

Marital Conflict in Older Adults: Endocrinological and Immunological Correlates

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Objective: To assess endocrinological and immunological correlates of marital conflict and marital satisfaction, 31 older couples (mean age 67 years) who had been married an average of 42 years were studied. **Method:** Couples were admitted to the Clinical Research Center and a catheter was placed in each subject's arm. Blood was drawn on entry for immunological assays; for hormone analyses, five blood samples were drawn during a 30-minute conflict discussion and a 15-minute recovery session. The conflict session was recorded on videotapes that were later coded for problem-solving behaviors using the Marital Interaction Coding System (MICS). **Results:** Among wives, escalation of negative behavior during conflict and marital satisfaction showed strong relationships to endocrine changes, accounting for 16% to 21% of the variance in the rates of change of cortisol, adrenocorticotropic hormone (ACTH), and norepinephrine (but not epinephrine). In contrast, husbands' endocrine data did not show significant relationships with negative behavior or marital quality. Both men and women who showed relatively poorer immunological responses across three functional assays (the blastogenic response to two T-cell mitogens and antibody titers to latent Epstein-Barr virus) displayed more negative behavior during conflict; they also characterized their usual marital disagreements as more negative than individuals who showed better immune responses across assays. **Conclusion:** Abrasive marital interactions may have physiological consequences even among older adults in long-term marriages.

Key words: stress hormones, psychoneuroimmunology, marriage, aging, conflict.

ACTH = adrenocorticotropic hormone; Con A = concanavalin A; CPQ = Communications Patterns Questionnaire; CRC = Clinical Research Center; EBV = Epstein-Barr virus; EPI = epinephrine; GH = growth hormone; HLM = hierarchical linear model; IF = immunofluorescence; MANOVA = multivariate analysis of variance; MAT = Marital Adjustment Test; MICS = Marital Interaction Coding System; NEPI = norepinephrine; OMSP = Oregon Marital Studies Program; PHA = phytohemagglutinin; PSS = Perceived Stress Scale.

INTRODUCTION

On the average, married people enjoy better mental and physical health than the unmarried (1, 2).

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Received for publication January 17, 1996; revision received August 12, 1996.

However, the simple presence of a spouse is not necessarily protective: a troubled marriage may simultaneously provide a prime source of stress while limiting a partner's ability to seek support in other relationships (3).

Underscoring possible risks of troubled relationships, marital interaction studies have demonstrated autonomic, endocrinological, and immunological correlates of negative behavior during marital conflict. For example, a 10-minute marital problem-solving task produced clinically significant blood pressure increments in hypertensive subjects (4), and increases in blood pressure were specifically associated with negative marital interactions: neither supportive nor neutral behaviors produced significant changes.

We found parallel data in a sample of 90 newlywed couples: negative behavior during marital conflict was associated with increased levels of epinephrine (EPI), norepinephrine (NEPI), growth hormone (GH), and adrenocorticotropic hormone (ACTH), as well as greater immunological change over the subsequent 24 hours (5, 6). Negative behavior in these newlyweds was also associated with antibody titers to latent Epstein-Barr virus (EBV), suggesting that differences in cellular immune function preceded the 24-hour period of study; the cellular immune response is responsible, in part, for the steady state expression of latent EBV (7).

Across these studies, wives have demonstrated greater and more persistent physiological changes related to marital conflict than husbands (4-6, 8). Moreover, wives' physiological changes have been more closely linked to conflict behavior and marital adjustment than husbands' responses (4, 6, 8-10). In addition, longitudinal data from one study suggested that wives' physiological responses to conflict may have greater predictive power than husbands': comparisons of couples at high or low risk for marital dissolution showed that high risk wives showed greater autonomic arousal during conflict than low risk wives, whereas high and low risk husbands did not differ (11). Thus, women seem to show greater physiological change related to marital conflict than men.

These marital interaction studies have focused on young and middle-aged couples; older adults have not been as well-studied (12, 13). It is possible that the greater predictability of conflicts in longer term marriages might blunt physiological responses over time. In fact, recent data suggest that older couples display less negative behavior and more affectionate behavior during conflict than middle-aged couples (12), so physiological responses might similarly be muted.

Alternatively, the number of relationships diminishes as people age, making the quality of relationships more salient (14). As a consequence of smaller social networks, troubled marital relationships could have a greater impact on older adults' mental and physical health (13). Thus, to assess the generalizability of physiological changes observed with young couples, we studied older couples' responses to marital conflict using the same paradigm employed with newlywed couples (albeit with a shorter hospital admission for older couples). In addition to self-rated marital satisfaction and simple frequencies of negative behavior, we were also interested in couples' propensity to escalate negative interactions, i.e., responding to negative behavior in kind, one "signature" of marital distress observed in both older and younger couples (12, 15, 16).

We expected that higher frequencies of negative behavior and greater escalation or reciprocity of negative behavior would be inversely related to marital satisfaction. In addition, we expected that negative behavior and lower marital satisfaction would be associated with steeper increases in stress hormones during conflict, as well as poorer immune function. Finally, we hypothesized that women would show greater physiological responsiveness to conflict than men.

METHODS

Subjects

The subjects, 31 older couples who ranged in age from 55 to 75 years, were recruited from newspaper advertisements, notices posted in senior citizen centers, and referrals from other participants. When subjects called the research office, we asked several brief questions, sending those who seemed to qualify a detailed letter describing the project, including a full description of the conflict resolution task. Those who returned the postcard enclosed with the letter underwent a 15-minute interview that included a medical history; these data were later reviewed by the project's research nurse and a physician. Couples were scheduled for an 8-hour Clinical Research Center (CRC) admission if they met the criteria described below, with the informed consent form signed on entry to the CRC. The resulting sample of couples had a mean age of 66.75 years (SEM = 0.62), had been married 42.28 years (SEM = 1.67), and had 11.26 (SEM = 0.85) years of education.

