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Post-stroke fatigue: course and its relation to personal and stroke-related factors

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Abstract

Objectives To describe the course of fatigue during the first year post stroke and to determine the relation between fatigue at 1 year post stroke and personal characteristics, stroke characteristics, and post-stroke impairments.

Design Inception cohort.

Setting Rehabilitation center.

Participants Patients (N=167) with a first-ever supratentorial stroke admitted for inpatient rehabilitation.

Interventions Not applicable.

Main Outcome Measure The Fatigue Severity Scale measured the presence and impact of fatigue at admittance for inpatient rehabilitation, as well as at 6 months and 1 year post stroke.

Results At admission, 6 months and 1 year post stroke, fatigue was present in 51.5%, 64.1% and 69.5% of the patients respectively. Fatigue impact 1 year post stroke was greater among patients with more depressive symptoms, higher age, females and patients with a locus of control more directed to powerful others.

Conclusions Because fatigue impact is an increasing problem during the first year post stroke, it deserves more attention in clinical practice and scientific research. Locus of control and depression are related to post-stroke fatigue and might be important foci for future interventions.

Introduction

Fatigue is a common complaint in stroke patients[1,2] and can contribute to functional limitations[1,3], institutionalization and mortality[3]. Only a few articles have described the results of studies on self-reported fatigue in a population of stroke patients.
The percentage of stroke patients reporting fatigue problems ranges from 39 to 68%[1-4]. These estimates are based on studies with cross-sectional designs. There is little data available on the course of post-stroke fatigue. In cross-sectional studies[1,2,4], no association was found between the post-stroke time interval and fatigue. Longitudinal data have not yet been published.
Little evidence is available on factors associated with post-stroke fatigue. Depression is the only post-stroke impairment with an undeniable relation to post-stroke fatigue[5]. Nevertheless, it is important to realize that post-stroke fatigue can also develop independently of depression[1-4]. Other factors must therefore play a role in the development of post-stroke fatigue. Contradictory results have been found for the relation of personal factors, such as age and sex, to post-stroke fatigue[1,3,4]. Glader et al. found that patients who lived alone were more fatigued than patients who lived with a partner[3]. Moreover, they found that fatigue was more common in patients who were ADL dependent before their stroke[3], indicating that prestroke health condition and comorbidity could be of importance. Several authors[6,7] have suggested that fatigue could be the result of inadequate coping with the consequences of a stroke, and recommended to examine prestroke psychological factors in future studies. With respect to stroke-related variables, no relation has been found between post-stroke fatigue and type of stroke or hemisphere[1,3,4]. With respect to post-stroke impairments, cognitive disorders seem to play an important role in post-stroke fatigue on clinical grounds. Self-experienced neuropsychological problems showed some association to post-stroke fatigue in a study of van de Werf et al[2]. Sleeping problems have frequently been reported post stroke[8] and a relation with post-stroke fatigue seems likely.
We conclude that evidence on determinants of post-stroke fatigue is still limited. Results were not always unequivocal, and difficult to compare because of differences in the determinants studied and the post-stroke time interval between and within studies[1,2,4]. Like other authors[9,10] we conclude that more attention should be given to exploring the factors contributing to post-stroke fatigue, as this could lead to the development of treatment options.
Our study aimed: (1) to describe the course of fatigue during the first year post stroke and (2) to determine the relation between fatigue 1 year post stroke and personal characteristics, stroke characteristics, and post-stroke impairments.

Methods

Participants

Subjects were selected from stroke patients consecutively admitted to four Dutch rehabilitation centers according to the following inclusion criteria: (1) admittance for inpatient rehabilitation, (2) first-ever stroke, (3) unilateral supratentorial lesion, and (4) age above 18. Exclusion criteria were (1) disabling comorbidity (prestroke Barthel Index score below 18), (2) inability to speak Dutch and (3) aphasia. The medical ethical committees of University Medical Center Utrecht and the participating rehabilitation centers approved the study.

