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# Trait positive affect and antibody response to hepatitis B vaccination

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**Abstract**

Recent evidence suggests that dispositional positive affect may be associated with decreased vulnerability to upper respiratory infections. To explore a potential pathway of this relationship, we examined whether trait positive affect is related to an in vivo immune response relevant for host resistance to infection. Eighty-four healthy, graduate students who tested negative for prior expose to the hepatitis B virus were administered the standard hepatitis B vaccination series. Five months after the first dose, a blood sample was collected for the measurement of specific antibody response to the vaccine and subjects completed a battery of psychosocial questionnaires. Higher scores on a measure of dispositional positive affect were associated with a greater antibody response to hepatitis B vaccination. This relationship occurred after controlling for demographics and body mass and was largely independent of concomitant levels of dispositional negative affect, optimism, and extraversion. In the presence of dispositional positive affect, there was no independent effect of trait negative affect on antibody response. Physical activity played a protective role for individuals low in positive affect, being related to higher antibody responses. These data provide initial evidence that individual differences in dispositional positive affect may be of health significance, being related to an in vivo immune response relevant for protection against infection.


*Keywords:* Psychoneuroimmunology; Positive affect; Emotion; Hepatitis B vaccine; Vaccination response; Optimism; Extraversion; Physical activity

## 1. Introduction

In support of popular belief, recent findings suggest that individuals who characterize themselves by moods such as happy, pleased, relaxed, and lively are less vulnerable to upper respiratory infections (Cohen et al., 2003). These findings add to a developing literature suggesting that dispositional positive affect may play a role in health improvement (Pressman and Cohen, in press). In their study, Cohen and colleagues experimentally inoculated 334 healthy, adult volunteers with common cold viruses and then quarantined and monitored them for the development of biologically verified upper respiratory infections. Findings demonstrated a dose–response relationship between higher positive emotional styles measured before the inoculation and lower risk of developing a cold. In contrast, there was no relationship between negative emotional styles and colds. A large number of control factors (including age, sex, education, negative affect, and virus-specific antibody status before challenge) were not able to explain decreased risk for colds among persons reporting higher dispositional PA.

A number of potential pathways exist through which an association between PA and infectious disease susceptibility might occur, including behavioral and immune mechanisms. A positive emotional style could promote health through health-enhancing behaviors (Myers and Diener, 1995). For example, better sleep quality and more exercise have been associated with high PA (Bardwell et al., 1999; Cohen et al., 2003), better immune function (Kiecolt-Glaser and Glaser, 1988) and decreased susceptibility to the common cold (Cohen et al., 1997). Another pathway through which emotions could influence infectious pathology is via

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modulation of immune function, influencing host susceptibility to infectious pathogens. Here, there is extensive evidence for direct anatomical and functional links between the central nervous and immune systems, providing a biological pathway for the influences of emotions on response to viral pathogens (Rabin, 1999). However, in contrast to a large literature examining the relationship between negative emotions and compromised immune function (Kiecolt-Glaser et al., 1992; Sergerstrom and Miller, 2004), only a few studies have examined immune function that accompanies PA. Initial findings suggest immune benefits of daily fluctuation in positive mood, including increased antigen-specific secretory immunoglobulin A response to an ingested innocuous protein (Stone et al., 1987) and increased natural killer cell cytotoxicity (Valdimarsdottir and Bovberg, 1997). To date, immune changes that accompany more enduring PA remain unknown. It is likely that dispositional (trait) PA would be associated with larger and more stable immune differences that would alter the ability of the body to resist viral infections.

The goal of the following study is to further explore the relationship between trait levels of PA and infectious disease susceptibility, by examining whether trait positive emotional style is associated with antibody response to hepatitis B vaccination. We define PA as the feelings that reflect a level of pleasurable engagement with the environment (Clark et al., 1989). We have previously reported that trait negative affect is associated with a reduction in antibody response to this vaccine (Marsland et al., 2001). Recent interest in the influence of PA on health and findings suggesting decreased disease risk among persons with a positive emotional style (Pressman and Cohen, in press), led us to examine whether trait PA is associated with antibody response and, if so, whether this relationship is independent of trait NA.

While there is much current debate regarding the structure of affect (e.g., Izard, 1977; Larsen and Diener, 1992; Watson and Tellegen, 1985), there is a growing consensus that positive and negative affect are broad, underlying dimensions of basic emotions that consistently emerge across studies (Watson and Tellegen, 1985). However, 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 (Cohen et al., 2003; Diener and Emmons, 1985). Recent evidence demonstrates that positive and negative affective styles are associated with 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, 2000). Consequently, we expected that PA would be associated with better antibody response, even after controlling for the influences of NA.

