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#### **Research Article**

# Disability Benefits and Chronic Fatigue Syndrome: A Populationbased Study of the Nature and range of Work-Related Impairment

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- Chronic fatigue syndrome
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#### Abstract

Aim: To compare disease impact on functioning in patients with chronic fatigue syndrome receiving disability benefits and patients recovered and returned to work.

Methods: Eighteen patients with CFS living in a Western Norway community with 11,500 inhabitants were included. Self-report questionnaires included the physical functioning scale of SF-36 (SF-36 PF); perception of effort during exercise, the Rate of Perceived Exertion scale (RPE); cognitive problems, the Chalder Fatigue Scale, (CFQ, questions 8-11). Objective tests were the Hand Grip Strength test (HGS); sub-maxima exercise testing, the 6-min Walk Test (6MWT); cognitive performance was the Paced Auditory Serial attention Test (PASAT).

**Results:** Twelve patients received disability benefits. Patients who received disability benefits scored worse than the recovered patients did on these measures: SF-36 PF (13 vs 29), RPE (15.9 vs 9.7), and (CFQ) (9.5 vs 4.8). Patients receiving disability benefits had lower maximum voluntary contraction values on HGS test (107 vs 128), decreased 6MWT (448 m vs 560 m).

**Conclusion:** Awarded disability benefits to CFS patients were associated with high levels of functional impairment, severe fatigue, poor physical functioning, memory and concentration problems, and increased perception of effort compared to recovered patients. Self-reported functional status correlated well with the objective tests.

# **INTRODUCTION**

Chronic fatigue syndrome (CFS) is a complex multi-system illness characterized by severe fatigue of new onset, substantial reduction in previous levels of occupational, educational, social and personal activities, and concurrent occurrence of four or more of the following symptoms: impaired short-term memory or concentration, sore throat, tender lymph nodes, muscle pain, multi joint pain, headache of a new type, unrefreshing sleep, and post-exertional malaise [1]. The excessive fatigue and fatigability with disproportionately prolonged recovery after exercise or activity is the cardinal symptom [2,3]. The etiology of CFS is largely unknown. Nevertheless, significant evidence of neurological, immunological, autonomic and energy metabolism impairments were reviewed in the 2015 Institute of Medicine (IOM) report 2015 [4].

Population-based epidemiological studies have estimated an overall yearly CFS incidence of 0.015% in England [5], and 0.025% in Norway [6]. CFS occurs in individuals during peak years of employment (age 20-50). A systematic review of literature on employment data found that 54% of patients with CFS were unemployed [7]. Work-related physical and cognitive impairments are demonstrable with prolongation and recurrence of sickness absence episodes that can be the first step in a process leading to medical retirement and awarded disability benefits [8,9]. The Norwegian Social and Insurance Scheme accepted in 1995 CFS to be a medico-legal diagnosis (ICD10 code: G 93.3) entitled to disability benefits on the ground of ill health [10]. In 2012, 32.1 % of the 5775 CFS patients registered in the Norwegian National Patient Registry received disability pension. In Australia the majority of patients diagnosed with CFS by primary care physicians were unemployed (26.7%), or on disability pension (34.2%) [11].

Knowledge about long-term disability in CFS is important as it relates to several aspects of the illness: information and advice to newly diagnosed patients, planning of health care and rehabilitation strategies that focus on volitional and social aspects of re-employment [12]. The objectives of this study were to identify factors associated with work cessation in a communitybased cohort of younger, adult CFS patients awarded disability benefits. We used recommended reproducible questionnaires.

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Objectively measured physical and cognitive functional capacity have the potential to improve the validity of questionnaire measures [13,14]. We included two objective tests of physical capacity.

The aim of this study was to compare clinical characteristics and functioning of a community-based cohort of younger CFS patients awarded disability benefits with a reference group of CFS patients who had recovered and returned to work.

## **MATERIALS AND METHODS**

#### **Geographical note**

Bømlo municipality with a population of 11,500 is situated at the southwest coast of Norway. One large and hundreds of smaller islands cover an area of 247 square km. Tourism, fishery, and offshore-related work are the major industries.

