Neural Correlates of Giving Support to a Loved One

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Objective: Social support may benefit mental and physical well-being, but most research has focused on the receipt, rather than the provision, of social support. We explored the potentially beneficial effects of support giving by examining the neural substrates of giving support to a loved one. We focused on a priori regions of interest in the ventral striatum and septal area (SA) because of their role in maternal caregiving behavior in animals. **Methods:** Twenty romantic couples completed a functional magnetic resonance imaging session in which the female partner underwent a scan while her partner stood just outside the scanner and received unpleasant electric shocks. **Results:** Support giving (holding a partner's arm while they experienced physical pain), compared with other control conditions, led to significantly more activity in the ventral striatum, a reward-related region also involved in maternal behavior (*p* values < .05). Similar effects were observed for the SA, a region involved in both maternal behavior and fear attenuation. Greater activity in each of these regions during support giving was associated with greater self-reported support giving effectiveness and social connection (*r* values = 0.55–0.64, *p* values < .05). In addition, in line with the SA's role in fear attenuation (presumably to facilitate caregiving during stress), increased SA activity during support giving was associated with reduced left (r = -0.44, p < .05) and right (r = -0.42, p < .05) amygdala activity. **Conclusions:** Results suggest that support giving may be beneficial not only for the receiver but also for the giver. Implications for the possible stress-reducing effects of support giving are discussed. **Key words:** providing social support, ventral striatum, septal area, caregiving, human, fMRI.

VS = ventral striatum; SA = septal area; ROI = region of interest.

INTRODUCTION

t is well established that social support relates to greater mental and physical well-being (1,2). Although most research has assumed that these benefits are due to *receiving* support from others, a less-explored possibility is that some of these benefits are due to the act of *giving* support to others (3). Empirical evidence has begun to show that individuals who provide support fare better in physical and mental health. Older adults who provided support to others close to them displayed lower mortality rates during a 5-year period compared with those who did not (3). Similarly, those who provided more support, after the loss of a spouse, exhibited an accelerated decline in depressive symptoms (4). Finally, giving more social support has been associated with lower blood pressure and mean arterial pressure during a 24-hour period (5).

Together, this work begins to establish an important relationship between support giving and mental and physical health. However, the directionality of these effects (owing to the correlational nature of these studies) and the underlying mechanisms that link support giving with health and well-being are not clear. Here, we used an experimental paradigm to examine the neural correlates associated with support giving to begin to explore the mechanisms that might ultimately link support giving with health and well-being. To identify the neural correlates of support giving, we borrowed from work on maternal caregiving behavior in animals—a likely substrate for support giving in humans. In animals, maternal caregiving behavior, which includes providing support and care for offspring, relies in part on activity in the ventral striatum (VS), a reward-related neural region. In humans, VS activity increases in anticipation of winning money, and this activity correlates with self-reported happiness in response to winning (6). The VS is also critical for maternal caregiving behavior, in part, because it may directly reinforce caregiving behavior (7). Thus, maternal behavior leads to increased VS activity (8); cocaine injected directly into the VS, which acts on reward-related dopaminergic receptors, impairs maternal behavior (9), and VS lesions disrupt maternal behavior, reducing approach and interaction with pups (10).

Maternal behavior also relies on activity in the septal area (SA), a region originally identified as a reward-related "pleasure center" (11) but, more recently shown to be involved in fear reduction as well. Electrical stimulation of the SA inhibits fear responding to aversive stimuli (12), leading to cardiac deceleration (13) and reductions in blood pressure (14). Conversely, septal lesions increase startle responses and other fearrelated behaviors (15). Evidence suggests that the SA reduces fear, in part, through inhibitory connections with the amygdala, a region involved in fear responding (16). With regard to maternal behavior, lesions to the SA dramatically disrupt maternal behavior, cutting the survival rates of pups in half (17). To the extent that the SA reduces fear responding, it has been suggested that the SA may contribute to maternal behavior by facilitating adaptive caregiving during stress or threat (18).

