THE STABILITY OF AND INTERCORRELATIONS AMONG CARDIOVASCULAR, IMMUNE, ENDOCRINE, AND PSYCHOLOGICAL REACTIVITY[1,2]

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ABSTRACT

One hundred fifteen college students were exposed to an evaluative speech task twice, separated by 2 weeks. At both sessions, we assessed cardiovascular, endocrine, immune, and psychological response at baseline and during the task. We found stability across sessions for stress-induced increases in anxiety and task engagement, heart rate, blood pressure, norepinephrine (but not epinephrine), cortisol, natural killer cell cytotoxicity, and numbers of circulating CD3+, CD8+, and CD56+ (but not CD4+ or CD19+) lymphocytes. The stable cardiovascular, immune, and endocrine reactivities were intercorrelated, providing evidence of a unified physiological stress response across these outcomes. Although stable stress-induced increases in task engagement were associated with the physiological stress responses, stress-induced anxiety was not.

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INTRODUCTION

The concept of stress reactivity refers to a stable individual difference in response to stressors. This concept was originally conceived of in relation to cardiovascular disease, with persons showing a disposition toward greater cardiovascular response thought to be at greater risk for stress-induced heart disease (1,2). More recently, reactivity has been applied to immune response as well (3,4). In this case, greater immunosuppression in response to stressors is thought to be associated with greater risk for stress-induced infectious, autoimmune, or malignant diseases. An integrated view of reactivity was suggested by Boyce et al. (3) who proposed a unified biological response to stressors. This was referred to as "psychobiological" reactivity. Such an approach suggests that there are close interrelations between cardiovascular, endocrine, and immune responses to stress. Consequently, persons reactive on one of these measures will be reactive on the others as well. It follows that such persons would be at risk for disease across multiple physiological systems.

Traditional research paradigms in this area have determined reactivity from a single response to an acute stressor in the laboratory (see 5). However, reactivity is thought to be an enduring trait and one-shot measures do not provide information about the stability of response over time. Moreover, seldom have responses from multiple physiological systems been assessed simultaneously. Consequently, it is unclear whether responses cohere across a common dimension, or each response domain represents a partly or entirely independent system. In this article, we address whether psychological, endocrine, cardiovascular, and immune responses to acute laboratory stressors are stable over time. We also investigate whether reactivity across response domains constitutes a unified psychobiological response or identifies individual differences in independent response modalities.

Evidence for the stability of cardiovascular response is provided by research on effects of acute laboratory stressors. In a review of 21 studies with intervals ranging from 2 days to a few months, Manuck (5) reported average correlations of .60 for heart rate (HR) response, .51 for systolic blood pressure (SBP), and .34 for diastolic blood pressure (DBP) response. However, higher correlations have been obtained with careful standardization of test stimuli and aggregation of responses over multiple tasks and occasions of measurement (6).

Only one study has examined the stability of functional immune response to an acute stressor task across testing periods. Marsland et al. (7) reported diminished proliferative response to phytohemagglutinin (PHA) and concanavalin A (ConA) when subjects gave a public speech. Although stress-induced changes in PHA response were stable across two testing periods (r = .50),

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ConA response was not ($r = .04$). Two studies have reported test–retest correlations of changes in enumerative measures of immunity (circulating white blood cell populations) in response to acute stressors (7,8). These studies found that a number of cell populations fluctuated with stress. However, significant correlations across sessions were found only for increases in circulating natural killer (NK) (CD56+) cells (Marsland et al. [7]: $r = .42$; Mills et al. [8]: $r = .41$) and T-cytotoxic/suppressor (CD8+) cells (Marsland et al. [7]: $r = .53$; but not Mills et al. [8]: $r = .14$, *ns*) and for a decrease in the helper–suppressor (CD4+:CD8+) ratio (Mills et al. [8]: $r = .60$). A moderate but nonsignificant correlation ($r = .31$) was also found by Marsland et al. (7) for stability of stressor-induced decrease in number of circulating B (CD19+) lymphocytes.

Acute stressors have also been found to produce changes in concentrations of circulating hormones. The hormones most often studied in acute laboratory stress paradigms are epinephrine (epi) and norepinephrine (norepi)—products of sympathetic nervous system activation, and cortisol—a product of the hypothalamic–pituitary–adrenal (HPA) axis. All three hormones are commonly found to increase in response to acute psychological stressors (e.g. catecholamine changes in 9,10; cortisol in 11,12). Two studies have addressed the stability of catecholamine reactivity. Mills and colleagues (13) found participants exhibited stable stressor-induced increases in both epinephrine (intersession $r = .41, p < .01$) and norepinephrine (intersession $r = .36$, $p < .01$) to the same acute laboratory stressor given 10 days apart. Lundberg and colleagues (14) compared both catecholamine and cortisol reactivities taken in the laboratory to those taken in a naturalistic (workplace) setting, separated by 4 months. Catecholamine intersession correlations across the same time of day (done to control for diurnal variation) are comparable to those of Mills et al. (epinephrine: $r = .47$, $p < .05$; norepinephrine: $r = .37$, $p < .05$). Yet cortisol intersession reactivity correlations across the same time of day did not reach significance ($r = .10$, *ns*). In a study of the stability of laboratory stressor-induced cortisol response, Kirschbaum et al. (15) found cortisol levels were elevated in response to an acute laboratory stressor on each of 5 days with intersession reliability of cortisol response ranging from $r = .38$ to $r = .60$.