#### Patients

During 1998-2010 eighteen patients, 14 females and 4 males referred from Bømlo municipality to the Outpatient Clinic of the Department of Neurology, Haukeland University Hospital, were diagnosed with CFS according to the 1994 Fukuda criteria [15]. The patients received a written self-management program including information about the illness, the fatigue experience, and active strategies for daily life. The family doctor and the local National Sickness Benefit Scheme office (NAV) received a specialist report on the medical history, clinical symptoms, fatigue severity and work capability.

At follow-up in 2012, all patients completed questionnaires: functional impairment, fatigue, physical and cognitive functioning, perceived effort of exertion, anxiety and depression. Tests of physical capacity were handgrip strength and sub-maximal exercise assessment. A cognitive test measured attention, memory and processing speed.

#### Employment

Current employment status was recorded as employed (full-time or part-time studies/work), or unemployed (not participating in studies/work).

#### **Self-reported measures**

**Functional impairment, WSAS:** The Work and Social Adjustment Scale (WSAS) is a 5-item self-report scale that measures perceived functional impairment, the reduced ability to carry out every day activities: work, home management, social and private leisure activities and close relationships. Each of the five items is rated on a nine-point scale ranging from 0 (not at all a problem) to 8 (severely impaired). The total scores range between 0 and 40. A score above 20 was used as a threshold to indicate moderately severe functional impairment [16].

**Fatigue, FSS:** Fatigue was self-rated with the Fatigue Severity Scale (FFS), a 9-item scale that measures the severity of fatigue

and its effect on daily living. Each item is rated from 1 "completely disagree" to 7 "completely agree". Examples of the items are: "my motivation is lower when I am fatigued", "exercise brings on my fatigue" and "I am easily fatigued". Patients with a mean FSS score > 5 are defined as having severe fatigue [17].

**Perception of effort, RPE:** Perceived effort during physical activity was rated with the Borg Rating of Perceived Exertion Scale (RPE) immediately after the 6-minute's Walk Test. RPE is a numerical scoring system that ranges from 6 (no exertion) to 20 (maximal exertion) [18].

**Cognitive symptoms, CFQ:** Cognitive impairments were measured with four questions on mental symptoms from the Chalder Fatigue Scale (CFQ): 8). do you have difficulty concentrating, 9). thinking clearly, 10). Find the correct word, and 11). How is your memory. Four options were used: "better than normal", "not more than usual", "worse than usual", "much worse than usual" [19].

**Physical functioning, SF-36:** Physical functioning, the ability to undertake everyday activities, was measured with the 10 item SF-36 Physical Functioning scale [20]. Patients scored 0 ("Yes, limited a lot"), 5 (Yes, limited a little), or 10 ("No, not limited at all"), range 0-100.

**Anxiety and depression, HADS:** Hospital Anxiety and Depression Scale (HADS) includes seven items each to assess anxiety and depression symptoms (the HADS-A and HADS-D, respectively), with each item answered on a four-point (0-3) scale. The total score on each subscale is obtained by adding together the items, and thus ranges from 0-21, with higher scores indicating more severe symptoms [21]. Case-level anxiety and depression are defined as scores on the HADS > 8 [22].

#### **Objective measures**

**Physical tests:** 6-min Walk Test (6MWT) was used to measure sub-maximal exercise capacity. It measures the distance an individual is able to walk over a time of six minutes on a hard flat surface [23]. Score range for healthy adults is 400-700.

Handgrip strength (HGS) was used to measure maximum voluntary contraction (MVC) with a hand-held dynamometer. Normative data for handgrip strength are 27 kg in males and 16 kg in females [24].

**Cognitive test:** We used Paced Auditory Serial Addition Test (PASAT) to measure sustained attention, memory and information processing speed [25].

#### **Statistics**

Student's t-test, and pairwise correlation analyses were performed when appropriate. Table 2-4 shows univariate (pairwise correlation tests), and multivariate (linear regression) analyses adjusting for sex and age. STATA/SE 17.0 (Statacorp 4905 Lakeway Drive, College Station, Texas 77845 USA) was used for analyses.

