Stress and the Memory T-Cell Response to the Epstein-Barr Virus in Healthy Medical Students


This study investigated the memory T-cell proliferative response to several early and late Epstein-Barr virus (EBV) polypeptides. Blood samples were collected twice, 1 month before a 3-day block of examinations and again on the last day of the exam series. Ss were 25 healthy, EBV seropositive medical students. The proliferative response to 5 of the 6 EBV polypeptides significantly decreased during examinations. In addition, Ss high (above the median) in seeking support, as measured by the COPE, had lower proliferative responses to 3 EBV polypeptides (p17, p52/50, and p85), as well as higher levels of antibody to EBV virus capsid antigen. The data provide further evidence that psychological stress can modulate the cellular immune response to latent EBV.

Key words: stress, support seeking, Epstein-Barr virus, blastogenesis

The interactions among the central nervous system (CNS), the endocrine system, and the immune system are complex. The CNS communicates with the immune system in a number of ways. For example, the immune system receives signals indirectly from the CNS by way of neuroptides and direct wiring and from the endocrine system through, for example, glucocorticoids (Felten et al., 1988; Goetzl & Spector, 1989; Munck & Guyre, 1991). Feedback from the immune system to the CNS has also been demonstrated. For example, interleukin-1 (IL-1), released after an infection, can interact with the hypothalamus, modulating the hypothalamic/pituitary/adrenal (HPA) axis (Dunn, 1988). A variety of psychological stressors can modulate the HPA axis, regulating different aspects of the immune response (Ader, Felten, & Cohen, 1991).

One of the areas on which we have focused in our laboratory has been the impact of relatively commonplace stressful events on the modulation of the immune response (e.g., Kiecolt-Glaser et al., 1986). Evidence for the down regulation of cellular immunity was demonstrated by decreases in natural killer (NK) cell activity, decreases in the proliferative response of peripheral blood leukocytes (PBLs) to mitogens, decrements in gamma-interferon (IFN-γ) synthesis by mitogen-stimulated PBLs, and an inhibition of the expression of the IL-2 receptor and its mRNA in PBLs obtained from medical students during examinations relative to lower stress baseline blood samples drawn 1 month earlier (Glaser et al., 1987, 1990; Kiecolt-Glaser & Glaser, 1988, 1991). Similarly, Dobbin, Harth, McCain, Martin, and Cousin (1991) reported that medical students taking examinations had significant decreases in lymphocyte responsiveness to both Concanavalin A (Con A) and pokeweed mitogen. Furthermore, production of IFN-γ was suppressed and IL-1β was significantly elevated after exam stress.

Typically, primary infection with the Epstein-Barr virus (EBV), a human herpesvirus, occurs during adolescence. About 40% of those with primary EBV infections present with infectious mononucleosis, with the remainder showing no clinical signs of infection (Henle & Henle, 1982). After infection, EBV latentely infects B-lymphocytes, resulting in a situation in which cells latently infected with EBV persist for the life of the individual. If the virus is reactivated in these latently infected cells, viral antigens will be expressed. Some of these antigens are the products of early virus transcription (synthesized independently of virus DNA synthesis), and some are the products of late transcription that depend on the synthesis of new viral DNA. In either case, the memory cellular and humoral responses are triggered, resulting in increased antibody levels to the early antigen (EA) and late antigen (virus capsid antigen, or VCA) complexes.

Cellular immune competence is a critical factor in controlling primary herpesvirus infections (including EBV) and maintaining virus latency (Glaser & Gotlieb-Stematsky, 1982). An increase in EBV-VCA Immunoglobulin G (IgG) antibody indicates exposure to the virus or reactivation of EBV from...
latent infection. Therefore, antibody titers to EBV can provide one measure of the cellular immune system's control over latent virus (Glaser & Gottlieb-Stematsky, 1982). For example, patients undergoing immunosuppressive therapies (e.g., chemotherapy) and those infected with human immunodeficiency virus 1 (HIV-1) have characteristic elevations in herpesvirus antibody titers. The increased herpesvirus antibody production in immunosuppressive conditions is thought to reflect the humoral immune system's response to an increased load of viral antigens resulting from virus reactivation.

