Negative Behavior During Marital Conflict Is Associated With Immunological Down-Regulation

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Although increased morbidity and mortality have been reliably associated with social isolation and less satisfying personal relationships, relatively little is known about the underlying biopsychosocial mechanisms. We assessed problem-solving behaviors and changes in immune function in 90 newlywed couples who were admitted to a hospital research unit for 24 hours. Subjects who exhibited more negative or hostile behaviors during a 30-minute discussion of marital problems showed greater decrements over 24 hours relative to low negative subjects on four functional immunological assays (natural killer cell lysis, blastogenic response to two mitogens, and the proliferative response to a monoclonal antibody to the T3 receptor), as well as larger increases in the numbers of total T lymphocytes and helper T lymphocytes. High negative subjects had higher antibody titers to latent Epstein-Barr virus than low negative subjects, consistent with down-regulated immune function. Women were more likely to show negative immunological changes than men.

The discussion of marital problems also led to larger increases in blood pressure that remained elevated longer in high negative subjects than low negative subjects. Positive or supportive problem-solving behaviors were not related to either immunological or blood pressure changes.

These physiological differences were particularly noteworthy because marital satisfaction was high in both groups, and couples had been selected on the basis of stringent mental and physical health criteria. These data provide additional support for the link between personal relationships and immune function.

Key words: Psychoneuroimmunology, hostility, immunity, personal relationships, marriage.

The link between personal relationships and immune function is one of the most robust findings in psychoneuroimmunology (PNI) (1). For example, lonelier medical students had lower natural killer (NK) cell activity than fellow students who were not as lonely (2). Higher NK activity and a stronger proliferative response to mitogen stimulation were associated with higher social support in women whose husbands were being treated for urologic cancer (3). Medical students who reported greater social support mounted a stronger immune response to hepatitis B vaccine than those with less support (4).

The support provided by certain key personal relationships is obviously more important than others: data from national surveys suggest that marital happiness contributes far more to global happiness than any other variable, including satisfaction with work and friendships (5). The loss of a spouse, either through bereavement (6, 7) or divorce (8, 9) has been linked to the down-regulation of cellular immunity.

Although loss of a spouse can provoke adverse mental and physical health changes, the simple presence of a spouse is not necessarily protective; a troubled marriage is itself a prime source of stress, while simultaneously limiting the partner's ability to seek support in other relationships (10). Troubled marriages are reliably associated with increased distress, and unmarried people are happier, on the average, than unhappily married people (5). In fact, depression is strongly associated with marital discord, e.g., Weissman (11) found that unhappy marriages were a potent risk factor for major depressive disorder, associated with a 25-fold increase over untroubled marriages. Moreover, unhappily married individuals reported poorer physical health than either happily married or divorced people of the same race, sex, and age (12).

Recent physiological data provide evidence of multiple pathways through which marital relationships may influence health (13). Ewart and colleagues (14) suggested that chronically abrasive marital relationships might contribute to hypertension and atherogenesis; using a sample of 43 patients with essential hypertension, they demonstrated that a 10 minute marital problem-solving task produced clin-
ically significant increases in blood pressure, with subjects reaching a mean of 160/100 mm Hg. The increases were specifically associated with hostile marital behaviors: neither supportive nor neutral behaviors produced significant changes. A 20-couple subsample of these subjects subsequently completed marital communications training, and their blood pressure reactivity to marital arguments was reduced compared with those who did not undergo training (15, 16); although the communications training emphasized the importance of increasing supportive and problem solving behaviors while reducing hostile behaviors, only hostile behaviors changed after training.

Marital discord has other important physiological correlates. In two small cross-sectional studies, we found that marital strife was associated with poorer immune function as well as greater depression and loneliness (8; 9). Although these data were provocative, the cross-sectional designs precluded inferences about the direction of causality, e.g., people who were more depressed might have viewed their marriages as less supportive, and their depressive symptoms might have also potentiated the down-regulation of immune function (17). However, we speculated that the immunological differences we observed reflected endocrinological changes related to the heightened autonomic arousal associated with marital discord (14-16, 18, 19). We designed this prospective longitudinal study to test these hypotheses.

As described earlier, blood pressure increases during conflict have been specifically associated with hostile marital interactions, not supportive or neutral behaviors (14). Across a large number of marital studies, negative communication indices provide much more discriminative and predictive power than positive indices (20), and distressed and nondistressed couples show reliable and stable behavioral differences during conflict. Dissatisfied couples behave more negatively toward each other, and they are more likely to reciprocate their partner's negative behaviors (21). Nondistressed couples are better able to set limits on negative communication and its reverberations than distressed couples (21, 22). Thus, we expected that negative communication would be much more strongly related to immune function and immunological changes over 24 hours than positive aspects. In addition, we expected that support in other relationships would not fully compensate for marital distress.

### METHOD

#### Subject Selection

Immunological, endocrinological, psychophysiological, behavioral, and self-report data were collected from 90 newlywed couples during a 24-hour admission to the Ohio State University Clinical Research Center (CRC), a hospital research unit. A three-stage process was used for screening and recruitment.