Finally, in addition to biological reactivity to stressors, psychological responses (primarily emotions) have also been studied. In response to acute laboratory stressors, participants report increases in negative moods such as anger and anxiety (e.g. 16,17) and decreases in positive moods such as calmness and well-being (e.g. 16). Although psychological response to acute stressful events is often referred to as having a basis in stable traits (e.g. 18), to our knowledge, only one study has addressed the stability of psychological responses over time. Mills and colleagues (13) found participants to exhibit stable increases in anxiety when exposed twice to a mental arithmetic task with a 10-day intersession interval (intersession $r = .32, p < .01$).

We are also interested in the extent to which stable dispositions to respond to stressors in different biological domains (cardiovascular, endocrine, immune) are interrelated. Boyce et al. (3) used cardiovascular and immune reactivities interchangeably to characterize individual differences in children susceptible to upper respiratory infection, yet they did not report relations between cardiovascular and immune response. There is evidence, however, that some (but not other) immune responses to stress are moderately correlated with concomitant cardiovascular and plasma catecholamine responses. Stress-induced changes in immunity associated with greater cardiovascular and catecholamine response include decreased PHA (19,20; but not in 21) and ConA (21) stimulated lymphocyte proliferation, and increased numbers of CD8+ (19,20) and CD16+/56+ cells (19) in circulation. Adrenoreceptor blocking studies have also provided support for the coordination of cardiovascular and immune response. These studies demonstrate that laboratory stressor induced changes in mitogen-stimulated lymphocyte proliferation, natural killer cell activity, and numbers of circulating lymphocytes do not occur with inhibition of adrenergic stimulation of lymphocytes (16,22). In this study, we investigate whether reactivity across endocrine (epi, norepi, and cortisol), cardiovascular (HR and blood pressure [BP]), and immune (NK activity and lymphocyte subsets) response domains constitutes a unified psychobiological response or identifies individual differences in independent response modalities.

Finally, we are interested in the extent to which stable biological response to stressors might be mediated by stable psychological responses. Psychological stress theory (23) argues that the physiological changes associated with stress occur in response to the emotions that are elicited when stressors are appraised as threatening. Although there is evidence that manipulating emotions can alter a range of biological responses (e.g. 24–27), it is not clear that emotional response to acute stress in the laboratory is either highly correlated with or responsible for stress-induced biological responses (28). Acute stressor-induced increases in epi have been associated with concomitant increases in tenseness (29), while increases in cortisol have been associated with stress-induced increases in anxiety (11), boredom, impatience, tiredness, and irritation (29). We felt that these investigations had tapped two very different types of emotions—those that reflected the threat posed by stressors (e.g. anxiety and tenseness) and those that reflected the extent of engagement in the stressor task (e.g. boredom and impatience). It has been suggested that sympathetic nervous system activation in stress–reactivity tasks (even those specifically designed to elicit threat) may be driven less by threat than by task engagement (30). This is in contrast to the generally accepted view that these tasks primarily model threat-mediated responses to acute stressors (e.g. 28).

In the study we report in this article, we exposed the same participants to two versions of an evaluative speech task separated by 2 weeks. Our first goal was to assess the stability of individuals' cardiovascular (HR, SBP, DBP), immune (NK cell cytotoxicity and numbers of lymphocyte subsets), endocrine (epi, norepi, and cortisol), and psychological (anxiety and task engagement) responses to a psychological stressor across the two testing periods. The temporal stability of NK cell cytotoxicity and engagement response to stress had not been assessed before. We expected that these parameters would be stable over time. Moreover, we expected to replicate earlier evidence for test–retest stability in the case of BP and HR (5), select white blood cell populations (7,8), epi and norepi (13,14), anxiety (13), and cortisol (14,15).

Our second goal was to examine the interrelations between those responses that demonstrate trait-like (stable) characteristics. First, we expected that responsiveness in biological domains (cardiovascular, endocrine, and immune) would be moderately intercorrelated. Although some correlations have been reported in the past, none have included HPA response (cortisol) or examined natural killer cell cytotoxicity. Second, we expected that trait-like emotional responsivity would also be correlated with trait-like biological response. We thought that rises in anxiety would represent a stable disposition to respond to acute laboratory stressors with psychological threat, while task engagement would represent a stable disposition to respond with increased attention

and motivation. The relative contribution of these separate emotional responses provides a window to the psychological components of the reactivity paradigm that are responsible for biological changes induced by stressor task.