In previous studies from our laboratory, we found that examination stress modulated the control of latent herpesvirus infections, particularly EBV. Higher antibody levels (IgG) to EBV were associated with a variety of psychological stressors, including academic stress (Glaser et al., 1987), divorce (Kiecolt-Glaser et al., 1988), and caregiving for a family member with Alzheimer's disease (Kiecolt-Glaser, Dura, Speicher, Trask, & Glaser, 1991). Furthermore, the reactivation of latent EBV in medical students at the time of examinations may be incomplete; we found evidence to suggest that only some EBV polypeptides (antigens) may be synthesized under times of higher stress. Antibody levels in the same plasma samples to three of four purified EBV polypeptides tested did not change over time; antibody levels to the fourth EBV polypeptide (an EBV EA polypeptide) did change. This suggested that partial reactivation of the latent EBV genome had occurred, resulting in the expression of a limited number of viral proteins (i.e., not all viral genes were expressed; Glaser et al., 1991). In addition to changes in antibody titers associated with stress, we found a decrease in the memory cytotoxic T-cell response to EBV growth-transformed B-lymphocytes during examinations relative to lower stress baseline periods (Glaser et al., 1987).

In addition to the evidence linking examination stress with decrements in cellular immunity, there is a growing literature relating individual differences in social support to modulation of the immune response (Irwin et al., 1990; Levy et al., 1990). For example, the perception of high-quality emotional support from a spouse or intimate other and higher social support from a physician was associated with higher NK cell activity in early-stage breast cancer patients (Levy et al., 1990). Furthermore, Baron, Cutrona, Hacklin, Russell, and Lubaroff (1990) found that spouses of cancer patients who reported higher social support had higher NK cell cytotoxicity and a stronger proliferative response to phytohemagglutinin (PHA) than did those who reported less support.

Animal models have also been useful in investigating the relationship between peer contact and immune function. For example, Coe, Rosenberg, and Levine (1988a, 1988b) demonstrated alterations in macrophage activity and abnormal T-cell proliferation using peer or maternal separation paradigms with nonhuman primates. In their studies, separated infants showed behavioral signs of distress (e.g., low rates of vocalization), increases in plasma cortisol, and increased activation of macrophages (Levine, Johnson, & Gonzales, 1985). Moreover, placement of the infant with peers or with another adult female after maternal separation moderated these distress-related changes (Coe et al., 1988b).

Besides peer contact and support from spouse or physician, marital disruption and feelings of loneliness have been associated with greater depression and poorer control of latent EBV (Kiecolt-Glaser et al., 1987, 1988). Poorer marital quality was associated with higher EBV-VCA antibody titers, as well as a poorer blasticogenic response to PHA and Con A (Kiecolt-Glaser et al., 1987). Others have shown that patients with syndromal depression show poorer control of latent EBV than do nondepressed subjects (DeLisi, Nurnberger, Goldin, Simmons-Ailing, & Gershon, 1986). Greater loneliness has also been associated with poorer immune function, including higher antibody titers to EBV (Glaser, Kiecolt-Glaser, Speicher, & Holliday, 1985; Kiecolt-Glaser et al., 1984).

Social contact and perceived support are conceptually different from support-seeking behavior. The seeking of social support is intimately linked to social resources, whereas perceived support is linked to cognitive interpretations. Specifically, social support seeking yields a set of predictions regarding the choices of both strong and weak supports a person should make in solving different types of problems (Granovetter, 1973; House, 1981; Lin, 1982). According to this theory, the strength of strong supports is their ability to satisfy expressive needs, whereas the strength of weak supports is their ability to satisfy instrumental needs. Therefore, an individual will selectively seek support within his or her personal network on the basis of the perceived needs created by the problem. It is possible that any problem for which individuals might seek support contains both an emotional and a practical component. This would be consistent with Folkman and Lazarus's (1980) finding that individuals use both emotion-focused and problem-focused coping strategies for all types of problems.

Within the social support literature, few studies have explicitly examined subjects' reports of support seeking (Coyne, Ellard, & Smith, 1990). Although the data are limited, there is some evidence that people who are most distressed are also most likely to seek support. Averill (1979), working within Lazarus's (1966) appraisal model, suggested that support seeking occurred in response to heightened perceptions of threat, especially when additional information regarding the stressor might be available within the social support network. In fact, people who are facing the greatest stressors may both seek and elicit more support (Coyne et al., 1990).

