

Positive Affect and Immune Function

ANNA L. MARSLAND, SARAH PRESSMAN, AND SHELDON COHEN

I. INTRODUCTION	761
II. POSITIVE AFFECT	761
III. THE EMPIRICAL EVIDENCE FOR AN ASSOCIATION BETWEEN PA AND IMMUNE FUNCTION	762
IV. CLINICAL CONTEXT: POSITIVE AFFECT AND HEALTH	769
V. POTENTIAL PATHWAYS LINKING PA AND IMMUNE FUNCTION	771
VI. TRAIT PA AND OTHER RELATED PERSONALITY CONSTRUCTS	773
VII. PSYCHOLOGICAL INTERVENTIONS	773
VIII. SUMMARY	774

I. INTRODUCTION

It is now over 40 years since it was first hypothesized that emotions could influence immunity and disease (Ader et al., 1987; Solomon and Moos, 1964). Since then, reliable associations have been found between immune function and depression, stress, and anxiety (see reviews by Herbert and Cohen, 1993a, 1993b; Segerstrom and Miller, 2004). In contrast, there has been little work on the effects of *positive* emotions on immunity and immune-mediated disease (Pressman and Cohen, 2005). Indeed, a search of PsycINFO revealed almost 100 times more studies on "depression and immunity" than there are on "happiness and immunity." The goal of this chapter is to review evidence for a relationship between positive emotions and immune function, and to explore the implications of this connection for health.

II. POSITIVE AFFECT

Although the literature examining positive psychological constructs and health is growing rapidly, there is little consensus in the field regarding a single definition of positive affect (PA). In this chapter, we define PA as the feelings that reflect a level of pleasurable engagement with the environment such as happiness, joy, excitement, enthusiasm, and contentment (Clark et al., 1989). There are other "positive" psychological constructs used in studies of immunity and health that have similarities to PA. Some are cognitive and motivational constructs such as self-esteem, optimism, extraversion, purpose, and mastery (DeNeve and Cooper, 1998; Lyubomirsky et al., 2005; Ryff, 2003; Salovey et al., 2000; Zautra, 2003), while others are complex measures like quality of life and subjective well-being (e.g., Diener, 1984; McDowell and Newell, 1996; Weisman, 1979) that combine PA in an undifferentiated manner with other constructs. Because our focus is on the influence of affect, we limit this review to studies using scales or experimental manipulations that primarily or solely address emotional response.

PA can be brief, longer lasting, or more stable trait-like feelings. Although some use the terms *affect*, *mood*, and *emotion* to distinguish duration, these uses are not applied consistently in the literature, and thus we use these terms interchangeably. We, however, distinguish between studies using measures that assess more stable disposition-like PA, which we refer to as *trait PA*, and those measuring or manipulating relatively

short-term bouts of positive emotions, which we refer to as *state PA*. For the purpose of this chapter, we consider *state* a measurement of moment-to-moment affect lasting up to a day in duration and *trait* a measure of affect assessed over at least 1 week and often evaluated as how people “typically” feel. The status of measures reflecting the experience of emotion over a few days is less clear, and they are generally thought of as longer-lasting state appraisals.

An important consideration for immunology researchers interested in studying emotion is the debate regarding the structure of affect (e.g., Ekman, 1992; Izard, 1977; Larsen and Diener, 1992; Russell, 1980; Watson and Tellegen, 1985). There is a growing consensus that positive and negative affect (NA) are broad, underlying dimensions of basic emotions that consistently emerge across studies (Watson and Tellegen, 1985). However, whether they represent two ends of a continuum or are independent concepts is controversial. Should positive and negative affect lie on opposite ends of a bipolar scale, then any effect of PA may merely reflect the absence of NA and vice versa. On the other hand, should they reflect relatively independent constructs, they may have distinctive influences on physiology. Given the strong evidence for the relation between NA and immunity, the magnitude of the correlation between NA and PA is key to understanding the importance of PA. To date, it appears that short-term (minutes, day) measures of PA and NA are strongly negatively correlated, while the longer the period that the measure covers (weeks, months, years, typically), the more independent they become (e.g., Diener and Emmons, 1985; Diener et al., 1985; Watson, 1988).

In addition to a positive versus negative valence dimension (e.g., happy versus sad), emotions are often categorized along a second dimension, high versus low activation (aroused versus unaroused), according to a circumplex model (e.g., Russell, 1980). Thus, emotions can be categorized by where they fall on these two dimensions. For example, excitement is positive valence/high activation, and sad is negative valence/low activation. While there are other ways of distinguishing between emotions, this system appeals to health researchers who equate emotional activation with physiological arousal, which is thought to be a primary pathway through which emotions may influence immunity and health (Cohen et al., 1997b; Krantz et al., 1981).

The majority of naturalistic studies examining relations between PA and immune function employ self-report measures of affect, using adjective checklists such as the Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988) or the vigor subscale

from the Profile of Mood States (POMS) (McNair et al., 1971). Both of these scales have been demonstrated to provide valid and reliable assessments of affect, with a bias towards positive valence/high activation emotions. Depending on the time frame employed when considering the experience of affect, these (and similar) scales are used to measure state (current mood) or trait (typical mood) PA.

There are also a number of experimental studies examining associations between PA and immunity utilizing mood manipulation paradigms to determine the impact of transient emotional experiences (states) on immune function. Mood inductions include a number of methods, for example, imagining previous positive events, listening to positive music, making facial expressions, reading emotional statements, and watching films. These procedures are effective in inducing changes in mood that typically last for 10 to 15 minutes (e.g., Frost and Green, 1982).

III. THE EMPIRICAL EVIDENCE FOR AN ASSOCIATION BETWEEN PA AND IMMUNE FUNCTION

A recent survey of Medline and PsycINFO and a review of the reference sections of identified papers revealed 25 studies examining the relationship between state or trait PA and immune function (Pressman and Cohen, 2005) (see Tables 1 and 2). The majority of these studies focus on the impact of the experimental induction of state positive moods, while the remainder involve naturalistic assessments of PA and immunity.

A. Mood Induction Studies

Of the 15 studies that examined mood induction, 8 assessed the effects of state PA on levels of secretory immunoglobulin A (sIgA) measured in saliva. sIgA is an antibody that provides the main immunological defense of mucosal surfaces and plays an important role in primary defense against viral and bacterial infection. Early studies measured the absolute concentration of total sIgA in saliva samples and were criticized because of the possibility that mood might alter saliva flow rate (Stone et al., 1987a). However, later studies controlling for saliva flow (using secretion rate or adjusting sIgA concentration for flow rate) have found similar results. In short, various forms of positive mood induction, including watching films, listening to positive music, or reflecting on positive personal experiences increase total sIgA levels in saliva. (Dillon et al., 1985; Harrison et al., 2000; Hucklebridge et al.,

TABLE 1 Summary of Mood Induction and Immune Function Studies (From Pressman and Cohen, *Psychological Bulletin*, 2005. Copyright 2005 by the American Psychological Association. Adapted with permission).

Study	Participants	Mood induction	Dependent measure	Findings
Berk et al., 2001	52 healthy men (M = 27)	Humorous film (No control condition)	NKCC; Plasma Ig A, G, M; # T- and B-cells; IFN gamma	Increased NKCC; IgG, A, & M; activated T, cytotoxic T, helper- T, B, and NK cell numbers; total leukocytes, and IFN gamma.
Dillon et al., 1985	10 students (M = 23)	Humorous film and control condition	SIgA	SIgA increased from baseline in mood induction, but not during control condition.
Futterman et al., 1992	5 actors (ages 25–38)	Monologue based on personal happy, sad, or neutral experience	NKCC; Cell subtype numbers (CD56, CD57, T-cell subgroups)	More immune fluctuation (combined) for affect inductions versus neutral condition and for aroused conditions (happy, anxious) than unaroused (depression, neutral).
Futterman et al., 1994	14 male actors (M = 35)	Five mood inductions on separate days; induced high/low arousal PA and NA by reading scenarios and using personal memories (No control)	NKCC; lymphocyte proliferation to PHA; Cell subtype numbers (CD57, NK, and T-cells)	All mood states were associated with NKCC and NK cell percent. Response to PHA increased after positive moods and decreased after negative moods.
Harrison et al., 2000	30 students (M = 21)	Humor and excitement inducing films and control condition	SIgA (measured 2 months after each film)	SIgA increased in response to all 3 films.
Hucklebridge et al., 2000 (2 studies)	Study 1: 19 female students Study 2: 41 male and female students (M = 20)	Study 1: Self-reflection on happy versus guilty life experience Study 2: Happy versus sad music No control condition	SIgA	SIgA increased with both manipulations regardless of valence. More pronounced elevation for happy mood.
Knapp et al., 1992	20 volunteers (ages 19–30)	Two 2.5 hour sessions on different days. Recall of positive or negative personal event and re-enactment	Lymphocyte proliferation to PHA, ConA, and PWM; NKCC; T-cell subsets	PHA stimulated proliferation decreased for PA and NA inductions (Con A decreased with NA only).
Labott et al., 1990	39 women (M = 22)	Humorous and sad films and control condition	SIgA	Humorous film associated with increased SIgA.
Lambert and Lambert, 1995	39 5th grade students	Humorous program and control condition	SIgA	SIgA increased in response to the humorous, but not the non-humorous, film.
McCraty et al., 1996	10 healthy volunteers (M = 41)	Music inducing calm with energetic alertness and self-induced positive emotional states of appreciation versus non-appreciation. No control condition	SIgA	SIgA increased by 55% with calm/alert music and by 50% with appreciation induction. Simultaneous calm/alert music and appreciation produced a 141% increase.
Mittwoch-Jaffe, 1995	123 students (M = 23)	Positive (humorous) and negative films. No control condition	IL-1beta, IL-2, IL-3, IL-6, TNF-alpha	Positive mood induction associated with decreased TNF and increased IL-2 and IL-3.
Njus et al., 1996	50 students	Writing about humorous or negative film or neutral control topic	SIgA	Writing about positive or negative films associated with increased SIgA when compared with writing about neutral topic.
Perera et al., 1998	16 students (M = 25)	Humorous or neutral film	SIgA and salivary lysozyme	Both lysozyme and SIgA increased with humorous versus neutral film.
Yoshino et al., 1996	26 women with rheumatoid arthritis and 31 healthy controls	3 hour performance of "Rakugo" (Japanese comedy). No control condition	Substance P, CD4:CD8 ration, NKCC, IL-6 and IFN-gamma	Comedy associated with decreased IL-6 in arthritic patients, and a decrease in IFN-gamma in both groups.
Zachariae et al., 1991	11 hypnotizable students	Hypnotized to feel happiness and well-being versus anger and depression. No control condition	Monocyte chemotaxis	Chemotactic index was higher after happy-relaxed induction versus baseline and NA states.
Zachariae et al., 2001	15 hypnotizable students	Hypnotized to feel sadness, happiness, and anger. No control condition	Hypersensitivity response to histamine	No effect of induced emotion was found on the size of the wheal reaction.

