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Can Stress Make You Sick?

The Effect of Cardiovascular Reactivity to and Recovery from Stress on Immune Response

Katherine Farner
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Abstract

From folklore and mass media to empirical research, stress has long been seen to weaken an individual's immune system, rendering them vulnerable to disease. This study asks, "How do individuals' reactions to and recovery from stressful events affect their susceptibility to disease?" It was hypothesized that individuals who display greater reactivity to a laboratory stress-task and slower recovery would have weaker immune function. As part of the Vaccination Immunity Project, I have been given access to data for 153 participants measuring their cardiovascular stress reactivity and recovery and their immune response to an immunization. Stress reactivity and recovery were measured as changes in heart rate and blood pressure in response to a laboratory stress-task simulating public speaking. Immune response was examined by measuring production of antibody in response to the standard Hepatitis B vaccine series. The stressor task caused significant increases in the cardiovascular markers, which returned towards baseline during the recovery period. Both the reactions of their cardiovascular markers and their recovery to baseline were highly correlated across two stress sessions approximately four weeks apart. Neither individual differences in stress reactivity nor recovery was found to significantly predict antibody response to the Hepatitis B vaccine. The effect of diastolic blood pressure on second antibody response and cardiovascular recovery on third antibody response approached significance. The findings on stress and the immune system conflict with previous research thus demonstrating the

complexity of the association between stress and immunity and the difficulty in measuring and operationalizing these variables.

Introduction

While psychological stress is known to effect susceptibility to disease, not all individuals who experience stress develop disease. This study explores individual differences in stress reactivity that may predict increased susceptibility to infectious disease. With this review of the literature I intend demonstrate that the cardiovascular variables used in this study, specifically heart rate and blood pressure, increase due to stress in a means consistent over time. Furthermore I will present studies linking stress and stress reactivity to antibody response in order to inform the reader the literature most related to this experiment.

Does stress influence the cardiovascular markers?

Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) all reliably increase in response to laboratory stressor tasks (Marsland, Cohen, Rabin and Manuck 2001; Cohen et al., 2000; Evans, Allen, Tafalla and O'Meara 1996; Sgoutas-Emch et al., 1994). In Marsland et al. (2001) and Cohen et al. (2000) HR, SBP, DBP were found to significantly increase in response to a five-minute evaluative speech task. Evans, Allen, Tafalla and O'Meara (1996) found significant increases in diastolic and systolic blood pressure due to performance of a speech task and exposure to a noxious noise. In addition, Evans et al. (1996) found that exposure to multiple stressors, such as a speech task and a noxious noise, causes greater increase in blood pressure than a singular stressor, such as a speech task alone, demonstrating that greater increases in blood pressure occur with greater stress.

Sgoutas-Emch et al. (1994) found SBP, DBP and HR to increase due to either a three-minute evaluative speech task or a two-minute mental arithmetic task.

Are cardiovascular responses consistent across sessions?

The literature shows that the reaction of the cardiovascular markers is a characteristic of the individual, consistent across laboratory sessions (Cohen et al., 2000; Sgoutas-Emch et al., 1994). Cohen et al. (2002) and Cohen et al. (2000) found that increases of in SBP, DBP and HR due to a laboratory speech task are significantly correlated across lab sessions run two weeks apart. Similarly, Sgoutas-Emch et al. (1994) found HR reactivity due to a speech task and an arithmetic stressor task given approximately three weeks apart to be consistent. This provided further evidence that stress reactivity is a stable characteristic of individuals, even across stressor tasks.

Do individual differences in stress reactivity in the laboratory predict immune response outside of the lab?

The literature supports that increased stress and stress reactivity is associated with weaker immune function (Cohen et al., 2002; Marsland et al., 2002; Cohen et al., 2001; Marsland et al., 2001; Sgoutas-Emch et al., 1994). Cohen et al. (2002) found that, for those reporting higher levels of stressful life events, higher cortisol reactivity and lower CD8+ reactivity during a laboratory stress session was associated with increased incidence of upper respiratory infection (URI) during a twelve-week

follow-up. No association or interaction with life events was found between cardiovascular reactivity and immune susceptibility. This study shows that an individual's stress reactivity impacts their immune competence, and suggests cortisol as a possible mediator between stress reactivity and immune competency.

A review by Marsland, Bachen, Cohen, Rabin and Manuck (2002) demonstrates that immune suppression due to laboratory-induced stress predicts real life immune reactivity to a Hepatitis B vaccine. Furthermore, this review establishes that individual differences in immune reactivity, such as proliferative response to PHA and the numbers of circulating cytotoxic T and natural killer (NK), are stable between laboratory stress sessions given two weeks apart. This demonstrates that immune reactivity is stable and that some individuals are always "high immune reactors", potentially causing them to be more susceptible to disease.

