Chapter 9

Personality and Human Immunity

Sheldon Cohen, Denise Janicki-Deverts, Crista N. Crittenden, and Rodlesia S. Sneed

Abstract
We review evidence on the role of personality traits in immune function including studies of enumerative and functional immune markers and of host resistance to infectious illness. We begin by discussing a series of pathways through which traits may influence immunity: immune-altering behaviors; concomitant activation of physiological systems; aggravation or attenuation of the activating effects of environmental demands or stressors; or selection into environments that alter immunity. We focus on the “Big Five” personality factors—extraversion, agreeableness, neuroticism, conscientiousness, and openess to experience but also address other trait characteristics that do not cleanly fit into the Big Five typology including dispositional optimism, trait positive affect, hostility, and social inhibition. We conclude that the literature on personality and immunity is in its infancy and not developed enough to make any definitive conclusions. We can say that there is evidence of possible associations with immunity across all the traits, with existing data suggesting some reliable associations. We suggest the importance of future works being based in trait-specific theory and outline a number of important methodological concerns.

Key Words: personality, Big Five, extraversion, agreeableness, neuroticism, conscientiousness, openness to experience, optimism, positive affect, hostility, social inhibition, immunity, immune function, host resistance, infectious disease

Introduction
The terms “personality” and “personality trait” generally refer to stable individual differences in a person’s characteristic patterns of behavior, thoughts, and feelings. A prototypic text on personality discusses dozens if not hundreds of possible personality traits. However, the literature addressing the role of personality in immunity is much more constrained, focusing on less than a dozen personality factors. One of the major theories of personality posits five superordinate independent traits (McCrae & Costa, 1987; Goldberg, 1992). The so called “Big Five” are extraversion, agreeableness, neuroticism, conscientiousness, and openness to experience. Here we review the existing literature examining the association of each of the Big Five factors with human immunity, as well as literature on four other trait characteristics that have been studied in relation to immunity: trait positive affect, optimism, hostility, and social inhibition.

How Could Personality Traits Influence Immunity?
A trait may influence the likelihood of an immune altering behavior. For example, persons high in conscientiousness are more likely to take care of themselves (refrain from smoking, drink alcohol moderately, exercise, get sufficient sleep) hence increasing the possibility of a better functioning immune system. Some traits covary with levels of nervous or endocrine system activation through which they may modulate immunity. For example,
neuroticism is thought to be a manifestation of high levels of cortical activation. Relatedly, a trait could operate by either aggravating or attenuating the activating effects of environmental demands or stressors. Neuroticism is thought to aggravate stress responses and optimism to reduce them. Personality traits may also result in a tendency to select environments that alter immunity. For example, those high in hostility tend to seek out and create social conflicts and, in turn, experience their activating properties. In contrast, agreeable persons are most likely to seek our positive interactions with others. Of course, there is also the possibility that associations between traits and immunity occur because either stable differences in our immune function influence our behavior or third factors, such as sex, age, genetics, or differences in the function of other physiological systems influence both our personalities and our immune responses.

Most of the literature we review is focused on the main effects of personality characteristics on measures of basal immunity. However, because personality may influence immunity by exacerbating or attenuating the activating effects of stress, we also discuss evidence on stress-by-personality interactions.

**How is Personality Measured in this Literature?**

There are two standard strategies for assessing personality. The most common is to ask people about the extent to which various statements or adjectives describe “how they usually are.” These assessments are most often collected at a single point in time. Although rare, a better strategy would be to collect these data at two or more points, the further apart the better, and average the scores. This approach maximizes the stable aspects of responses to the items and minimizes responses that might reflect experiences/feelings surrounding the time of questionnaire administration. Overall, this retrospective methodology is often criticized as heavily reflecting a person’s reconstruction of their memory for their own behavior based on their beliefs and recent experiences rather than accurately reflecting how they usually behave. An alternative approach uses the same items but asks people to rate the extent to which the items reflect how they are right now (or over a short period like a day). With this procedure the instrument is administered on multiple days, optimally covering a relatively long interval, and the personality score is based on average response over the repeated administrations of the scale. This strategy both avoids the retrospective reconstruction and the potential threats to reliability inherent in basing a personality score on an assessment administered at only one point in time. Although the single assessment retrospective technique is the one used most often in the personality and immunity literature, averaging over multiple state reports is also used in a handful of studies.

**Which Immune Outcomes are Addressed in this Literature?**

As difficult, if not more difficult, than defining and measuring personality in an integrated and comprehensive manner, is addressing how one should define and assess immune competence. We will not directly address the definition of immunocompetence and its appropriate measurement here for two reasons. First, we expect these issues to appear in multiple chapters in this volume, but more importantly, there are relatively few immune outcomes used in this literature, and, hence, what is important in this context is the nature of these specific outcomes.

The most common measures of immunity used in this literature include enumerations of leukocytes, antibody response to immunization, natural killer (NK) cell cytotoxicity, mitogen-stimulated lymphocyte proliferation, delayed-type hypersensitivity (DTH), antibody level to herpes viruses, stimulated production of pro-inflammatory cytokines, and circulating markers of inflammation. Although some of these measures are (at least in theory) interpretable in terms of their implications for host resistance (e.g., greater NK cytotoxicity, greater lymphocyte proliferation), others (e.g., numbers of leukocytes when counts fall within normal ranges, stimulated production of pro-inflammatory cyto-kines) are not.

Our review goes beyond the standard immune measures in that we also address literatures on the role of personality in the onset or exacerbation of infectious disease. The major function of the immune system is identifying and destroying infectious agents. As we have noted, individual measures of either enumerative or functional immunity seldom have straightforward implications for overall immunocompetence. Consequently, we view host resistance to infection as the ultimate downstream marker of immunocompetence. Infectious diseases that have been studied in relation to personality traits include the common cold, HIV/AIDS, and genital herpes.
Can We Make Causal Inferences?

Work on the role of personality and immunity is challenging to interpret in regard to the direction of causal inference. Personality is not generally thought to be manipulable, and, hence, experiments are not possible. Because traits are stable over long periods, it is assumed that related immunity would also be stable and hence prospective studies would be no more useful (no change to predict) than cross-sectional studies. The exception is studies that examine a critical point in the development of the immune system (when immunity would change). Exclusion of alternative causal explanations is, however, possible by controlling for third factors (e.g., sex, age, genetics, various physiological states) that may contribute both to personality and immunity, and we place special emphasis on appropriate use of this technique.

The Big Five Personality Factors

The Big Five traits are most often assessed by the Neuroticism Extraversion Openness Personality Inventory (NEO PI; Costa & McCrae, 1985), or one of its revisions: the NEO PI-R and the 60-item NEO Five-Factor Inventory (NEO-FFI) (Costa & McCrae, 1992), or a version of the Goldberg trait adjective scales (Goldberg, 1992). Extraversion and neuroticism are also often assessed using the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1968) or the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975).

Each of the Big Five is thought to be composed of six constituent facets or subtraits (Costa & McCrae, 1995). The NEO scale (but not others) allows the assessment of subtraits as well as factors. Although most of the studies we report in this section are focused on the associations of the factors with immune markers, some investigations assess subtrait scores. Which level of analysis (factor or subtrait) is best is debatable. Many believe that a focus that is limited to the five factors results in the loss of explanatory power (Paunonen & Ashton, 2001). Others, however, argue that the use of only the five factors allows for a more intuitive and easier interpretation of results (Carver & Scheier, 2008).

Within the literature reviewed here, most studies are limited to the factor level. However, we will briefly define the subtraits for each factor and will review any results reported at the subtrait level.

Extraversion

Extraversion/introversion is the extent to which individuals are sociable and outgoing. Subtraits of extraversion include friendliness, gregariousness, assertiveness, activity level, excitement seeking, and cheerfulness. Eysenck (1967) hypothesized that extraverts are motivated to seek out social activity and other forms of external stimulation in order to compensate for low levels of basal cortical arousal, whereas introverts avoid social interaction and other forms of external excitation in order not to further heighten an already hyperaroused basal state.

Susceptibility to Infectious Disease

Some of the earliest work to explore the immunological correlates of extraversion examined the importance of this personality characteristic in predicting susceptibility to infectious disease. Tostman, Kiff, Reed, and Craig, (1980) employed a viral challenge design to address the question of whether extraversion is associated with the likelihood of developing signs and symptoms of upper respiratory infection (URI). Following completion of the EPI, 52 healthy volunteers (mean age 30.9 years, range 18 to 49; 67% female) were exposed to one of two rhinoviruses that cause the common cold (Rhinovirus [RV] 2 or RV31). During the 5 days after exposure, the investigators collected nasal secretions on a daily basis to assess the amount of virus shedding (replication), an indication of having been infected with challenge virus. They also collected daily self-reported symptoms, and they monitored for the presence of fever and the number of tissues used. Analyses controlling for viral antibody level to the challenge virus before exposure showed that those with lower scores on the extraversion scale (i.e., those who were more introverted) shed more virus, and reported more cold symptoms than those with higher scores (i.e., those who were more extraverted). Extraversion was not, however, related to fever or tissue usage.

Similar findings were reported by Broadbent, Broadbent, Phillpotts, and Wallace (1984). These authors examined 173 men and women (over several different studies) who had completed the EPQ and were then exposed to either RV9, a combination of RV9 and RV14, or either of two strains of influenza virus (A/Munich [H1N1] or A/California [H1N1]). Nasal virus shedding, number of tissues used, and the weight of nasal secretions in the 5 days following virus exposure were employed as markers of illness susceptibility. The analysis aggregated data across the rhinovirus studies, and controlled for virus strain and viral-specific prechallenge antibody. Introvers (scoring <13) shed more virus than extraverts (>13), but no associations were found...
with tissue use or nasal secretion. Among the influenza studies, extraversion was not correlated with any of the markers of illness susceptibility.