TABLE 2 Summary of Naturalistic Mood Studies and Immune Function (adapted from Pressman and Cohen, 2005)

Study	Participants	Design/Independent measure	Dependent measure	Findings
Costanzo et al., 2004	18 older males and females (M = 84)	Cross-sectional. PA and NA measured using short form of POMS based on how they felt during the past week and optimism	Production of IL-2, IFN-gamma, and IL-10 by PBMCs stimulated with live influenza virus and vaccine	PA and optimism positively associated with T-helper type 1 cytokine responses to live virus and vaccine. Higher NA associated with lower cytokine responses.
Evans et al., 1993	12 students (Age approx. 20)	Longitudinal—2 weeks ambulatory monitoring of mood (Nowlis Mood Adjective Checklist)	SlgA	Within subject analysis showed higher SlgA levels on days with negative mood.
Logan et al., 1998	9 healthy subject with history of cold sores (ages 20–40)	Longitudinal—3 months daily mood report on bipolar mood continuums (e.g., happy-unhappy) also Affect Intensity Scale	Weekly blood draw to measure T lymphocytes and NK cell number	More contentment correlated with lower NK level and elevated CD8+ cells the week before cold sore outbreak. Greater depression (combination of low happiness, low hopefulness) associated with lower CD8+ numbers.
Lutgendorf et al., 2001	30 older adults moving to assisted living and 28 non-moving controls (M = 78)	Longitudinal (1 month before move and 2 weeks and 3 months post-move). PA and NA measured using short form of POMS based on how they felt during the past week.	NKCC, IL-6, and IgG antibody titers to EBV	Across both groups and all time-points, higher PA was associated with greater NKCC. At the 2-week post-move time-point, higher PA associated with lower EBV titers across both groups.
Marsland et al., 2006	84 healthy graduate students (M = 24)	Cross-sectional. PA assessed with adjective checklist based on how they usually are as compared to peers and measured after first 2 vaccinations in 3-vaccine sequence	Antibody response to hepatitis B vaccination	Trait PA was associated with higher levels of antibody production, independently of NA and closely related constructs such as optimism and extraversion.
Moss et al., 1989	10 healthy subjects (M = 24)	Longitudinal—4 weeks of weekly mood questionnaires and blood draws. PA assessed with POMS	NKCC	No correlation between any mood item (NA or PA) and NKCC.
Ryff et al., 2004	135 older women (ages 61–91)	Cross-sectional—4 days of mood report on PANAS, short form of Watson MASQ (happy, cheerful, fun over past week) and Ryff eudaimonic well-being scale and 1 blood draw	IL-6	No association between mood and IL-6, but eudaimonic factors (high life purpose) correlated with lower IL-6.
Stone et al., 1987	30 graduate students (M = 24.5)	Longitudinal—4 weeks ambulatory monitoring of daily mood (Nowlis Mood Adjectives)	Antigen-specific SlgA in response to novel antigen-rabbit albumin	SlgA higher on days with high PA and lower on days with high NA.
Stone et al., 1994	96 adults (M = 42)	Longitudinal—12 weeks ambulatory monitoring of daily mood with PANAS	Antigen-specific SlgA in response to novel antigen-rabbit albumin NKCA	SlgA higher on days with high PA and lower on days with high NA.
Valdimarsdottir and Bovbjerg, 1997	48 healthy women (M = 39)	Cross-sectional—2 days of mood report on subject of POMS adjectives from factor analysis	NKCA	PA associated with higher NKCA, NA associated with lower. Significant interaction where PA is only beneficial when some NA present.

2000; Labott et al., 1990; Lambert and Lambert, 1995; McClelland and Cheriff, 1997; McCraty et al., 1996; Njus et al., 1996; Perera et al., 1998).

All of these studies examined healthy, young adults except the study by Lambert and Lambert (1995), which demonstrated the same effect in a sample of fifth grade children. All but two (Lambert and Lambert, 1995; McCraty et al., 1996) studies confirmed that the mood induction was successful. Furthermore, the majority of the studies included an emotionally neutral condition to control for diurnal variation, passage of time, and other contextual factors. Plasma levels of immunoglobulins G, A, and M have also been shown to increase in response to a film designed to stimulate mirthful laughter (Berk et al., 2001).

Two studies in this literature have examined whether mood-induced increases in sIgA are valence specific (Hucklebridge et al., 2000; Njus et al., 1996). Njus and colleagues (1996) examined the impact of writing about films designed to arouse positive or negative moods (a Bill Cosby performance or a documentary about the death of a child) on salivary sIgA levels among 50 healthy, undergraduate volunteers. After watching one of the two films, subjects were instructed to write about either the film or a mundane topic (their shoes). Saliva samples were obtained before and immediately after the writing exercise and again 24 and 48 hours later. Manipulation checks (self-reported moods) confirmed that the films were effective at inducing positive and negative affect, respectively. Moreover, subjects who wrote about either film had higher concentrations of salivary sIgA than the control groups who wrote about their shoes. There was *no differential effect* of positive versus negative mood states on sIgA. Similarly, Hucklebridge et al. (2000) reported on two separate experiments examining the impact of positive and negative mood induction on sIgA concentration. In the first, 19 healthy female subjects attended two laboratory sessions and were asked to write for 10 minutes about a past situation in which they had been either "very happy" or "very guilty." Mood ratings validated the efficacy of the manipulation. In the second study, 41 healthy male and female undergraduates listened to music that had previously been demonstrated to induce sad and happy mood states. Both experiments showed a significant elevation in sIgA concentration and secretion rate in response to mood manipulations *regardless of the valence* of the induced emotion. Thus, although there is consistent evidence for mood-induced increases in total sIgA concentration, it appears to be the activation dimension of the emotion, rather than the valence, that is associated with increased antibody levels. This conclusion is consistent with the studies showing an

increase in total salivary sIgA levels in response to acute laboratory stress tasks that typically induce negative mood states (e.g., Bristow et al., 1997; Willemson et al., 1998).

Induced positive emotions have also been shown to affect a handful of other immunologic parameters, although these findings are more difficult to interpret. A few studies have examined positive mood-induced changes in the numbers of immune cells in peripheral circulation. Here, findings are mixed, with some studies showing increases in the percentage of NK cells and in absolute numbers of circulating B-cells, T-cells, T-helper cells, cytotoxic T-cells, and total leukocytes (Berk et al., 2001; Futterman et al., 1992, 1994), and another showing no change (Knapp et al., 1992). The effect of induced PA on measures of cellular immune function has also received little attention. A few studies have examined NK cell cytotoxicity (NKCC), and initial findings suggest a mood-induced increase in this measure (Berk et al., 2001; Futterman et al., 1994), but it is not clear that this is specific to moods of positive valence (Futterman et al., 1994). Findings from the two studies examining phytohemagglutinin (PHA)-induced proliferation of lymphocytes are also mixed. Futterman et al. (1994) found that induced positive moods were associated with increases and induced negative moods with decreases in this measure. In contrast, Knapp et al. (1992) found decreases in PHA-elicited proliferation with both positive and negative mood inductions. Overall, interpretation of these few mixed findings is limited by small sample sizes and a general failure to include an emotionally neutral control condition or to differentiate between high and low activated positive states, making it premature to form any conclusions.

More recent attention in the field of psychoneuroimmunology has turned to relationships between emotions and the concentration of cytokines in peripheral circulation. The health significance of circulating levels of cytokines is difficult to interpret, as it reflects regulation of levels in response to specific demands. Nevertheless, the few studies that have examined cytokine levels in response to positive mood induction provide some evidence that state PA is associated with increases in interleukin (IL)-2, IL-3, and decreases in tumor necrosis factor-alpha (Berk et al., 2001; Mittwoch-Jaffe et al., 1995). Findings are less consistent for interferon gamma, with one study showing PA-related increases (Berk et al., 2001) and another showing decreases (Yoshino et al., 1996). Finally, a study examining circulating levels of IL-6 among patients with rheumatoid arthritis demonstrated that watching a comedy performance was associated with a decrease in levels of this pro-inflammatory cytokine (Yoshino

et al., 1996) that may be a marker of a short-term beneficial health effect.

A few studies have examined whether induced PA is associated with a more clinically meaningful measure of cellular immune function, allergic hypersensitivity reactions in response to allergen, or histamine exposure in allergic subjects. In support of a health benefit of state PA, a reduction in allergic response (wheal size) was found when pleasantness and relaxation were induced by hypnotic suggestion (Laidlaw et al., 1996) and when humor was induced by watching a film (Kimata, 2001). In contrast, Zachariae and colleagues (2001) did not find an effect of hypnotically induced positive or negative moods on magnitude of hypersensitivity response.

In sum, the most consistent findings from studies examining the effects of brief positive mood induction on immune function in healthy individuals support PA-related increases in sIgA levels, numbers of immune cells in peripheral circulation, and possibly NK cell activity, suggesting an upregulation of parameters of innate immunity. These findings are consistent with those found in response to acute laboratory stress tasks designed to elicit negative moods, such as speech and mental arithmetic tasks (for review, see Segerstrom and Miller, 2004). Similar immune responses to positive and negative mood states suggest that it is the increase in affective arousal, rather than the positive or negative valence of the emotion, that contributes to immunological variability. Further evidence for this is derived from the few studies that have induced both positive and negative moods in the laboratory and show similar immune effects (Futterman et al., 1992; Knapp et al., 1992; Hucklebridge et al., 2000; Njus et al., 1996). To date, the majority of positive mood induction protocols have induced activated positive states, such as humor and excitement. It remains to be determined whether low activation positive mood states such as calm and pleasure are associated with similar immune responses.

There is now a large body of literature demonstrating that immune changes in response to acute laboratory stress are largely mediated by activation of the SNS (Marsland et al., 2001a). For example, it has been demonstrated that immune outcomes assessed after a laboratory stressor covary with the magnitude of sympathetic activation elicited under the same stimulus conditions (e.g., Manuck et al., 1991). Pharmacological studies provide further support for this pathway, with the administration of physiological doses of sympathetic stimulants (e.g., exogenous catecholamines) invoking functional modulation of innate immunity that is similar to that seen during mental stress (van

Tits et al., 1990). Furthermore, acute stress-related immune responses are blocked by adrenergic receptor inhibition (Bachen et al., 1995). Given the similarity in immune responses to both positive and negative mood induction, it is possible that the arousal dimension of these mood states induces activation of the SNS and an upregulation of innate immunity. It has been proposed that brief increases in innate immune function in response to acute challenge are adaptive, reducing risk of infection and aiding in wound healing (Segerstrom and Miller, 2004).

B. Naturalistic Studies of Positive Emotional States

Others have studied self-reports of PA and their relations with immune outcomes in naturalistic settings. These studies utilize daily diary measures of mood states and examine mood-related immune function. A well-designed study by Stone and colleagues (1987) had volunteers ingest a capsule containing an innocuous novel antigen (rabbit albumin) daily for 10 weeks so that the researchers could determine the *specific* sIgA response to the novel antigen, unlike other studies that look at more general total (non-specific) levels of this marker. For the latter 8 weeks of this period, volunteers also completed daily diaries, recording positive and negative mood states, and gave daily saliva samples to assess specific sIgA to the novel antigen. Within subjects, analyses revealed that antigen-specific sIgA was higher on days with higher positive mood relative to days with lower positive mood. Conversely, sIgA was lower on days with high negative mood relative to days with lower negative mood (Stone et al., 1987). These results were replicated in a subsequent study by the same group that monitored mood and antibody levels over a 12-week period (Stone et al., 1994).

Evans et al. (1993) examined relationships between daily mood and non-specific sIgA over a 2-week measurement period. Although they found no associations between positive mood and total sIgA, negative mood was associated with higher total sIgA concentration and secretion rate. It may be that these results differ from the studies discussed above because the specific marker of immune activity in response to an antigenic challenge used in Stone's work better gauges immune function than the non-specific and unstimulated marker used here. Further naturalistic studies are indicated to aid in better understanding relationships between acute mood states and immune function and disentangling the differential roles of emotional valence and arousal.

