HEALTH PSYCHOLOGY, 1989, 8(6), 747-752

Issues in Psychoneuroimmunology Research

Jeffrey Ratliff-Crain
University of Minnesota

Lydia Temoshok
Walter Reed Army Medical Center

Janice K. Kiecolt-Glaser
Ohio State University School of Medicine

Lawrence Tamarkin
National Institute of Mental Health

Psychoneuroimmunology describes a new multidisciplinary area of research that has as its focus the dynamic interactions among behavioral factors, the central nervous system (CNS) and the endocrine and immune systems. The long-range goal of this research is to provide a comprehensive understanding of the role that behavior might play in promoting health and provoking illness. In identifying research questions in psychoneuroimmunology, this task force noted that the problems present in this area of research, such as the choice of measures and subject populations to study, although similar to those in other areas, can be more complex and limiting due to the multidisciplinary nature of the work. The suggestions offered here are neither comprehensive nor exhaustive but are illustrative of issues that the task force members felt needed to be addressed for the field to progress.

THE IMMUNE SYSTEM

CNS and Immune System Communication

How the CNS and the immune system interact is still a major question that needs to be answered. Although there is relatively new evidence showing bidirectional communication (e.g., Grota, Ader, & Cohen, 1987), how that

Requests for reprints should be sent to Jeffrey Ratliff-Crain, Social Sciences Division, University of Minnesota, Morris, MN 56267.

communication is achieved is unclear; this is an example of basic information that is not available at this time. Assumptions can be made by observing changes in health and behavior and by making various measurements that reflect aspects of immunologic function. However, continued efforts to pinpoint the mechanisms underlying CNS and immune system interactions are needed to go beyond the state of hypotheses and assumptions.

Understanding cellular communication is an example of a challenge that will require close cooperation among psychologists, endocrinologists, and immunologists. Current knowledge in immunology points toward myriad peptides and proteins forming a communication network among cells of the immune system. Immunologists traditionally view these molecules as autocrines or paracrines whose role is restricted solely to the immune system. New data have indicated that molecular communication can occur between the immune system, the endocrine system, and the CNS and that these molecules can affect cells outside the immune system (Berkenbosch, van Oers, del Rey, Tilders, & Besedovsky, 1987; Bernton, Beach, Holaday, Smallridge, & Fein, 1987; Sapolsky, Rivier, Yamamoto, Plotsky, & Vale, 1987). Assessment of how these cells communicate might be critical for understanding how the CNS and the immune system interact.

Measurement

Measurement of immune function, the most likely dependent measure for studies in this area of research, is a complex issue. Quantitative/enumerative and qualitative/functional assays of immunocompetence may not be correlated. Moreover, different measures of the same type may produce inconsistent results from one time to another, further complicating critical decisions about which measures to use. Another basic problem is revealed by the debate about what individual measures mean and what constitutes a clear and accurate picture of the potential of the immune system to respond to an immunologic challenge. This creates a central concern for psychologists studying the interactions among the environment, behavior, and immune function. Choosing a set of immune measures that will be appropriate, predictive of clinical outcome, and accepted by the immunology community is necessary for conducting effective research.

The dynamic interaction between the CNS and the immune system resembles a jigsaw puzzle with some, if not many, missing pieces. Putting the picture together is nearly impossible until measures are developed that provide a "snapshot" of both the percentage and functional capacity of each immune cell subset. This latter aspect may require an *in vivo* measure of the blood concentrations of some of these peptides to provide a more accurate picture of the immune system. Specifically, the task ahead includes an understanding of the regulation of immune factors—interleukins, interferons,

and tumor necrosis factor—as modulators of immune responses and as possible communicating signals to neuroendocrine targets.

PSYCHOLOGICAL AND ENVIRONMENTAL MEDIATORS

In addition to studying the underlying mechanisms involved in the interaction between the CNS and the immune system, future research in this area will need to focus on how environmental and mental events influence changes in immunologic function and, ultimately, in health. Careful research questions and designs are needed to clearly describe what role environmental, behavioral, and emotional events play in the development of illness by affecting the immune system.

Physiological and psychological reactions to events can be mediated by several factors, including sociodemographic variables that cannot be easily controlled experimentally. A complete understanding requires taking into account all the complexities of the person-situation interaction. For example, whether a stressful event is chronic or acute, controllable or not, or whether actions taken to cope with a situation are successful or not can all influence patterns of reactions to a situation. These factors need to be incorporated into the current field of psychoneuroimmunology.

