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LENDING A HAND: SOCIAL REGULATION OF THE NEURAL RESPONSE TO THREAT

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ABSTRACT

Social contact promotes enhanced health and well being, likely as a function of the social regulation of emotional responding in the face of various life stressors. For this functional magnetic resonance imaging (fMRI) study, 16 married women were subjected to the threat of electric shock while either holding their husband's hand, holding the hands of anonymous male experimenters, or holding no hand at all. Results indicated a pervasive attenuation of activation in the neural systems supporting emotional and behavioral threat responses as a function of spousal handholding. A more limited attenuation of activation in these systems occurred as a function of stranger handholding. Most strikingly, the effects of spousal handholding on neural threat responses varied as a function of marital quality, with higher marital quality predicting less threat-related neural activation in the right anterior insula, superior frontal gyrus and hypothalamus during spousal, but not stranger, handholding.

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Social bonding and soothing behaviors mitigate the destructive effects of negative environmental events and promote enhanced health and well being (Berscheid, 2003). Indeed, social isolation is now considered a major health risk (House, Landis, & Umberson, 1988). Moreover, married people tend on average to be happier and healthier than unmarried people (Wood, Rhodes, & Whelan, 1989), and among married individuals, higher marital quality is associated with decreased risk of infection, faster recovery from injury, and a lower rate of mortality following a diagnosis of life threatening illness (Coyne, Rohrbaugh, Shoham, Sonnega, Nicklas, & Cranford, 2001; Robles & Kiecolt-Glaser, 2003).

The likely mechanism underlying these effects is the social regulation of emotional responding (Diamond, 2001; Hofer, 1984). Theorists have long argued that relationships serve security-provision and distress-alleviation regulatory functions on negative affect and arousal (Bowlby, 1969/1982; Mikulincer, Shaver, & Pereg, 2003). Supportive social behaviors are known to attenuate stress-related activity in the autonomic nervous system (ANS), and hypothalamic-pituitary-adrenal (HPA) axis (DeVries, Glasper, & Detillion, 2003). Maternal grooming behaviors even affect glucocorticoid receptor gene expression underlying hippocampal and HPA axis stress reactivity in rat pups (Weaver, Diorio, Seckl, Szyf, & Meaney, 2004). It is becoming increasingly clear that the neural systems supporting social affiliation are implicated in more general emotional responding. For example, the neuropeptides oxytocin and arginine vasopressin have emerged as important mediators of social affiliation (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005; Young & Wang, 2004), and receptors for both are found in a network of emotion-related cortical and sub-cortical structures among monogamous non-human mammals (Insel, 1997).

Recent human functional neuroimaging studies of maternal affection and romantic attachment have implicated structures associated with reward seeking, including caudate-putamen and ventral tegmentum, as well as portions of the dorsolateral and ventrolateral prefrontal cortex (PFC) (Aron, Fisher, Mashek, Strong, Li, & Brown, 2005; Bartels & Zeki, 2004). Interestingly, *deactivations* in structures associated with the regulation of negative emotion, such as the medial prefrontal and ventral paracingulate cortex, have also been observed in some of these studies (Bartels & Zeki, 2004). Although interesting, research of this sort has focused on putative neural responses to higher order constructs (e.g., love, friendship) that are in fact difficult or impossible to capture directly using most neuroimaging technology (cf., Cacioppo, Berntson, Lorig, Norris, Rickett & Nusbaum, 2003). By contrast, simple threat cues possess discrete stimulus properties that are well suited to neuroimaging. Despite this advantage, no work to date has identified the distress-alleviating effects of romantic relationships on the neural circuitry supporting threat responding.

In this functional magnetic resonance imaging (fMRI) experiment, handholding and threat of electric shock were used to investigate the social regulation of neural systems underlying response to threat (cf., Dalton, Kalin, Grist, & Davidson, 2005). Because most married people in the United States identify their spouse as their central adult relationship (Lugaila, 1998), married women in highly satisfactory relationships were asked to view images indicating either safety or threat under three counterbalanced conditions while brain images were collected. In one condition, women held their husband's hand. In the other two, they either held the hand of an anonymous male experimenter or no hand at all. Handholding was selected as a means of supportive social behavior because it 1) is a common nonverbal mode of expressing social support and affection, 2) has been observed in non-human primates during periods of dyadic reconciliation and soothing (de Waal, 2000), 3) has been shown to reduce autonomic arousal and reports of anxiety under stressful conditions (Jung-Soon & Kyung-Sook, 2001), and 4) offered a method that was easily implemented in the fMRI environment.

