Personality and Tonic Cardiovascular, Neuroendocrine, and Immune Parameters

Gregory E. Miller,*·†·[1] Sheldon Cohen,† Bruce S. Rabin,‡ David P. Skoner,‡·§
and William J. Doyle‡·§

*Western Psychiatric Institute and Clinic and †Carnegie Mellon University, Pittsburgh, Pennsylvania
15213; ‡University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15260;
and §Children's Hospital of Pittsburgh, One Children's Place, 3705 Fifth Avenue,
Pittsburgh, Pennsylvania 15213*

Although there is now abundant evidence that certain personality features constitute risk factors for negative health outcomes, personality measures have received little attention to date in the behavioral immunology literature. The present study assessed the relationship between major dimensions of personality and tonic cardiovascular, neuroendocrine, and immunologic parameters in 276 healthy adults. Participants who scored low in agreeableness tended to have higher levels of systolic blood pressure, diastolic blood pressure, and epinephrine. Low levels of extraversion were associated with higher blood pressure, epinephrine, norepinephrine, and natural killer cell cytotoxicity. Neuroticism was generally unrelated to physiologic outcomes. Personality was not associated with leukocyte subset counts. The magnitude of relationships between personality and physiology was modest, with personality measures accounting for 1 to 7% of the variance in selected physiological parameters. Health practices did not mediate associations between personality and physiologic outcomes. However, a substantial proportion of the relationship between extraversion and natural killer cell cytotoxicity was accounted for by their common association with epinephrine and to a lesser extent norepinephrine. These findings are consistent with the notion that personality contributes to basal physiology and provide a foundation for further research on the relationship between personality and natural killer cell cytotoxicity.   © 1999 Academic Press

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INTRODUCTION

Over the past 3 decades, an impressive collection of evidence has accumulated showing that individuals who possess certain personality features are at elevated risk for negative health outcomes. The strongest evidence for this phenomenon comes from studies of coronary heart disease, which have documented elevated rates of morbidity and mortality among patients who exhibit a constellation of personality characteristics known as cynical hostility (for reviews see Matthews, 1988; Miller et al., 1996). Other personality features that have been linked to objective health outcomes include pessimism/fatalism (Reed et al., 1994; Scheier et al., 1989), conscientiousness (Friedman et al., 1993), extraversion (Broadbent et al., 1984; Cohen et al., 1998; Totman et al., 1980), and interpersonal rejection sensitivity (Cole, Kemeny, Taylor, & Fahey, 1996).

Despite the promise that personality variables have shown in explaining health outcomes, they have received relatively little attention in behavioral immunology

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[1] To whom correspondence should be addressed at Department of Psychology, Carnegie Mellon University, Pittsburgh, Pennsylvania 15213. E-mail address: gmiller@andrew.cmu.edu.

research, where most studies have focused on immunologic changes that occur in response to acute laboratory stressors or more enduring stressful circumstances. This may be attributable to the theoretical frameworks that guide research in behavioral immunology, which downplay the contribution that individual difference variables make to health outcomes (see Cohen, Kessler, & Gordon, 1995; Keller et al., 1994). To address this problem, the present study explored how tonic cardiovascular, neuroendocrine, and immunologic parameters relate to three dimensions of personality that have proven important in previous studies of psychosocial factors and health. These personality dimensions are agreeableness, extraversion, and neuroticism.

Agreeableness is the dimension of personality that underlies interpersonal attitudes and behavior (Costa & McCrae, 1992). Individuals who fall toward the positive pole of this dimension are characterized as helpful, sympathetic, and trusting. Individuals who fall toward the negative pole are characterized as uncooperative, suspicious, and cynical. Although agreeableness has not been studied extensively in the context of health, correlational and factor analytic studies suggest that its negative pole reflects the personality feature of cynical hostility (Costa, McCrae, & Dembroski, 1989; Friedman, Tucker, & Reise, 1995), which has been defined as a set of ''negative attitudes, beliefs, and appraisals concerning others . . . as frequent and likely sources of mistreatment, frustration, and provocation'' (Smith, 1992, p. 139). Compared to their nonhostile peers, hostile individuals have higher ambulatory blood pressure and higher levels of epinephrine, norepinephrine, and cortisol during daily life (Jamner et al., 1991; Pope & Smith, 1991; Suarez & Blumenthal, 1991) and exhibit more pronounced cardiovascular and neuroendocrine responses to psychological stress (Suarez et al., 1998). These exaggerated physiologic responses are thought to predispose hostile individuals to premature mortality from cardiovascular as well as other causes (for reviews see Matthews, 1988; Miller et al., 1996). Based on the assumption that cynical hostility is a component of the higher order personality dimension of agreeableness, we expected that participants in the present study who were low in agreeableness would show physiological profiles similar to those found among high hostile individuals. That is, to the extent that they reported low agreeableness, we expected participants to exhibit higher basal levels of blood pressure, heart rate, catecholamines, and cortisol.