In another viral challenge study that focused on the effects of social ties on susceptibility to the common cold, extraversion was examined as a control variable (Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997). After completing a modified version of Goldberg's trait adjective scales, 276 healthy adults between the ages of 18 and 55 (mean age 29.1 ± 9.1; 55% female) were experimentally exposed to one of two rhinoviruses (RV39 or Hanks), and then sequestered in a hotel for 5 days. Infection was defined as viral shedding or a fourfold or greater increase (from pre-viral exposure to 4 weeks postexposure) in virus-specific antibody titer. Disease expression was defined objectively as increased mucus production or decreased nasal mucociliary clearance function (a marker of congestion). Colds were defined as the combination of infection and expressing signs of illness. Those scoring below the median on the extraversion scale were more likely to develop a cold even after controlling for prechallenge antibody, body mass index (BMI), season of the year, age, race, sex, virus type, and education.

Cohen, Doyle, Turner, Alper, and Skoner (2003a) again made use of the viral challenge paradigm to examine the association of extraversion and cold risk in a different sample of 334 healthy adults (mean age 28.8 ± 10.4 years; 52% female). Participants completed the Goldberg scales and were then exposed to one of two rhinoviruses (RV39 or RV23) and sequestered for 5 days. Colds were defined using the objective criteria described earlier, and the same 8 control variables were included in the analysis. Consistent with the findings from Cohen et al. (1997), higher extraversion scores were associated with fewer colds for both viruses.

ANTIBODY RESPONSE TO VACCINATION

Pressman, Cohen, Miller, Barkin, Rabin, and Treanor (2005) recruited 37 male and 46 female college freshmen for a study examining the role of psychosocial factors in antibody response to a trivalent influenza vaccine. Participants were 18 to 25 years of age (96.4% were 18–19 years old). Extraversion was assessed 5 to 6 days prior to immunization using the Goldberg trait adjective scales. Participants were immunized in conjunction with university-wide flu vaccine clinics. Vaccine antibody levels were assessed at baseline (day of immunization) and again one and four months postimmunization. Extraversion was not related to vaccine antibody response at either the 1-month or 4-month follow-up.

ENUMERATIVE MEASURES OF IMMUNITY

Two published studies have addressed the question of whether extraversion is associated with circulating numbers of total lymphocytes and lymphocyte subsets. In the first of these, Miller, Cohen, Rabin, Skoner, and Doyle (1999) observed no association between scores on Goldberg’s extraversion scale and numbers of circulating total T lymphocytes (CD3+), helper T lymphocytes (CD4+), cytotoxic/suppressor T lymphocytes (CD8+), B cells (CD19+), or NK cells (CD3+CD16+CD56+) in the 276 healthy men and women (ages 18 to 55 years) who participated in the Cohen et al. (1997) study.

The second study, by comparison, did find an association between extraversion and enumerative immune measures. Using an elderly adult sample comprised of 11 medicated depressives (mean age 71 ± 8 years; 73% female), 10 unmedicated depressives (mean age 76 ± 7 years; 70% female), and 23 nondepressed controls (mean age 70 ± 7 years; 30% female), Bouhuys, Flentge, Oldhinkel, and van den Berg (2004) examined the association of extraversion, as assessed by the EPQ, with counts of CD3+, CD8+, and CD3-CD16+CD56+ cells, and the CD4+/CD8+ ratio. The authors found that greater extraversion was related to greater CD3-CD16+CD56+ counts and lower CD4+/CD8+ ratios, independent of depression group and age. However, extraversion was not related to either total CD3+ or CD8+ counts.

IMMUNE FUNCTION MEASURED IN VITRO

Gonzales-Quijano, Martin, Millan, and Lopez-Calderon (1998) examined the role of extraversion in lymphocyte proliferative response to phytohemagglutinin (PHA) in a sample of 28 male undergraduate students in Madrid, Spain (mean age 19 ± 0.2 years). Extraversion was assessed with a Spanish version of the Sixteen Personality Factors (16PF) Questionnaire (Cartell, 2005). The authors found that proliferative responses decreased with decreasing levels of extraversion. In studies described in the previous section, Miller, Cohen, et al. (1999) found lower extraversion to be associated with reduced NK cell cytotoxicity in a relatively large sample of healthy young to middle aged adults, whereas Bouhuys et al. (2004) found no association of extraversion with lipopolysaccharide (LPS)-stimulated production of the pro-inflammatory
cytokine interleukin (IL)-6 in a small sample that consisted primarily of depressed elderly.

**HIV**

Ironson, O' Cleirigh, Weiss, Schneiderman, and Costa (2008) examined whether extraversion was related to the average rate of change in CD4+ counts and viral load over a 4-year period in a sample of 104 HIV patients (mean age 38 ± 8.5 years; 32% female). All participants were free of AIDS-defining illnesses and had midrange CD4+ counts (150 to 500) at baseline. Data on all variables including extraversion, as measured by the NEO PI-R and blood samples for measurement of CD4+ cells and viral load were collected every 6 months over 4 years. Covariates included antiretroviral use, medication adherence, baseline CD4+ or viral load, race, sex, age, education, and time since baseline. Greater extraversion was associated with both a lower average rate of increase in viral load and a slower average rate of decline in CD4+ cell count over the 4-year period.

**HERPES RECURRENCES**

In a sample of 116 men and women with previously diagnosed culture-positive HSV2 (genital herpes) (mean age 35.3 years, range 21–69; 59% female), Cassidy, Meadows, Catalan, and Barton (1997) examined whether extraversion was related prospectively to number of genital herpes recurrences over a 6-month period. Extraversion was measured using the EPQ, and recurrence was determined by patient report. Results indicated no association between extraversion and symptom recurrence.

**MODERATING THE EFFECTS OF STRESS ON IMMUNITY**

In their sample of 28 male undergraduates, Gonzalez-Quijano and colleagues (1998) also explored the possibility that extraversion might buffer the expected attenuation of lymphocyte proliferative response following exposure to psychological stress. Stress was assessed with a questionnaire that asked participants to list the number of major life changes that occurred over the previous year. There was no interaction between stressful life events and extraversion and, hence, no evidence for extraversion buffering the effects of stress.

**CONCLUSIONS**

Studies of extraversion suggest that it may play a role in host resistance. Data from prospective (viral-challenge) cold studies are quite consistent in indicating that introverted persons are more susceptible to developing colds following experimental exposure to rhinovirus than their more extraverted counterparts. The single influenza study, however, failed to observe an association between extraversion and URI risk. In a single study of persons with HIV, greater extraversion was associated with a slower rate of decline in CD4+ cells in addition to a smaller increase in viral load.

The evidence in relation to immune markers is limited, but when associations were found, they were in the expected direction. Greater extraversion was associated with increased lymphocyte proliferative response and greater NK cell cytotoxicity. However, extraversion was unrelated to stimulated IL-6 production or to antibody response to a trivalent influenza vaccine. Moreover, among persons infected with HSV2, extraversion did not predict symptom recurrence. In general, extraversion appears not to be related to enumerative measures in healthy populations, although Boulhuys et al. (2004) found greater extraversion to be associated with greater numbers of NK cells, and lower CD4+/CD8+ ratios in their older adult sample.

Why is there more consistency in extraversion’s association with host resistance than with its associations with specific markers of immunity? Host resistance is a downstream response that integrates the dynamic and interactive roles of various aspects of functional immunity. A change in any relevant component of the immune response might (under the right conditions) result in a change in host resistance. However, many of the immune measures studied in this literature may have little or no implications for host resistance and hence we may not even expect them to be correlated with host resistance or for that matter with extraversion just because it predicts host resistance.

**Neuroticism**

Neuroticism reflects the extent to which individuals tend to experience negative emotional states, including anxiety, depression, and anger (Costa & McCrae, 1992). Accordingly, this construct also has been referred to as trait negative affectivity (NA), negative emotional style (NES), and negative emotionality. Individuals who score high on measures of neuroticism view the world as threatening, are easily distressed, and have difficulty coping with stressful situations, whereas those who score low on neuroticism are calm, emotionally stable, and cope well in the face of stress. Accordingly, the neuroticism
substrates include anxiety, depression, anger, self-consciousness, immoderation, and vulnerability to stress.

Eysenck (1967) theorized that neurotic tendencies derive from an innate predisposition toward low-threshold, high-intensity, and long-lasting autonomic activation in response to sensory stimuli. Accordingly, some interpreting high levels of neuroticism as being analogous to a high-stress condition with accompanying sympathetic and hypothalamic-pituitary-adrenal (HPA) activation (Miller, Cohen, et al., 1999). Moreover, because higher levels of neuroticism are thought to be associated with increased stress-related activation, neuroticism is also thought to exacerbate stress effects on immune function.

As discussed earlier, neuroticism frequently is assessed by questionnaire. Another approach is the assessment of individuals’ levels of negative mood daily for a week or more, and then creating a summary measure (average across days) of typical NA or NES.

**Susceptibility to Infectious Disease**

In their sample of 334 healthy men and women, Cohen, Doyle, Turner, Alper, and Skoner (2003b) used an interview measure to examine the association of NES with susceptibility to the common cold. During the month prior to being exposed to either of two rhinoviruses (RV39 or RV23), participants were interviewed nightly over a period of seven days. Interviewers asked participants to rate nine negative adjectives in regard to how accurately each of the adjectives described how they were feeling that day. Adjectives represented three subcategories of negative emotion: depression (sad, depressed, unhappy), anxiety (on edge, nervous, tense), and hostility (hostile, resentful, angry). NES scores were computed by averaging participants’ daily negative mood scores across the seven days. Following exposure to the challenge virus, participants were sequestered in a hotel for five days, and monitored for the development of infection and signs of illness. NES was unrelated to the risk of developing a cold.

Cohen, Alper, Doyle, Tranor, and Turner (2006) replicated these findings in a different sample of 193 healthy adults (mean age 37.3 ± 8.8 years, 51% female), using a modified version of the procedures employed in their previous study (Cohen et al., 2003b). NES again was measured by nightly telephone interview, but over the course of two weeks, and asking participants to rate their mood based on six, rather than nine adjectives (sad, unhappy, on edge, tense, hostile, angry). Participants subsequently were exposed to either RV39 or to A Texas/36/91 (H1N1) influenza virus, sequestered in a hotel for five (RV39) or six (influenza) days and monitored for signs and symptoms of URI. Colds were defined using the criteria described earlier. Consistent with their earlier findings, NES was unrelated to colds, regardless of the criteria used to define them.