To begin to explore the mechanisms that might underlie the relationship between support giving and well-being in humans, we examined the neural correlates of giving support to a loved one in need, focusing on anatomically defined regions of interest (ROIs) in the VS, SA, and amygdala. Specifically, here we focused on the neural correlates of giving support to a relationship partner in need. Building on animal models of maternal caregiving, we hypothesized that support giving would lead to increased activity in the VS and SA, regions central to maternal behavior. In addition, to the extent that the SA is involved in fear inhibition, presumably to facilitate responsive caregiving during times of threat, we hypothesized that SA

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activity during support giving would correlate negatively with amygdala activity.

METHODS Participants

Twenty right-handed female participants in long-term relationships (mean = 23.6 months) completed the session with their male partners. Data were collected during an 11-month period between 2009 and 2010. Both members of the couple were scanner safe (i.e., no metal in their bodies). The final sample of females was ethnically diverse: 45% Asian, 30% white, 15% Hispanic, and 10% "other." Procedures were approved by the institutional review board of the University of California, Los Angeles.

Procedures

Females were scanned, as their male partners stood outside the scanner and received unpleasant electric shocks. On arrival, two shock electrodes were applied to the man's left forearm, leaving his right arm free so that the woman could support him by holding this arm. Physical touch was used as the supportive behavior because it is a common way of expressing social support and is easily implemented in the scanning environment (19). Each woman was explicitly instructed to provide her partner with support during the appropriate condition (see the next section). Shocks were delivered via Biopac's STMISOL (Biopac Systems, Santa Barbara, CA) and calibrated to each man's pain threshold (a score of "10," corresponding to moderate discomfort on a 0–20 scale). Males actually received only two shocks per run. Before entering the scanner, one shock was also delivered to each female to familiarize her with the sensation that her partner would be experiencing.

Once in the scanner, females completed four conditions during two functional runs. In the primary condition of interest, the participant held her partner's arm while he received shock (support giving; Fig. 1). Activity in this condition was then contrasted with three control conditions in which the female participant: a) held a squeeze ball while her partner received shock (*no support giving*), b) held her partner's arm while he did not receive shock (*arm holding*), and c) held a squeeze ball while her partner did not receive shock (*ball-only*). Each condition consisted of the following: a) a cue indicating whether the male partner would receive a shock (2 seconds), b) instructions asking the female participant to take either her partner's arm or the squeeze ball (10 seconds), c) a progress bar during which time the male partner would receive shock ("shock anticipation period," 10 seconds), and d) a rest period (8 seconds). In addition, each condition was presented four times during each of the two functional runs. To implement this, there were two separate scripts, each of which presented the four conditions in a pseudorandom order. The order with which the two scripts were viewed was counterbalanced across participants.

After the scan, females indicated how effectively they had supported their partners ("support effectiveness") and their feelings of social connection (i.e., how connected/supportive they felt) during each of the four conditions. All ratings were made on a 7-point scale, from 1 (not at all) to 7 (very much so). Any outliers (>2.5 standard deviations [SD] from the sample mean) were winsorized (moved to 2.5 SDs from the sample mean without the outlier included) and included in the final analyses (however, results did not change significantly when the outliers were removed or not winsorized). In addition, to ensure a fairly uniform experience across participants, we also asked participants about their overall relationship satisfaction and their level of comfort with touch. Thus, female participants completed an item measuring relationship satisfaction ("how happy are you in your current relationship" on a scale of 1 [extremely unhappy] to 7 [perfect] (20)). In addition, participants rated how comfortable they felt touching their partners on a 1 (not at all) to 7 (very much so) scale. Behavioral results reported later are from the full sample (n = 20).

Imaging Acquisition and Analysis

Data were acquired on a 3T Siemens Trio magnetic resonance imaging scanner. Head movements were restrained with foam padding. For each participant, a high-resolution structural T2-weighted echo-planar imaging volume (spin echo, repetition time = 5000 milliseconds, echo time = 34 milliseconds, matrix size = 128×128 , resolution = $1.6 \times 1.6 \times 3$ mm, field of view = 200 mm, number of slices = 36, thickness = 3 mm, flip angle = 90 degrees, bandwidth = 1302 Hz/pixel) was acquired coplanar with the functional scans. Two functional scans, lasting approximately 8 minutes each, were acquired (gradient echo, repetition time = 2000 milliseconds, echo time = 30 milliseconds, matrix size = 64×64 , resolution = $3.1 \times 3.1 \times 4.0$ mm, field of view = 200 mm, number of axial slices = 33, thickness = 4 mm, flip angle = 90 degrees, bandwidth = 2604 Hz/pixel).

