

AMAZING PAPERS IN NEUROSCIENCE

Psychosocial Stress, Health, and the Hippocampus

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Psychoneuroimmunology (PNI) is an interdisciplinary field that examines the relationships between psychological factors and changes in endocrine and immune function, with possible consequences for health status. There is a growing literature suggesting that psychosocial stressors can impact negatively on health through deleterious changes in immune function. In their 2005 review, Glaser and Kiecolt-Glaser examined the mechanisms by which these changes might occur, and summarized some of the findings showing stress-related health consequences in a number of human populations. Buchanan et al. (2009)

examined the cortisol response in individuals sustaining damage to the hippocampus, when challenged with a psychosocial stressor. Individuals with damage to the hippocampus, but not those with damage in other regions of the brain, showed abnormal cortisol responses to the psychosocial stressor. These papers were used successfully in an undergraduate Neuroscience course to stimulate class discussion; other possible uses for these articles are discussed.

Key words: Psychosocial stressors; health consequences of stressors; hippocampus; cortisol

The notion that psychosocial stressors might impact one's health is not a new one. However, it was not until the 1970s that research exploring the interactions between psychological, neural, and immune systems began to increase, due in part to Ader and Cohen's demonstration of behaviorally-conditioned immunosuppression in rodents (Ader and Cohen, 1975). In that study, mice were given saccharin-flavored water (CS) paired with an injection of cyclophosphamide (UCS), a drug that suppresses immune function. Following acquisition, animals continued to show immunosuppression when presented with saccharin-flavored water alone (conditioned immunosuppression), suggesting that immune responses were susceptible to conditioning. Ader and Cohen's work led to the birth of the new interdisciplinary field, Psychoneuroimmunology (PNI).

Glaser and Kiecolt-Glaser (2005), pioneers in the field of PNI, provide a well-written review of potential health consequences of psychosocial stressors. The paper begins with a brief discussion of how researchers study the stress response using paper-and-pencil questionnaires and blood sample analysis, and a longer discussion of the mechanisms by which the nervous, endocrine, and immune systems communicate. This communication involves hormone receptors on immune cells and feedback from immune cells to the hypothalamus, which regulates production of corticotropin-releasing hormone (CRH), a critical step in the "classic" stress pathway (the hypothalamic-pituitary-adrenal system).

The paper then addresses potential health consequences of stressors. Citing now-classic research from their laboratory, as well as the work of others, the authors describe how the cellular (T cell mediated) and humoral (B cell mediated) immune responses may be negatively affected by stressors resulting in increased susceptibility to infectious disease, including the common cold; dysfunctions in the body's antibody response to vaccination; faster rates of progression of HIV in men infected with the virus; and impaired wound healing. The

studies are described in adequate detail, providing the reader with the rationale for the work, as well as the general methods used to arrive at the conclusions of the work cited. In the final section of the paper, Glaser and Kiecolt-Glaser present some of the work linking inflammation to suppressed immunity, with particular attention to the role of stress and inflammation in the aging process. The instructor can easily integrate findings from more recent work when using this paper in class.

Buchanan et al. (2009) provide a nice follow-up to the Glaser and Kiecolt-Glaser review article. The authors examined dysfunctions in the glucocorticoid response to stress in individuals sustaining bilateral hippocampal damage. Participants included individuals with damage to the medial temporal lobe (including the hippocampus; experimental group) and comparison participants with damage in the lateral temporal lobe, parietal lobe, occipital lobe, as well as neurologically-intact controls.

The Trier Social Stress Test (TSST) was given to all participants. This widely-used instrument, requiring participants to deliver a speech and engage in mental arithmetic problems in front of a small group of experimenters, reliably induces stress in participants. Buchanan et al. collected three cortisol samples from participants, including at the time of arrival to the lab, and at two time points following completion of the TSST. In addition, heart rate measures were obtained throughout the protocol period, including measures at baseline and during the TSST. Finally, measures of emotion were obtained to assess positive and negative affect. Although no differences were found between participants with hippocampal damage and comparison, participants on measures of heart rate, there were significant differences between groups on cortisol measures and on subjective reports of negative affect. Specifically, individuals with hippocampal damage and those with damage outside of the hippocampus showed pre-TSST CORT levels that were higher than non-damaged controls. However, CORT levels in hippocampal-damaged participants fell

significantly lower than both groups at 10 and 30 minute time points following the psychosocial stressor, suggesting that the hippocampus is critical to the response to psychosocial stressors. Moreover, although there were no group differences in pre-TSST negative affect scores, nor were there differences in pre- or post-TSST ratings of positive affect, hippocampal-damaged individuals reported significantly higher post-test ratings of negative affect than other groups, although negative affect was elevated in all groups following the TSST. The results suggest that multiple physiological systems are involved in the response to psychosocial stressors (e.g., the HPA pathway, autonomic control of heart rate, subjective reports of stress), and elucidate the role of the hippocampus in one of these “pathways” (the glucocorticoid response).

VALUE

The two papers complement each other well, providing valuable and important information to students studying the potential health consequences of psychosocial stressors, and the role of the hippocampus in the responses to psychosocial stressors. The Glaser and Kiecolt-Glaser review provides critical foundational information, including the basics of the immune system and of the immune response, as well as methodological considerations for researchers in the field of PNI. The Buchanan et al. paper reinforces the importance of the hippocampus in the stress response, and also provides students with reminders about some of the unique methodological considerations when engaged in human PNI research (e.g., the need to include a group of individuals with damage outside of the hippocampus in addition to neurologically-intact controls, the benefit of multiple dependent measures). In addition, the paper demonstrates that, in addition to the hypothalamus and pituitary, other important forebrain areas are critical to an organism’s response to psychosocial stressors.

AUDIENCE

These papers were used in an Advanced Neuroscience course, the capstone course for our students pursuing the

Neuroscience concentration. The course examines a number of contemporary topics in Neuroscience, generally by having students read and discuss primary source literature related to each topic. Generally, each topic is covered in two to three class periods. Students enrolled in the course have completed an introductory course in Neuroscience, as well as several elective courses in Psychology, Biology and Chemistry, and therefore have adequate background to understand and discuss these papers.

The papers could be integrated into an upper level course in Biological Psychology or Neurophysiology, as well, provided that students have sufficient background in Biology or Psychology. Discussion sessions could be led by the course instructor or by a student. In addition, one could structure the course in such a way that students are responsible for presenting the paper contents to the class and subsequently leading discussion, thereby providing an opportunity to sharpen oral communication skills.

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