Procedure

At the start of inpatient rehabilitation, patients were invited by their rehabilitation physician to participate in the study. Informed consent was obtained from all patients. Personal and stroke characteristics were recorded at the first assessment, which took place as soon as possible after admission. Post-stroke impairments were assessed at 1 year post stroke. Fatigue was measured at the first assessment, and then 6 months and 1 year post stroke. All assessments were carried out by trained research assistants.

Measures

Fatigue. The Fatigue Severity Scale[4,11] (FSS) (Appendix) was used to evaluate post-stroke fatigue. It assesses the impact of fatigue on daily life. The FSS is a brief and simple instrument and therefore feasible for stroke patients. It consists of 9 statements about fatigue scored on a 7-point scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The total score is the mean of the nine item scores. The higher the FSS score, the more impact fatigue has on daily life. The FSS was originally designed to evaluate the impact of fatigue in patients with multiple sclerosis[11], but it has also been used in the stroke population[4]. In the current study the internal consistency of the FSS, measured using the Cronbach α, was .89. Fatigue was scored as present if the FSS score was above 4[12]. A score above 4 indicates a moderate to high impact of fatigue on daily living.

Personal characteristics. Data on age, sex, marital status and comorbidity were obtained from medical records. Locus of control is a psychological characteristic defined as "the degree to which individuals perceive events in their lives as being the consequence of their own actions, and thereby controllable (internal control), or as being unrelated to their own behavior, and therefore beyond personal control (external control)". The Multidimensional Health Locus of Control Scale[13] (MHLC) focuses on perceptions concerning the locus of control over health-related outcomes. The MHLC has three

subscales, each consisting of 6 items scored on a 6-point scale. The Internal subscale assesses the extent to which a person believes health is a function of his/her own behavior. The two other subscales assess the externally orientated beliefs. The Chance subscale assesses the degree to which a person believes his health is unpredictable, a matter of fate, luck or chance. The Powerful Others subscale assesses the extent to which a person believes that health is largely determined by the actions of physicians.
Stroke characteristics. Data on type of stroke and hemisphere were obtained from medical records. Type of stroke was classified as ischemic versus hemorrhagic (intracerebral hemorrhage and subarachnoid hemorrhage)
Post-stroke impairments. The Motricity Index[14,15] (MI) is a brief assessment method for motor impairment that scores the level of hemiparesis from 0 (paralysis) to 100 (normal strength). Cognitive functions were evaluated using two methods. First, the Mini Mental State Examination[16] (MMSE) is a widely used brief screening instrument. It tests orientation, memory, attention, calculation, language and construction functions. A subject who scored less than 24 on the MMSE was considered to have cognitive impairments. Second, the Trail Making Test part B[17] (TMT-B) indicates the level of executive functioning. It involves complex visual scanning, motor speed and attention. The participant has to connect 25 encircled numbers and letters, as quickly as possible, alternating between numbers and letters (1-a-2-b-3-c etc.). Both the time taken to complete the tests and the number of correct connections are recorded. We used the Center of Epidemiologic Studies Depression scale[18] (CES-D) to assess depression. It is a self-reporting questionnaire with 20 items and investigates mood over the past 7 days. A subject scoring above 16 was considered to be depressed[19]. One item of the Rehabilitation Activities Profile[20] was used to evaluate the presence of sleeping problems.

Statistical Analysis
We used descriptive statistics (means and standard deviations [SDs]; medians and interquartile ranges) to describe the baseline characteristics. A one-way repeated-measures analysis of variance was performed to compare FSS scores at admission, 6 months and 1 year post stroke. We used univariate analysis to examine the relations between the FSS scores and the independent variables (ie, personal characteristics, stroke characteristics and post-stroke impairments.) Variables with a significance level below 0.5 in the univariate analysis were selected for the multivariate regression analysis. Backward linear regression analysis was used until the remaining variables had a significance level below 0.1. This selection, with a more liberal significance level, increased the power for selection of true associated determinants and limited the bias in the regression coefficients[21].

Results

A total of 228 patients were included in the study. Eight patients died before 1-year follow-up, 15 had a recurrent stroke, 21 refused further participation and 17 patients had missing scores on 1 or more measures. Thus, data from 167 patients were available for analysis.