METHODS

Participants

Participants were solicited via electronic bulletin boards, school newspaper, and word of mouth to be part of a larger study entitled, "Stress Reactivity and Susceptibility to Upper Respiratory Infection." They were eligible to participate if they were aged 18–30 years, students of either the University of Pittsburgh or Carnegie Mellon University, had no infectious illness within 2 weeks of the session, no chronic illness, no personal history of cancer, no autoimmune disorders, no current or history of psychological disorder, consumed no more than 12 alcoholic beverages on average per week, did not use street drugs, and were not currently pregnant or lactating. One-hundred fifty-one people met these criteria. Of those potential participants, 115 (71%) participated. The main reason for nonparticipation was due to potential participants not showing for their scheduled appointments (85%); the remaining (15%) had difficulty with catheterization. The sample was 47% male, 53% female; 92% single; 76% Caucasian, 10% African–American, 7% Asian, 2% Hispanic, and 5% "other race"; and had a mean age of 21.11 years (SD = 2.66 years). Participants received $50 for participation in the two sessions.

Procedures

All participants attended two laboratory sessions, each lasting approximately 2 hours. The sessions, which were exactly 2 weeks apart, were scheduled at the same hour of the day (either 7:00 a.m. or 9:30 a.m.). Two weeks between testing was chosen for both practical and theoretical reasons. We thought it was long enough to provide a feel for reliability, but it was short enough so we could complete the study within a semester. Experimental procedures at the two testing sessions were nearly identical. Participants were asked to abstain from tobacco products, vigorous exercise, caffeine, and food or beverages (except water) for 8 hours before sessions and to abstain from over-the-counter medication for 24 hours before sessions. After obtaining informed consent and administering questionnaires to collect demographic, health, and personality information, participants were seated upright in a recliner and an occluding cuff was placed on the left arm for automated measurement of HR and blood pressure (Dinamap XL Vital Sign Monitor or Citikron Dinamap). Three cardiovascular measurements were taken to accustom subjects to the measurement procedure, and the details of the session were then explained. Next, an intravenous catheter was inserted into the antecubital fossa of the participant's right arm for collection of blood samples. Participants were then instructed to sit quietly for 30 minutes. Baseline cardiovascular measures were taken 25, 27, and 29 minutes into the rest period. At the conclusion of the rest period, the first 15 ml blood sample was taken for baseline immune and catecholamine (last 58 participants only) measures. Baseline emotion was also collected at this point.

A video camera was then placed approximately 2 feet in front of the subject and the task instructions were explained. As in Marsland et al. (7), participants were asked to perform a simulated public speaking task, consisting of 2 minutes preparation for a speech defending themselves against an alleged transgression (shoplifting or traffic violation), followed by 3 minutes of videotaped speech delivery. In the first situation, the transgression involved being wrongly accused of stealing a belt by a department store security guard; in the second, it involved being detained by a police officer for driving through a stop sign. The two transgression scenarios were counter-balanced across sessions. Cardiovascular measures were assessed every 90 seconds during speech preparation and performance, and a second 15 ml blood sample was collected 2 minutes into speech presentation to assess task-related immune and catecholamine (last 58 participants only) responses. Immediately after completing the speech, mood was assessed again and participants began the 20-minute recovery period. Because the maximal cortisol response occurs 20–30 minutes after stressor onset, the salivary cortisol[3] measure intended to assess the response to the speech was collected 15 minutes into the recovery period (approximately 22 minutes following the beginning of speech preparation). In order to obtain a baseline sample not influenced by anticipation of the laboratory task visit, the last 58 participants[4] also provided baseline salivary cortisol samples taken in a naturalistic setting 1 week after their laboratory visits. To control for the diurnal rhythm of cortisol, these samples were collected at the same interval between wake-up and sample collection as passed between wake-up and laboratory stress-induced sample collection (approximately 3 hours, although it varied between participants). Participants were informed to proceed with their usual days and to collect the sample at the appropriate time.

Measures

Emotion Measures: Participants were asked to rate "how they feel right now" after baseline and immediately posttask using 11 items from the anxiety (on edge, nervous, tense, uneasy), calm (at ease, calm, relaxed, comfortable), boredom (bored), and fatigue (sleepy, worn out) subscales of the Profile of Mood States (see 31). Each adjective was rated from 0 (*not at all*) to 4 (*extreme*). The 11 items (baseline data from the first task session) were entered into a varimax rotation factor analysis that resulted in two independent factors: anxiety and task engagement. Anxiety included the 8 items from anxious and calm (reversed) subscales. The factor loadings ranged from .52 to .80. Task engagement included the 3 items from the boredom and fatigue subscales (all reversed). The factor loadings ranged from .56 to .87. (The item "bored" was added in the second part [N = 58] of the study.) We view the anxiety factor as assessing threat posed by the task and the task engagement factor as assessing task interest and engagement.

Immune Assays: Enumerative assays were assessed in whole blood using dual color fluorescence analysis with a Becton Dickinson FACScan flow cytometer (San Jose, CA). Lymphocyte subsets were analyzed using monoclonal antibodies labeled with either fluorescein or phycoerythrin to quantify CD3+ (total T), CD3+CD4+ (T-helper), CD3+CD8+ (T-suppressor/cytotoxic),

[3] Saliva was used instead of blood for the determination of cortisol because it offers a less expensive, yet accurate reflection of blood cortisol levels (correlations in the literature frequently reach or exceed 0.9 [14]) and could easily be obtained by the participants in their homes for the nonvisit baseline measure.

