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Factors associated with multidimensional aspect of post-stroke fatigue in acute stroke period

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ABSTRACT

Background: Post-stroke fatigue (PSF) is a frequent and distressing consequence of stroke, and can be both acute and long lasting. We aimed to investigate multidimensional aspects of acute PSF and to determine the clinical factors relevant to acute PSF.
Methods: We collected data of 101 patients admitted to the hospital for acute stroke. PSF was assessed using the Multidimensional Fatigue Inventory within 2 weeks of stroke. Measures included Mini-Mental State Examination, Hospital Anxiety and Depression Scale, and Functional Independence Measure. Stroke character, lesion location, and clinical variables that potentially influence PSF were also collected.
Results: The prevalence of pathological fatigue is 56.4% within 2 weeks of stroke. Binary logistic regression analysis revealed that anxiety was the only predictor for presence of PSF (OR = 1.32, 95% CI: 1.13–1.53, $P < 0.001$). Multivariate stepwise regression analysis showed anxiety, right lesion side, thalamus, and/or brainstem were independently associated with general fatigue, right lesion side, depression, diabetes mellitus, and anxiety with physical fatigue, depression with reduced activity, depression, and BMI with reduced motivation, depression, and diabetes mellitus with mental fatigue.
Conclusions: PSF was highly prevalent in the acute phase, and specific factors including lesion location (right side lesion, thalamic and brainstem lesion), anxiety, and depression were independently associated with multidimensional aspects of PSF. Further study is needed to elucidate how specific structural lesions and anxiety symptoms relate to the development of early fatigue following stroke.

1. Introduction

Post-stroke fatigue (PSF) is one of the most prevalent and distressing symptoms of stroke, with 23–75% prevalence (Ingles et al., 1999; Staub and Bogousslavsky, 2001; Choi-Kwon and Kim, 2011). It may substantially persist after stroke and negatively impact rehabilitation, functioning, and quality of life (van der Werf et al., 2001; Snaphaan et al., 2011; Radman et al., 2012). Fatigue is a complex, multifaceted, and entirely subjective construct. PSF differs from normal fatigue resulting from overexertion and is not relieved by rest (Chaudhuri and Behan, 2004; Wu et al., 2015). Despite its prevalence, little is known about the underlying mechanism and related factors. Many studies have demonstrated a robust relationship between PSF and post-stroke depression (van der Werf et al., 2001; Lerdal et al., 2011). However, PSF can also occur in the absence of depression (van der Werf et al., 2001), and that post-stroke depression and PSF are dissociated from each other. In addition to post-stroke depression, post-stroke anxiety is also important neuropsychiatric consequences of stroke, and has been recently investigated (Campbell Burton et al., 2013). The association between PSF and post-stroke anxiety has been controversial (Wu et al., 2014).

Considering PSF etiology, both the direct consequence of neurologic insult and psychosocial factors are thought to be involved. The stroke itself may be more influential in the early period, while psychosocial factors become more dominant in the chronic phase. A recent study (Lerdal and Gay, 2013) reported that acute phase fatigue is a significant predictor of later fatigue. However, studies investigating PSF in the acute phase, such as the first or second week following stroke, are scarce (Chaudhuri and

Abbreviations: PSF, post-stroke fatigue; MFI, multidimensional fatigue inventory; SIAS, stroke impairment assessment set; MMSE, mini-mental state examination; HADS, hospital anxiety and depression scale; HADS-A, hospital anxiety and depression scale anxiety subscale; HADS-D, hospital anxiety and depression scale depression subscale; FIM, functional independence measurement; BMI, body mass index.

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Behan, 2004; Schepers et al., 2006; Christensen et al., 2008). Because the acute phase may represent a critical period for functional recovery, it is important to clarify the prevalence, characteristics, and possible contributing factors of PSF.

This study thus investigated the prevalence and characteristics of PSF among stroke patients admitted on the acute ward using multidimensional fatigue inventory and determined the relationship between clinical variables including affective symptoms and PSF.

2. Methods

2.1. Subject

One hundred one patients with acute stroke participated in the study, recruited from 220 consecutive stroke patients admitted to the acute ward of Azumino Red Cross Hospital between October 2012 and November 2013. Inclusion criteria were ischemic or hemorrhagic stroke diagnosed by clinical and radiographic findings. Severe confusion, severe aphasia, or severe motor complications with immobility that could impede active rehabilitation were not excluded. A cross-sectional, descriptive analysis design was developed. All interviews and assessments were conducted within 2 weeks after stroke and were administered by the authors (H. M, T. F, A. H and A. S: certified occupational therapists trained for this study). The Ethical Review Board of Azumino Red Cross Hospital and the Ethical Committee of Shinshu University approved this study. Participating patients or their relatives gave informed consent.