Patients were relatively young, and the majority lived with a partner (table 1). Infarctions were more frequent than hemorrhages. At 1 year post stroke 11.4% of the patients were considered cognitively impaired as indicated by the score on the MMSE. The CES-D score indicated a depression in 25.7% of patients.

Table 1. Descriptives of personal characteristics, stroke characteristics, and post-stroke impairments

Characteristic	Subjects (N=167)
Personal characteristics	
Mean age ± SD (y)	56.4 ± 11.4
Sex (% women)	41.3
Comorbidity (% present)	55.1
Marital status (% living with partner)	73.7
Mean MHLC ± SD	
Internal subscale	21.8 ± 5.0
Chance subscale	20.8 ± 5.4
Powerful others subscale	20.3 ± 5.4
Stroke characteristics	
Weeks post stroke (median, IQR)	6.0 (4.0)
Hemisphere (% right)	58.7
Type of stroke (% ischemic)	68.9
Impairments at 1 year post stroke	
Mean Motricity Index ± SD	70.7 ± 25.4
Mini Mental State Examination (median, IQR)	28.0 (3.0)
Trail Making Test part B	
Time (median, IQR) (s)	123.0 (87.0)
Number of correct connections (median, IQR)	24.0 (4.0)
Mean CES-D ± SD	10.7 ± 8.2
Sleeping problems (% present)	33.5

Abbreviations: SD, standard deviation; MHLC, Multidimensional Health Locus of Control scale; IQR, interquartile range; CES-D, Center of Epidemiologic Studies Depression scale

Course of post-stroke fatigue

Fatigue was present at admission, and at 6 months and 1 year post stroke in 51.5%, 64.1% and 69.5% of the patients respectively (table 2). In 37.7% of the patients, fatigue was present at all three assessments (fig 1); fatigue was only absent at all three assessments in 17.4% of the patients. A more variable course of fatigue during the first year post stroke was shown in the remaining 44.9% of the patients. Of the patients who reported fatigue at 1 year post stroke, 29.3% were also depressed. Table 2 presents means and SDs of FSS scores at the different post-stroke time intervals. There was a significant effect of time ($F_{2,165}$ = 10.95, P<.000.)

Table 2. Descriptive statistics for Fatigue Severity Scale (FSS) scores for admission to rehabilitation center, 6 months and 1 year post stroke (N=167)

Measurement period	% Fatigued	Mean FSS score ± SD
Admission	51.5	4.1 ± 1.3
6 months post stroke	64.1	4.5 ± 1.2
1 year post stroke	69.5	4.7 ± 1.3

Abbreviation: SD = standard deviation

Figure 1. Number (and proportion) of patients who reported fatigue at admission, 6 months and 1 year post stroke (N=167)

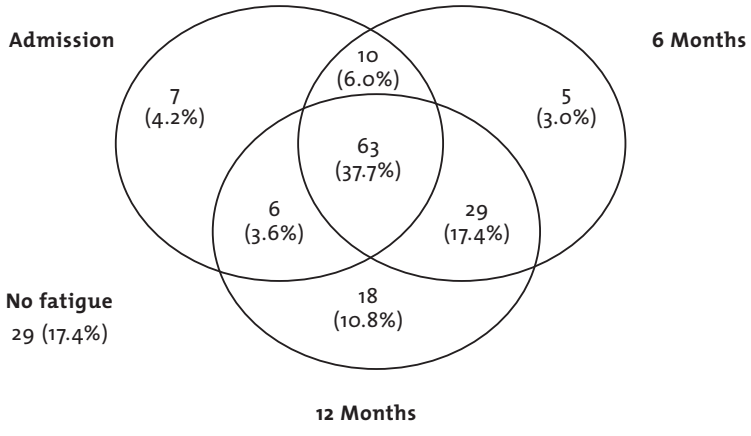

Table 3. Univariate and multivariate analyses between personal characteristics, stroke characteristics, and post-stroke impairments and the Fatigue Severity Score 1-year post stroke (N=167)

