This was noteworthy because of the immunologic mechanisms involved in the control of the EBV. After the initial active EBV infection, the virus genome is repressed in a latent state within host B-lymphocytes. It is thought that cellular latency is important in the regulation of latent infections associated with EBV and other herpes viruses (15). Research has also suggested that the higher antibody levels found in the higher cellular transformation levels (11). The implications of these data are discussed in reference to the cellular immune response.

**METHOD**

**Subjects**

Newly admitted nonpsychotic psychiatric inpatients at the Ohio State University Hospital were used as subjects in the research. Mentally retarded patients, those with any physical problems that might have had a significant immunologic component, and those with any evidence of recent alcohol or drug abuse were excluded from the study. The final sample consisted of 21 women and 12 men, with an age range of 18-52 and a mean age of 34.0. Subjects completed a brief interview and the questionnaires, and allowed additional blood to be drawn at the time of the routine admission blood draw.

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NK Activity

NK activity was assayed on day 1 as the difference in death cell numbers.

NK assay was performed on monocytes isolated from peripheral blood. Monocytes were isolated by density gradient centrifugation on Ficoll-Hypaque and stained with trypan blue. The monocytes were then assayed for cytotoxic activity in a chromium release assay.

RESULTS

There were significant differences in NK activity between the high and low loneliness groups. The high loneliness group had significantly higher NK activity than the low loneliness group, F (1, 29) = 4.22, p < 0.05. The mean level of the high loneliness group was 30.77%, while the low loneliness group had a mean of 16.56%.

Self-Report Measures

Self-report measures included the Minnesota Multiphasic Personality Inventory (MMPI), the Interview Life Events Scale (PERI), and the Weighted POMS. The MMPI is a self-report measure of psychological distress that includes 10 subscales. The PERI is a brief subjective measure of the adequacy of interpersonal relationships. The Weighted POMS is a self-report measure of psychological distress that includes 6 subscales.

Table 1: Mean MMPI T-Scores

<table>
<thead>
<tr>
<th>Scale</th>
<th>Loneliness Low</th>
<th>Loneliness High</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Hypochondriasis)</td>
<td>64.41</td>
<td>63.00</td>
</tr>
<tr>
<td>2 (Depression)</td>
<td>83.88</td>
<td>74.69</td>
</tr>
<tr>
<td>3 (Hysteria)</td>
<td>69.82</td>
<td>69.13</td>
</tr>
<tr>
<td>4 (Psychopathic Deviate)</td>
<td>82.65</td>
<td>74.94</td>
</tr>
<tr>
<td>5 (Masculinity-Femininity)</td>
<td>53.00</td>
<td>52.06</td>
</tr>
<tr>
<td>6 (Paranoia)</td>
<td>76.94</td>
<td>69.75</td>
</tr>
<tr>
<td>7 (Psychasthenia)</td>
<td>80.18</td>
<td>69.38</td>
</tr>
<tr>
<td>8 (Schizophrenia)</td>
<td>84.06</td>
<td>71.50</td>
</tr>
<tr>
<td>9 (Hypomania)</td>
<td>61.94</td>
<td>63.50</td>
</tr>
<tr>
<td>10 (Social Introversion)</td>
<td>68.29</td>
<td>59.75</td>
</tr>
</tbody>
</table>

The data was analyzed using an analysis of variance design, with two between subjects variables, loneliness and stressful life events. The initial analysis also included sex as a variable in subsequent analyses. The majority of results were significant, with respect to age, loneliness, stressful life events, urinary cortisol levels, immunologic competence, or distress on any of the diagnostic categories.

Urinary Cortisol

Urinary cortisol levels were measured by a competitive binding assay. Cortisol levels were normalized against random urine samples instead of 24-hr collections. The data were analyzed using an analysis of variance design, with two between subjects variables, loneliness and stressful life events.

Table 1: Mean Cortisol Levels

<table>
<thead>
<tr>
<th>Subject Group</th>
<th>Cortisol Level (µg/g creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Loneliness</td>
<td>30.77</td>
</tr>
<tr>
<td>Low Loneliness</td>
<td>16.56</td>
</tr>
</tbody>
</table>

There were significant differences in urinary cortisol levels between the high and low loneliness groups. The high loneliness group had significantly higher levels of urinary cortisol than low loneliness subjects, F (1, 29) = 4.22, p < 0.05. The mean level of the high loneliness group was 16.56 µg/g creatinine, in contrast to the low loneliness group's mean of 16.56 µg/g creatinine.

