Loneliness, Social Network Size, and Immune Response to Influenza Vaccination in College Freshmen

Sarah D. Pressman and Sheldon Cohen
Carnegie Mellon University

Gregory E. Miller
University of British Columbia

Anita Barkin
Carnegie Mellon University

Bruce S. Rahn
University of Rochester

John J. Teasor
University of Pittsburgh

Antibody response to the influenza vaccination was investigated in 83 first-year, healthy, university freshmen. Elevated levels of loneliness throughout the semester and small social networks were independently associated with poorer antibody response to 1 component of the vaccine. Those with both high levels of loneliness and a small social network had the lowest antibody responses. Loneliness was also associated with greater psychological stress and negative affect, less proactive affect, poorer sleep efficiency and quality, and elevations in circulating levels of cortisol. However, only the stress data were consistent with mediation of the loneliness–antibody response relation. None of these variables were associated with social network, and hence none were potential mediators of the relation between network size and immunization response.

Keywords: loneliness, social network size, vaccination, sleep, stress

Social isolation is the objective condition of having few contacts with family and community (Townsend, 1968; Studies of isola-

tion may include the number of individuals with whom a person interacts, the frequency of interactions, the number of types of relationships (e.g., married, friends, social and religious group members), or even the degree of intimacy (Douglas, 1967). There is considerable evidence that social isolation is associated with poorer health. Those with more types of relationships and those who spend more time in social activities are at lower risk for disease and mortality than their more isolated counterparts (see reviews in Berkman, Vaccination, & Seeman, 1993; Cohen, 1988; House, Landis, & Umberson, 1988). Although evidence for the association between numbers of network members and health is less consistent (see review in Cohen, 1988), low number of network members have been associated with increased suicide risk (Trot, 1940), increased risk of functional decline (Bueno et al., 2003; Mendes De Leon, Gold, Glass, Kaplan, & George, 2001), poor mental health (Mendes De Leon et al., 2001), and increased risk-factor levels for heart disease (i.e., higher cholesterol and blood pressure, or higher levels of smoking; O'Reilly & Thomas, 1989).

Loneliness has similarly been associated with poorer health. Although conceptually similar to social isolation, loneliness is the feeling or perception of being alone (Peplau & Perlman, 1982). It has also been defined as the evaluation that one is not achieving a desired level of social interaction (Peplau & Peplau, 1981). In some cases, social isolation and loneliness are not highly corre-

lated (Carona, 1982); for example, a person with a large social network can experience loneliness (e.g., if they lack intimacy in their relationships), whereas a person who has only a few close social ties may not feel lonely at all (Peplau & Perlman, 1982).
Feeling lonely has been associated with poorer self-reported physical health (Berg, Mellstrom, Persson, & Svenson, 1981; Fees, Martin, & Poos, 1999; Mahon, Yarcheski, & Yarcheski, 1993), postpartum surgery mortality (Herlitz et al., 1999), and abnormal hemodynamic functioning (Cacioppo, Hawkley, Crawford, et al., 2002; Sarkin, Rook, & Lu, 2002). Loneliness has also been associated with poorer immune status, including poorer natural killer cell function (Kiecolt-Glaser, Glaser, & Currer, 1984), smaller proliferative responses to phytohemagglutination stimulation (Kiecolt-Glaser, Ricker, et al., 1984), and higher levels of antibody (Ab) to the Epstein-Barr virus (suggesting less immune control over this pathogen; Glaser, Kiecolt-Glaser, Steeple, & Holloway, 1985). In contrast, feelings of loneliness predicted less rapid decline in numbers of CD24+ cells in HIV-positive men over a 3-year follow-up, suggesting a slower progression of infection (Miller, Kemeny, Taylor, Cole, & Visscher, 1997), and were unrelated to Ab formation in response to a low-dose hepatitis B vaccine (Zahbuz, 1993).