Another issue that requires clarification in the literature linking PA to health is the role of psychological concepts that are closely related to PA, such as optimism and extraversion. These factors have been related to improved objective health outcomes (e.g., Cohen et al., 1997; Scheier and Carver, 1987) and to improved immune function (Miller et al., 1999; Sergerstrom et al., 1998). Furthermore, extraversion has been associated with decreased susceptibility to upper respiratory infections (Broadbent et al., 1984; Cohen et al., 1997; Totman et al., 1980). Thus, it is possible that these dispositional characteristics account for associations between PA and infectious disease susceptibility. In this study, we controlled for these third factors and explored the independent contributions of optimism, extraversion and trait PA to antibody response. Finally the possibility that health practices, including smoking, alcohol use, and physical activity mediate the relationship between trait PA and antibody response was explored.

For this study, we chose to examine the influence of affective style on secondary immune response to a novel antigen, hepatitis B vaccination. This decision was based on an existing literature suggesting that trait affect has its greatest impact on secondary as opposed to primary immune response to vaccination (as reviewed by Cohen et al., 2001). In the case of antibody response to hepatitis B vaccine series, this phase occurs after the second vaccination, a period when it has been demonstrated that psychosocial factors are associated with magnitude of antibody response (e.g., Jabaai et al., 1993; Marsland et al., 2001). A second reason to focus on antibody responses to the second vaccination in this 3 dose sequence is the typical titer response to each of the vaccinations. There is little variability in response across individuals following either the first vaccination, when only about 25% of individuals have discernable levels of antibody, or the third vaccination, when the majority of recipients have mounted maximal antibody responses. In contrast, there is widespread interindividual variability in the magnitude of antibody response following the second vaccination (Szmuness et al., 1980). At this timepoint, the majority of individuals have mounted an antibody response; however, the range of antibody responses is widely dispersed, enabling us to explore emotional factors associated with individual difference in response.

## 2. Method

### 2.1. Participants

The participants were 51 male and 33 female graduate students ages 21–33 years (mean = 24) who volunteered to participate in a study investigating whether psychological factors influence immune response to hepatitis B vaccination. Three participants were dropped from data analyses due to problems collecting blood samples, leaving a final sample of 81. All subjects were of normal weight, healthy, endorsed no history or symptoms of systemic diseases known to affect the immune system and were native English

speakers. All reported no previous hepatitis B vaccination. The vaccine was not available or a routine component of the childhood vaccination sequence when the participants were in early childhood. No subjects had evidence of current or past infection with hepatitis B virus as indicated by the absence of existing hepatitis B surface antigens or antibodies to core antigens. All subjects gave informed consent to participate in this investigation, which was approved by the IRB of the University of Pittsburgh.

### 2.2. Procedures

All participants received the standard course of three 20 μg doses of recombinant hepatitis B vaccine (Heptavax B, Smithkline Beecham), administered intramuscularly into the deltoid muscle. The first two injections were given six weeks apart, followed by a booster injection at 6 months. Five months following the initial vaccination, all subjects attended a brief laboratory visit scheduled in the morning. Subjects were asked to fast for 12 h before this visit, when a 10-ml of blood was drawn for the determination of antibody response to the hepatitis B surface antigen (time 1 sample) and subjects received a battery of questionnaires to take home, complete and return within a week. Participants received $10 for participating in the laboratory visit. There was a second phase to the study which occurred 2–4 months following the final booster vaccination when the participants returned to the laboratory 2–4 months following completion of the hepatitis B vaccination series to participate in an acute psychophysiological reactivity session, results of this assessment are reported elsewhere (Marsland et al., 2001). A second blood sample was drawn at this time for the reassessment of hepatitis B antibody response (time 2 sample).

### 2.3. Hepatitis B measures

Blood samples for the determination of hepatitis B surface antigen (HBsAG), and antibodies to hepatitis B surface and core antigens (anti-HBs and anti-HBc) were centrifuged and the serum was frozen at −80 °C until analysis. Antibody titers were determined by enzyme-linked immunoassay (EIA), using commercial kits (kindly donated by Abbot Laboratories). Briefly, polystyrene beads coated with human HBsAG were incubated at room temperature for 18 h with serial two-fold dilutions of each serum sample. After washing, HBsAG, conjugated to biotin, and rabbit anti-biotin antibody, conjugated with horseradish peroxidase, were incubated with the beads. After incubation with substrate solution (*O*-phenylone diamine, 2 HCl, and 0.02% hydrogen peroxide), absorbency of the controls and test serum samples was determined. Antisera with known titers was used to determine the International Units (IU)/ml of antibody in each sample.