A review by Cohen et al. (2001) supports an association between self-reported psychological stress and suppression of the immune response such that individuals with higher levels of stress consistently produced a lower second antibody response. Because this review did not find a consistent association between stress and primary antibody response it also supports the use of repeated secondary antibody response as an outcome variable.

Marsland et al. (2001) found that stress impacts the immune system in the laboratory and individual reactions to stress are predictive of immune response to a Hepatitis B vaccine. This study found that numerous T-cell measures and NK cell counts

increase along with SBP, DBP and HR due to a five-minute laboratory speech task. Responses to PHA, Con A and PWM decreased in response to a stressor task – showing an effect of stress on the immune system within the laboratory. Additionally, lower antibody responses a Hepatitis B vaccine were associated with high trait negative affect and low T-cell response to PHA – showing that immune suppression due to stress measured in the laboratory is related to real life immune reactivity. Cardiovascular reactivity to the stress session was not found to be associated with antibody response.

Sgoutas-Emch et al. (1994) found that the magnitude of an individual's cardiovascular reactivity to stress is associated with their increases in cortisol levels and NK cell cytotoxicity due to stress, showing a possible mechanism for the proposed link between cardiovascular reactivity and immune response.

Do individual differences in stress recovery in the laboratory predict immune response outside of the lab?

Another approach to assessing individual differences in response to stress is to measure how long it takes an individual them to recover from stress. However, there is no evidence on the reliability of cardiovascular recovery from stress measure across sessions, and on whether it predicts later immune response. Therefore the hypotheses on cardiovascular recovery have been extended from the findings in the body of literature on reactivity.

Based on my review of previous literature there are many unanswered questions about the effect of psychological stress on immune response. This study examines some of the individual characteristics that predict increased susceptibility to infectious disease based on exposure to stress. More specifically, it addresses two questions: "Is cardiovascular reactivity to stress related to immune response?" and "Is cardiovascular recovery from stress related to immune response?" For the purpose of this experiment cardiovascular reactivity is defined as the increase in SBP, DBP and HR from a baseline condition to a stressor condition. Those who have greater reactivity are seen as having less effective physical and psychological mechanisms for handling stressful situations. Cardiovascular recovery is defined as the speed of and the extent that heart rate returns to baseline following exposure to a stressor condition. Those who take less time to recover are seen as having a more effective mechanism for cardiovascular recovery. For the purpose of this study immune response will be measured using antibody response to the second (6 weeks from first) and third (6 months from first) of the three hepatitis B vaccinations given in its standard series (Marsland et al., 2001). A higher antibody response to the vaccine indicates a stronger immune response to invading antigens and is a measure of immune competency (Marsland et al., 2002; Cohen et al., 2001; Cohen et al., 1997).

The hypothesis for reactivity is that individuals with greater increases in HR, DBP and SBP from baseline to a stressor condition will produce fewer antibodies in response to the second and third vaccinations. Cohen et al. (2002), Marsland et al. (2002) and Cohen et al. (2001) and Marsland et al. (2001) all find associations between measures

of stress reactivity and later immune response. While both Cohen et al. (2002) and Marsland et al. (2001) examined cardiovascular reactivity and immune response neither found a significant association. A methodological problem in Marsland et al. (2001) is that the reactivity stress sessions were run after administration of the Hepatitis B vaccine and therefore stress reactivity cannot be seen as predictive of the vaccine. In this study both stress reactivity sessions were performed prior to the vaccination in hopes of finding an association between stress reactivity and immune response. Sgoutas-Emch et al. (1994) shows that an individual's cardiovascular reactivity is related to weakened NK cell responses that indicated decreased immune strength. When surveying the literature, no research was found on the effect of cardiovascular recovery on immune response – making this both a novel and important subject of inquiry. Based on the proposed effect of reactivity, the hypothesis for recovery is that individuals who show a faster and greater heart rate recovery from a stressor condition back to baseline will produce more antibodies in response to the second and third vaccinations.

Primarily, stress reactivity is thought to influence immune competence because it is a marker of activation of the sympathetic nervous system. Activation of the sympathetic nervous system results in increased arterial blood pressure, and changes in the regulation of the receptors and cytokines involved in immune function (Marsland et al., 2002). An increase in blood pressure causes fluid to enter extra vascular spaces resulting in an increase in all the non diffusible blood components, which explains some of the increase in circulating cytotoxic T and NK cells (Marsland et al., 2002). Finally it has been found that activation of the sympathetic nervous system results in changes in

the adhesion molecules of lymphocytes, causing them to be released for general circulation.