# **RESULTS**

This population based study showed that 18 persons developed CFS between 1998 and 2010 (14 females and 4 males) in the population of 11,500 in Bømlo municipality, Norway.

The crude annual incidence rates for CFS in the population  $\geq$ 15 years was 0.017% (0.007% for males and 0.027% for females). Point prevalence on January 1 2012 was 0.14%. The mean age at the onset of symptoms was 26 years (SD, 13 years) (range 15-57 years).The mean age on follow-up was 39 years (SD, 18 years) for males, and 35 years (SD, 11 years) for females. The mean time from onset of symptoms to follow-up was 8.5 years (SD, 4.7 years).

At follow-up in 2012, twelve patients did not have work capacity and got disability benefits (seven patients WAA and five patients DP). Six patients (all females) obtained significant clinical improvement and had returned to part-time or full-time work.

Table 1 compares different scores in patients with CFS and patients who had recovered. All scores except PASAT, HADS-A and HADS-D were significantly worse among CFS patients.

Table 2 shows univariate and multivariate analyses with FSS as dependent variable. FSS had high association with unemployment, Borg RPE scale, 6-minutes Walk Test, handgrip strength in female, SF-36 Physical Function, but no association with PASAT and HADS-D scores. Replacing FSS with WSAS gave almost identical results.

Table 1: Different scores (mean, SD) in patients with CFS compared to recovered patients

	CFS N=12	Recovered N=6	Р
Age	36 (13)	35 (12)	.83
WSAS	31 (4.0)	12.5 (9.8)	<.001
FSS	6.5 (.5)	3.5 (1.1)	<.001
SF-36 PF <sup>1</sup>	18 (4.8)	29 (1.5)	<.001
Borg RPE scale	16 (3)	8 (1.8)	<.001
Six minute walk test	448 (130)	662 (58)	.002
Handgrip (females)	90 (16)	128 (17)	.002
Cognitive symptoms	2.6 (.7)	8.5 (1.4)	<.001
PASAT	42 (8)	41 (18)	.9
HAD anxiety	6.7 (4.7)	3.3 (2.8)	.13
HAD depression	3.9 (4.0)	2.3 (2.3)	.39

<sup>1</sup>PF = physical function

 Table 2: Univariate and multivariate analyses with FSS as dependent variables in patients with CFS and recovered patients

	Univariate		Multivariate		
Independent variables	R	Р	Beta <sup>1</sup>	Р	<b>R-squared</b>
Employment	90	<.001	91	<.001	.82
WSAS	.66	.004	.68	.008	.44
SF-36 PF <sup>2</sup>	.79	<.001	.76	.001	.65
Six minute walk test	71	.003	71	.003	.62
Handgrip	37	.20	97	.002	.64
Borg RPE scale	.79	<.001	.78	.001	.68
Cognitive function	.65	.005	.62	.01	.47
PASAT	02	.93	04	.90	.55
HAD anxiety	.48	.054	.47	.059	.32
HAD depression	.24	.36	.36	.25	.16

<sup>1</sup>Adjusted for sex and age <sup>2</sup>PF = physical function

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Table 3 shows univariate and multivariate analyses with the physical function subscore of SF-36 as dependent variable. Except PASAT all scores were significantly associated with low physical function. This pertained especially to unemployment, 6-minutes Walk Test, Borg RPE scale and CFQ.

Table 4 shows univariate and multivariate analyses with Borg RPE as dependent variable. Except PASAT, HADS-A and HADS-D, Borg RPE was significantly associated with all scores and unemployment.

