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Social Networks and Immunosuppression During Stress: Relationship Conflict or Energy Conservation?

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Abstract

Despite the apparent health benefits of social relationships, some studies indicate that larger social networks can be associated with greater vulnerability to infectious disease, particularly if stressors are also present. Two possibilities for such effects are, first, that more social contacts lead to more negative affect and social conflict during stressors, or second, that maintaining more social contacts is an energetically costly activity, and ecologically motivated immunosuppression is one means of providing energy to maintain social resources. First-year law students (N = 76) completed questionnaires and had delayed-type hypersensitivity skin tests at five time points during their first 6 months of law school. Both moving away from home and a smaller social network associated with larger DTH responses (both $p < .05$) across all time points. However, negative affect, either broadly defined or as specific affects (hostility, sadness, guilt), did not mediate social network effects, suggesting that negative affect and social conflict are less plausible explanations than ecological immunosuppression. Ecological models would predict that temporary immunosuppression is less harmful to health in the long run than loss of social resources.

Social relationships seem to yield significant health benefits, with the mortality risk of a small social network approximately equaling that for cigarette smoking (House et al., 1988). One potential pathway between social connectedness and clinical health is physiological: higher social support is associated with lower tonic blood pressure, reduced cardiovascular reactivity, and higher functional immune assays (e.g., natural killer cell cytotoxicity) and, conversely, loneliness is associated with elevated cortisol and lower functional immune assays (see Cacioppo et al., 2000; Uchino et al., 1996; for reviews). Beneficial effects of social relationships extend to non-human animals. For example, juvenile macaques separated from their mothers had higher lymphocyte proliferative responses if they were housed with conspecifics with whom they had "significant, complex relationships" than if they were housed alone; furthermore, proliferative responses were positively correlated with degree of affiliation with others during the separation (Boccia et al., 1997, p. 193).

However, there are some notable cases in which a larger number of social relationships negatively correlated with immunity and health. Miller and Cole (1998) reviewed 10 studies of social relationships and HIV progression. In these studies, loneliness and other measures of low emotional satisfaction with social relationships associated with faster HIV progression. However, larger social network size and other measures of greater social integration such as intent to participate in social activities and greater affinity with social networks also associated with faster progression. An interaction between stress and social connectedness was observed

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among healthy college students experiencing multiple negative life events, who had significantly higher numbers of upper respiratory infections if they had more diverse social networks, a social measure that correlates highly with total number of social relationships (Hamrick et al., 2002). One possibility raised in the latter study is that social connectedness provides more opportunities for infection; combined with immune changes associated with negative life events (Segerstrom and Miller, 2004), these opportunities could result in more clinical infections. However, HIV studies that controlled for sexual contacts still found that social integration predicted disease progression (Miller and Cole, 1998).

What, then, accounts for negative relationships between social integration and immunity, particularly under stress? Two possibilities arise. The first is that the quality of social relationships changes under stress. For example, one of the main consequences of negative life events is negative affect such as depression. In turn, negative affect can adversely impact relationships (Strack and Coyne, 1983). Adverse changes in relationships can reciprocally increase negative affect and, importantly, negatively toned relationships can also impact the immune system (Kiecolt-Glaser, 1999). Therefore, the relationship between greater integration and worse immune function could be accounted for by a larger number of social relationships that “go sour” under stress, more pervasive interpersonal conflict, and more negative affect.

The second possibility is energetic rather than affective. Ecological immunology posits that in light of finite sources of energy, immune function can and perhaps should be compromised in the service of maintaining or attaining important resources (Barnard and Behnke, 2001; Segerstrom, in press). In murine models, for example, immunity was compromised when animals had the opportunity to gain social or physical resources such as mating opportunities or nestboxes (Barnard and Behnke, 2001). Given that both the immune system and social relationships take energy to maintain, there may be situations in which the human immune system is downregulated in order to make energy available to pursue and protect social resources. Primates, including humans, are highly dependent on social relationships to survive and thrive, and so it seems plausible that ecological mechanisms that shifted energy away from immunity to support social activity would be conserved during the evolution of higher mammals. Unlike the case of social conflict, however, ecological immunosuppression may not be associated with negative affect. Affective changes are not typically observed after difficult goal pursuit in the lab, although increased fatigue is occasionally but not consistently reported (e.g., Baumeister et al., 1989). In naturalistic settings, the resource maintenance and growth resulting from goal pursuit are likely to protect against distress (Hobfoll, 1989).