Another mechanism linking cardiovascular reactivity and decreased immune response is based on the impact of hormones involved in the stress reaction that are released in conjunction with cardiovascular response and are know to influence immune competence. The stress reaction causes "potentially pathogenic states" due to the stress-elicited release of several hormones such as epinephrine, norepinephrine and cortisol (Cohen et al., 2001; Marsland et al., 2001; Krantz et al.1984). These hormones directly bind to and interact with cells involved in antibody response (Marsland et al., 2001). In the case of cortisol there is there is a strong body of evidence associating elevated levels of this hormone and "longer-term down regulation of cellular immune function" which would make individuals more susceptible to disease (Marsland et al., 2002).

The proposed mechanism between speed of cardiovascular recovery and immune response is based on the mechanism for reactivity. Just as having a greater response to a stress condition will result in wear on immune components through hormones, a stress response of longer duration will result in greater impact on these immune components. If an individual takes longer to recover from a stressor situation, then they will spend more time in this "potentially pathogenic state" each day for a given number of stressors, resulting in greater impact.

Methods

Participants

The participants in this study are 153 of the total 182 participants of the Vaccination Immunity Project (PI : Marsland, A). This sample was selected due to the availability of cardiovascular and antibody response data on these participants. The subjects are healthy male and female adults between 40 and 60 years of age. The sample is 41.8% male and 58.2% female. Racially, the sample is slightly skewed towards Caucasians but numerous backgrounds are represented. The sample is 88.2% Caucasian, 9.8% African American, 1.3% Hispanic and 7% Asian. Participants came from a range of different socioeconomic backgrounds, as assessed by their income and education. The subjects' incomes ranged from under $5000 to over $100,000 a year with the most frequent response being in the range of $25,000-34,999 a year. The education levels ranged from no education following 9th grade to a doctoral degrees with the most frequent response being a college degree.

Subjects were included based on the following major criteria: between 40-60 years old, English speaking, less than 30% overweight for their height and sex, resting blood pressure in normal range (<140/100 mmHg) and no history of psychiatric disorder. Participants were excluded based on the following criteria: prior hepatitis B vaccination or infection, pregnancy or intention to become pregnant in the next 20 months, having smoked a cigarette in the past 20 months, regular illicit drug use, history of a psychiatric disorder. Participants were also excluded for either taking medications known to affect

the endocrine or immune systems other than contraceptives, which affect the endocrine system. Participants were excluded for having symptoms of a disease involving either the nervous, endocrine or immune systems.

Subjects were recruited by advertisements in local and university news papers, mass mailings, campus voice mail announcements, electronic bulletin boards and radio and television public service announcements. Postage-paid response cards were distributed to locations such as doctor's offices, clinics and other research studies waiting areas.

Procedures

There were three phases to this study, two lab sessions testing physiological reactivity, a vaccination phase administering the hepatitis B vaccine and a follow-up period measuring the subject's response to the vaccine.

Reactivity Lab Session

The two reactivity lab sessions were three hours each and occurred approximately four weeks apart. All of the reactivity sessions start between 7 and 9 AM. Prior to the sessions the subjects were asked to abstain from alcohol for the 48 hours prior, from exercise and non-prescription medication for the 24 hours prior and from food and caffeine for the 12 hours prior. Informed consent was obtained at a separate visit before the lab session.

Background information was collected using questionnaires. The subject variables collected which were used as controls in this experiment include height, weight and initial resting blood pressure. A catheter was inserted in to the participants' arms by the Research Nurse and was used to collect blood throughout the lab session in order to measure variables not covered in this article. Next an automatic blood pressure cuff was placed on the arm without the catheter to collect the diastolic and systolic blood pressure data used in this study. Three EKG electrodes were applied, one on each shoulder and one at the xyphoid process. A respiration belt was also worn during the lab session to collect data not used in this research.

The participants sat quietly for 30 minutes to adjust to the laboratory. During the last six minutes of the adjustment phase four baseline readings of HR and BP were taken. The stressor task followed this period. Subjects were required to perform a public speaking task defending themselves against either a shoplifting charge or a traffic violation. They were given 2 minutes to prepare their speech and three minutes to deliver their speech to a video recorder. Following the stressor task the participants rested quietly for 30 minutes and recovery readings were taken. Heart rate and blood pressure was measured every 90 seconds during the stressor task (both performance and preparation) and during the last six minutes of the recovery period. Following the lab session all of the testing instruments were removed and additional measured unrelated to this report were collected.

Hepatitis B Vaccination Phase

In the vaccination phase of this study the participants received the standard series of 3 x 20 ug injections of recombinant hepatitis B vaccine, Engerix-B, manufactured by GlaxcoSmithKline. The first vaccination was received four weeks after the final reactivity lab session. The second dose was received four weeks after the first and the final 6 months after the first. All of the vaccinations were administered by the research nurse with the supervision of a medical doctor. The vaccines were not given if, when questioned, a female participant indicated that there is a possibility she may be pregnant.