Our predictions about how agreeableness would relate to immune parameters were somewhat more tentative, however, given the scarcity of data linking personality to immunity. We derived two competing predictions in this regard. The first was that participants who were low in agreeableness would show greater numbers of circulating natural killer cells and higher natural killer cell cytotoxicity. This prediction was based on the assumption that disagreeable individuals would have higher circulating concentrations of epinephrine and norepinephrine, which in turn would selectively mobilize natural killer cells into the circulation and upregulate their function. A number of laboratory studies have demonstrated that epinephrine can have this effect acutely (Bachen et al., 1995; Benschop et al., 1994, 1997; Schedlowski et al., 1993). The competing prediction was that individuals who endorsed low levels of agreeableness would have fewer circulating natural killer cells and diminished natural killer cell cytotoxicity. This prediction was based on the assumption that chronically high circulating catecholamine levels would lead to a downregulation of adrenergic receptor function on natural killer cells, through decreases in receptor density, binding

affinity, or receptor sensitivity. Such a downregulation could lead to a decrease in circulating natural killer cells and diminished natural killer cell cytotoxicity. This prediction would be consistent with studies showing that chronic psychological stress is associated with decrements in natural killer cell cytotoxicity (e.g., Esterling, Kiecolt-Glaser, Bodnar, Glaser, 1994; see Herbert & Cohen, 1993, for a review) and with studies showing that adrenergic receptor function on lymphocytes is downregulated among individuals high in cynical hostility (Suarez et al., 1997).

Extraversion is the personality dimension that reflects an individual's preferences for social settings (Costa & McCrae, 1992). Eysenck (1967) argued that individuals who are low in extraversion find social interactions to be aversive because they have a relatively low threshold for activation of the ascending reticular activating system (ARAS), which mediates diffuse autonomic nervous system arousal. He argued further that extraverted individuals have a higher threshold for activation of the ARAS, such that they find a given level of social interaction less physiologically arousing than their less extraverted counterparts. Studies examining basal physiological differences between extraverts and introverts have yielded mixed results, with some studies showing that individuals low in extraversion are characterized by higher resting levels of electrocortical and sympathetic nervous system activity and others showing null findings (for reviews, see Geen, 1997; Stelmack & Geen, 1992). We predicted that in the present study, extraversion would be associated with greater activation of the sympathetic nervous system and the hypothalamic–pituitary–adrenal axis. That is, we expected that participants who described themselves as low in extraversion would exhibit higher levels of blood pressure, heart rate, epinephrine, norepinephrine, and cortisol. With respect to the immune parameters, there is a paucity of data linking extraversion to the immune system. We therefore derived two competing predictions about how extraversion would relate to immune parameters. These predictions parallel those described above for agreeableness.

The personality dimension of neuroticism reflects an individual's propensity to experience negative emotional states such as anxiety, depression, and anger (Costa & McCrae, 1992). Although individuals who are high in neuroticism report more somatic complaints than their emotionally stable peers, they do not show different profiles on more objective, biological markers of disease. This has been demonstrated in numerous studies of healthy individuals (Watson & Pennebaker, 1989) and in the context of coronary heart disease (Costa, 1987) and upper respiratory infection (Cohen et al., 1995). Given that neuroticism functions as more of a marker of somatic sensitivity than a predictor of objective health outcomes (Watson & Pennebaker, 1989), we hypothesized that it would be unrelated to cardiovascular, neuroendocrine, and immunologic parameters in the present study.

A second goal of the present study was to identify potential mediators of the relationship between personality and cardiovascular, neuroendocrine, and immunologic parameters. We were particularly interested in determining whether epinephrine, norepinephrine, or cortisol could account for the relationship between personality dimensions and immune parameters. We hypothesized that epinephrine and norepinephrine would emerge as statistical mediators of any relationship between personality and natural killer cell numbers or cytotoxicity. Because the personality dimensions examined in this study have been linked to health practices that could conceivably influence basal physiology (e.g., Lipkus et al., 1994; Vingerhoets et al., 1990), we also explored

whether these practices could explain any associations documented between personality and cardiovascular, neuroendocrine, or immunologic parameters.

METHODS

Participants

Two-hundred seventy-six participants were recruited from the Pittsburgh, Pennsylvania, area through advertisements in local newspapers. The sample was composed of 125 men (45%) and 151 women (55%). Participants ranged in age from 18 to 55 years, with an average of 29.13 years (SD = 9.08). Twenty percent of the participants had completed a high school education or less, 58% had completed some college, and 22% had been awarded a bachelor's degree or higher. The ethnic breakdown of the sample was 81.2% Caucasian, 15.2% African-American, 2.2% Asian-American, and 1.4% Hispanic. Participants were paid $800 upon completion of the study.