[4] After preliminary analysis of the first 57 participants' cortisol data, we discovered that the cortisol sample intended to represent baseline levels (precatheterization) was higher than that of the sample taken to reflect task-induced increases, possibly reflecting anticipatory anxiety. Although there may have been similar sympathetic nervous system and immune responses at entering the lab, these responses are relatively short-lived (return to baseline in minutes), while cortisol rises continue for 30 minutes to an hour.

TABLE 1

Mean Values for Cardiovascular, Immune, Endocrine, and Psychological Parameters During Rest, Task, and Hemoconcentration-Adjusted Task (Immune Only) Conditions on Testing Sessions 1 and 2 (Standard Deviations in Parentheses)

	Session 1			Session 2		
	Rest	Task	Adjusted Task	Rest	Task	Adjusted Task
Systolic Blood Pressure (mmHg)	108 (9)	128 (15)		108 (10)	123 (15)	
Diastolic Blood Pressure (mmHg)	62 (7)	77 (10)		63 (7)	73 (10)	
Heart Rate (bpm)	64 (9)	80 (13)		64 (9)	78 (12)	
CD3+ (cells/mm^3)	1228 (388)	1291 (388)	1216 (346)	1302 (461)	1316 (429)	1283 (424)
CD4+ (cells/mm^3)	794 (252)	814 (248)	788 (244)	825 (292)	816 (265)	801 (270)
CD8+ (cells/mm^3)	447 (178)	592 (227)	564 (210)	469 (181)	536 (190)	525 (180)
CD19+ (cells/mm^3)	213 (107)	226 (126)	205 (100)	217 (112)	221 (115)	205 (88)
CD56+ (cells/mm^3)	139 (67)	335 (213)	319 (191)	130 (63)	251 (187)	225 (136)
Natural Killer Cell Cytotoxicity	39 (15)	72 (32)		39 (17)	59 (30)	
Epinephrine (pg/ml)	57 (19)	80 (31)		54 (17)	69 (23)	
Norepinephrine (pg/ml)	219 (67)	272 (79)		198 (58)	233 (63)	
Cortisol (nmol/l)	9 (5)	13 (6)			12 (7)	
Anxiety Factor	7.91 (4.85)	14.22 (5.44)		7.73 (4.74)	12.83 (4.88)	
Engagement Factor	7.04 (2.05)	9.75 (1.70)		6.79 (2.37)	9.21 (2.51)	

Note: Adjusted = adjusted for hemoconcentration.

CD3+CD19+ (B), and CD3−CD16+CD56+ (NK) cells. Absolute numbers of cells were calculated from a complete blood count. Pretask and task blood samples were assayed in the same batch on each occasion of testing.

A whole blood chromium^{51} release assay (32) was used to determine percent cytotoxicity to the NK-sensitive erythroleukemic K562 cell line. Pretask and task blood samples were assayed in the same batch.

Cortisol Assay: Saliva samples collected via Salivettes were centrifuged at 3000 rpm for 5 minutes and a 1 ml sample was obtained. Levels of salivary cortisol were determined via time-resolved immunoassay with fluorometric end point detection (DELFIA) and are expressed in units of nmol/l (12).

Catecholamine Assays: Blood samples were anticoagulated with EDTA, chilled, and centrifuged; plasma was then removed and frozen at −70°C until analysis. High performance liquid chromatography determinations of epi and norepi, following extraction with alumina, were conducted using a Phase II, reverse phase, 3-micron column. Peak catechol heights were measured automatically by Chromatochart-PC (BAS/IMI) and are expressed in pg/ml.

RESULTS

Missing Data

Home baseline salivary cortisol sample collections, laboratory catecholamine collections, and a single item of the task engagement scale (boredom) were added midway through data collection, and thus are only available for the last 58 participants. Participants' scores were excluded from any particular analysis in the study if their measure was greater than 2.5 standard deviations from the mean for that outcome (mean % lost across variables = 4.5%, *SD* = 2.5%). Other data were missing due to Dinamap error or blood clotting (mean % lost = 3.25%, *SD* = 2.8%). Number of participants included for each outcome is the following: cardiovascular = 102 (89% of 115); immune = 95 (83% of 115); endocrine = 50 (86% of 58); anxiety = 114 (99% of 115); and engagement = 52 (90% of 58).

Data Reduction

Baselines for each cardiovascular measure were calculated by averaging measures taken at 25, 27, and 29 minutes after catheterization. Values for cardiovascular response during the stressor task were similarly reduced by averaging over the two measurements taken during performance of the speech.

Changes in numbers of cells in circulation can be affected by cells moving in or out of circulation but can also be influenced by transient shifts in plasma volume. Because there is a decrease in the fluid content of blood (hemoconcentration) in response to stressors (33), we adjusted the number of lymphocytes under stress (in both sessions) for hemoconcentration and report these in addition to the unadjusted values. To adjust the numbers, we estimated percent change in plasma volume (%ΔPV) from changes in hemoglobin level and hematocrit (34). Then, adjusted task values (Xt − c) were calculated from simple task values (Xt) using the following formula: $Xt - c = Xt/[1 - (\%\Delta PV/100)]$ (33).