Follow up Period

During the follow up period blood samples were taken to determine each individual's antibody response to vaccine injections. At the second and third vaccination visits a blood sample was drawn to determine the hepatitis B antibody levels. Blood samples were also taken at either laboratory or home visits 6 and 12 months following the final vaccination. The blood samples taken were analyzed for hepatitis B antibody titer. Repeated antibody responses, secondary antibody response and tertiary antibody response, were used because the plateau phase following repeated responses is on the order of 10x greater than the primary response. Also, as established in Cohen (1997), there is more measureable variance in repeated antibody responses making them better suited to compare the relative strengths of individual immune responses.

Statistical Analysis

Each cardiovascular reactivity variable – systolic blood pressure and diastolic blood pressure and heart rate – was calculated by averaging across time period (baseline, stress-task and recovery). These values were found to be significantly correlated across the two laboratory sessions and were averaged across sessions to determine the effect of the stressor task on cardiovascular recovery and reactivity. Also, average heart rate was calculated for five separate time periods during the recovery portion of the laboratory session with the first three periods lasting 90 seconds and the following two lasting five minutes.

Standardized residuals were calculated for each variable with a linear regression predicting the task average from the baseline average. These residuals represent the difference between the expected and actual increase in each variable from baseline to task and were used to demonstrate greater or lesser increase in these variables while controlling for baseline. Residuals of the cardiovascular reactivity markers were each found to have a normal distribution for both sessions.

The predictor variable for recovery, RecovHR, was calculated using the EEG data from both laboratory stress sessions. Recovery was estimated as the integral of heart rate during the recovery period. Baseline heart rate was controlled for by subtracting the integral of heart rate during the baseline period. For RecovHR higher scores indicate a slower recovery. This variable was found to be highly correlated between sessions and was averaged to obtain a value closer to each participant's true mean.

A natural log scale transformed the two outcome variables, second antibody response and third antibody response, in order to obtain a more normal distribution. Because second antibody response still deviated from a normal distribution this variable was coded into three categories: no response, response below mean and response above mean. For second antibody response, 11.4% of the subjects displayed no antibody response to the vaccine, for third antibody response, only 3.2%. For second antibody response the non-responding group was dropped in order to analyze the data by logistic regression. The non-responders were retained for third antibody, which was analyzed by linear regression. All analyses controlled for (covaried) sex (M, F) and race (Caucasian, African American, Hispanic, Asian, Native American or Other).

Results

Did stress influence the cardiovascular markers?

Reactivity

One-sample T tests found that each of the cardiovascular markers have a significant increase due to the laboratory stressor task (SBP mean increase = 17.27 mmHg, $t(114) = 15.71$, $p > .001$; DBP mean increase = 8.71 mmHg, $t(114) = 20.19$, $p > .001$; HR mean increase = 9.27 mmHg, $t(114) = 15.61$, $p > .001$). This data is displayed in Figures 1-3.

Recovery

One-sample T tests found that each of the cardiovascular markers have a significant decrease following the laboratory stressor task (SBP mean decrease = 14.27 mmHg, $t(114) = 13.40$, $p > .001$; DBP mean decrease = 7.71 mmHg, $t(114) = 19.15$, $p > .001$; HR mean decrease = 8.83 mmHg, $t(114) = 14.47$, $p > .001$). This data is also displayed in Figures 1-3.

The markers all return to values close to baseline (Figures 1-3). Both systolic and diastolic blood pressures are significantly higher for the recovery period than baseline (SBP mean difference = 3.00, $t(114) = 6.041$, $p > .001$; DBP mean difference = 1.00, $t(114) = 3.975$, $p > .001$). The difference between heart rate during baseline and recovery was not significant (HR mean difference = .43, $t(114) = 1.67$, $p = .097$).

When comparing heart rate averages within five different time points during recovery, while controlling for baseline heart rate, the values show a steady decrease

(Figure 4). However, even after five minutes the mean heart rate was still three beats per minute above baseline (Figure 4)