**Antibody Response to Vaccination**

Marsland, Cohen, Rabin, and Manuck (2001) examined whether neuroticism was associated with antibody response to Hepatitis B (HBV) vaccine in 84 healthy, HBV seronegative graduate students (mean age 24 years, range 21–33; 39% female). Participants received three doses of HBV vaccine: baseline, six weeks postenrollment, and six months postenrollment. Five weeks after the initial HBV vaccination, participants completed a battery of psychological questionnaires. Neuroticism was measured using subscales from four instruments: anxiety and depression from the POMS Affect Scale; emotional stability from the Goldberg trait adjective scales; unpleasant affect and activated unpleasant affect from the Larsen and Diener Circumplex (Larsen & Diener, 1992); and positive loading for stress from the Mackay Circumplex (Mackay, Cox, Burrows, & LaCasse, 1978). Antibody response to HBV vaccine was measured following the second vaccination, and participants were identified as being low (n = 40) or high (n = 41) antibody responders. Results of logistic regression analysis controlling for age, sex, and BMI showed that neuroticism independently predicted antibody response to HBV vaccine such that greater neuroticism was associated with a greater likelihood of being in the low response group.

Phillips, Carroll, Burns, and Drayson (2005) examined whether neuroticism, as assessed by the EPQ, was associated with antibody response to a trivalent influenza vaccine in a sample of 57 healthy university students (mean age 19.8 ± 2.3 years; 46% female). After completing demographic and psychological questionnaires, participants received an influenza vaccination containing three viral strains: A/Panama (H3N2); A/New Caledonia (H1N1); and B/Shangdong. Baseline antibody titers were assessed prior to vaccination, and antibody response to vaccination was measured 5 weeks and 5 months later. Although neuroticism was unrelated to baseline antibody titers, persons scoring higher on neuroticism had lower antibody titers to A/Panama at both 5 weeks and 5 months. Neuroticism was unrelated to antibody response to the A/New Caledonia and B/Shangdong viral strains.
In a study of the role of neuroticism in the vaccine response of children, Morag, Morag, Reichenberg, Leric, and Yirmiya (1999) studied 240 female students (mean age 12.4 ± 0.2 years) recruited from 8 public schools in Israel. Two weeks prior to vaccination, neuroticism was assessed using the Junior EPI (Eysenck, 1965). Baseline rubella antibody titers were determined 2 weeks later, immediately prior to vaccination with a live-attenuated rubella virus. Participants were divided into a seronegative group (no immunity prior to vaccination; \( n = 60 \)) and a seropositive group (immunity prior to vaccination; \( n = 180 \)). Infection with rubella, as determined by a fourfold increase in antibody titers to the virus, was assessed 10.5 weeks later. Only infected participants were included in analyses. Among those in the seronegative group, higher neuroticism was associated with reduced antibody production following viral infection. By comparison, neuroticism was unrelated to antibody titers in the seropositive group in which, as expected, there was considerably less change in antibody in response to the vaccine.

As described in the extraversion section, Pressman and colleagues (2005) examined the role of personality in immune response to influenza vaccination in 83 college freshman. The authors found that neuroticism, as measured by the Goldberg emotional stability scale, was not related to vaccine antibody response at either the 1- or 4-month follow-ups.

**ENUMERATIVE MEASURES OF IMMUNITY**

Two of the studies described in the extraversion section also examined the association of neuroticism with circulating lymphocyte counts (Bouhuyts et al., 2004; Miller, Cohen et al., 1999), and in neither study was neuroticism related to total lymphocytes or lymphocyte subsets. Shea, Burton, and Grgic (1998) also examined the association of neuroticism with lymphocyte counts (total lymphocytes, CD4+, CD8+, and CD4+/CD8+ ratio) in a sample of 39 female undergraduates (from a sample of 220) who scored extremely high and extremely low on both the Willoughby Neuroticism scale (Willoughby, 1932) and an absorption questionnaire. Again, neuroticism was unrelated to cell numbers.

**IMMUNE FUNCTION MEASURED IN VITRO**

Two studies described earlier also addressed the role of neuroticism in functional immunity. Miller, Cohen et al. (1999) found no association between neuroticism and NK cell cytotoxicity in a sample of healthy adults. In contrast, Bouhuyts et al. (2004) found higher neuroticism scores to be associated with greater stimulated IL-6 production in a sample including mostly depressed elderly.

Three additional studies examined the role of trait anxiety, a well-studied trait of neuroticism, in cellular immune function. In their previously described cross-sectional study of 28 male undergraduates, Gonzalez-Quijano and colleagues (1998) did not find an association between anxiety and lymphocyte proliferative response to PHA. By comparison, Arranz, Gruyberas, and De la Fuente (2007) found anxiety to be associated with several in vitro measures of immune function, including proliferative response, in a sample of 66 healthy Spanish women (mean age 43.3 ± 2.1 years). Anxiety was assessed with the Beck Anxiety Inventory (Beck, Epstein, Brown, & Steer, 1988), and participants were divided into high (score >30) and low (score <29) anxiety groups. Functional immune measures included PHA-stimulated lymphocyte proliferation, PHA-stimulated lymphocyte productions of tumor necrosis factor (TNF-\( \alpha \), and IL-2; chemotaxis: lymphocyte adherence capacity (ability of lymphocytes to adhere to endothelial cells); phagocytosis; and NK cell cytotoxicity. When compared to those with low anxiety, highly anxious women showed decreases in PHA-stimulated lymphoproliferation, stimulated IL-2, lymphocyte chemotaxis, phagocytosis, and NK cell activity, and increases in stimulated TNF-\( \alpha \). The groups did not differ in adherence capacity.

Esterling, Antoni, Kumar, & Schneiderman (1993) used circulating levels of antibody to Epstein-Barr virus (EBV) to examine whether trait anxiety was associated with cellular immune function in a sample of 54 EBV seropositive undergraduate students (age range 17–25 years). EBV is a latent virus that is held in check by the cellular immune system. Poorer cellular immunity is thought to result in activation of the virus, and in turn an increase in the production of viral specific antibody. Thus, in contrast to vaccination studies wherein higher viral antibody concentrations are indicative of well-functioning humoral immunity, here, higher concentrations of circulating antibody are suggestive of impaired cellular immunity. They reported that greater anxiety, as measured by the Taylor Manifest Anxiety Scale (Taylor, 1953), was associated with greater EBV antibody levels and, thus, poorer cellular immunity.

Finally, in their sample of 39 female undergraduates, Shea and colleagues (Shea et al., 1993) examined the association of neuroticism with DTH skin
responses to seven antigens: tetanus, diphtheria, streptococci, tuberculin, candida, trichophyton, and protozoa, as well as to a glycerin control. Those high in neuroticism showed greater induration (i.e., better cellular immunity) in response to streptococcus, candida, and tuberculin than those low in neuroticism.

CIRCULATING MARKERS OF INFLAMMATION

In a sample of 855 relatively healthy middle-aged adults (mean age 45 ± 7 years; 50% female), Marsland, Prather, Peterson, Cohen, and Manuck (2008) examined whether trait NA, as assessed with the Multidimensional Personality Questionnaire—Short Form (MPQ-SF; Tellegen, 1982) was associated with circulating concentrations of IL-6 and C-reactive protein (CRP). Greater NA was associated with greater circulating concentrations of both IL-6 and CRP, independent of age, sex, race, years of education, and medical conditions or medications known to influence inflammation.

Similar results were reported by Sutin, Terracciano, Deiana, Nairz, Ferrucci, Ulda et al. (2009) in a sample of 5,119 residents of the Italian island of Sardinia (mean age 39.3 ± 14.7 years; 55% female). Higher levels of neuroticism as assessed by the Italian version of the NEO PI-R (Terracciano, 2003) were associated with higher concentrations of both IL-6 and CRP independent of age, sex, BMI, aspirin use, and disease burden (sum of current diseases).

HIV

Tomakowsky, Lumley, Markowitz, and Frank (2001) examined the cross-sectional association of trait NA, as assessed by the Positive and Negative Affect Schedule (PANAS), with HIV disease status, as indicated by CD4+ cell count, in a sample of 78 HIV-infected men (mean age 39 ± 7.8 years) who were free of AIDS-defining illnesses. Negative affectivity was not associated with CD4+ count. Similarly, in their 4-year prospective study of personality and disease progression in persons with HIV, Ironson and colleagues (2008) found no association between neuroticism, as assessed by the NEO PI-R, and change in either CD4+ cell count or viral load.

HERPES RECURRENCES

In their prospective study of personality and genital herpes symptom recurrence described earlier, Cassidy and colleagues (1997) found that neuroticism was unrelated to number of recurrences over a 6-month period.

MODERATING THE EFFECTS OF STRESS ON IMMUNITY

Borella, Bargellini, Rovesti, Pinelli, Vivoli, Solfini, et al. (1999) examined whether neuroticism moderates the effects of a brief naturalistic stressor (first semester at an Italian military academy) on NK cell function. Stressors of this sort tend to be associated with decreases in NK cell cytotoxicity (Segerstrom & Miller, 2004). Neuroticism was assessed in 39 male cadets using a composite measure combining the Goldberg emotional stability scale, the Trait Anxiety Scale from the State-Trait Anxiety Inventory, and the neuroticism items from the EPI. Results supported an exacerbating effect of neuroticism on the stress-related changes in NK cell cytotoxicity, such that those with high neuroticism scores experienced a decline in NK cell activity from the beginning of the semester to final examinations, whereas those with midrange scores showed no change in cytotoxicity. Interestingly, low neuroticism scores were associated with an increase in NK cell cytotoxicity from the beginning to the end of the semester. All findings were independent of coffee consumption and smoking status.