### 2.4. Psychosocial measures

Participants completed a series of psychosocial questionnaires evaluating trait positive and negative affect, extraversion, optimism, depression and health behaviors around the time of their initial laboratory visit. To assess affective styles, including trait positive and negative affect and extraversion, participants completed an 88-item adjective rating scale. This scale included subscales taken from four widely used and well-validated measures of affect: Profile of Mood States (POMS) Affect Scale (Usala and Hertzog, 1989), Goldberg's Big-5 Factor Scales (Goldberg, 1992), Larsen and Diener Circumplex (Larsen and Diener, 1992) and Mackay Circumplex (Mackay et al., 1978). 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 and approximate age on a 5-point likert scale ranging from 0 (not at all accurate) to 4 (extremely accurate). This scale included 9 positive (lively, full-of-pep, energetic, happy, pleased, cheerful, at-ease, calm, and relaxed) and 9 negative (sad, depressed, unhappy, on-edge, nervous, tense, hostile, resentful, and angry) mood adjectives derived from a factor analysis of affect items (Usala and Hertzog, 1989) and used by Cohen et al. (2003) as a measure of positive and negative emotional style. Cohen et al. (2003) found that this measure of dispositional style 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. Thus, we chose to employ the same mood adjectives to measure PA and NA. The internal-reliabilities (αs) in this sample were .71 for the positive and .76 for the negative mood scale.

### 2.5. Control variables

A number of control variables were assessed that might provide alternative explanations for associations between trait positive affect and response to hepatitis B vaccination. These included age, sex, body mass index, and depression, assessed by the Beck Depression Inventory (BDI; Beck et al., 1961). In addition, optimism was evaluated using the Life Orientation Test (LOT: Scheier and Carver, 1987), a well validated, 12-item scale designed to measured dispositional optimism. To assess extraversion, we used a modified 10-item version of the extraversion subscale from Goldberg's Big-5 Factor Scale (Cohen et al., 1997; Goldberg, 1992).

### 2.6. Health practices

Finally, health practices were evaluated as possible pathways linking PA to antibody response. These measures included smoking (average number of cigarettes/day) and drinking alcohol (average number of alcoholic drinks/week). Physical activity was also measured using three questions taken from the Paffenbarger Activity Scale (Paffenbarger et al., 1993). The questions were: (1) How many flights of stairs do you walk up each day? (2) On average, how many city blocks of their equivalent do you walk each day as part of your normal routine? And (3) List any sports or recreation

you have participated in during the past month. Please include only the time when you were physically active.

### 2.7. Statistical analysis

An initial examination of the distribution of the antibody responses to hepatitis B surface antigen measured at time 1, 5 months after the initial vaccination, revealed the expected widespread interindividual variability. Antibody responses ranged from no discernable antibody to the maximal antibody response quantifiable by our methods −150 mIU/ml. Because the distribution of responses was bimodal, with most individuals falling at the extremes, parametric analyses were not justified. Instead, two groups of subjects were identified by dividing the distribution of time 1 antibody responses at the median, permitting identification of individuals with "High Ab" or "Low Ab" responses (mIU/ml: Low Ab ($n=41$): mean = 16; High Ab ($n=40$): mean = 120). A series of stepwise logistic regression analyses was then performed examining whether trait positive affect predicted the binary antibody outcome. For these analyses, standard control variables (sex, age, and BMI) were entered in the initial step, followed by trait positive affect in step two. A further series of analyses was performed entering third variables (trait negative affect, optimism, and extraversion) at the same time as trait PA to determine whether the association between PA and antibody response is substantially reduced after controlling for the contribution of these factors. Finally, we examined whether health behaviors mediate the relationship between PA and antibody response. For this purpose, any health behaviors that were associated with PA and predicted variations in antibody responses were entered into a regression model containing PA to determine whether they significantly reduced the relationship between PA and antibody response. We report the regression coefficient, its standard error, and probability level. In addition, we also include odds ratios (*OR*) and 95% confidence intervals as an estimate of relative risk.

## 3. Results

### 3.1. Comparison of antibody groups on control factors

Preliminary analyses were conducted using *t* tests to compare the two antibody response groups on a number of control measures that may influence magnitude of antibody response (Table 1). High and Low Ab subjects did not differ in mean age or sex distribution. As expected based on previous findings (Wood et al., 1993), individuals in the Low Ab group had greater mean body mass index than their High Ab counterparts ($t(79)=2.17$, $p<.03$). BMI, sex, and age were entered as covariates in all regression analyses.