We sought to test three major hypotheses. First, we hypothesized simply that both spouse and stranger handholding would attenuate threat responsive neural activity. Second, we hypothesized that attenuation of the neural threat response would be maximized during spousal handholding. Finally, we hypothesized that attenuation of the neural threat response would be a partial function of marital quality, with higher marital quality predicting greater attenuation.

METHOD

PARTICIPANTS

16 highly satisfied married couples were selected to participate (mean husband and wife ages were 33 [s.d. = 5] and 31 [s.d. = 5], respectively). 15 couples identified as Caucasian and one identified as Asian. Participants were recruited from the greater Madison, WI area via newspaper advertisements, and respondents were excluded if they had current or past psychopathology, were pregnant, or exhibited any risk for incident in the magnetic environment of the fMRI scanner. Because previous research suggests the distress-attenuating effects of relationships should be strongest in those that are highly satisfactory (Coyne et al., 2001), both wife and husband marital quality ratings were assessed using the satisfaction subscale of the Dyadic Adjustment Scale (DAS; Spanier, 1976). The DAS is a widely used measure of relationship quality comprised of four correlated subscales and one overall composite score (the DAS score). Higher DAS scores indicate relationships of putatively higher quality. In the initial telephone screening, the satisfaction subscale of the DAS was used to rapidly screen out couples who were dissatisfied with their marriage. This subscale ranges from 0 to 50, with 50 representing the highest level of satisfaction. Husbands and wives scoring lower than 40 on this subscale were excluded from the study. The total DAS score has a theoretical range extending from 0 to 151, with scores lower than 100 thought to indicate distressed marriages. Phone screening on the satisfaction subscale resulted in husband and wife mean DAS scores of 126 (SD = 10) and 127 (SD = 6), respectively, indicating a generally high level of marital quality among the couples in this sample. The Pearson correlation between husband and wife DAS scores was $r = .20$, $p = \text{ns}$. Composite DAS scores were used for analyses reported below. Only wives were tested in the scanner. Husbands completed questionnaires and provided handholding. All participants gave written informed consent in agreement with the Human Subjects Committee (HSC) of the University of Wisconsin medical school and were paid for participation.

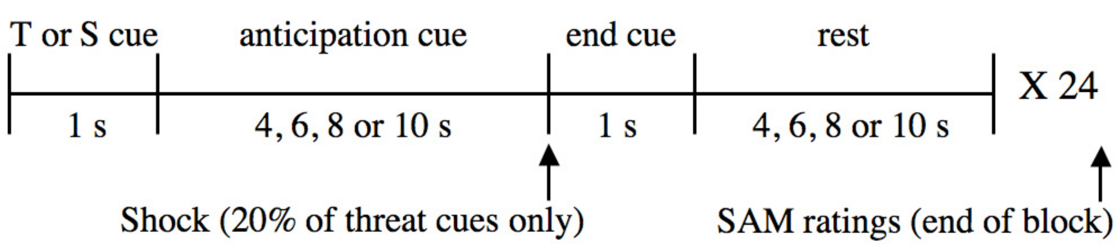
PROCEDURE

Interested participants were screened via telephone. Eligible participants were told they were participating in a study of handholding, and scheduled for two visits to the laboratory. During the first, a battery of questionnaires selected to assess marital quality and various aspects of personality were completed before participants underwent an imaging "trial run" in the laboratory's mock fMRI scanner. Mock scanning familiarizes participants to the scanning environment, allowing assessment of comfort with that environment and practice using experimental devices (e.g., button box). Although all couples were fully informed about the electric shocks involved in visit two, no sample shocks were delivered during visit one.

The second visit occurred approximately one week later, and consisted of the experimental brain imaging procedure. Couples were brought to a waiting room where they completed an additional fMRI safety assessment as 2 Ag-AgCl shock electrodes were applied to the wife's right or left ankle (counterbalanced across participants). The wife was then led to the fMRI chamber, where high-resolution anatomical scans were collected before the beginning of the experiment.

For the experiment, the wife observed 12 threat (T) and 12 safety (S) cues, in random order, within each of three counterbalanced blocks of 24 total cue trials (see figure 1) Trials were randomized within subjects and block order was counterbalanced between subjects. During one block, the wife held her husband's hand. During another, she held the hand of an unseen, anonymous male experimenter. (Wives were not introduced to the anonymous male handholder until after the experiment was completed.) For the remaining block no handholding was provided. Subjects' right hands were used for all handholding; left hands were used for providing ratings of subjective experience. With the exception of three participants, all participants held the hand of the same male experimenter. Two other male volunteers served as the stranger on the occasions the standard stranger was unavailable. Threat cues (a red "X" on a black background) indicated a 20% likelihood of receiving an electric shock to the ankle. Safety cues (a blue "O" against a black background) indicated no chance of shock. Electric shocks were delivered using an isolated physiological stimulator (Coulborn Instruments, L. L. C., Allentown, Pennsylvania) with 20 ms duration at 4 mA. All subjects received two shocks per block.