In this study, we examined the relationship between examination stress and the specific memory T-cell proliferative response of PBLs to purified EBV polypeptides. This study extends previous investigations involving academic stress and EBV latency. We hypothesized that the proliferative response to several EBV polypeptides (i.e., early and late proteins) would decrease during examinations and that these effects would be magnified by degree of seeking support.

Method

Subjects

Thirty 1st-year medical students volunteered for a research project on stress and the immune response. The 1st-year medical student curriculum is such that students have seven or eight 3-day examination blocks during the academic year. The 1st-year medical student class, as a group, cycles through these examination periods, and they are aware
of all examination dates at the beginning of the academic year. Blood samples were obtained 3 weeks before, and at the end of, a 3-day examination sequence. All blood samples were collected between 11:00 a.m. and 1:00 p.m. to control for diurnal variation.

Of the initial 30 subjects recruited, 25 were EBV seropositive as determined by the indirect immunofluorescence (IF) test, which measures antibody titers to EA/VCA. The 5 EBV seronegative subjects were excluded from further analyses because they would not have been latently infected with the virus. The average age of the 16 men and 9 women was 22.4 years. Each time blood was drawn, subjects were asked to indicate how many hours they had slept in the last 3 days, any change in their weight in the last week, and the number of alcoholic and caffeinated drinks they had consumed in the last 48 hr. They were also asked to list any medications they had taken in the last week, either prescription or nonprescription.

Support Seeking as a Moderator of Stress

The COPE (Carver, Scheier, & Weintraub, 1989) was used, at baseline, to assess the degree to which subjects sought others for emotional or instrumental social support. The COPE is a 52-item dispositional inventory yielding 13 theoretically and conceptually distinct scales. Overall, this inventory has excellent internal and test–retest reliability, as well as discriminant and convergent validity. Because we were interested in support-seeking behaviors, two scales—seeking social support for emotional reasons and seeking social support for instrumental reasons—were used; because they were significantly correlated ($r = .74, p < .001$), they were summed to yield a total seeking-support score. Individuals scoring high on seeking support could be described as seeking others for advice, assistance, or information or, alternatively, seeking others for moral support, sympathy, or understanding with the purpose of ventilating their feelings (Carver et al., 1989). A median split (i.e., 24) was used to divide subjects into two groups (high or low in support seeking).

Social Contacts and Loneliness

The Social Network Index (SNI; Cohen, 1991) was used to assess social contact at baseline. This assessment provided data on number of roles (e.g., spouse, parent, child, and student) and number of relationships across these roles (Cohen, 1991). Test–retest reliability over 6 months was .82 (Cohen, 1991). We obtained reports for each of eight social integration domains: (a) parents, (b) other relatives, (c) members of religious groups, (d) members of leisure groups, (e) co-workers (if the subject worked), (f) classmates, (g) friends, and (h) neighbors. For each domain, subjects reported the number of persons with whom they interacted at least once during a typical 2-week period, either in person or by telephone. Thus, we did not measure specific contact during either time point; rather, we measured potential social contacts over time. From this assessment, three primary scales were computed; these scales reflected total number of roles, total number of contacts, and total number of roles by contacts.

The Shaver, Furman, and Buhrnester (1984) State Loneliness Scale was used to assess loneliness. This scale combines eight items from the UCLA Loneliness Scale (Russell, 1980) and three items from the NYU Loneliness Scale (Rubinstein & Shaver, 1982); both of these scales have adequate reliability and validity (e.g., Russell, 1982). The resulting State Loneliness Scale had a coefficient alpha of .65 and correlated significantly with the UCLA Loneliness Scale.

Distress

Two self-report measures provided data on stress and anxiety. The Profile of Mood States (POMS; McNair, Lorr, & Dropelman, 1981) is one of the best self-report measures for identifying and assessing transient, fluctuating mood states. It is widely used, has excellent normative data, and is very strong psychometrically in terms of both reliability and validity (McNair et al., 1981). We were particularly interested in the Tension–Anxiety scale, the most responsive scale in our medical student population to the short-term increases in distress associated with examinations. The POMS was administered each time blood was drawn.

