Stress, immune reactivity and susceptibility to infectious disease

Anna L. Marsland[a,*], Elizabeth A. Bachen[b], Sheldon Cohen[c], Bruce Rabin[d], Stephen B. Manuck[a]

[a] [illegible]
[b] [illegible]
[c] [illegible]
[d] [illegible]

Received 5 July 2002; accepted 30 August 2002

Abstract

Psychological stress is known to affect immune function and to predict infectious disease susceptibility. However, not all individuals who are stressed develop disease. In the present article, we report on a series of studies from our laboratory describing interindividual variability of immune responses to psychological stress. In our initial series of experimental investigations, we demonstrated that acute laboratory stress alters both quantitative and functional components of cellular immunity. An examination of response variability revealed that individuals differ substantially in the magnitude of these immune responses. These differences were found to parallel (and be predicted by) interindividual variability in stress-induced sympathetic nervous system activation. Further investigation revealed that individuals vary consistently in the magnitude of their immune responses to stress, making it conceivable that individual differences in immune reactivity provide a vulnerability factor mediating relationships between stress and disease. In support of thistrese.7(relatpossiy)-353.revea,.7(immunw-35e.1(imm

against an alleged transgression (shoplifting or traffic violation), followed by 3 min of videotaped speech delivery. The Stroop task was a 21-min computerized version of the Stroop Color–Word Interference Test. In this task, the subject is presented with one of four-color names, appearing in an incongruent color. The subject is required to identify, from a response selection of four-color names (also in incongruent colors), the color name corresponding to the

responses to different acute stressors [27]. In this study, subjects were exposed to a speech task and a mental arithmetic task on the same occasion of testing. Intertask correlations were significant for the magnitude of decrease in proliferative response to PHA (=.76, <.0001) and increase in the number of circulating NK cells (=.46, <.005). Taken together, these findings and those of others suggest that individuals vary consistently in the magnitude of their cellular immune reactivity to acute stress [17,28].

4. Individual differences in immune reactivity and vulnerability to disease

The existence of such enduring characteristics makes it conceivable that individual differences in immune reactivity moderate associations between psychological stress and susceptibility to infectious disease. In this regard, we have hypothesized that individuals who show exaggerated immune responses to laboratory stressors exhibit similarly exaggerated reactions to everyday hassles, e.g., work demands and time pressures, rendering them more or less susceptible to infectious disease. To begin to explore this possibility, we examined whether immune reactivity predicts antibody response to hepatitis B vaccination, a real-life measure of host resistance [29]. In the initial study, 84 healthy, male and female graduate students (ages 20–35) who tested negative for prior exposure to hepatitis B virus were administered the standard series of three hepatitis B vaccinations. The first two vaccinations were given 6 weeks apart, with a follow up booster dose administered 6 months following the first shot. Five months after the first dose, each subject completed a battery of psychosocial measures, assessing levels of stress during the past 12 months, and a blood sample was drawn to assess hepatitis B surface antibody levels. Four to six weeks following completion of the vaccination series, subjects returned to the laboratory to perform an acute laboratory stress protocol, measuring immunologic responses to an evaluative speech task.

Consistent with prior findings, acute laboratory stress was associated with a significant increase in numbers of circulating cytotoxic T and NK cells, and a significant decrease in proliferative responses to PHA, Con A and pokeweed mitogen (PWM). The primary question of interest in this study was whether individual differences in the magnitude of these immune responses to acute stress were related to subjects' ability to mount an antibody response to the vaccine. In this regard, we found that, when compared with high antibody responders, subjects who mounted lower antibody responses to hepatitis B vaccination following the first two doses displayed greater stress-induced suppression of immune function, as measured by proliferative response to PHA (=.000001, <.04) (see Fig. 3). A similar pattern was observed for relationships between antibody response to the vaccination and Con-A induced proliferation; however, these findings did not achieve significance. Enumerative measures and proliferative response to PWM were unrelated to antibody response. These findings lend some support to the hypothesis that individual differences in the magnitude of acute stress-induced modulation of immune function may have clinical significance, being related to an in vivo immune response relevant for protection against infection.

A relationship was also observed between trait negative affect, also known as neuroticism, and antibody response to the vaccine. Subjects who described themselves as having higher levels of negative affect than their peers mounted lower antibody responses to the vaccine, as measured 5 months after the initial vaccination (= –.65, <.02). These data provide an important extension of past research on psychosocial factors and immunity. To date, research has focused on demonstrating associations between state psychological measures and laboratory assays of immunity. Relations between trait characteristics and immunity have received little attention, even though there is a large literature relating trait negative affect to health (see Ref. [30] for a review). Results of this study extend previous findings to demonstrate a relationship between trait negative affect and a measure of immune function of health significance. The relationship between trait negative affect and antibody response in this study was not explained by individual differences in immune reactivity to stress. Thus, lower antibody response to hep13.2(-438.3(of)n4y)]TJal-4e.2c4(egative51Tive)-2

lower final antibody response (as measured 1–2 months

[22] Felten SY, Olschowka J. Noradrenergic sympathetic innervation of the spleen: II. Tyrosine hydroxylase (TH)-positive nerve terminals for synaptic like contacts on lymphocytes in the splenic white pulp. J Neurosci Res 1987;18:37–48.
[23] Plaut M. Lymphocyte hormone receptors. Annu Rev Immunol 1987;5: 621–69.
[24] Dimsdale JE, Young D, Moore R, Strauss HW. Do plasma norepinephrine levels reflect behavioral stress? l
.
[25] Kamarck TW, Jennings JR, Manuck SB. Psychometric applications in the assessment of cardiovascular reactivity. Homeostasis 1993;34: 229–43.
[26] Mills PJ, Berry CC, Dimsdale JE, Nelesen RA, Ziegler MG. Temporal stability of task-induced cardiovascular, adrenergic, and psychological responses: the effects of race and hypertension. Psychophysiology 1993;30:197–204.
[27] Marsland AL, Henderson BN, Chambers WH, Baum A. Stability of individual differences in cellular immune responses to two different laboratory tasks. Psychophysiology [in press].
[28] Mills PJ, Haeri SL, Dimsdale JE. Temporal stability of acute stressor-induced changes in cellular immunity. Int J Psychophysiol 1995;19: 287–90.
[29] Marsland AL, Cohen S, Rabin BS,1993;30:11.9(ltlai7gy)-324rcNh
St1(in2937428t)FeBsaudility r-nt
–