	Univariate analysis		Multivariate analysis	
Determinants	**Pearson r**	**P**	**ß**	**P**
Personal characteristics				
Age	.18	.02*†	.17	.02*
Sex (women)	.15	.06*†	.14	.06*
MHLC Internal subscale	-.07	.35†		NS
Chance subscale	.12	.12†		NS
Powerful Others subscale	.24	.002*†	.12	.09*
Comorbidity (present)	.04	.64		NA
Marital status (living with partner)	-.11	.18†		NS
Stroke characteristics				
Hemisphere (right)	.03	.73		NA
Type of stroke (ischemic)	.06	.41†		NS
Post-stroke impairments				
Motricity Index	-.05	.53		NA
Mini Mental State Examination	.03	.68		NA
TMT B Time	.03	.67		NA
Number of correct connections	-.03	.67		NA
CES-D	.39	<. 001*†	.34	<. 001*
Sleeping problems (present)	.12	.11†		NS

Abbreviations: MHLC = Multidimensional Health Locus of Control scale; TMT B = Trail Making Test Part B; CES-D = Center of Epidemiologic Studies Depression scale; NA = Not applicable; NS = Not significant

* P<0.1, † Determinants included in multivariate regression analysis

Regression analyses

Table 3 presents univariate correlation coefficients between FSS scores 1 year post stroke and the independent variables (ie, personal characteristics, stroke characteristics and post-stroke impairments.) The highest correlation coefficients were found for the CES-D, followed by the MHLC Powerful Others subscale and age. The variables included in the multivariate backward analysis were age, sex, all subscales of the MHLC, marital status, type of stroke, CES-D and sleeping problems. The multivariate model (see table 3)

included age, sex, MHLC Powerful Others subscale and the CES-D, and explained 21% of the total variance (adjusted R^2 = .20) of FSS scores 1 year post stroke.

Discussion

The percentage of patients reporting fatigue increased over time: its prevalence increased from half of the patients at admission to two-thirds of the patients at 1 year post stroke. Fatigue impact scores increased significantly during the first year post stroke. Fatigue impact at 1 year post stroke was greater among patients with more depressive symptoms, higher age, female sex and patients with a locus of control more directed to powerful others. The prevalence of post-stroke fatigue was comparable to the estimates in the literature which range from 39 to 68%[1-4]. The relatively low percentage of 39% was found in a study that excluded patients who reported that they always felt depressed[3]. The impact of fatigue increased during the first year post stroke. This might be because in the first phase after their stroke, patients have to deal with many consequences. They could experience fatigue as a "minor" problem compared with their other impairments and functional limitations. At 1 year post stroke when most of the recovery has taken place, fatigue could remain as an important problem with disabling consequences for every-day life. The impact of fatigue could become more relevant as patients try to resume their work and social activities, and the demands of daily life increase.

In patient education, which is a first and important step in the management of fatigue problems, health care professionals must inform patients about the likelihood of experiencing fatigue after suffering a stroke, even long after the event. This will enable patients and their families to anticipate future problems and allows them to gain recognition for this problem. This may diminish distress and misunderstanding when fatigue problems occur[22].

Depression was an important determinant of fatigue impact in our study and this agrees with earlier findings[1-3]. Nevertheless, depression and fatigue must be seen as distinct post-stroke consequences[1-5] because three quarters of the patients with moderate to high fatigue impact were not depressed. Other factors were also related to post-stroke fatigue. The demographic variables age and sex were significantly related to post-stroke fatigue as was found by Glader et al[3]. Moreover our study investigated the health locus of control beliefs. The Powerful Others subscale, one of the externally orientated subscales, was found to be related to post-stroke fatigue. A higher belief of control directed to physicians was associated with higher levels of fatigue impact. Some others found associations between locus of control and health outcome. A high internal

locus of control was associated with faster recovery from physical disability in stroke patients[23]. A low internal locus of control or high external locus of control was associated with more fatigue problems in patients with chronic fatigue syndrome[24] and with a chronic anxiety disorder[25]. A more favorable outcome was also shown to be related to high internal and low external control in other patient groups, i.e. patients with traumatic brain injury[26], spinal cord injury[27] and chronic low-back pain[28].

