Research Article

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 holding their husband’s hand, the hand of an anonymous male experimenter, or no hand at all. Results indicated a pervasive attenuation of activation in the neural systems supporting emotional and behavioral threat responses when the women held their husband’s hand. A more limited attenuation of activation in these systems occurred when they held the hand of a stranger. Most strikingly, the effects of spousal hand-holding 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, hand-holding.

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 et al., 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 that influence negative affect and arousal (Bowlby, 1969/1982; Mikulincer, Shaver, & Peregr, 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 subcortical structures in monogamous nonhuman 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 (Aron et al., 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 et al., 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, hand-holding 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 partner (Lugaila, 1998), we asked married women in highly satisfactory marital relationships 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 held either the hand of an anonymous male experimenter or no hand at all. Hand-holding was selected as a supportive social behavior because it (a) is a common nonverbal mode of expressing social support and affection, (b) has been observed in nonhuman primates during periods of dyadic reconciliation and soothing (de Waal, 2000), (c) has been shown to reduce autonomic arousal and reports of anxiety under stressful conditions (Jung-Soon & Kyung-Sook, 2001), and (d) 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 hand-holding would attenuate threat-responsive neural activity. Second, we hypothesized that attenuation of the neural threat response would be maximized during spousal hand-holding. 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
Sixteen highly satisfied married couples were selected to participate; mean ages of the husbands and wives were 33 (SD = 5) and 31 (SD = 5), respectively. Fifteen couples identified themselves as Caucasian, and one identified themselves 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 that highly satisfactory relationships should have the strongest distress-attenuating effects (Goyne et al., 2001), both wives and husbands rated their marital quality using the Satisfaction subscale of the Dyadic Adjustment Scale (DAS; Spanier, 1976). The DAS is a widely used measure of relationship quality comprising 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. Scores on this subscale range 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. Later, total DAS scores were recorded from both husbands and wives. The total DAS score has a theoretical range extending from 0 to 151, with scores lower than 100 thought to indicate distressed marriages. Mean total DAS scores were 126 (SD = 10) and 127 (SD = 6) for husbands and wives, respectively, indicating a generally high level of marital quality among the couples in this sample. The Pearson correlation between husbands’ and wives’ DAS scores was .20, n.s. Total DAS scores were used for the analyses reported here.

Only wives were tested in the scanner. Husbands completed questionnaires and provided hand-holding. All participants gave written informed consent in agreement with the Human Subjects Committee 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 hand-holding, and scheduled for two visits to the laboratory. During the first visit, participants completed a battery of questionnaires selected to assess marital quality and various aspects of personality (results not reported here) before undergoing an imaging trial run in the laboratory’s mock fMRI scanner. Mock scanning familiarizes participants with the scanning environment, allows them to express any discomfort with that environment, and gives them practice using experimental devices (e.g., button box). Although all couples were fully informed about the electric shocks that would be involved in the second visit, no sample shocks were delivered during the first visit.

The second visit, which occurred approximately 1 week later, consisted of the experimental brain-imaging procedure. Couples were brought to a waiting room, where they completed an additional fMRI safety assessment as two 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 and 12 safety cues, in random order, within each of three counterbalanced blocks, for a total of 24 cue trials (see Fig. 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 hand-holder until after the experiment was completed.) For the remaining block, no hand-holding was provided. Subjects’ right hands were used for all hand-holding; left hands were used for providing ratings of subjective experience. With the exception of 3 participants, all participants held the hand of the same male experimenter. Two other male
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Statistical Regions of Interest (ROIs)