The present study reports on the relationships among social network parameters, affect, and delayed-type hypersensitivity skin test results (DTH) in first-year law students. The first year of law school is extremely stressful for students, and one source of that stress is the degree to which law school takes time and energy away from maintaining relationships with friends and family outside of law school (Segerstrom, 1996). Therefore, law school is a model situation for studying a potential energetic trade-off between immunity and social pursuits during a stressor. Analyses tested the prediction that larger social networks would be inversely associated with DTH response during the stressful first year of law school. The DTH skin test provides an in vivo assessment of cellular (Th1) immune responses, such that larger indurations reflect more robust cellular immunity. Further analyses then tested whether negative affect could mediate between social network parameters and DTH (c.f., Segerstrom, 2006). If stress contaminates social relationships, then one would expect negative affect to mediate any inverse relationship between social connectedness and immunity; however, if stress results in ecological immunosuppression in order to maintain relationships, mediation by negative affect is less likely.

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Method

Subjects

Subjects were 76 first-year law students from three consecutive entering classes. They were nearly equally male (47%) and female (53%). The majority was Caucasian (86%), with the remainder African-American (10%), Asian-American (1%), or multiple races (3%). Mean age was 24.4 years (SD = 3.3). The majority was unmarried (68%), with the remainder divorced (8%), married but not living together due to law school (3%), or married and living together (21%). Six percent had children. Academically, they were representative of the law school as a whole, with a median LSAT score of 160 and interquartile range of 5 (law school median for same years, 160, interquartile range, 6) and median undergraduate GPA of 3.60 and interquartile range of 0.50 (law school median for same years, 3.56, interquartile range, 0.51). Approximately half (53%) relocated to attend law school.

Method

During the summer before their first year of law school, all matriculating students were sent information about the study and screening materials to be returned if they were interested. Eligible students were in good mental health (e.g, no psychotropic medication, no self-reported history of impairment of function for 2 weeks or more), physical health (e.g., no immunologically mediated disease, no contraindications for skin testing, no immunotropic medication), and did not report substantial substance use (e.g., more than two drinks of alcohol every day). They were subsequently contacted by telephone to be enrolled into the study and scheduled for their initial visit.

At each of 5 waves (beginning of first semester, middle of first semester, finals week, beginning of second semester, middle of second semester), students completed questionnaires (including the Measures below) and were given a DTH skin test. The five time points reflected five qualitatively different law school experiences. Although experience naturally varied across students, they generally represented, respectively, the anticipation of entering law school, uncertainty about performance, examination stress, the return of first-semester grades, and the beginning of interviews for summer internships. Table 1 given the means and standard deviations for study variables across the five waves. Participants were paid $50 for their participation at each wave. After accounting for missing data, drop-outs, and excluded data (see Controls below), the 76 students yielded 317 observations for analysis.

Measures

Social network parameters—Social network size was operationalized with two variables. The first variable was whether or not the student was relocated, that is, he or she moved away from home to go to law school, versus resident, that is, did not move away from home. Relocation can reduce the magnitude of social goals and obligations, and so students who relocate may have fewer opportunities for negatively toned social contacts, fewer energetic demands from their social networks, or both. Relocation was measured by self-report at the first time point. In order to confirm that relocation was associated with reduced network demands, goal descriptions collected at selected waves from the second and third cohorts (n = 58) were examined. Among resident students, 24 goals concerned relationship initiation or maintenance. Among relocated students, there were 29 such goals. The proportion of these goals having to do with new relationships (e.g., “meet new people”) was only somewhat higher among relocated students (45% vs. 33% for residents), and the proportion having to do with staying in touch with others (e.g., “keep up with my friendships”) was also somewhat higher among relocated students (38% vs. 25% for residents). However, the proportion having to do with spending time with others (e.g., “make time for friends and family”) was markedly higher among resident students (42% vs. 17% for relocated). These descriptive data suggest that being

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resident was, in fact, associated with more social goals and obligations having to do with spending time with others (cf., Segerstrom, 2006).