CONCLUSIONS

The most consistent evidence to support an association between neuroticism and immunity derives from the vaccination studies, wherein three of four studies found greater neuroticism to be associated with attenuated antibody response (Marsland et al., 2001; Morag et al., 1999; Phillips et al., 2005). By comparison, neuroticism was unrelated to developing a common cold following experimental exposure to any of several cold viruses (Cohen et al., 2006; Cohen et al., 2003b). The research has also consistently failed to show any association between neuroticism and enumerative measures. Whether neuroticism is associated with functional measures of immunity, however, is less clear. Arranz et al. (2007) found higher levels of neuroticism to be associated with poorer lymphocyte proliferation, NK cell cytotoxicity, phagocytosis, chemotaxis, and stimulated IL-2 production. Both Arranz et al. (2007) and Bouhuys et al. (2004) found higher levels of neuroticism to be associated with greater stimulated production of two pro-inflammatory cytokines, TNF-α and IL-6, respectively, and Shea et al. (1993) observed greater DTH responses among young women who scored high relative to low in neuroticism. By comparison,
Gonzalez-Quijano et al. (1998) observed no association between neuroticism and lymphocyte proliferation, and Miller, Cohen et al. (1999) observed no association with NK cell cytotoxicity. Neuroticism also was unrelated to HIV progression, as indicated by either CD4+ counts or viral load, or to genital herpes recurrence. Sex differences in the association of neuroticism with immune activity might account for these inconsistent findings. For example, Arranz et al. (2007) and Shea et al. (1993) employed entirely female samples, whereas Gonzalez-Quijano et al. (1998) and Tomakowsky et al. (2001) studied only men. In regard to integrating stress in the relationship between neuroticism and immunity, the single published study (Borella et al., 1999) suggests that stress and neuroticism may have a synergistic, dysregulating effect on immune functioning.

With only three studies, it is hard to interpret the impact of the neuroticism trait, anxiety, on immunity. Overall, the results were mixed, with anxiety predicting poorer cellular immunity in some cases but not in others. Moreover, since the associations of anxiety and immunity were not compared to other traits or even to neuroticism, little can be said about whether it is the or merely a central component of neuroticism in terms of its potential to influence immunity.

Conscientiousness

Conscientiousness is a personality trait that includes as its traits self-efficacy, orderliness, dutifulness, achievement-striving, self-discipline, and cautionfulness. Individuals with high levels of conscientiousness demonstrate greater self-discipline, greater adherence to ethical/moral standards, and a strong sense of order (e.g., neatness, organization). Further, they strive for achievement and are cautious in their actions. Conscientiousness is most likely to influence immunity through its relationship with better health practices and adherence to medication regimens. The association between conscientiousness and immunity has been addressed in only four studies, two of which have their methods described in detail in previous sections (Cohen et al., 1997; Pressman et al., 2005).

Susceptibility to Infectious Disease

In Cohen and colleagues’ (1997) prospective study of psychosocial factors and susceptibility to the common cold in healthy adults, conscientiousness, as measured with Goldberg’s trait adjectives, was unrelated to the likelihood of developing a cold following experimental exposure to one of two viruses.

Antibody Response to Vaccination

In their prospective study of healthy young adults who also assessed personality with the Goldberg scales, Pressman and colleagues (2005) found no association between conscientiousness and antibody response to influenza vaccine either 1 or 4 months after immunization.

Circulating Markers of Inflammation

In contrast, findings from Sutin and colleagues’ (2009) study of 5,119 Italian men and women suggest that conscientiousness might be associated with reduced inflammation in healthy adults. In this large sample, lower conscientiousness scores on the NEO PI-R were associated with higher concentrations of both IL-6 and CRP, independent of age, sex, BMI, aspirin use in the last two weeks, and disease burden. Less smoking among those scoring higher in conscientiousness partially mediated the relationship between IL-6 levels and five conscientiousness subcomponents: competence, dutifulness, achievement striving, self-discipline, and deliberation. The mediation tests for the association of total conscientiousness with IL-6, and analyses with CRP as the outcome, were not reported.

HIV

O’Cleirigh, Ironson, Weiss, and Costa (2007) used a prospective design to examine the association of conscientiousness with HIV disease progression among 119 HIV-positive adults (mean age 37 years; 34% female). Conscientiousness, assessed with the NEO PI-R, CD4+ cell counts, and viral load were measured at baseline and one year later. Covariates included age, race, sex, antiretroviral medication use, and baseline CD4+ or viral load levels. Higher conscientiousness at baseline was related to a slower decline in CD4+ levels and an attenuated increase in viral load from baseline to 1-year follow-up. None of the potential mediators tested (depression, perceived stress, coping style, and medication adherence) explained the association of conscientiousness with either outcome. In their longitudinal analysis of 104 surviving participants from this sample, Ironson and colleagues (2008) found that greater conscientiousness was associated with a slower average rate of increase in viral load over the course of 4 years. In this case, however, conscientiousness was not related to changes in CD4+ count.
CONCLUSIONS

To date, available information on the relation of conscientiousness to immunity is insufficient to draw any meaningful conclusions. Conscientiousness appears not to be related to the likelihood of developing a cold following experimental exposure to viruses that cause URI, nor to antibody response to influenza vaccination. However, lower levels of conscientiousness may be associated with elevated circulating markers of inflammation. Among HIV patients, conscientiousness has been associated with slower increases in viral load, and inconsistently with a slower decline in CD4+ cells. It is not clear, however, whether these associations are mediated by better health behaviors (e.g., diet, physical activity, smoking) and medication adherence among more conscientious persons or is via some other pathway.

Agreeableness

Agreeableness refers to being concerned with and contributing to the maintenance of relationships with other persons. Persons who score high on agreeableness tend to be pleasant and accommodating, and place considerable importance on maintaining harmony in their interpersonal relationships. Agreeable persons also tend to hold optimistic views of human nature. Subtraits of agreeableness include trust, morality, altruism, cooperation, modesty, and sympathy. Agreeableness has rarely been examined in relation to immunity. The findings summarized next derive from four studies (all described earlier) that were conducted with healthy adults, and one HIV study. In most cases, agreeableness was one of several personality characteristics that were examined or was included as a control variable. Two healthy population studies examined whether Goldberg’s agreeableness subscale was related to susceptibility to the common cold (Cohen et al., 1997; Cohen et al., 2003a). Whereas the earlier study conducted in a sample of 193 found no relation between agreeableness and cold susceptibility, the later study, conducted in a larger sample of 334, found greater agreeableness to be associated with greater resistance (Cohen et al., 2003a). Other outcomes examined in healthy adults included antibody response to vaccination (Pressman et al., 2005), enumerative measures of immunity (i.e., total lymphocytes and lymphocyte subsets; Miller, Cohen et al., 1999) and NK cell cytotoxicity (Miller, Cohen et al., 1999). Agreeableness was unrelated to any of these outcomes. The HIV study similarly found no associations between agreeableness and changes in CD4+ counts or viral load across 4 years (Ironson et al., 2008).

Openness

Openness to experience, or simply openness, refers to the extent to which individuals are appreciative of new or different ideas and experiences. Persons scoring high on measures of openness tend to be curious, imaginative, and reflective, whereas those scoring low on openness tend to be more conventional and less given to abstract thought. Subtraits of openness include imagination, artistic interests, emotionality, adventurousness, intellect, and liberalism. To date, only three studies have examined whether openness is associated with measures of immunity in samples of healthy adults, and only one study in persons with HIV. All of these studies were described previously, and all examined openness as a secondary variable. Among the studies conducted in healthy populations, the assessed immune outcomes were susceptibility to the common cold (Cohen et al., 1997), antibody response to vaccination (Pressman et al., 2005), and circulating markers of inflammation (Sutin et al., 2009). In none of these studies was openness associated with immune outcomes. In the HIV study, neither changes in CD4+ or viral load were associated with openness across the 4-year follow-up (Ironson et al., 2008).

Other Personality Characteristics

In addition to the Big Five personality characteristics, four other personality traits have been examined in regard to associations with immune function: dispositional optimism, trait positive affect, hostility, and social inhibition. We discuss these traits separately from the Big Five because none is encompassed by a single Big Five category. For example, hostility is thought to include dimensions of both agreeableness and neuroticism; trait positive affect, agreeableness and extraversion; social inhibition, agreeableness, extraversion, and neuroticism; and optimism, possibly all five factors.

Dispositional Optimism

Dispositional optimism reflects the extent to which individuals hold generalized favorable expectancies for their future, and pessimism reflects the extent to which they hold unfavorable expectancies (Carver, Scheier, & Segerstrom, 2010). Optimism is most often assessed by the Life Orientation Test (LOT; Scheier & Carver, 1985; revised version
LOT-R; Scheier, Carver, & Bridges, 1994). Higher scores on this questionnaire suggest strong agreement with the expectation of favorable experiences and strong disagreement with the expectation of unfavorable experiences. The LOT also contains subscales that can be used to assess optimism and pessimism separately. Another approach to optimism focuses on attributional styles—how people explain events. In this approach, optimistic justifications of negative experiences are attributed to factors outside the self (external), that are not likely to occur consistently (unstable), and are limited to specific life domains (specific). In contrast, optimistic interpretations of positive experiences would be labeled as the opposite: internal, stable, and global. Pessimistic attributional styles are defined as the opposite of the optimistic styles. Attributional styles are assessed by the Attributional Style Questionnaire (ASQ; Peterson et al., 1982) or the Content Analysis of Verbatim Explanations (CAVE; Peterson, Luborsky, & Seligman, 1983) technique, in which interview answers or archival data are content analyzed for attributional styles. The attributional style measures are only modestly associated with measures of generalized expectancies (Ahrens & Haaga, 1993; Peterson & Vaidya, 2001). Thus, expectancy and attribution measures cannot be considered interchangeable.

**ENUMERATIVE MEASURES OF IMMUNITY**

Kamen-Siegel, Rodin, Seligman, and Dwyer (1991) examined whether pessimistic attributional style, as measured by the CAVE, was associated with percentages of CD3+, CD4+, and CD8+ cells in 26 men and women between the ages of 62 and 83 years (mean age 70.4 years). Analyses that controlled for lag in days between CAVE interview and blood tests, general health, and depressive symptoms revealed that pessimistic explanatory style was correlated with low CD4+/CD8+ ratios, and was accounted for largely by the association between more pessimistic style and a higher percentage of CD8+ cells. No results were reported for analyses predicting CD3+ cells.

Brennan & Charnetski (2000) investigated whether attributional style, as assessed by the ASQ, was associated with total salivary secretory immunoglobulin A (slgA) concentrations. In a sample of 112 undergraduates (mean age 18.8 years, range 16 to 23; 63% female). Neither total ASQ scores nor scores on the optimistic style subscale were related to slgA. However, higher scores on the pessimistic style subscale were associated with lower slgA levels.