Figure 1

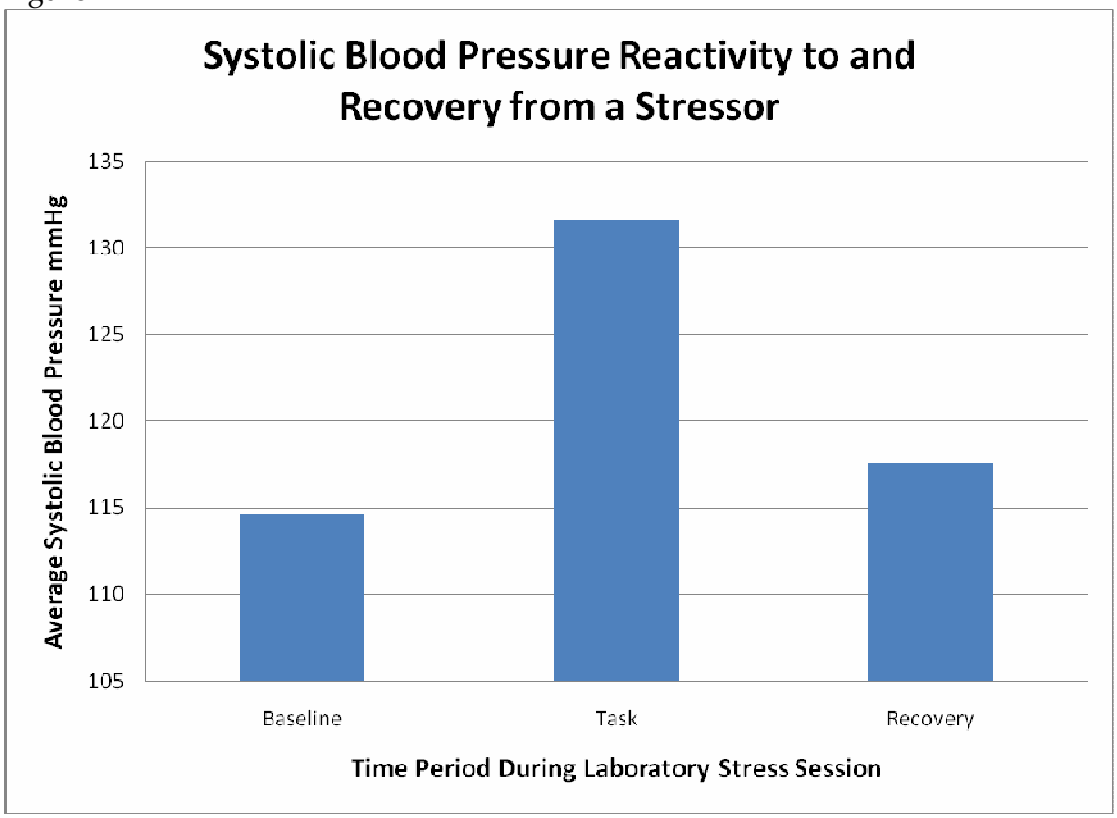


Figure 2

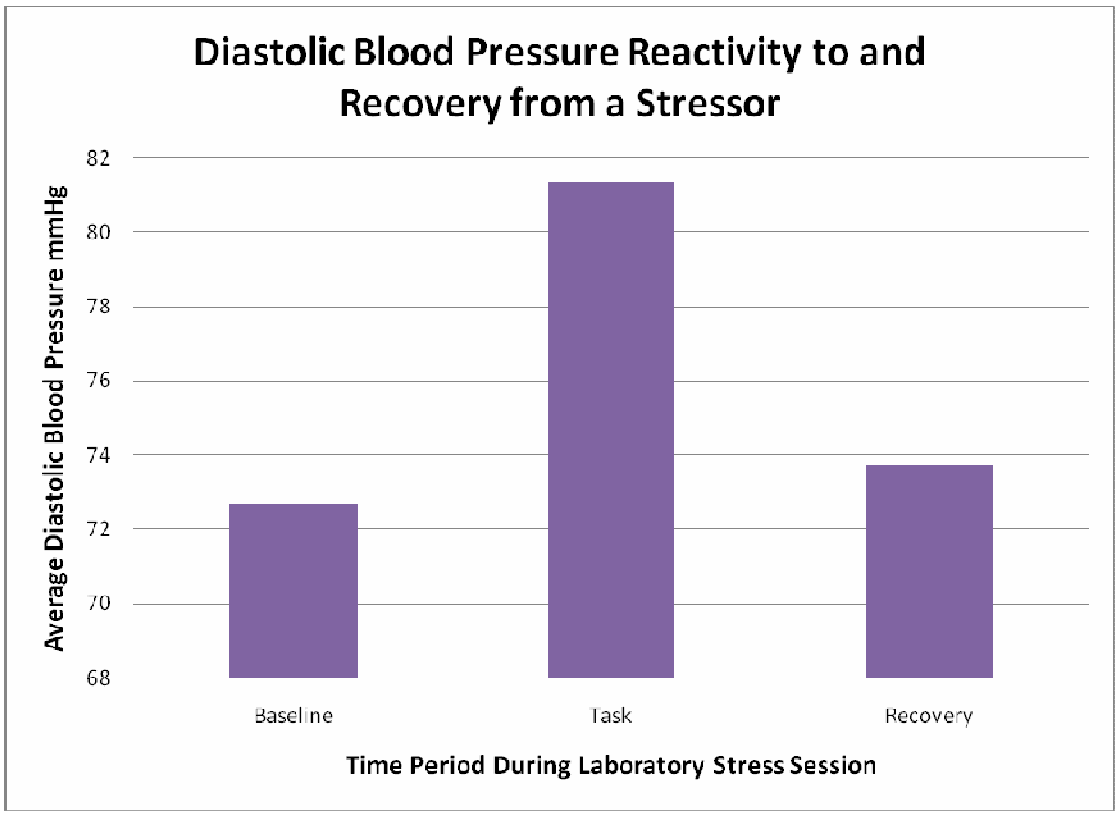

Diastolic Blood Pressure Reactivity to and Recovery from a Stressor
Average Diastolic Blood Pressure mmHg
82
80
78
76
74
72
70
68
Baseline
Task
Recovery
Time Period During Laboratory Stress Session

