 160 mmHg) did not perform the chair rise assessment since that requires high physical exertion that may lead to a further rise in BP.

From 2009 to 2011, eligible subjects received a postal questionnaire and a letter with information about the CAMB survey. In addition, subjects were asked to visit the National Research Centre for the Working Environment and participate in a health examination and physical assessments. During the visit the subjects received oral information about the study, and both oral and written informed consent was obtained. Non-respondents were sent a reminder 4 weeks after the first invitation, which was repeated at the end of the data collection period if subjects had not responded. The study protocol was approved by the local ethics committee (number H-A-2008-126) and the Danish Data Protection Agency (number 2008-41-2938).

Of the 17,937 invited subjects, 4,964 (28%) completed the postal questionnaire, the chair rise, and the handgrip test. Compared with non-participants, participants did not differ much with regard to educational levels, but higher proportions of participants were employed (16). However, the number of general practitioner visits in 2009 did not differ between participants and non-participants, which suggested that participants do not have better health (16).

Measures

Self-reported fatigue. Fatigue was assessed with the self-reported MFI-20, comprising 5 subscales: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue (15). Each subscale consists of 4 items rated on a 5-point Likert-scale (1 = yes, it is true; 5 = no, it is not true) with positively and negatively phrased items. The items are summed to calculate a subscale score with a theoretical range of 4–20 (higher scores indicate more fatigue). Examples of the items include: “I feel tired” (general fatigue); “Physically I feel I am in a bad condition” (physical fatigue); “I get little done” (reduced activity); “I dread having to do things” (reduced motivation); and “It takes a lot of effort to concentrate on things” (mental fatigue). Several studies report the MFI-20 as a feasible, reliable, and valid measure (12, 15, 20).

Physical function. Physical function was measured by two tests: (*i*) the maximal number of chair rises the subject was able to perform in 30 s, with their arms crossed against their chest and their knees fully extended before starting to descend (21). During the test, the subject’s back did not need to touch the backrest. The test was performed using a chair with a seat-height of 45 cm. A mechanical contact was connected to a signal-conditioning interface that automatically recorded the number of transitions. (*ii*) Maximal handgrip strength, in kg, of the dominant hand was measured with a dynamometer, as well as being recorded automatically (22). Subjects were instructed to squeeze their hand as hard and quickly as they could for about 3 s. Subsequently, participants could rest for 30 s until the next trial. Subjects completed 3–5 trials according to the following rule: If the force of the third handgrip trial exceeded both preceding trials by more than 5%, subjects performed a fourth trial. A fifth trial was done if the force of the fourth trial exceeded the third trial by more than 5%. The highest score on the 3–5 trials was selected for the analyses.

Health examination and assessment of covariates. The health examination included the measurement of height, body mass, and blood pressure. Blood pressure was measured to assess the subject’s eligibility for participation in the chair rise test. In addition to sociodemographic data (age, sex, education, and living situation), subjects’ occupational social class was derived by classifying occupation into social classes I–VI, according to the Danish occupational social class classification standard. Accordingly, social classes I–V comprise economically active individuals ranging from professional occupation in social class I to unskilled occupation in social class V. Social class VI represents people on public transfer income, including sickness benefits and disability pension. Depressive symptoms were assessed by the Major Depression Inventory (MDI), which comprises 10 items (including 2 sub-items) with a 6-point Likert-scale to measure symptom frequency during the previous 2 weeks (0 = at no time; 5 = all the time; theoretical score range 0–50, higher scores indicate higher levels of depressive symptoms) (23). To assess present morbidity and other health problems, such as stroke and osteoarthritis, 19 items from the Danish National Health Interview Survey were used and 2 questions were added on kidney stones and gallstones (a total of 21 items) (23, 24).

Statistical analyses

Before calculating sum scores of the MFI-20 subscales, per participant missing responses were replaced by the respondent’s mean scores for completed items of the same subscale when at least half of the subscale responses were valid. Likewise, total scores were calculated for the MDI. No other data were imputed.