Figure 1



<u>Experimental procedure</u>. Trials consisted of a 1s T or S cue, and a 4 to 10 s anticipation period, a 1 s end cue, and a 4 to 10 s resting period. At the end of each handholding condition, subjects completed ratings of unpleasantness and arousal.

Cues each lasted 1 s, followed by an anticipation period that was varied from between 4 and 10 seconds. Subjects were instructed to focus their attention on a fixation cross, "+," during the anticipation period, and the end of each cue trial was indicated with a small circle, "•." Subjects were instructed to rest until the next trial began. The resting period presented a black screen, which also varied between 4 and 10 seconds. At the end of each block, subjects completed unpleasantness and arousal ratings using the Self-Assessment Manikin (SAM) scales (Bradley & Lang, 1994). Subjects provided one unpleasantness and arousal rating for each handholding condition selecting their scores using a button box placed in their left hands.

FMRI IMAGE ACQUISITION AND DATA ANALYSIS

Functional magnetic images were acquired using a General Electric (Fairfield, CT) Signa 3.0 Tesla high-speed magnetic imaging device, with a quadrature head coil. 215 functional images were collected per block, in volumes of 30 4mm sagital echo-planar (EPI) slices (1-mm slice gap) covering the whole brain. A repetition time (TR) of 2 s was used, with an echo time (TE) of 30 ms, a 60° flip, and a field of view (FOV) of 240 X 240 mm, with a 64 X 64 matrix, resulting in a 3.75 X 3.75 X 5 mm voxel size. Prior to collection of functional images, a T1 weighted SPGR anatomical scan consisting of 124 1.2mm slices to assist with localization of function.

Using Analysis of Functional Neural Images (AFNI) software (v. 2.52; Cox, 1996), raw data were reconstructed offline with a 1-voxel in-plane FWHM Fermi window, 6-parameter rigid body motion correction, high pass filtering of 1/60 s (to remove signal unrelated to stimulus presentation), and removal of ghost and skull artifacts. Trials during which participants actually received shocks were excluded from analysis in order to minimize movement artifacts. Time series were fit with a least squares general linear model to an ideal hemodynamic response with the motion parameters entered as covariates. The resultant beta-weights were converted to percent signal change, and the maps transformed into standardized Talairach space (Talairach, 1988).

STATISTICAL REGIONS OF INTEREST (ROIS).

An intermediate data reduction step involved determination of the normative neural threat response. To accomplish this, activation to threat (T) and safety (S) cues were contrasted (T – S) within the no-handholding condition. T – S multi-subject regions of interest (ROIs) were identified via $p < .005$ (corrected), voxel-wise t-tests that indicated areas of greater activation in threat than safety cue trials, with corrections estimated from Monte Carlo simulations. As expected, this procedure revealed activation in a network of regions associated in numerous studies with neural response to threat, negative affect or anticipation of pain, such as the anterior cingulate (ACC), ventral ACC, right dorsolateral prefrontal cortex (DLPFC), right inferior frontal gyrus, right superior frontal gyrus, right anterior insula, caudate / nucleus accumbens (NAcc), putamen, hypothalamus, right postsentral gyrus, superior colliculus/midbrain, posterior cingulate, and left supramarginal gyrus (see table 1 for all ROIs) (Davidson & Irwin, 1999; Ploghaus, Tracey, Gati, Clare, Menon, Matthews, & Rawlins, 1999; Salomons, Johnstone, Backonja, & Davidson, 2004; Wager, Rilling, Smith, Skolnik, Casey, Davidson, Kosslyn, Rose, & Cohen, 2004). Average values across ROIs for each subject were used in subsequent comparisons of handholding condition and tests of covariation with marital quality.

Table 1. Statistical ROIs (with centroid coordinates and cluster size) determined by no-hand T – S ($p < .005$, $P_{rep} \geq .97$, corrected) contrasts, and their effects across handholding conditions.