We initially identified couples through Franklin County Court records for the Columbus metropolitan area. We sent letters to demographically "appropriate" couples (first marriage, ages 20-40, no children) who had obtained marriage licenses 4 to 6 months previously. The first phase of the study was described as a phone survey of newlyweds' health and happiness, and subjects were told that they would be paid $10 per couple for interviews concerning their physical and mental health if they returned an enclosed postcard; 2249 individuals were interviewed of 4758 who received letters, representing a 47% response rate. Eight percent of the couples who returned our original postcards were eventually admitted to the CRC.

We eliminated couples from further consideration if either spouse reported any acute or chronic health problems that might have immunological or endocrinological consequences, if they took any medications except birth control pills, if they drank more than 10 alcoholic drinks per week or used any street drugs, if they smoked, if they used caffeine excessively, or if they were not within 20% of their ideal weight for their height. We explored the reasons for past surgeries or hospitalizations, as well as any psychological/psychiatric treatment. Women were asked about any menstrual problems, because of their endocrinological relevance. Couples who were planning to move or to have children within the next 2 years were excluded, since they might be lost to follow-up.

We also administered the telephone version (23) of the Marital Adjustment Test (MAT) (24). The MAT mean for the telephone interview sample was 126.98 (SEM = 0.33); higher MAT scores indicate greater marital satisfaction. Couples were targeted for additional screening if they met the above criteria, and if either member of the couple scored 130 or greater or 118 or less on the MAT (in an attempt to maximize the marital satisfaction range among our sample).

During the second set of phone interviews we collected both current and lifetime psychiatric disorder data as well as a detailed medical history; for the latter, the interviewer completed a standard medical history/review of systems form that was later reviewed by the project's research nurse and a physician. Subjects received $15 each for these 30- to 90-minute interviews administered by postdoctoral fellows and advanced clinical psychology graduate students. Comparisons of physical health and depression data collected through telephone or in-person interviews suggest that the two methods produce comparable data (25).

We excluded subjects who had met DSM-III-R criteria for any psychotic diagnosis, any depressive or anxiety disorder other than simple phobia, or substance abuse. These criteria were designed to exclude previously impaired or vulnerable individuals whose psychopathology might produce marital discord (26), as well as associated endocrinological or immunological alterations, e.g., the hypercortisolemia or altered immune function associated with clinical depression (17). We eliminated individuals with any history of major depression or dysthymia, since impairments in marital and other close relationships can persist for 4 years or more after an acute episode (27).

Of the 313 individuals who completed the second set of interviews (14% of the original interview sample of 2249), 58% of these...
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Subjects (90 couples) were eventually admitted to the CRC. Aside from our stringent mental and physical health criteria, couples were eliminated if they reported any needle or hospital phobias, if they could not be scheduled for their CRC admission within 14 months of their marriage, or if one spouse could not be reached to complete the interviews. Because all CRC evaluations had to be scheduled during the follicular phase of the woman's menstrual cycle (days 5-9), matching couples' schedules with CRC availability was particularly problematic.

The sociodemographic characteristics of our final sample were as follows: the average age of wives and husbands was 25.21 (SEM = 0.32) and 26.13 (SEM = 0.32), respectively, with a range from 20 to 37. Couples were well-educated: 6.1% were high school graduates, 23.3% had some college training, 53.3% were college graduates, and 17.2% had additional postgraduate training. The average couple's combined income was $43,464 (SEM = 1764.44). The majority were white (95%). Couples dated an average of 36.58 months (SEM = 2.60) before marriage, and 55 couples (61.11%) lived together before marriage. An average of 10.44 months (SEM = 0.15; range = 6-14) elapsed between their marriage and their CRC admission.

CRC Admission

After admission to the CRC hospital unit at 7:00 AM, a heparin well was inserted in each subject's arm so we could draw blood regularly across the 24-hour stay and minimize additional discomfort. We asked couples not to drink or eat anything after midnight; all couples were served the same meals, controlling dietary factors such as sodium, and beverages were caffeine-free. Couples remained together in the same CRC room for 24 hours, assuring consistent physical activity across couples (Table 1).

After the 1½-hour adaptation period after insertion of the heparin well, subjects were positioned in chairs facing each other in front of a curtain. The couples completed several questionnaires (described below), then sat quietly for 10 minutes.

For frequent, unobtrusive endocrine sampling during the interaction tasks, a long polyethylene tube was attached to the heparin well, so nurses could draw blood samples at set intervals, out of subjects' sight; the polyethylene tube was easily accessible to two nurses who sat behind the curtain. Two psychology team members were also seated behind the curtain during the interviews, monitoring the videotaping and adjusting the remote-controlled cameras.

At the end of the baseline period a psychology graduate student or postdoctoral fellow conducted a brief interview (10-20 minute) to help identify the best topics for the problem discussion. Based on this interview and their ratings from the Relationship Problem Inventory (28), couples were asked to discuss and try to resolve two or three marital issues that the interviewer judged to be the most conflict-producing. During the 30-minute problem discussion that followed immediately, the research team remained out of sight behind the curtain. After a 30-minute break, the couples responded to questions about the history of their relationship (29), with the latter interview generally a pleasant one for most couples, lasting 30 to 45 minutes.