The Perceived Stress Scale (PSS; Cohen & Williamson, 1988) is a 14-item instrument that assesses global perceptions of stress and measures the degree to which individuals appraise situations in their life as unpredictable, uncontrolable, and overloading over the past week. Normative data are available from a national probability sample. The PSS was also administered each time blood was drawn.

Preparation of Purified EBV Polypeptides

The following purified EBV polypeptides were prepared: gp250, gp125, p160, p85, p52/50, and p17 (as previously described; Goldschmidt, Luka, & Pearson, 1987; Kishishita, Luka, Vroman, Poduslo, & Pearson, 1984; Luka, Chase, & Pearson, 1984; Luka, Miller, Jormwall, & Pearson, 1986; Pearson et al., 1983; Vroman, Luka, Rodriguez, & Pearson, 1985). Briefly, HR-1 tumor cells expressing the different EBV antigens were used as a source to prepare the polypeptides. An extraction buffer containing 0.5% NP-40 was used to prepare extracts (Luka et al., 1984). Cell-free supernatants were passed sequentially over affinity columns prepared with monoclonal antibodies (MAbs) to the respective polypeptides. The bound proteins were eluted from each column with 3 M MgCl$_2$ and 20 mM tris-HCl, pH 7.4, and dialyzed against 20 mM NH$_4$HCO$_3$, buffer overnight. The purity of each EBV-specific polypeptide was monitored by immunoblotting (as previously described; Goldschmidt et al., 1987; Pearson et al., 1983).

Measurement of the EBV Specific T-Cell Response

Mononuclear cells from 60 cm$^2$ of blood treated with heparin were separated with Hypaque-Ficoll density gradients, washed twice with Mg$^{2+}$ and Ca$^{2+}$ free phosphate buffered saline, counted with a Coulter counter, and then used as described. The polypeptides were prepared in complete RPMI 1640 medium. One hundred $\mu$l of cell suspension was placed in 90-well flat-bottom microtiter plates. The final concentration per well was 3 $\times$ 10$^5$ PBLs; triplicate wells were prepared. One hundred $\mu$l of each EBV-specific polypeptide (containing 25 $\mu$g/ml or 5 $\mu$g per well) were then added. We determined that a sufficient blastogenic response was induced by 5 $\mu$g per well of each polypeptide. Because it is extremely difficult to obtain large amounts of purified polypeptide, we decided to use only the 5-$\mu$g concentration for each assay for each polypeptide, which provided adequate numbers of subjects to perform the study. Triplicate wells were also set up as media controls. The cells were incubated at 37 °C in an atmosphere of 5% CO$_2$ for 112 hr and, then pulsed with $^3$H-TdR for the final 8 hr of incubation (1 $\mu$Ci per well, specific activity 6.7 Ci/mM). A Beckman LS-7000 scintillation counter was used to quantitate $^3$H-thymidine incorporation by liquid scintillation counting; the data are expressed as the stimulation index.

Measurement of Antibody to EBV

The indirect IF test was used to measure antibodies to EBV-VCA IgG to determine which subjects were latently infected with the virus and, therefore, expected to have memory cytotoxic T-lymphocytes (Glaser et al., 1987). Smears of HR-1 cells were used to assay antibody titers. Cells were fixed in acetone at room temperature for 10 min and
adsorbed with twofold dilutions of plasma prepared in phosphate buffered saline (pH 7.4) for 30 min at 37°C. The cells were washed with phosphate buffered saline, counterstained with Evans blue, mounted in Protex, and examined with a Zeiss UV microscope. Antibody titers were determined by the highest dilution of plasma still able to demonstrate a positive IF response. All slides were read blind coded. All antibody titer values are reported as the mean log-transformed dilution factor.

Results

Health Behaviors

Students reported significantly less sleep in the 3 days before the examination blood draw than they had experienced before the baseline period. They reported a mean and standard error of 22.32 ± 0.97 hr of sleep before baseline relative to 17.48 ± 0.74 hr before the examinations, F(1, 24) = 15.49, p < .01. Hours of sleep were significantly correlated with the blastogenic response to two of the polypeptides at baseline (r = -.47, p < .05, for gp250 and r = -.46, p < .05, for p160) but not during the examinations (r = -.25 for gp250 and r = -.09 for p160). Examination of baseline data showed that 1 subject reported only 4 hr of sleep, which was more than three standard deviations below the mean. When this outlier was removed from the calculations, the correlations fell sharply (r = -.33, ns, for gp250 and r = -.32, ns, for p160), suggesting that the outlying value was responsible for the significant correlations. Consistent with other medical student data from our laboratory, it appears that sleep is not reliably related to correlations. Consistent with other medical student data from our laboratory, it appears that sleep is not reliably related to correlations.