### 3.2. Does trait PA predict antibody response?

In support of our hypothesis, when examined as an individual predictor, higher levels of trait PA were associated with higher antibody responses to the vaccination ($b=.54$ [±.25], $p<.03$; $OR=1.73$ [1.05–2.84]). Thus, the odds of an individual with high trait PA belonging to the high antibody response group are 1.73 times that of an individual with low trait PA. These findings are displayed in Fig. 1, which shows that individuals who mounted higher antibody responses to hepatitis B vaccination endorsed higher levels of trait PA than their low antibody response counterparts.

Table 1
Characteristics of low and high antibody groups (standard deviations in parentheses)

| | Low Ab | High Ab |
|---|---|---|
| *N* | 41 | 40 |
| Antibody level (mIU/ml) | | |
| Time 1 | 16 (17) | 120 (35) ** |
| Time 2 | 92 (61) | 150 (1) ** |
| Age | 25 (3) | 24 (3) |
| Sex | | |
| Male | 29 | 22 |
| Female | 12 | 18 |
| Body mass index | 24.7 (4.5) | 22.8 (2.9)* |

Antibody responses >10 mIU/ml are considered protective.
* $p<.05$.
** $p<.00001$.

Affect is frequently conceptualized according to a circumplex structure with two dimensions: valence (e.g., positive versus negative) and activation/arousal (aroused versus unaroused) (Russell, 1980). Thus, affect can be described by where it falls on this two-dimensional plane. We took a closer look at the valence of the positive emotions to determine whether the relationship between positive affect and antibody response was specific to emotions of low or high activation/arousal. For this purpose, we examined the three positive subscale scores: well being (happy, pleased, and cheerful), calm (at-ease, calm, and relaxed: low arousal) and vigor (lively, full-of-pep, and energetic: high arousal) as independent predictors. There was a trend for all three

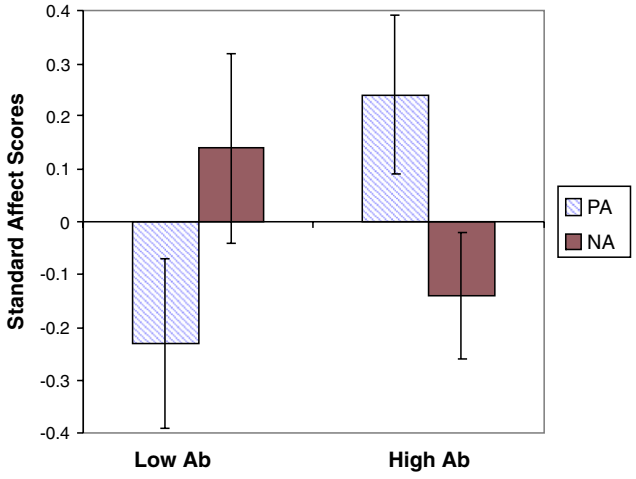


Fig. 1. Positive and negative affect standardized scores among individuals high and low in antibody response after controlling for age, BMI, and sex.

subscales to be similarly associated with higher antibody responses: Vigor ($b = .16$ [±.09], $p < .07$; $OR = 1.17$ [0.98–1.40]); Calm: ($b = .14$ [±.08], $p < .09$; $OR = 1.15$ [0.97–1.35]); well-being ($b = .18$ [±.10], $p < .06$; $OR = 1.20$ [0.99–1.45]), suggesting that the associations between positive affect and antibody response are equivalent irrespective of activation/arousal dimension.

### 3.3. Is the relationship between trait PA and antibody response independent of trait NA?

We have previously reported that trait negative affect is significantly related to lower antibody responses to hepatitis B vaccination (Marsland et al., 2001). This raises the possibility that the current findings reflect the absence of NA rather than the presence of positive emotional styles. Consistent with the literature, our findings revealed that PA and NA are negatively correlated ($r = -.53$, $p < .0001$). Based on current conceptualizations, we hypothesized that these factors although related would have a distinct effect on vaccination response and would not be merely opposites on the same continuum. Thus, we anticipated that the relationship between trait PA and antibody response would be independent of the influences of NA. When the two affect measures were entered into the regression simultaneously to test the independent contribution of each factor, PA remained the dominant factor marginally predicting antibody group ($\beta$ changed from .54 to .46 [±.29], $p < .11$; $OR = 1.58$ [.9–2.78] with NA in the model). In contrast, no independent influence of trait NA was observed ($b = -.19$ [±.31], $p < .54$; $OR = .82$ [.45–1.53]). Finally, we added the interaction between PA and NA to the regression model. This interaction did not approach significance. These findings suggest that, although related, positive and negative emotional styles are distinct concepts, with individuals who endorse higher levels of trait PA tending to mount better in vivo antibody responses to vaccination even when concomitant levels of NA are taken into account.