The independent physical function measures were dichotomized at their sex-specific medians (see notes in Tables II and III for more details). Since MFI-20 subscale scores as the outcome variables did not meet the linear regression assumptions, it was decided to perform multivariate logistic regression analyses and use sex-specific medians as cut-offs (see notes in Tables II and III for more details). In addition to analyses of the total group, analyses were stratified by sex and adjusted for age, height, body mass and, in the total group only, sex (model 1). In subsequent models the following covariates were added: present morbidity (model 2) and present morbidity and depressive symptoms (model 3). The selection of the covariates age, height, body mass, sex, present morbidity, and depressive symptoms was based on previous studies (5–10, 25, 26). In *post-hoc* analyses gender differences were studied by entering the Sex × Physical function interaction terms in models 1–3.

All statistical analyses were performed with SPSS 20. The level of significance was set at $p = 0.05$.

RESULTS

Participants

Table I shows that the 4,964 participants comprise 2 age-groups: 2,175 subjects, age range 49–53 years (44%) and 2,789 subjects, age range 56–63 years (56%); with a median age of 50 years for women and 57 years for men. Of the subjects, 90% had a job, 55% were overweight (BMI ≥25) and two-thirds had one or more diseases. Concerning subscales of self-reported fatigue, higher median levels were reported on general fatigue and physical fatigue (9.0) in comparison with the other 3 subscales (7.0). The mean value for

Table I. *Characteristics of participants, by sex*

	Total (*n*=4,964)	Men (*n*=3,331)	Women (*n*=1,633)
Age			
49–53 years, *n* (%)	2,175 (44)	904 (27)	1,271 (78)
56–63 years, *n* (%)	2,789 (56)	2,427 (73)	362 (22)
Median age (IQR; range)	56 (50–57; 49–63)	57 (51–57; 49–63)	50 (50–52; 49–63)
Living alone, *n* (%)			
No	4,180 (84)	2,818 (85)	1,362 (83)
Yes	765 (15)	498 (15)	267 (16)
Unknown	19 (<1)	15 (<1)	4 (<1)
Occupational social class, *n* (%)[a]			
Class 1 and 2	2,073 (42)	1,466 (44)	607 (37)
Class 3 to 5	2,367 (48)	1,522 (46)	845 (52)
Class 6	469 (9)	315 (9)	154 (9)
Other	55 (1)	28 (1)	27 (2)
Present smoker, *n* (%)[b]			
No	3,812 (77)	2,548 (76)	1,264 (77)
Yes	1,147 (23)	779 (23)	368 (23)
Unknown	5 (<1)	4 (<1)	1 (<1)
Height, cm, mean (SD)	175.2 (8.9)	179.6 (6.5)	166.3 (6.2)
Body mass, kg, mean (SD)	80.0 (15.3)	85.0 (13.6)	69.6 (13.3)
BMI (kg/m^2):			
Mean (SD)	26.0 (4.2)	26.3 (3.8)	25.2 (4.7)
Overweight (≥25), *n* (%)	2,747 (55)	2,029 (61)	718 (44)
Present morbidity: *n* (%)[c]	3,344 (67)	2,222 (67)	1,122 (69)
Allergy	1,045 (21)	644 (19)	401 (25)
Arthritis	994 (20)	634 (19)	360 (22)
Hypertension	863 (17)	638 (19)	225 (14)
Depressive symptoms – MDI, median (IQR; range)[d]	5.0 (3.0–9.0; 0–48)	5.0 (2.0–8.0; 0–48)	6.0 (3.0–10.0; 0–48)
Fatigue – MFI-20[e]			
General fatigue			
Mean (SD)	9.6 (3.9)	9.3 (3.8)	10.1 (4.2)
Median (IQR; range)	9.0 (6.0–12.0; 4–20)	9.0 (6.0–12.0 ; 4–20)	10.0 (7.0–13.0; 4–20)
Physical fatigue			
Mean (SD)	9.1 (3.8)	8.9 (3.7)	9.6 (4.0)
Median (IQR; range)	9.0 (6.0–12.0; 4–20)	8.0 (6.0–11.0; 4–20)	9.0 (6.0–12.0; 4–20)
Reduced activity			
Mean (SD)	7.9 (3.3)	8.0 (3.3)	7.9 (3.5)
Median (IQR; range)	7.0 (5.0–10.0; 4–20)	7.0 (6.0–10.0; 4–20)	7.0 (5.0–10.0; 4–20)
Reduced motivation			
Mean (SD)	7.2 (2.5)	7.3 (2.5)	6.9 (2.5)
Median (IQR; range)	7.0 (5.0–9.0; 4–20)	7.0 (5.0–9.0; 4–20)	6.0 (5.0–8.0; 4–18)
Mental fatigue			
Mean (SD)	7.7 (3.3)	7.6 (3.2)	7.8 (3.5)
Median (IQR; range)	7.0 (5.0–9.0; 4–20)	7.0 (5.0–9.0; 4–20)	7.0 (5.0–10.0; 4–20)
Physical function, mean (SD)			
Handgrip strength, kg	43.5 (11.4)	49.6 (8.4)	31.3 (5.3)
Chair rise, *n*/30 s	21.7 (5.7)	22.0 (5.7)	21.2 (5.7)