The study we report compared the effects of social isolation and loneliness on a component of health: immune competence as assessed by the amount of Ab produced in response to an immunization. It also attempts to identify specific pathways that might link isolation and loneliness to immunity. One potential pathway is the elevation in immune-modulating glucocorticoids. Elevated cortisol levels have been found in chronically lonely college students (Cacioppo et al., 2000), lonely psychiatric inpatients (Kiecolt-Glaser, Ricker, et al., 1984), and socially isolated pre-school children (Sánchez-Martín et al., 2001). Another potential pathway is via differences in health practices (e.g., smoking, exercise; Cacioppo, Hawkley, & Bermond, 2001; Cohen, 1998; Rock, 1984). Although some studies have not found differences between lonely and nonlonely individuals (Cacioppo et al., 2000; Cacioppo, Hawkley, Crawford, et al., 2002); loneliness has been found to be associated with alcoholism (Nerviano & Gross, 1978), and isolation has been found to be associated with smoking, alcohol consumption, and poorer exercise habits (Berkman & Syme, 1979). It has also been postulated that these differences in restorative processes (e.g., sleep behaviors) that serve to repair and maintain physiological function may be responsible for the health consequences of loneliness and related factors (Hawkley & Cacioppo, 2003). Research to date suggests that the lonely sleep less effectively and less efficiently than do their nonlonely counterparts (Berg et al., 1981; Cacioppo et al., 2000; Cacioppo, Hawkley, Brenton, et al., 2002), and studies have shown that social isolation is related to poor sleep habits and insomnia (Berkman & Syme, 1979; Cohen, Doyle, Rabin, & Gwaltney, 1997; Hanslo, & Oostergen, 1987). It seems plausible then that restorative behaviors and/or health practices mediate the associations between loneliness and/or social network size and health-related outcomes. Others theories of how isolation and loneliness might influence health have also been raised. Hawkley and Cacioppo (2003) argued that social isolation might also influence health via feelings of loneliness because loneliness gauges dissonance over the current social status quo. Cacioppo et al. (2003) suggested that lonely and isolated individuals have higher levels of stress in their lives and that this contributes to wear and tear on the body, which may in turn influence health. Rock (1984), however, suggested that loneliness and isolation may operate via health-related stress pathways. Rock specifically suggested that loneliness alters well-being via elevated stress and depression, whereas social isolation is harmful because of an absence of others to prompt positive health practices and deter deviant ones. There may also be alternative factors that are similar to loneliness and isolation that give rise to the associations between isolation, loneliness, and physical well-being. Loneliness is strongly correlated with such personality characteristics as low self-esteem, introversion, hostility, and neuroticism (Berg et al., 1981; Cacioppo, 1982; Levin & Stokes, 1986; Russell, Pepels, & Curowo, 1980). Because many of these variables have also been correlated with impaired immune functioning, poor physical health, and greater symptom reporting (e.g., Cohen, Turner, Alper, & Skoner, 2003; Feldman, Cohen, Doyle, Rabin, & Gwaltney, 1999; Miller, Cohen, Rabin, & Doyle, 1999), they may be what underlies associations among loneliness, isolation, and health.

We assessed the value of social network size and loneliness in predicting immune function by monitoring Ab response to an influenza immunization in a group of college freshmen who reported that this was their first influenza vaccination. Immunization studies are desirable not only because of their clinical significance but also because of their ability to assess in vivo functional immunity (Cohen, Miller, & Rabin, 2001). We chose to study incoming freshmen because this period of their lives is often coupled with feelings of loneliness (Curowo, 1982; Weiss, 1973). It is also a time when they radically change their health behaviors (e.g., sleeping patterns, alcohol usage), which may provide the opportunity to determine whether lonely and/or isolated individuals are more likely to engage in detrimental health behaviors and whether these in turn mediate the relationship between social factors and immunity.

