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Psychological influences on the perception of immune function

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ABSTRACT

Background. Perception of deficiencies in immunity are common in a number of patient complaints. However, little is known about the way in which individuals form perceptions about the competence of their immune system. In two studies we examined the relationship between subjects' perceptions of their immune functioning, physical symptoms, mood and measures of immunity.

Methods. In Study 1, 20 healthy volunteers completed global ratings of their immune system functioning, as well as mood and symptom reports, twice a week for 5 weeks. At the same time, blood samples were taken to assess serum IgA, IgG, and IgM antibodies. In Study 2, another sample of 58 subjects completed the same measures weekly for 5 weeks and their blood was tested for concentrations of CD3, CD4, CD8, and CD16 lymphocytes.

Results. We found perceptions of immune functioning to be unrelated to the concentrations of serum antibodies or blood lymphocytes. Immune perceptions were strongly related to mood and in particular, feelings of fatigue and vigour. The experience of recent physical symptoms, while not as strong as mood variables, was also important in perceptions of immune functioning.

Conclusions. Mood seems to be an important determinant in the perception of immune function, and complaints about immune dysfunction in clinical situation should be investigated with this possibility in mind.

INTRODUCTION

Many patients visit doctors with symptoms and conditions that are attributed by the patient to deficiencies in their immune system. Over the past 10 years the immune system has gathered increased prominence in public discourse about health and is generally seen as being weakened by modern stresses, food and pollutants (Wessely, 1997). The relative strength of the immune system is popularly seen as providing the key to avoiding many illnesses including cancer. Numerous alternative therapies and medicines are marked to the public as bolstering or boosting the immune system. Such products usually claim to provide nutrients essential to immune system potency and, therefore, health. Little is known, however, about why individuals determine that their immune system is at a stage where it needs such an upgrade.

Disorders such as chronic fatigue syndrome (CFS), multiple chemical sensitivity, candida infection, and specific food allergies are often seen by patients as being the result of an immune system that has become depleted, over-challenged, or unresponsive (Ax *et al*. 1997). This is clear in the way CFS is also labelled 'Chronic Fatigue and Immune Dysfunction Syndrome' by the major CFS patient organization in the United States. Although studies have failed to find consistent immune correlates of these illnesses (Simon *et al*. 1993; Hotopf & Wessley, 1994; Wilson *et al*. 1994) and many reported

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food allergies (Young *et al.* 1987), a dysfunctional immune system is still perceived by patients and the general public to play a critical role (Maclean & Wessley, 1994).

Information on how individuals make judgements about the functioning of their immune system would be useful in order to understand the factors that influence patient complaints of immune deficiency. As with many internal physiological states that we cannot assess directly, it is likely that individuals use heuristic models based on other physical and psychological states that are experienced more immediately (Pennebaker, 1982). For instance, previous work has shown hypertensive patients to base (erroneously) their perception of blood pressure on such signs as ringing in the ears, headaches and feeling stressed (Meyer *et al.* 1985). Similarly, insulin-dependent diabetic patients usually have clear beliefs about which symptoms indicate hypoglycaemia or hyperglycaemia, although studies have shown these personal symptom indicators are often not accurate and can lead to errors in treatment (Gonder-Frederick & Cox, 1991).

Such research on the ability of individuals to judge internal physiological states such as blood pressure has shown that estimates are often only poorly or moderately correlated with actual physiological activity. Moreover, judgements can be strongly influenced by symptoms, mood, situational factors and dominant cognitive schemas (Baumann & Leventhal, 1985; Pennebaker & Watson, 1988; Salovey *et al.* 1989; Watson & Pennebaker, 1989).