[a]Class 1–2 – job requires ≥3 years of theoretical or university training or management of ≥11 subordinates; class 3–5 – job requires no to 1.5 years of theoretical training or management control of ≤10 subordinates; class 6 – economically inactive (transfer income); other – students, housewives/husbands, and individuals with no or insufficient job information.
[b]Daily and not daily smoking.
[c]≥1 self-reported somatic or psychiatric disease or health problem; including the 3 most prevalent diseases or health problems.
[d]Major Depression Inventory (MDI, theoretical range 0–50, higher scores indicate higher levels of depressive symptoms).
[e]Multidimensional Fatigue Inventory (MFI-20, higher scores indicate more self-reported fatigue).
IQR: interquartile range; SD: standard deviation.

handgrip strength was lower in women (31.3 kg) than men (49.6 kg), but the results on the chair rise test appeared similar (21.2 and 22.0).

Handgrip strength

In the total group the associations were the strongest between handgrip strength and self-reported physical fatigue (Table II). In contrast to associations with other subscales of self-reported fatigue, the associations of handgrip strength with physical fatigue and reduced motivation were still statistically significant after adjustments for age, sex, body mass, height, present morbidity, and depressive symptoms in the total group (model 3 – physical fatigue; odds ratio (OR) 0.75

Table II. *Odds ratios (OR) and 95% confidence intervals (95% CI) from multiple logistic regression analyses of handgrip strength with dimensions of self-reported fatigue, by sex*

	General fatigue OR (95% CI)	Physical fatigue OR (95% CI)	Reduced activity OR (95% CI)	Reduced motivation OR (95% CI)	Mental fatigue OR (95% CI)
Total (*n*=4,964)					
Model 1	0.79 (0.70–0.89)***	0.70 (0.62–0.79)***	0.85 (0.75–0.95)**	0.78 (0.69–0.87)***	0.90 (0.80–1.01)
Model 2	0.79 (0.70–0.89)***	0.70 (0.62–0.79)***	0.85 (0.75–0.95)**	0.78 (0.69–0.88)***	0.90 (0.80–1.01)
Model 3	0.89 (0.77–1.04)	0.75 (0.66–0.86)***	0.94 (0.83–1.07)	0.85 (0.75–0.96)*	1.03 (0.90–1.18)
Men (*n*=3,331)					
Model 1	0.82 (0.71–0.95)**	0.72 (0.62–0.83)***	0.86 (0.74–0.99)*	0.78 (0.67–0.90)***	0.88 (0.76–1.01)
Model 2	0.82 (0.70–0.94)**	0.71 (0.61–0.83)***	0.86 (0.74–0.99)*	0.78 (0.67–0.90)***	0.88 (0.76–1.01)
Model 3	0.94 (0.79–1.13)	0.77 (0.66–0.91)**	0.96 (0.82–1.12)	0.85 (0.73–0.99)*	1.00 (0.85–1.17)
Women (*n*=1,633)					
Model 1	0.71 (0.57–0.88)**	0.66 (0.53–0.82)***	0.81 (0.66–1.01)	0.75 (0.61–0.93)**	0.93 (0.76–1.15)
Model 2	0.71 (0.57–0.89)**	0.66 (0.53–0.83)***	0.82 (0.66–1.02)	0.75 (0.61–0.93)**	0.94 (0.76–1.16)
Model 3	0.77 (0.58–1.01)	0.71 (0.56–0.90)**	0.91 (0.72–1.16)	0.82 (0.65–1.03)	1.10 (0.87–1.40)

$^*p \leq 0.05$; $^{**}p \leq 0.01$; $^{***}p \leq 0.001$.