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 drank more than 14 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 excluded subjects who were taking β blockers or calcium channel blockers because they could interfere with sympathetic nervous system (SNS) responses to conflict. Similarly, eight subjects (five men, three women) were Type 2 (noninsulin dependent) diabetics, recruited for a pilot study on diabetes; their data were excluded from the present immunological and endocrinological analyses because of the commonly observed alterations in SNS responses and immune and endocrine function. Eighteen of the women in the sample were taking either estrogen or Provera supplements; women on supplements were evaluated during the estrogen-only phase of their cycle. Other prescription medications taken by subjects included diuretics (two women, two men), thyroid supplements (two women), nonsteroidal antiinflammatory medication for arthritis (three women, three men), and antacids (two women, two men).

CRC Admission

Subjects were admitted to the CRC at 7:00 AM. We asked couples not to drink or eat anything after midnight, and couples were all served the same meals during their 8-hour admission.

Approximately 90 minutes after a heparin well had been inserted in each subject's arm, the conflict resolution task began. Couples sat in chairs that faced each other, with a curtain separating them from the data team (two psychology team members and two nurses). Polyethylene tubes were attached to the heparin wells, allowing the nurses to draw blood samples without being observed. The conflict resolution task included a 10-minute baseline, 15- to 25-minute problem identification interview, and a 30-minute problem-solving discussion.

At the end of the 10-minute baseline a psychology graduate student or postdoctoral fellow conducted a brief interview to help identify the best topics for the problem discussion based on the ratings each spouse had made independently on the Relationship Problem Inventory (17); the subjects had provided ratings from 0 to 100 of the intensity of their disagreements about 10 common relationship issues (e.g., in-laws, finances, leisure time). The interviewer talked with couples about the topics rated highest by both.

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and 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.

Five blood samples were drawn across the conflict interaction (including the baseline and postconflict samples), with the timing of each illustrated in Figures 1 and 2. See Malarkey et al. (5) for a more detailed description of the sampling procedure.

Marital Interaction Coding System (MICS).

The Marital Interaction Coding System-IV (MICS) (18-23) provided data on problem solving behaviors during 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. Several studies have shown that the MICS discriminates well between happy and unhappy couples, and marital therapy studies show changes in MICS-coded behaviors from pre- to posttreatment (21, 22). 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 re-coded when agreement was 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 (23); generalizability and error

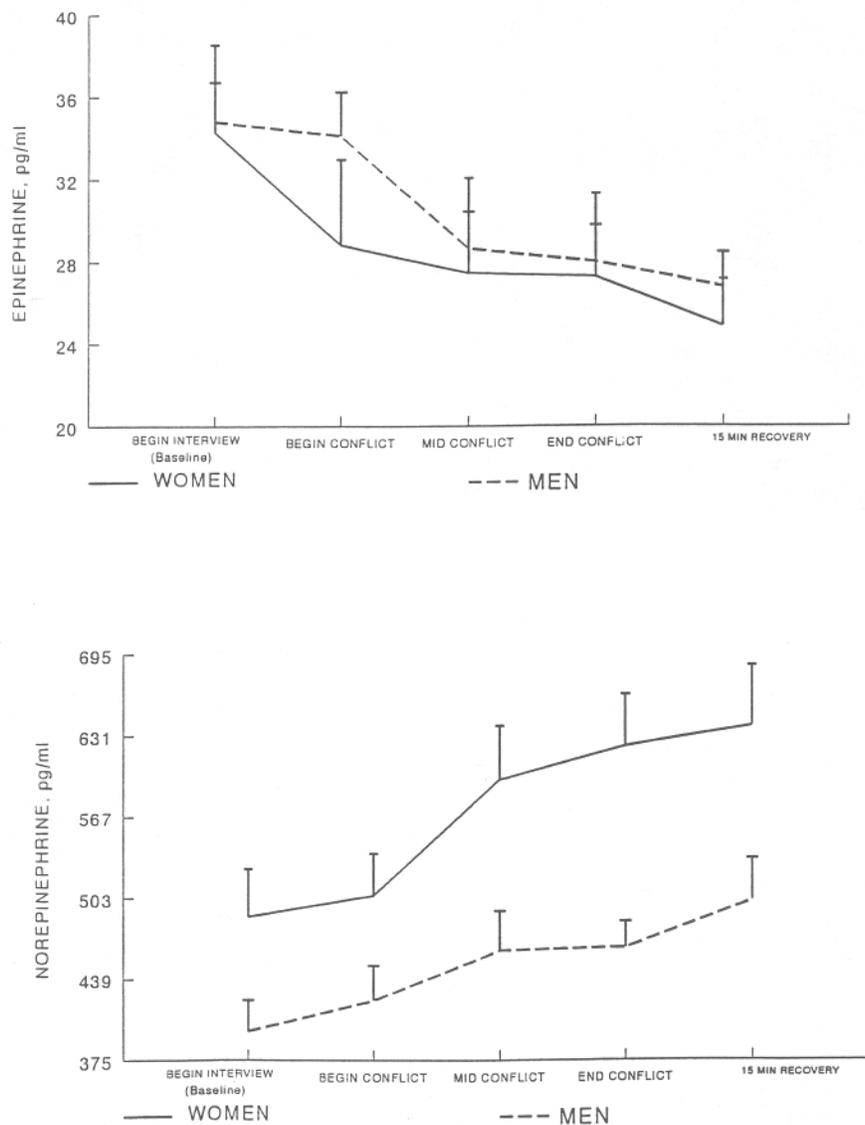


Fig. 1. Mean (+ SEM) values are shown at each point in time for men and women for epinephrine (*top*) and norepinephrine (*bottom*).