C. Naturalistic Studies of Positive Emotional Traits

1. General Findings

Other naturalistic research has explored the relationship between longer-lasting PA and NKCC. For example, Lutgendorf et al. (2001) employed a sample of 58 older adults (65–89 years), 30 of whom were moving to an assisted living facility. They measured mood over the past week using the POMS and assessed NKCC on three occasions, 1 month before the move, and 2 weeks and 3 months after the move. Across the whole sample and study period, higher levels of vigor were associated with greater NKCC. Higher vigor was also associated with lower IgG antibody titers to Epstein-Barr Virus (EBV), as measured at the 2-week post-move assessment. These results suggest that a trait PA measure is associated with increased cellular immune competence, including more effective immune control of latent EBV.

Valdimarsdottir and Bovbjerg (1997) also found a relationship between PA (averaged over a 2-day period) and NKCC. In this study, 48 healthy female volunteers completed a positive and negative adjective checklist derived from the POMS on 2 consecutive days. Overall, higher levels of PA were associated with greater NKCC. Conversely, when compared with women who endorsed no NA, the 26 women who endorsed some NA had lower NKCC. Interestingly, there was also an interaction between PA and NA scores in predicting NKCC, with individuals who endorsed both lower levels of PA and the presence of some NA showing lower NKCC than individuals with either higher PA or no negative mood. Thus, it is possible that PA is protective for individuals who also experience negative mood traits. In contrast to the above two studies, Moss et al. (1989) tracked relationships between weekly positive moods and NKCC for 4 weeks during summer vacation among 10 healthy professional students and found no consistent effects of mood on NKCC. These findings are more difficult to interpret as a consequence of a large interindividual variability in NKCC (Moss et al., 1989).

Evidence suggesting that trait PA is associated with more effective cellular immune function is provided by a recent study examining *in vitro* cytokine responses to live influenza virus and to influenza vaccine among 18 healthy older adults (75–91 years) who had previously received the influenza vaccine (Costanzo et al., 2004). The POMS was employed here as a measure of affect over the course of the past week. Higher levels of PA (and optimism) were associated with greater T-helper type 1 (T_H1) cytokine (IL-2 and IFN-gamma) responses to *in vitro* stimulation of peripheral blood

mononuclear cells with live influenza virus or vaccine. Conversely, higher NA was associated with lower T_H1 cytokine responses, indicating a potential influence of affect on cell memory. T_H2 cytokine responses were largely unaffected by mood. It is unclear whether these findings reflect independent effects of PA and NA.

Two other studies have examined associations between trait affect and immune responses among individuals with immune-related diseases. For example, Logan et al. (1998) followed 10 individuals with a history of herpes labialis (cold sores) over a 3-month period, recorded daily state measures of PA and NA, and drew blood each week for the determination of numbers of circulating T lymphocytes and NK cells. In the week prior to a cold sore outbreak, individuals who endorsed being more content demonstrated higher numbers of NK cells and cytotoxic T-cells than individuals who were discontent. Conversely, individuals who reported low happiness/hopefulness showed lower CD8+ cell numbers than those at the other end of the happiness continuum. Similarly, Laidlaw et al. (1994) found that individuals with allergies who endorsed greater liveliness on a bipolar continuum from liveliness to listless and more vigor on the POMS, as averaged over a 2-week period, had smaller mean hypersensitivity skin responses to allergens than their more listless and lower vigor counterparts. Because positive and negative affect were assessed in these studies on a single continuum, it is impossible to know whether one or both valences contributed to the reported associations.

In sum, available evidence from the few naturalistic studies examining mood across periods ranging from a few days to a couple of weeks suggests that PA is associated with markers of immune function, including higher NK cell number and activity, greater control of latent EBV, and increased T_H1 cytokine responses to *in vitro* stimulation with live influenza virus. Of greater potential clinical relevance are studies linking PA to an increasing number of circulating CD8+ and NK cells among individuals with herpes and a reduction in allergic response in individuals with allergies. Although this literature is not yet convincing, these findings raise the possibility that PA-related changes in immune function confer a health benefit. However, because these studies used scales that included adjectives that primarily tapped vigor (for example, *energetic*, *peppy*, and *vigorous*), it is possible that the association of PA with immunity reported here merely occurs because the PA measures that were used assessed underlying health status.

To date, the majority of studies examining relationships between trait affect and immunity have focused on mood averaged across relatively short periods

(days to a couple of weeks). In contrast, the literature examining relationships between emotions and health has focused on stable, dispositional characteristics, which may be associated with more stable immune differences of greater potential health significance. There is no single accepted method of measuring stable dispositions; however, one method that is widely employed is to ask people to characterize themselves as they *typically* are. Using this method, a large literature has demonstrated a reliable association between self-endorsed NA and immune function (for reviews, see Herbert and Cohen, 1993a; Kiecolt-Glaser et al., 2002). In contrast, relations between dispositional PA and immunity have received little attention.

2. Trait PA and Vaccination Response: The Pittsburgh Hepatitis B Study

We recently reported results of one of the first studies to explore relationships between a dispositional measure of PA and immune function, examining whether individuals' perceptions of their positive affective style were associated with antibody response to hepatitis B vaccination (Marsland et al., 2006). In this study, 84 healthy male and female graduate students (ages 20–35) who tested negative for prior exposure to hepatitis B virus were administered the standard series of three hepatitis B vaccinations. The first two vaccinations were given 6 weeks apart, with a follow-up booster dose administered 6 months following the first shot. Five months following the initial vaccination, each subject completed a battery of psychosocial measures, assessing trait positive and negative affect, extraversion, optimism, depression, and health behaviors, and a blood sample was drawn to assess hepatitis B surface antibody levels. Our measure of trait PA was derived from a factor analysis of the POMS affect scale (Usala and Hertzog, 1989) and included nine positive (*lively, full-of-pep, energetic, happy, pleased, cheerful, at-ease, calm, and relaxed*) and nine negative (*sad, depressed, unhappy, on-edge, nervous, tense, hostile, resentful, and angry*) mood adjectives. For each item, subjects were required to rate how accurately the trait described them as they typically are, as compared with other persons of the same sex. Cohen et al. (2003) found that this measure of dispositional affect correlated highly with an aggregate measure of mood averaged across a 7-day period and that it predicted vulnerability to upper respiratory infections equivalently to the aggregated measure.

Our decision to focus on the influence of affective style on antibody response after the second vaccination in the sequence was based on (1) an existing literature suggesting that trait negative affect has its greatest impact on secondary as opposed to primary immune

response to vaccination (as reviewed by Cohen et al., 2001); (2) evidence that psychosocial factors are associated with magnitude of antibody response at this time (e.g., Jabaa et al., 1993; Marsland et al., 2001b); and (3) evidence that there is widespread interindividual variability in the magnitude of antibody response following the second vaccination in the sequence (Szmunn et al., 1980), enabling us to explore emotional factors associated with individual difference in response.

The primary question of interest in this study was whether individual differences in trait PA were related to subjects' ability to mount an antibody response to the vaccine. In this regard, we found that, when compared with low antibody responders, subjects who mounted higher antibody responses to hepatitis B vaccination following the first two doses displayed higher levels of trait PA ($b = .54, p < .03$), with the odds of an individual with high trait PA belonging to the high antibody response group being 1.73 times that of an individual with low trait PA. These findings are displayed in Figure 1. A large number of control factors (including age, sex, body mass, smoking, alcohol use, and exercise) failed to explain the higher antibody responses among individuals high in trait PA. We next took a closer look at the activation level of the positive emotions to determine whether the relationship between PA and antibody response was specific to emotions of low or high activation/arousal. The relationship between PA and higher antibody response was similar for three subgroups of positive emotions: (1) well-being (*happy, pleased, cheerful*); (2) calm (*at-ease, calm, relaxed*: low arousal); and (3) vigor (*lively, full-of-pep, energetic*: high arousal), suggesting that the associations between trait PA and antibody

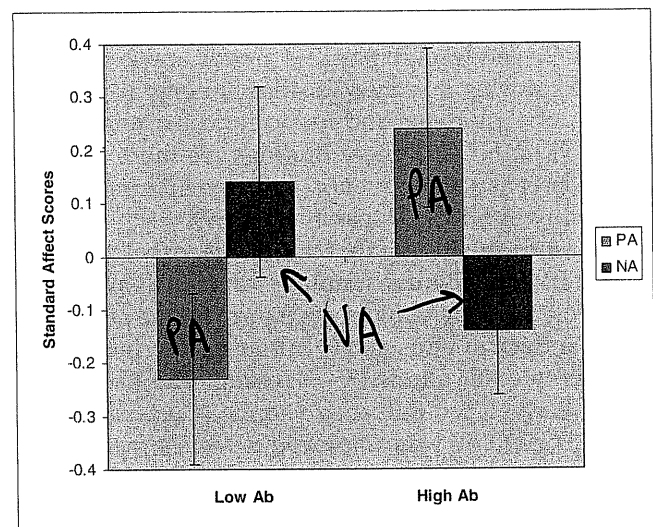


FIGURE 1 Standardized positive and negative affect scores among individuals high and low in antibody response. (From Marsland et al., 2006. *Brain, Behavior and Immunity*.)

response are equivalent irrespective of activation/arousal dimension.

We previously reported that trait NA is significantly related to lower antibody responses to hepatitis B vaccination (Marsland et al., 2001b), raising the possibility that the findings we reported above reflect the absence of NA rather than the presence of positive emotional styles. Thus, we next examined whether the relationship between trait PA and antibody response was independent of the influences of trait NA. When the two affect measures were entered into the regression model simultaneously to test the independent contribution of each factor, PA remained the dominant factor predicting antibody group. In contrast, no independent influence of trait NA was observed.

To date, the literature has focused on the relationships between trait NA and immune function and health, with little consideration of the role of trait PA. Our findings suggest that, in the presence of PA, there is no independent effect of trait NA on antibody response. Furthermore, previous studies, including our own, that find a relationship between trait NA and immune response may reflect the absence of PA, rather than the presence of distinct negative feelings. This interpretation is consistent with findings of Cohen et al. (2003) that positive, but not negative, emotional styles predict the incidence of upper respiratory infections.

IV. CLINICAL CONTEXT: POSITIVE AFFECT AND HEALTH

In general, the literature examining the association between PA and health has not focused on the role of PA in specific immune-mediated diseases. Instead, it primarily includes studies with unspecified pathologies (e.g., total mortality) and studies of a broad range of diseases, some with obvious (e.g., infection) or possible (e.g., coronary heart disease) immune etiology. Because the literature is small, and because immune function could play a role in many of the pathological processes involved, we provide an overview of the entire literature examining objective health outcomes, rather than focusing on only those studies that are obviously immune mediated.

A. Positive Affect and Mortality

A recent review provides evidence for an association between PA and decreased mortality rates in the community-residing elderly (Pressman and Cohen, 2005). For example, Ostir and colleagues (2000) followed 2,282 older Mexican Americans (65–99 years) for 2 years and found that, after controlling for base-

line medical conditions, body mass index, smoking, drinking, sociodemographic characteristics (including age), and levels of negative affect (NA), individuals who scored higher PA were half as likely to die during the follow-up than those who endorsed lower levels of PA. Other prospective studies have similarly demonstrated that PA is associated with lower mortality among community-residing elderly samples (e.g., Kawamoto and Doi, 2002; Levy et al., 2002; Maier and Smith, 1999; Parker et al., 1992). However, the evidence from two studies of seniors institutionalized in nursing homes looks quite different from that found for those residing in the community. In these cases, higher levels of PA were associated with *increased* risk for mortality (Janoff-Bulman and Marshall, 1982; Stones et al., 1989). Moreover, the few studies of other populations are inconsistent and include evidence that PA is not associated with mortality (Kaplan and Camacho, 1983), is associated with a decreased risk (Koivumaa-Honkanen et al., 2000, 2001), and is associated with an increased risk (Friedman et al., 1993).

In sum, existing evidence suggests that trait PA is associated with greater longevity in the relatively healthy community-residing elderly. Work with other populations is limited to date but suggests the possibility that PA may not always be beneficial.