Threat Responsive Regions	x	y	z	t-score	Size in mm^3	Condition effect	Spouse effect	Stranger effect
Frontal / Anterior Cingulate Regions								
Supplementary motor	4	6	46	3.63	4043			
Superior frontal gyrus	-10	-8	59	3.82	907			
	9	-9	64	3.89	435			
Ventral ACC	-12	39	-1	3.55	358	✓	✓	✓
	3	44	2	3.81	296			
DLPFC	32	34	30	3.78	350	✓	✓*	
Precentral gyrus	-39	-4	37	3.73	336			
Ventromedial PFC	12	45	-6	3.77	275			
Inferior frontal gyrus	-36	35	21	4.05	572			
Insular / Subcortical Regions								
Anterior insula	37	16	3	4.33	6213			
	-28	20	3	3.92	4937			
Caudate	8	7	8	3.89	2092			
	-10	-3	21	3.75	491			
Caudate / NAcc.	-8	4	2	3.71	1390	✓	✓	
Putamen	28	4	-3	3.72	192			
Ant. thalamic nucleus	-11	-14	11	3.63	418			
Hypothalamus	1	-13	-5	3.72	1441			
Superior colliculus	3	-28	-2	3.77	1316	✓	✓	
Parietal / Posterior Cingulate Regions								
Posterior cingulate	9	-55	19	3.65	645			
	-9	-28	38	3.93	381	✓	✓	✓
	14	-33	38	3.53	249	✓	✓	✓
Postcentral gyrus	30	-50	63	3.73	390	✓	✓	✓
Supramarginal gyrus	-53	-29	20	3.54	298	✓	✓	✓
	50	-28	17	3.73	231			

Spouse effect = threat activity during spouse < no hand; Stranger effect = threat activity during stranger < no hand
*indicates spouse < stranger; No instances of stranger < spouse were observed

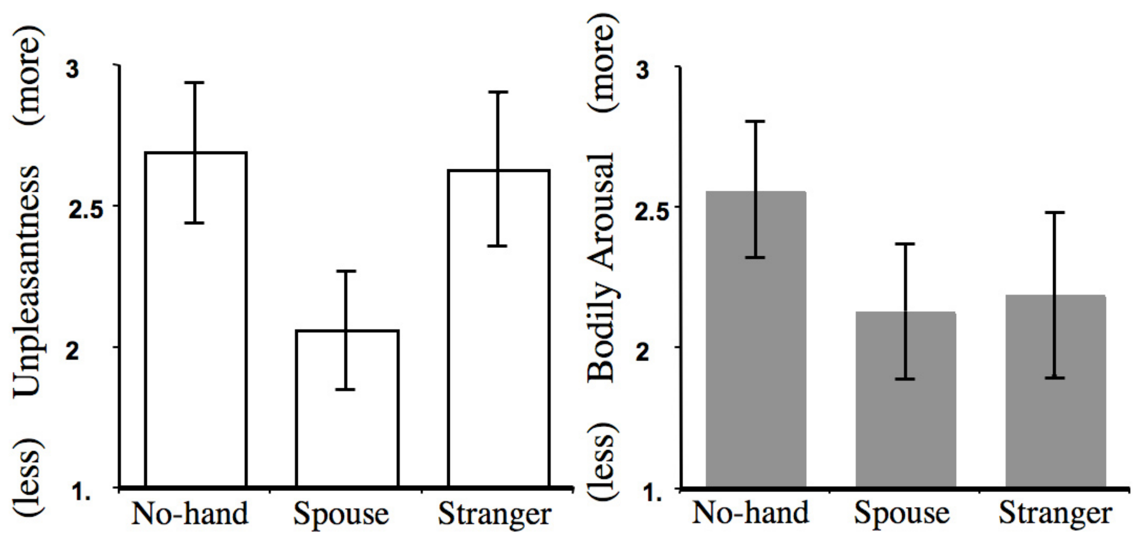
To examine the effects of handholding on threat-related ROI activation, two general data analytic techniques were employed. First, the repeated measures general linear model (GLM) was used to test for effects of handholding condition in all ROIs. Second, following identification of ROIs showing main effects of Condition, planned comparisons were conducted to determine whether specific condition contrasts (spouse v. stranger v. no-hand) were statistically significant. Third, in testing relationships between threat related neural activation and marital quality, SPSS's linear mixed model module was used to test for differences in slopes between brain activation and DAS scores as a function of handholding condition.