**Table 3:** Univariate and multivariate analyses with the physical function subscore of

 SF-36 as dependent variable in patients with CFS and recovered patients

	Univariate		Multivariate		
	R	Р	Beta <sup>1</sup>	Р	<b>R-squared</b>
Employment	.80	<.001	.81	<.001	.68
WSAS	80	<.001	78	<.001	.65
FSS	79	<.001	80	.001	.63
Six minute walk test	.90	<.001	.90	<.001	.82
Handgrip	.44	.09	.79	.01	.44
Borg RPE scale	83	<.001	87	<.001	.71
Cognitive function	.85	<.001	.88	<.001	.72
PASAT	.18	.47	.14	.6	.08
HAD anxiety	64	.004	64	.005	.48
HAD depression	61	.008	63	.007	.45

<sup>1</sup>Adjusted for sex and age

	Univ	Univariate		variate	
	R	Р	Beta <sup>1</sup>	Р	<b>R-squared</b>
Employment	83	<.001	89	<.001	.78
WSAS	.83	<.001	.81	<.001	.74
FSS	.79	<.001	.82	.001	.66
Six minute walk test	82	<.001	80	<.001	.72
Handgrip	37	.18	65	.04	.41
Cognitive function	87	<.001	91	<.001	.81
PASAT	14	.59	04	.90	.10
HAD anxiety	.42	.10	.47	.08	.31
HAD depression	.37	.16	.46	.09	.30

 Table 4: Univariate and multivariate analyses with Borg RPE Scale as dependent variable in patients with CFS and recovered patients

<sup>1</sup>Adjusted for sex and age

Excluding recovered patients, 6-minutes' Walk Test was correlated to SF-36 Physical Functioning (r=.80, P=.005), WSAS (r=-.84, P=.002), HADS-A (r=-.68, P=.03), HADS-D (r=-.71, P=.02), and possibly Borg RPE (r=-.60, P=.07), but not FSS, CFQ or PASAT (all P>.1).

#### DISCUSSION

Despite limited number of cases, this CFS patient cohort appear to be representative. Rates of both annual incidence, 0.017%, and 30% awarded disability pension are similar to the estimates for Norway. Moreover, the recovery rate of 30%, 6 patients returning to work (2 patients full time and 4 patients part time) is comparable to the 10% total and 22,5% partial remission rates in a population-based 3 year follow-up of 40 patients in Wichita, Kansas [26].

A multi-dimensional approach using questionnaires identified the following determinants of work disability: high levels of perceived functional impairment, profound fatigue, and poor physical function, and cognitive difficulties. Objective measures of physical functioning including six minutes Walk Test and handgrip test were associated with unemployment.

#### Functional impairment and unemployment

Our study confirm that the use of WSAS is an acceptable measure of disability. CFS patients awarded disability benefits had high WSAS scores that correlated significantly with fatigue, physical activity, perception of effort, cognitive complaints, and 6-min Walk Test.

A study of the psychometric properties of the WSAS in two large cohorts of CFS patients suggested that WSAS is an appropriate measure of disability in both research and in everyday clinical context. Higher levels of disability were associated with higher fatigue and depression scores, and lower SF-36 physical function scores. Associations between objective tests of physical fitness, such as the 6 minutes Walk Test and a step test, although significant, were small [27]. In our long-term follow-up of employment, status in patients with CFS after mononucleosis the WSAS score was significantly associated with disease duration, depression and post-exertional malaise [28]. A recent study of factors associated with work status in CFS included 508 patients of whom 45% reported temporary or permanently interrupted employment. Fatigue severity, poorer physical functioning and job demands were associated with unemployment. Multivariate analyses suggested that currently not working was most strongly associated with perceived functional impairment, WSAS, older age and depression symptoms [29].

#### Fatigue

The Fatigue Severity Scale (FSS) measure severity of fatigue and its effect on daily living [17]. Our study shows that fatigue is severe in CFS patients receiving disability benefits. The degree of fatigue correlated with the levels of perceived functional impairment, physical functioning, perception of effort, reduced walking distance, and reduced handgrip strength in women.

Higher scores for fatigue, neurological symptoms, pain, depression, autonomic and sleep dysfunction were all associated with higher risk of work disability in a community-based study [30]. Physical fatigue was significantly associated with long-term sickness absence for patients with CFS at an out-patient treatment service [8]. This is consistent with previous research that suggests that physical functioning plays an important role in the persistence of fatigue complaints and work disability in employees on sick leave [31]. By performing repeated hand grip and quadriceps strength measurements muscular fatigue and fatigability were objectively detected [3].