Figure 3

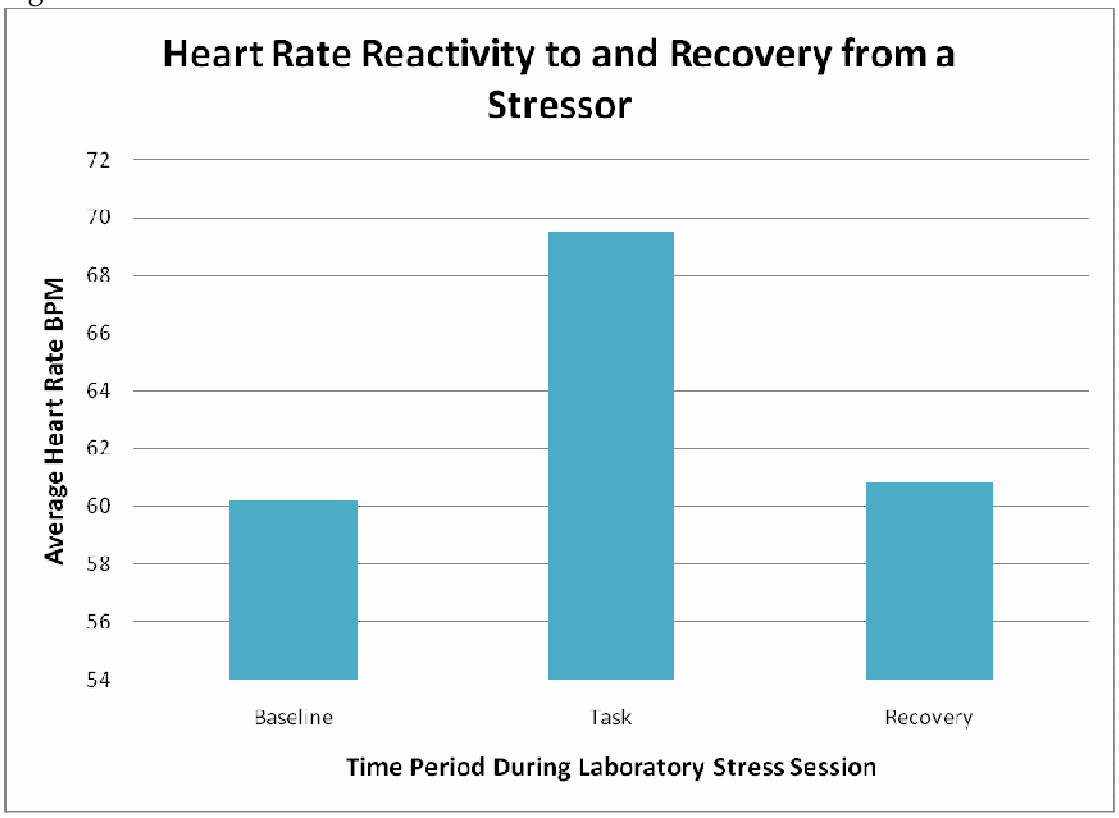
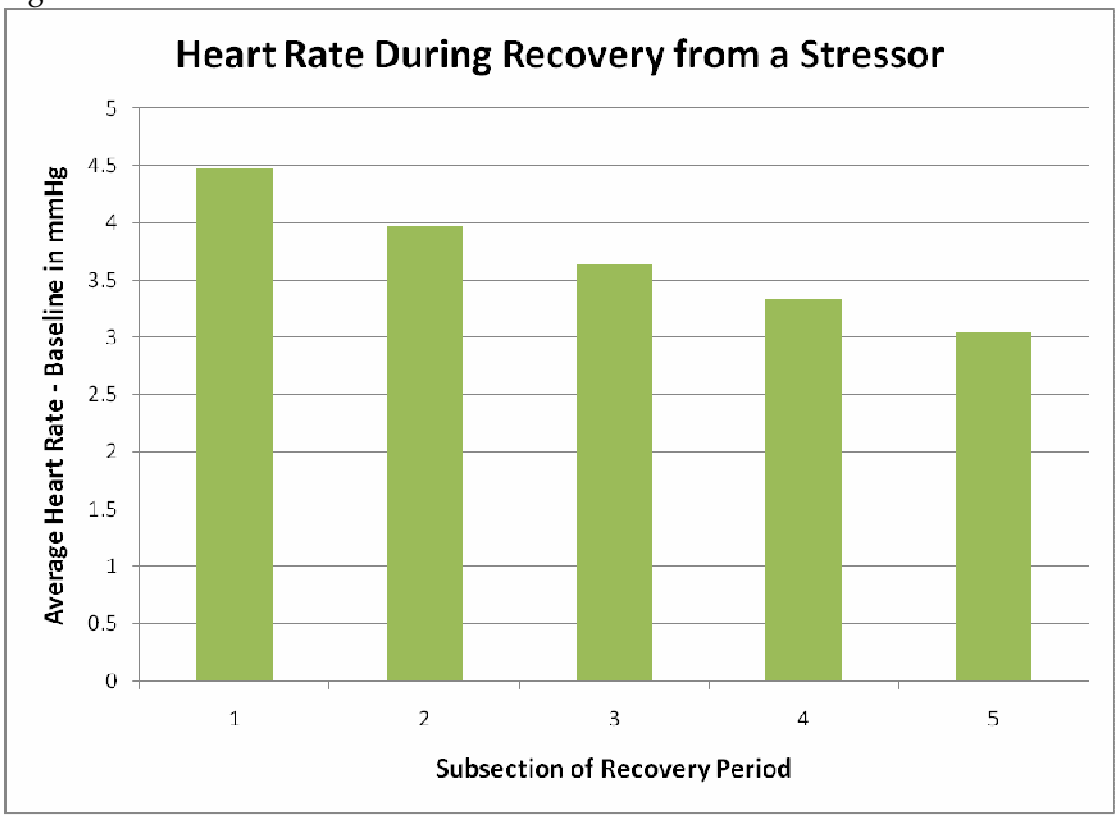

