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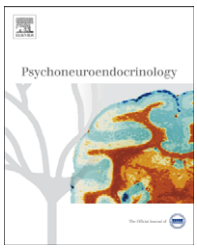

REVIEW

An extended concept of altered self: Chronic fatigue and post-infection syndromes ☆

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Summary
Sickness behavior in active infectious diseases is defined here as the responses to cytokines and other mediators of inflammation as well as the adaptability of a pre-existing integrated immunological, psychological, neurological, and philosophical self. These complex behaviors are biologically advantageous to the afflicted individual, but they also impact surrounding individuals. If chronic conditions, such as chronic fatigue syndrome or post-infection fatigue, exhibiting these behaviors follow infection in the absence of ongoing changes in immunological self associated with an active infection or subsequent injury, they are currently considered illness states rather than true diseases. Self-referential recognition (interoception) of bodily processes by the brain and subsequent unconscious and conscious adaptive responses arising in the brain, i.e., in the endocrine system and immune systems, which are initiated during the infection and would normally lead to positive maintenance, may become maladaptive and lead to an "extended altered self state." Exploratory measurements of such alterations using a "top-down" approach such as monitoring responses to appropriate challenges can be obtained using functional brain imaging techniques. Once identified, processes remediable to biological/pharmacologic and/or psychological intervention can be targeted in directed trials.
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1. Introduction

This hypothesis-generating essay addresses the questions: (1) Why do people feel sick during an infection? (2) Are there long term consequences of acute infection-related disease responses that require an expanded approach in considering pathophysiology of chronic illnesses? The essay addresses these questions based on the model of "altered self" as established in immune responses to infection, but extends it into a brain function model applicable to chronic illness syndromes in general and proposes testable hypotheses.

Acute infectious diseases are defined by the type of infectious agent, its target organs, and by the cellular and humoral immune responses that collectively lead to specific tissue injury and clinical consequences, such as cough in pneumonias and generalized signs such as fever. The sickness behavior complex accompanying these diseases, experienced as fatigue, malaise, irritability, disturbed sleep, and inability to concentrate, also results from activation of the immune response network (Hart, 1988; Dantzer, 2001; Vollmer-Conna et al., 2004). The individual's life history, knowledge, and perception of illness contribute to sickness behavior (Imboden et al., 1959). Dantzer (2004) suggested a motivational component to its purposes, implying conscious or unconscious recognition of a baseline state from which referential actions are elicited.

2. Disease, illness, and sickness

Because of the divergent disciplines called upon in this essay, a discussion of the meanings of the words disease, illness, and sickness illness is necessary. The issue is compounded by the attribution of an altered state of health to all three terms. Comparison of the origins of the words "ill," "sick," "illness," "sickness," and "disease" shows their interdependency (Oxford English Dictionary, 2007). Several authors, for example, Twaddle and Nordenfelt (1994) and Hofmann (2002) attribute disease to "an organic phenomenon (physiologic event) independent of subjective experience and social convention." Whereas illness is considered a subjective undesirable state of health or a feeling state referred to by expression of symptoms. Although only "somatic" conditions are included in the Hofmann, Twaddle, and Nordenfelt discourses, psychiatric conditions such as depression would qualify for the illness label based on its definitional requirements, but as the biology of depression becomes clear, it will likely be considered a disease. In order to fulfill Twaddle's definition of sickness (Twaddle and Nordenfelt, 1994), a societal recognition of a disease or illness that frees the individual from ordinary duties of work and makes him or her eligible for economic assistance is required. Hofmann (2002) suggests that the three constructs may occur in varying combinations. The first is illness and sickness in the absence of disease, such as low back pain; a construct on the surface that is germane to this essay. He also suggests that disease and illness may coexist in the absence of sickness, such as in the common cold or aging, because society does not accept a sick role for these individuals (perhaps it should). The third situation is disease and sickness in the absence of illness leading to physician intervention, such as in pre-clinical diabetes mellitus. Eisenberg (1977), writing from a medical rather than a sociological point of view, shares the concepts of a biological origin for disease and a subjective origin for illness.

3. Sickness behavior

The term "sickness behavior" appears in two divergent contexts in the 20th century. It appears to have been introduced in evaluation of the sick role or illness behavior associated with people who were considered to be sick in a sociological construct by Parsons (1958). The concept was expanded to include the term sickness behavior by Twaddle (1979) who, as seen above, previously addressed the triad of disease, illness, and sickness. More recently, descriptions of the specific behavior of diseased animals and humans as it relates to the consequences of infections and host responses to endogenously produced cytokines (Hart, 1988; Dantzer et al., 1998) also used the term sickness behavior (see Section 8). In infectious diseases, sickness behavior constitutes part of the disease process; it includes biological responses that are processed and perceived in turn as subjective symptoms. In modern immune concepts of disease, Twaddle's concept of progression of disease to illness to sickness (Twaddle and Nordenfelt, 1994) could now be considered one of simultaneous events. In a classical medical model, tissue responses brought about by the actions of the infecting agent, the host's responses to them, and the symptoms produced during these processes

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