# **Physical functioning**

The 36-item Short-Form Health Survey (SF-36) has been

used to assess the disability criteria for the case definition: substantial reductions of occupational, educational, social, and personal activities [32]. CFS patients on average scored lower on most subscales of the SF-36 in comparison with healthy controls and other chronic diseases [5,33]. The loss of functional status was greater in patients with CFS than in patients with multiple sclerosis and heathy controls [34].

In the present study CFS patients receiving disability benefits had reduced SF-36 physical functioning scores that correlated with severe fatigue, greater perceived effort scores, cognitive complaints, reduced hand grip strength in women, and decreased walking distance. A comprehensive UK study identified older age, male sex, duration of illness, fatigue and physical functioning to be associated with cessation of employment. In a multivariate model, physical functioning remained an independent predictor [35].

The relationship between subjective interpretations of physical activity level and objective measures of physical activity has been assessed empirically. The scores of the physical functioning scales were significantly correlated with the number of steps on an activity meter, and % VO2 of a cardiopulmonary exercise test [36]. A meta-analysis of RPE responses to aerobic exercise in CFS compared with healthy controls confirmed that perception of effort is elevated in people with CFS [37]. Compared to fitness-matched controls, cardiopulmonary responses to exercise in CFS are characterized by inefficient exercise ventilation and augmented perception of effort [38]. Although it is generally agreed that perception of effort reflects neural integration and processing of sensory signals, the exact causes are still unclear [37].

Fatigue is common in patients with neurological disorders including Parkinson's disease [39]. Patients with CFS have been shown to exhibit symptoms suggestive of decreased basal ganglia function including motor slowing that correlated with severity of fatigue [40]. Improvement in exercise tolerance and ratings of perceived exertion (Borg RPE) were observed after exercise training in patients with Parkinson's disease [41]. Functional magnetic resonance imaging to examine neural activation showed that patients with CFS exhibited significant reduced basal ganglia activation compared to healthy controls [42]. A systematic review of neurologic impairments in CFS using neuroimaging techniques suggested disruption of autonomic nervous system network, white matter abnormalities and aberrations in functional connectivity. However, these findings are not consistent across studies, and the origins of these abnormalities remain unknown [43]. A recent regional cerebral blood flow study in CFS patients showed low perfusion in several brain regions of the limbic system, including the anterior cingulate cortex, putamen, pallidum, and ventral insular area that may contribute to the CFS pathogenesis [44].

The main weakness of the present study is the low number of patients. Strengths include population based design and the use of both questionnaires and objective physical measures.

# **CONCLUSION**

In conclusion, compared to recovered patients, patients with CFS scored significantly worse on all questionnaires and objective physical tests except depression and anxiety questionnaires.

