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BOOK REVIEW

Fatigue as a Window to the Brain

Edited by John DeLuca

The MIT Press, 2005

This edited volume, organized by Professor John DeLuca, at the College of Medicine of New Jersey, is ahead of the curve in at least two ways: medical and intellectual. Regarding medicine, it comprises a welcome addition to the neuroscience of a set of syndromes that are emerging from vagueness toward clear definition. Only recently has the CDC recognized fatigue syndromes as legitimate. Scientific work on these syndromes has been underfunded. Useful chapters in this volume offer good definitions of chronic fatigue states (CFS) and good approaches to their measurement. Among possible mechanisms, abnormalities in the neuroendocrine axis from the hypothalamus to the pituitary to the adrenal gland clearly dominate the thinking of some researchers. The book also reviews credible brain imaging evidence of differential activation in CFS patients, and summarizes certain sleep disorders that are clearly associated with CFS.

The relation of depression to fatigue is complex. Simply calling CFS patients "depressed" would not fit the evidence. Furthermore, when the two conditions are indeed correlated, would the depression be a cause or an effect?

Important information in this book deals with contributions to CFS from abnormalities of immune systems. Altered levels of cytokines such as interleukin-6 have been reported. This review brings into play a new field pioneered by Ader at the University of Rochester and currently represented by labs such as that of Sternberg (at NIMH), Bullock (at Rockefeller), and Maier (at Colorado). Proinflammatory cytokines certainly cause behavioral changes, with an emphasis on fatigue. Their effects in CNS deserve more attention.

The book would have been strengthened by more extensive consideration of other syndromes such as fibromyalgia syndrome (FMS) and the Gulf War syndrome. Furthermore, the prominent sex differences in these syndromes are underrepresented. CFS is found more often in women, and Gulf War in men. A more systematic evaluation of the balance of neural, hormonal, and immunological causes of CFS would have been appreciated.

The book is also ahead of the curve, intellectually. Twentieth century neuroscience could be termed "the hunt for specificity." It featured questions of the form: "Why does this particular stimulus (and no other stimulus) evoke that particular response (and no other response)?" In contrast, 21st century neuroscience is likely to emphasize changes of state in the CNS—state changes that help to explain entire constellations of stimulus–response causal relationships. This reviewer has argued that the state of elementary arousal of the mammalian CNS is a function of the most fundamental force in the CNS, generalized arousal, supplemented by a host of specific arousal states. Such a concept subsumes sleep/wake neurophysiology and circadian rhythms as well as fatigue states. Therefore, studies of fatigue states will provide some of the important clinical applications dependent on mechanisms of CNS arousal. However, in both medical and intellectual terms, work on CNS arousal and fatigue is in its early days.

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