Table 1

<table>
<thead>
<tr>
<th>Scale</th>
<th>Baseline</th>
<th>Examination</th>
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<tbody>
<tr>
<td>Profile of Mood States</td>
<td>43.04 ± 1.58</td>
<td>57.17 ± 2.14</td>
</tr>
<tr>
<td>Tension-Anxiety</td>
<td>18.76 ± 1.34</td>
<td>27.88 ± 1.96</td>
</tr>
</tbody>
</table>

*p < .01.

Self-Reported Distress

A repeated measure analysis of variance with one within-subjects variable (change from baseline to examination) and one between-subjects variable (seeking support) was used to analyze the data. Consistent with our interpretation of the examination periods as higher stress periods, subjects reported significantly greater anxiety, F(1, 24) = 51.31, p < .001, and stress, F(1, 24) = 33.28, p < .001, during the examinations relative to baseline (Table 1). Furthermore, those subjects who were high in seeking support reported significantly more stress at baseline than did those who were low in seeking support, F(1, 23) = 4.70, p < .05, and the Seeking Support x Time interaction was not significant, F(1, 23) = 2.52.

Blastogenesis assays using PBLs obtained at baseline and during the examination block were performed to explore the specific T-cell response (memory) to several EBV polypeptides. The polypeptides that were selected included two late glycoproteins expressed on the surface of EBV-infected cells (gp250 and gp125), one late protein (p160), and three early proteins (p17, p52/50, and p85). The selection of these polypeptides was based on the specific MAbs available at the time; these MAbs were subsequently used to obtain the purified polypeptides. The results are expressed as the stimulation index and the standard error for each peptide. Significant decreases in T-lymphocyte proliferation from baseline to the examination period were found in response to gp250, F(1, 23) = 11.04, p < .001; p160, F(1, 23) = 5.97, p < .02; p17, F(1, 23) = 4.50, p < .05; p52/50, F(1, 23) = 9.99, p < .004; and p85, F(1, 23) = 6.59, p < .02 (Table 2). In addition, there was a marginally significant decrease in the proliferative response to gp125, F(1, 23) = 3.09, p < .09.

The EBV-specific T-lymphocyte proliferative response was significantly lower for the EBV proteins in subjects high in seeking support than in those scoring below the median on seeking support.1 That is, the proliferative responses to p17, F(1, 23) = 5.68, p < .05; p52/50, F(1, 23) = 5.34, p < .03; and p85, F(1, 23) = 6.67, p < .02, were significantly lower in the former group (Figure 1). No significant differences were found for p160, F(1, 23) = 1.16; gp125, F(1, 23) = 2.18; or gp250, F(1, 23) = 1.07. Also, no significant interactions were found between seeking support and change from baseline to examinations for any of the EBV polypeptides (all Fs > 1).

Antibody titers to EBV-VCA were significantly higher in the high support seekers than in their low-seeking counterparts (Figure 2), F(1, 23) = 6.45, p < .02. Analyses of antibody titers

1 No significant effect of gender was found with respect to levels of seeking support, F(1, 23) = 2.97, ns.

Significant weight changes were reported throughout the study. Alcohol use was minimal (M = -0.32 drinks), with only 2 subjects reporting consumption (6 and 2 drinks, respectively) over the previous 48 hr. Alcohol and caffeine use were not significantly correlated with any immune measure at baseline (rs = .14 to .21 and .05 to .09, respectively) or during the examination period (rs = .00 to .13 and .01 to .07, respectively). Furthermore, self-reported medication use (both prescription and nonprescription) was minimal, limited to birth control pills, vitamins, and analgesics.
that psychological stress can adversely affect the ability of stressors (Glaser et al., 1985, 1987, 1991). We have also found evidence that latent EBV can be modulated by psychological contacts.