Levels of loneliness, social network size, health behaviors, and restorative behaviors were assessed at baseline. We also measured self-esteem, hostility, neuroticism, and extraversion at baseline as possible third (spurious) factors that could bias both in loneliness and immune suppression. We then monitored loneliness, health behaviors, and mood, and stress with electronic daily diaries for 2 consecutive weeks starting 2 days before vaccination, along with salivary cortisol, which was assessed for 5 days during this period starting 1 day pre-vaccination. The diary period was followed by 3.5 months of biweekly questionnaires assessing symptom levels of loneliness, stress, and mood. AB levels were determined via blood samples drawn at baseline (the day of vaccination), 1 month (the point at which maximal stressors should be reached), and 4 months to determine if differences between groups were maintained over time.

Method

Participants

Participants were college freshmen (37 men and 46 women) at Carnegie Mellon University, aged 18-23 years (62% were 18-19 years), who responded to e-mail advertisements and posters and were recruited in four separate cohorts (September 2000 and 2001 and November 2000 and 2001). All reported to be healthy, non-smokers, no more than 60 minutes of moderate exercise per week (with the exception of birth control), and good health prior to study onset. Individuals who had ever been vaccinated for influenza, who were pregnant or breast-feeding, or who had immunologically missed health problems were excluded. All participants were paid $120 for their participation. Our preregistered completed all components of the study ex-
Participants were summarized in conjunction with university-wide flu vaccination rates (Figures 3A and 4). Demographic, psychological, and health practice questionnaires were administered 5 to 6 days prior to immunization. Two days prior to immunization, participants began 13 days of psychological assessment (ENA; Stone & Shiffman, 1994) by using a paper computer. Participants gave saliva samples at least twice a day, at the same time that they completed their questionnaire. Following the last day of ENA, two-way mail reminders were administered to assess salivary, stress, and mood over the following 14 weeks. All levels were assessed at baseline (day of immunization) and in 1-4 months postimmunization.

Materials

Stressors of loneliness and social network size. Loneliness was assessed at study baseline by using the University of California-Los Angeles Loneliness Scale (Russell, 1996). This eight-item scale measures the extent to which the participant feels lonely and isolated (α = .69). To capture feelings of loneliness over the ambulatory and follow-up period, we asked participants to estimate the extent to which they felt lonely and isolated at each diary entry (from never feel lonely to always feel lonely). A score of 0 indicated no loneliness and an average of 8 indicated high loneliness. The ENA data were averaged across the four daily assessments (Mean 9.77). An index of loneliness was constructed as the average of the 5 days loneliness scores and an average of all the follow-up scores had a correlation of .80. When the 13 ENA and seven follow-up scores were entered into a principal component analysis, all loaded at .50 or better on the same factor. Consequently, across the entire ENA daily and follow-up assessments to construct a single loneliness score. We defined social isolation as the objective condition of having few contacts with family and community (Twible-Bean, 1988). Studies of isolation have focused on both total isolation and social network size (e.g., Calz & Gove, 1978) and decreased contact and communication with others (e.g., Tomil, 1988). Because we were studying college students, we felt that traditional measures of social integration were not appropriate and instead focused on the issue of contact. We administered the Social Networks in Adult Life (SNA; Deinen and Allen, 1987) at baseline to 4 weeks social network size. Participants were presented with these conceptual circles and told to write the initials of a maximum of 20 people that they knew well and were in contact with at least once a month in the circles. Instructions specified that “People in the innermost circle are those who are close and important to you, and without whom your life would be difficult to imagine. The remaining two circles are for people who are successively less close.” Total social network size was estimated by summing the number of initials within all three levels.

Personality scales. Neuroticism test extraversion were assessed at baseline by using a modified version of the scale (see Feldman et al., 1999, for modifications) from Goldberg's Big Five Scale (10 items each: Goldberg, 1992) that required participants to indicate how accurately a trait of 0 (e.g., anxious, extraverted, and, superficially reflected how they generally feel on a scale from 1 to 5 at all other times) to 4 (e.g., anxious, accurate). The alpha for neuroticism and extraversion was .86 and .79, respectively. Participants also completed the four-item version of the Rosenberg Self-Esteem Scale (Rosenberg, 1965) at study baseline. They were assessed at study baseline by using the 30-item version of the Cock-Medley Social Power Scale (Cock-Medley, 1977). Participants completed 20 true-false questions indicating their hostile affect, cyanotic, and aggressive responding.6 Agreement (counterbalanced) items were reversed, and the number of counterbalanced items was then summed to construct a total hostility score (α = .63).