The effects of marital conflict on heart rate and blood pressure were determined by measurements made immediately after the conflict. The nurses used a stethoscope and a sphygmomanometer to measure blood pressure and heart rate. Readings were taken at the end of the 10-minute baseline, at the end of the 30-minute conflict task, at the end of the 30-minute break between the conflict and the oral history interviews, and at the end of the oral history interview.

The couples had no additional experimental tasks until 5:00 that afternoon when we assessed cardiovascular reactivity during 2-minute mental arithmetic serial subtraction tasks. After a 2-minute baseline, each member of the couple performed serial subtraction alone, then in the presence of his/her spouse. Cortronics 7000 units were used for continuous assessment of heart rate, and systolic and diastolic blood pressure.

Early the next morning couples completed self-report measures and discussed their reactions to the visit. Couples were paid $350 for their time in the CRC.

Marital Interaction Coding System (MICS)

The Marital Interaction Coding System-IV (MICS; 30) provided data on problem solving behaviors in the 30-minute marital conflict resolution task. The videotapes were coded by the Oregon Marital Studies Program (OMSP) under the direction of Robert L. Weiss.
The MICS, the most widely used marital behavioral coding system, is designed to describe couples' behaviors as they attempt to resolve a relationship issue (31). A number of studies have shown that the MICS discriminates well between distressed and nondistressed couples, and marital treatment studies show changes in MICS-coded behaviors from pre- to posttreatment (32, 33). After OMSP coding conventions, each coder maintained code-by-code agreement with a master coder of at least 70% on a random sample of 20% of the tapes. Tapes were recorded when agreement fell below this criterion.

One study that used generalizability theory as a method for evaluating the dependability of the MICS produced impressive evidence supporting its reliability (33); generalizability and error coefficients computed for samples collected under five different conditions showed that most of the variation in marital interaction samples was a function of differences among couples and cross-situational differences within couples, with no evidence of observer drift, coder biases across couples or occasions, or reactivity from the first to the second sampling occasion. Moreover, distressed couples' negative behaviors showed strong cross-situational consistency, despite discussion topic differences and sampling on two occasions (33).

Most marital communication studies utilize a positive/negative distinction when assembling summary codes (34), because distressed marriages are characterized by negative affect, conflictual communication, and poor listening skills (20, 21). To capture these dimensions in composite indices, we conducted separate factor analyses of MICS code frequencies for the positive and negative dimensions. Three positive factors emerged that had eigenvalues greater than one, and were similar or identical to the dimensions described by Weiss and Summers (30): a problem solving/proposal change cluster (negative solution, problem description, compromise, and positive solution), a positive behavior or validation/facilitation cluster (agree, approve, accept responsibility, assent, and positive mind reading), and a humor cluster (humor, compliance, and smile/laugh). Although there was not a clear factor solution for negative codes, two clusters emerged that were consistent with the dimensions used by other investigators (16, 30); the first cluster included "active" negative behaviors (criticize, disagree, deny responsibility, excuse, interrupt, negative mind reading, noncompliance, put down, turn off, disapprove, and dysphoric affect). These behaviors represent the combined blame and invalidation categories from Weiss and Summers (30); in addition, they are the same as those used by Ewart et al. (16) for their "hostile" dimension, with four exceptions: disapprove and dysphoric affect were not included in their earlier version of the MICS, and interrupt and noncompliance were not codes they used. Our second negative dimension tapped avoidance or withdrawal behaviors (not tracking, withdrawal, off-topic, and disengage). Husbands show much greater withdrawal from marital conflict than wives, and it has been suggested that men's exclusion is related to greater conflict-related physiological arousal (29). Several codes were excluded, either because they did not clearly fit either the positive or negative dimensions (talk, question, paraphrase, and command), their nonoccurrence was related to experimental constraints (positive physical contact), or they overlapped with other codes (attention and not tracking are correlated, \( r = .98, p < .001 \)).

As in other studies (16), husbands' and wives' negative or hostile behaviors were significantly correlated, \( r = .74, p < .001 \), so we summed them for each couple, after the convention in other marital research (16, 35); also, we were interested in the couple's negative behavior total because we assumed that one partner's behavior affected the other. We divided the resulting frequencies at the median, 105, to form high and low negative groups for the first series of immunological change analyses, with higher scores on this dimension reflecting higher frequencies of negative or hostile behaviors. Thus, our MICS groups were defined solely on the basis of high or low hostile or negative behavior, not avoidant or positive behaviors.

**Psychological Assessment**

The Structured Clinical Interview for DSM-III-R, nonpatient version (SCID-NP) is designed to enable a clinically trained interviewer to make rapid and valid DSM-III-R diagnoses for both lifetime and current psychopathology (36). We used the SCID-NP to exclude vulnerable individuals, as described earlier. Interrater reliability for SCID-NP diagnoses, calculated using randomly selected audiottaped interviews for 10% of the sample, had acceptable reliability based on the resulting kappa coefficient of .74.