The second variable was network number from the Social Network Index (Cohen et al., 1997). This variable reflects the total number of people with whom the individual has contact in a 2-week time frame. In addition, social network diversity was operationalized with network diversity from the Social Network Index. This variable reflects the number of roles in which the person has any social contact in a 2-week time frame. Because network size but not diversity should increase immunosuppressive effects of social networks, network diversity allows for a critical test of the specificity of the effects of network size on immune function. However, it should be noted that network number and diversity were positively correlated at all time points ($r = .52 - .83$), and so the critical test becomes the effects of diversity above and beyond network number (and vice versa). The Social Network Index was administered at each time point.

Negative affect—Affect was measured with the PANAS-X (Watson and Clark, 1994), which was administered daily for 3 days (the day preceding and two days of the skin test assessment) at each time point. Alpha reliability for all subscales was >.72 for across the three days, and so each time point was represented by an average of the scores over the three days. The PANAS-X yields scores for negative affect (NA) and specific negative affects including sadness, hostility, guilt, and fatigue. The global negative affect measure used for this study was the mean of the NA and sadness subscales; the original PANAS NA scale (Watson et al., 1998) has been criticized for not including low-arousal negative affect, and including sadness ensures that both high- and low-arousal negative affect is represented. In addition to this global negative affect variable, specific affects that can be associated with negatively toned social interactions (i.e., sadness, guilt, and hostility) and possibly with difficult goal pursuit (i.e., fatigue) were tested.

DTH—Cellular immunity was measured at each time point by delayed-type hypersensitivity responses to Candin skin test antigen (ALK Laboratories, Wallingford, CT), a preparation of *Candida albicans* yeast. A nurse injected 0.1 ml of Candin intradermally in the participant's nondominant arm. Induration was measured 48 hours later using the ballpoint pen method (Longfield et al., 1984). All skin test administrations and readings took place between 7 and 10 am to control for diurnal variation.

Controls—Control variables were assessed at each time point (except sex, age, marital status, and parental status). Data from 6 time points (4 subjects) were excluded for use of idiosyncratic medications and drug use (e.g., benzodiazepine, marijuana, narcotic) at that time point. Other potential person and behavioral influences on DTH responses were examined, including sex, age, marital status (living with spouse vs. unmarried, separated, divorced), parental status (with vs. without children), menstrual phase, 6 types of prescription medication (antihistamine, antibiotic, topical steroid, hormonal birth control, acid inhibitor, antidepressant, and decongestant), alcohol use, caffeine use, smoking, exercise, cold symptoms during the 48 hours of the skin test, and acute allergy or asthma symptoms during the 48 hours of the skin test. Only sex and caffeine use were significantly associated with induration size, with female sex ($p < .0001$) and higher caffeine use ($p < .03$) associated with larger induration. However, controlling for these factors did not substantively affect the results reported below, except that the effect for social network size was notably increased after controlling for caffeine use. Therefore, these controls are not discussed further. All analyses controlled for antigen batch, which varied between but not within participant cohorts.