although there was no difference in number of friends or stress and loneliness than did their low-seeking counterparts, EBV-VCA. Subjects higher in seeking support reported more subjects higher in seeking support had lowered proliferative responses to all of the early EBV polypeptides (i.e., p17, p45, p62, p85), as well as higher levels of antibody to p52/50, and p85), and p85*, gp125, gp250**, p50**, and p17*. Subjects who scored high on seeking support reported greater loneliness than those their low-seeking counterparts. The groups did not differ in regard to total number of contacts, roles, or contacts by roles (Fs < 1). Levels of perceived stress at baseline or examination were not correlated with seeking support or loneliness (rs = .09 to .27). Investigation of whether loneliness was related to any of the immune measures, independent of the other variables, revealed no significant correlations at either baseline or examination (rs = .01 to .21).

Discussion

We explored the relationship between examination stress and a specific immune response to EBV: the memory T-cell response, as measured by the ability of peripheral blood T-lymphocytes to respond to EBV specific polypeptides. Significant decreases in memory T-cell proliferation were found during the examination time point relative to pre-exam levels for five of the six EBV polypeptides tested. In addition, subjects higher in seeking support had lowered proliferative responses to all of the early EBV polypeptides (i.e., p17, p52/50, and p85), as well as higher levels of antibody to EBV-VCA. Subjects higher in seeking support reported more stress and loneliness than their low-seeking counterparts, although there was no difference in number of friends or contacts.

In previous work from our laboratory, we have found evidence that latent EBV can be modulated by psychological stressors (Glaser et al., 1985, 1987, 1991). We have also found that psychological stress can adversely affect the ability of medical students to respond to a recombinant hepatitis B vaccination (Glaser, Kiecolt-Glaser, Bonneau, Malarkey, & Hughes, 1992). In this study, we demonstrated that psychological stress in this medical student model can down regulate the EBV-specific T-cell response, as measured by a decrease in the proliferation of lymphocytes when they are exposed to viral proteins. These new data are consistent with the reliable changes in aspects of immune function related to control of latent EBV found in our previous studies and now confirmed by others (Esterling et al., 1992).

A number of studies have shown that stress is associated with a poorer proliferative response to mitogens (Ader et al., 1991). Mitogens stimulate the replication of lymphocytes in a nonspecific manner (i.e., the response does not require binding to the T-cell receptor) and do not require the presence of previously primed lymphocytes. In contrast, our data show a specific response using EBV proteins (antigens) that bind to the T-cell receptor on lymphocytes previously primed by exposure to the virus (memory), demonstrating the universality of the stress response on proliferation of T-lymphocytes.

Although we did not find a change in antibody titers to EBV-VCA due to examination stress in this particular case, this could be a result of the timing of the study. In a previous study, we found that during this time of year (third quarter of the academic year), there was no change in EBV antibody titers as a function of examination stress, although there were significantly higher antibody titers at both baseline and examination than after summer vacation (3 months later) in the same medical student subjects (Glaser et al., 1985).

Support seeking has been associated with greater distress in prior research (Brown, 1978), and there is some evidence that explicit support seeking may be an ineffective means of coping and a poor way to obtain support (Coyne, 1976; Coyne, Aldwin, & Lazarus, 1981; Lieberman & Mullan, 1978). We found that subjects who reported more support-seeking behavior also described themselves as more stressed and lonelier than their low-seeking counterparts. The groups did not differ on reports of number of contacts, roles, or roles by contacts. In previous studies, greater loneliness has been associated with higher EBV-VCA antibody titers (Glaser et al., 1985; Kiecolt-Glaser et al., 1987) and lower levels of NK cell activity (Kiecolt-Glaser et al., 1984). In this study, those subjects who

Table 2
Effect of Examination Stress on the Memory T-Cell Response to Purified Epstein-Barr Virus Polypeptides