B. Positive Affect and Morbidity

1. General Findings

A large cross-sectional literature has examined PA among people with chronic disease. Not surprisingly, they find lower levels of PA among individuals with physical health problems than among healthy controls and declines in PA with increasing severity of disease. For example, patients with lupus (Pfeiffer and Wetstone, 1988), gastrointestinal cancer (Hornquist et al., 1992), hypertension (Knox et al., 1988), fibromyalgia (Celiker and Borman, 2001), arthritis (Celiker and Borman, 2001), and increasing numbers of chronic medical conditions (Jelicic and Kempen, 1999) report lower PA than healthy controls. It is likely that this reflects the influence of the disease on PA, rather than the influence of PA on disease. Interestingly, however, there is some recent evidence that individuals with chronic illness adapt over time, with PA levels eventually returning to similar levels to those reported by healthy controls (e.g., Riis et al., 2005).

The more conservative prospective studies of PA provide stronger support for the hypothesis that PA contributes to better health (Pressman and Cohen, 2005). Here, trait PA is assessed in people who are healthy at baseline and correlated with later (months to years) disease onset. In these studies, trait PA has

been associated with lower rates of stroke among non-institutionalized elderly (Ostir et al., 2001), lower rates of re-hospitalization for coronary problems (Middleton and Byrd, 1996), fewer injuries (Koivumaa-Honkanen et al., 2000; Smith et al., 1997), and improved pregnancy outcomes among women undergoing assisted fertilization (Klonoff-Cohen et al., 2001). These community studies are often limited by a lack of control for factors that may influence both PA and disease susceptibility, and many do not rule out the possibility that PA itself (e.g., endorsing of items such as *energetic*, *full-of-pep*, and *vigorous*) is merely a marker of sub-clinical disease processes.

2. PA and Susceptibility to Upper Respiratory Infection: The Pittsburgh Cold Study

Viral challenge studies resolve some of the limitations of community studies by selecting disease- and symptom-free volunteers and experimentally exposing them to a virus after assessment of PA and other factors that may influence susceptibility to upper respiratory infection. A recent viral challenge study from our group provides initial evidence to corroborate prospective findings from community studies by demonstrating that individuals who characterize themselves by moods such as *happy*, *pleased*, *relaxed*, and *lively* are less susceptible to upper respiratory infections (Cohen et al., 2003). In this study, 334 healthy male and female volunteers (18–54 years) were interviewed by telephone three times per week for 2 weeks to assess daily levels of PA and NA using an adjective checklist derived from the POMS (Usala and Hertzog, 1989). Adjective ratings were averaged over the 2 weeks to obtain an estimate of trait PA and NA. Subjects were then quarantined, and a baseline assessment of respiratory symptoms (including self-reported symptoms, two objective indicators of illness: nasal mucociliary clearance and nasal mucus production, and pre-challenge antibody titer) was performed before they were experimentally inoculated with one of two rhinoviruses. Quarantine continued for 5 days after exposure. On each day, subjects completed a respiratory symptoms questionnaire and were tested for the two objective markers of illness. Presence of an infection was biologically verified by viral isolation in nasal secretion samples and four-fold increases in virus-specific antibody in serum. Volunteers were considered to have a cold if they were both infected and met illness criteria. Finally, on the day before viral-challenge, 12 saliva samples were obtained for the measurement of salivary cortisol.

Figure 2 depicts the study's major finding. For both viruses, higher trait PA was associated (in a dose-

response manner) with lower risk of developing a cold. In contrast, there was no relationship between trait NA and susceptibility to colds, and the association of PA and colds was independent of NA. A large number of control factors (including age, sex, education, race, body mass, season, and pre-challenge virus-specific antibody) were not able to explain the decreased risk for colds among persons reporting higher dispositional PA. Consistent with findings from other studies (reviewed in Pressman and Cohen, 2005), individuals high in trait PA also reported fewer and less severe symptoms in response to verified upper respiratory infection (Cohen et al., 2003). Although trait PA was associated with lower levels of epinephrine, norepinephrine, and cortisol and better health practices, including better sleep quality and efficiency and more exercise, none of these accounted for the PA association with colds. However, higher PA was also associated with less production of IL-6 (in nasal secretions) in response to infection, and the data were consistent with IL-6 partly mediating the association of PA and upper respiratory disease (Doyle et al., 2006).

C. Positive Affect and Disease Course

1. Survival

Comparatively few studies have examined whether PA predicts survival among people with chronic disease, and available findings are mixed. Based on their review of the literature, Pressman and Cohen (2005) concluded that higher levels of trait PA may be

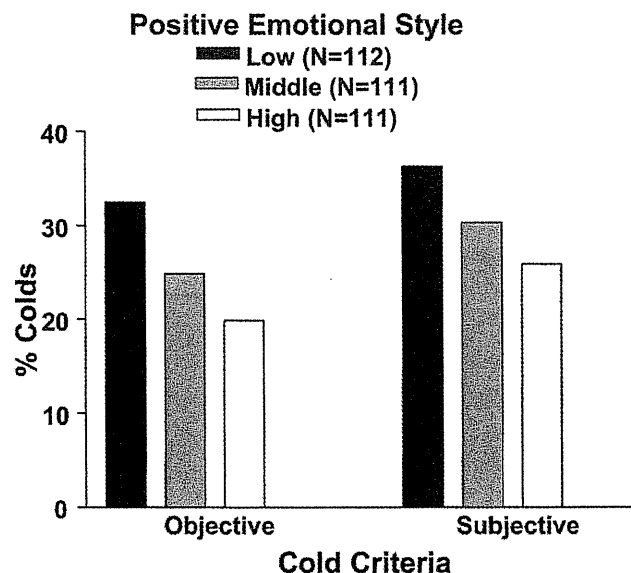


FIGURE 2 Positive emotional style and incidence of clinical colds using objective and subjective criteria for illness. (From Cohen et al., 2003. *Psychosomatic Medicine*, 65, 652–657.)

detrimental to the health of individuals who have advanced disease with a poor short-term prognosis, such as patients with melanoma (Brown et al., 2000), metastatic breast cancer (Derogatis et al., 1979), and end-stage renal disease (Devins et al., 1990), possibly as a consequence of underreporting of symptoms or a lack of adherence to treatment. In contrast, individuals with diseases that have better prospects for longer-term survival, such as AIDS (Moskowitz, 2003), breast cancer (Levy et al., 1988), and coronary heart disease (van Domburg et al., 2001), were generally benefited by PA.

2. Asthma Severity

In contrast, there is a growing literature on the role of state PA in triggering asthma attacks (see review in Pressman and Cohen, 2005). In laboratory studies of asthmatics, acute states of arousal (either induced PA or NA) appear to worsen pulmonary outcomes (e.g., Ritz et al., 2000a; Ritz et al., 2000b; Ritz et al., 2001; Florin et al., 1985). In contrast, naturalistic studies typically found that state PA was associated with improved lung function (e.g., Apter et al., 1997). The reason may be that most laboratory inductions are associated with more intense and arousing emotions as compared to the day-to-day fluctuations that occur in naturalistic follow-ups. In fact, Ritz and Steptoe (2000) found that there was a decrease in pulmonary function in a naturalistic study on the occasions that adult asthmatic subjects reported their *most extreme levels* of positive and negative moods. Hence, the association between state PA and lung function outcomes may be curvilinear, with small to moderate changes in mood improving function but truly intense emotions having detrimental effects associated with arousal. This is consistent with findings that strong emotional arousal, irrespective of valence, activates the immune system, increasing the likelihood of an inflammatory response and associated airway constriction in the lungs of asthmatics.

V. POTENTIAL PATHWAYS LINKING PA AND IMMUNE FUNCTION

The pathways through which PA influences immune function are not entirely clear. To help provide a theoretical framework to guide future research, we propose two models linking trait PA to immune function: a main (direct) effect model and a stress-buffering model (Figures 3 and 4; adapted from Pressman and Cohen, 2005). In the first case, PA has a direct effect on behavioral and biological mechanisms that influence immune

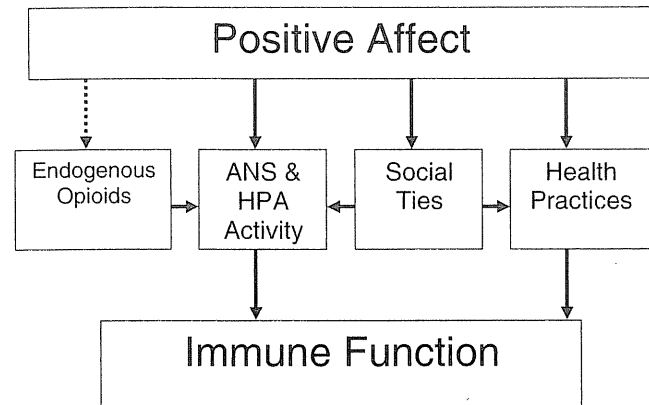


FIGURE 3 The Direct Effect Model: Direct pathways through which PA might influence onset and progression of immune system-mediated disease. (From Figure 1, Pressman and Cohen, 2005. *Psychological Bulletin*. Copyright (c) 2005 by the American Psychological Association. Adapted with permission.)

function. In the second model, PA acts as a buffer of behavioral and physiological responses to stress. We realize that these models represent oversimplifications, considering pathways in only one direction from PA to immune function. No lack of alternative paths is implied.

A. The Direct Effect Model

A number of direct pathways link psychological variables to immune function, including behavioral, neurological, and endocrine mechanisms. In the first case, positive emotional styles could directly influence immunity through favorable health habits (Myers and Diener, 1995). For example, better sleep quality, more exercise, and more and higher quality social relationships have been associated with more positive dispositional styles (Bardwell et al., 1999; Berry et al., 2000; Cohen et al., 2003; Ryff et al., 2004; Watson et al., 1992; but not Diener and Seligman, 2002). Better health practices, including nutritional status, not smoking, exercise, social support, and sleep, have also been associated with more positive immune status and lower risk for morbidity and mortality (e.g., Berkman and Breslow, 1983; Cohen et al., 1993; Kiecolt-Glaser and Glaser, 1988; Kronfol et al., 1989; Luoto et al., 1998; Uchino et al., 1996; Wingard et al., 1994).

PA may also directly alter immune function through the activation of neurological and neuroendocrine pathways and the release of hormones and neurotransmitters, such as cortisol and catecholamines. Here, there is extensive evidence for direct anatomical and functional links between the central nervous and immune systems, as indicated by the sympathetic

and parasympathetic innervation of lymphoid organs (Felten and Olschowka, 1987; Livnat et al., 1985) and the presence of receptors on immune cells for a variety of hormones and neurotransmitters that are released in response to emotional stimuli, including catecholamines (epinephrine and norepinephrine), corticosteroids, and opiates (Rabin, 1999). Aroused positive and negative emotional states are associated with activation of the sympathetic branch of the autonomic nervous system (e.g., Futterman et al., 1994; Knapp et al., 1992; Neumann and Waldstein, 2001). It is well accepted that activation of this pathway drives the upregulation of innate immune function that follows acute stress (Marsland et al., 2001a), making it likely that it also accounts for the similar immune responses that accompany the induction of activated positive moods. In contrast, less activated positive emotional states (e.g., calm) have been associated with decreases in SNS activation and possible activation of the parasympathetic branch (PNS) of the autonomic system (e.g., Bacon et al., 2004, but not Frazier et al., 2004). Interestingly, recent findings demonstrate that PNS activation is associated with a downregulation of inflammation (Borovikova et al., 2000; Tracey, 2002). Thus, relationships between low arousal positive moods and immune function warrant investigation.