#### REFERENCES

- Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. Ann Intern Med. 1994; 121: 953-959.
- Paul L, Wood L, Behan WM, Maclaren WM. Demonstration of delayed recovery from fatiguing exercise in chronic fatigue syndrome. Eur J Neurol. 1999; 6: 63-69.
- Jakel B, Kedor C, Grabowski P, Wittke K, Thiel S, Scherbakov N, et al. Hand grip strength and fatigability: correlation with clinical parameters and diagnostic suitability in ME/CFS. J Transl Med. 2021; 19: 159.
- Clayton EW. Beyond myalgic encephalomyelitis/chronic fatigue syndrome: an IOM report on redefining an illness. JAMA. 2015; 313: 1101-1102.
- Nacul LC, Lacerda EM, Pheby D, Campion P, Molokhia M, Fayyaz S, et al. Prevalence of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in three regions of England: a repeated crosssectional study in primary care. BMC Med 2011; 9: 91.
- Bakken IJ, Tveito K, Gunnes N, Ghaderi S, Stoltenberg C, Trogstad L, et al. Two age peaks in the incidence of chronic fatigue syndrome/ myalgic encephalomyelitis: a population-based registry study from Norway 2008-2012. BMC Med. 2014; 12: 167.
- Ross SD, Estok RP, Frame D, Stone LR, Ludensky V, Levine CB. Disability and chronic fatigue syndrome: a focus on function. Arch Intern Med. 2004; 164: 1098-1107.
- Knudsen AK, Henderson M, Harvey SB, Chalder T. Long-term sickness absence among patients with chronic fatigue syndrome. Br J Psychiatry. 2011; 199: 430-431.
- Taylor RR, Kielhofner GW. Work-related impairment and employ ment-focused rehabilitation options for indviduals with chronic fatigue syndrome: A review. J Mental Health. 2005; 14: 253-267.
- Haukenes G, Aarli JA. [Postviral fatigue syndrome]. Tidsskr Nor Laegeforen 1995; 115: 3017-3022.
- 11. Johnston SC, Staines DR, Marshall-Gradisnik SM. Epidemiological characteristics of chronic fatigue syndrome/myalgic encephalomyelitis in Australian patients. Clin Epidemiol 2016; 8: 97-107.
- Vink M, Vink-Niese F. Work Rehabilitation and Medical Retirement for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Patients. A Review and Appraisal of Diagnostic Strategies. Diagnostics. 2019; 9.
- Lawrie SM, MacHale SM, Cavanagh JTO, O'Carroll RE, Goodwin GM. The difference in patterns of motor and cognitive function in chronic fatigue syndrome and severe depressive illness. Psychological Med. 2000; 30: 433-442.
- Meeus M, Ickmans K, Struyf F, Kos D, Lambrecht L, Willekens B, et al. What is in a name? Comparing diagnostic criteria for chronic fatigue syndrome with or without fibromyalgia. Clin Rheumatol. 2016; 35: 191-203.
- Naess H, Sundal E, Myhr KM, Nyland HI. Postinfectious and chronic fatigue syndromes: clinical experience from a tertiary-referral centre in Norway. In Vivo. 2010; 24: 185-188.

- Mundt JC, Marks IM, Shear MK, Greist JH. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry. 2002; 180: 461-464.
- 17. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol. 1989; 46: 1121-1123.
- Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc. 1982; 14: 377-381.
- Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. J Psychosom Res. 1993; 37: 147-153.
- Ware NC, Kleinman A. Culture and somatic experience: the social course of illness in neurasthenia and chronic fatigue syndrome. Psychosom Med. 1992; 54: 546-560.
- 21. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983; 67: 361-370.
- Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res. 2002; 52: 69-77.
- Lipkin DP, Scriven AJ, Crake T, Poole-Wilson PA. Six minute walking test for assessing exercise capacity in chronic heart failure. Br Med J (Clin Res Ed). 1986; 292: 653-655.
- 24. Dodds RM, Syddall HE, Cooper R, Benzeval M, Deary IJ, Dennison EM, et al. Grip strength across the life course: normative data from twelve British studies. PLoS One. 2014; 9: e113637.
- 25. Gronwall DM. Paced auditory serial-addition task: a measure of recovery from concussion. Percept Mot Skills. 1977; 44: 367-373.
- Nisenbaum R, Jones JF, Unger ER, Reyes M, Reeves WC. A populationbased study of the clinical course of chronic fatigue syndrome. Health Qual Life Outcomes. 2003; 1: 49.
- 27. Cella M, Sharpe M, Chalder T. Measuring disability in patients with chronic fatigue syndrome: reliability and validity of the Work and Social Adjustment Scale. J Psychosom Res. 2011; 71: 124-128.
- Nyland M, Naess H, Birkeland JS, Nyland H. Longitudinal follow-up of employment status in patients with chronic fatigue syndrome after mononucleosis. BMJ Open. 2014; 4: e005798.
- 29. Stevelink SAM, Fear NT, Hotopf M, Chalder T. Factors associated with work status in chronic fatigue syndrome. Occup Med (Lond) 2019; 69: 453-458.
- 30. Castro-Marrero J, Faro M, Zaragoza MC, Aliste L, de Sevilla TF, Alegre J. Unemployment and work disability in individuals with chronic fatigue syndrome/myalgic encephalomyelitis: a community-based cross-sectional study from Spain. BMC Public Health. 2019; 19: 840.
- Leone SS, Huibers MJ, Kant I, Van Schayck CP, Bleijenberg G, Andre Knottnerus J. Long-term predictors of outcome in fatigued employees on sick leave: a 4-year follow-up study. Psychol Med. 2006; 36: 1293-1300.
- 32. Reeves WC, Wagner D, Nisenbaum R, Jones JF, Gurbaxani B, Solomon L, et al. Chronic fatigue syndrome--a clinically empirical approach to its definition and study. BMC Med. 2005; 3: 19.
- 33. Jason L, Brown M, Evans M, Anderson V, Lerch A, Brown A, et al. Measuring substantial reductions in functioning in patients with chronic fatigue syndrome. Disabil Rehabil. 2011; 33: 589-598.
- 34. Kingdon CC, Bowman EW, Curran H, Nacul L, Lacerda EM. Functional Status and Well-Being in People with Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome Compared with People with Multiple Sclerosis and Healthy Controls. Pharmacoecon Open. 2018; 2: 381-392.