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Analysis

The data were analyzed using multi-level models and SAS PROC MIXED. The multi-level models allowed social network parameters, affect, and immunity to covary both within-subjects (level 1) and between-subjects (level 2). The level 1 model specified that induration size (Y_{ij}) was a function of person j's intercept (β_{0j}), a slope associated with social network number across all waves (β_{1j}), and an error term (R_{ij}).

$$Y_{ij} = \beta_{0j} + \beta_{1j}(\text{network size}_{ij}) + R_{ij}$$

The level 2 model specified that the differences in induration size between people after including the effects of network size (i.e., β_{0j}) was a function of a grand mean (γ_0), differences in relocation (γ_{01}), and an error term (U_j), constraining the effect of social network size to be the same across people (γ_{10}). The constraint was justified by the lack of significant variation in this parameter when it was modeled as a random variable ($\tau^2 = 0.34$, SE = 1.12). This was, therefore, a *random intercept* model.

$$\beta_{0j} = \gamma_{00} + \gamma_{01}(\text{relocation}_j) + U_j$$

$$\beta_{1j} = \gamma_{10}$$

Therefore, in the complete model, the fixed parameters to be estimated were γ_{00} (the intercept), γ_{10} (effect of network size), and γ_{01} (effect of relocation).

$$Y_{ij} = \gamma_{00} + \gamma_{10}(\text{network size}_{ij}) + \gamma_{01}(\text{relocation}_j) + U_j + R_{ij}$$

Gamma weights, the estimates reported, are analogous to unstandardized beta weights (i.e., mm change in induration associated with the group difference or a 1-unit change in the predictor; because continuous predictors were standardized before analysis, the unit change is equivalent to 1 SD). Extensions of this model included between- (e.g., sex) and within-subjects (e.g., caffeine use) controls, additional predictors (e.g., network diversity), and exploration of variance with regard to between-subjects and within-subjects effects. Because network size has both person j and wave i variance, it can explain both between-subjects and within-subjects variance. To separate these sources of variance, the network size variable was divided into the mean network size for each person j and deviations from that mean at each wave i, with the deviation score associated with the level 1 equation and the mean score associated with the level 2 equation.

Results

Social networks and cellular immunity

Consistent with predictions, both relocation and social network number were associated with smaller indurations, that is, less robust cellular immunity. With both predictors in the model and controlling for antigen batch, resident students had predicted DTH indurations 2.69 mm smaller than relocated students (SE = 1.36, t (240) = -1.98, $p < .05$). With regard to social network number, each additional standard deviation increase in social network number predicted 0.94 mm smaller indurations (SE = 0.40, t(240) = -2.35, $p < .05$). Separating within-subjects and between-subjects variance in social network number, the effect was primarily due to changes in social network number over time. Between-subjects mean differences were associated with nonsignificantly smaller (-.42 mm) indurations (SE = 0.94, t(240) = -0.44, $p > .05$), but within-subjects changes were associated with significantly smaller (-1.10 mm) indurations (SE = 0.45, t(240) = -2.47, $p < .05$). An additional model tested for the interaction between relocation and social network size, but the interaction was not significant. Therefore, relocation and social network number independently predicted immunity. Furthermore, these

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effects were consistent across all assessments, as there was not a significant interaction between relocation or network number and assessment time.

Figure 1 shows predicted DTH induration size for resident and relocated students crossed with large (+1 SD) or small (-1 SD) social network number. Resident students with large social networks had the smallest DTH responses, whereas relocated students with small social networks had the largest DTH responses.

Network diversity, however, did not significantly predict cellular immunity. After controlling for both measures of social network size, there was a nonsignificant tendency for more social network diversity to predict larger induration, with each standard deviation increase in social network diversity associated with 0.87 mm larger indurations (SE = 0.56, t(238) = 1.55, $p > .05$). Both measures of network size remained significant predictors; if anything, their effects increased after controlling for social network diversity.

The role of affect

A possible role for negative affect in these relationships was tested by adding total negative affect to the model first; supplemental models tested specific negative affective states that could be associated with negatively toned relationships, specifically, hostility (e.g., “angry”, “hostile”), guilt (e.g., “guilty”, “ashamed”), and sadness (e.g., “sad”, “alone”, “lonely”). None of these affective states individually predicted DTH (all $t < 1$), and, therefore, none accounted for the effects of social network size on DTH. Likewise, fatigue neither predicted DTH ($t < 1$) nor accounted for the effects of social network size. Therefore, the effects of social network size appeared to be independent of affect.