Imaging data were analyzed using SPM 5 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK). Images for each subject were realigned to correct for head motion, normalized into a standard stereotactic space, and smoothed with an 8-mm Gaussian kernel, full-width at half-maximum, to increase the signal-to-noise ratio. For each participant, the 10-second shock



Figure 1. Sample support giving trial.

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anticipation periods for each of the four conditions were modeled as blocks, and rest periods comprised the implicit baseline. Linear contrasts (shock anticipation periods for the support giving condition relative to each of the other conditions) were computed for each participant. These individual contrast images were then used in group-level analyses. Three participants were removed for signal dropout; therefore imaging results are based on 17 participants.

ROI analyses focusing on the left and right VS and the SA were performed. VS ROIs were structurally defined by combining the caudate and putamen from the automated anatomical labeling atlas (21) and constrained at -24 < x < 24, 4 < y < 18, and -12 < z < 0. The SA ROI was created using MarsBaR (http:// marsbar.sourceforge.net) and was centered at (0, 2, -4), with a 5-mm radius based on an average from previously published articles on prosocial behavior (22,23). We examined the activity within these three ROIs for each of the four conditions. Finally, left and right amygdala ROIs were structurally defined using the automated anatomical labeling atlas. There was one outlier on amygdala activity during support giving and ball-only conditions; the individual's data were winsorized as described previously and included in the final sample. Based on convention, all neuroimaging analyses were one-tailed.

RESULTS

Behavioral Analyses

Overall, participants in the present study scored relatively high in relationship satisfaction and showed high levels of comfort with touch. Thus, on average, women reported being "very" to "extremely" happy in their current relationship (mean [SD] = 5.6 [0.68] on a 1–7 scale), and no subjects rated their satisfaction lower than 4, corresponding to "happy." Moreover, participants reported feeling very comfortable touching their partners (mean [SD] = 6.85 [0.37] on a 1–7 scale), and there was very little variability in this rating (range, 6-7).

Consistent with the manipulation of support giving, participants reported higher levels of support effectiveness during the support giving condition (mean [SD] = 5.50 [1.05]) compared with the arm holding (mean [SD] = 4.70 [1.63], t = 2.22, df = 19, p < .05), no support giving (mean [SD] = 2.21 [1.42], t = 7.42, df = 19, p < .01), and ball-only (mean [SD] = 2.02 [1.12], t = 13.39, df = 19, p < .01) control conditions. Interestingly, participants also felt more connected to their partners during the support giving (mean [SD] = 5.75 [0.90]) compared with the arm holding (mean [SD] = 5.45 [1.11], t = 2.26, df = 19, p < .05), no support giving (mean [SD] = 2.23 [1.10], t = 10.44, df = 19, p < .01), and ball-only (mean [SD] = 2.23 [1.03], t = 18.54, df = 19, p < .01) control conditions.

Neuroimaging Analyses

As predicted, participants showed greater right VS activity during the support giving condition compared with the no support giving condition (t = 1.93, df = 16, p < .05; Fig. 2A) and the ball-only condition (t = 1.99, df = 16, p < .05). Perhaps surprisingly, VS activity was also more active during the support giving condition compared with the arm holding condition (t = 2.10, df = 16, p < .05). In addition, greater VS activity during support giving (versus the ball-only condition) was associated with greater self-reported support effectiveness (r = .64,



Figure 2. Ventral striatum and septal area responses during each condition. (A) Parameter estimates from right ventral striatum and septal area regions-of-interest during each condition versus the rest period. (B) Scatterplot showing the correlation between felt social connection with right ventral striatum and septal area activity. (C) Scatterplot showing the correlation between septal area and amygdala activity (during support giving versus ball-only conditions).

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p < .05) and feelings of social connection (r = .55, p < .05; Fig. 2B) (during the support giving versus ball-only condition).

The SA showed a similar pattern; there was more SA activity during the support giving condition compared with the arm holding condition (t = 2.09, df = 16, p < .05) and marginally more activity during the no support giving (t = 1.20, df = 16, p = .12) and ball-only conditions (t = 1.40, df = 16, p = .09; Fig. 2A). In addition, greater SA activity during support giving (versus the ball-only condition) was associated with greater support effectiveness (r = .60, p < .05) and feelings of social connection (r = .63, p < .05; Fig. 2B) (during the support giving versus ball-only condition).