In the two studies reported here we investigated the relationship between subjects' perceptions of the current state of their immune system and its relationship to actual immune activity, as well as current mood and recent physical symptoms. In the first study, we examined these relationships twice a week for 5 weeks using the three major classes of serum antibodies; IgG, IgM and IgA. IgG is the predominant class, while IgM is produced early in primary response to foreign antigen and serum IgA correlates with mucosal IgA concentrations secreted to protect the internal surfaces of the body. Serum immunoglobulin levels in all three classes have been reported as being influenced by psychological states such as stress (Vassend & Halvorsen, 1987; Orth Gomer & Eneroth, 1990) and relaxation (Green *et al.* 1988). In the second study, using a similar design we assessed the relationship of immune perceptions, symptoms and moods to the concentrations of blood lymphocyte subpopulations.

METHOD

Study 1

Participants and procedure

Twenty healthy subjects (8 men, 12 women) were recruited through an advertisement on the local medical school computer network. All subjects were staff working at the school over the summer vacation. Ages ranged from 22–48 (mean = 31·1). With ethical committee approval and informed consent, subjects completed questionnaires and had blood samples taken twice a week for 5 weeks. Blood samples were taken at the same time of day on each occasion. All subjects completed the study and were paid NZ$50 for their participation.

Measurement

All subjects completed the following measures at the time of each blood draw.

Immune system perception

Subjects were asked to respond on a 10 cm visual analogue scale labelled from 'poor' to 'excellent' to the following instruction; 'Please mark on the line what you think to be the state of your immune system today'.

Mood

The Profile of Mood States (POMS; McNair *et al.* 1971) was used to assess mood. Participants were asked to describe their mood 'right now' using the 65 descriptors on 5-point Likert scales ranging from 'not at all' to 'very much'. Items are summed to form six mood scales; tension, depression, anger, vigour, fatigue, and confusion.

Physical symptoms

A modified version of the PILL symptom checklist (Pennebaker, 1982) was used to assess symptoms. Subjects were asked to mark any symptoms from a list of 54 that they had experienced since the last blood draw.

Immune measures

On each occasion, a 5 ml blood sample was

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collected by venipuncture, allowed to clot at 4 °C for 3 h, then centrifuged, and serum collected and stored at −20 °C. All blood was drawn between 9 a.m. and 11 a.m. at the beginning and end of the working week (i.e. 3 or 4 days apart). Concentrations of the three major classes of antibodies (IgG IgM and IgA) were determined using standard nephelometric techniques conducted on all serum samples at the same time at the Auckland Hospital immunology diagnostic laboratory.

Study 2

Participants and procedure

The subjects in this study were 58 medical students who volunteered for a study to evaluate psychological influences on immunity. They were aged from 19 to 33 years (mean = 21·5). There were 33 females and 25 males in the sample, comprising 42 Caucasian, 7 Maori, 7 Asian and 2 Polynesian. Subjects completed questionnaires and had blood samples taken once a week for 5 weeks at the same time of day. All subjects completed the study and were paid NZ$50 for their participation.

Measures

Pencil and paper measures

Subjects completed the immune perception item, POMS questionnaire, and the modified PILL symptom checklist as described in Study 1. Again, all psychological measures were completed at the time of each blood draw.

Immune measures

Blood (10 ml) was drawn into heparinized tubes. Standard haematological markers relating to white blood cells, red blood cells and platelets, together with white blood cell differential counts were determined using a Bayer Technicon H1 Hematology Analyzer. Proportions of mononuclear cells in the blood bearing the markers CD3 (T lymphocytes), CD4 (T helper lymphocytes), CD8 (T cytotoxic/suppressor lymphocytes) and CD16/56 (natural killer (NK) cells) were determined using flow cytometry in a Becton Dickinson FACScan Cell Analyzer with Becton Dickinson Simultest fluorescent antibody reagents. Absolute numbers of CD3, CD4, CD8 and NK cells were calculated using these proportions and lymphocytes concentrations from the haematological screen.