Procedures

As part of a larger study investigating psychosocial factors and susceptibility to upper respiratory infection (Cohen et al., 1997, 1998), all participants underwent a medical eligibility screening that consisted of a physical examination and laboratory testing. Candidates were excluded from participation if they (a) reported a history of asthma, cardiovascular disease, or nasal/otologic surgery, (b) were infected with the human immunodeficiency virus, (c) were currently pregnant or lactating, (c) were on a regular medication regimen other than oral contraceptives, (d) had abnormal laboratory findings on complete blood count, urinalysis, or blood enzymes, or (e) showed nutritional deficiencies on any of three nutritional markers (albumin, transferrin, or retinol binding protein). Also, during the eligibility screenings, information regarding participants' demographic characteristics, health behavior practices, and height and weight data were collected.

Participants who met the medical eligibility criteria returned to the hospital 4 and 5 weeks later. On both occasions they completed personality measures and provided blood samples. The blood samples were used to measure plasma cortisol levels, circulating numbers of leukocyte subsets, and natural killer cell cytotoxicity. These sessions were scheduled for the morning hours to control for diurnal variations in immune parameters. Blood samples were collected under resting conditions, such that participants had sat quietly for a 30-min adaptation period before blood was drawn.

One week later participants entered quarantine. Nasal examinations and washes were conducted within 24 h of admission. Participants who showed evidence of concurrent viral infection were excluded from further participation. During this time participants also provided 24-h urine samples which were used to assess levels of epinephrine, norepinephrine, and cortisol. Twenty-four hours into the quarantine period participants were administered nasal drops containing one of two rhinoviruses. For the next 5 days, they were monitored for the development of symptoms and signs of upper respiratory infection (for additional details, see Cohen et al., 1997). Throughout the quarantine period, blood pressure and heart rate were measured each morning using an automated blood pressure monitor. Blood pressure and heart rate readings were collected following a 20-min rest period during which participants sat quietly.

Measurement of Psychosocial Parameters

Personality. Three dimensions of personality were assessed in the present study: agreeableness, extraversion, and neuroticism. This was accomplished using 30 items (three 10-item scales) based on Goldberg's (1992) adjectives. The scales showed high levels of internal consistency, with Cronbach's αs for the dimensions ranging from .79 to .87. Because participants completed the personality measure on two occasions, the average of the two assessments was utilized. Correlations between the subscales at the two administrations were high: .84 for agreeableness, .86 for extraversion, .79 for neuroticism.

Health practices. We assessed several health practices that could explain an association between personality measures and cardiovascular, endocrine, and immune parameters. These included smoking, alcohol consumption, exercise, sleep, and body mass index. Participants were classified as smokers or nonsmokers based on whether they reported smoking cigarettes, cigars, or pipes on a daily basis (Cohen, Tyrell, Russell, Jarvis, & Smith, 1993). Alcohol use was assessed by calculating the average number of alcoholic drinks an individual had reported consuming per day over the previous week. A drink was considered a bottle or can of beer, a glass of wine, or a shot of hard liquor (Cohen et al., 1993). Exercise was measured by participants' reports of the number of times per week a participant engaged in an activity long enough to work up a sweat, get the heart thumping, or get out of breath (Paffenbarger, Blair, Lee, & Hyde, 1993). Sleep habits were assessed with the sleep efficiency scale of the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Sleep efficiency is defined as the proportion of time in bed a participant spends sleeping. Body mass index was computed as weight in kilograms divided by the square of the participant's height in meters.

Measurement of Biological Parameters

Cardiovascular parameters. Blood pressure and heart rate were assessed each morning of the quarantine using an automated blood pressure monitor (Marshall TM94). To create indices reflecting tonic cardiovascular parameters, blood pressure and heart rate values were averaged across the quarantine period. Ten participants had missing blood pressure data from at least 1 day of the quarantine and 23 had missing heart rate data. In no case was a subject missing more than three data points. To preserve statistical power, blood pressure and heart rate indices were computed using available data points. (A reanalysis excluding subjects with any missing data points did not alter any of our substantive conclusions.) All three cardiovascular parameters—systolic blood pressure, diastolic blood pressure, and heart rate—were stable across the 6 days of quarantine (Cronbach's αs = .87, .87, and .86, respectively).