Depression symptoms, affect, and psychological symptoms. Depression symptoms were assessed at baseline by using the 15-item version of the Center for Epidemiologic Studies—Depression Scale (CES-D; 10-Andersen, M. A., & Patrick, 1994). The items were scored on a 4-point scale on which 0 indicated that the symptom occurred rarely or none of the time and 3 indicated most of the time. Individual items were totaled to yield a summary score, with higher scores indicating more symptoms of depression (α = .79).

Blood was assessed at each study diary by using four negative tests associated with two subgroups of negative affect (NA) and eight items associated with positive affect (PA). NA items included anxiety, depression, and nervousness (unhappy, sad), whereas PA included indicators of vigor (active, intense, lively, enthusiastic), well-being (happy, cheerful), and calm (calm, relaxed). Each item was rated on a scale from 1 (not at all accurate) to 4 (extremely accurate) according to how much the week when participants felt at least at each moment. For each interview, appropriate means were summed to create separate NA and PA scales. The overall alpha for the four NA items on the 13 interviews ranged from .81 to .91. The overall alpha for the eight PA items on the 13 interviews ranged from .86 to .90. The same items in each diary portion of the study were assessed by asking participants how they have felt over the previous 2 weeks. Average NA and PA scores across the study were created by taking the mean of the item means. To construct a composite measure of NA and PA across the entire 13 diary days and the seventh (k=2) questionnaire items (NTA = .92). PA = .94.

Psychological stress data were also gathered at each diary entry as well as weekly, monthly, and yearly. As an example, in the last interview, the participants were asked how often they have used: smoking, alcohol abuse, and eating habits. The overall alpha for the four NA items on the 13 interviews ranged from .62 to .79. We took the means of the two questionnaires at each assessment, averaged the means within a day, and then created an average daily score by taking the means of all days assessed.

Health practices and restrained behavior. Health practices were assessed by questionnaire at baseline with an inventory that had been used in published studies by Cohen et al. (1997). Participants were classified as smokers if they had used cigarettes, pipe, or cigars or a combination of the above. Alcohol use was determined by counting the number of alcoholic drinks consumed during a typical week. A typical week was defined as the period in which the participants engaged in heavy drinking (at least 5 days) over the past month. Participants were assessed by asking the participants how often they engaged in vigorous activity (number of days) each week by using an item from the Physical Activity Quantity Questionnaire (Paffenbarger, Lin, & Hey, 1983). All of the health practices were also assessed once each day by EMA and were averaged across the 13 EMA days. Alcohol consumption and smoking were determined by number of drinks and units smoked; physical activity was measured by the number of times and number of minutes of exercise.
stimulation (to control for possible differences in the vaccines and assays), race (Caucasian, other), and baseline Ab levels (for immunization response analyses) followed by the appropriate psychological variables in a second step. A third step was included when interactions were tested. Separate regressions were done for each of the three components of the trivalent vaccine according to the suggestion of Cohen et al. (2001). We report the change in multiple correlation-squared values and F values when there was a main effect of the regression step. Participants who had maximal responses at baseline were excluded from immune analyses because of our inability to gauge their response to the antigen (New Caledonia, n = 9; Papua New Guinea, n = 6; both Ab viruses, n = 0). Loneliness was associated with baseline titers of Ab/new Caledonia (r = .35, p < .01) but with no other antigens, whereas social network size was not associated with baseline levels of Ab in any influenza strain.