Sex-specific cut-offs (medians) for: General fatigue ≤ 10 (=”low”) vs > 10 (=”high”) (females), ≤ 9 (=”low”) vs > 9 (=”high”) (males); Physical fatigue ≤ 9 (=”low”) vs > 9 (=”high”) (females), ≤ 8 (=”low”) vs > 8 (=”high”) (males); Reduced activity ≤ 7 (=”low”) vs > 7 (=”high”) (females/males); Reduced motivation ≤ 6 (=”low”) vs > 6 (=”high”) (females), ≤ 7 (=”low”) vs > 7 (=”high”) (males); Mental fatigue ≤ 7 (=”low”) vs > 7 (=”high”) (females/males); Handgrip strength ≤ 31.1 (=”weak”) vs > 31.1 (=”strong”) (females), ≤ 49.4 (=”weak”) vs > 49.4 (=”strong”) (males).

Model 1: adjusted for age, body mass, height, and – in total group only – sex; Model 2: adjusted for age, body mass, height, sex (total group only), and present morbidity; Model 3: adjusted for age, body mass, height, sex (total group only), present morbidity, and depressive symptoms.

(95% confidence interval (CI) 0.66–0.86); $p \leq 0.001$; – reduced motivation; OR 0.85 (95% CI 0.75–0.96); $p \leq 0.05$). This suggests that participants with a stronger handgrip were 25% less likely to report physical fatigue and 15% less likely to report reduced motivation than participants with a weaker handgrip. Without adjustments for depressive symptoms (models 1 and 2), handgrip strength, in the total group and in men and women separately, was statistically significantly associated with all subscales of self-reported fatigue, except for mental fatigue (total group, men, and women) and reduced activity in women.

Chair rise test

Table III shows that in the total group, after adjustments for age, sex, body mass, height, present morbidity, and depressive symptoms (model 3), results on the chair rise test were statistically significantly associated with self-reported physical fatigue (OR 0.61 (95% CI 0.53–0.69); $p \leq 0.001$), general fatigue (OR 0.72 (95% CI 0.62–0.84); $p \leq 0.001$), reduced activity (OR 0.79 (95% CI 0.70–0.90); $p \leq 0.001$) and reduced motivation (OR 0.84 (95% CI 0.74–0.95); $p \leq 0.01$). For example, in contrast to subjects with a poor performance

Table III. *Odds ratios (OR) and 95% confidence intervals (95% CI) from multiple logistic regression analyses of the chair rise test with dimensions of self-reported fatigue, by sex*

