Poststroke Fatigue
A Hint, But No Definite Word on Therapy Yet

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The diagnosis of chronic fatigue is largely based on exclusion of other conditions, shows frequent comorbidities, has no known neuropathological basis, and no confirmed single etiology, pathogenesis or established treatment. It is not easily accepted by patients and caregivers alike, and probably the most effective remedy up to now has been to find patients with similar conditions to share experiences. Chronic fatigue is an accepted medical term, especially when presenting in chronic multiple sclerosis or other mostly postviral conditions. In these patients, cognitive behavior therapy and graded exercise therapy have recently been shown to moderately improve outcome.1

In stroke patients, however, fatigue has not been clearly defined, and interventions tested in these populations have only been based on very small numbers. In one review, poststroke fatigue has been described as “a feeling of early exhaustion developing during mental activity with weariness, lack of energy, and aversion to effort.”2 However, the most striking feature of chronic fatigue is that it is always present. It does not go away when resting and impedes all domains of daily life and can persist for years. It can coexist with a number of other chronic poststroke conditions including depression and dementia. None of the scales used for measuring fatigue has been specifically developed for poststroke conditions; the cutoffs used for making the diagnosis with these scales also vary between studies, and no consistent correlation with stroke characteristics has been found.3 In addition, there is a notable prevalence of fatigue in the general population up to 2.6%.1

Is it possible to test an intervention in a poststroke condition that is so ill-defined? Zedlitz et al.,4 from Nijmegen, The Netherlands, do think so. In this issue of Stroke, they report the results of a multicenter trial performed in 83 stroke patients that were randomized into two treatment groups. Both groups received cognitive therapy (CO), which consisted of weekly 2-hour sessions “including elements of cognitive behavioral therapy and teaching of compensation strategies aimed at pacing and relaxation,” and only 1 of the 2 groups additionally underwent graded activity training (GRAT), which consisted of “of walking on a treadmill, strength training, and physical fitness home work assignments.” Latter intervention was applied for 2 hours twice weekly for the duration of the 12-week study.

Inclusion was based on self-reported severe fatigue corresponding to 40 or more points on the subscale Fatigue of the Checklist Individual Strength. Among a number of other conditions, depression was an exclusion criterion. After 12 weeks of interventions, the subscale fatigue showed improvement for both groups, with more significant changes in the combined treatment group receiving both CO and GRAT. The domains pain and anxiety (which are not considered part of the fatigue syndrome) were not influenced.

Considering the suffering of such patients, the results are certainly worth reporting. It is unclear, however, to which extent these results will have an impact on routine therapy. First, the trial results reported here are not easily replicated. Many patients had their stroke several years back, some of them even more than 10 years ago. There are no data on other therapies that had been tested in these patients. The data on stroke are scarce and of questionable relevance for either the inclusion or the results. There is a large heterogeneity of stroke etiologies, although a subanalysis excluding subarachnoid hemorrhage cases was performed. Additionally, the absence of a control group and the termination of the study after 12 weeks do not allow firm conclusions about effect size and sustainability of these effects.

How can this unclear situation be clarified? Inevitably, prospective epidemiological studies are needed in the normal population as well as in well-described stroke cohorts. Only then will we know how frequent this condition is and to what extent it is based on other factors or comorbidities. This will allow for more homogenous study protocols to be developed.

To broaden the knowledge and base for future clinical trials, a closer definition of the poststroke fatigue syndrome should be undertaken. Possibly, there is more than 1 complaint under this umbrella. One could be the loss of “sense of effort” that had been puzzling the neuroanatomist Alf Brodal when he had suffered a stroke: “It was a striking and repeatedly made observation that the force needed to make a severely paretic muscle contract is considerable. Subjectively, this is experienced as kind of mental force, a power of will. In the case of a muscle just capable of being actively moved, the mental effort needed was very great. Subjectively, this it felt as if there was a resistance which could be overcome by very strong voluntary innervation. This force of innervation is obviously some kind of mental energy, which cannot be quantified or defined more closely.”5
Another issue is a need for a neuropathological hypothesis, which should be investigated in stroke patients. Only 1 study has found a correlation with posterior circulation strokes.\(^6\) We therefore need well-designed, controlled studies confirming the efficacy of cognitive and behavioral interventions in patients with a chronic fatigue condition that has a plausible correlate with the initial stroke.

**Disclosures**

None.

**References**


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