The Hamilton Depression Rating Scale (HDRS) (37), a 24-item, interviewer-rated depression scale, administered after the SCIDNP, provided additional information on depressive symptomatology during the week before the interview. Interrater reliability, calculated for 10% of the sample, was excellent, \( r = .96 \).

The Marital Adjustment Test (MAT) (24), used to assess marital satisfaction, was administered during the initial telephone screening interview. The MAT is widely used in marital research because of its reliability and validity in discriminating satisfied and dissatisfied couples (23). Lower scores indicate lower marital satisfaction.

Subjects completed the revised Social Support Questionnaire (SSQ) (38) during their CRC visit. The SSQ yields scores for both the perceived number of social supports and satisfaction with available support. Each item asks subjects to list the people to whom they can turn and/or on whom they can rely in any given circumstance, and also to indicate how satisfied they are with each of these supports. The scale provides a way to separate the support provided by the spouse from support provided by other people.

The Profile of Mood States (POMS) (39), one of the best self-report measures for identifying and assessing transient, fluctuating affective states, was administered at baseline before the interview began at the end of the conflict task and oral history interviews, and at the end of the 24-hour CRC admission. The POMS has excellent norms, and psychometrically is very strong in terms of both reliability and validity (39). The POMS measures six identifiable and factorially distinct affective states; we were particularly interested in changes on the hostility and anxiety scales.

The Positive and Negative Affect Schedule (PANAS) (40) includes two 10-item mood scales. The two scales are largely uncorrelated, and show good convergent and discriminant validity when related to state mood scales and other variables (40). We included the scale because health complaints, perceived stress, social activity, and exercise have been related to these two affective dimensions (41).

The Marlowe-Crowne Social Desirability Scale (42) was included because high scorers characteristically avoid conflict, even when provoked (43, 44). High scorers also tend to describe themselves in unrealistically positive ways on self-report measures (42).
Immunological Methods

The two blood samples for immunological analyses were drawn at the beginning and the end of couples’ 24-hour CRC visit, between 6:00 and 8:00 AM each time to minimize diurnal variation. The immunological battery provided data on both functional and quantitative in vitro changes in a spectrum of cellular immunological functions. Quantitative assays included assessment of total T lymphocytes, helper T cells, suppressor T cells, B lymphocytes, and neutrophils. Assays used to study functional changes included NK cell lysis, IFN-γ production by lymphocytes stimulated with concanavalin A (Con A), the blastogenic response to Con A, and phytohemagglutinin (PHA), and to a monoclonal antibody (MAB) to the T3 receptor. We also measured antibody titers to a latent herpesvirus, Epstein-Barr virus (EBV). We have found stress-related differences using these assays in our previous research (1, 2, 8, 9, 45-47).

Measurement of NK Cell Lysis. This protocol has been previously reported (2). Briefly, cells were prepared to make a 50:1, 25:1, and 12.5:1 effector to target cell ratios and seeded in triplicate, in 96-well microtiter plates. Additional wells containing only target cells (K562) in medium or target cells in a medium containing 5% sodium dodecyl sulfate were used to determine spontaneous and maximum release of radioactivity, respectively. Plates were incubated for 5 hours in a 5% CO2 atmosphere at 37°C, supernatants were harvested and activity was determined by the release of 3H into the supernatants. Supernatants were counted using a Beckman 9000 gamma counter.

Measurement of IFN-γ. The measurement of IFN-γ was obtained using procedures previously described (45). Briefly, PBLs, 5 x 10⁶, were prepared in complete RPMI 1640 medium supplemented with 5.0% of fetal bovine serum (Hyclone). To each culture, 10 µg of Con A was added. Cells, 1 x 10⁵/well, were incubated for 92 hours at 37°C in 96-well round-bottom plates, then pulsed for 4 hours with 3H TdR (0.5 µCi/well, specific activity 1 mCi/ml). All samples were run in triplicate (47). To measure the blastogenic response to the T, monoclonal antibody (MAB) we have found three different concentrations of the Coulter MAB that work satisfactorily, 1:128, 1:256, 1:512. These dilutions were prepared in RPMI 1640 medium with 5% fetal bovine serum. Cells were incubated in 96-well round-bottom plates for 70 hours, then pulsed for 22 hours with 3H TdR (0.5 µCi/well specific activity). The cells were harvested and counts/min (CPM) determined for each dilution.

EBV Antibody Titters. The EBV VCA antibody titers (IgG) were assayed by the indirect immunofluorescence (IF) test using HR-1 cells by procedures previously described (46, 47). Because the method of doubling dilutions was used to obtain EBV antibody titers, a logarithmic conversion was used to normalize the distribution and reduce variance for statistical purposes (49). For descriptive purposes the geometric mean titers (GMTs) are also presented to allow comparisons with prior research.

Quantitative/enumerative assays: Total T lymphocytes, helper and suppressor T lymphocytes, macrophages, and neutrophils. Monoclonal antibodies were used to provide data on certain quantitative aspects of immune function, using the methods described previously (8, 9, 47).