These findings raise the question of whether there is an independent effect of trait negative affect on antibody response. Our previous publication based on this data set suggested that this was the case (Marsland et al., 2001). The measure of trait NA employed in this earlier study was somewhat broader than the measure of affective tone used in this analysis. The broader measure was derived from a factor analysis of 17 negative mood adjectives taken from four instruments: anxiety and depression from the POMS Affect Scale (Usala and Hertzog, 1989), emotional stability from Goldberg's Big-5 Factor Scales (Goldberg, 1992), activated unpleasant affect and unpleasant affect from the Larsen and Diener Circumplex (Larsen and Diener, 1992) and positive loading for stress from the Mackay Circumplex (Mackay et al., 1978). Although all the adjectives loaded highly on a single negative affect factor, the list includes subscales that assess depression (sad, depressed, unhappy, blue, and resentful), anxiety (on edge, nervous, tense, uneasy, anxious, worried, fearful, and touchy), and stress (distressed, uptight, bothered, and irritable). In contrast, the 9-item adjective measure of emotional style used in the current paper (Usala and Hertzog, 1989), includes subscales that assess depression (sad, depressed, unhappy), anxiety (on edge, nervous, and tense) and anger (resentful, angry hostile).

To further tease out the relationship between NA and vaccination response, we next examined whether both measures of NA (the 17-item scale and the 9-item scale) were independent predictors of antibody response group. As reported previously, the 17-item measure of NA was a significant predictor of lower antibody response $b = -.65$ [±.29], $p < .02$; $OR = .52$ [.30–.91]. However, a parallel analysis using the 9-item measure of negative emotional style revealed only a marginal relationship between higher NA and lower antibody response ($b = -.43$ [±.28], $p < .12$; $OR = .65$ [.38–1.11]). Although both measures of NA were highly correlated ($r = .94$, $p < .0001$), there were some differences between the measures that may account for the different findings. One notable difference was the inclusion of adjectives measuring anger in the 9-item scale, but not in the 17-item version. Given that High and Low Ab subjects did not differ in the magnitude of their responses to the anger adjectives ($t(78) = .27$, $p < .78$), we explored the impact of dropping anger from the 9-item measure. Consistent with the findings from the earlier study, this abbreviated measure of trait NA was an independent predictor of antibody response group ($b = -.12$ [±.06], $p < .03$; $OR = .89$ [.80–.99]), suggesting that trait levels of anxiety and depression, but not anger, are related to decreased vaccination response.

In the case of all three measures of trait NA (17-item measure, 9-item measure, and the abbreviated 6-item measure), the relationship between trait NA and antibody response was reduced substantially and below significance when trait PA was entered simultaneously into the model. This suggests that previous studies, including our own, that find a relationship between trait NA and immune response may be partially evaluating the absence of PA rather than the presence of negative feelings.

### 3.4. Is the relationship between trait PA and antibody response independent of optimism, extraversion, and depression?

To assess whether the association of PA and antibody response was independent of any association with optimism or extraversion, we first examined Pearson product-moments correlations between these psychological constructs. As expected, trait PA was closely related to optimism ($r = .52$, $p < .0001$) and extraversion ($r = .51$, $p < .0001$). However, independent $t$ tests comparing the two antibody response groups on these variables revealed no significant differences in optimism ($t(78) = -1.42$, $p < .16$) or extraversion ($t(78) = -.44$, $p < .66$). In light of the trend for a between-group difference for optimism, we also ran a regression analysis, entering trait PA and optimism

together in the second step. Adding optimism to the model only resulted in a small drop in the PA effect size ($\beta$ changed from .54 to .41[±.29], $p < .16$; $OR = 1.51$[.85–2.66]), with no independent relationship between optimism and antibody response group ($b = .07$, $p < .33$). This conservative analysis suggests that PA influences health independently of optimism. Others have proposed that PA, optimism and extraversion reflect a common underlying construct and should not be separated (Gable et al., 2003). To explore whether this approach would alter the outcome, we entered the three variables into a principal component factor analysis. Because all three loaded on the same factor, we calculated an aggregate measure of the three by averaging the standardized scores. This combined score accounted for little variability in antibody response grouping over that associated with PA alone ($\beta$ changed from .54 with PA in model to .57 [±.26], $p < .03$; with the aggregate measure). Overall, these findings suggest that the association between trait PA and antibody response is largely independent of the related constructs of optimism and extraversion. Finally, there was no relationship between depression, as measured by the BDI and antibody response.