Effect of the Speech Tasks on Cardiovascular, Immune, Endocrine, and Mood Measures

Cardiovascular, lymphocyte subsets (both adjusted and unadjusted for hemoconcentration), NK cytotoxicity, epi, norepi, cortisol, and mood data were subjected to 2 ($Session_{first,second}$) × 2 ($Condition_{rest,task}$) repeated measures analyses of variance (ANOVAs). Means and standard deviations are presented in Table 1. A condition main effect was found for all variables except CD4+ lymphocytes (Table 2).

Across sessions, increases relative to baseline measures were found during the task for SBP; DBP; HR; CD3+, CD8+, CD19+, and CD56+ cell numbers; NK cell cytotoxicity; epi; norepi; cortisol; and anxiety and engagement. To be sure that the effect of the task on NK cytotoxicity was not merely due to the increase in NK cell number, NK cell number was added as a covariate in the analysis. The effect of the stress task on NK cytotoxicity remained, despite controlling for NK cell number ($F(1, 96) = 23.50, p < .01$).

Session main effects were significant for SBP, DBP, CD56+ cell number, NK cytotoxicity, epi, norepi, anxiety, and task engagement, reflecting overall decreases in these measures be-

TABLE 2

ANOVA Summaries and Test–Retest (i.e. Between-Sessions) Correlations for Baseline, Task, and Baseline-Adjusted (Residualized) Change Scores Both Unadjusted and Adjusted for Hemoconcentration

	ANOVA Summary			Correlations Between Sessions				
	F Stress Main Effect	*F* Session Main Effect	*F* Stress × Session	*r* Baseline	*r* Task	*r* Task (Adjusted)	*r*Δ Scores	*r*Δ Score (Adjusted)
Systolic BP (mmHg)	311.75**	14.49**	30.87**	.75**	.85**		.67**	
Diastolic BP (mmHg)	411.71**	11.65**	39.21**	.73**	.76**		.50**	
Heart Rate (bpm)	357.93**	1.57	5.44*	.63**	.72**		.64**	
CD3+ (cells/mm^3)	6.76*	2.35	4.94*	.71**	.60*	.60*	.24*	.26*
CD4+ (cells/mm^3)	..32	.73	2.62†	.75**	.63**	.65**	.04	.08
CD8+ (cells/mm^3)	81.23**	1.94	31.32**	.64**	.71**	.77**	.50*	.54**
CD19+ (cells/mm^3)	5.15*	.03	1.60	.77**	.78**	.68**	.08	.03
CD56+ (cells/mm^3)	92.91**	37.21**	32.09**	.63**	.76**	.69**	.69**	.63**
NK Cytotoxicity	143.59**	12.98**	26.75**	.56**	.67**		.52**	
Epinephrine (pg/ml)	100.55**	5.66*	4.17*	.51**	.23†		−.05	
Norepinephrine (pg/ml)	66.88**	9.37*	5.26*	.43**	.41*		.32*	
Cortisol (nmol/l)	15.56**			.50**			.37*	
Anxiety Factor	149.42**	6.34*	5.69*	.57**	.68**		.64**	
Engagement Factor	97.97**	4.33*	1.01	.67**	.68**		.59**	

Note: Δ = residual change, BP = blood pressure, NK = natural killer, Adjusted = adjusted for hemoconcentration.
† $p < .10$, * $p < .05$, ** $p < .001$.

tween Sessions 1 and 2 (refer to Tables 1 and 2). Session by Condition interactions were found for SBP; DBP; HR; CD3+, CD8+, and CD56+ cell number; NK cell cytotoxicity; epi; norepi; and anxiety, reflecting larger effects of the stressor in the first session (see Tables 1 and 2).

Temporal Stability in Cardiovascular, Immune, Endocrine, and Mood Responses

Correlations were calculated between corresponding measurements obtained at the two laboratory sessions to determine the stability (test–retest reliability) of each response measure. A higher correlation allows more confidence in the existence of stable individual responses. In calculating change scores, it is desirable to control for the possibility that a measure's value at baseline influences the magnitude of possible change. To control for this possibility, we computed residualized values that resulted from separate analyses of each session. In each case, we regressed responses to the stressor task onto corresponding baseline responses. We used these values as baseline-adjusted change scores for each cardiovascular, immune, endocrine, and mood variable.

Because there is disagreement about the appropriate way to analyze change scores, we also did all of the analyses using two other procedures. In one, we calculated the residuals in a pooled regression equation where each subject is entered into the equation twice, once for each session. We then calculated their residual scores for each session based on the single equation (instead of basing them on separate equations for each session). This procedure eliminates the possibility that any anomalies in data at either session (e.g. subjects with extreme scores) would bias the regression coefficients and hence the calculation of the residualized change scores. In another, we used raw difference scores. There were no substantial differences in results irrespective of the means of calculating difference scores, and hence we report only results based on residual change scores calculated in separate equations.