Nutritional Markers, Albumin, and Transferrin

Nutritional status was assessed to evaluate the possibility that any immune differences were a function of poor nutrition. Although tests for carbohydrates and fat can be used to assess nutritional status, protein tests are better because their nutritional building blocks are more varied, and their synthetic pathways are complex. Albumin has a half-life of 2 to 3 weeks, compared to 8 days for transferrin. The procedures used to measure albumin and transferrin are described in Kiecolt-Glaser et al. (50).

Data Analyses

Data for NK cell lysis, Con A, PHA, and T, receptor-induced blastogenesis were analyzed using MANOVA's with two within-subjects variables (change between CRC entry and exit, and change across the three ratios or concentrations), as well as two between-subjects variables, gender and high vs. low negative behaviors on the Marital Interaction Coding System (MICS). Analyses for the remaining immunological variables and self-report data were similar, but used only one within-subjects variable, change between entry and exit. Nine subjects did not have blood drawn on exit from the CRC, either because they needed to leave too early or because of catheter problems. Measures that were taken on a single occasion, e.g., EBV antibody titers, were analyzed using MICS group and gender. Behavioral data from the MICS were analyzed using gender as a within-dyad (repeated measures) factor, as recommended by Kenny and Kashy (51), since the interactional behaviors were interdependent.

RESULTS

The high and low negative MICS groups did not differ on age, education, or income, Fs < 1. The two groups did not differ either on the length of the time they had dated before marriage, F(1, 88) = 1.52, or on the number of months between their wedding and CRC visit, F(1, 88) = 1.06.

Questionnaire Data

High negative subjects reported significantly lower marital satisfaction on the MAT than low negative subjects, F(1, 178) = 4.50, p < .05. The mean for high negative subjects was 125.90 (SEM = 1.73), compared with 130.47 (SEM = 1.33) for low negative subjects. Men and women did not differ, F(1, 176) = 1.76, and the interaction between gender and MICS group was not significant, F < 1.

High and low negative MICS groups did not differ at baseline on either the POMS hostility or anxiety scales, Fs < 1. Similarly, we found no evidence of baseline group differences using the PANAS positive affect scale, F(1, 169) = 1.49, or negative affect, F < 1. Depression as measured by the Hamilton Depres-
pression Rating Scale (administered during the screening interviews) was unrelated to gender, MICS group, or their interaction, $F_{S} < 1$. The absence of any baseline affective differences between groups is important because of evidence that individuals high in neuroticism or negative affectivity may show an enhanced stress response and report more health complaints (41).

We also assessed changes in hostility and anxiety over time. Both MICS groups showed the same decline in hostile affect over time, with their highest scores at baseline, $F(2, 175) = 52.95, p < .001$; in addition to the main effect for time, however, there was also a significant interaction between group and time, $F(2, 175) = 4.08, p < .05$, with higher hostility reported by high negative subjects at the end of conflict (Figure 1). The pattern for anxiety self-reports was quite similar, with the group by time interaction approaching significance, $F(2, 175) = 2.75, p < .06$. There were not significant effects associated with gender, but the POMS T-scores that we used for analyses have gender-adjusted norms.

Using SSQ data (38), high and low negative MICS subjects did not report differences in either the number of nonspousal support persons listed across questions, $F(1, 173) = 1.31$, or their satisfaction with nonspousal social support, $F < 1$. Women reported greater numbers of supports than men, $F(1, 173) = 7.14, p < .01$, and higher satisfaction as well, $F(1, 160) = 5.36, p < .05$. Neither of the group by gender interactions was significant, $F_{S} < 1$.

The MICS groups did not differ on social desirability, $F(1, 172) = 1.87$, and the group by gender interaction was nonsignificant, $F < 1$. Women had higher Marlowe-Crowne scores than men, $F(1, 172) = 5.94, p < .05$.

**Behavioral Data.** Table 2 provides the values for each of the five behavioral dimensions as a function of gender and negative MICS group. Husband and wife were included as a within-subjects variable for analyses with these behavioral data as described earlier (51). Although the negative MICS groups obviously differed on the dimension used to dichotomize them, it is also apparent that women had significantly higher frequencies of negative behavior than men, $F(1, 88) = 6.43, p < .01$, consistent with the

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**Fig. 1.** POMS hostility scores at baseline, at the end of the 30-minute conflict task, and at the end of 24 hours in the CRC as a function of high or low negative MICS behaviors. Although high and low negative MICS groups did not differ on hostility at baseline or at the end of their CRC admission, high negative subjects reported more hostility at the end of the conflict task.
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There was not a significant main effect for group or for gender, and the group by gender interaction was not significant, $F$s < 1. However, although the means for the low negative group were the same or higher after 24 hours across all three concentrations, the values for high negative subjects decreased across two of the three concentrations, producing a significant group by concentration by time interaction, $F(2, 160) = 2.95$, $p < .05$. Gender was not a significant factor for Con A, either for the gender by concentration interaction, the group by gender by concentration interaction, the gender by concentration by day interaction, or the four-way interaction, all $F$s < 1. The three Con A concentrations produced the usual differences in proliferation, $F(2, 160) = 38.39$, $p < .001$, as well as a time by concentration interaction, $F(2, 160) = 86.70$, $p < .001$. No other main effects or interactions were significant.