In addition to autonomic pathways, it is widely accepted that psychological factors can regulate immune function by direct activation of the hypothalamic-pituitary-adrenal (HPA) axis and release of hormones, including cortisol, from the adrenal cortex. A number of studies have demonstrated that higher levels of trait PA are associated with lower levels of cortisol (Buchanan et al., 1999; Cohen et al., 2003; Smyth et al., 1998; Steptoe et al., 2005). However, not all findings are consistent (Ryff et al., 2004; van Eck et al., 1996). Other studies have demonstrated that low levels of trait PA are associated with dysregulated cortisol rhythms, with higher cortisol levels in the afternoon and evening (Polk et al., 2005). Glucocorticoid receptors are expressed on a variety of immune cells, and ligand binding to these receptors has a number of immune inhibitory effects (e.g., Almawi et al., 1996; Cato and Wačé, 1996). Other hormones are also found to increase in response to positive emotions, including growth hormone (Berk et al., 1989), prolactin (Codispoti et al., 2003), and endogenous opioids (Gerra et al., 1996, 1998), which might also play a role in the regulation of immune function.

B. The Stress-Buffering Model

PA may also act as a buffer of the immune influences of stressful life events. Although there is a sub-

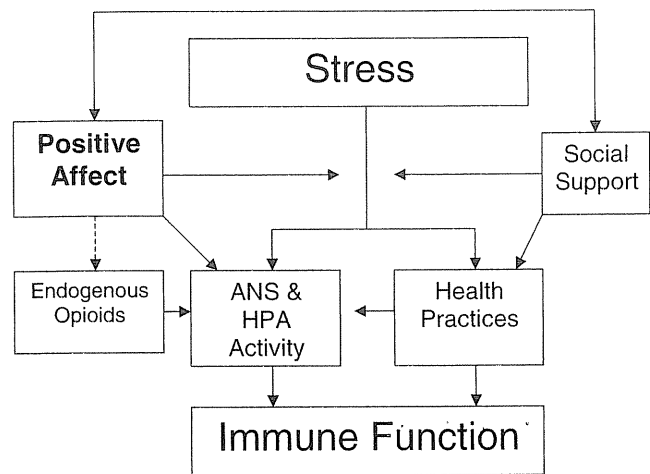


FIGURE 4 The Stress-Buffering Model: Pathways through which PA might influence onset and progression of immune system-mediated disease though the buffering of stress effects. (From Figure 2, Pressman and Cohen, 2005. *Psychological Bulletin*. Copyright (c) 2005 by the American Psychological Association. Adapted with permission.)

stantial literature demonstrating that psychological stress dysregulates immune function, not all individuals display immune changes following stressful life events. Variability among individuals in the magnitude of their immune responses to stress is attributed to their level of perceived stress. A psychological stress response composed of negative cognitive and emotional states is proposed to be the consequence of perceptions that demands imposed by events exceed individuals' abilities to cope (Lazarus and Folkman, 1984). It is these stress responses that are thought to influence immune function through their effects on health behaviors and neuroendocrine responses. Trait PA may act as a buffer of stress responses, acting to reduce negative appraisals of events and to facilitate adaptive coping. In this way, PA may ameliorate stress-related ANS and HPA activation. PA may also encourage restorative coping activities such as sleep, exercise, relaxation, social support, and vacation (Smith and Baum, 2003). These hypotheses are consistent with Fredrickson's proposal that positive emotions broaden and diversify individuals' thoughts and actions, which enable them to build "enduring personal resources," including social contacts that can be drawn on when facing environmental threats (Fredrickson, 1998). In addition to buffering the effects of stress, PA may also facilitate faster recovery from stress-related psychological and physiological activation. In support of this possibility, Fredrickson and associates (2000) demonstrated that inducing PA following a stressful stimulus resulted in faster recovery to baseline levels of heart rate and blood pressure.

VI. TRAIT PA AND OTHER RELATED PERSONALITY CONSTRUCTS

A. Optimism and Extraversion

An issue that requires clarification in the literature linking trait PA to immunity and disease is the role of psychological concepts that are related to trait PA, such as optimism and extraversion. These constructs are typically moderately correlated with PA (e.g., Roysamb et al., 2002). Indeed, a recent meta-analysis of 137 studies examining the relationship between current conceptualizations of personality and positive emotional traits found that trait positive affect was correlated with extraversion ($r = .20$) and agreeableness ($r = .17$) (DeNeve and Cooper, 1998). Optimism and extraversion have also been related to improved objective health outcomes (e.g., Cohen et al., 1997a; Scheier and Carver, 1987), including decreased susceptibility to upper respiratory infections (Broadbent et al., 1984; Cohen et al., 1997a; Totman et al., 1980) and improved immune function (Miller et al., 1999; Segerstrom et al., 1998). Thus, it is possible that these dispositional characteristics account for associations between PA and immune function. To date, the majority of studies examining relations between PA and immune function or health have failed to assess and evaluate the role of these overlapping cognitive and motivational concepts, making it difficult to parse out the unique effects of PA. In our recent vaccination study (Marsland et al., 2006), trait PA was related to optimism ($r = .52$) and extraversion ($r = .51$). However, high and low antibody responders did not differ on these constructs. Furthermore, trait PA predicted greater production of antibody after controlling for both constructs, suggesting that the association between trait PA and antibody response is largely independent of the related constructs of optimism and extraversion. However, it remains likely that personality and coping styles predispose individuals to stable affective dispositions, which, in turn, mediate physiological responses, including regulation of immune function.

B. Relationships between Trait PA and NA

Although there is growing acceptance that positive and negative affect are broad, underlying dimensions of basic emotions that consistently emerge across studies (Watson and Tellegen, 1985), the relationship between them remains unclear. Rather than being opposite extremes of the same underlying construct, trait measures of emotional style are thought to be

mutually independent, with PA conferring health benefits independently of NA levels (Diener and Emmons, 1985). The few studies that have examined both constructs generally support their independent influence on immune function (Marsland et al., 2006) and susceptibility to disease (Cohen et al., 2003; Ostir et al., 2001; Smith et al., 1997). Further evidence for trait PA and NA as separate constructs is derived from their asymmetrical activation of regions of the prefrontal cortex in the brain (Davidson et al., 1999). Individuals who show high levels of left-sided prefrontal activation endorse higher levels of dispositional positive affect and also show improved immune function as measured by increased natural killer cell activity, when compared with their right-frontally activated counterparts who endorse more dispositional negative affect (Davidson et al., 1999; Davidson et al., 2000). Neurotransmitters may also respond differently to PA than NA. For example, trait PA was associated with increased serotonergic function after controlling for NA (Flory et al., 2004). Taken together, these findings suggest that trait PA is not simply the absence of trait NA or vice versa, and the independent influences of both emotional traits on immunity warrants further investigation.

VII. PSYCHOLOGICAL INTERVENTIONS

If there is a link between PA and regulation of immune function, interventions designed to increase PA might bring about positive health outcomes by improving immunocompetence. To our knowledge, no studies to date have directly examined the health benefit of interventions designed to increase PA. However, a number of studies have investigated whether psychological interventions designed to decrease NA can alleviate the immune dysregulation that accompanies stress. A meta-analysis of this literature concluded that there is only modest evidence that interventions can reliably alter immune parameters (Miller and Cohen, 2001). The many null findings were attributed to theoretical and methodological limitations of existing studies, including a general failure to focus on individuals with high levels of NA, to use interventions demonstrated to be effective at reducing NA, or to measure immune parameters that are typically dysregulated by NA (Miller and Cohen, 2001). In fact, if you focus on the few studies that have recruited populations experiencing high levels of NA, results are more consistent and document intervention-related improvements in immune function (Antoni et al., 1991; Fawzy et al., 1990; Goodkin et al., 1998; Lutgendorf et al., 1994). To date, these interventions have employed

stress management techniques, including coping skills training, cognitive restructuring, relaxation training, and social support, and the extent of immune system change has been shown to covary with reductions in NA (Antoni et al., 1991; Fawzy et al., 1990). The possibility that these interventions might also influence immunity by increasing PA remains to be explored. Further evaluation and development of psychological interventions designed to increase PA may shed light on causal relationships between PA and immune function, and have valuable clinical implications. It is advisable, however, to proceed with caution. Given that it is *trait* PA that is most consistently associated with immune and health outcomes, to see any long-term health benefit, the improvement in PA will need to be long lasting. It is, however, controversial whether one can alter trait PA. Historically, it has been considered a stable characteristic of the individual that is relatively impervious to manipulation. However, more recently it has been argued that powerful positive events can alter trait affect (Diener et al., unpublished).

VIII. SUMMARY

Recent attention has turned to the potential immune benefits of positive emotions. In contrast to the large established literature showing associations between NA and immune function (for review, see Kiecolt-Glaser et al., 2002), the literature examining PA and immune function is in its infancy. In this chapter, we review findings from 25 studies examining relationships between state or trait PA and immune function. The majority of these studies (15/25) have examined the impact of the experimental induction of state positive moods in the laboratory, with the remainder examining concomitants of naturalistic state and trait mood. Overall, findings from studies examining transient mood states suggest that activated positive moods (e.g., excitement, humor, joy) are associated with an upregulation of components of the innate immune system among healthy volunteers, including increases in total and antigen-specific salivary sIgA levels, numbers of immune cells in peripheral circulation, and possibly NK cell activity. Induced positive mood states have also been associated with a reduction in allergic responses among allergy sufferers. In general, these findings are consistent with immune responses to activated negative mood states, as induced by laboratory stress tasks, suggesting that it may be the increase in affective arousal, rather than the positive or negative valence of the emotion, that is responsible for immune modulation. Future work is needed to disentangle the

valence and arousal dimensions of mood states in a more sophisticated manner.

Other limitations of the current mood induction literature necessitate caution in interpreting findings and drawing definitive conclusions. To date, many of the studies employ insufficient sample sizes to provide enough power, so it is important to weigh results accordingly. Furthermore, a number of studies fail to include either an emotionally neutral but interesting condition to control for diurnal variations, passage of time, and factors associated with the manipulation itself (e.g., distraction) or conditions examining the induction of other types of emotion (e.g., NA or differing types of PA). Without these controls interpretation of the true effect of PA is difficult, and it becomes impossible to address the valence/arousal question raised earlier. If one is interested in specific emotions, it is also important to understand the precise nature of the induced state. For example, humor is often used to induce PA, so without measuring, it is impossible to know whether a change in physiology is due to increases in humor or PA (see Martin, 2001, for a review of humor and health). More problematic for interpretation purposes is that these studies employ manipulations that result in only momentary mood changes. Aside from studies that have demonstrated associations between highly activated emotional states and poorer lung function among asthmatics, the majority of studies demonstrating associations between PA and health have focused on trait affect, leaving the influence of induced state PA on actual health unclear.

Of greater potential relevance for health are the small number of naturalistic studies that examine relationships between longer-lasting PA and immune function. Here, findings are promising and provide initial support for a relationship between trait PA and more effective cellular immune function, including higher NK cell numbers and activity, increased T_{H1} cytokine responses to *in vitro* stimulation of mononuclear cells with influenza virus or vaccine, higher antibody responses to hepatitis B vaccination, and decreased hypersensitivity skin responses to allergens among allergy sufferers. These findings raise the possibility that PA-related immune function is one mediator of observed associations between positive emotional states and better general health. However, again, caution is warranted in interpreting these early findings. Before firm conclusions can be drawn, more studies are necessary to replicate initial findings and address gaps in our knowledge of PA-immune-disease relationships. Indeed, it remains to be determined whether the nature and magnitude of immunologic alterations associated with PA bear relevance to decreased disease susceptibility, especially in light of

the fact that immune responses that accompany psychosocial parameters typically fall within normal ranges (Rabin et al., 1989). To date, few studies have examined immune function as a mediator of associations between trait PA and immune-mediated disease susceptibility, and other possible pathways exist, including the likely role of health behaviors. Additional studies that employ longitudinal designs, measure dispositional PA, adequately control for both objective and perceived health at baseline, predict immune mediators relevant for disease, control for health behavior, and document related health outcomes are needed. These studies will need to examine the independent contributions of closely related constructs, including trait NA, optimism, and extraversion, and begin to explore behavioral, psychological, and biological mechanisms that may link positive affective styles to immune function.