J Neurol Disord Stroke 10(1): 1200 (2023)

- 35. Collin SM, Crawley E, May MT, Sterne JA, Hollingworth W, Database UCMNO. The impact of CFS/ME on employment and productivity in the UK: a cross-sectional study based on the CFS/ME national outcomes database. BMC Health Serv Res. 2011; 11: 217.
- 36. van Campen CMC, Rowe PC, Verheugt FWA, Visser FC. Physical activity measures in patients with myalgic encephalomyelitis/chronic fatigue syndrome: correlations between peak oxygen consumption, the physical functioning scale of the SF-36 questionnaire, and the number of steps from an activity meter. J Transl Med. 2020; 18.
- Barhorst EE, Andrae WE, Rayne TJ, Falvo MJ, Cook DB, Lindheimer JB. Elevated Perceived Exertion in People with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Fibromyalgia: A Meta-analysis. Med Sci Sports Exerc. 2020; 52: 2615-2627.
- Cook DB, VanRiper S, Dougherty RJ, Lindheimer JB, Falvo MJ, Chen Y, et al. Cardiopulmonary, metabolic, and perceptual responses during exercise in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): A Multi-site Clinical Assessment of ME/CFS (MCAM) substudy. PLoS One. 2022; 17: e0265315.
- Chaudhuri A, Behan PO. Fatigue in neurological disorders. Lancet. 2004; 363: 978-988.

- 40. Majer M, Welberg LA, Capuron L, Pagnoni G, Raison CL, Miller AH. IFN-alpha-induced motor slowing is associated with increased depression and fatigue in patients with chronic hepatitis C. Brain Behav Immun. 2008; 22: 870-880.
- 41. Koseoglu F, Inan L, Ozel S, Deviren SD, Karabiyikoglu G, Yorgancioglu R, et al. The effects of a pulmonary rehabilitation program on pulmonary function tests and exercise tolerance in patients with Parkinson's disease. Funct Neurol. 1997; 12: 319-325.
- 42. Miller AH, Jones JF, Drake DF, Tian H, Unger ER, Pagnoni G. Decreased basal ganglia activation in subjects with chronic fatigue syndrome: association with symptoms of fatigue. PLoS One. 2014; 9: e98156.
- 43. Maksoud R, du Preez S, Eaton-Fitch N, Thapaliya K, Barnden L, Cabanas H, et al. A systematic review of neurological impairments in myalgic encephalomyelitis/ chronic fatigue syndrome using neuroimaging techniques. PLoS One. 2020; 15: e0232475.
- 44. Li X, Julin P, Li TQ. Limbic Perfusion Is Reduced in Patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Tomography. 2021; 7: 675-687.