In clinical practice, stroke patients who have made a good physical recovery often have disabling fatigue problems. Patients with a lacunar infarction, who all had a maximum score on the Barthel Index, reported many emotional disturbances and fatigue problems[29]. Patients with good physical recovery seemed to be the most disabled by fatigue[6]. We did not find support for this idea, as motor impairment was not associated with fatigue impact. In our study population, patients with both good and poor motor recovery experienced fatigue problems.

Cognitive impairments were studied because on clinical grounds, it could be expected that these would be related to fatigue impact. Limited attentional capacity was found in patients with lacunar infarction who also reported fatigue[29]. As a result of cognitive problems many tasks cost more mental effort and it seems plausible that this would give rise to fatigue. However, we did not find a relation between fatigue impact and cognitive disorders. This might have been attributable to our assessment methods for cognitive impairments: the MMSE, which is only a global screening instrument, and one test for executive functioning (the TMT-B), were the instruments we used. To clarify the relation between cognitive impairments and post-stroke fatigue, additional research with more extensive neuropsychological assessments is needed.

The determinants depression, age, sex and locus of control explained one fifth of the variance of fatigue impact scores. Therefore, most fatigue impact remained unexplained. We expect that a number of factors we did not take into account might be associated with post-stroke fatigue. For example, the level of physical fitness[30,31] could be an important factor contributing to post-stroke fatigue. Fatigue could be the side effect of using certain medications[10]. Sleep apnea, which is commonly associated with stroke[8], might also be important[32]. Environmental factors and personal characteristics, such as coping strategies, might be relevant for post-stroke fatigue as well. Additional research is needed to clarify the impact of such factors on post-stroke fatigue.

We studied the factors potentially associated with post-stroke fatigue because exploring the underlying mechanism of post-stroke fatigue could support the development of intervention strategies. Depression is probably an important focus for interventions for post-stroke fatigue. It is known that depressive symptoms can improve with medication.

The preference is currently given to the selective serotonin reuptake inhibitors[5]. The question is whether administration of an antidepressant that alleviates the symptoms of depression could also reduce fatigue problems. There are indications that selective serotonin reuptake inhibitors sometimes reduce fatigue levels in patients with multiple sclerosis and cancer[10]. Additional research is needed to examine the effects of antidepressants on post-stroke fatigue in both depressed and non-depressed patients.
In addition to depression, locus of control could be an interesting focus for future interventions. Some consider locus of control to be a fairly stable psychological characteristic. However, it is far more likely that health locus of control beliefs can change over time. Changes in locus of control beliefs were found after dramatic illness-related experiences[33]. A multidisciplinary treatment program was shown to be effective in changing locus of control beliefs in chronic pain patients[34]. It would be interesting to investigate whether locus of control beliefs can be changed in stroke patients and whether these changes would have a positive effect on health outcome. Indications for this can be found in studies of other patient populations. In cancer patients, tailored counseling was shown to be effective with respect to locus of control and fatigue[35]. A mind-body wellness intervention for older adults with chronic illness led to a significant decrease in external locus of control and a decrease in sleeping problems, pain, anxiety and depression[36].

Conclusions

Fatigue is an important post-stroke impairment and its impact on every daily life increased during the first year post stroke. Depression, age, sex and health-related locus of control were related to post-stroke fatigue. Patient education on post-stroke fatigue should be routinely given to patients and their families. Depression and locus of control could become important foci for interventions. Future research should focus on a more detailed exploration of the determinants of post-stroke fatigue and on evaluating interventions for this.

Appendix

The Fatigue Severity Scale (FSS)

Statement
1. My motivation is lower when I am fatigued.
2. Exercise brings on my fatigue.
3. I am easily fatigued.
4. Fatigue interferes with my physical functioning.
5. Fatigue causes frequent problems for me.
6. My fatigue prevents sustained physical functioning.
7. Fatigue interferes with carrying out certain duties and responsibilities.
8. Fatigue is among my three most disabling symptoms.
9. Fatigue interferes with my work, family, or social life.

Patients are instructed to choose a number from 1 to 7 that indicates the degree of agreement with each statement where 1 indicates strongly disagree and 7 strongly agree.

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