	General fatigue OR 95% CI	Physical fatigue OR 95% CI	Reduced activity OR 95% CI	Reduced motivation OR 95% CI	Mental fatigue OR 95% CI
Total (*n*=4,964)					
Model 1	0.62 (0.55–0.70)***	0.54 (0.48–0.61)***	0.68 (0.61–0.77)***	0.73 (0.65–0.82)***	0.83 (0.74–0.93)**
Model 2	0.64 (0.57–0.72)***	0.55 (0.49–0.62)***	0.70 (0.62–0.78)***	0.74 (0.66–0.83)***	0.85 (0.76–0.95)**
Model 3	0.72 (0.62–0.84)***	0.61 (0.53–0.69)***	0.79 (0.70–0.90)***	0.84 (0.74–0.95)**	1.02 (0.90–1.16)
Men (*n*=3,331)					
Model 1	0.64 (0.55–0.74)***	0.55 (0.47–0.63)***	0.71 (0.62–0.82)***	0.76 (0.66–0.88)***	0.89 (0.77–1.02)
Model 2	0.66 (0.57–0.76)***	0.56 (0.48–0.65)***	0.72 (0.63–0.83)***	0.77 (0.67–0.89)***	0.90 (0.78–1.04)
Model 3	0.71 (0.60–0.85)***	0.60 (0.52–0.71)***	0.81 (0.69–0.94)**	0.86 (0.74–1.00)	1.07 (0.91–1.25)
Women (*n*=1,633)					
Model 1	0.59 (0.48–0.73)***	0.53 (0.43–0.65)***	0.64 (0.52–0.79)***	0.66 (0.54–0.82)***	0.72 (0.59–0.89)**
Model 2	0.61 (0.50–0.76)***	0.54 (0.44–0.67)***	0.65 (0.53–0.81)***	0.68 (0.55–0.83)***	0.74 (0.60–0.91)**
Model 3	0.74 (0.56–0.96)*	0.61 (0.49–0.77)***	0.77 (0.61–0.97)*	0.80 (0.63–1.00)*	0.91 (0.72–1.15)

$^*p \leq 0.05$; $^{**}p \leq 0.01$; $^{***}p \leq 0.001$.

Sex-specific cut-offs (medians) for: General fatigue ≤ 10 (=”low”) vs >10 (=”high”) (females), ≤ 9 (=”low”) vs > 9 (=”high”) (males); Physical fatigue ≤9 (=”low”) vs > 9 (=”high”) (females), ≤8 (=”low”) vs > 8 (=”high”) (males); Reduced activity ≤7 (=”low”) vs >7 (=”high”) (females/males); Reduced motivation ≤6 (=”low”) vs > 6 (=”high”) (females), ≤ 7 (=”low”) vs > 7 (=”high”) (males); Mental fatigue ≤ 7 (=”low”) vs > 7 (=”high”) (females/males); Chair rise test ≤20.6 (=”poor function”) vs >20.6 (=”good function”) (females), ≤21.8 (=”poor function”) vs >21.8 (=”good function”) (males).

Model 1: adjusted for age, body mass, height, and – in total group only – sex; Model 2: adjusted for age, body mass, height, sex (total group only), and present morbidity; Model 3: adjusted for age, body mass, height, sex (total group only), present morbidity, and depressive symptoms.

on the chair rise test, subjects with a good performance had a 39% lower risk to report physical fatigue, 28% lower risk to report general fatigue, 21% lower risk to have a reduced activity level, and 16% lower risk to report reduced motivation. Without adjustments for depressive symptoms (models 1 and 2), all associations between chair rise performance and subscales of self-reported fatigue were statistically significant in the total group and in men and women, except for mental fatigue in women.

Post-hoc analyses

Post-hoc analyses including interaction terms for sex by physical function measures showed that all terms were statistically non-significant.

DISCUSSION

The main finding in this population study in late mid-life men and women is that, after adjusting for potential confounding variables, physical function, as measured by handgrip strength and the chair rise test, was most strongly associated with the MFI-20 physical fatigue subscale. Apparently the self-reported physical fatigue subscale reflects both muscle strength as measured by the handgrip test and also a broader concept of physical function, i.e. the chair rise test, including muscle strength, balance and mobility (27, 28), and maybe also aerobic capacity. In addition, the association between function and self-reported fatigue is independent of gender in this late mid-life cohort.

The present study expands our knowledge of the physiological basis of the MFI-20 subscales, since, except for a study in patients with fibromyalgia, to our knowledge no population studies have examined the associations between these subscales and measures of physical function (29). In addition, it complements previous cross-sectional population studies of other self-reported fatigue measures that are significantly associated with measures of physical function, such as handgrip strength (30, 31) and the chair rise test (32). To represent physical function, we selected the widely used handgrip strength and chair rise tests that predict cognitive decline, disability, and mortality (25, 26, 33, 34). Handgrip strength is strongly associated with other measures of muscle strength and can be considered as a marker of physiological reserve in middle-aged and older adults (25, 26). We also used the chair rise test because it is a robust measure of physical function and quantifies the function of physiological systems associated with muscle strength and aerobic capacity. Performance in chair rise is also a strong indicator of mobility (27, 28).