Because the cardiovascular data were collected in the days following viral challenge, it was possible that any relationship documented between personality and cardiovascular parameters was inflated or spurious. In other words, an association could have arisen because participants with certain personality characteristics (e.g., low extraversion or agreeableness) showed greater cardiovascular changes in response to illness or infection. To examine this possibility, we compared participants who did and did not develop clinical colds on the three cardiovascular parameters. Participants

who developed a cold did not differ from participants who did not develop a cold with respect to systolic blood pressure [M = 115.91, SD = 11.31 versus M = 117.13, SD = 10.36; $t(274) = 0.90$, $P = .37$]. The cold and noncold groups also did not differ with respect to diastolic blood pressure [M = 72.77, SD = 8.73 versus M = 73.77, SD = 8.32; $t(274) = 0.95$, $P = .34$]. However, participants who developed a cold showed higher heart rates (M = 77.91; SD = 9.25) than participants who did not (M = 74.57; SD = 10.52), $t(274) = -2.70$, $P = .006$. We also examined whether cardiovascular parameters differed as a function of whether participants became infected with the experimental virus. These analyses revealed no differences in tonic cardiovascular parameters between infected and noninfected participants, all ts < 1.00. On the basis of these findings, we statistically controlled for participants' cold status in all analyses involving heart rate.

Neuroendocrine parameters. Epinephrine, norepinephrine, and cortisol were measured in 24-h urine samples collected during the first day of quarantine and prior to viral exposure. Catecholamine assays were performed at the Clinical Analytical Laboratory of the University of Pittsburgh School of Medicine using high-performance liquid chromatography with electrochemical detection. The interassay coefficients of variation were 1.49 and 3.49% for norepinephrine and epinephrine, respectively. Cortisol assays were performed using a double antibody competitive radioimmunoassay at the Clinical Chemistry Laboratory of the University of Pittsburgh School of Medicine. The interassay coefficient of variation was 10%.

Immune parameters. Blood for immunologic measures was drawn 1 and 2 weeks prior to quarantine. Immunologic assays were performed at the Immunologic Monitoring and Diagnostic Laboratory of the University of Pittsburgh School of Medicine. Leukocyte subsets were enumerated using a complete blood count with differential and flow cytometry with three-color immunofluorescence (see Kirkwood et al., 1997). We assessed total white blood cells, as well as circulating numbers of total T lymphocytes ($CD3^+$), helper T lymphocytes ($CD3^+/CD4^+$), cytotoxic/suppressor T lymphocytes ($CD3^+/CD8^+$), B cells ($CD19^+$), and natural killer cells ($CD3^-/CD16^+/CD56^+$). Cell counts were averaged across the two blood draws. Correlations between the two assessments were high (average $r = .78$; range .62–.82, $P < .001$).

Natural killer cell cytotoxicity was measured using a whole blood assay at effector to target cell ratios of 100:1, 50:1, 25:1, and 12.5:1 (Fletcher, Baron, Ashman, Fischl, & Klimas, 1987). To assess the reliability of the natural killer cell cytotoxicity assay, duplicate blood samples were collected from 60 participants and submitted to the laboratory for analysis. Laboratory technicians were blind to this procedure. Values derived from the duplicate samples were highly correlated, $r = .92$, $P < .001$. In order to obtain a maximally reliable assessment of basal natural killer cell cytotoxicity, values obtained from the two blood draws were averaged. The association between cytotoxicity measures at the two blood draws was $r = .50$, $P < .001$. Values were expressed in cytotoxicity units.

RESULTS

Our first step was to examine the distributions of all variables for departures from normality. This was accomplished by inspecting histogram plots for each variable and computing skew and kurtosis statistics. These procedures revealed normally distributed personality and cardiovascular data. However, the majority of the neuroendocrine and immunologic variables were distributed in a leptokurtic fashion. To address

TABLE 1
Descriptive Statistics for Personality, Health Practice, and Physiological Measures

Measure	Mean	SD
Personality measures		
Agreeableness (0–40)	27.85	6.53
Extraversion (0–40)	28.30	5.29
Neuroticism (0–40)	28.53	5.63
Health practices		
Percentage of smokers	34.40	—
Average number of alcoholic drinks per day, past week	1.14	2.42
Average number of exercise episodes per week	2.55	2.39
Sleep efficiency (percentage of time in bed spent asleep)	0.90	0.11
Body Mass Index	25.63	5.16
Cardiovascular parameters		
Systolic blood pressure (mmHg)	116.13	10.25
Diastolic blood pressure (mmHg)	73.18	8.37
Heart rate (BPM)	75.62	10.14
Neuroendocrine parameters		
Urinary epinephrine (μg/total volume)	4.36	2.54
Urinary norepinephrine (μg/total volume)	31.91	14.80
Urinary cortisol (μg/total volume)	36.33	24.48
Plasma cortisol (μg/dl)	16.41	8.04
Immunologic parameters		
White blood cell count	6340	1715
T lymphocytes (CD3$^+$)	1360	390
Helper T lymphocytes (CD3$^+$/CD4$^+$)	670	230
Cytotoxic T lymphocytes (CD3$^+$/CD8$^+$)	350	130
B cells (CD19$^+$)	270	140
Natural killer cells (CD3$^-$/CD16$^+$/CD56$^+$)	85	38
Natural killer cell cytotoxicity (cytotoxicity units)	56.68	23.32

Note. $N = 276$. Leukocyte counts are expressed as cells/mm^3 of peripheral blood.

this problem, we performed log 10 transformations on all neuroendocrine and immunologic data. Although these transformations helped to normalize distributions, when correlations were computed between personality and biological measures, only negligible differences in results emerged between the transformed versus raw data. We therefore elected to present the neuroendocrine and immune data in their raw form. Means and standard deviations for personality, health practice, and physiological variables are presented in Table I.

