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Subjective General Health and the Social Regulation of Hypothalamic Activity

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Abstract

Objective—Social support is associated with better health. This association may be partly mediated through the social regulation of adrenomedullary activity related to poor cardiovascular health and glucocorticoid activity known to inhibit immune functioning. These physiological cascades originate in the hypothalamic areas that are involved in the neural response to threat. We investigated whether the down regulation, by social support, of hypothalamic responses to threat is associated with better subjective health.

Methods—A diverse community sample of seventy-five individuals, ages 23–26, were recruited from an ongoing longitudinal study. Participants completed the Short Form Health Survey (SF-36) a well-validated self report measure used to assess subjective general health. They were scanned, using fMRI, during a threat of shock paradigm involving various levels of social support, which was manipulated using hand-holding from a close relational partner, a stranger, and an alone condition. We focused on a hypothalamic region of interest (ROI) derived from an independent sample to examine the association between hypothalamic activity and subjective general health.

Results—Results revealed a significant interaction between handholding condition and self-reported general health, $F(2, 72) = 3.53$, $p = .032$, partial $\eta^2 = .05$. Down regulation of the hypothalamic ROI during partner handholding corresponded with higher self-ratings of general health, *ß*☐= −.31, *p* =.007.

Conclusion—Higher self-ratings of general health correspond with decreased hypothalamic activity during a task that blends threat with supportive handholding. These results suggest that associations between social support and health are partly mediated through the social regulation of hypothalamic sensitivity to threat.

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Keywords

health; social support; hypothalamus; emotion regulation

INTRODUCTION

Rewarding social relationships correspond with better health and longevity (1). Social isolation entails a mortality risk comparable in magnitude to that of smoking, a sedentary lifestyle, obesity, and alcohol abuse (2). The buffering hypothesis suggests that social support affects health by attenuating the physiological effects of psychosocial stress (3). The hypothalamic pituitary adrenal axis and sympathetic adrenomedullary pathway are both reliably activated during perceived threats, and are thus thought to be key mechanisms through which psychosocial stress affects health (4). Chronic activation of these systems may lead to poor cardiovascular health, inhibition of inflammatory and immune responses, and decreased activity of hormones controlling reproduction and growth (5; 6). Moreover, their chronic activation contributes to poor insulin control, decreased adipose tissue metabolism, diminished bone mass, and a general increase in susceptibility to disease (7; 8). Activation of both the hypothalamic pituitary adrenal axis and the sympathetic adrenomedullary pathway are mediated through threat-related activity within the hypothalamus (9).

Social support may mitigate the physiological sequelae of stress by attenuating hypothalamic responses to perceived threat. Social support corresponds with diminished circulating glucocorticoid activity (10; 11), more rapid wound healing (12), and attenuated sympathetic cardiovascular reactivity (13; 14). Even simple hand holding by a high quality relationship partner can reduce hypothalamic reactivity to the threat of electric shock (15). Similar findings obtain in children (16), and in larger samples utilizing different modes of threat and social support provision (17).

Neuroimaging studies of the effects of social support during threat reveal activity in regions other than the hypothalamus (18, 19, 20). But multiple lines of evidence suggest a critical role for the social regulation of hypothalamic activity in mitigating the physiological sequelae of stress through supportive social interaction. This in turn suggests a specific hypothesis: that individuals with lower threat-related hypothalamic reactivity during the receipt of social support should report better general health.

To our knowledge, no research to date has demonstrated an association between subjective health and the direct regulation of hypothalamic activity by social support. Below, we show that the social regulation of threat-related hypothalamic activity is stronger among people who report better subjective general health.

Method

Participants

Seventy-five participants brought an opposite-sex partner to the scanner. Of the seventy- five dyads, 25 identified as friends, 23 were dating, 24 were cohabitating, and 3 were married.

Scanned participants were recruited from the KLIFF/VIDA longitudinal study of adolescence (21), and their partners provided handholding. Of scanned participants, 45% were men, 55% were women, and ages ranged from 23–26 years. Approximately 57% of scanned participants self-identified as white, 37% as African-American, and 6% as other ethnicities. Participants rated their income in brackets, and all but 15 participants fell below $29,999 pre-tax annual income. Only 2 participants identified as students.