### 3.5. Do health behaviors mediate the relationship between PA and vaccination response?

We explored the possibility that heath behaviors mediate the association between trait PA and antibody response. Descriptive statistics for these measures are presented in Table 2. Preliminary analyses using $t$ tests to compare the two antibody response groups on a number of health behaviors revealed no significant difference between High and Low Ab subjects in alcohol use or smoking status. On evaluation of the three exercise questions, there was no difference between the groups in the number of flights of stairs climbed each day. In contrast, high antibody responders endorsed walking more city blocks per day as part of their normal routine ($t(78) = -1.95$, $p < .05$) and spending more time exercising ($t(78) = -1.90$, $p < .06$) than low antibody subjects. Further analyses revealed a significant correlation between PA and time spent exercising each week ($r = .24$, $p < .03$), but not number of city blocks ($r = .09$, $p < .38$). Thus, time spent exercising was assessed as a possible pathway linking PA to vaccination response. Adding PA and exercise time to the equation (including standard controls) revealed relatively independent influences of PA ($\beta$ changed from .54 to .48 [±.26], $p < .06$; $OR = 1.62$ [.97–2.69] with exercise time in the model) and exercise time $b = .17$ [±.10], $p < .09$; $OR = 1.19$ [.98–1.44] on classification of individuals into the antibody response groups. Finally, there was a significant effect of adding the interaction between PA and exercise time to the model ($b = -.24$ [±.11], $p < .03$; $OR = .78$ [.63–.98]). Further examination of this interaction (Fig. 2) revealed that Low PA is associated with lower antibody response among those exercising fewer hours but not among those exercising longer.

Table 2
Health behaviors of low and high antibody groups (standard deviations in parentheses)

| | Low Ab | High Ab |
|---|---|---|
| # Alcoholic drinks/week | 3.6 (4.7) | 3.4 (4.0) |
| # Active smokers | 2 | 4 |
| # Flights of stairs/day | 7.4 (5.6) | 8.7 (8.6) |
| # City blocks/day | 13.9 (8.6) | 18.7 (13.1)* |
| Hours spent exercising/week | 2.4 (2.5) | 3.5 (2.6)* |

* $p < .05$.

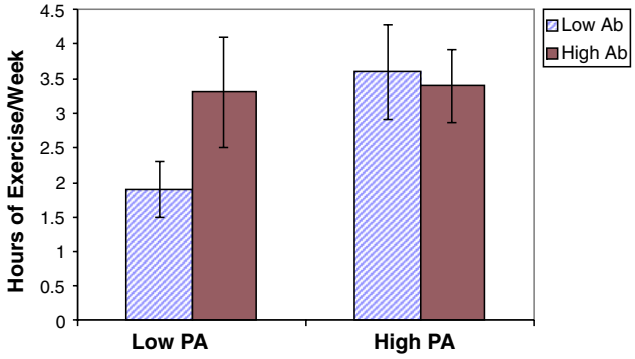


Fig. 2. Number of hours of exercise per week among individuals high and low in positive affect (median split) and antibody response.

To determine whether relationships between PA and exercise in predicting antibody response were the consequence of negative mood, we re-ran the exercise mediation analyses adding trait NA (9-item measure) and depression as controls to the model and again found independent influences of PA ($b = 1.27$ [±.52], $p < .02$; $OR = 3.55$ [1.28–9.83]), exercise time ($b = .22$ [±.11], $p < .05$; $OR = 1.25$ [1.00–1.55]), and the interaction between PA and exercise time ($b = -.24$ [±.11], $p < .04$; $OR = .79$ [ .63–.99]) on antibody response classification.

## 4. Discussion

This study provides evidence for an association between dispositional positive affect and magnitude of secondary antibody response to hepatitis B vaccination, an in vivo measure of host resistance to viral infection. Consistent with a growing literature suggesting that positive affect is associated with improved immune function (Stone et al., 1987; Valdimarsdottir and Bovberg, 1997) and better health outcomes (Pressman and Cohen, in press), we found that subjects who mounted higher antibody responses to hepatitis B vaccination endorsed more dispositional positive affect than subjects who mounted lower antibody responses. This association occurred after controlling for age, sex and body mass and did not differ among high and low activation/arousal positive emotions. A positive relationship between PA and antibody response raises the possibility that the recently reported dose–response relationship between increased positive emotional style and decreased susceptibility to upper respiratory illness

(Cohen et al., 2003) could be mediated through differences in ability to mount a protective immune response.