Correlation coefficients that reflect the stability of baseline, task, and residualized change scores across Sessions 1 and 2 are presented in Table 2. Correlations across sessions for stress-induced changes in enumerative immune response were significant except for CD4+ and CD19+ cells, and ranged from .24 to .69. Correlations based upon changes in enumerative immune values adjusted for hemoconcentration yielded similar results. Cross-session correlations for cardiovascular (range .50 to .67), emotion (.68 for both scales), NK cytotoxicity (.52), norepi (.32), and cortisol changes in response to stress (.37) were all significant at the .05 level. Epi response to the stressors was not stable across sessions (−.05).

General Psychophysiology Issue

We averaged the residualized change scores across the two sessions to create a stable reactivity measure for each of the response variables.[5] This procedure was limited to those responses that were both affected by the stress task (i.e. a main effect in Table 2) and exhibited reliability across visits (i.e. significant test–retest correlation). We removed CD3+ number from these analyses because the other enumerative immune outcomes were subsets of this variable. In addressing the general psychophysiological issue, we computed correlations within and between response domains (refer to Table 3).

All of the cardiovascular reactivity parameters correlated with each other and these correlations ranged from .49 to .77 ($ps < .01$). Because cardiovascular response and catecholamine response are both indicators of sympathetic nervous system (SNS) response, one could also view the correlations between cardiovascular and norepi responses as indicative of a single system response (see factor analyses below). Changes in norepi were, in fact, correlated between .38 and .45 ($ps < .05$) with the cardiovascular measures. The intraimmune reactivity parameter correlations were all significant as well, and ranged from .61 to .84 ($ps < .05$). Cortisol reactivity was moderately, but not significantly, correlated with norepi reactivity. The anxiety and engagement scales (which were intended as relatively independent factors) were marginally correlated ($p < .10$).

[5] Averaging across sessions might obscure specific interrelationships among reactivity measures during a given session. To address this issue, we ran correlations between the stable reactivity measures separately for Sessions 1 and 2. The matrices were virtually identical, suggesting comparable effects at both sessions.

TABLE 3

Correlations of Average Cardiovascular, Immune, Endocrine, and Mood Reactivities (Residual Change Scores) Across the Two Sessions, Correlations Within Domains are Boxed

	DBP	HR	NK % CYT	CD8#	CD56#	Norepi	Cortisol	Anxiety Factor	Engagement Factor
SBP	.77**	.54**	.60**	.49*	.66**	.43*	.39*	−.05	.46**
DBP		.49**	.50**	.34*	.53**	.45*	.34*	−.05	.51**
HR			.49**	.43**	.65**	.38*	.29*	−.04	.28*
NK % CYT				.61**	.84**	.45*	.20	.06	.37*
CD8#					.76**	.52**	.18	−.04	.30*
CD56#						.50**	.27*	.04	.34*
Norepinephrine							.13	−.10	.23†
Cortisol								−.21	.22
Anxiety Factor									.22†

Note: SBP = systolic blood pressure, DBP = diastolic blood pressure, NK % CYT = natural killer percent cytotoxicity, Norepi = norepinephrine.
** $p < .001$, * $p < .05$, † $p < .10$.

All cardiovascular and immune interdomain correlations were significant and ranged from .34 to .66 ($ps < .05$). All of the cardiovascular–endocrine interdomain correlations were significant, as well (range: .29–.45). All of the immune reactivity outcomes were correlated with norepi reactivity (range: .45–.52), while only CD56+ number reactivity was correlated with cortisol reactivity.

To further address the issue of intercorrelation between biological response domains, we created single variables to represent each domain. We had insufficient numbers of subjects (only 40) with data on all of the biological measures to conduct a single factor analysis entering all the variables. So we performed separate factor analyses (varimax rotation) within each reactivity domain. Our intention was to create reliable domain factors based upon the individual variables that had displayed adequate stability in terms of their response to the stressor tasks across sessions. Norepi loaded with the cardiovascular responses to form a single sympathetic nervous system factor (SBP .86, DBP .81, HR .72, and norepi .69) and the immune measures all loaded on a single immune system factor (NK .90, #CD56+ .95, #CD8+ .86). To create factor scores, we summed the standardized residualized change scores of each of the measures in a factor. Because we had only a single measure of HPA axis response, changes in cortisol were used to represent this system. We then correlated the three biological systems factors with each other. SNS response was highly correlated with immune response (.70, $p < .001$, $N = 102$), and moderately correlated with cortisol response (.34, $p < .02$, $N = 53$). Cortisol response was marginally correlated with immune response (.25, $p < .08$, $N = 51$).