Scanned participants were initially recruited in 1998 for the KLIFF/VIDA longitudinal study of adolescence from the seventh and eighth grades of a public middle school in the southeastern United States that drew from urban and suburban populations (21). Beginning in 2009, participants from the longitudinal study were recruited via telephone or email to participate in the current neuroimaging study at the University of Virginia. Neuroimaging data collection began in the winter of 2009 and continued through the spring of 2012. All willing participants concurrently participating in the longitudinal study who met inclusion criteria were included in this sample. To be included, participants needed to have a friend or romantic partner of the opposite sex who was willing to visit the lab to provide handholding. Participants were excluded from participation if they were pregnant or exhibited any risk of danger in the environment of the scanner. Informed consent was obtained from both members of each dyad, and all participants were paid $160 for participation. All study procedures were approved by the Institutional Review Board at the University of Virginia.

Procedure

We tested the association between subjective general health and the social regulation of hypothalamic activity using the 36-Item Short-Form Health Survey (SF-36), a well-validated self-report measure of general health (22), and an fMRI task that blends the threat of electric shock with supportive handholding. Specifically, 75 participants were scanned during a threat of shock paradigm involving various levels of social support (15), including handholding by either a familiar partner (friend or romantic), a stranger, or no handholding at all. Each participant underwent each social support condition in a counterbalanced order (within subjects design). During scanning, participants viewed a series of threat and safety cues. Threat cues consisted of a red ‘X’ on a black background and indicated a 17% chance of electric shock while safety cues consisted of a blue ‘O’ on a black background, indicating no chance of shock. The presentation of the threat or safety cue was followed by a brief anticipation period. Then, a small dot appeared during which shocks were delivered 17% of the time to the participants’ ankle in shock trials only. Each block of trials (alone, stranger, familiar partner) consisted of 10 threat cues with no shock, 2 with shock, and 12 safety cues in variable order. After each block participants rated their subjective assessment of their current emotional arousal and valence using the pictorial Self-Assessment Manikin (SAM) Scales while in the scanner (23).

Participants provided their BMI, smoking status, average number of alcoholic beverages consumed per week, and reported on whether they had ever done hard drugs. Participants also responded to a qualitative question about specific health concerns, “In the past two years, have you been under the care of a physician for any medical conditions? If yes, what are the conditions?” We quantified their responses to this question by counting the number of health problems each individual listed (0–2).

Participants also completed a self-report measure of relationship quality. Participants who brought a friend to the scanner completed the Friendship Quality Questionnaire (FQQ; 24), and participants who brought a romantic partner to the scanner completed the Dyadic Adjustment Scale (DAS; 25). These widely used measures of relationship quality demonstrate good reliability and validity (24,25).

We focused on a hypothalamic region of interest (ROI) derived from an independent sample of participants who completed the same fMRI paradigm (15). Specifically, we utilized the peak hypothalamus coordinates reported in Coan et al (15) that were significantly more active during threat than during safety trials while alone in the scanner. We created a 5X5X5 voxel mask within the hypothalamus surrounding these coordinates. To confirm that the manipulation of social support via handholding had subjective effects with this particular sample, we conducted a within subjects ANOVA on SAM ratings of arousal and valence.

Given the hypothesis that the link between social support and health is partially mediated through the social regulation of hypothalamic activity (1; 8), we limited our analysis to the association between hypothalamic activity and subjective general health as a function of handholding condition, expecting a negative association between threat-related hypothalamic activity during partner handholding and subjective health. For each individual, we extracted the average percent signal change within the hypothalamic ROI from each of the handholding conditions, and conducted a repeated measures general linear model covarying subjective general health. Specifically, the model included handholding condition (alone, familiar, stranger, within-subject), and SF-36 reports of general health (between subjects).

To assess the impact of relationship status and relationship quality, dummy variables were created for relationship status with friends as the reference group. Additionally, we calculated a relationship quality composite score by z-scoring the FQQ and DAS scores independently and averaging them. We then used linear regression to examine the relationship between hypothalamic activity in the partner handholding condition and self-reported general health after adjusting for relationship status and our relationship quality composite variable. We also used linear regression to examine the relationship between hypothalamic activity in the partner handholding condition and self-reported general health after adjusting for the number of medical conditions participants reported.