RESULTS

HANDHOLDING REDUCES SUBJECTIVE UNPLEASANTNESS AND AROUSAL

Tracking subjective experience reports provides an important check on the efficacy of the experimental manipulation. Thus, at the end of each block of trials, subjects completed emotional valence and bodily arousal ratings using the Self-Assessment Manikin (SAM) scales (Bradley & Lang, 1994): 5-point non-verbal pictorial instruments for measuring degrees of unpleasantness (valence) and agitation (arousal). Repeated measures ANOVAs revealed main effects of handholding condition on ratings of both valence, $F(2,14) = 8.30$, $p = .004$, $P_{rep} = .98$, $\eta_p^2 = .54$, and arousal, $F(2,14) = 3.62$, $p = .05$, $P_{rep} = .92$, $\eta_p^2 = .34$). Planned comparisons revealed spouse handholding ratings were significantly less unpleasant than both stranger hand, $F(1,15) = 4.77$, $p = .05$, $P_{rep} = .93$, $\eta_p^2 = .24$ and no-hand, $F(1,15) = 16.30$, $p = .001$, $P_{rep} = .99$, $\eta_p^2 = .52$, conditions. By contrast, planned comparisons of arousal ratings across handholding conditions revealed that although spouse and stranger hand conditions were both less arousing than no hand, these comparisons only approached statistical significance, with $F(1,15) = 3.85$, $p = .07$, $P_{rep} = .90$, $\eta_p^2 = .20$ for spouse hand and $F(1,15) = 3.46$, $p = .08$, $P_{rep} = .89$, $\eta_p^2 = .19$ for stranger hand (see figure 2).

Figure 2



Main effects of handholding condition on unpleasantness and arousal ratings

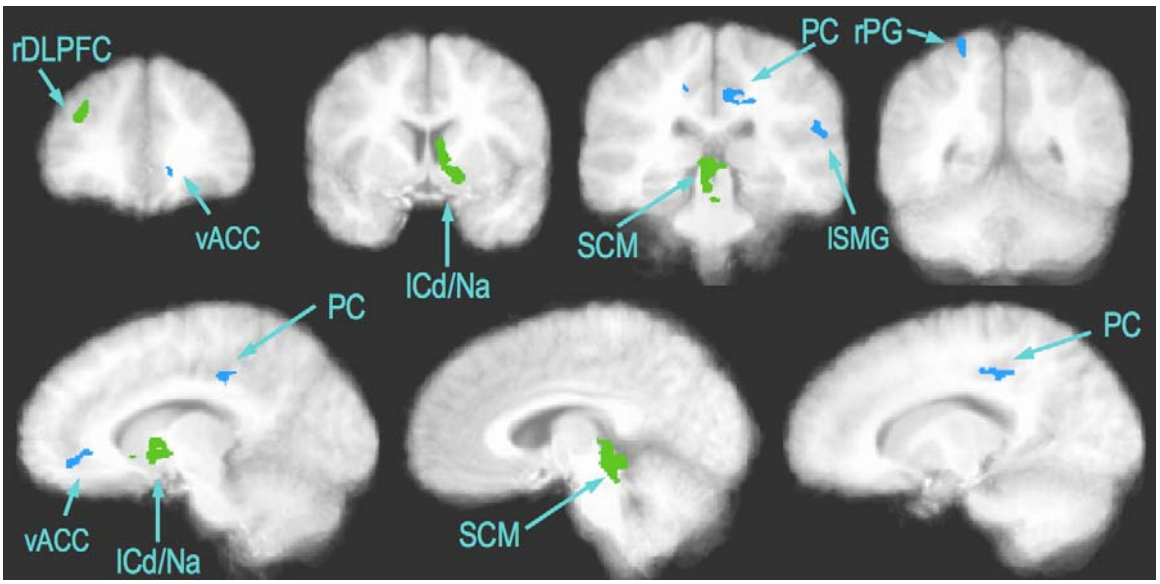
HANDHOLDING ATTENUATES NEURAL THREAT RESPONSES

Main effects. Significant main effects of handholding condition were found in ventral ACC, right DLPFC, left caudate, superior colliculus/midbrain, two regions of the posterior cingulate, left supramarginal gyrus, and right postcentral gyrus, all $Fs(2,14) \geq 3.62$, $ps \leq .05$, $P_{rep}s \geq .92$, $\eta_p^2 \geq .20$ (see figure 3).

Spouse effects. Planned comparisons revealed that neural activation to threat (T – S) during the spouse condition was significantly less than the no-hand condition in the ventral ACC, left caudate, superior colliculus/midbrain, posterior cingulate, left supramarginal gyrus and right postcentral gyrus, all $Fs(1,15) \geq 4.52$, $ps \leq .05$, $P_{rep}s \geq .92$, $\eta_p^2 \geq .23$. Neural activation to threat during spouse hand holding was also significantly less than the stranger condition in the right DLPFC, $F(1,15) = 6.89$, $p = .02$, $P_{rep} = .95$, $\eta_p^2 = .32$, though attenuation in this region in comparison to no hand only approached significance, $F(1,15) = 3.54$, $p = .08$, $P_{rep} = .89$, $\eta_p^2 = .19$.