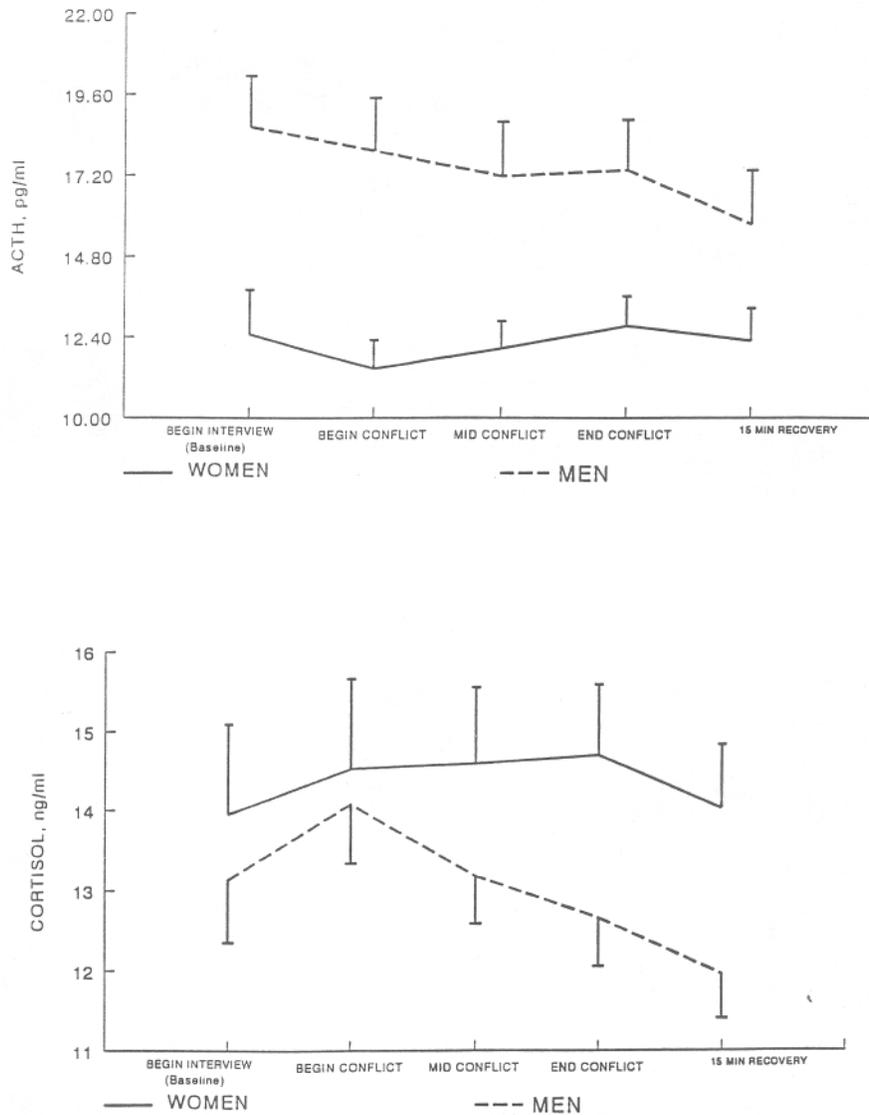


Fig. 2. Mean (\pm SEM) values are shown at each point in time for men and women for ACTH (top) and cortisol (bottom).

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 time couples were seen. Moreover, distressed couples' negative behaviors showed strong cross-situational consistency, despite discussion topic differences and sampling on two occasions (23). Indeed, couples' negative behaviors were so consistent and stable across both topics and situations that the authors described them as "more traitlike than statelike" (p. 476), in accord with communication deficit theories of marital distress. Other research has similarly confirmed the consistency of couples' negative behaviors (24).

Unhappy marriages are reliably characterized by negative affect, conflictual communication, and poor listening skills (4, 18-24). For these reasons, the MICS codes of greatest interest

were those that assessed negative behaviors (criticize, disagree, deny responsibility, excuse, interrupt, negative mind reading, noncompliance, put down, turn off, disapprove, and dysphoric affect); our negative escalation data included only these negative behaviors, not avoidant or positive behaviors. These negative behaviors are consistent with those used in prior studies (4-6, 18, 19, 23); see also Jacob and Krahn (19) for a discussion of classification strategies.

Psychological Assessment

The telephone version (25) of the Marital Adjustment Test (MAT), administered during the telephone screening interview, provided data on marital satisfaction (26). Widely used in marital research because of its reliability and validity in discriminating

satisfied and dissatisfied couples (26), lower scores indicate poorer marital satisfaction.

The short form of the Communications Patterns Questionnaire (CPQ; 27) was used to assess spouses' perception of their typical communication patterns during relationship problem discussions. Two items were summed that assessed the propensity for a constellation of negative behaviors (mutual blame, accusations, criticism, and threats), whereas three items assessed constructive communication strategies (e.g., suggesting possible solutions or compromises, expressing feelings). Three items were summed that assessed wife demand/husband withdraw communications, with three identical (role reversed) items for husband demand/ wife withdraw. Each item was rated from 0 (very unlikely) to 9 (very likely).

Two measures were administered on entry to the CRC to assess recent perceived stress and depression. The 10-item Perceived Stress Scale (PSS) (28) measured the degree to which subjects perceived their daily life during the prior week as unpredictable, uncontrollable, and overloading. The short version of the Beck Depression Inventory (29) provided information on the severity of depressive symptoms. The 13 items on the short Beck cover affective, cognitive, and vegetative depressive symptoms, with the severity of each symptom rated from 0 to 3.