Results

Table 1 displays participant characteristics related to perceived health. Subjective general health was not related to age, $R=.10$, $p=.39$, sex, $F(1,74)=.81$, $p=.37$, BMI, $R=-.10$, $p=.42$, smoking status, $F(1,74)=.32$, $p=.57$, or whether participants had ever used hard drugs, $F(1,74)=.46$, $p=.50$. There was a marginal association between number of alcoholic drinks consumed per week and subjective health, $R=-.22$, $p=.057$. In response to the qualitative question about health problems, 26 participants reported one or more health problems, including problems with obesity, asthma, drug and alcohol use, aneurisms, herniated discs, chronic pain, prostatitis, seizures, glaucoma, head injury, migraines/headaches, dizziness, arrhythmias, interstitial cystitis, dizziness, stomach and bowel problems, and musculoskeletal problems, indicating that roughly 35% of participants had health concerns. Participants who reported more medical conditions in response to the qualitative question reported significantly lower subjective general health, R=−0.29, p=.029.

Self-reported levels of arousal did not differ across the handholding conditions, F(2, 70) = .32, p = .73. However, valence levels differed significantly across handholding conditions, F(2, 65) = 9.32, p < .001, partial η^2 = .13, such that participants felt most positive in the partner condition (M = 5.92, SD = 1.98), followed by the alone condition (M = 5.23, SD = 1.83), and the stranger condition (M = 4.83, SD = 1.97). Similar subjective results obtain when more participants were added to this sample who did not concurrently participate in the KLIFF/VIDA longitudinal study of adolescence (c.f., 26).

Analyses of hypothalamic activity revealed a main effect of handholding condition, F(2, 72) = 3.79, p = .025, partial η^2 = .05, such that percent signal change in the hypothalamic ROI was highest in the alone condition (M= .032 SD=.09), followed by the partner handholding condition (M=.030 SD=.07) and stranger handholding condition (M=.022 SD=.08).

Results also revealed a significant interaction between handholding condition and self-reported general health, F(2, 72) = 3.53, p = .032, partial η^2 = .05, see Figure 1. Regression weights revealed no significant associations between self-reported general health and hypothalamic activation in the alone, *ß* = −.06, *t*(74) = −.49, *p* =.62, or stranger conditions, *ß* =.13, *t*(74) = 1.15, *p* =.25. But greater self-reported general health corresponded with lower hypothalamic activity during the familiar partner handholding condition, *ß* = −.31, *t*(74) = −2.78, *p* =.007. If anything, this latter association was potentiated after adjusting for both relationship status and relationship quality, *ß* = −.33, *t*(74) = −2.91 *p* =.005, and after adjusting for the number of medical conditions participants reported in response to the qualitative question, *ß* = −.32, *t*(73) = −2.69 *p* =.009. Similar results obtain using a hypothalamus ROI defined by the portions of the hypothalamus that were active in a whole brain corrected cluster analysis from threat minus safe contrasts of the alone condition within the current sample (see text, Supplemental Digital Content 1, for greater detail).

Discussion

Individuals with lower threat-related hypothalamic activity during familiar partner handholding reported greater general health. By contrast, threat-related hypothalamic activity either while alone or during stranger handholding was not associated with subjective general health. These findings suggest that individuals reporting higher levels of general health may have lower hypothalamic activity in response to periods of perceived threat when receiving social support from close-relational partners.

It is widely accepted that a lack of social support relates to lower perceptions of health, and ultimately constitutes a major risk factor for morbidity and mortality. Moreover, a wealth of evidence suggests that social contexts can alter neural functioning (27, 28, 29). But the biobehavioral mechanisms linking attenuated neural threat responding in supportive social contexts to perceived health remain poorly understood. On the one hand, heightened stress has been linked to poor health behaviors including higher fat diet, smoking, and less frequent exercise (30). This suggests that the stress buffering neural effects of social support may indirectly decrease the risk of poor health behaviors by first decreasing general stress. On the other hand, hypothalamic activity creates a direct link between stress and poor health through the chronic activation of neuroendocrine and sympathetic systems (4). This suggests that social support promotes health in part by directly attenuating hypothalamic responses to stress (3). Our findings are consistent with this hypothesis, linking perceptions of general health to reduced hypothalamic activity, in vivo, during the receipt of social support.

Strengths and Limitations

The current study employed a large and diverse community sample of participants, and an experimental manipulation of social support through handholding by social partners and strangers in the scanning environment. While the fMRI task and self-report measure of health are both well-validated, the current study is limited by its lack of objective health measures. Moreover, while the SF-36 has been validated in clinical populations, these validation studies typically utilize older subjects who likely have greater health impairments compared to our sample of 23–26 year old adults. In the current sample, the SF-36 may capture a general concept of health related quality of life, limiting its generalizability to populations with greater physical health impairments. Future research should investigate specific and objective physical health outcomes in conjunction with this paradigm to better understand direct associations between the regulation of hypothalamic activity via social support and physical health status.