In contrast to the huge literature showing associations between dispositional negative affect and vulnerability to disease (e.g., Krantz and McCeney, 2002; Taylor, 1990), relatively few studies have examined the relationship between positive affect and physical health outcomes. Indeed, it is only in recent years that attention has turned to the health benefits of positive emotions. Available findings are encouraging and a recent review of prospective studies in the literature (Pressman and Cohen, in press) concludes that higher levels of trait PA are associated with increased longevity and decreased morbidity. However, to date, the mechanisms through which positive emotions influence health have been unknown. Our findings demonstrate a direct link between dispositional PA and an in vivo measure of immune function, which is clinically relevant for protection against viral infection. This suggests that one potential pathway to health is via changes in immune function.

A couple of alternate mechanisms could underlie associations between positive affect and antibody response. First, there is converging evidence that the central nervous and immune systems are linked by neuroendocrine pathways. Emotions are associated with activity along two physiologic pathways (1) the hypothalamic-pituitary-adrenal axis and (2) the sympathetic nervous system, both of which have been shown to play a role in the modulation of immunity (Ader, 2000; Felten and Olschowka, 1987; Plaut, 1987). Positive affect may alter immune function via the dampening of activity along these pathways. In support of this possibility, lower circulating concentrations of epinephrine, norepinephrine and cortisol have been shown to accompany higher levels of trait PA (Cohen et al., 2003; Kugler and Kalveram, 1987; Smyth et al., 1998). Furthermore, the few available studies examining biological mediators suggest that cortisol may be one pathway linking emotions to antibody response (e.g., Burns et al., 2002); however, to date, no studies have directly explored this possibility. In their study, Cohen and colleagues (2003) found no evidence that catecholamine or cortisol release over the course of a 24-h period accounted for the association between PA and susceptibility to upper respiratory infections.

Trait PA may also influence immunity via changes in health practices that affect immune function. There is evidence that individuals high in trait PA endorse more exercise and better overall sleep quality, than their low PA counterparts (Cohen et al., 2003). Consistent with these findings, our data support a positive relationship between trait PA and a subjective measure of time spent exercising per week. Sleep quality was not assessed in the current study and we found no relationship between PA and alcohol use or smoking. Interestingly, in addition to being associated with PA, physical activity was related to vaccination response, with individuals who mounted higher antibody responses endorsing walking more per day as part of their normal routine and a tendency to spend more time exercising per week than low antibody responders. These findings are consistent with those of other investigators who have reported an association between lifestyle exercise and enhanced antibody response to influenza immunization (Kohut et al., 2002) and improved general immune function (e.g., Kiecolt-Glaser and Glaser, 1988; Nieman et al., 1993; Shinkai et al., 1995). Further examination of our findings revealed that the influences of PA and physical activity on antibody response were largely independent. Indeed, we reran the analyses dropping the PA adjectives that overlap with the exercise dimension (energetic, lively and full-of-pep) from the model and found that the relationship between PA and antibody response remained significant ($b = .11$ [$\pm.05$], $p < .05$). However, less physical activity appeared to be deleterious for the low PA group, with individuals who endorsed lower levels of PA and fewer hours spent exercising per week mounting lower antibody responses than their high PA counterparts. In contrast, individuals who endorsed low PA and more hours of exercise mounted similar antibody responses to individuals with high PA. This relationship remains after statistically controlling for levels of depression and trait negative affect, suggesting that it is not the consequence of underlying negative mood. Thus, it appears that physical activity can be protective for individuals who characterize themselves as low in positive affect. It is possible that both physical activity and positive affect activate the same physiological pathways, for example, the sympathetic nervous system, resulting in a similar influence on antibody production in response to vaccination.

We have previously reported that trait negative affect is associated with lower antibody response in this sample (Marsland et al., 2001). This raises the possibility that the association between trait positive affect and increased antibody responses reflects the absence of negative affect, or the opposite end of the same continuum, rather than the specific effects of positive mood characteristics. An initial examination of findings revealed the expected correlation between trait PA and NA, as measured in this study ($r = -.53$, $p < .0001$). It is likely that this resulted from the unit-weighting of items in the calculation of the PA and NA scale scores, which recaptures the natural covariation among items and suggests that these factors are not entirely independent. Despite this correlation, the association of trait PA with antibody response was largely independent of trait NA. Furthermore, there was no evidence that trait PA was beneficial only because it reduced the effects of trait NA (no significant interaction between PA and NA). Thus, the relationship between trait PA and improved antibody response was independent of trait NA.

