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Frequency, characterisation and therapies of fatigue after stroke

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Abstract Post-stroke objective or subjective fatigue occurs in around 50% of patients and is frequent (30%) even after minor strokes. It can last more than one year after the event, and is characterised by a different quality from usual fatigue and good response to rest. Associated risk factors include age, single patients, female, disability, depression, attentional impairment and sometimes posterior strokes, but also inactivity, overweight, alcohol and sleep apnoea syndrome. There are few therapy studies, but treatment may include low-intensity training, cognitive therapy, treatment of associated depression, wakefulness-promoting agents like modafinil, correction of risk factors and adaptation of activities.

Keywords Fatigue · Stroke · Cognitive · Modafinil · Depression

Definition of fatigue

Fatigue is a multidimensional motor-perceptive, emotional and cognitive experience. Objective fatigue corresponds “to an observable and measurable decrement in performance occurring during the repetition of a physical or mental task”, and subjective fatigue [1] is characterised by “a feeling of early exhaustion, weariness and aversion to effort”, and is nearer (although different) to neurasthenia (ICD 10) and chronic fatigue syndrome (CFS). “Primary fatigue syndrome” can also be distinguished from “secondary fatigue syndrome” [2] as it appears in the absence of depression, significant cognitive alteration or any other causes that could lead to fatigue, such as anti-hypertensives, neuroleptics, antidepressants, decreased ferritin level (<50 mg/l), lifestyle, obesity, addictions, infections such as EBV or HIV, and depression (25%–30% of fatigue in primary care). Post-stroke fatigue (PSF) is generally thought to be a primary subjective fatigue but some participating causes are often present. Cardiac disease, sleep apnoea syndrome and vitamin D deficiency also increase fatigue.

Frequency of post-stroke fatigue

Fatigue frequency in post-stroke survivors ranges from 29% to 68% (20% in the control groups) [3–5] and seems to be correlated to functional disability and cognitive impairment. The large variability across studies is probably due to the inclusion criteria and the fatigue scales used. Nevertheless, this symptom is also frequent (29%) after minor strokes [6]. Particularly mental fatigue is also observed even in the case of a single or small infarct.

Concerning time dynamics, PSF seems stable across time. A longitudinal study showed some increased percent-

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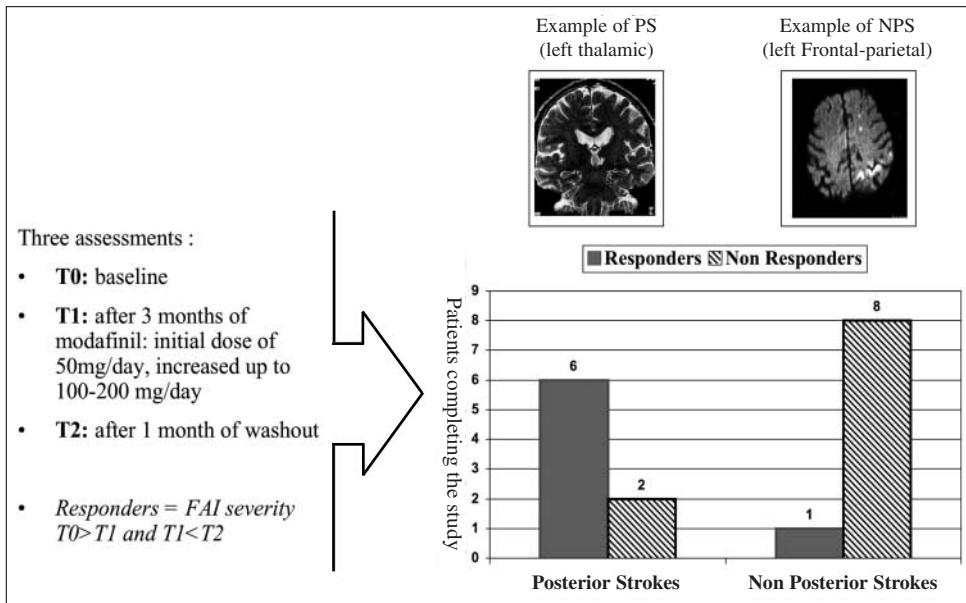


Fig. 1 Three-months pilot study showing the differential effect of modafinil on fatigue in patients with posterior (brainstem or thalamic) strokes and non-posterior stroke ($c2, p=0.01$). Responder's profile was defined according to the FAI (Fatigue Assessment Inventory, Schwartz et al., 1993, [11]) scores. Sleepiness was not affected by therapy [12]

ages of self-rated fatigue between admission (51.5%), 6 months (64.1%) and one-year (69.5%) follow-ups [5], suggesting that fatigue may appear as activity increases. Two thirds of tired patients at 6 months will continue to complain from fatigue after 1 year.

Characterisation of post-stroke fatigue

PSF is qualitatively different from the fatigue experienced by patients before stroke. It is exacerbated by stress and physical exercise, and responds well to rest, sleep and low temperature (the last points being rarely described in CFS or in depression). The severity scores are generally lower in stroke patients than in matched multiple sclerosis (MS) patients; moreover, PSF seems slightly more “physical” and less “psychic” than MS-related fatigue [6]. PSF seems to be favoured by disability, cognitive dysfunction, biographical factors (single before stroke, female gender, higher age) and psychic post-stroke factors (depression, anxiety, perception by the patient of having little control over his health [6]). PSF can also be weakly influenced by lesion site, particularly by posterior strokes [7]. Clinical cohort analysis suggests that there are in fact different types of fatigue in stroke: a “task-specific” fatigue linked to cognitive or physical sequels (such as residual aphasia, when mental fatigue appears after speaking for a certain length of time) and a more “primary” PSF linked to subtle attention difficulties after vertebro-basilar strokes impairing the cortex activating system [1].

Since fatigue can be a key feature of depression, overlap between both syndromes is unquestionable. In our cohort, the presence of significant fatigue scores and depression criteria 6 months after stroke were predictors of depression at 12 months. Nevertheless, fatigue can also occur in the absence

of depression. For example, only 38% of patients with severe fatigue after stroke met the criteria for depression [8].

Therapies of post-stroke fatigue

There are very few controlled studies on therapy of PSF. Fluoxetine 20 mg/day does not improve PSF but it decreases depressive symptoms [9]. Improvement of sleep disordered breathing (with a CPAP) does not seem to be effective in PSF unless the patients have a symptomatic sleep apnoea syndrome [10]. Recently, we conducted a pilot study (40 patients with chronic stroke and MS) with a wakefulness-promoting agent (modafinil). Side effects led to a drop-out of 25% of patients. In the remaining patients, preliminary results show that modafinil decreased fatigue severity scores in MS and in brain-stem or thalamic strokes, but not in cortical stroke infarcts (Fig. 1). Such findings tend to confirm that PSF characteristics may vary depending on aetiology and site of lesions.

Studies on fatigue in cancer and CFS patients may also provide some cues for PSF therapy. In 2006, Gliessen and collaborators showed that cognitive behavioural therapy (based on the model of precipitating and perpetuating factors of post-cancer fatigue) has long-lasting positive effects on severely fatigued disease-free cancer patients [13]. In CFS patients, regular exercise training for 6 weeks (particularly low-intensity exercises) decreased feelings of fatigue, independently from changes in aerobic muscular parameters [14]. In conclusion, there seem to be pharmacological and non-pharmacological cues to alleviate fatigue symptoms, but one of the most important is the necessity to adapt patients' activities.

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Conflict of Interest statement The Authors declare that they have no conflict of interest related to the publication of this manuscript

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