In sum, initial evidence suggests the possibility of a relationship between PA and immune parameters of relevance to health. This is clearly a potential pathway through which PA may modulate host resistance to disease onset or progression and provides one of the most exciting recent developments in the field of PNI. It is time for researchers interested in psychological influences on health to move beyond the role of situational stress and negative affect to further explore the impact of positive emotions on health-related immune function.

Acknowledgments

Dr. Marsland was supported during the preparation of this work by grant R01 NR008237 from the National Institute of Nursing Research (ALM), Ms. Pressman by a Post-Graduate Scholarship from the Natural Science & Engineering Research Council of Canada, and Dr. Cohen by a grant to the Pittsburgh NIH Mind-Body Center (HL65111 and HL65112). The authors thank Jeffrey Horn for helpful comments on an earlier version of the manuscript and Ellen Conser for assistance with manuscript preparation.

References

- Ader, R., Cohen, N., and Felten, D. L. (1987). Brain, behavior, and immunity. *Brain Beh. Imm.*, *1*, 1–6.
- Almawi, W. Y., Beyhum, H. N., Rahme, A. A., and Rieder, M. J. (1996). Regulation of cytokine and cytokine receptor expression by glucocorticoids. *J. Leukoc. Biol.*, *60*, 563–572.
- Antoni, M. H., Baggett, L., Ironson, G., LaPerriere, A., Sugust, S., Klimas, N. G., Schneiderman, N., and Fletcher, M. A. (1991). Cognitive-behavioral stress management intervention buffers distress responses and immunologic changes following notification of HIV-1 seropositivity. *J. Consult. Clin. Psychol.*, *59*, 906–915.
- Apter, A. J., Affleck, G., Reisine, S. T., Tennen, H. A., Barrows, E., Wells, M., Willard, A., and ZuWallack, R. L. (1997). Perception of airway obstruction in asthma: sequential daily analyses of symptoms, peak expiratory flow rate, and mood. *J. Allergy Clin. Immunol.*, *99*, 605–612.
- Bachen, E. A., Manuck, S. B., Cohen, S., Muldoon, M. F., Raible, R., Herbert, T. B., and Rabin, B. S. (1995). Adrenergic blockade ameliorates cellular immune responses to stress in humans. *Psychosom. Med.*, *57*, 366–372.
- Bacon, S. L., Watkins, L. L., Babyak, M., Sherwood, A., Hayano, J., Hinderliter, A. L., Waugh, R., and Blumenthal, J. A. (2004). Effects of daily stress on autonomic cardiac control in patients with coronary artery disease. *Am. J. Cardiol.*, *93*, 1292–1294.
- Bardwell, W. A., Berry, C. C., Ancoli-Israel, S., and Dimsdale, J. E. (1999). Psychological correlates of sleep apnea. *J. Psychosom. Res.*, *47*, 583–596.
- Berk, L. S., Felten, D. L., Tan, S. A., Bittman, B. B., and Westengard, J. (2001). Modulation of neuroimmune parameters during the eustress of humor-associated mirthful laughter. *Altern. Ther. Health Med.*, *7*, 62–76.
- Berk, L. S., Tan, S. A., Fry, W. F., Napier, B. J., Lee, J. W., Hubbard, R. W., Lewis, J. E., and Eby, W. C. (1989). Neuroendocrine and stress hormone changes during mirthful laughter. *Am. J. Med. Sci.*, *298*, 390–396.
- Berkman, L., and Breslow, L. (1983). *Health and ways of living: the Alameda County study*. New York: Oxford University Press.
- Berry, D. S., Willingham, J. K., and Thayer, C. A. (2000). Affect and personality as predictors of conflict and closeness in young adults' friendships. *J. Res. Pers.*, *34*, 84–107.
- Borovikova, L. V., Ivanova, S., Zhang, M., Yang, H., Botchkina, G. I., and Watkins, L. R. (2000). Vagus nerve stimulation attenuates the systemic inflammatory response to endotoxin. *Nature*, *405*, 458–461.
- Bristow, M., Hucklebridge, F., Clow, A., and Evans, P. (1997). Modulation of secretory immunoglobulin A in relation to an acute episode of stress and arousal. *J. Psychophys.*, *11*, 248–255.
- Broadbent, D. E., Broadbent, M. H. P., Phillpotts, R. J., and Wallace, J. (1984). Some further studies on the prediction of experimental colds in volunteers by psychological factors. *J. Psychosom. Res.*, *28*, 511–523.
- Brown, J. E., Butow, P. N., Culjak, G., Coates, A. S., and Dunn, S. M. (2000). Psychosocial predictors of outcome: time to relapse and survival in patients with early stage melanoma. *Br. J. Cancer*, *83*, 1448–1453.
- Buchanan, T. W., al'Absi, M., and Lovallo, W. R. (1999). Cortisol fluctuates with increases and decreases in negative affect. *Psychoneuroendocrinology*, *24*, 227–241.
- Cato, A. C. B., and Wade, E. (1996). Molecular mechanisms of anti-inflammatory action of glucocorticoids. *Bioessays*, *18*, 371–378.
- Celiker, R., and Borman, P. (2001). Fibromyalgia versus rheumatoid arthritis: a comparison of psychological disturbance and life satisfaction. *J. Musculoskel. Pain*, *9*, 35–45.
- Clark, L. A., Watson, D., and Leeka, J. (1989). Diurnal variation in the positive affects. *Motiv. Emot.*, *13*, 205–234.
- Codispoti, M., Gerra, G., Montebanocci, O., Zaimovic, A., Raggi, M. A., and Baldaro, B. (2003). Emotional perception and neuroendocrine changes. *Psychophysiology*, *40*, 863–868.
- Cohen, S., Doyle, W. J., Skoner, D. P., Rabin, B. S., and Gwaltney, J. M. (1997a). Social ties and susceptibility to the common cold. *JAMA*, *277*, 1940–1944.
- Cohen, S., Doyle, W. J., Turner, R. B., Alper, C. M., and Skoner, D. P. (2003). Emotional style and susceptibility to the common cold. *Psychosom. Med.*, *65*, 652–657.
- Cohen, S., Kessler, R. C., and Underwood Gordon, L., Eds. (1997b). *Measuring stress: a guide for health and social scientists*. London: Oxford University Press.

- Cohen, S., Miller, G. E., and Rabin, B. S. (2001). Psychological stress and antibody response to immunization: a critical review of the human literature. *Psychosom. Med.*, 63, 7–18.
- Cohen, S., Tyrrell, D. A., Russell, M. A., Jarvis, M. J., and Smith, A. P. (1993). Smoking, alcohol consumption, and susceptibility to the common cold. *Am. J. Pub. Health*, 83, 1277–1283.
- Costanzo, E. S., Lutgendorf, S. K., Kohut, M. L., Nisly, N., Roseboom, K., Spooner, S., Benda, J., and McElhaney, J. E. (2004). Mood and cytokine response to influenza virus in older adults. *J. Gerontol.*, 12, 1328–1333.
- Davidson, R. J., Coe, C. C., Dolski, I., and Donzella, B. (1999). Individual differences in prefrontal activation asymmetry predict natural killer cell activity at rest and in response to challenge. *Brain Behav. Imm.*, 13, 93–108.
- Davidson, R. J., Jackson, D. C., and Kalin, N. H. (2000). Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. *Psychol. Bull.*, 126, 890–909.
- DeNeve, K. M., and Cooper, H. (1998). The happy personality: a meta-analysis of 137 personality traits and subjective well-being. *Psychol. Bull.*, 124, 197–229.
- Derogatis, L. R., Abeloff, M. D., and Melisaratos, N. (1979). Psychological coping mechanisms and survival time in metastatic breast cancer. *JAMA*, 242, 1504–1508.
- Devins, G. M., Mann, J., Mandin, H., Paul, L. C., Hons, R. B., Burgess, E. D., Taub, K., Schorr, S., Letourneau, P. K., and Buckle, S. (1990). Psychosocial predictors of survival in end-stage renal disease. *J. Nerv. Ment. Dis.*, 178, 127–133.
- Diener, E. (1984). Subjective well-being. *Psychol. Bull.*, 95, 542–575.
- Diener, E., and Emmons, R. A. (1985). The independence of positive and negative affect. *J. Pers. Soc. Psychol.*, 47, 1105–1117.
- Diener, E., Larsen, R. J., Levine, S., and Emmons, R. A. (1985). Intensity and frequency: dimensions underlying positive and negative affect. *J. Pers. Soc. Psychol.*, 48, 1253–1265.
- Diener, E., Lucas, R. E., and Scollon, C. N. (2005). Beyond the Hedonic treadmill: revisions to the adaptation theory of well-being. Unpublished.
- Diener, E., and Seligman, M. E. (2002). Very happy people. *Psychol. Sci.*, 13, 81–84.
- Dillon, K. M., Minchhoff, B., and Baker, K. H. (1985). Positive emotional states and enhancement of the immune system. *Int. J. Psychiatry Med.*, 15, 13–18.
- Doyle, W. J., Gentile, D. A., and Cohen, S. (2006). Emotional style, nasal cytokines, and illness expression after experimental rhinovirus exposure. *Brain Beh. Imm.*, 20, 175–181.
- Ekman, P. (1992). Are there basic emotions? *Psychol. Rev.*, 99, 550–553.
- Evans, P., Bristow, M., Hucklebridge, F., Clow, A., and Walters, N. (1993). The relationship between secretory immunity, mood and life-events. *Brit. J. Clin. Psychol.*, 32, 227–236.
- Fawzy, F. I., Kemeny, M. E., Fawzy, N. W., Elashoff, R., Morton, D., Cousins, N., and Fahey, J. L. (1990). A structured psychiatric intervention for cancer patients: changes over time in immunological measures. *Arch. Gen. Psychiatry*, 47, 729–735.
- Felten, S. Y., and Olschowka, J. (1987). Noradrenergic sympathetic innervation of the spleen. II. Tyrosine hydroxylase (TH)-positive nerve terminals for synaptic like contacts on lymphocytes in the splenic white pulp. *J. Neurosci. Res.*, 18, 37–48.
- Florin, I., Freudenberg, G., and Hollaender, J. (1985). Facial expressions of emotion and physiologic reactions in children with bronchial asthma. *Psychosom. Med.*, 47, 382–393.
- Flory, J. D., Manuck, S. B., Matthews, K. A., and Muldoon, M. F. (2004). Serotonergic function in the central nervous system is associated with daily ratings of positive mood. *Psychiatry Res.*, 129, 11–19.
- Frazier, T. W., Strauss, M. E., and Steinhauer, S. R. (2004). Respiratory sinus arrhythmia as an index of emotional response in young adults. *Psychophysiology*, 41, 75–83.
- Fredrickson, B. L. (1998). What good are positive emotions? *Rev. Gen. Psychol.*, 2, 300–319.
- Fredrickson, B. L., Mancuso, R. A., Branigan, C., and Tugade, M. M. (2000). The undoing effect of positive emotions. *Motiv. Emot.*, 24, 237–258.
- Friedman, H. S., Tucker, J. S., Tomlinson-Keasey, C., Schwartz, J. E., Wingard, D. L., and Criqui, M. H. (1993). Does childhood personality predict longevity? *J. Pers. Soc. Psychol.*, 65, 176–185.
- Frost, R. O., and Green, M. L. (1982). Duration and post-experimental removal of Velten mood induction procedure effects. *Pers. Soc. Psychol. Bull.*, 8, 341–347.
- Futterman, A. D., Kemeny, M. E., Shapiro, D., and Fahey, J. L. (1994). Immunological and physiological changes associated with induced positive and negative mood. *Psychosom. Med.*, 56, 499–511.
- Futterman, A. D., Kemeny, M. E., Shapiro, D., Polonsky, W., and Fahey, J. L. (1992). Immunological variability associated with experimentally-induced positive and negative affective states. *Psychol. Med.*, 22, 231–238.
- Gerra, G., Fertomani, G., Zaimovic, A., Caccavari, R., Reali, N., Maestri, D., Avanzini, P., Monica, C., Delsignore, R., and Brambilla, F. (1996). Neuroendocrine responses to emotional arousal in normal women. *Neuropsychobiology*, 33, 173–181.
- Gerra, G., Zaimovic, A., Franchini, D., Palladino, M., Giucastro, G., Reali, N., Maestri, D., Caccavari, R., Delsignore, R., and Brambilla, F. (1998). Neuroendocrine responses of healthy volunteers to 'techno-music': Relationships with personality traits and emotional state. *Int. J. Psychophysiol.*, 28, 99–111.
- Goodkin, K., Feaster, D. J., Asthana, D., Blaney, N. T., Kumar, M., Baldewicz, T., Tuttle, R. S., Maher, K. G., Baum, M. K., Shapshak, P., and Fletcher, M. A. (1998). A bereavement support group intervention is longitudinally associated with salutary effects of CD4 cell count and number of physician visits. *Clin. Diagn. Lab. Immunol.*, 5, 382–390.
- Harrison, L. K., Carroll, D., Burns, V. E., Corkill, A. R., Harrison, C. M., Ring, C., and Drayson, M. (2000). Cardiovascular and secretory immunoglobulin A reactions to humorous, exciting, and didactic film presentations. *Biol. Psychol.*, 52, 113–126.
- Herbert, T. B., and Cohen, S. (1993a). Depression and immunity: a meta-analytic review. *Psychol. Bull.*, 113, 472–486.
- Herbert, T. B., and Cohen, S. (1993b). Stress and immunity in humans: a meta-analytic review. *Psychosom. Med.*, 55, 364–379.
- Hornquist, J. O., Hansson, B., Akerlind, I., and Larsson, J. (1992). Severity of disease and quality of life: a comparison in patients with cancer and benign disease. *Qual. Life Res.*, 1, 135–141.
- Hucklebridge, F., Lambert, S., Clow, A., Warburton, D. M., Evans, P. D., and Sherwood, N. (2000). Modulation of secretory immunoglobulin A in saliva: response to manipulation of mood. *Biol. Psychol.*, 53, 25–35.
- Izard, C. E., Ed. (1977). *Human emotions*. New York: Plenum Press.
- Jabaaaj, L., Grosheide, P. M., Heijntink, R. A., Duivenvoorden, H. J., Ballieux, R. E., and Vingerhoets, A. J. J. M. (1993). Influence of perceived psychological stress and distress on antibody response to low dose rDNA hepatitis B vaccine. *J. Psychosom. Res.*, 37, 361–369.
- Janoff-Bulman, R., and Marshall, G. (1982). Mortality, well-being, and control: a study of a population of institutionalized aged. *Person. Soc. Psych. Bull.*, 8, 691–698.
- Jelicic, M., and Kempen, G. I. J. M. (1999). Chronic medical conditions and life satisfaction in the elderly. *Psychol. Health*, 14, 65–70.