**IMMUNE FUNCTION MEASURED IN VITRO**

Kamen-Siegel and colleagues (1991) also examined whether pessimistic attributional style was associated with PHA-stimulated lymphocyte proliferation. A more pessimistic style was associated with a lower proliferative response, but only when stimulated with a 0.5 μg/mL dose of PHA and not 10.0 μg/mL. In a study of the potential role of optimism in response to an immunization, Kohut, Cooper, Nicklaus, Russell, and Cunick (2002) administered the LOT to 56 healthy men and women aged 62 years and older (63% female) who were vaccinated with a trivalent influenza vaccine. Blood for immune assessments was drawn 14 weeks postvaccination. Outcomes included influenza-specific lymphocyte proliferation and influenza vaccine-stimulated productions of IL-2, IL-10, and IFN-γ. Optimism was unrelated to any of these measures.

**ANTIBODY RESPONSE TO VACCINATION**

Kohut et al. (2002) also examined whether optimism was related to IgG and IgM antibody response to the trivalent influenza vaccine. The LOT was not related to response of either antibody.

**CIRCULATING MARKERS OF INFLAMMATION**

Two recent studies examined whether optimism is associated with circulating markers of inflammation. In a sample of 36 healthy nonsmoking postmenopausal women (mean age 60.7 ± 6.7 years), O’Donovan, Lin, Dhabhar, Wolkowitz, Tillie, Blackburn, and Eple (2009) found that higher scores on the pessimism subscale of the LOT-R were associated with higher IL-6 concentrations, independent of age, caregiver status, and optimism subscale scores. Optimism, by comparison, was unrelated to IL-6 even when adjusting only for age. In another multivariate model that included a group of hypothesized mediators (neuroticism, perceived stress, physical activity, and sleep quality) in addition to age, caregiver status, and optimism, the association of pessimism with IL-6 was slightly reduced; evidence consistent with the hypothesis that one or more of these variables (or their combination) may act as pathways linking optimism to IL-6 concentrations.

Roy, Diez-Roux, Seeman, Ranjit, Shea, and Cushman (2010) also tested the hypothesis that lower optimism and higher pessimism each would be related to greater circulating markers of inflammation. However, in addition to IL-6, Roy and colleagues measured CRP, fibrinogen, and
homocysteine. Participants were drawn from the 6,195 men and women (mean age 62.2 years, range 45 to 84; 53% female) who took part in the first MultiEthnic Study of Atherosclerosis (MESA) follow-up examination (n = 5,220 to 5,358, depending on outcome). Bivariate analysis showed that higher scores on the pessimism subscale of the LOT-R were associated with higher concentrations of all four inflammatory markers, independent of age, race, and sex. By comparison, lower scores on the optimism subscale showed only a marginal association with higher homocysteine, and were unrelated to IL-6, CRP, and fibrinogen. The authors further explored the associations of pessimism with inflammatory markers by conducting three additional sets of multivariate analyses. In the first, which controlled for age, sex, fasting, recent infections, and medication use, greater scores on the pessimism subscale remained an independent predictor of greater IL-6, CRP, and fibrinogen, respectively, but not of homocysteine. In the second model, including additional controls for race, education, income, depression, cynical distrust, smoking status, exercise, and diet, the associations of pessimism with CRP and fibrinogen remained, but the association with IL-6 lost significance. A final model entered three potential mediators, BMI, diabetes, and hypertension as additional controls. The results were consistent with the hypothesis that one or more (or a combination) of these variables act as pathways linking optimism to inflammatory response. In contrast, the association between pessimism and fibrinogen was reduced only minimally, a finding inconsistent with mediation in this case.

TELOMERE LENGTH IN LEUKOCYTES

In addition to examining an association between optimism and pessimism with IL-6, O’Donovan et al. (2009) also explored the association of these traits with telomere length in leukocytes. Telomeres are regions of repetitive DNA that form at the ends of chromosomes and function to protect the chromosome terminus from deterioration subsequent to repeated replication. Leukocyte telomere length may serve as an indicator of immunosenescence, with shorter telomeres indicating more DNA replications, and thus more aged or compromised immunity. Age-adjusted analyses showed higher pessimism subscale scores to be associated with shorter telomeres. Optimism scores, by comparison, were unrelated to telomere length. When entered into a model that controlled for age, caregiver status, optimism, perceived stress, neuroticism, BMI, exercise, and sleep, pessimism remained an independent correlate of telomere length.

HIV

Several studies have explored the relation of optimism to disease progression in HIV-infected individuals. Ironson and colleagues (2005) examined the prospective association of optimism with change in CD4+ counts and viral load among 177 HIV-infected adults (mean age 37.5 years; 30% female) with midrange CD4+ counts and no AIDS defining illnesses at baseline. Dispositional optimism was measured at baseline using a composite of the LOT and the LOT-R. CD4+ counts, viral load, and potential psychosocial (depression, perceived stress, coping) and behavioral mediators (medication adherence, substance use, sleep, exercise, condom use, procreative disease behaviors) were measured every 6 months over a 2-year period. Covariates included time since study entry, viral load or CD4+ count at study entry, use of antiretroviral medications, race, sex, age, education, route of infection, and sexual orientation. Greater optimism at baseline was associated with both a slower average decline in CD4+ counts and a slower average increase in viral load across the two years of follow-up. Further, analyses were consistent with less depression, more proactive disease behavior (e.g., information seeking, health behavior change), and less avoidant coping among those with greater optimism partially mediating the association of optimism with CD4+ count, and less depression alone playing a mediating role in the association of optimism with viral load.

Milam, Richardson, Marks, Kemper, and McCutchan (2004) explored similar research questions in a prospective study conducted among 412 HIV-infected men and women attending 6 public HIV clinics in California (mean age 39.0 ± 7.9 years; 12% female). All participants were on antiretroviral therapy at study entry. Optimism and pessimism were measured at baseline using separate subscales of the LOT-R. Other baseline measurements included age, race, sex, diagnosis date, exercise, diet, tobacco use, depression, illicit drug use, viral load, and CD4+ count. Viral load and CD4+ count were measured again 18 months later, as was antiretroviral adherence. Greater pessimism at baseline was associated with a greater increase in viral load over 18 months. This association was not explained by any of the behavioral variables. By comparison, although greater optimism was related cross-sectionally to lower viral load at baseline, optimism did not predict viral load at follow-up. Neither
pessimism nor optimism was linearly related to follow-up CD4+ counts. However, optimism showed a curvilinear association with CD4+ counts such that individuals with moderate optimism scores displayed higher counts than those with either low or high scores. This association was not explained by health behaviors or depression.

In the sample of HIV-positive men described in the section on neuroticism, Tomakowsky and colleagues (2001) examined both cross-sectional and prospective associations of optimism with disease progression using two models of optimism: dispositional optimism, as measured by the LOT, and optimistic attributional style, as measured by the Expanded Attributional Style Questionnaire (EASQ; Peterson & Villanova, 1988). All 78 men were included in the cross-sectional analyses, and a subset of these men (n = 47) who had survived and remained in treatment at the clinic 2 years after the initial enrollment were included in the 2-year prospective follow-up analyses. Health status at baseline and follow-up was assessed with CD4+ cell counts. Fully adjusted models controlled for demographics, length of diagnosis, antiretroviral drug use, and negative affectivity. Prospective models included additional control for baseline CD4+ counts.

Surprisingly, results indicated that those scoring higher on optimistic explanatory style displayed more advanced disease at baseline and experienced a greater decline in health status over the subsequent two years. Optimism as measured by the LOT was neither cross-sectionally nor prospectively associated with HIV disease progression.

MODERATING THE EFFECTS OF STRESS ON IMMUNITY

In a three-month prospective study conducted among 39 healthy white women (mean age 32.0 ± 6.6 years), Cohen, Keanney, Zegans, Kemeny, Neubauer, and Stites (1999) evaluated whether dispositional optimism buffers the effects of stress on lymphocyte percentages and NK cell cytotoxicity. Dispositional optimism was evaluated using total LOT scores. Participants’ experiences of acute stress (less than one week) and persistent stress (more than one week) were assessed with weekly stress logs. Enumerative measures included percentages of CD4+ and CD8+ cells. In light of evidence suggesting that phenotypically different CD8+ cells may have different functions, the authors also measured two subsets of CD8+ cells, CD8+CD11b- and CD8+CD11b+, to explore whether these subsets show differential responses to stress. The authors observed interactions of optimism with acute stress in the prediction of CD8+CD11b- cell percentages, and with persistent stress in the predictions of CD8+CD11b- percentages and NK cell cytotoxicity. Only in the case of acute stress, however, was the moderating effect consistent with a buffering role for optimism—that is, acute stress-related increases in CD8+CD11b+ cells were less pronounced at higher relative to lower levels of optimism. Unexpectedly, the persistent stress-associated decreases in CD8+CD11b- percentages and NK cell cytotoxicity were more pronounced at higher levels of optimism.

Using data from 59 male university students (age range 18 to 30), Brydon, Walker, Wawrzynek, Chart, and Steptoe (2009) examined whether optimism would moderate the combined effects of psychological and immune (i.e., vaccination for typhoid) challenge on immunity. After the assessment of optimism using the LOT-R, participants were randomized into one of four conditions: vaccine/stress; placebo/stress; vaccine/rest; and placebo/rest. Vaccination (or placebo) was administered 30 minutes prior to laboratory stress (or rest). The stress condition involved both a Stroop task and a public-speaking task. Circulating serum IL-6 and typhoid antibody were both measured before vaccination. IL-6 was measured again 3 hours after vaccination, and antibody to the vaccine 3 weeks later. The results were consistent with a stress-buffering hypothesis. Among persons in the combined vaccine/stress and placebo/stress conditions, IL-6 increased from baseline to posttask at low levels of optimism, and the magnitude of this increase became less apparent as LOT-R total scores increased. Among persons in the vaccine-stress group only, the expected acute stress-associated increase in antibody production was evident at high but not low levels of optimism.