Common hand effects. Neural activation to threat during both the spouse and stranger conditions was significantly less than the no-hand condition in the ventral ACC, posterior cingulate, left supramarginal gyrus and right postcentral gyrus, all $Fs(1,15) \geq 5.76$, $ps \leq .03$, $P_{rep}s \geq .94$, $\eta_p^2 \geq .28$.

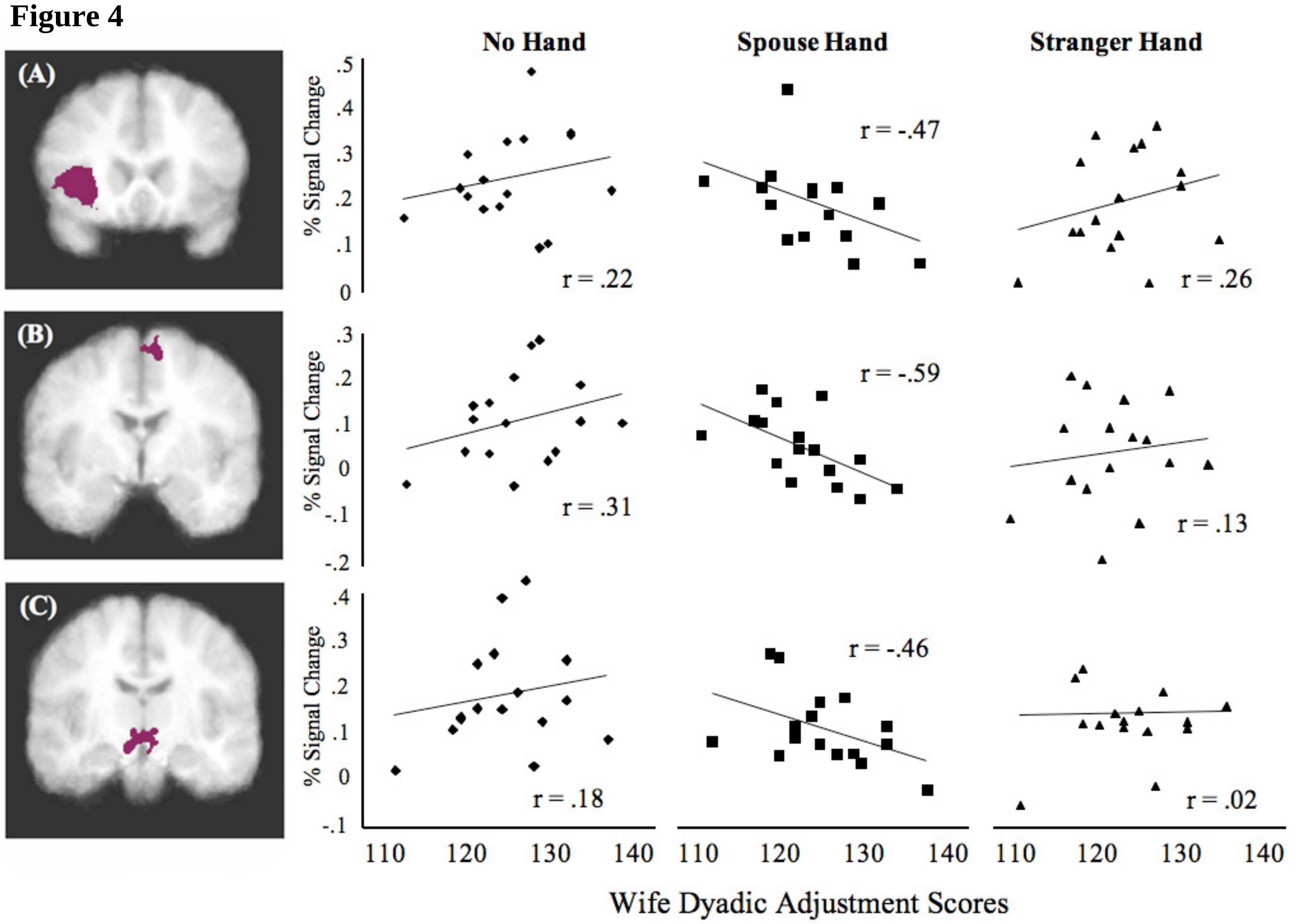
Figure 3



Threat responsive ROIs affected by handholding condition. Green clusters highlighting right DLPFC, left caudate/nucleus accumbens (lCd/NAcc), and superior colliculus/midbrain (SCM) indicate spouse related attenuation. Blue clusters highlighting the ventral ACC (vACC), posterior cingulate (PC), right postcentral gyrus (rPG) and left supramarginal gyrus (lSMG) indicate attenuation associated with both spouse and stranger handholding. Section plane coordinates are (from left to right): top row: Y = +34 mm, +3mm, -29 mm, -49 mm; bottom row: X = -10 mm, +2 mm, +14 mm.