Data from the T<sub>3</sub> receptor-induced blastogenesis assay (Figure 3) showed no overall group difference, $F(1, 85) = 2.10$. Neither the main effect for gender nor the group by gender interaction was significant, $F$s < 1. The high negative subjects started lower and displayed greater downward change than low negative subjects, with group differences over time most apparent at higher dilutions, producing a significant group by time by concentration interaction, $F(2, 170) = 6.61$, $p < .002$, without a significant main effect for time, $F(1, 85) = 3.04$. The assay was not added to the study at the beginning, so subject numbers are lower than other assays. There was also a significant main effect for differences in concentration, $F(2, 84) = 3.79$, $p < .05$. No other interactions among these variables were significant. These data complement the PHA and Con A results by showing that the physiological changes induced by a stressor can affect how cells respond when their receptor is triggered by this MAB.

Analysis of NK cell lysis data (Figure 4) across the three effector: target ratios showed that the lysis activity of high negative subjects started higher and declined more sharply than low negative subjects, producing a significant group by time interaction, $F(1, 158) = 3.73$, $p < .05$. Men had higher values than women, $F(1, 158) = 5.15$, $p < .05$. The three effector: target ratios produced the expected differences in lysis, $F(2, 316) = 136.65$, $p < .001$, and subjects showed greater change at lower ratios, resulting in a time by ratio interaction, $F(2, 316) = 529.21$, $p < .001$. No other main effects or interactions were significant.

Gamma interferon production by lymphocytes did not change significantly over 24 hours, $F(1, 166) = 2.93$, and did not differ as a function of group or...
Fig. 2. A and B, Changes in blastogenic response to PHA and Con A between entry and exit to the CRC as a function of high or low negative MICS behaviors. Although there were differences between mitogens and across concentrations, the blastogenic response of high negative subjects showed greater downward change after 24 hours in the CRC than that of low negative subjects.

gender, $F_s < 1$. The group by time interaction was not significant, $F(1, 166) = 3.12$.

The numbers of total T lymphocytes (T₃) and the helper/inducer T-cell subset (T₄) followed very similar patterns: both increased significantly between CRC entry and exit, with greater increases in high than low negative subjects (Table 3). For T₃ cells, the interaction between group and time was $F(1, 142) = 9.80, p < .01$; for T₄ cells, $F(1, 144) = 6.40, p < .01$. The increase between entry and exit resulted in significant main effects on T₃ cells, $F(1, 142) = 50.38, p < .001$; for T₄ cells, the time effect was $F(1, 144) = 65.06, p < .001$. Women had higher values
Fig. 3. Change in blastogenic response to a monoclonal antibody to the T<sub>3</sub> receptor between entry and exit to the CRC as a function of high or low negative MICS behaviors. High negative subjects had lower values at baseline and displayed greater downward change than low negative subjects.

Fig. 4. Change in natural killer cell lysis between entry and exit to the CRC as a function of high or low negative MICS behaviors. The lytic activity of high negative subjects started higher and declined more sharply over 24 hours than that of low negative subjects.
than men on both assays, \( p < .01 \), without significant effects for group or the remaining interactions.

Although the numbers of suppressor/cytotoxic (T₈) lymphocytes also increased over the 24-hour period, \( F(1, 143) = 39.67, p < .001 \), the group by time interaction was not significant, \( F(1, 143) = 1.05 \). Women again had higher values than men, \( F(1, 143) = 11.85, p < .001 \), without significant effects for group, or for any of the remaining interactions, \( F < 1 \).

Not surprisingly, changes in the T₄/T₈ ratio reflected the greater increases in T₄ subsets in high negative subjects over the 24 hours, producing a significant group by time interaction, \( F(1, 142) = 5.20, p < .05 \). The gender by MICS group interaction approached significance, \( F(1, 142) = .63, p < .06 \).

EBV VCA IgG antibody titers, assayed only once because of the temporal stability of IgG, were significantly higher in the high negative group than the low, \( F(1, 165) = 6.63, p < .01 \). Higher antibody titers to a latent herpesvirus suggest that the cellular immune response is less competent in controlling the latent virus (8, 9, 45-47). Women had higher titers than men, \( F(1, 165) = 4.42, p < .05 \). The group by gender interaction was negligible, \( F < 1 \). The GMTs for low and high MICS women were 348.43 and 480.87, respectively, compared to 304.56 and 333.15 for low and high men.