Finally, consistent with the notion that SA activity during support giving may be associated with reductions in fear responding, greater SA activity during the support giving (versus ball-only) condition was associated with reduced activity in both left (r = -0.44, p < .05) and right (r = -0.42, p < .05) amygdala ROIs (Fig. 2C). VS activity was not (p values > .22).

DISCUSSION

Although previous work suggests that support giving may benefit health, the directionality of these effects and the underlying neural mechanisms have not yet been explored. The current study examined the neural correlates associated with giving support to a loved one in need. Importantly, we experimentally manipulated support giving to directly compare the neural underpinnings of giving versus not giving support. In doing so, we were able to elucidate some of the ways in which support giving might be beneficial for the support giver without the influence of confounds, such as differences in the amount of psychological resources of the support giver at baseline. These results demonstrated that support giving activated neural regions involved in reward and maternal caregiving in nonhuman mammals—a possible substrate of support giving in humans more generally.

Specifically, the VS was more active when women supported their partners compared with when they did not. Interestingly, support giving activated the VS more than just holding the partner's arm when the partner was not in pain, suggesting that it may be more rewarding to help a loved one in need than to engage in passive physical contact with them. The notion that support giving activates reward-related neural regions may shed light on some possible mechanisms underlying the benefits of support giving (3,24). Activation of the mesolimbic dopaminergic system, especially the VS, has been shown to play a role in analgesia (25). In animals, stimulation of dopamine receptors within the VS reduces flinching to a noxious stimulus (26). To the extent that providing support to another activates the VS, thereby decreasing the distressing experience of physical pain, providing support may confer similar benefits.

Another intriguing result from the current study involves the negative correlation between the SA and amygdala during support giving. The SA has an inhibitory influence on stressrelated responding in the amygdala and hypothalamic-pituitaryadrenal (HPA) axis (16). Thus, electrical stimulation of the

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SA leads to decreases in blood pressure, heart rate, pituitaryadrenal function, and galvanic skin responses (16), whereas stimulation of the amygdala exerts opposite effects (27). Moreover, septal lesions lead to increases in fear-related responding (14) and enhanced HPA activation to stress (28). If providing support to another increases SA activity, which relates to reduced amygdala and HPA axis activity, then providing support may also reduce physiological stress responding. However, future work will need to directly examine the effects of support giving on the physiological stress response.

Of note here is the potential role of oxytocin (OT) in the neural correlates of providing care to others. OT is a neuropeptide associated with maternal and affiliative behaviors and the regulation of stress (29,30). Administration of OT to virgin female rats induces maternal behavior toward pups (31), whereas an OT antagonist eliminates this behavior (32). Moreover, OT aids the regulation of stress by dampening physiological stress responses, leading to an anxiolytic, calming effect (33,34) and reduced amygdala activity to fearful stimuli (35). The anxiolytic effects of OT have been suggested to facilitate maternal behavior through the reduction of fear responding (36). Finally, in line with OT's potential role in support giving, the neural regions highlighted as important for the provision of support here, namely, the VS, SA, and amygdala, have high densities of OT receptors (37). Therefore, OT may play a role in facilitating the rewarding and potentially stress-reducing effects of support giving found here; however, a direct test of OT's role in support giving by administering an OT antagonist, for example, is needed.

Although the detrimental effect of prolonged caregiving (e.g., caring for a spouse who is disabled) is well established (38), prior studies have not yet disentangled the effects of support giving itself from the effects of other psychological processes involved in this type of caregiving-such as seeing a loved one deteriorate or mourning their potential loss. For example, most caregiving studies have compared caregivers (e.g., spouses of individual's with Alzheimer's disease) with individuals who are both not caregivers and not dealing with a spouse who is experiencing a deteriorating condition (38-41). Thus, although assumed, it is not clear if the negative effects of prolonged caregiving are due to the act of support giving itself or the first-hand witnessing of the failing health of a spouse; future work will be necessary to disentangle these caregivingrelated subprocesses. In addition, the current study represents a single instance of support giving in a controlled setting and not a prolonged episode such as those that occur in more traditional caregiving studies. Thus, caregivers from these previous studies may experience more burnout because they are providing support for longer periods. They may also feel more obligated and responsible for the person they are supporting, whereas participants in the current study were likely giving support to their partners because it was a nice thing to be able to do. Therefore, the neural correlates of this more prolonged caregiving might involve different neural regions than the type of caring behavior studied here; future work will also need to examine the neural correlates of prolonged support giving.