Heart Rate Reactivity to and Recovery from a Stressor
Average Heart Rate BPM
72
70
68
66
64
62
60
58
56
54
Baseline
Task
Recovery
Time Period During Laboratory Stress Session

Figure 4



Were cardiovascular responses consistent across sessions?

Reactivity

Individuals' average SBP, DBP and HR during baseline and task periods was found to be highly correlated across sessions (Table 1). Increases in the cardiovascular markers were found to be highly correlated across sessions (SBP $r = .729$, $p < .001$; DBP $r = .431$, $p < .001$; HR $r = .628$ $p < .001$).

Recovery

The individuals' average of each cardiovascular marker during the recovery period was found to be highly correlated across sessions (Table 1). RecovHR, measuring

the time and extent of heart-rate recovery, was found to be highly correlated across sessions ($r = .488$, $p < .001$).

Table 1: Correlations in Cardiovascular Markers Across Lab Sessions

Marker	Period During Laboratory Session		
	Baseline	Task	Recovery
SBP	$r = .864$, $p < .001$	$r = .881$, $p < .001$	$r = .834$, $p < .001$
DBP	$r = .875$, $p < .001$	$r = .849$, $p < .001$	$r = .863$, $p < .001$
HR	$r = .829$, $p < .001$	$r = .817$, $p < .001$	$r = .699$, $p < .001$

Did individual differences in average cardiovascular response predict antibody response?

Reactivity

Second Antibody Response

Logistic regression, controlling for sex and race, was run to determine the impact of the three measures of cardiovascular reactivity, systolic blood pressure and diastolic blood pressure and heart rate, on low or high second antibody response. Average increases in systolic blood were not significantly associated with second antibody response ($B = .204$, $SE = .242$, $p = .399$). The association between diastolic blood pressure and second antibody response was marginally significant with higher

average increases in diastolic blood pressure resulting in greater second antibody response (B = .496, SE = .281, p = .077). Average increases in heart rate were not significantly associated with second antibody response (B = -.014, SE = .227, p = .953).

Third Antibody Response

Linear regression, controlling for sex and race, was run to determine the impact of the same three measures of cardiovascular reactivity on third antibody response. Average increases in systolic blood pressure were not significantly associated with third antibody response (B = .160, SE = .264, p = .546). The association between average increases in diastolic blood pressure and third antibody response was not significant (B = .330, SE = .108, p = .265). Linear regression demonstrated that average increases in heart rate were not significantly associated with second antibody response (B = .160, SE = .260, p = .540).

Recovery

Second Antibody Response

Logistic regression, controlling for sex and race, showed that the RecovHR, measuring the time and extent of heart-rate recovery, was not significantly associated with second antibody response (B = .000, SE = .000, p = .223).

Third Antibody Response

Linear regression, controlling for sex and race, shows a marginal association between RecovHR and third antibody response such that slower recovery is associated with greater antibody response ($B = .000$, $SE = .000$, $\beta = .183$, $p = .098$).

Discussion

Did stress influence the cardiovascular markers?