Because our sampling schedule was designed to capture diurnal fluctuations in mood and cortisol, it was important to carefully monitor participants' compliance with the ambulatory monitoring procedures. On an as-needed basis, we chose to include only those diary entries within 60 min of target in either direction. When this definition was applied, 3.756 of the 4.316 diary entries (87%) met our criteria for compliance. Only these values were used in the analyses below (e.g., computing average loneliness scores, average NA, average PA, cortisol levels).

Social Network Size, Loneliness, and Ab Response

Separate analyses assessed whether social network size and loneliness were associated with Ab response at both follow-up points for the various antigens/components. Smaller social networks were associated with lower Ab production at both 1 month (ΔR² = .07), F(2, 71) = 4.91, p < .05, and 4 months (ΔR² = .28), F(2, 70) = 5.53, p < .01, in response to the Ab/new Caledonia virus but not to the Ab/Papua or the Ab viruses. In both cases, the association with Ab/New Caledonia was attributable to lower Ab production in the most isotolerant set (see Figure 1).

The two measures of loneliness—total loneliness score (4-month mean) and the UCLA Loneliness Scale—were correlated (r = .49, p < .01). We examined response to the immunization at 1 month and 4 months by using both the UCLA scale and the total loneliness score in separate analyses. Higher levels of total loneliness were associated with lower Ab levels at both 1 month (ΔR² = .04), F(1, 72) = 4.79, p < .05, and 4 months (ΔR² = .04), F(1, 71) = 5.04, p < .05, for the Ab/new Caledonia vaccination but again not for the other vaccine components. As apparent from Figure 2, the association was linear with each increase in loneliness associated with lower Ab production. The UCLA scale was not related to Ab responses; therefore, our subsequent loneliness analyses focus on the total loneliness measure. Furthermore, because the Ab/New Caledonia virus was the only component associated with loneliness and isolation, further analyses focus on this element of the Ab response.

Test of Spurious (Third Factor) Explanations

It is possible that personality characteristics that are thought to influence the development of social networks and our perceptions of them might account for the relations we found by affecting...
isolation and loneliness as well as immune response to the vaccine. Bivariate correlations revealed that loneliness was associated with elevated levels of neuroticism (r = .34, p < .01), higher hostility scores (r = -.30, p < .01), and marginally lower levels of extraversion (r = -.19, p = .09) but was not associated with self-esteem. Analyses of variance examining the independent relationships between social network tertiles and these potential third factors revealed no associations, with the exception of extraversion (r = -2.2, p < .05). None of these variables were associated with A/New Caledonia Ab levels, and covarying them did not greatly reduce the association between social network and immune response or between loneliness and immune response.

Test of Mediators

We were interested in whether stress and mood, health and restorative behaviors, or context operated as pathways linking social variables with immunization response. For a variable to be considered a mediator, it must correlate with the independent predictor and account for variations in the dependent variable, and when controlled for, the relationship between the independent and the dependent variable must be significantly reduced (Baron & Kenny, 1986). We began by examining the potential roles of stress and affect. Loneliness was positively correlated with NA (r = .74, p < .01), psychological stress (r = -3.1, p < .01), and depressive symptoms (r = .52, p < .01) and negatively correlated with PA (r = -.31, p < .01). Individual analyses of variance assessing the relationship between each of these variables and social network-size tertiles revealed no associations. To test the hypothesis that distress mediates the influence of loneliness on health outcomes, we tested each of NA, PA, stress, and depression in independent regressions to determine if they were associated with Ab response. Only psychological stress was significantly associated with response to A/New Caledonia; 1 month (ΔR² = .04), F(1, 72) = 4.83, p < .05; 4 months (ΔR² = .04), F(1, 71) = 4.91, p < .05. This is similar to our previous finding that stress over the EMA period was related to Ab levels (Miller et al., 2004). We also entered these variables into a stepwise regression to determine whether they would lessen the association between loneliness and Ab response. Only stress entered the first step of the equation, and when loneliness was added to a second step, stress reduced the association of loneliness with Ab levels reported earlier by 50%: 1 month (ΔR² = .02), F(1, 71) = 2.8, p = .10; 4 months (ΔR² = .02), F(1, 70) = 5.1, p = .08. In contrast, a similar analysis substituting social network size for loneliness did not indicate any reduction of the association when stress was added to the equation.