Endocrinological and Immunological Assays

The ACTH, cortisol, and catecholamine assays were performed with well-established methods, described in detail elsewhere (5). ACTH levels were determined by an IRMA assay using materials supplied by Nichols Institute (Capistrano, CA). Plasma cortisol was assayed using a fluorescent polarization technique (TDX; Abbott Laboratories, Chicago, IL). The plasma catecholamine concentrations (NEPI and EPI) were determined by high-performance liquid chromatography (HPLC) using a Waters system.

The indirect immunofluorescence (IF) assay was used to measure antibody titers to EBV virus capsid antigen (VCA) immunoglobulin G (IgG), as previously described (6, 30). All slides were read blind coded.

Mononuclear cells from 30 cc of blood treated with heparin were separated using Hypaque-Ficoll density gradients, washed two times with Mg-, Ca-, and phosphate-free buffer, counted in a Coulter Counter, then used as described in detail elsewhere (6, 30). Lymphocyte proliferation was assessed in response to both concanavalin A (Con A) and phytohemagglutinin (PHA), with assays performed in triplicate. Mitogens were used at a final concentration of 2.5, 5.0, 10.0, and 20.0 µg/ml in complete RPMI 1640 media supplemented with 5% fetal bovine serum (FBS), as previously described (6, 30). The data were analyzed as counts per minute (cpm) in the stimulated samples minus the cpm for unstimulated samples (δ cpm). A base 10 logarithmic transformation was performed on the resulting values.

Sequential Analyses

Bakeman's (31) lag sequential analysis program, ELAG, was used to assess negative escalation across the 30-minute conflict task. In such analyses, the base rate or unconditional probability of a target behavior is compared to its conditional probability, i.e., the probability of the target behavior given the occurrence of a particular criterion behavior. This difference is then divided by an estimate of the SE of the difference, thereby expressing the relationship between the conditional and unconditional probab-

ilities as a z statistic. Positive z statistics indicate that the criterion behavior increases the likelihood of the target behavior (i.e., a facilitative effect), whereas negative z statistics indicate that the criterion behavior decreases the likelihood of the target behavior (i.e., an inhibitory effect). For example, in the case of negative escalation, the larger the z score, the greater the probability that a spouse responded to negative behavior in kind, one behavioral "signature" • ' of marital distress (12, 15, 16). We used lag 1 data (the immediate response of one spouse to the other) for our analyses; the z scores always reflect alternating patterns of wife-husband or husband-wife behavior.

Analysis of Change Using Multilevel Models

The primary focus of data analyses involved the study of a) individual differences in patterns of change in hormone levels during the conflict discussion, and b) the prediction of such individual differences as a function of psychological variables and aspects of the couples' interaction during the conflict. Multilevel models were used to address these questions. Such models have been used to study the structure of longitudinal data of many kinds, such as depression (32), psychological change in married couples (33), adolescent attitudes toward deviance (34), and human growth (35). In the current context, let y_{it} represent the measure for individual i at occasion t for any one hormone, and let x_t represent an index for the occasion, where $x_t = 0, 1, 2, 3, 4$ for the five measurement occasions. Then the hormone level is predicted as a linear function of time according to the model

$$y_{it} = \beta_{0i} + \beta_{1i}x_t + e_{it} \tag{1}$$

where β_{0i} is the intercept or initial level for individual i , β_{1i} is the slope or rate of linear change for individual i , and e_{it} is the error in predicting the hormone level from time and has variance σ_e^2 . By comparing this residual variance to a corresponding variance obtained from a baseline model, omitting time as a predictor, one can determine the proportion of variance in the hormone level accounted for by time. The intercept and slope in Equation 1 are considered as varying randomly across subjects, where this random variation is represented by .

$$\beta_{0i} = \beta_0 + r_{0i} \tag{2}$$

$$\beta_{1i} = \beta_1 + r_{1i} \tag{3}$$

Here β_0 and β_1 represent the mean intercept and slope (called fixed effects), respectively, and r_{0i} and r_{1i} represent the random variation of individual intercepts and slopes around their respective mean values. The variance of r_{0i} and r_{1i} , and their covariance, are represented as φ_{00} , φ_{11} , and φ_{01} , respectively. Fitting this model to sample data yields estimates of the means, variances, and covariance of the intercepts and slopes, as well as the residual variance σ_e^2 , along with significance tests for these parameter estimates. (This linear change model can be extended to a variety of nonlinear forms. A linear model was used in the present study due to the rather small number of measurement occasions. Efforts to fit a nonlinear model of change by introducing a quadratic effect of time in Equation 1 did not yield systematic interpretable results, and visual inspection of plots of individual raw data indicated that, with few exceptions, individual patterns of change could be reasonably well approximated using a linear model.) If there exists substantial variance in the intercepts and slopes, then it is potentially useful to attempt to explain some portion of that variance using variables measured on the individual subjects. In the present context we were especially interested in predicting

individual differences in slopes on various hormones, thus potentially identifying predictors of variation in endocrinological responsiveness to the conflict discussion. This was achieved by extending the model in Equations 2 and 3 by introducing predictor variables. Letting w_{i1} be the score for individual i on the MAT, w_{i2} be the z score for individual i on wife's negative escalation, and w_{i3} be the score reflecting frequency of negative behaviors by the couple during the conflict discussion, Equations 2 and 3 are extended as follows:

$$\beta_{0i} = \beta_0 + \gamma_{01}w_{i1} + \gamma_{02}w_{i2} + \gamma_{03}w_{i3} + r_{0i} \quad (4)$$

$$\beta_{1i} = \beta_1 + \gamma_{11}w_{i1} + \gamma_{12}w_{i2} + \gamma_{13}w_{i3} + r_{1i} \quad (5)$$

Here γ_{01} , γ_{02} and γ_{03} are weights for predicting the intercepts from the three background variables, and γ_{11} , γ_{12} , and γ_{13} are weights for predicting the slopes from the same three variables. Variances of r_{0i} and r_{1i} now represent the residual variance in the intercepts and slopes, respectively. i.e., variance not accounted for by the three background variables. Fitting this model to sample data yields estimates of the γ s as well as of all of the parameters specified in the earlier model, and corresponding significance tests. Variance accounted for by the background variables can be determined by calculating the reduction in the residual variance from Equations 2 and 3 to Equations 4 and 5.