- Kaplan, G. A., and Camacho, T. (1983). Perceived health and mortality: a nine-year follow-up of the human population laboratory cohort. *Am. J. Epi.*, 117, 292-304.
- Kawamoto, R., and Doi, T. (2002). Self-reported functional ability predicts three-year mobility and mortality in community-dwelling older persons. *Geriatrics & Gerontology International*, 2, 68-74.
- Kiecolt-Glaser, J. K., and Glaser, R. (1988). Methodological issues in behavioral immunology research with humans. *Brain Beh. Imm.*, 2, 67-78.
- Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., and Glaser, R. (2002). Emotions, morbidity, and mortality: new perspectives from psychoneuroimmunology. *Ann. Rev. Psychol.*, 53, 83-107.
- Kimata, H. (2001). Effect of humor on allergen-induced wheal reactions. *JAMA*, 285, 738.
- Klonoff-Cohen, H., Chu, E., Natarajan, L., and Sieber, W. (2001). A prospective study of stress among women undergoing in vitro fertilization or gamete intrafallopian transfer. *Fertil. Steril.*, 76, 675-687.
- Knapp, P. H., Levy, E. M., Giorgi, R. G., Black, P. H., Fox, B. H., and Heeren, T. C. (1992). Short-term immunological effects of induced emotion. *Psychosom. Med.*, 54, 133-148.
- Knox, S., Svensson, J., Waller, D., and Theorell, T. (1988). Emotional coping and the psychophysiological substrates of elevated blood pressure. *Beh. Med.*, 14, 52-58.
- Koivumaa-Honkanen, H., Honkanen, R., Viinamaeki, H., Heikkilae, K., Kaprio, J., and Koskenvuo, M. (2001). Life satisfaction and suicide: a 20-year follow-up study. *Am. J. Psychiatry*, 158, 433-439.
- Koivumaa-Honkanen, H., Honkanen, R., Viinamaki, H., Heikkila, K., Kaprio, J., and Koskenvuo, M. (2000). Self-reported life satisfaction and 20-year mortality in healthy Finnish adults. *Am. J. Epi.*, 152, 983-991.
- Krantz, D. S., Glass, D. C., Contrada, R., and Miller, N. E. (1981). Behavior and health: mechanisms and research issues. *Soc. Sci. Res. Council: ITEMS.*, 35, 1-6.
- Kronfol, Z., Nair, M., Goodson, J., Goel, K., Haskett, R., and Schwartz, S. (1989). Natural killer cell activity in depressive illness: a preliminary report. *Biol. Psychiatry*, 26, 753-756.
- Labott, S. M., Ahleman, S., Wolever, M. E., and Martin, R. B. (1990). The physiological and psychological effects of the expression and inhibition of emotion. *Behav. Med.*, 16, 182-189.
- Laidlaw, T. M., Booth, R. J., and Large, R. G. (1994). The variability of type I hypersensitivity reactions: the importance of mood. *J. Psychosom. Res.*, 38, 51-61.
- Laidlaw, T. M., Booth, R. J., and Large, R. G. (1996). Reduction in skin reactions to histamine after a hypnotic procedure. *Psychosom. Med.*, 58, 242-248.
- Lambert, R. B., and Lambert, N. K. (1995). The effects of humor on secretory immunoglobulin A levels in school-aged children. *Pediatr. Nurs.*, 21, 16-19.
- Larsen, R. J., and Diener, E. (1992). Promises and problems with the circumplex model of emotion. In M. S. Clark (Ed.), *Emotion* (pp. 25-59). Thousand Oaks, CA: Sage Publications.
- Lazarus, R. S., and Folkman, S. (1984). *Stress, appraisal, and coping*. New York: Springer.
- Levy, B. R., Slade, M. D., Kunkel, S. R., and Kasl, S. V. (2002). Longevity increased by positive self-perceptions of aging. *J. Pers. Soc. Psychol.*, 83, 261-270.
- Levy, S. M., Lee, J., Bagley, C., and Lippman, M. (1988). Survival hazards analysis in first recurrent breast cancer patients: seven-year follow-up. *Psychosom. Med.*, 50, 520-528.
- Livnat, S., Felten, S. Y., Carlson, S. L., Bellinger, D. L., and Felten, D. L. (1985). Involvement of peripheral and central catecholamine systems in neural-immune interactions. *J. Neuroimm.*, 10, 5-30.
- Logan, H. L., Lutgendorf, S., Hartwig, A., Lilly, J., and Berberich, S. L. (1998). Immune, stress, and mood markers related to recurrent oral herpes outbreaks. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.*, 86, 48-54.
- Luoto, R., Prattala, R., Uutela, A., and Puska, P. (1998). Impact of unhealthy behaviors on cardiovascular mortality in Finland, 1978-1993. *Prev. Med. Int. J. Devoted Practice and Theory*, 27, 93-100.
- Lutgendorf, S. K., Antoni, M. H., Kumar, M., and Schneiderman, N. (1994). Changes in cognitive coping strategies predict EBV-antibody titer change following a stress disclosure induction. *J. Psychosom. Res.*, 38, 63-78.
- Lutgendorf, S. K., Tripp Reimer, T., Harvey, J. H., Marks, G., Hong, S.-Y., Hillis, S. L., and Lubaroff, D. M. (2001). Effects of housing relocation on immunocompetence and psychosocial functioning in older adults. *J. Geront.*, 56A, M97-105.
- Lyubomirsky, S., King, L., and Diener, E. (2005). The benefits of frequent positive affect: does happiness lead to success? *Psychol. Bull.*, 131, 803-855.
- Maier, H., and Smith, J. (1999). Psychological predictors of mortality in old age. *J. Gerontol. B Psychol. Sci. Soc. Sci.*, 54, P44-P54.
- Manuck, S. B., Cohen, S., Rabin, B. S., Muldoon, M. F., and Bachen, E. A. (1991). Individual differences in cellular immune response to stress. *Psychol. Sci.*, 2, 111-115.
- Marsland, A. L., Bachen, E. A., Cohen, S., and Manuck, S. B. (2001a). Stress, immunity and susceptibility to infectious illness. In A. Baum, T. A. Revenson, and J. E. Singer (Eds.), *Handbook of health psychology* (pp. 683-695). New Jersey: Lawrence Erlbaum Associates.
- Marsland, A. L., Cohen, S., Rabin, B. S., and Manuck, S. B. (2006). Trait positive affect and antibody response to hepatitis B vaccination. *Brain. Beh. Imm.*, 20, 261-269.
- Marsland, A. L., Cohen, S., Rabin, B. S., and Manuck, S. B. (2001b). Associations between stress, trait negative affect, acute immune reactivity, and antibody response to hepatitis B injection in healthy young adults. *Health Psychol.*, 20, 1-8.
- Martin, R. A. (2001). Humor, laughter, and physical health: methodological issues and research findings. *Psychol. Bull.*, 127, 504-519.
- McClelland, D. C., and Cheriff, A. D. (1997). The immunoenhancing effects of humor on secretory IgA and resistance to respiratory infections. *Psychol. Health*, 12, 329-344.
- McCraty, R., Atkinson, M., Rein, G., and Watkins, A. D. (1996). Music enhances the effect of positive emotional states on salivary IgA. *Stress Med.*, 12, 167-175.
- McDowell, I., and Newell, C. (1996). *Measuring health: a guide to rating scales and questionnaires* (2nd ed.). New York: Oxford University Press.
- McNair, D. M., Lorr, M., and Droppleman, L. F. (1971). *Profile of mood states manual*. San Diego: Educational and Industrial Testing Service.
- Middleton, R. A., and Byrd, E. K. (1996). Psychosocial factors and hospital readmission status of older persons with cardiovascular disease. *J. App. Rehab. Counsel.*, 27, 3-10.
- Miller, G. E., and Cohen, S. (2001). Psychological interventions and the immune system: a meta-analytic review and critique. *Health Psychol.*, 20, 47-63.
- Miller, G. E., Cohen, S., Rabin, B. S., Skoner, D. P., and Doyle, W. J. (1999). Personality and tonic cardiovascular, neuroendocrine, and immune parameters. *Brain Beh. Imm.*, 13, 109-123.