We then considered the roles of health and restorative behaviors. Social network size was not related to any of the health or restorative behaviors. Loneliness (controlling for sex, cohort, and race) was associated with poorer sleep efficiency assessed at baseline (ΔR² = .07), F(1, 72) = 6.34, p < .05, and marginally associated with higher sleep loss (ΔR² = .04), F(1, 78) = 3.16, p = .08, and poorer sleep quality (ΔR² = .06), F(1, 78) = 3.42, p = .07, over the diary period, but not with any of the other behaviors. However, none of these variables associated with loneliness were significantly related to Ab levels; therefore, none were potential mediators.
Finally, we examined whether cortisol could have acted as a mediating pathway. Neither network size nor total loneliness was associated with average cortisol AUC or with mean levels at the four time points (controlling for sex, cohort, and race). Because cortisol levels were sampled only during the first week of the study, we examined whether cortisol was related to loneliness over the surrounding EMA period. Although it was not related to average AUC, further analysis revealed that diary loneliness was associated with higher average cortisol levels at the early morning (1-hr postwakeup) and evening samples (11-hr postwakeup) 1 hr later (\( \Delta R^2 = .10 \), F(1, 50) = 7.0, \( p < .05 \); 11 hr \( \Delta R^2 = .00 \), F(1, 50) = 4.4, \( p < .05 \). However, none of the variables associated with loneliness were significantly related to AB levels, therefore, none were potential mediators.

**Loneliness as a Mediator of the Association of Social Network Size and Immunity**

Rawley and Cacioppo (2003) predicted that one way that social network size could influence health is via perceptions of loneliness. Social network size and loneliness were not correlated (\( r = -.09 \), \( p = .40 \)). Alone, social network size accounted for approximately 7% of the AB response to A/New Caledonia at both time points. When loneliness was entered in the first block, the network effects were reduced to 0% at 1 and 4 months but remained statistically significant (\( p = .02 \) for both). Hence, loneliness accounted for only 14% of the variability (initial \( \Delta R^2 = \) new \( \Delta R^2 \) / initial \( \Delta R^2 = .07 / .06 = .07 / 07 = .14 \) initially accounted for by social network size.

**Interaction of Loneliness and Social Network Size**

To examine possible synergistic effects of loneliness and social network size on AB response, we entered loneliness and social network size together followed by the product of the two in the next step. When loneliness and social network size were included in the same regression to test for independent associations with AB change, neither association was reduced substantially—loneliness: 1 month (\( \Delta R^2 = .03 \), F(1, 70) = 3.62, \( p = .06 \); 4 months (\( \Delta R^2 = .04 \), F(1, 69) = 3.49, \( p = .07 \); and social network size: 1 month (\( \Delta R^2 = .06 \), F(2, 70) = 4.00, \( p < .05 \); 4 months (\( \Delta R^2 = .06 \), F(2, 69) = 4.26, \( p < .05 \). The interaction between social network size and loneliness was significant at both 1 month (\( \Delta R^2 = .08 \), F(2, 68) = 6.24, \( p < .01 \); and 4 months (\( \Delta R^2 = .06 \), F(2, 67) = 5.03, \( p < .01 \). Figure 3 shows the interaction at 1 month. The 4th month #3 in not depicted graphically, but it is identical to the findings at 1 month. Individuals most at risk were those who were socially isolated by baseline as well as alone throughout the 4 months of the study. Furthermore, we found that loneliness was not associated with lower AB response when social network size was large, whereas network size was not associated with AB response when loneliness was low.

