

Correspondence

To the Editor:

FATIGUE IN MULTIPLE SCLEROSIS

The role of the cognitive dimension of fatigue in multiple sclerosis (MS)¹ is supported by working memory impairment in persons with chronic progressive MS² and by the contribution of articulatory rehearsal to working memory.³ These findings prompt the assessment of fatigue in the MS patient¹ by analyzing speech pauses on a time-base.⁴

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Reply from the author:

Dr. Friedman has made an important comment concerning the relationship between the perceived impact of fatigue on cognitive functioning and working memory impairment in MS patients. Recent studies¹⁻³ do suggest that MS patients have reduced working memory capacity, with particular difficulties in articulatory rehearsal. However, it is unclear from Dr. Friedman's comment whether he is implying that the patients' perception of the impact of fatigue on cognitive activities is wholly accounted for by a working memory impairment, i.e., "the role of the cognitive dimension of fatigue in multiple sclerosis (MS) is supported by working memory impairment. ..." While it is true that the effects of a working memory impairment may overlap considerably with those of fatigue (e.g., perceived difficulties with concentration, organization of thoughts, forgetfulness, slowed thinking, and making decisions), we suggest that the effects of fatigue on cognition and working memory impairment are separable but may co-occur in the same individual. Fatigue may exacerbate the effects of an impairment in working memory but it is not the impairment. Little is known about the neuropathologic basis of either fatigue or working memory impairment in MS but accumulating research on prefrontal cortex⁴ suggests that the cognitive deficits observed in MS patients may occur as a consequence of disruption of white matter fiber tracts connecting periventricular areas to dorsolateral areas of frontal cortex. The experience of fatigue, on the other hand, may reflect disruption of white matter fiber projections to basomedial prefrontal cortex which is thought to be important for motivation and arousal. Fatigue may also occur as a consequence of peripheral neuropathy, e.g., impaired neural transmission. Research attempting to disentangle the two may be illuminating and is certainly a worthwhile pursuit.

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To the Editor:

NEUROBIOLOGY OF WORKING MEMORY

Turnbull et al.¹ report that hippocampal stimulation of fornical-lesioned rats improves working memory. On selected test days, lesioned animals received a stimulation train through the electrode in the dentate gyrus and the perforate path of the right hemisphere. The neurobiology is suggested by operant conditioning of hippocampal CA1 pyramidal cell bursting at different concentrations of dopamine lateralized to the right hemisphere, showing a sharp peak at 1 mM and falling off abruptly when this optimal concentration of dopamine was either halved or doubled.² This hypothesis is supported by profound effects on neuronal integration due to either an increase or a decrease in monoaminergic inputs³ and by dopamine release in passive avoidance impairment after ischemia. It is also supported by the contribution of articulatory rehearsal to short-term memory² guiding the temporal organization of behavior,³ by optimal response organization at intermediate dopamine tone in a medial-frontal-striatal activation system, by the concept of cellular tone, and by a neurochemical model underlying differences in reaction times between introverts and extroverts. The fact that delay-dependent speeding of reaction time, indicating motor readiness, is abolished by depletion of dopamine, prompts the evaluation of the neuromodulation⁴ of cortical silent periods⁵ in the detection of a missing temporal or "clocking cue" by monitoring temporal features of expressive activity. This method is supported by the construct validity of response latencies, easily obtainable through microcomputer testing.⁴ This strategy may be implemented by monitoring speech hesitation and switching pauses in emotionally charged dialogues, reflecting properties of neuronal activity and firing.²

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