Chronic Versus Acute Stress

"Stress" is one of the psychological variables implicated most often as having effects on immunologic function. *Stress,* however, is a broad term incorporating a variety of stimuli and reactions. Physiological reactivity in response to stressors can be affected by the time course of an event—whether it is chronic or acute. The following examples illustrate how chronicity of a stressor may play either a direct or indirect role in stress reactions and immune function. In studies on unemployment, subjects who had been unemployed for a short period of time (fewer than 3 weeks) reacted to laboratory challenges differently from those who had been unemployed for at least 2 months (Baum, Fleming, & Reddy, 1986). Short-term unemployment was associated with increased sympathetic reactivity and greater persistence on an unsolvable task, whereas longer term unemployment was associated with decreased reactivity and task persistence, reminiscent of learned helplessness. Due to these psychological and physiological differences in reactions to chronic and acute stressors, there are likely to be differential immunologic effects as well. More directly, the chronicity of pharmacological challenge has been shown to determine whether cellular immune response is decreased or increased in rats (Paciotti, Skwerer, & Tamarkin, 1987). Studying the time course of stressors on immunologic vari-

ables will be necessary before clear conclusions can be made about the connections between stress and immune function.

Severity of an Event

It is not clear from the literature in psychoneuroimmunology how severity of an event is related to a person's reaction to the event or to noticeable and/or clinically meaningful immunologic changes. Most of the current literature has addressed the occurrence of certain events (e.g., bereavement, divorce) and a variety of immunological measures. There is little information, however, about the degree of severity or duration or about the type of events that are necessary to evoke specific changes in the functioning of the immune system. Evidence that different emotional events can lead to different patterns of endocrinologic responses (Mason, 1975) underscores the relevance of this question.

Perceived Control and Coping

How much control people feel they might have over an event and how they attempt to cope with that event might be important factors in determining long-term physiological effects. The resulting variability in response to similar stressors may play an indirect role in the variability of immunologic changes. For example, perception of greater loss of control has been associated with increased signs of stress in both laboratory (e.g., Glass & Singer, 1972) and field (e.g., Davidson, Baum, & Collins, 1982) studies. On the other hand, different coping behaviors can result in either a decrease or an increase in behavioral, emotional, or physiological responses to stress depending on the strategy used and the situation. With a chronic stressor, such as living near the Three Mile Island nuclear power plant before and after the time of the accident, an emotion-focused coping strategy was associated with lower stress effects than was a strategy using denial or problem-oriented methods (Baum, Fleming, & Singer, 1983). In contrast, with another life event, acute surgical stress, use of denial as a coping strategy was associated with shorter hospital stays and the use of fewer analgesics (Wilson, 1981). Whether the use of different coping styles in different situations has direct or indirect effects on the immune system needs to be determined. Additionally, certain behaviors often used as part of coping might have their own independent effects on immune function. One behavior of this type, drug use—either illegal, over the counter, or common (caffeine, nicotine, or alcohol)—deserves more careful consideration when evaluating the effects of events on the immune system.

SUMMARY AND CONCLUSIONS

Careful design of studies is crucial for meaningful progress in this area of inquiry. Along with systematic evaluation of immunologic factors, clear un-

derstanding of antecedent factors is also important. Age, sex, and other sociodemographic factors might play a major role in how an individual reacts to a given situation when compared with another individual. Assessment of the impact of these factors on the immune system might be further complicated by immunosuppressive viruses like HIV or by the use of many common medications such as beta-blockers for hypertension (Kiecolt-Glaser & Glaser, 1988). Longitudinal studies are needed to understand the process of change and the dynamic patterning of psychosocial and immunologic relationships over time. Additionally, use of multimodal measures to assess psychological events such as stress is imperative (Baum, Grunberg, & Singer, 1982). It will not serve our understanding of psychological influences on the immune system to jump to the conclusion that an event is "stressful" because it seems as if it *should* be.

Finally, establishing a "core" battery of widely accepted immune tests will be important in establishing comparability across studies. The standardization and acceptance of specific biochemical measures will facilitate the infusion of talented clinical and basic scientists into the area of psychoneuroimmunology.

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