Summary immune change measures. In addition to the analyses for each of the immunological parameters, described above, we were interested in assessing overall gender differences in change and the possible contributions of withdrawal and positive behaviors. To address these questions, we computed residualized change scores (to adjust for baseline differences) for each of the immunological measures on which we had found either a significant main effect for change over time, or an interaction between MICS group and change over time (NK cell lysis, Con A, PHA, blastogenesis with the MAB for the T₃ receptor, percent of macrophages, and numbers of T₃, T₄, and T₈ lymphocytes). We converted each set of residualized change scores to z-scores and computed the mean for the eight scores (after reversing the sign on z-scores for T₃, T₄, and T₈), with lower scores indicating greater negative change between CRC entry and exit. Because of occasional missing data (i.e., the nine subjects who had only one immunological blood draw, the absence of CBC data for the first six couples in the study, and the later addition of the T₃ receptor blastogenesis assay to the study), we only included subjects for whom we had at least six of the eight measures (80% of the sample).

We used this summary immune change score as the dependent measure in two multiple regression analyses. Gender was entered on the first step, and then each subject's frequency data for all five of the MICS behavior categories (negative behavior or hostile behavior, withdrawal/avoidance, positive behavior, problem solving/proposal change, and humor) were entered on the second step, in a stepwise fashion following Ewart et al. (14). Women showed significantly greater immunological down-regulation than men, \( \beta = .20, p < .02, R^2 = .04 \). For the second step, only the active negative code category was a significant predictor of immunological change, \( \beta = -.26, p < .001, R^2 = .11 \). In a second regression

<table>
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<th>TABLE 3. Changes in mean (±SEM) T lymphocytes and T lymphocyte subsets, macrophages, and neutrophils over 24 hours</th>
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<td><strong>T3 lymphocyte numbers</strong></td>
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<td><strong>T4 lymphocyte numbers</strong></td>
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we again entered gender on the first step, with stepwise entry allowed on the second step for three variables: MICS negative behaviors, the subject's MAT score (to provide a subjective estimate of marital quality), and the total frequency of nonspouse support from the SSQ (38). The SSQ data allowed us to test the possibility that support from other relationships would compensate for marital difficulties. Again, only gender and negative behaviors provided significant contributions, with is < 1 for MAT and SSQ scores.

Heart Rate and Blood Pressure Changes During and After Conflict

High and low negative subjects did not show even marginal differences at baseline on heart rate or blood pressure (SBP and DBP), all Fs < 1, and the gender by MICS groups interactions were similarly nonsignificant, F(1, 155) = 1.03 for heart rate, Fs < 1 for SBP and DBP. Men had higher SBP and DBP values than women, although women had higher heart rates than men, ps < .01.

Although MICS groups did not differ at baseline, SBP and DBP showed very different patterns of change after conflict and after the 30-minute break before the oral history interview (Figure 5). The MANOVA for SBP (using change scores) reflected the significantly greater change in SBP for the high negative group, F(1, 154) = 4.22, p < .05, without significant effects for gender, F(1, 154) = 2.62, for time, F < 1, or for any of the interactions, Fs < 1. Similarly, DBP differences between MICS groups were significant, F(1, 154) = 11.57, p <.001, without any other significant main effects or interactions, all Fs < 1. Heart rate increased significantly during conflict and returned to baseline levels after the break, but change analyses did not show significant group effects or interactions with group, Fs < 1.

Following the model for regressions with the summary immune change measure described above, we assessed the contributions of the five MICS categories to changes in SBP and DBP during conflict. After entering gender on the first step, only negative behavior made a significant contribution to DBP on the second (beta = .27, p < .001), accounting for an additional 5% of the variance. None of the five MICS dimensions was significant in the SBP regression.

Cardiovascular Reactivity

The high and low negative MICS groups did not differ on the baseline data collected for the cardiovascular reactivity task in the late afternoon, with all Fs < 1 for heart rate, DBP, and SBP. Similarly, the two MICS groups did not show even marginal differences.
differences in change on any of these indices during mental arithmetic (alone condition), all $F$s < 1; the math task produced the expected significant increases across heart rate, SBP, and DPB, $p$s < .01. Thus, the MICS group differences in blood pressure and immune function did not seem to be related to underlying stable individual differences in cardiovascular reactivity (52, 53).

Nutrition and Health-Related Behaviors

We assessed nutrition and health-related behaviors because they can affect immune function (54). All subjects fell within the normal ranges on our two protein markers, albumin and transferrin, and the two MICS groups did not differ, $F$s < 1. Similarly, MICS groups did not differ in caffeine or alcohol intake or hours of exercise per week, $F$s < 1. Our average subject drank less than one cup of coffee per day, averaged 2.28 alcoholic drinks per week, and reported 4.86 hours of vigorous physical activity during a typical week.

DISCUSSION

We found that couples who were more negative or hostile during a 30-min marital problem discussion also showed greater immunological change after 24 hours together in the CRC: relative to the low negative MICS subjects, high negative subjects declined on four functional assays (NK cell lysis and the blastogenic response to Con A, PHA, and a monoclonal antibody to the T$_3$ receptor). High negative subjects also showed relatively greater reductions in the percentage of macrophages. High negative subjects had higher antibody titers to latent EBV than low negative subjects, suggesting that the cellular immune response of the former was less competent in controlling this latent virus (46). High negative subjects had more neutrophils than low negative subject, similar to other reports of stress-associated immune alterations (55).