An intermediate data-reduction step involved determining the normative neural threat response by contrasting activation to threat cues and activation to safety cues (threat minus safety) within the no-hand-holding condition. Multisubject ROIs were identified via voxel-wise *t* tests that indicated areas of greater activation in threat- than safety-cue trials (*p* < .005 corrected, with corrections estimated from Monte Carlo simulations). As expected, this procedure revealed activation in a network of regions that numerous studies have shown to be associated with neural response to threat, negative affect, or anticipation of pain, such as the ventral anterior cingulate cortex (vACC), right dorsolateral prefrontal cortex (right DLPFC), right inferior frontal gyrus, left superior frontal gyrus, right anterior insula, caudate–nucleus accumbens (NAcc), putamen, hypothalamus, right postcentral gyrus, superior colliculus, posterior cingulate, and left supramarginal gyrus (Davidson & Irwin, 1999; Ploghaus et al., 1999; Salomons, Johnstone, Backonja, & Davidson, 2004; Wager et al., 2004). Table 1 lists all the ROIs. These ROIs were used in subsequent comparisons of hand-holding conditions and tests of covariation with marital quality.

To examine the effects of hand-holding on threat-related ROI activation, we employed three general data-analytic steps. First, the repeated measures general linear model was used to test for effects of hand-holding 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 vs. stranger vs. no hand) were statistically significant. Third, in testing relationships between threat-related neural activation and marital quality (DAS scores), we used SPSS’s linear mixed-model module to examine differences in slopes as a function of hand-holding condition.

RESULTS

Hand-Holding Reduces Subjective Unpleasantness and Arousal

Tracking reports of subjective experience provided an important check on the efficacy of the experimental manipulation. Repeated measures analyses of variance revealed main effects of hand-holding condition on SAM ratings of both valence, *F*(2, 14) = 8.30, *p* = .004, *p*<sub>rep</sub> = .97, η<sup>2</sup><sub>p</sub> = .54, and arousal, *F*(2, 14) = 3.62, *p* = .05, *p*<sub>rep</sub> = .88, η<sup>2</sup><sub>p</sub> = .34. Planned comparisons

<table>
<thead>
<tr>
<th>T or S Cue</th>
<th>Anticipation Cue</th>
<th>End Cue</th>
<th>Rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 s</td>
<td>4, 6, 8, or 10 s</td>
<td>1 s</td>
<td>X 24</td>
</tr>
</tbody>
</table>

Shock (20%) of Threat Cues Only

SAM Ratings (End of Block)

\( \text{Z} \approx 0.88, 0.97, 0.88, \)
revealed that unpleasantness ratings were significantly lower in the spousal-hand-holding condition than in both the stranger-hand-holding condition, $F(1, 15) = 4.77, p = .05, r_{rep} = .88, \eta_p^2 = .24$, and the no-hand condition, $F(1, 15) = 16.30, p = .001, r_{rep} = .99, \eta_p^2 = .52$. By contrast, planned comparisons of arousal ratings across hand-holding conditions revealed that although the spouse and stranger conditions were both less arousing than the no-hand condition, these comparisons only approached statistical significance, $F(1, 15) = 3.85, p = .07, r_{rep} = .85, \eta_p^2 = .20$, and $F(1, 15) = 3.46, p = .08, r_{rep} = .83, \eta_p^2 = .19$, respectively (see Fig. 2).

**Hand-Holding Attenuates Neural Threat Responses**

Table 1 provides a guide to the main effects and planned comparisons, with centroid coordinates and cluster size for each ROI. Significant main effects of hand-holding condition were found in vACC, right DLPFC, left caudate, superior colliculus, two regions of the posterior cingulate, left supramarginal gyrus, and right postcentral gyrus, all $F$s(2, 14) $\geq$ 3.62, $p$s $\leq$ .05, $r_{rep}$s $\geq .88, \eta_p^2$s $\geq .20$ (see Fig. 3).

Planned comparisons revealed that neural activation to threat (threat minus safety) was significantly lower in the spouse condition than in the no-hand condition for the following regions: vACC, left caudate, superior colliculus, posterior cingulate, left supramarginal gyrus, and right postcentral gyrus, all $F$s(1, 15) $\geq 4.52, p$s $\leq .05, r_{rep}$s $\geq .88, \eta_p^2$s $\geq .23$. Neural activation to threat was also significantly lower in the spouse condition than in the stranger condition in the right DLPFC, $F(1, 15) = 6.89, p = .02, r_{rep} = .93, \eta_p^2 = .32$, though attenuation in this region for the comparison between the spouse and no-hand conditions only approached significance, $F(1, 15) = 3.54, p = .08, r_{rep} = .84, \eta_p^2 = .19$.