These models were fit to data for husbands and wives separately, using each hormone in turn as the outcome variable. Model fitting was performed using the FILM software package (36).

This effort to represent and explain individual differences in patterns of change on each hormone gives rise to some related questions. For instance, are rates of change on different hormones related? Are husbands' and wives' rates of change on a given hormone related? Such questions can be addressed by extending the multilevel model described above to incorporate multiple response variables. A formal description of this extended model is well beyond the scope of the present article. Goldstein (35) presents a brief description, and a detailed presentation along with examples is given by MacCallum et al. (37). In the present study the multivariate multilevel model was used to evaluate

correlations between rates of change on different hormones and between spouse's rates of change on each hormone. These multivariate models were fit to data using the MLn program for multilevel modeling (38).

RESULTS

Endocrine Data

Table 1 presents results for HLM analyses of individual differences in patterns of change on EPI, NEPI, cortisol, and ACTH. The table contains a section for each hormone showing results of fitting a sequence of two models to measures on that hormone for wives and husbands separately. Within each such section the upper portion shows results for fitting a model represented by Equations 1 to 3 above. Results shown include the estimated mean and variance of the intercepts and slopes for both wives and husbands. Also shown is the estimated ratio of true parameter variance to total variance for intercepts and slopes; Bryk and Raudenbush (38) refer to this ratio as the "reliability" of the intercepts and slopes. The lower portion of results for each hormone in Table 1 includes the estimated regression weights for predicting intercepts and slopes using MAT and negative escalation. Based on literature that suggests that distressed wives are more likely than distressed husbands to respond in kind to negative messages (15, 16), we used the husband negative/wife negative z scores. However, the two negative escalation z scores (husband negative/wife

TABLE 1. Results of HLM Analyses

	EPI		NEPI		Cortisol		ACTH	
	Wives	Husbands	Wives	Husbands	Wives	Husbands	Wives	Husbands
Level 1 model								
Intercept Mean	28.68**	34.92**	486.76**	399.78**	14.29**	13.76**	14.03*	18.65**
Slope Mean	-1.69**	-2.20**	41.77**	24.84**	.04	-.38	.08**	-.65
Intercept Variance	101.90**	147.34**	24139.06**	16515.31**	36.54**	15.05**	25.64**	59.33**
Slope Variance	1.34	40.98*	1223.79**	992.95**	.70**	1.32**	2.66**	3.98**
Intercept Reliability ^a	.79	.83	.86	.84	.96	.92	.82	.87
Slope Reliability ^b	.23	.39	.65	.66	.74	.86	.74	.74
Level 2 model								
Intercept Model								
Intercept		36.22	455.46*	436.23	11.25	16.80*	14.31*	19.31
MAT		-.04	-.16	-.39	.01	-.02	-.03	-.02
Negative Escalation		-3.86	-54.62	-11.59	-1.43	-.05	-1.92*	-1.49
Slope Model								
Intercept		-8.19	135.41**	148.72*	.16**	-.56	1.15	-3.02
MAT		.05	-.79*	-.96	.00	-.01	.01	-.02
Negative Escalation		.46	-3.20	1.95	.37*	.07	.67*	.02

^a Ratio of parameter variance to total variance, intercept.

^b Ratio of parameter variance to total variance, slope.

* $p < .05$; ** $p < .01$.

negative, wife negative/husband negative) were significantly correlated ($r = .84, p < .001$); the use of wife negative/husband negative z score for husbands did not alter the nonsignificant HLM analyses for husbands, described below. Because spouses' negative behavior frequencies were also significantly correlated ($r = .85, p < .001$), we followed previously used procedures (5, 6) by summing the couples' negative behavior frequencies to produce a single measure. Results are not shown for frequency of negative behavior as a predictor of intercepts and slopes because inclusion of this measure as a predictor did not yield any significant effect on slope for any hormone for either husbands or wives.

Our first attempt to fit the model in Equations 1 to 3 to EPI data for wives resulted in an improper solution, with a parameter estimate well outside of its logical bounds. Inspection of detailed results and of raw data revealed a single outlier, a subject with a highly deviant slope and intercept. Removal of this subject resulted in a successful analysis, with results reported in Table 1. The linear effect of time on EPI levels accounted for 17.8% of the variance in EPI for wives and 30.8% for husbands. Thus, a linear change model explains a moderate portion of the variance in this hormone. Parameter estimates show a significant mean rate of linear change in EPI for both wives and husbands, with wives' EPI level declining an average of 1.69 units per occasion of measurement from an initial level of 28.68, and husbands' EPI level declining an average of 2.20 units per occasion of measurement from an initial level of 34.92. Reliability estimates for slopes are rather low in both groups, indicating that much of the observed variance in slopes is attributable to sampling variance rather than true parameter variance. Furthermore, the slope variance for wives is not significant, indicating an absence of significant variation in rate of linear change in EPI for wives; husbands' slope variance is significant. Because of the nonsignificant slope variance for wives, Level 2 results for wives are not included in Table 1. Level 2 results for prediction of husbands' slopes from MAT and negative escalation show neither predictor to have a significant weight. Less than 1% of the variance in EPI slopes for husbands was accounted for by these predictors.