**Discussion**

Low numbers of social ties were associated with a poorer immune response to one component of the influenza vaccination. Being in the lowest tertile of social network size (4–12 members in the total network) was associated with less AB production than
were the other two tertiles (ranging from 13 to 20 contacts). This association was independent of feelings of loneliness. College students have many opportunities for social contacts via roommates, dormitories, classes, and university organizations; consequently, availability of social ties is an unlikely explanation for isolation. Implications for health may arise because these individuals lack social support to buffer the stress that occurs during the first semester of school. Alternatively, individuals with few ties may perceive themselves to be stigmatized because of the relative embeddedness of their counterparts with larger social networks and the cultural values associated with being popular. However, these explanations seem unlikely because network size was not associated with stress, depression, or self-esteem. Finally, an explanation based on the hypothesis that greater network size is associated with greater probability of exposure to more virulent and hence development of immunity to the viruses in the vaccine does not appear to be the root of this finding as there were no social network group differences in baseline Ab levels.

Loneliness (as assessed by the diary and interview data) was associated with poorer Ab response to the A/New-Caledonia virus component of the vaccination at both 1 and 4 months postimmunization. Baseline levels of loneliness, as assessed by the UCLA scale, however, were not related to vaccination response. This was consistent with the failure of an earlier study (Zahariadis et al., 1993) to find an association of baseline loneliness as assessed by the UCLA scale and Ab response. We may have been able to tease out this association because the score was based on multiple measurements over 4 months and was both contemporaneous with the immunization response and a more reliable measure of chronic loneliness. In contrast, the baseline assessment may have merely picked up the transient loneliness associated with moving to a new school. This is consistent with the argument that chronic feelings of loneliness are more important predictors of health and well-being (Weiss, 1973). It may be that acute levels of loneliness do not have the same immune implications of chronic loneliness. This is in line with Cicchetti et al.'s (2003) argument that the two measures might have distinct mechanisms by which they operate on health.

We pursued the possibility of several mediating pathways that might have linked social isolation or loneliness to poorer immune response. Recall that Rook (1984) predicted that the association of social isolation and health would be mediated by health practices, whereas the association of loneliness and health would be mediated by stress and negative affect. Rook (1984) argued that social network may prevent deviant behavior during periods of rapid personal change. This suggests that socially isolated persons may have poorer health practices and restorative behaviors. However, neither health practices nor restorative behaviors were associated with network size in our freshmen. Because the first year of college is a period of transition, it is plausible that other unassessed behaviors (e.g., substance abuse, nutrition, caffeine intake) could mediate the association between social network size and immune function. For example, coping via substance abuse has been associated with poor Ab response to a hepatitis B vaccination.
Burns, Carroll, Ring, Harrison, & Drayson, 2002). Alternatively, health behaviors of freshmen may be too variable and influenced by external factors (e.g., exams and assignments altering sleep patterns, variable access to cigarettes and alcohol due to age restrictions) to be sensitive to the influences of social networks. In contrast to network size, high loneliness was associated with poorer sleep efficiency at baseline and marginally associated with more sleep less and poorer sleep quality over the diary assessment. These results are consistent with evidence from both the laboratory and field that lonely college students have poorer sleep efficiency (Cacioppo et al., 2000; Cacioppo, Hawkley, Berniss, et al., 2002). However, neither these particular restorative behaviors nor any of the health behavior measures were associated with response to the immunization. In some cases, the behaviors had low base rates restricting the possibility of associations (e.g., 78% did not smoke, and 50% did not drink alcohol). In contrast, the sleep habits of many of the students were highly irregular in November through December, when midterms, projects, and exams were prevalent (e.g., sleep less ranged from 0 to 120 min per night). These irregularities may have similarly clouded any possible relation.