Preliminary Analyses

Preliminary analyses revealed that the three dimensions of personality were intercorrelated. Participants who described themselves as high in agreeableness tended to endorse higher levels of extraversion, $r(276) = .28$, $P < .001$, and lower levels of neuroticism, $r(276) = -0.43$, $P < .001$. Extraverted individuals described themselves as low in neuroticism, $r(276) = -0.38$, $P < .001$. Compared to male participants, female participants endorsed higher levels of agreeableness [M = 32.88, SD = 5.14 versus M = 30.98, SD = 4.21; $t(274) = -3.37$, $P = .001$] and lower levels of extraversion [M = 26.14, SD = 6.57 versus M = 29.96, SD = 6.17; $t(274) = 4.05$, $P = .0001$]. No gender differences emerged with respect to neuroticism ($t <$

1.00). Independent-samples *t* tests comparing Caucasian and non-Caucasian partici-
pants with respect to personality dimensions yielded no significant differences ($ts <$
1.60, $Ps > .10$). Finally, no significant correlations emerged between the three per-
sonality dimensions and age or years of education, $Ps > 10$.

Personality and Cardiovascular, Neuroendocrine, and Immune Parameters

To examine the relationship between personality and cardiovascular, neuroendo-
crine, and immune parameters, we computed a series of Pearson correlations between
the personality dimensions of agreeableness, extraversion, and neuroticism and physi-
ological outcome measures. Tests of significance were two-tailed with α set at .05.
Given these constraints and a sample size of 276, Pearson correlation coefficients
with an absolute value of greater than or equal to .117 reached statistical significance.

Participants who scored low in agreeableness tended to have higher systolic blood
pressure, $r(276) = -0.12$, $P = .05$, diastolic blood pressure, $r(276) = -0.12$, $P =$
.05, and urinary epinephrine, $r(275) = -0.13$, $P = .04$. Agreeableness was not asso-
ciated with heart rate, norepinephrine, or cortisol levels (all $Ps > .15$). Agreeableness
was not associated with circulating numbers of leukocytes (total white blood cells,
total T lymphocytes, CD4$^+$ T lymphocytes, CD8$^+$ T lymphocytes, natural killer cells,
or B cells) or with natural killer cell cytotoxicity (all $Ps > .17$).

Participants who scored low in extraversion showed higher systolic blood pressure,
$r(276) = -0.17$, $P = .005$, and higher diastolic blood pressure, $r(276) = -0.17$, $P =$
.005. Low extraversion also was associated with higher levels of urinary epinephrine,
$r(275) = -0.26$, $P = .0001$, and norepinephrine, $r(275) = -0.17$, $P = .005$, with
higher numbers of total white blood cells, $r(275) = -0.12$, $P = .04$, and with greater
natural killer cell cytotoxicity, $r(276) = -0.14$, $P = .02$, even when numbers of
circulating natural killer cells were partialled out, partial $r(275) = -0.13$, $P = .04$.
Contrary to expectations, low extraversion also was associated with lower plasma
cortisol levels, $r(276) = .17$, $p = .004$. Extraversion was not associated with heart
rate or urinary cortisol ($Ps > .45$). It also was not related to circulating numbers of
total white blood cells, total T lymphocytes, CD4$^+$ T lymphocytes, CD8$^+$ T lympho-
cytes, natural killer cells, or B cells (all $Ps > .50$).

Participants who reported high levels of neuroticism tended to have higher plasma
cortisol levels, $r(276) = .18$, $P = .002$. Neuroticism was not associated with blood
pressure, heart rate, urinary cortisol, or epinephrine and norepinephrine levels. It also
was not associated with circulating numbers of leukocytes (total white blood cells,
total T lymphocytes, CD4$^+$ T lymphocytes, CD8$^+$ T lymphocytes, natural killer cells,
or B cells) or with natural killer cell cytotoxicity.

Extraversion, Natural Killer Cell Cytotoxicity, and Neuroendocrine Levels

Our next step was to determine whether epinephrine, norepinephrine, or cortisol
levels could account for the relationship between extraversion and natural killer cell
cytotoxicity. To accomplish this, we followed the recommendations of Stone (1992)
for identifying *statistical* mediation. Stone describes three criteria that need to be
met for data to be consistent with a mediational model. First, the predictor variable
(in this case personality) must be associated with the proposed mediator (in this case
neuroendocrine levels). Second, the predictor variable must be associated with the
outcome variable (in this case natural killer cell cytotoxicity). Third, the magnitude

of the association between the predictor variable and the outcome variable must be substantially reduced when the proposed mediator is statistically controlled.