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### Table 1

**Statistical Regions of Interest and Their Effects Across Hand-Holding Conditions**

<table>
<thead>
<tr>
<th>Region</th>
<th>Centroid coordinates</th>
<th>Size (mm$^3$)</th>
<th>Condition effect</th>
<th>Spouse effect</th>
<th>Stranger effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frontal and anterior cingulate regions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supplementary motor cortex</td>
<td>4 6 46</td>
<td>3.63</td>
<td>4,043</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>-10 -8 59</td>
<td>3.82</td>
<td>907</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventral ACC</td>
<td>-12 39 -1</td>
<td>3.55</td>
<td>358</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>DLPFC</td>
<td>3 44 2</td>
<td>3.81</td>
<td>296</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Insular and subcortical regions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior insula</td>
<td>37 16 3</td>
<td>4.33</td>
<td>6,213</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate</td>
<td>-28 20 3</td>
<td>3.92</td>
<td>4,937</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caudate–NAcc</td>
<td>-10 -3 21</td>
<td>3.75</td>
<td>491</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putamen</td>
<td>-8 4 2</td>
<td>3.71</td>
<td>1,390</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Anterior thalamic nucleus</td>
<td>28 -14 11</td>
<td>3.63</td>
<td>418</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>1 -13 -5</td>
<td>3.72</td>
<td>1,441</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior colliculus</td>
<td>3 -28 -2</td>
<td>3.77</td>
<td>1,316</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td><strong>Parietal and posterior cingulate regions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior cingulate</td>
<td>9 -55 19</td>
<td>3.65</td>
<td>645</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>-9 -28 38</td>
<td>3.93</td>
<td>381</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Supramarginal gyrus</td>
<td>30 -50 63</td>
<td>3.73</td>
<td>390</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Superior colliculus</td>
<td>-53 -29 20</td>
<td>3.54</td>
<td>298</td>
<td>√</td>
<td></td>
</tr>
</tbody>
</table>

Note. Regions of interest were identified as clusters that showed significantly greater activation on threat trials than on safety trials in the no-hand condition ($p < .005, r_{rep} \geq .97, \text{corrected}$). ACC = anterior cingulate cortex; DLPFC = dorsolateral prefrontal cortex; NAcc = nucleus accumbens; PFC = prefrontal cortex; spouse effect = threat activity in the spouse condition < threat activity in the no-hand condition; stranger effect = threat activity in the stranger condition < threat activity in the no-hand condition.