In three studies, Segerstrom and colleagues (Segerstrom 2006; Segerstrom, 2001; Segerstrom, Taylor, Kemeny, & Fahey, 1998) evaluated the potential moderating role of optimism in immune response to the stress of attending law school. In none of these studies, however, did optimism show the expected moderating effect.

The first study evaluated 50 first-year law students at the University of California at Los Angeles (Segerstrom et al., 1998). Data were collected during low (two weeks prior to law school orientation and the first day of classes) and high (during midsemester) stress periods. Dispositional optimism was measured using the LOT. Additional measures
conclusions

When examined collectively, research on dispositional optimism and immunity suggests that greater pessimism rather than less optimism may be the more important dimension of personality in regard to predicting individuals’ predispositions toward immune dysregulation. The link between pessimism and immunity has been demonstrated across several immune outcomes, with greater pessimism being associated with increased likelihood of exhibiting a pro-inflammatory phenotype, poorer cell-mediated immunity, reduced humoral immunity, and accelerated immunosenescence. There is evidence that at least some of the tie between pessimism and inflammatory markers may be mediated by lifestyle and risk behaviors and possibly perceived stress.

Evidence for links between optimism and immunity is weaker. None of the studies reviewed here observed a main effect association between optimism and immune outcomes in healthy adult samples, regardless of whether optimism was measured using total LOT scores, the optimism subscale of the LOT, or the optimistic-style subscale of the ASQ. By comparison, the HIV studies found associations between both optimism and pessimism with HIV disease status and progression, but the directions of these associations were inconsistent and often counterintuitive. For example, greater optimism has been associated cross-sectionally with lower viral load and lower CD4+ counts, and with less CD4+ decline over time, whereas optimistic attributional style has been associated cross-sectionally with higher CD4+ counts, and with greater CD4+ decline over time.

In contrast to the studies examining main effect associations of optimism with immune-related outcomes, there is evidence to suggest that optimism moderates the effects of stress on immunity. The findings of these studies, however, are difficult to interpret. Two studies provided support for the buffering hypothesis by showing that real life acute stress-related elevations in CD8+CD11b+ percentages and laboratory stress-related increases in IL-6, respectively, are reduced among persons with higher levels of optimism. These findings, however, appear to be the exception rather than the rule, because most of the studies we discuss here either reported no moderating effect of optimism or even an accentuating effect of optimism on stress-related changes in immunity. It is noteworthy that these studies all had relatively small samples (N = 22–59) and may have been underpowered to detect stress-buffering effects (Cohen & Edwards, 1989).
Trait Positive Affect/Positive Emotional Style

Positive affect (PA) is the experience of feelings that indicate a positive engagement or interaction with one's environment (Clark, Watson, & Leckman, 1989). Trait PA (also called positive emotional style [PES]) is a dispositional characteristic that reflects one's tendency to experience PA (Cohen et al., 2003b). An important aspect of the research on trait PA/PES and immunity is its emphasis on establishing whether associations of PES with immunity are independent of those of trait NA or neuroticism.

ANTIBODY RESPONSE TO VACCINATION

In a study described earlier in the section on neuroticism, Marsland, Cohen, Rabin, and Manuck (2006) also examined whether trait PA was associated with antibody response to Hepatitis B (HBV) vaccine in 84 healthy, HBV seronegative graduate students (mean age 24 years, range 21–33; 39% female). PA was measured using subscales from the POMS Affect Scale, the Goldberg Big Five Factor Scales (Goldberg, 1992), the Larsen and Diener Circumplex (Larsen & Diener, 1992) and from the Mackay Circumplex (Mackay, Cox, Burrows, & Lazarini, 1978). Results of logistic regression analysis controlling for age, sex, BMI and depression showed that trait PA independently predicted antibody response to HBV vaccine such that greater PA was associated with less likelihood of being in the low-response group. This effect was also independent of neuroticism (trait NA) and of other dimensions of personality that are closely related to PA such as optimism and extraversion.

SUSCEPTIBILITY TO INFECTIOUS DISEASE

The majority of this work has focused on the role of this personality characteristic in resistance to URI. In the initial study, Cohen and colleagues (2003b) used two methods to assess PES in the sample of 334 healthy men and women described in the extraversion and neuroticism sections. The first was a brief retrospective questionnaire that was administered six weeks prior to viral exposure and on which participants rated how accurately each of nine adjectives reflecting positive mood states (e.g., happy, enthusiastic, calm) described how they “usually” feel. The second was a multiple interview-based summary measure of daily mood. During the month prior to viral exposure, participants were interviewed by telephone on seven nights and asked to rate the same nine adjectives that were included in the questionnaire in regard to how accurately each of the adjectives described how they were feeling that day. Positive emotional style scores were computed by averaging participants’ daily positive mood scores across the seven days.

Higher scores on the interview-based PES measure were related in a dose-response manner to a lower risk of developing a cold. This association was independent of preexposure viral-specific-antibody level, age, race, sex, education, BMI, season of the year, and virus type. Results were also independent of trait NA. Inclusion of potential health-behavior mediators (smoking status, alcohol intake, exercise, and sleep quality) into the model did not diminish the association. Higher scores on the questionnaire measure of PES showed a similar association with reduced cold risk.

In a later paper based on data from the same sample, Doyle, Gentile, and Cohen (2006) examined the possibility that the aforementioned reported association of PES with signs of clinical illness may have been mediated by local (in nasal secretions) release of pro-inflammatory cytokines (IL-1β, IL-6, and IL-8). Results showed that higher scores on the interview measure of PES were associated with lower production of IL-6 in response to infection. Moreover, IL-6 accounted for 25–44% of the association of PES with signs of clinical illness, thus suggesting a mediational role for IL-6 in the association of PES with the expression of clinical colds. PES was not related to either IL-1β or IL-8.

In the sample of 193 healthy men and women described in the section on neuroticism, Cohen and colleagues replicated the association between higher PES and fewer colds using a modified version of the interview-based PES measure (Cohen et al., 2006). Prior to exposure to either RV39 or the A/Texas/36/91 (H1N1) influenza virus, participants were interviewed nightly over a period of two weeks and asked to report on their mood using the nine- adjective PA scale employed in Cohen et al. (2003b). Positive emotional style scores were computed by averaging daily mood scores across the two weeks. The remainder of the protocol was identical to the previous study, and the primary outcome was the development of a cold. Similar to the previous findings, increases in PES were associated with decreases in objectively diagnosed illness independent of age, sex, race, education, BMI, virus type, antibody levels, and NA.

IMMUNE FUNCTION MEASURED IN VITRO

Prather, Marsland, Muldoon, and Manuck (2007) explored whether trait PA is associated with
stimulated production of pro- and anti-inflammatory cytokines in vitro in a sample of 146 community volunteers (mean age 45.2 ± 6.2 years; 42.5% female). PA was assessed with the trait version of the PANAS. Productions of three pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) and one anti-inflammatory cytokine (IL-10) were measured following stimulation in whole blood with LPS in vitro. Higher trait PA was associated with lower productions of IL-6 and IL-10, but was not related to production of either IL-1β or TNF-α. A significant PA-by-sex interaction in the prediction of IL-10 revealed that the decrease in IL-10 production with increasing PA was apparent only in men. No PA-by-sex interactions were found for IL-6.

CONCLUSIONS

The data support a reliable association of greater trait PA (PES) with less expression of signs of illness in persons experimentally exposed to rhinoviruses. In addition, a single study suggests that PA is associated with a better secondary response to HBV vaccine. Another indicates the possibility of trait PA modulating lymphocyte production of pro-inflammatory cytokines. However, as there are no norms for appropriate levels of cytokine production in vitro, the implication of this association for immunocompetence is unclear.

Hostility

Hostility is often defined in terms of its cognitive, affective, and behavioral components. The cognitive component encompasses cynicism as well as hostile attributions, the affective component includes negatively charged emotions such as anger and annoyance, and the behavioral component includes verbal and physical aggression (Barefoot et al., 1991; Smith, 1992). Two of the more frequently used instruments to measure hostility are the Cook-Medley Hostility Scale (H; Cook & Medley, 1954; Barefoot, Dodge, Peterson, Dahlstrom, & Williams, 1989) and the Buss-Perry Aggression Questionnaire (BPAQ; Buss & Perry, 1992). Both scales are comprised of subsets of items reflecting the cognitive, affective, and behavioral dimensions of hostility. However, whereas the constructs measured by the Cook-Medley Ho are referred to as cynicism, hostile affect, and aggression, analogous constructs measured by the BPAQ are referred to as hostility, anger, physical aggression, and verbal aggression.

Much of the interest in exploring whether hostility is related to immune function stems from the well-established association of hostility with risk for cardiovascular disease (CVD) (e.g., Everson-Rose et al., 2006; Smith, 1992; Suls & Wan, 1993). Activities of the immune system, in particular inflammation, have come to be recognized as important contributors to the pathogenesis of atherosclerotic CVD (Ross, 1999). In light of evidence implicating inflammation in CVD pathogenesis, and evidence showing associations between the components of hostility and atherosclerotic CVD (Everson-Rose et al., 2006; Miller, Freedland, Carney, Steffler, & Banks, 2003), there has been considerable interest in the association between hostility and markers of inflammation.

STIMULATED PRO-INFLAMMATORY CYTOKINE PRODUCTION

In a sample of 62 healthy, nonsmoking men (mean age 25.4 ± 5.9 years), Suarez, Lewis, and Kuhn (2002) tested the hypothesis that greater levels of hostility, assessed with the BPAQ, would be associated with greater LPS-stimulated production of TNF-α. In analyses that controlled for age, race, education, and alcohol use, BPAQ total scores, as well as scores on the hostility and physical aggression subscales, were each associated with greater stimulated TNF-α production. The anger and verbal aggression subscales were not related to stimulated TNF-α.

In a later study of 44 healthy, nonsmoking premenopausal women (mean age 33.5 ± 8.2 years), Suarez, Lewis, Krishnan, and Young (2004) examined the association of cynical hostility, as assessed by the Cook-Medley Ho, with stimulated productions of three pro-inflammatory cytokines (IL-1α, IL-1β, TNF-α) and three chemokines involved in the recruitment of leukocytes to locations of injury (IL-8, monocyte chemotactic protein [MCP]-1, macrophage inflammatory protein [MIP]-1α). Analyses controlling for race, BMI, total cholesterol, and alcohol consumption indicated that greater hostility was associated with greater stimulated productions of IL-1α and IL-1β, but in contrast to the authors’ previous finding in men (Suarez et al., 2002), not with production of TNF-α. Greater hostility also was associated with greater stimulated IL-8, but was unrelated to productions of either of the other two chemokines.