DAS scores and neural response to threat. We next sought to predict threat related neural activation using DAS scores. First, a repeated measures ANCOVA revealed an interaction effect between handholding condition and wife DAS (WDAS) in predicting valence ratings, $F(2,13) = 5.16$, $p = .02$, $P_{rep} = .96$, $\eta_p^2 = .44$. Pearson correlations between WDAS and valence ratings were $r = -.46$, p = ns, $r = -.28$, p = ns, and $r = -.82$, $p < .001$, Prep = .99, for no-hand, spouse and stranger conditions, respectively. HDAS scores did not show any similar effects, nor were WDAS or HDAS scores associated with arousal ratings. Thus, it was necessary to determine whether DAS scores were capable of predicting threat-related neural activation independently of valence ratings. To accomplish this, linear mixed models containing valence ratings (a changing covariate), HDAS scores, and WDAS scores, as well as their interactions with handholding condition, were performed. No effect of HDAS or the HDAS by condition interaction was observed. As shown in figure 4, however, there were significant WDAS by condition interaction effects in the right superior frontal gyrus $F(2,26) = 4.84$, $p = .02$, $P_{rep} = .96$, right anterior insula, $F(2,23) = 4.33$, $p = .03$, $P_{rep} = .95$, and hypothalamus, $F(2,27) = 4.31$, $p = .02$, $P_{rep} = .95$. Inspection of separate regressions revealed these interaction effects to be driven by negative correlations between WDAS and threat related neural activation during the spouse condition alone. These correlations were $r = -.59$, $p = .02$, Prep = .95, $r = -.47$, $p = .07$, Prep = .90 and $r = -.46$, $p = .08$, Prep = .89, for right superior frontal gyrus, right anterior insula, and hypothalamus, respectively. In stranger and alone conditions, correlations between WDAS and threat related ROI activation was either slightly positive (less than .31) or near zero. Interestingly, main effects of valence were also observed in both the right anterior insula, $F(1,27) = 6.02$, $p = .02$, $P_{rep} = .96$, and the hypothalamus, $F(1,32) = 10.23$, $p = .003$, $P_{rep} = .99$, with average correlations of $r = .46$, $p = .08$, $P_{rep} = .89$ and $r = .65$, $p = .01$, $P_{rep} = .97$, for anterior insula and hypothalamus, respectively. These effects indicate that greater activation in both the anterior insula and the hypothalamus corresponded with greater levels of subjective unpleasantness, regardless of handholding condition.

Figure 4



Decomposed WDAS by handholding condition interaction effects. (A) Right anterior insula (Y = +19mm). (B) Right superior frontal gyrus (Y = -4mm). (C) Hypothalamus (Y = -13mm).

DISCUSSION

As hypothesized, both spouse and stranger handholding attenuated neural response to threat to some degree, but spousal handholding was particularly powerful. Moreover, even within this sample of highly satisfied married couples, the benefits of spousal handholding under threat were maximized in those couples with the very highest quality relationships.

Close inspection of the regions implicated in the main effects of handholding suggests the following:

1. Both spouse and stranger handholding confers a basic level of regulatory influence on the neural response to threat cues, especially with regard to structures implicated in the modulation of affect-related action and bodily arousal such as the ventral ACC (Allman, Hakeem, Erwin, Nimchinsky, & Hof, 2001), and visceral and musculoskeletal responses, such as the posterior cingulate, supramarginal gyrus and postcentral gyrus (Fulbright, Troche, Skudlarski, Gore, & Wexler, 2001; Liddel, Brown, Kemp, Barton, Das, Peduto, Gordon, & Williams, 2005; Rushworth, Krams, & Passingham, 2001).
2. Spousal handholding conferred these benefits and more, further attenuating threat related neural activation in areas implicated in the regulation of emotion (right DLPFC, caudate) and emotion-related homeostatic functions (superior colliculus/midbrain) (Damasio, Grabowski, Bechara, Damasio, Ponto, Parvizi, & Hichwa, 2000; Davidson & Irwin, 1999; Liddel et al., 2005). It is striking how this pattern of neural effects was echoed in subjective reports of experience: While both spouse and stranger handholding resulted in lower reports of bodily arousal, only spousal handholding provided the additional benefit of lowering subjective reports of task-related unpleasantness.
3. *Threat-related activation in the right anterior insula, superior frontal gyrus and hypothalamus was sensitive to marital quality.* This suggests individuals in higher quality relationships benefit from greater regulatory effects on the neural systems supporting the brain’s stress response, including the affective component of pain processing (e.g., in right anterior insula; cf., Ploghaus et al., 1999; Salomons et al., 2004; Wager et al., 2004).