RESULTS

Study 1

Correlations between immune perceptions and immune measures, symptom levels, and mood states over the 10 assessments were calculated for each participant, and the average correlations across participants are presented in Table 1. Participants' immune perceptions were not significantly associated with changes in their concentrations of IgA, IgG, or IgM. In contrast, their perceptions varied significantly with changes in their symptom levels and mood states, with the exception of tension. Immune perceptions were positively associated with vigour and negatively associated with symptoms, fatigue, confusion, depression and anger.

Comparisons of the average within-subject standard deviations (S.D.s) in relation to the observed ranges of values for the measures reveal differences in variability over time among the measures (see Table 1). The immune variables are relatively stable over time, with the average S.D.s being 4–6 % of the ranges in values observed across the sample. In contrast, the average S.D.s for the immune perceptions and mood measures are proportionally greater – being between 9 to 18 % of their respective ranges. Symptoms appear to be relatively more stable over time, with the average within-subject S.D. being ap-

Table 1. *Mean correlations and measure variability between immune perceptions and serum immunoglobulin levels, symptoms, and mood over the 5 week trial*

Measure	Mean correlation	S.D.	Mean within-subjects S.D.	Range
IgA	−0·02	0·30	0·15	3·72
IgG	0·09	0·26	0·78	13·43
IgM	0·08	0·37	0·12	2·94
Symptoms	−0·24**	0·36	2·47	36·00
Vigour	0·64**	0·30	5·48	30·00
Fatigue	−0·57**	0·26	4·51	26·00
Confusion	−0·48**	0·25	2·49	21·00
Depression	−0·30**	0·31	3·15	35·00
Anger	−0·24*	0·39	3·81	21·00
Tension	−0·11	0·36	3·57	27·00
Immune perceptions			15·28	98·00

$N = 20$; * $P < 0{\cdot}05$; ** $P < 0{\cdot}01$; S.D. is the standard deviation in the distribution of correlation coefficients. Mean within-subjects S.D. is calculated across the 10 assessments for the sample of 20 participants. Range refers to the total range of scores in the 200 observations.

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Table 2. *Summary of a hierarchical regression analysis for variables predicting immune perceptions*

Variables	*B*	S.E. *B*	*β*	R^2 change	*F*
Step 1				0·56	11·96**
Subjects†					
Step 2				0·01	0·44
Time‡					
Step 3				0·01	1·32
IgA	−10·82	11·67	−0·41		
IgG	0·90	0·57	0·09		
IgM	9·38	10·91	0·27		
Step 4				0·06	26·76**
Symptoms	−1·99	0·39	−0·45**		
Step 5				0·16	21·20**
Anger	−0·41	0·26	−0·08		
Confusion	−0·62	0·54	−0·09		
Depression	0·01	0·31	0·00		
Fatigue	−0·20	0·29	−0·05		
Tension	0·36	0·31	0·08		
Vigour	1·60	0·24	0·46**		
Total R^2				0·80	

Observations $N = 198$; ** $P = 0·001$.

† The subjects block includes 19 variables accounting for between-subjects variance.

‡ The time block includes nine variables accounting for variance in immune perceptions over the 10 assessments.

Table 3. *Correlations of immune status perceptions with blood lymphocyte subpopulations, symptoms and mood at weeks* 1 *and* 5

Variable	Week 1 ($N = 58$)	Week 3 ($N = 57$)	Week 5 ($N = 54$)
CD3	−0·06	0·02	0·11
CD4	−0·12	0·03	0·01
CD8	0·02	0·13	0·07
CD16	0·01	0·10	0·10
Symptoms	−0·12	−0·52**	−0·61**
Anger	0·14	−0·24	−0·11
Confusion	−0·27*	−0·33*	0·20
Depression	−0·08	−0·36**	0·04
Fatigue	−0·34**	−0·55**	0·32*
Tension	−0·20	−0·35**	−0·12
Vigour	0·38**	0·44**	0·52**

* $P < 0·05$; ** $P < 0·01$.

proximately 7% of the total range of symptom scores. Participants' ratings of their immune status and mood levels are more variable over time than their level of IgA, IgG, and IgM.