More recently, Janicki-Deverts, Cohen, & Doyle (2010) examined the association of hostility, as assessed by the Cook-Medley Ho, with stimulated productions of three pro-inflammatory (IL-2, TNF-α, INF-γ) and three anti-inflammatory (IL-4, IL-5, IL-10) cytokines in a sample of 153 healthy
men and women (mean age 37.3 ± 8.8 years; 51% female). The authors found that greater hostility was related to greater stimulated production of the pro-inflammatory cytokines TNF-α and IFN-γ, but was unrelated to production of IL-2 or to any of the anti-inflammatory cytokines. Further analysis of the subcomponents of hostility—cynicism, hostile affect, and aggression—showed that greater cynicism was related to greater productions of all three of the pro-inflammatory cytokines independent of age, sex, race, socioeconomic status, BMI, and health behaviors. Neither hostile affect nor aggression was related to any of the stimulated cytokine measures. These findings suggest that cynicism may be the key aspect of hostility associated with increases in stimulated pro-inflammatory cytokine production.

CIRCULATING MARKERS OF INFLAMMATION

Five published studies have examined the association of hostility with circulating markers of inflammation. Four of these used the Cook-Medley Ho to assess hostility, examined pro-inflammatory cytokines and/or CRP as outcomes, and included several control variables in their analyses. Suarez (2003) examined the association of hostility with IL-6 in 90 healthy, nonsmoking men (mean age 26.1 ± 6.8 years), and controlled for age, BMI, fasting total cholesterol, HDL cholesterol, resting diastolic blood pressure, and depressive symptoms. Miller, Freedland, Carney, Steefler, and Banks (2003) studied the relation of hostility to IL-1β, IL-6, and TNF-α in 100 healthy men and women (mean age 30.2 ± 10.0 years; 68% female), and controlled for demographic variables, smoker status, BMI, waist-hip ratio, cholesterol, mean arterial pressure, oral contraceptive use, and depressive symptoms. Stewart, Janicki-Deverts, Muldoon, and Kamarck (2008) examined the association of hostility with IL-6 and CRP in 316 healthy, older adults (mean age 60.6 ± 4.8 years; 49.1% female), and controlled for age, sex, race, education, BMI, blood pressure, cholesterol, triglycerides, glucose, insulin, health behaviors, and depressive symptoms. Most recently, Brummett, Boyle, Ortel, Becker, Siegler, and Williams (2010) examined circulating IL-6 and CRP concentrations in 525 younger adults (mean age 30.3 ± 9.0 years; 58% female) who were selected based on being either low (score of 9 or less) or high (score of 14 or more) in hostility, and controlled for age, race, sex, BMI, and sibship (some of the participants were related). Although Stewart and colleagues (2008) found greater hostility to be associated with greater IL-6 (but not greater CRP), none of the remaining studies observed an association between hostility and any of the measured circulating inflammatory markers.

In contrast to most of the aforementioned findings, Marsland and colleagues (2008) found hostility to be related to circulating markers of inflammation in their sample of 855 middle-aged adults (see study description in the neuroticism section). The authors used both the Cook-Medley Ho and the BPAQ to measure hostility, and created composite measures of the cognitive, affective, and behavioral dimensions by averaging standardized scores of the analogous subscales of the two hostility inventories. Circulating IL-6 and CRP concentrations were examined as outcomes. Results of analyses that controlled for age, sex, race, years of education, medical conditions, or medications known to influence inflammation, and trait NA revealed that higher scores on each of the three hostility subscales were associated with higher circulating concentrations of both inflammatory markers. The inclusion of health practices (BMI, smoking, exercise) as covariates reduced the association of hostile cognitions and hostile affect with IL-6 and CRP, consistent with the hypothesis that higher levels of BMI and smoking and lower levels of exercise may mediate these associations. By comparison, similar analyses did not support the hypothesis that health practices mediated the associations of hostile behavioral tendencies with IL-6 and CRP.

MODERATING THE EFFECTS OF STRESS ON IMMUNITY

As suggested earlier, it is possible that hostility moderates the immune system's response when individuals are subjected to stress. Findings from laboratory research suggest that exposure to acute psychological stressors—of either an interpersonal or noninterpersonal nature—gives rise to detectable changes in immunity (Segerstrom & Miller, 2004). Assuming that hostility may be associated with greater sensitivity to social stressors, one hypothesis that has been explored is that hostility should be associated with increased immune reactivity in response to interpersonal stress.

Mills, Dimsdale, Nelsen, and Dillon (1996) investigated whether changes in white blood cell (WBC) counts after participating in a public-speaking task (defending oneself against a false shoplifting accusation) differed depending on relative levels of hostility. A sample of 104 healthy adults (mean age 39.7 ± 10 years; 31% female) completed the
Buss-Durkee Hostility Inventory (BDHI; Buss & Durkee, 1957) and the Cook-Medley Ho within 48 hours of completing the stress task. Two factors related to the affective component of hostility were derived from BDHI scores, experience of anger (BD-experience), and expression of anger (BD-expression), and Cook-Medley Ho scores were used to measure total hostility (CM-hostility). Both before and after the task, participants completed the Spielberger State Anger Questionnaire, and blood was drawn for assessment of immune parameters (counts of CD3+, CD4+, CD8+, and CD19+ cells, two subsets of NK cells [CD56+ and CD57+], and total WBCs). The stress task was associated with increases over baseline in total WBCs, CD8+, CD57+, and CD56+ cells, and decreases in CD4+ and CD19+ cells. Cook-Medley total hostility moderated the effect of the stress task on CD57+ cell counts, and BD-expression scores moderated the effect of stress on CD19+ and CD56+ counts, but the nature of these effects were contradictory. Whereas the stressor-associated increase in CD57+ cells was amplified among those with higher CM-hostility scores, the stress-related changes in CD19+ and CD56+ counts were reversed among those with higher BD-expression scores—that is, CD19+ cells increased and CD56+ cells decreased subsequent to stress among those with higher scores. Neither anger responses to the task nor BD-experience were associated with changes in any of the immune measures.

Christensen, Edwards, Wiebe, Benotsch, McKelvey, Andrews, and Lubrarroff (1996) addressed whether hostility might influence changes in immune cell function in response to an interpersonal stress task. Forty-three male undergraduates completed a battery of psychological questionnaires that included the Cook-Medley Ho. Participants were then randomly assigned to one of two public-speaking conditions: a self-disclosure condition that required participants to describe an intimate and troubling personal experience; or a non-self-disclosure (low-stress control) condition wherein participants read from a passage describing a hypothetical student’s stressful experience. NK cytotoxicity was measured before and after the task. The results were consistent with the hypothesis that hostility moderates response to interpersonal stressors. Those with low levels of hostility responded to the interpersonal stressor with a small increase in NK cytotoxicity (relative to the low stress control), whereas those with high levels of hostility responded with a substantial increase in NK cytotoxicity.

Miller, Dopp, Myers, Stevens, and Fahey (1999) explored the possibility that hostility might moderate the association of negative emotional response to interpersonal stress with immunologic reactivity. To address this question, 41 couples (wives mean age 31.0 ± 7.5 years; husbands mean age 31.9 ± 7.7 years) took part in a marital conflict discussion. Hostility was measured before the discussion using the Cook-Medley Ho and counts of CD4+, CD8+, and CD5 CD16+CD56+ cells, and NK cell cytotoxicity were measured both before and after the discussion. Emotional response during the discussion was coded by trained observers. The results were consistent with hostility moderating stress response to interpersonal stressors, but only for men. In low-hostility husbands, decreased anger was associated with a small increase in NK cell cytotoxicity at mid-discussion, with no difference at the end of recovery. In contrast, for high-hostility husbands, anger expression was associated with a substantial increase in NK cell cytotoxicity during the discussion and a decline after the discussion. In high hostile men, higher levels of anger also covaried with greater increases in CD3 CD16+CD56+ counts. Anger was unrelated to immune parameters among wives, irrespective of their levels of hostility.

Although the laboratory studies suggest a possible moderating role for hostility in the immune system’s response to acute stress, data from a single field study failed to observe a moderating effect of hostility on functional immune response (lymphocyte proliferation) to a relatively short-lived real-life stressor. Lee, Meehan, Robinson, Smith, and Mahn (1995) used the five-item hostility subscale of the Brief Symptoms Inventory to measure hostility in 89 male first-year United States Air Force Academy cadets. Hostility was assessed on three occasions, 2 weeks prior to arrival at the Academy (pre-orientation), orientation, and 4 weeks postorientation (i.e., during a stressful training period). Proliferative response was measured on two occasions—orientation and 4 weeks later—by stimulating mononuclear leukocytes with PHA, phorbol 12-myristate 13-acetate (PMA), or anti-CD3 antibody. There were no cross-sectional associations between hostility and proliferative response during either orientation or training nor were there any lagged correlations between hostility at either pre-orientation or orientation and proliferative response during training.

CONCLUSIONS
There is reasonably reliable evidence that greater hostility (particularly cynicism) is associated with
greater stimulated production of pro-inflammatory cytokines. Less clear is its relation to circulating inflammatory markers. In this case, three small studies of primarily young samples found no relation between hostility and several markers of inflammation. However, two studies showed strong associations of hostility with IL-6 (Marsland et al., 2008; Stewart et al., 2008) and CRP (Marsland et al., 2008). The use of what may be a more reliable assessment of hostility and a larger and older adult sample may account for the discrepancy in findings between Marsland et al. (2008) and most of the other studies. Age is an especially important issue—and one that may explain Stewart et al.'s (2008) significant finding, because inflammation and, in turn, the variability of inflammatory markers within a sample increase with age. The average ages of participants in the three studies that found no association between hostility and inflammatory markers were all less than 31 years, whereas the average ages of the Stewart et al. (2008) and Marsland et al. (2008) samples were 61 and 45 years, respectively.