Stress was predicted to play a role in the link between loneliness and response to the immunization (Cacioppo et al., 2003; Krok, 1984). In our sample, increased loneliness was associated with greater NA, depression, and psychosocial stress and with lower levels of PA. All of these variables have been related to matters of immunocompetence in earlier studies (e.g., Cohen, Doyle, Turner, Alpert, & Skoner, 2003; Cohen, Turner, et al., 2003; Marziali, Cohen, Ratto, & Manuck, 2001; Miller et al., 1999), and psychosocial stress has been associated with Ab response to immunization (e.g., Burns, Carroll, Drayson, Whisham, & Ring, 2003; Glaser et al., 1992; Glaser, Kiecolt-Glaser, Malarcher, & Sheridan, 1998; Miller et al., 2004; Vencha et al., 1999). When these variables were stepped in as covariates, only stress entered the regression, which decreased the association between loneliness and Ab response by 50%. This provides partial support for previous theories that suggest loneliness may impact health via feelings of distress (Cacioppo et al., 2003; Krok, 1984). However, approximately 50% of the variability explained by loneliness remained after controlling for stress, there are other pathways at work as well. Larger networks were not associated with any of these variables; therefore, they are not potential mediators. Overall, we tested whether cortisol levels could explain the associations between either network size or loneliness and immunity. Although loneliness was associated with cortisol levels, it was only for loneliness levels reported around the time of the cortisol sampling period. Furthermore, because none of the cortisol measures (AUC and at all time points) were related to Ab response, they are not plausible mediators. One possible explanation for this null finding may be the highly irregular sleep habits of students, as discussed earlier. Cortisol data from that period may be too irregular to capture associations with Ab months later.

In short, we have not found any possible pathways linking social isolation to immune response, although stress does seem to play a major role in linking loneliness to Ab response to the immunization. Hawkley and Cacioppo (2003) postulated that one way isolation might influence health is via perceptions of loneliness. However, in this study, social network size and loneliness were not correlated here, nor did covarying loneliness significantly reduce the association of isolation with immune response. There was, however, a synergistic effect of number of ties and loneliness that suggests that there may be some common mechanistic(s) we have not identified. Individuals who had low levels of loneliness were protected from the lower immune response associated with isolation, and those with high numbers of social contacts were protected from the lower response associated with loneliness. Relevant here is a study by Reynolds and Kaplan (1990) showing increased risk of cancer and cancer-related mortality in women who reported both fewer contacts and feelings of isolation, but some degree of protection for those who reported only one or the other. The ability of these two variables to substitute for one another suggests that there may be some common pathway that is influenced by extreme levels of both variables.

The prospective nature of our social network-immune finding precludes the possibility of reverse causality. Although we have excluded several key factors (personality measures), it is still possible that some unmeasured third variable may be responsible for both the low levels of network members and suppressed Ab response. The loneliness-finding, however, is cross-sectional, precluding causal influences about the relationship between loneliness and Ab response. Given that the central nervous system and the immune axis have bidirectional communication (Maier & Watkins, 1998), it is conceivable that immune processes cause feelings of loneliness or that there is another unconsidered variable responsible. We must also consider the clinical implications of suppressed immune response to an influenza immunization. Statistical significance is not clinical significance and may not mean that these individuals are less protected from the virus. If we chose 40 titers as a protective level (Cox et al., 2002), only 6%–7% of our participants would have been below this level during follow-up. It is interesting to note that all of these participants had both small social networks and high levels of loneliness. Nonetheless, it remains intriguing that there was sufficient variability in Ab response in a young healthy population to find the associations we report.

Why were social network size and loneliness related to only one of the four viruses in the influenza vaccine? There was no a priori prediction that these variables would be associated with only one component of the vaccination component; however, A-type viruses are known to show more antigens drift (i.e., mutate more easily and cause more infection; Nicholson, Webster, & Hay, 1998), which may play a role in individual variability in response. In line with this, previous studies have found psychological associations with only the A components of the same vaccination (e.g., Burns et al., 2003); however, because many psychoneuroimmunological studies average over viruses (see review in Cohen et al., 2001), it is impossible to say with which A viruses drove previsouvly found associations between psychological factors and immune response. It remains unclear why these factors were associated with only one of the two A viruses.

In sum, social network size and loneliness were independently associated with the production of less Ab in response to one component of the influenza immunization in a young, healthy population. Our evidence is consistent with stress partially mediating the association between loneliness and immune response, but we have no support for a pathway linking social isolation and response.