NK Activity

NK activity was assayed on day 1 as the difference in death cell numbers. NK activity was determined by a chromium release cytotoxicity method. Triplicate (0.1 ml) aliquots of lymphocyte and labeled target cell suspensions were placed in wells of 96-well plates. Effector to target cell ratios of 40:1, 20:1, and 10:1 were obtained by triplicate wells with target cells and media only, and target cells and detergent (1% sodium dodecyl sulfate) were prepared for baseline controls. One-tenth of a milliliter of PWM was added to 1 x 10^6 lymphocytes (in 0.1 ml plasma), and added to human plasma. One milliliter of Vitrogon (New England Nuclear) was added and the amount of radioactive binding was counted in a Beckman 9000 gamma counter. Results are reported as percent lysis using the formula:

\[ \text{Percent Lysis} = \frac{\text{maximal CPM} - \text{spontaneous release CPM}}{\text{maximal CPM}} \times 100 \]

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Blastogenesis

The high loneliness group had a poorer response to PHA stimulation, with significant differences at concentrations of 0.25 µg/ml (F(1, 29) = 4.40, p < 0.04), and 0.50 µg/ml (F(1, 29) = 5.03, p < 0.03), and a near significant difference at a concentration of 1.0 µg/ml (F(1, 29) = 2.27, p < 0.14). The difference was not significant for the 2.0 µg/ml concentration (F(1, 29) = 0.31). These data are shown in Figure 2.

There were no consistent significant effects in the subjects' response to PWM stimulation as a function of the independent variables. Although the interaction between stressful life events was significant for the 5.0 µg/ml concentration (F(1, 29) = 6.21, p < 0.02), this interaction was not significant for either the 2.5 pg/ml concentration (F(1, 29) = 0.70) or the 10.0 Ag/ml concentration (F(1, 29) = 1.18). The logarithmic means for the 5.0 µg/ml concentration were 0.75 for the low stress, low lonely group; 1.07 for the high stress, low lonely group; 1.14 for the high stress, high lonely group; and 0.82 for the high stress, high lonely group.

In order to evaluate the relative contributions of loneliness and distress to immunocompetency, multiple regression analyses were performed. For all three NK effector to target cell ratios and for all but two of the PHA dilutions, loneliness emerged as the best predictor of immunocompetence. Correlations among loneliness, MMPI scales, and the immunologic variables were low, however.

DISCUSSION

In this study we found a significant association between two components of the cellular immune response and loneliness, with high loneliness subjects having significantly lower NK activity as well as a poorer T-lymphocyte response to PHA, when compared to the low loneliness group. High loneliness subjects also had significantly higher urinary cortisol levels. The association between NK activity and loneliness followed the same pattern as was found previously in medical student subjects (7). The PHA data are consistent with other research on the responsiveness of T-lymphocytes to various stressors, as discussed earlier (3, 4), and provide further support for the interplay between psychosocial variables and the immune response.

The absence of any consistent significant association between the independent variables and the response of mixed T- and B-lymphocytes to PWM is not surprising. Although some researchers see cellular immunity as more responsive to various acute physical stressors than humoral immunity (20), the effects of stress on the humoral response have been documented in humans and animals (21). It is possible that the differences observed between the high and low loneliness groups in their T-lymphocyte response to PHA were not vigorous enough to be detected in the mixed cell population used.

There are several possible explanations for the absence of consistent effects for stressful life events in both the immunologic and self-report data. The extremely high levels of distress that frequently precipitate psychiatric admissions maybe of sufficient intensity to overpower more subtle distress-related indices. Also, the psychiatric population is far more heterogeneous with respect to socioeconomic and demographic variables than the medical student population in which significant effects for stressful life events were previously found. This variability may have overshadowed the effects of stressful life changes (22).

Although the effects of interpersonal support on health-related outcomes have received attention in the related social support literature, the association between loneliness and health has not been comparably addressed (23). The social support "buffering" hypothesis suggests that the effects of support on stress are interactive, with support presumably having little effect on health-related outcomes when stress is low; the protective effects of support are thought to be maximized during periods of high stress (24). Extrapolating from the buffering hypothesis to our loneliness data, it is possible that the relatively high levels of distress which both the inpatients and the previous medical student sample (7) were experiencing may have influenced the outcomes. It would be interesting to see if loneliness is significantly related to urinary cortisol levels and cell-mediated immunity in less distressed populations, or, alternatively, if persistent corticosteroid elevations and decreased cellular immunocompetency can be found.
This study examined the associations among loneliness, stressful life events, and urinary cortisol obtained from 33 psychiatric inpatients on the day after admission, at which time they completed the UCLA Loneliness Scale, the Psychiatric-Mental Health Inventory, the MMPI, and the Social Position Scale. The data were analyzed using correlation and regression analyses. The results showed that the high loneliness group had significantly higher urinary cortisol levels compared to the low loneliness group. The high loneliness group also had significantly lower levels of natural killer cell activity and a significantly poorer T-lymphocyte response to phytohemagglutinin. The high loneliness subjects described themselves as significantly more distressed than the low loneliness group. Furthermore, there were no consistent significant effects on either the immunologic measures or the MMPI associated with the PERT.

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CELLULAR IMMUNOCOMPETENCY AND LONELINESS