*In this comparison, threat-related neural activation was greater in the stranger condition than in the spouse condition. No instances of the opposite pattern were observed.*
Neural activation to threat was significantly lower in both the spouse and the stranger conditions than in the no-hand condition in the vACC, posterior cingulate, left supramarginal gyrus, and right postcentral gyrus, all \( F(1, 15) \geq 5.76, p \leq .03, \eta_p^2 \geq .90, \) for the no-hand condition; \(-.28, n.s.,\) for the spouse condition; and \(-.82, p < .001, \eta_p = .99,\) for the stranger condition. Husband’s DAS score (HDAS) did not show any similar effects, nor were WDAS and HDAS 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, we conducted linear mixed models containing valence ratings (a changing covariate), HDAS, and WDAS, as well as their interactions with hand-holding condition. Neither HDAS nor the HDAS-by-condition interaction was significant. As shown in Figure 4, however, there were significant WDAS-by-condition interaction effects in the left superior frontal gyrus, \( F(2, 26) = 4.84, p = .02, \eta_p = .93;\) right anterior insula, \( F(2, 23) = 4.33, p = .03, \eta_p = .90;\) and hypothalamus, \( F(2, 27) = 4.31, p = .02, \eta_p = .93.\) Inspection of separate regressions (one for each brain area and condition) revealed these interaction effects to be due to negative correlations between WDAS and threat-related neural activation in the spouse-hand-holding condition. These correlations were \(-.59, p = .02, \eta_p = .95\) for the left superior frontal gyrus; \(-.47, p = .07, \eta_p = .86\) for the right anterior insula; and \(-.46, p < .001, \eta_p = .83\) for the hypothalamus. In the stranger and no-hand conditions, correlations between WDAS and threat-related ROI activation were either slightly positive (e.g., \( r = .31\) in the no-
hand condition) or near zero. Interestingly, main effects of valence were also observed in both the right anterior insula, $F(1,27)=6.02, p=.02, p_{\text{rep}}=.92$, and the hypothalamus, $F(1,32)=10.23, p=.003, p_{\text{rep}}=.93$, for which the average correlations were $.46, p=.08, p_{\text{rep}}=.89$, and $.65, p=.01, p_{\text{rep}}=.95$, respectively. These effects indicate that greater activation in both the anterior insula and the hypothalamus corresponded with greater levels of subjective unpleasantness, regardless of hand-holding condition.

**DISCUSSION**

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

Close inspection of the regions implicated in the main effects of hand-holding suggests the following:

- Both spouse and stranger hand-holding conferred 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 vACC (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 et al., 2005; Rushworth, Krams, & Passingham, 2001).
- Spousal hand-holding 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; Damasio et al., 2000; Davidson & Irwin, 1999; Liddel et al., 2005). It is striking how this pattern of neural effects was echoed in subjective reports of experience: Although both spouse and stranger hand-holding resulted in lower reports of bodily arousal, only spousal hand-holding provided the additional benefit of lowering subjective reports of task-related unpleasantness.
- Threat-related activation in the right anterior insula, superior frontal gyrus, and hypothalamus was sensitive to marital quality. This suggests that 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 the hypothalamus suggests that these benefits may be pervasive, as the hypothalamus influences a cascade of neurochemical regulatory processes, such as the

![Fig. 4. Interactive effect of wife’s score on the Dyadic Adjustment Scale (DAS) and hand-holding condition on neural response to threat. Percentage signal change is graphed as a function of DAS score (with correlation coefficients included) and condition for the three brain regions showing a significant interaction: (a) right anterior insula ($y=+19$ mm), (b) left superior frontal gyrus ($y=-4$ mm), and (c) hypothalamus ($y=-13$ mm).](image-url)
release of corticotropin-releasing hormone, 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 specific to spousal hand-holding. This finding 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 apparent only 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; Cooney et al., 2001; Hofer, 1984, 1995; House et al., 1988; Mikulincer et al., 2003; Robles & Kiecolt-Glaser, 2003; Wood et al., 1989). The current results provide new insights into how these effects occur. At one level, hand-holding appears to produce a general regulatory effect on neural threat responses related to bodily attention and the coordination of motor responses; this suggests 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 hand-holding, which suggests that attachment figures act as emotion regulators in ways that strangers do not. Put another way, both stranger and spousal hand-holding appear capable of decreasing the need for a coordinated bodily response to threatening stimuli, but only spousal hand-holding 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 points the way toward the neural mediators of those effects. Particularly promising in this regard is the observed effect of marital quality on the hypothalamus, 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 (Uvnæs-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 et al., 1999), and physical contact alone has been associated with oxytocin release from the paraventricular nuclei of the hypothalamus (Uvnæs-Moberg, 1998), which may in turn increase endogenous opioid activity (Uvnæs-Moberg, 1998) and target dopamine receptors related to inhibitory motor control throughout the basal ganglia (Gimpl & Fahrenholz, 2001).

Of course, it is 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 WDAS and subjective unpleasantness ratings across the different hand-holding conditions. These and other questions await further evaluation. In the meantime, results presented here provide 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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