Fatigue, physical activity, and function in PD

Garber and Friedman examined the relationships between fatigue, physical activity, and physical function in patients with PD. Patients with more severe fatigue were more sedentary and had poorer physical function and functional capacity compared to patients with less fatigue.

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Are studies of fatigue worth the effort?

Commentary by Steven R. Schwid, MD

Fatigue is formally defined as a reduced capacity for work following a period of mental or physical activity. In casual use, however, patients and practitioners often use this word less precisely, making it a difficult symptom to address. Fatigue may be particularly complex in patients with neurologic disorders, who experience a number of potentially confounding symptoms. For example, when patients with multiple sclerosis state that fatigue is their most common and disabling symptom,¹ it is not clear that they are all complaining of the same thing or that it is distinct from weakness, spasticity, incoordination, cognitive impairment, sleepiness, or depression. Although fatigue has traditionally been studied with self-report questionnaires, these all have inherent limitations. First, questionnaires ask patients to rate fatigue without rigorously defining it, resulting in potential confounds as described above. Second, questionnaires are entirely subjective. Even if patients are appropriately rating the intended symptom, it is not clear that they can accurately rate fatigue any better than they could rate motor impairment, cognitive impairment, or other facets of their disease. For this reason, self-report scales may be particularly prone to placebo effects as wishful thinking fills in gaps in meaningful self-assessment. Third, questionnaires require retrospective assessments of fatigue over relatively long periods. This makes self-report scales subject to recall bias.² Reliance on self-report questionnaires as the primary method for determining the presence and severity of fatigue may be one of

A hypothetical force-vs-time curve generated during an isometric contraction sustained for 30 seconds. The shaded region reflects motor fatigue occurring after developing a maximal voluntary isometric contraction (MVIC) (Adapted from ⁶).

the biggest factors impeding studies of its characteristics, mechanisms, and therapeutics.

The main alternatives to self-report questionnaires are to assess worsening function directly during sustained activity³ or to quantify differences in function before and after a fatiguing task.⁴ Methods to do so have not yet been adequately standardized and may require specialized techniques and equipment to provide reproducible results, making these approaches difficult to apply in clinical settings. Furthermore, the amount of fatigue quantified with these techniques does not correlate well with patients' responses on self-report measures.⁵ The lack of association may be due to limitations of the assessments themselves or it may indicate that the declines in functional ability physiologists consider the hallmark of fatigue have a different mechanism than the lassi-

tude that dominates patient complaints. These limitations indicate that we have not yet identified a satisfactory substitute for self-report assessments of fatigue, so we must learn to interpret these assessments as thoughtfully as possible. The Garber and Friedman study⁶ demonstrates that PD patients who have high levels of self-reported fatigue are more sedentary and have worse physical function and functional capacity than patients with lesser complaints. Although these results may not establish that fatigue is a unique part of the PD experience, they do indicate that fatigue is a symptom associated with substantial morbidity. For that reason alone, we cannot afford to ignore it.

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DHEA Group (shown as a solid line) vs placebo (dotted line).

“Future investigation of DHEA will attract a more representative AD sample . . . if cholinesterase inhibitors are allowed.”

Dehydroepiandrosterone in AD

Wolkowitz et al. treated 58 AD patients with dehydroepiandrosterone (DHEA) (100 mg per day) or placebo for 6 months. DHEA was well tolerated but did not significantly improve cognition or global ratings. A transient but nonsignificant effect on cognition was seen at month 3.

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The accompanying editorial by Knopman and Henderson discuss the rationale and limitations of this trial—the first randomized, double blind trial of DHEA in AD. The trial excluded patients who were receiving anticholinesterase inhibitors, which may have both hindered recruitment and contributed to the high rate of attrition in the study.

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APOE-ε4 in longitudinal cognitive decline

In a longitudinal prospective study of high-functioning elderly, Bretsky et al. report that the APOE-ε4 allele was associated with significant decline in function across a spectrum of cognitive domains, with strongest effects at the 7-year vs 2.5-year follow-up.

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Are ALS patients cognitively normal?

Lomen-Hoerth et al. administered word generation tests to 100 consecutive ALS patients not known to have cognitive abnormalities and found 1/3 of patients tested abnormally. Cognitive abnormalities suggestive of frontotemporal dementia are often associated with ALS.

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Scalp DC-EEG: noninvasive detection of seizures by DC-shifts

Vanhatalo et al. used noninvasive DC-EEG recordings from the scalp to show that slow DC-shifts, lasting many seconds, are consistently detected during spontaneous temporal lobe seizures. These DC-shifts may demonstrate the hemisphere (side) of seizure origin in cases where conventional clinical EEG is equivocal.

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The accompanying editorial by Lagerlund and Gross notes that Vanhatalo et al. rely upon a phenomenon well-known for over 40 years. Since DC recording is relatively low-cost and easy to perform it deserves study as a new way to localize medication-resistant seizures.

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Factor VIII as a risk factor for cerebral venous thrombosis

Performing comprehensive screening for a hypercoagulable state in 16 consecutive cases of cerebral venous thrombosis (CVT), Cakmak et al. found eight patients with persistently elevated plasma factor VIII level, which is also a recognized risk factor for deep-vein thrombosis.

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Neurofibromatosis 1: natural history of MRI lesions and cognitive abilities

In an 8-year prospective study of 32 children with NF1, Hyman et al. found that despite the disappearance of MRI T2-hyperintensities cognitive ability did not improve. MRI T2-lesions can be used as biological markers of cognitive dysfunction only in the under-18 age group.

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Clinical features of headache at high altitude

The Silber et al. prospective study examined risk factors for and characteristics of high altitude headaches. Headaches were more common in younger subjects and more severe in women and those who reported headaches in daily life. There was a wide spectrum of headaches, some suggesting intracranial hypertension. They propose diagnostic criteria for altitude headache.

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DWI-localization of stroke with cortical dysarthria

Kim et al. described six patients who had isolated dysarthria due to small cortical strokes (five infarcts, one hemorrhage) located lateral to the precentral knob. Diffusion-weighted MRI identified the infarcts.

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Cerebellar ataxia and coenzyme Q10 deficiency

Lamperti et al. found that 13 of 135 patients with genetically undefined cerebellar ataxia and atrophy had markedly decreased coenzyme Q10 (CoQ10) concentration in muscle. A presumably primary ataxic presentation of CoQ10 deficiency is suggested and may be responsive to CoQ10 supplementation.

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