Correlations Between Affect Response and Biological Response

As is apparent from Table 3, changes in anxiety in response to the stressors were not associated with changes in any of the individual biological responses. In contrast, stress-induced changes in task engagement were associated with greater stress-induced increases in SBP, DBP, HR, NK percent cytotoxicity, and numbers of CD8+ and CD56+ cells in circulation. Task engagement reactivity was also marginally associated with both increases in cortisol and norepi. We also correlated changes in each of the three biological factors (SNS, immune, cortisol) with changes in the two emotional factors. Again, changes in anxiety were not associated with any of the biological outcomes, while increased engagement was associated with increases in SNS (.43, $p < .001$), immune (.37, $p < .01$), and cortisol (same as individual cortisol in Table 3) factors.

DISCUSSION

The first question we raised was whether cardiovascular, immune, endocrine, and psychological responses to an acute laboratory stressor are stable over time. The answer is that there is considerable stability across sessions in all of the response domains. The stability coefficients for cardiovascular responses were strikingly similar to those reported by others (e.g. 5,7,35). In the case of immune responses, we were the first to assess the stability of NK cell cytotoxicity and found a moderate correlation across sessions with cytotoxicity rising in response to the acute stressor. Others have found stable stress-induced decreases in mitogen stimulated lymphocyte proliferation (7). In the case of white blood cell populations, we found quite stable increases in circulating CD8+ and CD56+ cells respectively, relations similar to those reported by Marsland et al. (7) and Mills et al. (8). Additionally, we replicated Mills et al.'s (8) finding concerning a stable increase in the number of CD3+ cells in circulation, although the correlation here was much smaller than found for other cell populations (.24). We did not replicate the stable decrease in CD19+ cells reported by Marsland.

We partially replicate past findings (13,14) of stable catecholamine response to acute stressors. Interestingly, although both epi and norepi are found to increase in response to the stressor tasks, only norepi was found to exhibit stability (moderate) in response over time. Because norepi responses are, in part, attributable to sympathoadrenal activation, one might expect that they would resemble those of cardiovascular measures. Less clear is why epi responses were not stable across sessions. Because epi is a clear marker of sympathetic activation and because two other studies in the literature (13,14) do find stability in epi response, we are puzzled by the lack of stability. It is possible, however, that the relatively small epi response to the stressor in the second session resulted in a truncated distribution, hence, attenuating any correlation. We also replicated Kirschbaum et al.'s (15) finding of the stable tendency for participants to exhibit an increase in salivary cortisol response to acute stressor tasks with a similar moderate correlation.

We replicate Mills and colleagues' (13) finding of stable anxiety response, and present the first data concerning the stability of engagement response to acute stressors. As expected, both anxiety and task engagement were found to increase in response to

stressor exposure. Interestingly, task engagement was one of the only variables for which the response to stress was not attenuated across sessions. It is not clear why engagement was maintained when anxiety (and all the physiological responses) were reduced. Possibly, the tasks were challenging enough to keep subjects engaged over both sessions. Most importantly, responses of both of the affect measures were very stable across testing sessions (.59 and .64). This stability is requisite for the hypothesis that influences of stress on physiological response in this paradigm are primarily driven by affect.

In sum, we found rather large test–retest correlations for stress response as assessed by cardiovascular, immune, and affect measures, and moderate correlations in regard to endocrine responses. On the one hand, the stability (trait-like characteristic) of all of these responses is probably somewhat overestimated, because we used different versions of the speech task at each testing instead of totally different tasks (see below). On the other hand, the weaker stability coefficients for immune and endocrine measures may be attributable to the fact that they are based on single samples at baseline and task assessments. In contrast, BP and HR are based on the average of multiple measures at both baseline and during the task, and affect is based on multiple item scales. It is likely that under more similar measurement conditions, endocrine and functional immune responses would look more equivalent to cardiovascular response.

These data support the hypothesis that cardiovascular, immune, and endocrine responses to acute stress are stable (dispositional) characteristics. This trait-like response is essential to hypotheses predicting the importance of reactivity for disease susceptibility (4). There is increasing evidence in support of such hypotheses including associations between greater cardiovascular reactivity and reports of minor illnesses such as colds, flu, infections, and diarrhea (36), and between cardiovascular reactivity and increased risk for heart disease (37). Both cardiovascular and immune reactivity (at least in terms of increased white blood cells in circulation) have also been associated with increased incidence of upper respiratory infections under stressful conditions (3). Although these data are provocative, continued work is needed to establish the conditions under which reactivity in different domains predicts subsequent incidence of different types of diseases. The use of more stable (multiple measure) assessments of reactivity would strengthen the quality of this literature.

The second question we raised is whether stable responses to stress that occur in different biological domains are interrelated. The answer is that there is a coordination of cardiovascular, immune, and endocrine response. The strongest ties are between SNS response (cardiovascular + catecholamines) and immune response. More moderate relations exist between cortisol and SNS response and between cortisol and immune response. However, as noted earlier, the use of a single (and hence lower in reliability) measure of cortisol likely attenuates correlations with other response domains.