Discussion

Despite the apparent health benefits of social relationships, some literature indicates that larger social networks can be associated with poorer immunity and greater vulnerability to infectious disease, particularly if stressors are also present (Hamrick et al., 2002; Miller and Cole, 1998). In this sample of first-year law students experiencing various stressors associated with law school, social network size was inversely related to cellular immunity as measured by DTH response. These data suggest that increased susceptibility to infectious disease with more social contacts (Hamrick et al., 2002; Miller and Cole, 1998) is not only an effect of exposure to pathogens: immunity may also be compromised.

Two possible mechanisms for such compromise include social discord, the magnitude of which could be higher with more social contact, or ecological immunosuppression occurring in support of social resource maintenance. Because discord but not ecological changes should be associated with negative affect, these data favor the ecological interpretation. Distress, either broadly conceived as negative affect or narrowly conceived as hostility, sadness/loneliness, or guilt, did not predict DTH response and did not account for the effects of social network size. Furthermore, post hoc analyses indicated that network size was not related to distress. Although the quality of relationships may have deteriorated during law school with affective consequences, the quantity of relationships appeared not to be related to any such deterioration. Alternatively, there may have been affective consequences specific to interpersonal interactions, but if there were such effects, they were not of sufficient magnitude to influence daily affect.

Quantity of relationships could be logically related to the amount of energy required to maintain those relationships. Ecological models of stress, resources, and immunity predict decrements in immunity when finite energy is tapped to pursue or protect important resources. It has been argued that frequent, ongoing social contact represents one of the most important resources for

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humans, and that other psychological needs (e.g., achievement) are secondary to social needs (Baumeister and Leary, 1995). Other energetic needs, including immunity, could similarly be secondary. Rather than affect, daily measures of time and energy use, exertion, effort, and the like would be of interest and should be a focus of future research on ecological mechanisms. Potentially interesting physiological mediators associated with self-regulatory effort include heart rate variability and blood glucose (Gailliot et al., 2007; Segerstrom and Solberg Nes, 2007). Motivation to affiliate, affiliation stress, and inadequate affiliation have neuroendocrine correlates, including cortisol, oxytocin, and progesterone (Schultheiss et al., 2004; Taylor, 2006; Wirth & Schlultheiss, 2006), and the effects of and interactions among these neuroendocrine factors may account for specific effects of social affiliation on immune function.

Because social network changes had already occurred by the first wave of data collection, the question of whether social isolation was immunoenhancing (c.f., Cole et al., 1999), social integration was immunosuppressive, or both cannot be answered by these data. Furthermore, the effects were more like subtle differences in the robustness of cellular immunity than pathologically low or high responses; mean indurations were similar to that from a small normative sample for this antigen (11 mm, from the package insert). However, it should be noted as evidence for immunosuppression that the proportion of anergic responses (< 5 mm) was twice as high in the resident (32% of all responses) as in the relocating group (15%).

Effects on immunity consistent with ecological models have also been demonstrated with regard to optimism, a personality trait that is associated with more persistent and energetic goal pursuit (see Segerstrom, 2005, for a review). In some of those studies, the effects depended on one of the goals being social; it will be an interesting future direction to examine whether ecological predictions are more likely to be supported when social resources are threatened compared with other kinds of resources. Another future direction for this work is comparing effects of social networks during stressors with and without energetic demands. In one study, former dementia caregivers had a lower antibody response to pneumococcus vaccination if they were lonelier, but the reverse was true for current caregivers, who had a larger antibody response if they were lonelier (Jones et al., 2005). Both current and bereaved former caregivers report elevated distress (Robinson-Whelen et al., 2001), but former caregivers experience a significant reduction in the energetic demands of caregiving. Changes in the relationship between social relatedness and immunity that vary by energetic demands but not distress (i.e., current versus former caregivers) provide another good test of ecological predictions.