Considering next the results for NEPI, the linear effect of time accounted for 52.1% of the variance in NEPI for wives and 43.1% for husbands. Level 1 results in Table 1 show significant mean rates of linear change in NEPI for both husbands and wives. Wives' mean rate of increase during conflict discussion is estimated at 41.77 units per occasion of

measurement from an initial level of 486.76: husbands' corresponding estimates are 24.84 units per occasion from an initial level of 399.78. Reliability estimates for both coefficients in both groups are substantial, indicating that much of the observed variance in intercepts and slopes is due to parameter variance. Level 2 results show a significant weight for MAT in prediction of NEPI slopes for wives, and no significant weights for prediction of husbands' slopes. Variance accounted for in NEPI slopes by the Level 2 model is 17.23% for wives and 8.99% for husbands.

Considering corresponding results for cortisol, it was found that the linear effect of time accounted for 40.0% of the variance in cortisol for wives and 61% for husbands, again indicating substantial variance explained by a linear change model. Level 1 results in Table 1 show nonsignificant mean slopes for both wives and husbands, but significant variances, indicating significant individual differences in slopes. Reliabilities of intercepts and slopes are again substantial. Level 2 results for cortisol show negative escalation having a significant weight in the prediction of wives' cortisol slopes, but neither MAT nor negative escalation having significant weights for prediction of husbands' slopes. The Level 2 model was found to account for 21.3% of the variance in wives' slopes and 0% of the variance in husbands' slopes.

For ACTH it was found that the linear effect of time accounted for 40.3% of the variance in ACTH for wives and 42.2% for husbands. Table 1 shows nonsignificant mean slopes for both wives and husbands, but significant variance, again indicating significant individual differences in slopes. Reliabilities for intercepts and slopes were again found to be substantial. Level 2 results show significant weights for negative escalation in predicting wives' slopes, but no significant weights for the predictors of husbands' slopes. The Level 2 model was found to account for 15.99% of the variance in wives' ACTH slopes and 0% of the variance in husbands' ACTH slopes.

To summarize results for multilevel modeling of change in each hormone, it was found that the linear effect of time explained substantial portions of the variances in all four hormones, indicating significant linear change. For all analyses except wives' EPI, results showed significant variance in slopes, indicating significant individual differences in rates of linear change in hormone levels during the conflict discussion. Figures 1 and 2 show the average change in each hormone over time. The attempt to explain this variation using a Level 2 prediction model

showed significant effects of either MAT or negative escalation on wives' slopes for KEPI, cortisol, and ACTH, but no such effects for husbands. However, it should be noted that tests of the difference between husbands' and wives' coefficients for the effect of MAT on KEPI slopes, and the effect of negative escalation on cortisol and ACTH slopes, showed those gender differences to be nonsignificant. Nevertheless, the Level 2 model explained much higher portions of wives' slope variance for KEPI, cortisol, and ACTH than of husbands' slope variance. Thus, these analyses show clear evidence for change in hormone levels during the conflict discussion, as well as for individual differences in rates of change, and some indications that those individual differences may be related to negative behaviors and attitudes, with those relationships possibly being stronger for wives than for husbands.

Endocrine data were next analyzed using multivariate multilevel models to study relationships between rates of change on different hormones, as well as relationships between rates of change for husbands and wives. Analysis of three hormones, excluding KEPI because of the nonsignificant variance of slopes for wives, resulted in nonsignificant correlations of .08 between ACTH and NEPI slopes and .20 between NEPI and cortisol slopes. However, a significant correlation of .87 was found between ACTH and cortisol slopes, indicating a very strong association between rates of linear change during the conflict discussion for these two hormones, consistent with their biological substrates. A similar approach was used to study husband-wife slope correlations on each hormone. Nonsignificant correlations between husband and wife slopes were found for ACTH (.37) and NEPI (.03). A substantial and significant correlation of .62 ($p < .05$) was found between husband and wife slopes on cortisol, indicating an association between rates of linear change on cortisol during the conflict discussion for matched pairs of husbands and wives.

Immunological Analyses

Immunological data were first analyzed in multiple regression analyses using the same three variables as the HLM analyses: MAT score, the couple's frequency of negative behaviors, and negative escalation. These regression analyses with EBV antibody titers and proliferative responses to PHA and Con A (using the average of the two peak concentrations for each mitogen assay) as dependent variables did not produce significant models for any variable.

However, following prior work (6, 30), we were also interested in possible psychological differences between individuals who showed a pattern of higher or lower immune functioning across assays, reversing the direction for EBV antibody titers (7). Thus, subjects whose values were above the median for their gender for at least two of the three assays were designated "high immune response," whereas remaining subjects were called "low immune response."

These high and low immune response groups differed significantly in the frequency of negative behaviors displayed during conflict. High immune response subjects displayed significantly fewer negative behaviors during conflict than low immune response subjects, $F(1,50) = 5.66, p < .03$, with no differences related to gender or the interaction between gender and immunological group, $F_s < 1.01$. Low immune response subjects displayed an average of 56.33 (SEM = 4.95) negative behaviors, compared with 38.59 (SEM = 5.64) for high immune response subjects. Analyses for MAT scores and negative escalation, the other two variables included in the regression analyses, showed no significant main effects or interactions, $F_s < 1.80$.