As hypothesized, systolic and diastolic blood pressure, and heart rate all show a significant increase due to the laboratory stressor task and significant decreases during the recovery period. This demonstrates that the stress task was effective in eliciting a cardiovascular response, and that individuals recovered from this response during the 30-minute recovery period. The means for systolic and diastolic blood pressure during recovery were significantly higher than the means for baseline, while there was no significant difference for heart rate between baseline and recovery. This shows that heart rate may exhibit faster recovery from a stressor than blood pressure. When examining heart rate by the five different time points during recovery, while controlling for baseline heart rate, the values gradual decreased, which is as expected. These findings are consistent with the existing literature, which also establishes SBP, DBP and HR as measures of stress (Marsland et al., 2001; Cohen et al., 2000; Evans et al., 1996).

Were cardiovascular responses consistent across sessions?

Increases in the cardiovascular markers due to stress and the heart-rate recovery following stress were highly correlated across laboratory sessions held four weeks apart. This finding is well supported by the literature that also finds at the reaction of the cardiovascular markers to be consistent across laboratory sessions (Marsland et al., 2002; Cohen et al., 2000; Sgoutas-Emch et al., 1994). This study is relatively novel in its examination of the consistency of cardiovascular recovery, and demonstrates that

cardiovascular recovery is also consistent across laboratory sessions held four weeks apart. These findings both add to the body of evidence demonstrating the stability of individual differences in cardiovascular response to stress and extend the time of consistency further than previous research, which has examined stability over only two (Marsland et al., 2002; Cohen et al., 2000) or three (Sgoutas-Emch et al., 1994) weeks. Still, further research is needed to explore the stability of cardiovascular recovery and examine both reactivity and recovery over greater lengths of time.

Did the average cardiovascular response predict response to repeated antibody exposure (secondary or tertiary antibody response)?

Reactivity

Reactivity of the cardiovascular markers, SBP, DBP and HR, were not significantly associated with second or third antibody response. This finding conflicts with the literature, which supports that increased stress and stress reactivity negatively impacts immune function (Cohen et al., 2002; Marsland et al., 2002; Cohen et al., 2001; Marsland et al., 2001; Sgoutas-Emch et al., 1994). However the lack of a significant association between cardiovascular reactivity, specifically, and immune function is supported by many of the same literature sources. Marsland et al. (2001) found that the effect of cardiovascular reactivity on antibody response to the Hepatitis B vaccine was not significant. Given the similarity between Marsland et al. (2001) and this study – the variables of stress and immune strength are operationalized with the same markers and collected in very similar means – Marsland's previous research is consistent with our

findings. Cohen et al. (2002) similarly showed no main effect of cardiovascular reactivity, on incidence of upper respiratory infections.

The marginal association found between diastolic blood pressure and second antibody response is has similarities to the previous literature finding an association between stress and immune function, yet conflicts with this same literature in the direction of the finding (Cohen et al., 2002; Marsland et al., 2002; Cohen et al., 2001; Marsland et al., 2001; Sgoutas-Emch et al., 1994). This previous literature found that that higher stress results in lower antibody response, while I found that higher stress, as shown by greater diastolic blood pressure was marginally related to higher second antibody response. There is no obvious explanation for this association at this time.

Recovery

The speed and extent of heart-rate recovery was not significantly associated with either second or third antibody response. Because no literature sources were found on the association between cardiovascular recovery and antibody response this finding is neither supported or in conflict with the literature. However it was hypothesized that, since the literature supports an association between reactivity and antibody response, there would be a relationship between recovery and immune response. Furthermore, the marginal association found between heart-rate recovery and third antibody response, such that slower recovery was associated with greater antibody response, is in the opposite direction of expected. It was expected that slower recovery, an indication of less ability to manage stress, would be associated with a weaker immune response.

This marginal finding is consistent with the marginal finding for reactivity, which also was in the opposite direction of hypothesized. It may be possible that those who have poor cardiovascular mechanisms for handling stress, as shown by greater reactivity and weaker recovery, have stronger immune response. However, that these relations are marginal indicates that they may just be random.

Based on the lack of a significant association between cardiovascular reactivity or recovery and antibody response, it is possible that in this study, Marsland (2001), and Cohen (2002), BP and HR are indicative of a different psychophysiological processes than stress, although they both increase during the stressor condition. Furthermore, the association between cardiovascular responses to stress and antibody response may be subtle enough that a larger population is needed to find a significant association. This study and many in the literature have the major methodological weakness inherent in all correlational studies - a third variable could be affecting both stress and immune response. In this study sex and race were controlled for and associations between antibody response and age, income, education and body mass index were found to be insignificant, yet another third variable could be impacting both measures. Future research should examine the association between cardiovascular response to stress and immune strength with larger sample sizes. The impact of other measures of the stress response, such as cortisol (Cohen et al., 2002; Cohen et al., 2001; Sgoutas-Emch et al., 1994) trait negative affect (Marsland, 2001), on immune strength should be examined and may yield significant findings.

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