If immunity is compromised in order to maintain social relationships, how does better health (e.g., House et al., 1988) result? First, social relatedness is likely to be associated with better immunity under many, if not most, circumstances. Ecological immunosuppression is likely to be invoked only when energy is unusually limited and not during ordinary goal pursuit. Second, temporary immunosuppression in the service of preserving long-term resources is likely to be better for the individual than temporary preservation of immunity at the cost of long-term resources; this is the basic premise of ecological immunology. Over the long run, the benefit of social connectedness is likely to outweigh the cost of these changes in immunity.

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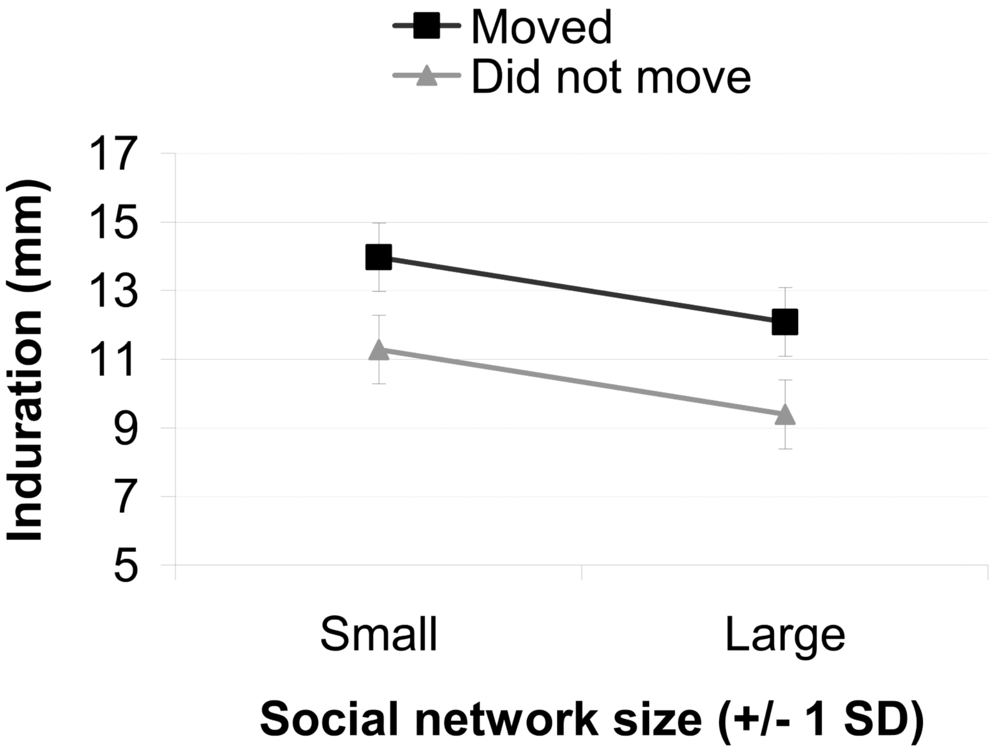

Figure 1.

Predicted DTH induration (mm) from the multi-level model showing effects of relocation and social network size across the first year of law school. Error bars show the pooled standard error of the estimates.

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Table 1

Means (SDs) of study variables across the 5 waves.

Variable	August	October	December	January	February
Network number[*]	18.8 (10.9)	29.8 (17.3)	27.5 (22.0)	32.9 (22.0)	34.2 (19.6)
Network diversity[*]	5.1 (1.5)	5.9 (1.9)	5.5 (1.7)	6.2 (1.8)	6.3 (1.9)
Negative affect[*]	1.6 (0.5)	1.7 (0.7)	1.8 (0.7)	1.6 (0.6)	1.6 (0.6)
DTH induration[*]	14.0 (8.1)	12.8 (8.7)	8.2 (6.4)	8.0 (4.0)	8.4 (6.2)

Note:

[*] $p < .05$ for effect of wave. DTH = delayed type hypersensitivity. Network number is total number of people contacted in a 2-week period; network diversity is up to 12 different contexts in which people are contacted; negative affect is on a 5-point scale; DTH induration is in mm.