In accord with the group differences in frequency of negative behavior, high and low immunological groups also differed in their perceptions of typical communication patterns during relationship problem discussions. A MANOVA that included the four CPQ scales showed a significant multivariate difference between immunological groups, $F(4,47) = 2.70, p < .05$, but not gender, $F < 1$, or the interaction between group and gender, $F(4,47) = 1.86$. Subsequent univariate comparisons showed that high immune function subjects reported that they were less likely to engage in negative behaviors than low immune subjects, $F(1,50) = 6.40, p < .02$; low immune response subjects had a mean of 5.00 (SEM = 0.58) for likelihood of negative behaviors, compared with 3.37 (SEM = 0.33) for high immune response subjects. Similarly, low immune response subjects had a mean of 9.44 (SEM = 0.80) for the three items tapping the likelihood of husband demand/wife withdraw, compared with 7.19 (SEM = 0.72) for high immune response subjects, $F(1,50) = 4.87, p < .04$. Univariate analyses revealed no differences in constructive behaviors or wife demand/husband withdraw, $F_s < 1$.

Additional analyses were conducted to assess the possibility that these immunological groupings might reflect differences in age, stress or depressive symptoms, or health behaviors. Importantly, individuals in the high and low groups did not show even marginal differences on age, $F < 1$, with a mean of 65 for both

groups. Neither immunological group, gender, nor their interaction was related to scores on the PSS and Beck. $F_s < 1$. For women, use of estrogen supplements was unrelated to immune group, $\chi^2 < 1$. Immunological groups were not related to body mass, caffeine intake, frequency of vigorous physical activity, or alcohol intake. and there were no significant gender by group interactions, all $F_s < 1$. Thus, lower immune response subjects described their marital disagreements as more negative on the CPQ, and they displayed more negative behaviors during conflict than subjects in the higher immune response group. and these differences were not related to affect, age, or health behaviors.

MICS-Coded Behavior and Self-Report Data

As expected, marital satisfaction as measured by the MAT was inversely related to higher frequencies of negative behavior, $r = -.33, p < .05$, as well as greater escalation of negative behavior, $r = -.31, p < .05$. The Communications Patterns Questionnaire (CPQ) (27), completed before the conflict discussion, was used to assess spouses' perceptions of their typical communication patterns during relationship problem discussions. The two CPQ items that were summed to provide a total for negative behaviors showed significant relationships with the frequency of MICS-coded negative behavior during conflict $r = .41, p < .01$. In addition, lower marital satisfaction was associated with greater self-reported negative behavior on the CPQ, $r = -.44, p < .01$. Thus, reports of "typical" conflict behaviors were significantly related to observed behavior, as well as marital satisfaction.

DISCUSSION

Results provide clear evidence for endocrine change during the conflict discussion, as well as for individual differences in rates of such change. Efforts to account for such individual differences using measures of marital satisfaction and negative escalation showed evidence for relationships of these variables to endocrine change, consistent with data from our studies of newlywed couples (5, 8). Among wives, lower marital satisfaction and greater negative escalation accounted for 16% to 21% of the variance in the rates of linear change of NEPI, cortisol, and ACTH over the course of the conflict discussion and 15-minute recovery period. In contrast, husbands' rates of linear change in hormone levels

did not show significant relationships with negative behavior or marital quality and showed much lower variance explained by those variables. Although several studies have shown that wives experience greater and more persistent physiological change associated with marital conflict than husbands (4-6, 8-10), the absence of statistically significant gender differences in these coefficients must moderate statements about gender differences for this sample.

Immunological data were also related to conflict behaviors. Both men and women who showed relatively poorer immunological responses across three functional assays displayed more negative behavior during conflict; they also described their usual marital disagreements as more negative.

In our earlier study of 90 newlywed couples, we found pervasive differences in endocrine and immune function associated with negative behaviors during marital conflict. Importantly, these differences were apparent even among very happy couples in their first year of marriage who had been selected on the basis of extremely stringent mental and physical health criteria (5, 6, 8). Similarly, the older couples in this study were, on the average, quite happy in marriages that had lasted for decades; only 13% of our older subjects in this study scored below 100 on the MAT, the traditional cutoff for marital distress (26). Moreover, in accord with the age-related diminution in negative behaviors described by Carstensen et al. (12), the older couples in this study exhibited 31% fewer negative behaviors and 20% more positive behaviors during the half-hour conflict than our newlywed sample. Despite these relative advantages, marital satisfaction and negative behavior during conflict showed significant relationships to endocrine and immune measures among this older adult sample, consistent with data from newlyweds.

Stress-related immunological alterations are likely to have greater health consequences for older adults than younger adults. Older adults have greatly increased morbidity and mortality from infectious illness as a consequence of normal age-related immunological down-regulation (40, 41). Furthermore, age and distress seem to interact to promote immune down-regulation: older adults show greater immunological impairments related to stress or depression than young adults (42, 43). Accordingly, troubled marriages might increase risk among older couples to a greater extent than young couples.

Other recent data from our laboratory have highlighted potential health consequences of chronic stress for older adults. We found large differences in both the antibody and virus specific T-cell responses

to influenza vaccination when we compared spousal caregivers for dementia sufferers and well-matched controls (44). Influenza and pneumonia are major causes of morbidity and mortality among older adults (40, 45); thus, it is of particular concern that older adults who show poorer responses to influenza vaccine and other antigenic challenges also experience higher rates of clinical illness, including influenza virus infection (40, 45).

Furthermore, stress-related immunological down-regulation has additional health implications beyond infectious disease: the immune system plays an important role in the wound healing process. We have also found that dementia caregivers showed a diminished pro-inflammatory cytokine response compared with controls, as well as slower wound repair (46); caregivers took an average of 9 days longer to heal a 3.5-mm punch biopsy wound than controls, i.e., 24% longer to repair a small, standardized wound. Consequently, stress-related alterations in immune function could have health repercussions across several domains, particularly among older adults.