Because it mediates broad physiological responses to stress, we have elected to limit our current analysis to the hypothalamus, and to the specific *a priori* hypotheses we have regarding its role in the salubrious effects of social support. Future research may well benefit from extending these analyses to other brain regions whose activity is altered as a function of social support (e.g., ventromedial prefrontal cortex, amygdala, etc.), and examining whether these regions show altered connectivity with the hypothalamus as a function of social support and general health. Moreover, future research would benefit from investigating the health implications of giving social support in addition to receiving support (31)

Conclusions

Higher self-ratings of general health are associated with decreased hypothalamic activity during a task that blends threat with supportive handholding. Although many have documented the attenuation of stress-related neuroendocrine activity by social support (32), results reported here provide direct evidence that the social regulation of threat-related hypothalamic activity, measured *in vivo*, corresponds with better subjective general health. Thus, these results provide new evidence that associations between social support and health may be mediated through the social regulation of hypothalamic sensitivity to threat.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

KLIFF/VIDA Kids	Lives, Families, and Friends/Virginia Institute for Development in Adulthood
fMRI	functional Magnetic Resonance Imaging
ROI	region of interest
SF-36	Short Form Health Survey
BMI	Body Mass Index
SAM	Self-Assessment Manikin
FQQ	Friendship Quality Questionnaire
DAS	Dyadic Adjustment Scale
M	Mean
SD	standard deviation
ANOVA	analysis of variance

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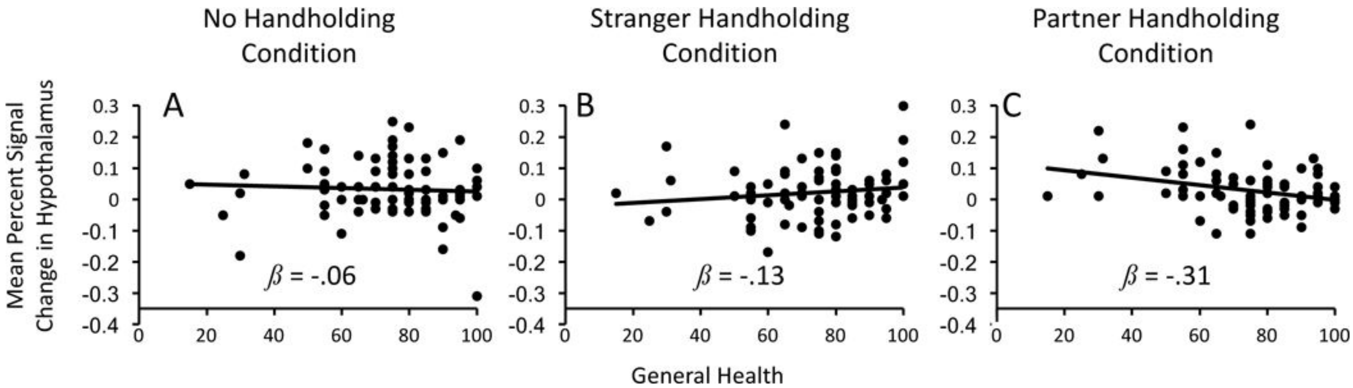

Figure 1.

The interaction between general health and handholding condition on threat-related hypothalamic activity. (A) Association between threat-related hypothalamic activity and general health while alone, □□= −.06, *t*(74) = −.49, *p* =.62. (B) Association between threat-related hypothalamic activity and general health during stranger handholding, □□=.13, *t*(74) = 1.15, *p* =.25. (C) Association between threat-related hypothalamic activity and general health during familiar partner handholding, □□= −.31, *t*(74) = −2.78, *p* =.007. In all graphs, the ordinate represents percent signal difference in hypothalamic threat-safe contrasts, and the abscissa represents SF-36 general health scores.

Table 1

Participant characteristics that may relate to subjective general health.

Variables	M (SD) or Ratio
Age, years	24.93 (0.84)
Male: Female	33:42
Body Mass Index	26.88 (7.20)
Smoker: Non-smoker	31:44
Number of alcoholic drinks per week	6.47 (11.29)
Used hard drugs: never used hard drugs	27:47
Subjective general health (SF-36)	73.68 (18.61)