This study shows that, after adjustments, the chair rise compared with the grip strength test was not only more strongly associated with the self-reported MFI-20 physical fatigue subscale, but also with general fatigue, reduced activity, and reduced motivation. These data suggest that these 4 subscales of self-reported fatigue also involve physical function in a broader sense. Rising from a chair compared with gripping requires the activation of a substantially larger muscle mass. In older adults especially, the activation of large muscle volume necessitates an effort that represents a relatively high proportion of the maximum capacity (35). In contrast with single, brief efforts of gripping, chair rise performance includes the repetitive activation of a larger muscle volume and is a more sensitive and comprehensive measure of physical function, including physical dimensions of fatigue. In total, the association between physical function as measured by grip strength and chair rise provides a physiological basis for MFI-20, especially for its physical dimensions.

Furthermore, adding morbidity to the first model did not affect the odds ratios. This is unexpected because previous studies in (older) adults showed that morbidity is associated with both self-reported fatigue and physical function (11, 36, 37). However, this finding might be explained by the included adjustments for age, body mass, height, and sex.

After the adjustments for confounders and adding depressive symptoms to model 3, the associations of the chair rise test with self-reported mental fatigue were no longer statistically significant. This suggests that depressive symptoms are an important factor in the association and that this subscale reflects mental components of perceived fatigue. Also, many previous population studies, with data from children and (older) adults, found depressive symptoms to be significantly associated with all MFI-20 subscales (11, 12, 20, 38, 39). The present findings are also congruent with previous data, showing that in older adults depressive symptoms, together with morbidity and sleep quality, substantially weakened the association between handgrip strength and a self-reported fatigue measure (31).

The last finding reflects the results of the *post-hoc* analyses of the interaction between sex and physical function. These analyses were performed because (*i*) previous studies reported gender differences on the MFI-20 subscales, handgrip strength, and chair rise test, and (*ii*) stratification was done in studies on the association between handgrip strength and self-reported fatigue (11, 12, 20, 31, 34, 38, 39). However, the present study showed that the association of physical function with subscales of self-reported fatigue is not different between men and women.

The present study has some advantages compared with previous studies on (self-reported) fatigue and physical function. To our knowledge, this is the first population study that linked measures of physical function with subscales of fatigue as measured by the MFI-20: it showed the difference between the associations of handgrip strength and the chair rise test vs more physical or psychological subscales of self-reported fatigue. Also, support for this cohort to be representative for the Danish population is found in another Danish population study that had a comparable mean age and similar mean scores of BMI and handgrip strength (40). Compared with men, women in the present study had much weaker handgrip strength but only slightly poorer performance on the chair rise test. This is congruent with previous studies, including the above-mentioned Danish population study and a study of a representative middle-aged group in the UK (37, 40, 41). However, a previous population study reported lower mean MFI-20 subscale scores for the age group of 40–59 years (interquartile range (IQR) 7.1–8.0 in men and 7.8–8.7 in women), than found in the present study (IQR 7.3–9.3 in men and 6.9–10.1 in women), which might be explained by the age-discrepancy (12). Other strengths of the present study are the large sample sizes for men and women, the age span limited to late mid-life, and the use of sex-specific cut-offs for each subscale that increased the statistical power of the analyses.

A limitation of the study is the quite low response rate. However, non-participants did not differ from participants on education level and the number of general practitioner visits in 2009, suggesting that, to some extent, it is possible to generalize the results to the general population. To delineate the direction of the association between physical function and self-reported fatigue, future follow-up studies should assess whether non-fatigued subjects with poor physical function have a higher incidence of becoming fatigued, than non-fatigued subjects with good physical function.

In conclusion, physical function, as measured by handgrip strength and the chair rise test, is associated with self-reported physical fatigue, general fatigue, reduced activity, and reduced motivation. Therefore this study supports the validity of the MFI-20. Knowledge about the features of physical functioning that are associated with subtypes of self-reported fatigue may contribute to the development of specific (preventive) interventions.

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