Epinephrine met all three criteria for statistical mediation. Participants who scored low in extraversion tended to show higher epinephrine levels. They also tended to exhibit higher natural killer cell cytotoxicity. Finally, when epinephrine levels were statistically controlled, the relationship between extraversion and natural killer cell cytotoxicity diminished in magnitude, partial $r(274) = -0.10$, $P = .09$.

To determine how much of the relationship between extraversion and natural killer cell cytotoxicity could be explained by a model including epinephrine, we calculated the percentage of variance in natural killer cell cytotoxicity accounted for by extraversion after controlling for epinephrine ($R^2 = -0.10^2 = .01$). This value was divided by the percentage of variance in natural killer cell cytotoxicity accounted for by extraversion alone ($R^2 = -0.14^2 = .0196$). One minus the ratio of these two values was equal to .49, suggesting that almost one-half of the relationship between extraversion and natural killer cell cytotoxicity was attributable to their common link with epinephrine.

Norepinephrine also met criteria for statistical mediation. Participants who were low in extraversion had higher norepinephrine levels. They also exhibited greater natural killer cell cytotoxicity. When norepinephrine levels were statistically controlled, the relationship between extraversion and natural killer cell cytotoxicity was reduced, partial $r(274) = -0.12$, $P = .05$. Norepinephrine explained a smaller proportion of the relationship between extraversion and natural killer cell cytotoxicity than epinephrine, however. The calculations described in the preceding paragraph revealed that it accounted for approximately one-fourth of this relationship.

Plasma cortisol did not emerge as a mediator of the relationship between extraversion and natural killer cell cytotoxicity. Although participants low in extraversion exhibited lower plasma cortisol levels, and had higher natural killer cell cytotoxicity, statistical controls for cortisol did not alter the magnitude of the association between extraversion and natural killer cell cytotoxicity, partial $r(274) = -0.14$, $P = .02$.

A model that simultaneously controlled for levels of all three stress hormones accounted for slightly more of the association between extraversion and natural killer cell cytotoxicity than models which controlled for any of the individual hormones alone. The correlation between extraversion and natural killer cell cytotoxicity, controlling for epinephrine, norepinephrine and cortisol, was partial $r(271) = -0.09$, $P = .12$. Cumulatively, then, the three stress hormones accounted for approximately 59% of the relationship between extraversion and natural killer cell cytotoxicity.

Personality, Health Practices, and Physiological Parameters

Next we determined whether any of the health practice variables—smoking, alcohol consumption, exercise, body mass index, or sleep habits—could account for the relationship between personality dimensions and physiological parameters. To accomplish this, we again followed Stone's (1992) recommendations for statistical mediation. Personality variables were used as predictors, health practice variables as potential mediators, and physiological variables as outcomes. Regression equations were computed only in those cases where personality had already been identified as a significant correlate of a cardiovascular, neuroendocrine, or immune parameter.

These analyses indicated that health practices did not explain the relationship between agreeableness and systolic blood pressure, diastolic blood pressure, and epi-

nephrine. This was evident when we tested Stone's first criterion for mediation and found that agreeableness was not associated with any of the four health practices (all Ps > .15).

Health practices also did not account for the relationship between extraversion and basal physiological parameters. Participants who scored low in extraversion did tend to have worse health practices—they were more likely to be smokers, β = .20, P = .002, exercised less, $r(276)$ = .17, P = .004, and had poorer sleep efficiency, $r(276)$ = .20, P = .001. As noted above, lower extraversion scores also were associated with higher systolic blood pressure, diastolic blood pressure, epinephrine, norepinephrine, and natural killer cell cytotoxicity. However, when partial correlations were computed controlling simultaneously for participants' smoking, exercise, and sleep habits, none of the associations between extraversion and a physiological outcome measure was attenuated.

The health practice variables also did not account for the relationship between neuroticism and cortisol. Participants high in neuroticism were more likely to smoke, β = .05, P = .05, and have poor sleep efficiency, $r(276)$ = .16, P = .08. And as noted above, neuroticism was associated with higher plasma cortisol levels. Nonetheless, the associated between neuroticism and cortisol was not diminished when health practices were statistically controlled, partial $r(274)$ = .19, P = .001.

