## NO TO POST-STROKE FATIGUE THERAPY TRIALS YET

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Chronic fatigue is a difficult diagnosis and is largely based on exclusion of other conditions. It shows frequent comorbidities, no known neuropathological basis, and no confirmed single etiology, pathogenesis, or established treatment.

Chronic fatigue is an accepted medical term esp when presenting in chronic multiple sclerosis patients. Recently cognitive behaviour therapy and graded exercise therapy has been shown to moderately improve outcome in such patients (White 2011).

In contrast, for stroke patients, fatigue has not been clearly defined. One description is "a feeling of early exhaustion developing during mental activity with weariness, lack of energy, and aversion to effort" (Staub and Bogousslavsky 2001). 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 post-stroke conditions and the cut-offs used for making the diagnosis with these scales also vary between studies. Thus, no robust endpoints can be defined for such studies.

Prospective epidemiological studies are needed in the normal population as well as in well-described stroke cohorts. Only then will we know the true frequency of this condition and to what extent it is based on other factors or comorbidities. This will allow for more homogenous study protocols to be developed.

In order to broaden the knowledge and base for future clinical trials, a closer definition of the post-stroke fatigue syndrome should be undertaken. Possibly, there is more than one complaint under this umbrella. One could be the loss of 'sense of effort' that had been puzzling a number of prominent stroke victims such as the neuroanatomist Alf Brodal or the physicist Ernst Mach when they reported their subjective feelings when they had suffered a stroke.

Another issue is a need for a neuropathological hypothesis which has not been investigated in stroke. Only one study has found a correlation with posterior circulation strokes. This might be in line with the finding of Constantin von Economo, a Viennese Neurologist and Neuropathologist who describes the essence of postviral fatigue in his famous book on the late observations of the Encephalitis lethargica cases he first described: According to him, it is "...essentially a disturbance of will, a psychic disturbance ...purely based on an organic lesion, probably involving the basal gray matter of the brainstem." We do not know how and whether this hypothesis which he formulated for postencephalitic cases applies to post-stroke conditions.