2.2. Assessment of fatigue

To characterize PSF, we employed Multidimensional Fatigue Inventory (MFI) as the main outcome measure (Smets et al., 1995; Sugaya et al., 2005). The MFI is a self-report questionnaire that assesses the impact of fatigue and comprises five dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. General fatigue measures overall feelings of tiredness, physical fatigue measures physical sensations related to feelings of tiredness, reduced activity measures amounts of daily activities, reduced motivation measures motivation level in daily activities, and mental fatigue includes deficits in cognitive functioning. MFI scoring ranges for each factor are 4–20, with higher scores indicating stronger fatigue.

2.3. Clinical characteristics

The following clinical information were collected: body mass index, medical complications (hypertension, myocardial infarction, angina, atrial fibrillation, arrhythmia, cardiac failure, and diabetes mellitus), stroke event (first or recurrent), and ischemic or hemorrhagic stroke.

Lesion side (right or left) and location were recorded with MRI or CT upon admission. The following lesion locations were used: frontal, temporal, occipital, parietal, basal ganglia, internal capsule, thalamic, brainstem, and cerebellar, divided into four groups according to their lesion location: cortical, thalamic and brainstem, basal ganglia and internal capsule, or cerebellar (Radman et al., 2012). In cases with multiple lesions, all of them were counted.

Impairment associated with stroke was assessed using Stroke Impairment Assessment Set (SIAS) (Chino et al., 1994). SIAS consists of nine functions: motor paralysis, muscle tone, sensory disturbance, range of motion, pain, trunk function, visuospatial perception, aphasia, and non-paretic limb function. Activities in daily living (ADL) were assessed using Functional Independence Measure (FIM) (Granger et al., 1993). FIM consists of motor and cognitive FIM. Thirteen items comprise motor FIM and five items comprise cognitive FIM. The scoring ranges of FIM are 18–126, with higher scores indicating higher ADL level. SIAS and FIM were administered by the authors within one week at admission. Global cognition was assessed by Mini-Mental State Examination (MMSE) (Folstein et al., 1975). Depression and anxiety symptoms were assessed by Hospital Anxiety and Depression Scale (HADS) (Sagen et al., 2010). HADS is a self-report questionnaire for psychological distress, including the HADS Anxiety subscale (HADS-A) and the HADS Depression subscale (HADS-D), each of which have seven items with responses ranging from 0 to 3. Scoring ranges of each scale are 0–21; higher scores indicate increased symptoms. The MFI, MMSE and HADS were performed during the second week of stroke.

2.4. Statistical analysis

All statistical analyses were performed with SPSS for Windows 22.0 (IBM, Chicago, USA). Correlations between parameters were computed using Spearman's correlation analysis. Cross-sectional predictive factors for PSF were determined by binary logistic regression analyses. Independent variables included age, sex, stroke event, stroke type, lesion side, lesion locations, medical complications, body mass index, FIM, MMSE, HADS-D, and HADS-A. We also collected SIAS motor paralysis and pain scores, because both severity of paralysis and pain were known to be possibly associated with PFS (Naess et al., 2010; Lerdal et al., 2011). For binary logistic regression models, lesion locations were bisected into two categories (e.g. thalamus or brainstem/other) and repeatedly analyzed by each four group.

Predictive factors of MFI in each dimension were determined by multivariate stepwise regression analyses. Independent variables were the same as in binary logistic regression analyses. In all analyses, a p-value <0.05 was considered statistically significant. In regression models, the variance inflation factor was also estimated to detect multicollinearity among predictors.

3. Results

3.1. Demographic information

Socio-demographic characteristics, cognitive status, medical complications, and SIAS scores are presented in Table 1. The mean age of the subjects was 74.4 ± 11.6 years, and 33.7% were female. Records of onset indicated that 73.3% were admitted with their first episode of stroke, and 75.2% of subjects suffered ischemic stroke. Lesion distribution was 46.5% right, 39.6% left, and 3.0% bilateral. Lesion locations were 58 cortical, 9 thalamic, 26 basal ganglia and internal capsule, 11 cerebellum, and 9 brainstem. Twelve patients had combination lesions; 7 cortical + basal ganglia and internal capsule, 2 cortical + cerebellum, 2 thalamus + basal ganglia and internal capsule and 1 cerebellum + brainstem. Mean MMSE score was 22.2 ± 7.8. SIAS at the time of admission indicated that 24.8% had severe motor paralysis and 15.8% had pain.

3.2. Fatigue, mood, and functional assessments

The means, standard deviations, and prevalence of pathological fatigue on MFI are presented in Table 2. With reference to cut-off values used in the literatures, we employed a general fatigue score ≥ 12 as clinically significant for pathological fatigue (Choi-Kwon et al., 2005; Christensen et al., 2008). The prevalence of pathological fatigue was 56.4%. Spearman's correlation was calculated for each MFI dimension to examine intercorrelation. MFI general fatigue and physical fatigue were moderately