A hierarchical regression analysis assessed the extent to which immune variables, symptoms, and mood states uniquely predicted immune perceptions (see Table 2). Sets of variables assessing between-subjects effects and time effects were entered in Steps 1 and 2, respectively. The immune measures were then entered in order: (*a*) to provide the strongest test of their possible association with immune perceptions; and (*b*) to control for these potential effects in assessing the contributions of symptoms and mood to immune perceptions. Symptoms and mood were then entered in steps 4 and 5, respectively. A set of variables assessing between-subjects effects was entered in Step 1, and the results indicated that individual subject differences in immune perceptions accounted for 56% of the total variance. Immune perceptions did not change significantly over the 10 assessments (as determined by a set of variables for time entered in Step 2). Although controlling for within-subject and time effects required the use of 28 independent variables in total in this analysis of 198 observations, power remained sufficiently high (0·85) to detect a change in R^2 of 0·03 using the significance level of $P < 0·05$.

Measures of IgA, IgG, and IgM (entered in Step 3) did not predict immune perceptions, whereas symptom levels (entered in Step 4) were significantly associated with lower immune perceptions and accounted for 6% of the total variance. The six mood measures were entered in the final step, and together they accounted for 16% of the total variance. Of these mood measures, only vigour uniquely predicted immune perceptions. Symptom levels remained a significant predictor in this final step of the analysis ($b = -1·24$, beta $= -0·28$, $t(159) = -3·83$, $P < 0·001$), indicating that symptoms and vigour independently predict immune perceptions. Analysis of the residuals supported the adequacy of the regression model by indicating the absence of curvilinearity, no outliers, and the absence of heteroscedasticity (Durbin–Watson statistic = 2·14).

Study 2

Of the 290 potential observations (58 participants with 5 assessments each), 8 were lost due to participants failing to attend sessions, 4 were lost due to failure to complete the symptoms and mood measures, and 3 were lost due to failure to

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Table 4. *Summary of a hierarchical regression analysis of variables predicting immune perceptions over a 5 week period*

Variables	*B*	S.E. *B*	*β*	R^2 change	*F*
Step 1				0·52	4·14**
Subjects†					
Step 2				0·05	0·19**
Time‡					
Step 3				0·00	0·00
CD3	−0·96	0·63	−0·20		
CD4	0·00	1·25	0·00		
CD8	−0·03	1·19	−0·01		
CD16	0·27	1·25	0·05		
Step 4				0·05	28·11**
Symptoms	−0·19	0·04	−0·43**		
Step 5				0·08	11·15**
Anger	−0·03	0·03	−0·08		
Confusion	−0·02	0·04	−0·04		
Depression	0·01	0·02	0·06		
Fatigue	−0·09	0·03	−0·30**		
Tension	0·03	0·03	0·08		
Vigour	0·06	0·03	0·18*		
Total R^2				0·71	

Observations $N = 275$; ** $P < 0·001$; * $P < 0·05$.

† The subjects block includes 57 variables accounting for between-subjects variance.

‡ The time block includes four variables accounting for variance in immune perceptions over the five assessments.

obtain immune assays. The final analyses were based on the remaining 95% of the observations ($N = 275$).

Because each participant was assessed only five times, there is insufficient data to calculate reliable within-subject correlations between immune perceptions and the variables associated with immune function, symptoms, and mood states. Instead, we computed between-subjects correlations at assessments 1, 3, and 5 to explore the nature and consistency in these correlations over the course of the trial (see Table 3). These data show that immune status perceptions were not associated with the circulating lymphocyte concentrations at any of the three time-points. Immune perceptions were not associated with symptom levels at the initial assessment, but strong correlations emerged by the third assessment. Fatigue and vigour ratings were significantly related to immune perceptions at all three time-points.