<table>
<thead>
<tr>
<th>Polypeptide</th>
<th>Baseline CPM</th>
<th>SI ± SE_M</th>
<th>Examination CPM</th>
<th>SI ± SE_M</th>
</tr>
</thead>
<tbody>
<tr>
<td>gp250**</td>
<td>12,734.02</td>
<td>1.54 ± 0.11</td>
<td>7,986.82</td>
<td>1.24 ± 0.09</td>
</tr>
<tr>
<td>gp125</td>
<td>13,478.60</td>
<td>1.63 ± 0.13</td>
<td>7,587.79</td>
<td>1.44 ± 0.13</td>
</tr>
<tr>
<td>p160*</td>
<td>11,792.41</td>
<td>1.42 ± 0.10</td>
<td>9,200.99</td>
<td>1.20 ± 0.11</td>
</tr>
<tr>
<td>p50*</td>
<td>9,771.88</td>
<td>1.15 ± 0.10</td>
<td>6,448.76</td>
<td>0.96 ± 0.08</td>
</tr>
<tr>
<td>p50**</td>
<td>10,113.31</td>
<td>1.21 ± 0.12</td>
<td>6,184.63</td>
<td>0.92 ± 0.11</td>
</tr>
<tr>
<td>p17*</td>
<td>11,440.76</td>
<td>1.39 ± 0.15</td>
<td>8,593.03</td>
<td>1.14 ± 0.14</td>
</tr>
</tbody>
</table>

Note. Stress was measured by proliferation of peripheral blood leukocytes in the presence of 5 μg of each polypeptide. All cultures were incubated for 112 hr, with a pulse with 1 μCi H3TdR for 8 hr. Background media control values were as follows: baseline, 7,757.36 ± 1,072.40, and examination 6,608.18 ± 798.63. CPM = counts per minute.

*p < .05. **p < .01.
reported higher levels of seeking support had higher antibody (VCA) titers to EBV, suggesting greater viral reactivation and more loss of control over latent virus. The proliferative response to several of the EBV polypeptides was also lower in subjects high in support seeking relative to their low-seeking counterparts. Furthermore, increased loneliness has been associated with higher recurrence rates for herpes simplex virus during a 5-week daily reporting period (McLarnon & Kaloupek, 1988).

EBV has been associated with chronic depression and may act as a cofactor in the development of chronic fatigue syndrome (Jones & Straus, 1987; Straus, 1988), as well as the development of the acquired immunodeficiency syndrome (AIDS; Antoni, Esterling, Lutgendorf, Fletcher, & Schneiderman, in press). Data from this study continue to support the hypothesis that psychosocial stressors can modulate EBV latency. Whether the changes observed in this and previous studies are related to clinical disease is still unknown, and future studies should clarify these linkages.

References


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**Call for Nominations**

The Publications and Communications Board has opened nominations for the editorships of *Behavioral Neuroscience*, the *Journal of Experimental Psychology: General*, and the *Journal of Experimental Psychology: Learning, Memory, and Cognition* for the years 1996–2001. Larry R. Squire, PhD, Earl Hunt, PhD, and Keith Rayner, PhD, respectively, are the incumbent editors. Candidates must be members of APA and should be available to start receiving manuscripts in early 1995 to prepare for issues published in 1996. Please note that the P&C Board encourages participation by members of underrepresented groups in the publication process and would particularly welcome such nominees. To nominate candidates, prepare a statement of one page or less in support of each candidate.

- For *Behavioral Neuroscience*, submit nominations to J. Bruce Overmier, PhD, Elliott Hall—Psychology, University of Minnesota, 75 East River Road, Minneapolis, MN 55455 or to psyjbo@vx.cis.umn.edu. Other members of the search committee are Norman Adler, PhD, Evelyn Satinoff, PhD, and Richard F. Thompson, PhD.

- For the *Journal of Experimental Psychology: General*, submit nominations to Howard E. Egeth, PhD, Chair, JEP: General Search, Department of Psychology, Johns Hopkins University, Charles & 34th Streets, Baltimore, MD 21218, to egeth@jhuvm.bitnet, or to fax number 410-516-4478. Other members of the search committee are Donald S. Blough, PhD, Martha Farah, PhD, and Edward E. Smith, PhD.

- For the *Journal of Experimental Psychology: Learning, Memory, and Cognition*, submit nominations to Donna M. Gelfand, PhD, Dean, Social and Behavioral Science, 205 Osh, University of Utah, Salt Lake City, UT 84112-1102 or to fax number 801-585-5081. Other members of the search committee are Marcia Johnson, PhD, Michael Posner, PhD, Henry L. Roediger III, PhD, and Richard M. Shiffrin, PhD.

First review of nominations will begin December 15, 1993.