Sociodemographic Variables

To rule out the possibility that sociodemographic characteristics inflated the relationship between personality and physiological outcome measures, we recomputed all correlations between personality dimensions and cardiovascular, neuroendocrine, and immunologic parameters, statistically controlling for participants' age, gender, ethnicity (Caucasian vs non-Caucasian), and educational status (High school diploma or less vs Some college vs Bachelor's degree or higher). Controls for these sociodemographic variables did not diminish any of the relationships between extraversion and tonic physiological parameters described above. These controls also did not attenuate the relationships between agreeableness and systolic blood pressure, diastolic blood pressure, and epinephrine. The only exception to this was gender, which reduced the magnitude of the relationships between agreeableness and systolic blood pressure (partial r = −0.09, P = .11), diastolic blood pressure (partial r = −0.07, P = .26), and epinephrine (partial r = −0.09, P = .14).

DISCUSSION

We hypothesized that participants who were low in agreeableness would exhibit higher blood pressure, heart rate, catecholamines, cortisol, and natural killer cell cytotoxicity. Partial support was found for this hypothesis. To the extent that they scored low in agreeableness, participants evidenced higher tonic levels of systolic blood pressure, diastolic blood pressure, and epinephrine. These findings are consistent with previous investigations showing higher ambulatory blood pressure and basal catecholamine levels among individuals high in cynical hostility (Jamner et al., 1991; Suarez & Blumenthal, 1991). However, it bears noting that a portion of the relationship between agreeableness and tonic physiology was attributable to these variables' common association with gender. In other words, the relationship between agreeableness and physiology may have arisen because male participants tended to score low in agreeableness and have higher levels of systolic blood pressure, diastolic blood

pressure, and epinephrine. It is not clear why no association emerged between agree-ableness and circulating leukocyte subsets counts or natural killer cell cytotoxicity. On the basis of their higher tonic levels of sympathetic nervous system activity, one might expect individuals who are low in agreeableness to show alterations in subset counts or natural killer cell cytotoxicity. On the other hand, previous studies have had little success in documenting a direct relationship between cynical hostility and immunity (see Miller et al., 1998; Christensen et al., 1996).

Our second hypothesis was that participants who were low in extraversion would exhibit higher levels of blood pressure, heart rate, catecholamines, and cortisol. This hypothesis received clear support. To the extent that they scored low in extraversion, participants evidenced higher systolic blood pressure, diastolic blood pressure, epinephrine, norepinephrine, and natural killer cell cytotoxicity. These findings replicate previous work showing that individuals who are low in extraversion are characterized by greater tonic sympathetic nervous system activity (see Eysenck, 1967; Geen, 1997; Stelmack & Geen, 1992). They extend this work by showing that low extraversion also is associated with higher basal natural killer cell activity. The magnitude of this relationship was fairly small—extraversion accounted for less than two percent of the variability in natural killer cell cytotoxicity. Extraversion was not associated with circulating numbers of natural killer cells or other leukocyte subsets.

The mechanisms by which extraversion comes to be associated with basal natural killer cell cytotoxicity are not fully understood. We can rule out the possibility that this effect was secondary to increased numbers of circulating natural killer cells. Extraversion was unrelated to natural killer cell counts, and the relationship between extraversion and cytotoxicity persisted even when numbers of natural killer cells were statistically controlled. Our mediational analyses, discussed in more detail below, are consistent with the possibility that the catecholamines epinephrine and norepinephrine operate as a pathway through which extraversion and natural killer cell cytotoxicity become associated. It is possible that individuals who are low in extraversion show higher basal catecholamine levels because they find day to day social interactions more arousing than their highly extraverted peers. Higher circulating catecholamine levels may in turn heighten natural killer cell cytotoxicity. This process would be consistent with epinephrine infusion studies (Schedlowski et al., 1993) and with studies showing adrenergic receptor-mediated increases in natural killer cell cytotoxicity during acute psychological stress (Bachen et al., 1995; Benschop et al., 1994, 1997). It would not be consistent with the chronic stress literature, however, which consistently demonstrates that prolonged psychological stress is associated with decrements in natural killer cell cytotoxicity (e.g., Esterling, Kiecolt-Glaser, Bodnar, Glaser, 1994; see Herbert & Cohen, 1993, for a review). It is not clear to us why personality relates to natural killer cell function in a way that is more consistent with the effects of acute stress than the effects of chronic stress.

Our third hypothesis was that neuroticism would be unrelated to the cardiovascular, neuroendocrine, and immunologic parameters assessed in the present study. The data were generally consistent with this hypothesis. Neuroticism was associated with higher levels of plasma cortisol, but not with blood pressure, heart rate, catecholamine levels, leukocyte subset counts, or natural killer cell cytotoxicity. Although we do not have any data that would help to explain why participants who were high in neuroticism tended to show greater plasma cortisol levels, we can offer some speculation. It is possible that neurotic individuals experienced greater psychological distress

in anticipation of the blood draw than their more emotionally stable counterparts, which raised their circulating cortisol level. It is also possible that the chronic dysphoria associated with neuroticism could result in higher tonic levels of cortisol. More generally, however, these findings provide support for the notion that neuroticism's relationship to health outcomes is mediated through increased symptom reporting and/or somatic sensitivity and not through modification of biological mediators of disease (Costa, 1987; Cohen et al., 1995; Watson & Pennebaker, 1989).