A hierarchical regression analysis of immune perceptions entered variable sets in the same order as used in Study 1 (see Table 4). The analysis first assessed the amount of variance in immune perceptions attributable to individual differences among participants (Step 1), and to general variations in immune perceptions over the course of the trial (Step 2). The set of variables assessing between-subjects effects accounted for 52% of the total variance, and the set of time variables significantly accounted for 5% of the total variance due to a general decrease in immune perceptions from Week 1 to Week 3. After entering the 61 variables associated with subjects and time effects, in this analysis with 275 observations, sufficient power remained to detect a change in R^2 of 0·03 at a significance level of $P = 0·05$ (power = 0·85).

The blood immune function variables, entered in Step 3, did not account for any of the variance in immune perceptions. Instead, symptoms (Step 4) and mood states (Step 5) significantly predicted immune perceptions. Of the mood states, only fatigue independently predicted immune perceptions. Consistent with Study 1, symptoms remained significant in Step 5 ($b = -0·15$, beta $= -0·33$, $t(202) = -4·03$, $P < 0·0001$), indicating that symptoms and mood independently predict immune perceptions. Analysis of the residuals (to evaluate the adequacy of the regression model) did not reveal any indications of problems due to curvilinearity, outliers, or heteroscedasticity (Durbin–Watson statistic = 2·23).

DISCUSSION

The results of both studies show remarkable consistency in the way individuals perceive the functioning of their immune system. In both studies, immune perceptions were not associated with actual measures of immune activity either in terms of serum antibody or blood lymphocyte concentrations. Although individuals' perceptions of their immune system function were markedly variable over time, the actual levels of immune activity we measured generally remained relatively stable. This is consistent with the finding in both studies that immune perceptions were most closely associated with mood. In particular, subjects' feelings of vigour and fatigue appear to be the main factors that individuals use to determine the state of their immune system.

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The presence of symptoms also seems to have an important independent effect on this judgement with individuals using recent symptoms as an indicator of poor immune functioning. Overall, these results suggest that an individual's perception that their immune system is functioning poorly is not likely to be associated with immune activity, but more likely in the presence of low feelings of vigour and high feelings of fatigue and a large number of physical symptoms. The fact that mood is the primary heuristic used by individuals when making inferences about how well their immune system is functioning may stem from the popular belief and observation that when we are tired and run down, we are more susceptible to infections and illness.

The strong influence of mood on perceived immune system effectiveness may have implications for unravelling complaints of immune deficiency in disorders such as CFS. We have found previously that the majority of CFS patients attribute their illness to a dysfunction of their immune system (Moss-Morris *et al*. 1996). Previous research has noted high rates of depression in CFS patients (Lane *et al*. 1991) and psychological morbidity has been associated with a poorer outcome (Wilson *et al*. 1994). Our findings highlight the possibility that some individuals may misattribute mood states, particularly the feelings of low energy associated with depression, as indicating an ongoing immune dysfunction. Previous studies on the way in which individuals use symptoms to infer internal physiological states suggest that once such beliefs are formed, they may be difficult to alter (Meyer *et al*. 1985). For CFS patients, such illness beliefs have been shown to be associated with chronicity and the maintenance of the disorder (Moss-Morris, 1997).

The present study found no relationship between immune perceptions and two components of the immune system. However, it is conceivable that other aspects of the immune system may be more closely related to perceived immune functions. Further evidence supporting these findings using other immune markers would be warranted before drawing firm conclusions regarding the independence of immune perceptions from immune activity. However, it is important to keep in mind that it is theoretically never possible to prove a null hypothesis. Yet of more critical importance to the primary goal of this study, controlling for these immune variables did not minimize the strong association of symptoms and mood with immune perceptions. It is also important to bear in mind that these studies were conducted with groups of healthy adults and it is possible that individuals with chronic or serious acute illnesses may perceive the function of their immune system in a qualitatively different way. Bearing these caveats in mind, the results of the present study suggest that perception of immune function is strongly influenced by mood and that complaints about immune dysfunction in clinical situations should be investigated with this possibility in mind.

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