The current findings of an independent relationship between PA and antibody response raise the possibility that our previous report that trait NA was associated with decreased antibody response was the consequence of lack of PA, rather than negative mood traits. We explored this possibility using the broader measure of trait NA employed in the prior publication and the measure of negative affective style used in the current analyses. A closer examination of the rela-

tionships between these different measures of trait negative affect and antibody responses revealed that higher scores on measures that assessed dispositional depression, stress and anxiety predicted lower antibody responses. In contrast, there was no association between trait anger and antibody levels. These findings are consistent with a literature demonstrating that trait anger is associated with a different pattern of physiological activity than the other negative emotions, including greater left frontal cortical activity (Harmon-Jones, 2003); a pattern that is posited to be associated with better physical health (Davidson, 1998). In all cases, relationships between negative mood traits and antibody responses disappeared once levels of PA were accounted for. This suggests that, in the presence of PA, there is no independent effect of trait NA on antibody response and that our past findings reflected the absence of PA, rather than the presence of distinct negative feelings. This interpretation is consistent with the findings of Cohen et al. (2003) that positive, but not negative emotional styles predicted the incidence of upper respiratory infections.

An issue in the literature examining the health benefits of positive affect is whether relationships are the consequence of a number of factors closely tied to PA and associated with improved health outcomes. These include the psychological characteristics: extraversion and optimism. Our findings demonstrated that although related, extraversion did not account for the relationship between PA and antibody response. In the case of optimism, PA remained the dominant predictor of antibody response after controlling for optimism, although it no longer achieved significance. Optimism was not an independent predictor of antibody response. These findings suggest that the association between trait PA and antibody response is largely independent of the related constructs of optimism and extraversion. In addition, we predicted antibody response from an aggregate measure including PA, optimism and extraversion to see if this represented a common underlying construct that was a better predictor than PA alone. It did not. In short, PA was clearly the driving force in accounting for antibody response.

Finally, it should be noted that the clinical significance of the observed differences in magnitude of antibody response for protection against hepatitis B infection is not clear. The study was conducted using young, healthy graduate students and a vaccination protocol designed to produce maximal immunity to hepatitis B in greater than 90% of individuals. As expected, the majority of subjects mounted an antibody titer that is considered to be protective against hepatitis B infection (>10 mIU/ml) by 1–2 months after the last vaccination. However, subjects who mounted a low antibody response after the second vaccination also had lower antibody levels after the booster vaccination than subjects who mounted a high response after the second dose ($X = 92$ versus 150 mIU/ml, respectively). Hence, the current findings suggest a relationship between trait positive affect and magnitude of antibody response as measured 1–2 months after the booster dose, which may be the consequence of rate of seroconversion. Antibody level is the main determinant of the duration of hepatitis B vaccine-induced immunity (Hollinger, 1989), with individuals who mount lower final antibody responses to this vaccine losing their protective status more quickly than individuals who mount higher responses (Horowitz et al., 1988). These data may help to explain interindividual variability in the maintenance of protective immunity over time.

Although it is likely that trait PA precedes the immune response to vaccination in this study, causation cannot be attributed solely on the basis of cross-sectional data. Indeed, it remains possible that trait PA is a consequence of the immune response to vaccination or increased immunocompetence. A growing literature supports immune-to-brain communication, with activation of peripheral immune cells signaling the brain and resulting in the so called "sickness syndrome," which includes depression of mood (Maier and Watkins, 1998). Thus, pathways exist between the immune system and brain regions involved in the regulation of affect, raising the possibility that improved immunocompletence results in improved PA. Alternatively, trait PA and ability to mount an antibody response may be related to a third factor, such as genetic predisposition. Further limitations of the current study include its retrospective design, with trait affect being measured on one occasion 5 months after the initial vaccination in the series used to predict antibody response. While it is likely that trait positive affect antecedes the immune response to vaccination in this study, we do not know that this is the case. A second limitation is the use of a single measurement of affect as a measure of dispositional emotional style. Future studies would benefit from the use of repeated measures across multiple occasions of testing to derive a more reliable measure of enduring dispositional style. In sum, before it can be concluded that individuals higher in dispositional positive affect are able to mount better in vivo immune responses to vaccination, prospective studies are required, employing more reliable measures of dispositional affect to predict clinically relevant antibody status.

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