Although the data from this study suggest that abrasive marital interactions may have endocrinological and immunological correlates among older adults, we do not have evidence of any health problems in this sample: we deliberately selected healthy couples and we only studied them at a single point in time. These older couples were generally quite happy, and their marriages had been quite stable and enduring (lasting an average of 42 years). Thus, although it is likely that these data underestimate the actual physiological impact of marital discord among older adults, they do provide a window on how such effects could be mediated. Close personal relationships clearly have important physiological correlates, in accord with the growing evidence demonstrating relationships between social support and physiological processes (47).

The study was supported in part by National Institute of Mental Health Grant MH44660, National Institutes of Health General Clinical Research Center Grant M01-RR-0034, and Ohio State University Comprehensive Cancer Center Core Grant CA16058.

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Multilevel Statistical Models for Psychosomatic Research

Psychosomatic medicine concerns the "impact of emotion, life events, social connectedness, and personality on normative physiology and pathophysiology (1)." For many research questions, a mere snapshot of an ongoing physiological process is inadequate, because it provides limited insight into the effects of personal and social factors on that process. One should aspire to observe the process as it unfolds and changes in response to social and psychological stimuli. However, organizing and understanding the data generated by an ongoing physiological process presents significant challenges. Recent improvements in computer technology and statistical methods now make it easier to address questions that require more than just a single snapshot of an unfolding process.

Kiecolt-Glaser et al. (2) study changes in the endocrine and immune systems of married couples during an experimental conflict resolution task. In their setup, endocrine measurements taken before, during, and after the experimental task are analyzed by a "multilevel model".¹ This model describes the time course of the average concentration of an endocrine variable. It describes how the time courses of individual subjects differ from one another, and it accounts for the effects of personal and situational factors on those individual courses. This model is carefully described by the authors, and a few minutes spent studying that description is rewarded by being able to interpret and appreciate the results in their Table 1.

The row labeled "Slope Variance" in their Table 1 is of special interest, because it quantifies the degree to which individuals differ in their response to the experimental task. Consider that the husbands' norepinephrine "Slope Variance" of 993 corresponds to a SD for the slopes of 32 (pg/ml per observation period) and compare this to the "Slope Mean" of 25 (pg/ml per observation period). The typical increase in norepinephrine is substantial across the four

observation periods, but there are some husbands whose increase is more than twice that and some who experience a substantial decrease. Thus, the experimental task is found to have substantially different effects on changes in the norepinephrine levels of different husbands, and this gives impetus to the search for factors that account for these individual differences. That search is performed in the Level 2 model, which estimates the effects of "negative escalation" and the Marital Adjustment Test. It happens that neither variable has a significant effect for husbands' norepinephrine levels. However, this negative finding does not reduce interest in the experimental model, because the "Slope Variance" showed that there are substantial individual differences, and some explanation of those differences is worth pursuing.

In addition to exploring the impact of social and behavioral factors on endocrine response, one can study the relationship between different response domains using multilevel models. Indeed, the authors do this elsewhere--studying the relationship of the responses of different hormones as well as the relationship of the responses of husbands to those of their wives. As a consequence, they have a better understanding of the impact of the experimental task than one obtains from the usual plots of means and SDS of the response variables.

The approach that Kiecolt-Glaser et al. (2) take to their data is made possible by recent developments in statistical methods (Gibbons et al. (3) review these for psychiatry researchers), by the availability of computer programs (4) that implement those methods, and by textbooks on these methods aimed at researchers and applied statisticians (5-7). Although these methods find application in such diverse areas as animal breeding research and seismology, their principal use in medical research is to estimate and summarize *person-specific effects* such as the endocrine response to a conflict resolution task. Often such person-specific effects (responses) are not directly measured but are inferred from the pattern seen in a series of measurements. In psychosomatic research, the patterns of most interest are often physiological responses to social or behavioral stimuli. And often, the variability of individual measurements makes it hard to determine whether apparent

¹ There are many terms used to describe this type of model: Multilevel model, hierarchical linear model, empirical Bayes model, random coefficient regression model, mixed linear model, and more. The multilevel model extends the familiar, classical models for linear regression and analysis of variance.

differences among patterns reflect true differences in the people studied or are merely chance artifacts. With multilevel models, the investigator can test for the presence of true differences among individuals and characterize their magnitude.

Experimental stimuli are often used to induce responses, but responses to naturally occurring stimuli can also be studied. Field studies pose special challenges, because the stimuli do not occur on a set schedule. Further difficulties are imposed by occasional missed measurements or irregularly timed measurements. Until fairly recently, such difficulties might have been dealt with by ad hoc methods such as omitting cases with missed measurements from the analysis, pretending that irregularly timed measurements were collected according to a regular schedule, and ignoring nuisance variation in measurements. At their best such ad hoc methods amount to discarding precious data; at their worst these methods distort the available data. By comparison, multilevel models provide a solid framework for characterizing responses using data from field studies. The investigation by Rose and Fogg (8) provides an example of some of the challenges of conducting psychosomatic field studies and the application of multilevel statistical models to those challenges. They studied the behavioral and physiological responses of air traffic controllers to variations in workload. In addition to documenting individual differences in responsiveness, they showed that the responses in different domains (i.e., cardiovascular, endocrine, and behavioral) were independent of one another.

Many advances in medical research have depended on improvements in the technology used to collect data and parallel improvements in the technology used to analyze those data, such as linkage analysis for the study of genetic determinants of

disease or survival analysis for studies of chronic disease risk factors and cancer therapies. It is becoming possible to collect extensive data on physiological response to social, behavioral, and environmental stimuli. Multilevel statistical models expand the analytical toolkit of researchers in psychosomatic medicine and will foster better understanding of those data.

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