Our fourth hypothesis was that a portion of the relationship between personality and natural killer cell cytotoxicity could be accounted for by a model that included epinephrine and norepinephrine. The data were consistent with this hypothesis. Statistical models indicated that epinephrine accounted for approximately 50% of the association between extraversion and natural killer cell cytotoxicity. Norepinephrine levels accounted for approximately 25% of this relationship. These data are consistent with the notion that epinephrine, and to a lesser extent norepinephrine, mediates the relationship between low extraversion and greater natural killer cell cytotoxicity. However, it is important to note that these data are not causally demonstrative of mediation. Such a demonstration would require experimental manipulations of the proposed mediator, similar to what has been performed in studies of short-term laboratory stress and immunity (e.g., Bachen et al., 1995; Benschop et al., 1994). The mediational analyses also indicated that cortisol could not account for the relationship between extraversion and natural killer cell cytotoxicity. This suggests that cortisol may play a less prominent role than epinephrine and norepinephrine in mediating the relationship between personality and natural killer cell cytotoxicity. It is possible that cortisol mediates relationships between other psychosocial factors and immune parameters. However, we are unaware of studies which provide direct evidence that cortisol plays this role in humans.

Our final hypothesis was that health practices would explain the relationship between personality and tonic cardiovascular, neuroendocrine, and immunologic parameters. We did not find any support for this hypothesis. None of the health practice variables that were examined—smoking, alcohol consumption, sleep efficiency, body mass index, or physical activity—could account for the associations between personality and physiological parameters. It is not clear why this occurred. Other analyses from this dataset have demonstrated that the health practice measures are reliable predictors of susceptibility to upper respiratory infection (Cohen et al., 1993, 1997).

The central limitation of the present study was its cross-sectional design, which precluded us from making any causal inferences about the influence of personality on tonic physiology. Another important limitation of this study is that not all of the data were collected simultaneously. For example, catecholamine data were collected 1 to 2 weeks after personality and natural killer cell cytotoxicity had been assessed. However, we do not believe that this temporal delay posed a major threat to the validity of our analyses because the psychological and physiological parameters assessed in the present study are highly stable over time. In any case, the net effect of this temporal delay should have been to reduce the magnitude of the relationship between any two variables that were not assessed cotemporally. Thus, the present study may have underestimated the true magnitude of the association between personality and tonic physiology. To assess the extent to which this occurred, we used a disattenuation formula provided by Pedhazur and Schmelkin (1991) to estimate what

the ''true'' magnitude of these relationships would be, assuming perfect stability over time. These calculations revealed that the ''true'' value of the correlations between personality and physiological parameters is an average of .06 larger than the observed value, with increases in magnitude ranging from .02 to .14. This rather modest amount of underestimation should have been counterbalanced to some extent by our strategy of aggregating across multiple measurements of psychological and physiological variables. This procedure reduces measurement error and therefore produces a more accurate (and more robust) estimate of the association between personality and tonic physiology.

To summarize, the present study indicates that dimensions of personality such as agreeableness and extraversion are reliably associated with tonic cardiovascular, neuroendocrine, and immune parameters. The magnitude of these relationships is relatively modest, with personality measures accounting for 1 to 7% of the variance in physiological parameters. Nonetheless, these findings represent a preliminary step toward integrating the concept of personality into behavioral immunology research. To provide a more complete understanding of how personality operates in the context of health, however, future research will need to address important issues, including why personality dimensions such as extraversion relate to natural killer cell cytotoxicity and others such as agreeableness do not and whether the contributions that personality makes to physiology are of sufficient magnitude and duration to be of clinical significance. It will also be important to address the issue of whether personality moderates individuals' physiological responses to stressful experiences. There is some evidence that personality's influence on physiology is more pronounced under conditions of stress. For example, a recent study (Miller et al., in press) found that among highly hostile men, anger expressed during marital conflict was associated with larger increases in systolic blood pressure, diastolic blood pressure, and cortisol. Highly hostile men also showed greater increases in circulating numbers of natural killer cells and heightened natural killer cell cytotoxicity. This contrasted with men low in cynical hostility, who showed *smaller* increases in natural killer cell cytotoxicity to the extent that they expressed anger during the conflict discussion. Finally, for personality to emerge as an important concept within behavioral immunology, existing theoretical models (e.g., Cohen, Kessler, & Gordon, 1995; Keller et al., 1994) will need to be refined so that they reflect the contribution that personality makes to immunologically mediated or resisted health outcomes.

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