The coordination in norepi, cardiovascular, and immune response is generally believed to occur because these reactivities stem from a common source. For example, there is evidence that sympathetic nervous system response drives the changes in immunity found in acute laboratory studies (e.g. 20,38). It is likely, however, that this relation is limited to certain types of immune response and that others may be more closely tied to activation of the hypothalamic–pituitary–adrenocortical axis and the consequent release of cortisol or to other mediating factors (39). Cortisol reactivity was associated with all three cardiovascular reactivities and with number of CD56+ cells, suggesting coordination of these responses. One reason that stress-induced changes in cortisol were not related to the other two stress-induced changes in immune outcomes (CD8+ cells and NK cytotoxicity) is that these increases in cortisol did not occur until 20 minutes after blood was taken for assessment of the stress immune outcomes. Consequently, stress-induced increases in cortisol could not act to influence (previously assessed) immune outcomes. Then, why would cortisol changes be related to CD56+ cell changes? We think that this is merely an artifact of the interrelation between sympathetic activation and the subsequent release of cortisol. In fact, in regressions where cardiovascular changes (each cardiovascular change score is entered in a separate regression) are entered before cortisol change, cortisol does not predict CD56+ changes (all $ps > .36$). On the other hand, when cortisol is entered first, the cardiovascular changes still predict changes in CD56+ cells (all $ps < .05$). These analyses suggest that cardiovascular change can account for the associations between stress-induced changes in cortisol and immunity.

Finally, we asked whether stable emotional response to acute stressors predicts stable biological response. Laboratory psychological stressors like public speaking are usually thought of as models of how threatening events elicit anxiety and, consequently, activation of various physiological systems. We found that participants reliably responded to the stressors with both increased anxiety and enhanced task engagement. Surprisingly, stress-induced changes in anxiety were not associated with any of the biological responses, while task engagement was associated with virtually all of the biological responses. The minimum we can say about our results is that, even in a task designed to provoke anxiety, engagement emotions seem to play a more important role. This raises serious questions about the extent to which laboratory "reactivity" tasks provide models of physiological response to the experience of threat and anxiety. Instead, they suggest that task effort, whether a product of the motivation to overcome the stressor or merely commitment to the study, is the primary psychological/behavioral concomitant of physiological response (40,41). These results also raise conceptual issues about what might trigger "stress-like" biological responses in the real world. For example, could it be that high levels of involvement in work or in social relationships elicit the same kinds of changes found in the laboratory?

Why did we not find associations between stress-elicited changes in anxiety and physiological response? It is possible that the kinds of acute stressors that we use in laboratory settings just do not elicit enough anxiety to drive physiological response. Public speaking is generally considered one of the most powerful threatening stressors in this setting. It is possible, however, that individual differences in the congruence between emotions and physiological response dampen this effect. For example, the correlation between anger (produced by harassment or conflict) and cardiovascular response has been found to be higher for those scoring high than those scoring low on a hostility scale (e.g. 42,43). Self-reports of emotion also vary across individuals, possibly attenuating congruence between anxiety and physiological responses. For example, Weinberger, Schwartz, and Davidson (44) found that a subset of people (called repressors) self-reported little anxiety, but physiologically displayed increases in heart rate and frontalis region electromyography (EMG), which would suggest that they were experiencing anxiety. Taking such individual differences into account might bring out otherwise undetected associations between anxiety and physiological response.

There are also characteristics of our study that might have dampened relations between anxiety and physiological responses. First, because we did not want to interfere with task performance, we assessed affect at the end (rather than during) the task. This "residual" affect is likely a less accurate marker of affect at the times the physiological measures were taken than the online measurement would have provided. There is also a specific problem with our attempt to associate stress-induced changes in affect (both anxiety and engagement) with cortisol. Although our baseline cortisol measure was taken outside of the laboratory, the baseline affect measure was taken in the laboratory. Because just entering the laboratory is potentially threatening to subjects, taking cortisol baselines in naturalistic settings can provide more valid baseline measurement. Similar arguments could be made about affect, and future work of this sort should include affect assessments in naturalistic settings as well.

Some limitations and words of caution must be stated. First, although participants completed the reactivity protocol on two occasions separated in time by 2 weeks, they performed a similar (speech) task both times. Further, these tasks were performed in a standardized laboratory setting on both occasions. Stability of cardiovascular reactivity has been found to vary according to the type of task used (45), as well as the setting in which the task is presented (46). Hence, the stability correlations we present may be overestimates of what would occur across more dissimilar situations. On a different note, the data on the association between task engagement emotions and physiological response are correlational. Consequently, we do not know whether engagement emotions are driving physiological response, physiological responses are driving engagement emotions (e.g. 47), or some unknown third factor is driving both. However, our data are consistent with increased sympathetic, HPA, and immune activation occurring in response to task engagement, but not to task-elicited anxiety.

In summary, we provide evidence of stability in behaviorally evoked psychological and physiological responses to similar evaluative speech tasks on two occasions, 2 weeks apart. These data provide validity for the existence of stable individual differences in reactivity within several response domains. We find evidence of a coordination of sympathetic, HPA, and immune response to stress and for the potential importance of stress-induced task engagement in eliciting these physiological responses. At the same time, we find that stress-induced anxiety did not play an important role in eliciting physiological response. Future research is needed to solidify the stability and intercorrelation issues, to identify emotions that might mediate physiological response to stress, and to explore the association of reactivity status and disease susceptibility.

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