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Although these results highlight the potentially beneficial properties of support giving, this study is only an initial step in understanding the relationship between support giving and well-being more broadly. Additional studies that directly manipulate support giving, assess health-relevant outcomes, and examine other types of supportive relationships will be needed to further examine the pathways that link support giving with health.

In sum, these data highlight the uniquely beneficial properties of support giving and suggest that supportive exchanges may increase the well-being not only of the receiver but of the giver as well.

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REFERENCES

- House JS, Landis KR, Umberson D. Social relationships and health. Science 1988;241:540–5.
- Berkman LF, Syme SL. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. Am J Epidemiol 1979;109:186–204.
- Brown SL, Nesse RM, Vinokur AD, Smith DM. Providing social support may be more beneficial than receiving it: results from a prospective study of mortality. Psychol Sci 2003;14:320–7.
- Brown SL, Brown RM, House JS, Smith DM. Coping with spousal loss: potential buffering effects of self-reported helping behavior. Pers Soc Psychol Bull 2008;34:849–61.
- Piferi RL, Lawler KA. Social support and ambulatory blood pressure: an examination of both receiving and giving. Int J Psychophysiol 2006;62:328–36.
- Knutson B, Adams CM, Fong GW, Hommer D. Anticipation of increasing monetary reward selectivity recruits nucleus accumbens. J Neurosci 2001; 21:RC159.
- Insel TR. Is social attachment an addictive disorder? Physiol Behav 2003; 79:351–7.
- Lonstein JS, Simmons DA, Swann JM, Stern JM. Forebrain expression of c-fos due to active maternal behaviour in lactating rats. Neuroscience 1997;82:267–81.
- Vernotica EM, Rosenblatt JS, Morell JJ. Microinfusion of cocaine into the medial preoptic area or nucleus accumbens transiently impairs maternal behavior in the rat. Behav Neurosci 1999;113:377–90.
- Hansen S. Maternal behavior of females rats with 6-OHD lesions in the ventral striatum: characterization of the pup retrieval deficit. Physiol Behav 1994;55:615–20.
- Olds J, Milner P. Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. J Comp Physiol Psychol 1954;47:419–27.
- Thomas E. Forebrain mechanisms in the relief of fear: the role of the lateral septum. Psychobiology 1998;16:36–44.
- Malmo RB. Slowing of heart rate after septal self-stimulation in rats. Science 1961;133:1128–30.
- Covian MR, Antunes-Rodrigues J, O'Flaherty JJ. Effects of stimulation of the septal area upon blood pressure and respiration in the cat. J Neurophysiol 1964;27:394–407.
- Brady JV, Nauta WJH. Subcortical mechanisms in emotional behavior: affective changes following septal forebrain lesions in the albino rat. J Comp Physiol Psychol 1953;46:330–46.
- Melia KR, Sananes CB, Davis M. Lesions of the central nucleus of the amygdala block the excitatory effects of septal ablation on the acoustic startle reflex. Physiol Behav 1991;51:175–80.
- Slotnick BM, Nigrosh BJ. Maternal behavior of mice with cingulate cortical, amygdala, or septal lesions. J Comp Physiol Psychol 1975;88:118–27.