The evidence suggests the possibility that hostility moderates the effects of experimental stress—in particular interpersonal stress, on NK cell cytotoxicity. Both studies of NK cell cytotoxicity showed stress-induced increases in immune function to be most apparent among the most hostile. Findings for changes in CD56+ counts are more difficult to interpret. For example, while Mills and colleagues (1996) found those who scored higher on trait anger expression decreased in CD56+ cells during acute stress, Miller and colleagues (1999) found highly hostile men who expressed anger during laboratory stress increased in CD56+ cells.

Social Inhibition

Social inhibition is a tendency to suppress the expression of emotions in social interactions, to demonstrate extreme sensitivity to social criticism, and to withdraw in uncertain or challenging situations (Asendorpf, 1993). Although social inhibition has been recognized as an enduring trait, no published and validated measures of this personality characteristic are presently available. Accordingly, the studies we describe below either employed study-specific measures or measures of closely related personality constructs.

DELAYED-TYPE HYPERSENSITIVITY RESPONSE

Cole, Kemeny, Wetzman, Schoen, and Anton (1993) evaluated the role of social inhibition in DTH responses to tetanus toxoid during social engagement. Participants were 36 men and women (86% female) with either functional bowel disease (FBD; 55%), fibromyalgia (15%), or both disorders (30%), who were enrolled in a study assessing the effectiveness of hypnosis and education interventions in immune function among persons with FBD. Social inhibition was measured using the UCLA Rejection Sensitivity Scale (UCLARS; Cole, 1996), and by combining items from the Restricted Expression, Social Apprehensiveness, and Intimacy Problems scales of the Dimensional Assessment of Personality and Psychopathology (DAPP; Livesley, Jackson, & Schroeder, 1992). The first DTH inoculation was administered during the low-social-engagement baseline period, and induration responses were read 48 hours later. Inoculations were then repeated 4 weeks later, during the high-social-engagement intervention period, and 6 weeks later, following completion of the intervention. Induration responses were read 48 hours after each inoculation with the larger of the two values taken as a measure of the maximal response during the intervention period. Socially inhibited participants (upper 15% of scores) displayed greater induration responses than their less-inhibited counterparts during the high-engagement intervention period but not during the low-engagement baseline, when the groups did not differ. The authors attributed the improved cellular immune response to inhibition-related “hyperresponsivity.”

HIV

Eisenberger, Kemeny, and Wyatt (2003) used a cross-sectional design to examine whether emotional expression was associated with CD4+ cell levels in a sample of 61 HIV-positive low-income minority women (mean age 37.2 ± 8.4 years). All participants took part in a 3- to 5-hour face-to-face interview that included open and closed-ended questions. Emotional expression was based on the percentage of negative (e.g., sad, hurt, hate, guilty) and positive (e.g., happy, joy, peaceful) emotion terms used during the coping with HIV component of the interview and emotional inhibition on the percentage of inhibition words used (e.g., inhibit, restrain, withhold, suppress, avoid). A blood draw at the time of the interview was used to evaluate CD4+ levels. Control variables included age, socioeconomic status, race, level of depression, recreational drug use, exercise, nutrition, sleep patterns, smoking, disease duration, HIV-related symptoms, HIV-related medication use, and sexually transmitted diseases. Emotional expression—either positive or
negative, was unrelated to CD4+ levels. However, greater emotional inhibition was associated with lower CD4+ levels.

Fincham, Smit, Carey, Stein, and Seedat (2008) used a cross-sectional design to evaluate the relationship between behavioral inhibition and CD4+ counts among 454 HIV-positive South Africans (mean age 33.7 ± 7.6 years; 75% female). Behavioral inhibition was assessed using the 30-item Retrospective Self-Report of Childhood Inhibition scale (RSRCSI; Reznick, Hegeman, Kaufman, Woods, & Jacobs, 1992), which comprised of two subscales: a social fears subscale and a general fearfulness subscale. CD4+ counts were obtained from participant medical records within four weeks of the interview assessment. Covariates included age, sexual orientation, antiretroviral drug use, race, and disease duration. CD4+ counts were not associated with the RSRCSI total scale or either of its subscales.

In a sample of 54 symptomatic HIV-infected gay men (median age 41 years, range 26–55), Cole, Kemeny, Fahey, Zack, and Nalliboff (2003) examined whether social inhibition influences changes in viral load and CD4+ cell counts over the course of 11 to 18 months, and if so, whether sympathetic nervous system (SNS) activity constitutes a possible explanatory mechanism. Social inhibition was measured using a composite of scales assessing introversion (extraversion subscale of the NEO-FFI; Costa & McCrae, 1992), social avoidance (DAPP social apprehensiveness and intimacy problems subscales; Cole et al., 1999; Livesley et al., 1992), emotional inexpression (Emotional Expressiveness Questionnaire; King & Emmons, 1996; DAPP restricted expression subscale), hostility (Cook-Medley Ho), and agreeableness (NEO-FFI). SNS activation was approximated using a composite score measuring skin conductance, brachial artery systolic blood pressure, and electrocardiogram data collected before, during, and after a serial subtraction stress task. HIV progression was assessed in terms of response to antiretroviral treatment (change in viral load and CD4+ count between baseline and follow-up). Control variables included age, race, income, education, substance use, sexual activity, infection duration, antiretroviral treatment, and baseline viral load or CD4+ count. Individuals scoring in the upper half of the social inhibition distribution had greater viral loads at baseline than those scoring below the median. Further, social inhibition was associated with poorer responses to antiretroviral treatment such that, relative to those who were less inhibited, inhibited persons demonstrated smaller CD4+ increases and smaller viral load declines following treatment with the antiretroviral medication. Socially inhibited persons also showed greater SNS activity in response to the stress task. Mediation analyses indicated that SNS activity accounted for 72% of the relationship between social inhibition and virologic response and 92% of CD4+ recovery following antiretroviral treatment.

CONCLUSIONS

The substantial differences in how social inhibition is measured across studies make it difficult to integrate the results. Even so, there is suggestive evidence that social inhibition is associated with poorer progression of disease among HIV-positive men. Evidence that this association may be mediated by SNS activity is also provocative.

Chapter Summary

The literature on personality and immunity is in its infancy. The lack of consistency of results across and within traits, and in what outcomes have been studied, makes it difficult to determine how reliable or meaningful associations are and whether different traits are important for different outcomes. Another limitation is the relative lack of evidence on the mediating pathways linking personality to various immune outcomes. It is only by understanding how specific traits may influence immunity that we could generalize existing findings to outcomes that have not yet received attention.

Overall, it is impossible to summarize this literature in any meaningful way. We can say that there is promising evidence across all the traits, with existing evidence at least suggesting some reliable associations and directions that future work might take to fill in voids in the literature.

Suggestions for Future Work

There is a clear need for adopting a strong theoretical stance in studying the association between personality traits and immunity. We have presented a general discussion of pathways that might link traits to immune function, but each trait has its own specific characteristics and each requires its own model. Such models should identify pathways and, in turn, outcomes that are most likely to be affected. For example, conscientiousness may be most closely tied to outcomes that respond to engagement in health-promoting behaviors and adherence to medical regimens, whereas extraversion might be more closely tied to outcomes influenced by physiological activation. Moreover, studies need to be designed
in response to these models. This includes not only appropriate choice of outcomes, but also assessment and testing of proposed mediating pathways.

As discussed earlier, each of the Big Five personality characteristics is comprised of several subtraits. For example, extraversion includes friendliness, gregariousness, assertiveness, activity level, excitement seeking, and cheerfulness. For the most part, personality subtraits are not individually studied in the literature. Future research might investigate the relative importance of factor subtraits in regard to immune function, and whether all subtraits of a given personality factor influence immunity via similar and/or complementary mechanisms. Distinguishing subtraits that are responsible for associations with immune outcomes can help in understanding the basis for personality-driven immunity, and it can help identify responsible mechanisms. Although not a Big Five factor, the work focusing on distinguishing the role of different aspects of hostility in immunity provides a good model. Here it seems that cynicism may be the driving force, suggesting that a particular component of hostility—general feelings of belief and trust in others—may be the important characteristic to focus on.

Stronger methodological approaches are also required. Especially in studies of markers of immunity, there is a tendency to use available samples, often students. However, in many cases young healthy adults are inappropriate because there is relatively little variance in their immune function and especially in markers of underlying disease such as chronic underlying inflammation (circulating CRP and IL-6). Moreover, the older one gets, the longer he or she has been exposed to the pathways linking personality to immunity, such as smoking or SNS activation. Similarly, and often because of the high cost of conducting studies, the sample sizes are small when considering the probable effect sizes and the noise often inherent in assessing functional immunity. Underpowered studies can mislead the field about the importance of addressing specific questions. Finally, there is a need to carefully consider controls for third factor variables in correlational studies. Personality traits and immunity both vary with demographics, with health, and with physical status (e.g., body mass); reasonable attempts to assess and control for these variables are imperative.

Finally, an important hypothesis concerns the potential role of personality in moderating the effects of stress on immunity. Here again, the development of appropriate theoretical approaches to each trait is essential. Why would we expect a trait to buffer or exacerbate the effects of stress? Should moderating effects look the same in healthy versus unhealthy (e.g., HIV) or younger versus older, or male versus female—populations? Should there be some kind of match between the type of stressor and type of trait? For example, hostility (a characteristic of social behavior) may exacerbate effects of social but not nonsocial stressors. Moreover, tests of interactions generally require large samples for adequate power. Finally, it is noteworthy that chronic and life-threatening diseases themselves often are major stressors, and associations between a personality trait and disease status or its progression may actually be driven by its moderating effects of the stress experience as opposed to a direct (main) effect on disease.

Related Chapters
For more information on concepts introduced in this chapter, see also Suarez; Pressman; and Booth, this volume.

Author Note
Preparation of this chapter was supported by AI066367, HL092858 and a minority supplement from the National Institute of Allergy and Infectious Diseases.

References
depression to immune function in elderly subjects. Psychiatry Research, 127(3), 237–245.


The Oxford Handbook of Psychoneuroimmunology

Edited by
Suzanne C. Segerstrom