In contrast to these downward functional changes, high negative subjects demonstrated relatively larger increases on enumerative assays (absolute numbers of T$_3$ and T$_4$ lymphocytes) than low negative subjects. We have found similar increases in lymphocyte numbers after a 12-minute math stressor (56), and other researchers have reported increases in lymphocyte numbers (and decreases in lymphocyte function) following short-term laboratory stressors or epinephrine injections (52, 53).

These epinephrine-induced changes in lymphocyte numbers are thought to reflect transient alterations in lymphocyte trafficking from lymphoid organs and peripheral blood mediated through adrenergic receptors on the lymphocytes or via the sympathetic innervation of lymphoid organs (57). Our newlywed couples' 30-minute problem-solving discussions also produced significant changes in plasma epinephrine levels, with larger and more persistent elevations in high negative subjects compared to the low negative group (58).

The discussion of marital problems led to larger increases in blood pressure that remained elevated longer in high negative subjects than low negative subjects, similar to the pattern reported by Ewart et al. (14). These changes appeared to be closely tied to behavior during the conflict discussion: high and low negative subjects did not differ either on baseline cardiovascular measures, or in their response to a standard cardiovascular reactivity task conducted later in the day. Moreover, low negative subjects reported greater reductions in hostility after the conflict task than high negative subjects.

Across both high and low negative MICS groups, the overall trend for immunological change was toward down-regulation. We believe this trend reflects our couples' response to a stressful situation. Admission to a hospital for 24 hours, insertion of a catheter, and couples' awareness that they would be asked to discuss areas of disagreement while being videotaped are all potential stressors. In this framework, the immunological differences between the high and low negative MICS groups may reflect the greater ability of the low negative couples to buffer or moderate the stressfulness of the shared experience for each other.

Analysis of our summary immune change measures and blood pressure change data suggested that only negative or hostile behavior was significantly related to physiological changes, not avoidant, positive, or problem-solving behaviors. In addition, neither a subject's self-reported marital quality nor support from other relationships seemed to moderate these effects. The specificity of the tie between negative behavior and immunological change parallels the link between MICS-coded hostile behaviors and elevated blood pressure reported by Ewart et al. (14); as those authors suggested in their title, "Not being nasty matters more than being nice" (p. 155).

Women were more likely to show negative immunological changes than men. Floyd and Markman (59) suggested that wives function as the "barometers" of distressed marriages: women are more sen-
sitive to negative marital interactions than men, and women may be more adversely affected by overt expressions of hostility in marital interactions than men (60). Wives are better at decoding their spouse’s emotional messages than husbands (61); distressed wives can more accurately decode their husbands’ negative messages than the reverse (62). Women in distressed marriages behave more negatively during conflict than men, and wives’ behaviors during conflict discriminate better between distressed and nondistressed couples than do their husbands’ (63). It is possible that the greater negative immunological change in women is simply a "barometer" effect, and men will eventually catch up and even surpass women in their immunological response to conflict; these are questions we will be addressing with subsequent data from this longitudinal study.

We assessed a number of psychological and physiological dimensions that might represent potential confounds in the behavioral data. The high and low negative MICS groups did not differ on admission to the CRC on negative or positive affect, hostility, or anxiety. Baseline heart rate and blood pressure did not differ between groups before the conflict discussion, and the two groups did not differ in cardiovascular reactivity to the mental arithmetic task in the afternoon; this latter similarity between groups is especially important in light of recent data linking cardiovascular reactivity with short-term endocrinological and immunological changes (52, 53, 56). We had stringent inclusion criteria that eliminated couples in which either spouse had current or past mental or physical health problems; as one consequence, our subjects were exceptional in their health habits, e.g., their commitment to regular exercise. By admitting couples to the CRC for 24 hours, we were able to control such factors as physical activity, diet, and caffeine intake that can influence immune and endocrine function (54), while simultaneously providing a uniform environment across couples. Thus, it seems reasonable to conclude that the behavior of the couples during their 24 hours together produced the observed immunological differences, rather than extraneous factors.

Couples’ fights at home are more negative and last longer than those studied in the laboratory (22). Our newlywed couples are, on the average, extremely happy in their marriages; only 3% of our subjects actually scored below 100 on the MAT, the traditional cutoff for marital distress (24). The intensity of marital conflict is lower during the early years of marriage, typically increasing over time (64, 65). Our couples are much better educated and have higher incomes than the average family in the United States, both factors that have been implicated in responses to stressful events (66). Despite these important differences between our newlywed couples and the average married couple, we found that those couples with more negative behaviors displayed larger immunological changes than couples with fewer negative behaviors. Thus, we believe our data are likely to underestimate the actual physiological impact of marital discord, because we selected individuals who were presumably the least vulnerable.

These data provide a window on the pathways through which close personal relationships may affect physiological functioning and health. If chronically abrasive relationships produce more frequent and more pronounced immunological, endocrinological, and cardiovascular changes, then individuals in troubled relationships could be at greater risk over time.

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REFERENCES

MARITAL CONFLICT AND IMMUNITY