- Stack EC, Balakrishnan R, Numan MJ, Numan M. A functional neuroanatomical investigation of the role of the medial preoptic area in neural circuits regulating maternal behavior. Behav Brain Res 2002;131:17–36.
- Coan JA, Schaefer HS, Davidson RJ. Lending a hand: social regulation of the neural response to threat. Psychol Sci 2006;17:1032–9.
- Spanier GB. Measuring dyadic adjustment: new scales for assessing the quality of marriage and similar dyads. J Marriage Fam 1976;38:15–28.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 2002;15:273–89.
- Krueger F, McCabe K, Moll J, Kriegeskorte N, Zahn R, Strenziok M, Heinecke A, Grafman J. Neural correlates of trust. Proc Natl Acad Sci U S A 2007;104:20084–9.
- Moll J, Zahn R, de Oliviera-Souza R, Bramati IE, Krueger F, Tura B, Cavanagh AL, Grafman J. Impairment of prosocial sentiments is associated with frontopolar and septal damage in frontotemporal dementia. Neuroimage 2011;54:1735–42.
- Brown SL, Smith DM, Schulz R, Kabeto MU, Ubel PA, Poulin M, Yi J, Kim C, Langa KM. Caregiving behavior is associated with decreased mortality risk. Psychol Sci 2009;20:488–94.
- Wood PB. Mesolimbic dopaminergic mechanisms and pain control. Pain 2006;120:230–4.
- Taylor BK, Joshi C, Uppal H. Stimulation of dopamine D₂ receptors in the nucleus accumbens inhibits inflammatory pain. Brain Res 2003;987:135–43.
- Davis M. The role of the amygdala in conditioned fear. In: Argon J, editor. The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction. New York, NY: Wiley-Liss Inc; 1991:255–305.
- Herman JP, Figueiredo H, Mueller NK, Ulirch-Lai Y, Ostrander MM, Choi DC, Cullinan WE. Central mechanisms of stress integration: hierarchical circuitry controlling hypothalamic-pituitary-adrenocortical responsiveness. Front Neuroendocrinol 2003;24:151–80.
- Carter CS. Biological perspectives on social attachment and bonding. In: Carter CS, Ahnert L, Grossman KE, Hrdy SB, Lamb ME, Porges SW, Sachser N, editors. Attachment and Bonding: A New Synthesis. Cambridge, MA: MIT Press; 2005:85–100.
- 30. Insel TR, Fernald RD. How the brain processes social information: searching for the social brain. Annu Rev Neurosci 2004;27:697–722.
- Pedersen CA, Prange AJ Jr. Induction of maternal behavior in virgin rats after intracerebroventricular administration of oxytocin. Proc Natl Acad Sci U S A 1979;76:6661–5.
- Olazabal DE, Young LJ. Oxytocin receptors in the nucleus accumbens facilitate "spontaneous" maternal behavior in adult female prairie voles. Neuroscience 2006;141:559–68.
- Heinrichs M, Baumgartner T, Kirschbaum C, Ehlert U. Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. Biol Psychiatry 2003;54:1389–98.
- Uvnas-Moberg K. Oxytocin may mediate the benefits of positive social interaction and emotions. Psychoneuroendocrinology 1998;23:819–35.
- Kirsch P, Esslinger C, Chen Q, Mier D, Lis S, Siddhanti S, Gruppe H, Mattay VS, Gallhofer B, Meyer-Lindenberg A. Oxytocin modulates neural circuitry for social cognition and fear in humans. J Neurosci 2005;25: 11489–93.
- Carter CS. Neuroendocrine perspectives on social attachment and love. Psychoneuroendocrinology 1998;23:779–818.
- Insel TR, Shapiro LE. Oxytocin receptor distribution reflects social organization in monogamous and polygamous voles. Proc Natl Acad Sci U S A 1992;89:5981–5.
- Schulz R, Beach SR. Caregiving as a risk factor for mortality: the caregiver health effects study. JAMA 1999;282:2215–9.
- Mausbach BT, von Kanel R, Aschbacher K, Roepke SK, Dimsdale, JE, Ziegler MG, Mills PJ, Patterson TL. Spousal caregivers of patients with Alzheimer's disease show longitudinal increases in plasma level of tissuetype plasminogen activator antigen. Psychosom Med 2007;69:816–22.
- Roepke SK, Chattillion EA, von Känel R, Allison M, Ziegler M, Dimsdale JE, Mills PJ, Patterson TL, Ancoli-Israel S, Calleran S, Harmell AL, Grant I. Carotid plaque in Alzheimer caregivers and the role of sympathoadrenal arousal. Psychosom Med 2011;73:206–13.
- Wu H, Wang J, Cacioppo JT, Glaser R, Kiecolt-Glaser JK, Malarkey WB. Chronic stress associated with spousal caregiving of patients with Alzheimer's dementia is associated with downregulation of B-lymphocyte GH mRNA. J Gerontol A Biol Sci Med Sci 1999;54:M212–5.

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