Indeed, regulation of structures like the hypothalamus suggests these benefits may be pervasive, as the hypothalamus influences a cascade of neurochemical regulatory systems, such as the release of corticotropin-releasing-hormone (CRH), which in turn stimulates the release of cortisol into the bloodstream—a process widely understood to hold implications for immune function and memory (Kemeny, 2003).

It is particularly noteworthy that the effects of marital quality were themselves specific to the spouse handholding condition. This is consistent with conceptualizations of attachment relationships as “hidden regulators”—“regulators,” because of the emotion-regulatory benefits attachment relationships confer, and “hidden” because those regulatory benefits are frequently only apparent when the attachment system, or one of the partners within that system, is under threat (Hofer, 1984, 1995).

It is already well known that social isolation is a major health risk, and that high quality attachment relationships mitigate the effects of stress, injury and infection (Berscheid, 2003; Coyne et al., 2001; Hofer, 1984, 1995; House et al., 1988; Mikulincer et al., 2003; Robles & Kiecolt-Glaser, 2003; Wood et al., 1989). These results provide new insights into how these effects occur. At one level, handholding appears to produce a general regulatory effect on neural threat responses related to bodily attention and the coordination of motor responses, suggesting that such processes may represent the most immediate or lowest level benefit of social soothing and support. At another level, structures associated with more evaluative, attentional and affective components of the threat response were attenuated more specifically by spousal handholding, suggesting that attachment figures act as emotion-regulators in ways that strangers do not. Put another way, both stranger and spousal handholding appears capable of decreasing the need for a coordinated bodily response to threatening stimuli, but only spousal handholding confers the additional benefit of decreasing the need for vigilance, evaluation and self-regulation of affect. Finally, the correspondence between the magnitude of threat-related neural responses and marital quality is consistent with known associations among measures of marital quality and health, and even point the way toward the neural mediators of those effects. Particularly promising in this regard is the effect of marital quality on the hypothalamus observed here, as links between the HPA-axis and various health related processes (e.g., immune function) suggest a bridge between findings reported here and general associations between marital quality and health reported elsewhere (Robles & Kiecolt-Glaser, 2003). Other links are possible as well. For example, oxytocin has been proposed as one of the mechanisms through which the positive benefits of social support are realized (Uvnaes-Moberg, 1998), and it is plausible that oxytocin activity served as a mediator of the attenuation of threat related neural activity reported here. Exogenous injection of oxytocin attenuates a variety of centrally mediated stress responses in rats (Izzo, Rotondi, Perone, Lauro, Manzo, Casilli, Rasile, & Amato, 1999) and physical contact alone has been associated with oxytocin release from the paraventricular nuclei of the hypothalamus (Uvnaes-Moberg, 1998), which may in turn increase endogenous opioid activity (Uvnaes-Moberg, 1998) and target dopamine receptors related to inhibitory motor control throughout the basal ganglia (Gimpl & Fahrenholz, 2001).

Of course, it remains important to note that these findings may not generalize to attachment relationships that are characterized by discord or that are otherwise unsatisfactory to one or the other partner. Indeed, the fact that threat-related neural activation was sensitive to marital quality even within highly satisfactory marriages suggests that many of these effects should not generalize to relationships of poorer quality. Moreover, it is well known that threat responses in the context of attachment relationships also vary as a partial function of attachment-related personality characteristics—individual differences in styles of relating to others while under stress (Bowlby, 1969/1982; Mikulincer& Shaver, 2005; Mikulincer et al., 2003). Indeed, such differences may have influenced the pattern of correlations observed between wife DAS scores and subjective unpleasantness ratings across the different hand holding conditions. These and other questions await further evaluation. In the meantime, results presented here have provided evidence of the neural systems and processes through which the distress-alleviating and health enhancing effects of social soothing in general, and high quality attachment relationships in particular, are realized.

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