- Mittwoch-Jaffe, T., Shalit, F., Srendi, B., and Yehuda, S. (1995). Modification of cytokine secretion following mild emotional stimuli. *Neuroreport*, 6, 789-792.
- Moskowitz, J. T. (2003). Positive affect predicts lower risk of AIDS mortality. *Psychosom. Med.*, 65, 620-626.
- Moss, R. B., Moss, H. B., and Peterson, R. (1989). Microstress, mood, and natural killer-cell activity. *Psychosom.*, 30, 279-283.
- Myers, D. G., and Diener, E. (1995). Who is happy? *Psychol. Sci.*, 6, 10-19.
- Neumann, S. A., and Waldstein, S. R. (2001). Similar patterns of cardiovascular response during emotional activation as a function of affective valence and arousal and gender. *J. Psychosom. Res.*, 50, 245-253.
- Njus, D. M., Nitschke, W., and Bryant, F. B. (1996). Positive affect, negative affect, and the moderating effect of writing on sIgA antibody levels. *Psychol. Health*, 12, 135-148.
- Ostir, G. V., Markides, K. S., Black, S. A., and Goodwin, J. S. (2000). Emotional well-being predicts subsequent functional independence and survival. *J. Am. Geriatr. Soc.*, 48, 473-478.
- Ostir, G. V., Markides, K. S., Peek, M. K., and Goodwin, J. S. (2001). The association between emotional well-being and the incidence of stroke in older adults. *Psychosom. Med.*, 63, 210-215.
- Parker, M. G., Thorslund, M., and Nordstrom, M. L. (1992). Predictors of mortality for the oldest old: a 4-year follow-up of community-based elderly in Sweden. *Arch. Gerontol. Geriatr.*, 14, 227-237.
- Perera, S., Sabin, E., Nelson, P., and Lowe, D. (1998). Increases in salivary lysozyme and IgA concentrations and secretory rates independent of salivary flow rates following viewing of a humorous video. *Int. J. Beh. Med.*, 5, 118-228.
- Pfeiffer, C. A., and Wetstone, S. L. (1988). Health locus of control and well-being in systemic lupus erythematosus. *Arthritis Care Res.*, 1, 131-138.
- Polk, D. E., Cohen, S., Doyle, W. J., Skoner, D. P., and Kirschbaum, C. (2005). State and trait affect as predictors of salivary cortisol in healthy adults. *Psychoneuroendocrinology*, 30, 261-272.
- Pressman, S., and Cohen, S. (2005). Does positive affect influence health? *Psychol. Bull.*, 131, 925-971.
- Rabin, B. S. (1999). *Stress, immune function, and health: the connection*. New York: Wiley-Liss.
- Rabin, B. S., Cohen, S., Ganguli, R., Lusle, D. T., and Cunnick, J. E. (1989). Bidirectional interaction between the central nervous and the immune system. *Crit. Rev. Imm.*, 9, 279-312.
- Riis, J., Loewenstein, G., Baron, J., Jepson, C., Fagerlin, A., and Ubel, P. A. (2005). Ignorance of hedonic adaptation to hemodialysis: a study using ecological momentary assessment. *J. Exp. Psychol. Gen.*, 134, 3-9.
- Ritz, T., Claussen, C., and Dahme, B. (2001). Experimentally induced emotions, facial muscle activity, and respiratory resistance in asthmatic and non-asthmatic individuals. *Brit. J. Med. Psychol.*, 74, 167-182.
- Ritz, T., George, C., and Dahme, B. (2000a). Respiratory resistance during emotional stimulation: evidence for a nonspecific effect of experienced arousal? *Biol. Psychol.*, 52, 143-160.
- Ritz, T., and Steptoe, A. (2000). Emotion and pulmonary function in asthma: reactivity in the field and relationship with laboratory induction of emotion. *Psychosom. Med.*, 62 (6), 808-815.
- Ritz, T., Steptoe, A., DeWilde, S., and Costa, M. (2000b). Emotions and stress increase respiratory resistance in asthma. *Psychosom. Med.*, 62, 401-412.
- Roy Samb, E., Harris, J. R., Magnus, P., Vitterso, J., and Tambs, K. (2002). Subjective well-being: sex-specific effects of genetic and environmental factors. *Personal. Indiv. Diff.*, 32, 211-223.
- Russell, J. A. (1980). A circumplex model of affect. *J. Personal. Soc. Psychol.*, 39, 1161-1178.
- Ryff, C. D. (2003). The role of emotion on pathways to positive health. In R. Davidson (Ed.), *Handbook of affective sciences* (pp. 1083-1104). London: Oxford University Press.
- Ryff, C. D., Singer, B. H., and Dienberg Love, G. (2004). Positive health: connecting well-being with biology. *Philos. Trans. R. Soc. Lond. B. Biol. Sci.*, 359, 1383-1394.
- Salovey, P., Rothman, A. J., Detweiler, J. B., and Steward, W. T. (2000). Emotional states and physical health. *Am. Psychol.*, 55, 110-121.
- Scheier, M. F., and Carver, C. S. (1987). Dispositional optimism and physical well-being: the influence of generalized outcome expectancies on health. *J. Personal.*, 55, 169-210.
- Seegerstrom, S. C., and Miller, G. E. (2004). Psychological stress and the human immune system: a meta-analytic study of 30 years of inquiry. *Psychol. Bull.*, 130, 601-630.
- Seegerstrom, S. C., Taylor, S. E., Kemeny, M. E., and Fahey, J. L. (1998). Optimism is associated with mood, coping, and immune change in response to stress. *J. Personal. Soc. Psychol.*, 74, 1646-1655.
- Smith, A. M., Stuart, M. J., Wiese-Bjornstal, D. M., and Gunnon, C. (1997). Predictors of injury in ice hockey players. A multivariate, multidisciplinary approach. *Am. J. Sports Med.*, 25, 500-507.
- Smith, A. W., and Baum, A. (2003). The influence of psychological factors on restorative function in health and illness. In J. Suls and K. A. Wallston (Eds.), *Social psychological foundations of health and illness* (pp. 431-457). Malden, MA: Blackwell Publishers.
- Smyth, J., Ockenfels, M. C., Porter, L., Kirschbaum, C., Hellhammer, D. H., and Stone, A. A. (1998). Stressors and mood measured on a momentary basis are associated with salivary cortisol secretion. *Psychoneuroendocrinology*, 23, 353-370.
- Solomon, G. F., and Moos, R. (1964). Emotions immunity, and disease. *Arch. Gen. Psychiatry*, 11, 657-674.
- Steptoe, A., Wardle, J., and Marmot, M. (2005). Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes. *Proc. Natl. Acad. Sci. USA*, 102, 6508-6512.
- Stone, A. A., Cox, D. S., Valdimarsdottir, H., Jandorf, L., and Neale, J. M. (1987). Evidence that secretory IgA antibody is associated with daily mood. *J. Personal. Soc. Psychol.*, 52, 988-993.
- Stone, A. A., Neale, J. M., Cox, D. S., Napoli, A., Valdimarsdottir, H., and Kennedy-Moore, E. (1994). Daily events are associated with a secretory immune response to an oral antigen in men. *Health Psychol.*, 13, 440-446.
- Stones, M. J., Dornan, B., and Kozma, A. (1989). The prediction of mortality in elderly institution residents. *J. Gerontology*, 44 (3), P72-P79.
- Szmunn, W., Stevens, C. E., Harley, E. J., Zang, E. A., Oleszko, W. R., William, D. C., Sadovsky, R., Morrison, J. M., and Kellner, A. (1980). Hepatitis B vaccine: demonstration of efficacy in a controlled clinical trial in a high-risk population in the United States. *N. Engl. J. Med.*, 303, 833-841.
- Totman, R., Kiff, J., Reed, S. E., and Craig, J. W. (1980). Predicting experimental colds in volunteers from different measures of recent life stress. *J. Psychosom. Res.*, 24, 155-163.
- Tracey, K. J. (2002). The inflammatory reflex. *Nature*, 420, 853-859.
- Uchino, B. N., Cacioppo, J. T., and Kiecolt-Glaser, J. K. (1996). The relationship between social support and physiological processes: a review with emphasis on underlying mechanisms and implications for health. *Psychol. Bull.*, 119, 488-531.
- Usala, P. D., and Hertzog, C. (1989). Measurement of affective states in adults: evaluation of an adjective rating scale instrument. *Res. Aging*, 11, 403-426.

- Valdimarsdottir, H. B., and Bovbjerg, D. H. (1997). Positive and negative mood: association with natural killer cell activity. *Psychol. Health*, 12, 319-327.
- van Domburg, R. T., Pedersen, S. S., van den Brand, M. J. B. M., and Erdman, R. A. M. (2001). Feelings of being disabled as a predictor of mortality in men 10 years after percutaneous coronary transluminal angioplasty. *J. Psychosom. Res.*, 51, 469-477.
- van Eck, M., Berkhof, H., Nicolson, N., and Sulon, J. (1996). The effects of perceived stress, traits, mood states, and stressful daily events on salivary cortisol. *Psychosom. Med.*, 58, 447-458.
- van Tits, L. J. H., Michel, M. C., Grosse-Wilde, H., Happel, M., Eigler, F. W., Soliman, A., and Brodde, O. E. (1990). Catecholamines increase lymphocyte beta-2 adrenergic receptors via a beta adrenergic, spleen-dependent process. *Am. J. Physiol.*, 258, E191-202.
- Watson, D. (1988). The vicissitudes of mood measurement: effects of varying descriptors, time frames, and response formats on measures of positive and negative affect. *J. Personal. Soc. Psychol.*, 55, 128-141.
- Watson, D., Clark, L. A., McIntyre, C. W., and Hamaker, S. (1992). Affect, personality, and social activity. *J. Personal. Soc. Psychol.*, 63, 1011-1025.
- Watson, D., Clark, L. A., and Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *J. Personal. Soc. Psychol.*, 54, 1063-1070.
- Watson, D., and Tellegen, A. (1985). Toward a consensual structure of mood. *Psychol. Bull.*, 98, 219-235.
- Weisman, A. D. (1979). *Coping with cancer*. New York: McGraw-Hill.
- Willemson, G., Ring, C., Carroll, D., Evans, P., Clow, A., and Hucklebridge, F. (1998). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and cold pressor. *Psychophysiology*, 35, 252-259.
- Wingard, D. L., Berkman, L. F., and Brand, R. J. (1994). A multivariate analysis of health-related practices: a nine-year mortality follow up of the Alameda county study. In A. Steptoe and J. Wardle (Eds.), *Psychosocial processes and health: a reader* (pp. 273-289). New York: Cambridge University Press.
- Yoshino, S., Fujimori, J., and Kohda, M. (1996). Effects of mirthful laughter on neuroendocrine and immune systems in patients with rheumatoid arthritis. *J. Rheumatol.*, 23, 793-794.
- Zachariae, R., Jorgensen, M. M., Egekvist, H., and Bjerring, P. (2001). Skin reactions to histamine of healthy subjects after hypnotically induced emotions of sadness, anger, and happiness. *Allergy*, 56, 734-740.
- Zachariae, R., Bjerring, P., Zachariae, C., Arendt-Nielsen, L., Nielsen, T., Eldrup, E., Larsen, C. S., and Gotliebsen, K. (1991). Monocyte chemotactic activity in sera after hypnotically induced emotional states. *Scand. J. Imm.*, 34, 71-79.
- Zautra, A. J. (2003). *Emotions, stress, and health*. London: Oxford University Press.