

Self-Transcendent Values and Neural Responses to Threatening Health Messages

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ABSTRACT

Objective: Prioritizing self-transcendent values such as family and friends more than nontranscendent values such as wealth and privilege is associated with lower stress response. In this study, we tested whether having self-transcendent values can reduce specific responses in the brain in the context of potentially threatening health communications.

Methods: Sedentary adults ($N = 67$) who would likely feel threatened by health messages that highlight the risk of sedentary behavior were recruited. Participants indicated the degree to which they prioritize self-transcendent values more than nontranscendent values. Using functional magnetic resonance imaging, participants' neural responses to health messages were assessed within neural regions implicated in threat responses, including bilateral amygdala and anterior insula (AI).

Results: A tendency to prioritize self-transcendent more than nontranscendent values was associated with lower reactivity during exposure to health messages within anatomically defined regions of left amygdala ($t(55) = -2.66, p = .010$, 95% confidence interval [CI] = -0.08 to -0.01), right amygdala ($t(55) = -2.22, p = .031$, 95% CI = -0.06 to 0.0), and left AI ($t(55) = -2.17, p = .034$, 95% CI = -0.04 to 0.0), as well as a mask functionally defined to be associated with "threat" using an automated meta-analysis ($t(55) = -2.04, p = .046$, 95% CI = -0.05 to 0.0). No significant effect was obtained within the right AI ($t(55) = -1.38, p = .17$, 95% CI = -0.04 to $.01$). These effects were partially enhanced by reinforcing important values through self-affirmation, remained significant after accounting for self-reported social connection, and were specific to health message processing (versus generic self-related information).

Conclusions: Attenuated neural reactivity to potentially threatening health messages may be a novel way that prioritizing self-transcendent values could lead to positive health behaviors.

Key words: amygdala, anterior insula, health communication, physical activity, self-transcendence, threat.

INTRODUCTION

Self-transcendence, generally defined as the process of psychological expansion beyond self-boundaries (1,2), is associated with mental and physical health benefits, including improved subjective well-being (3–6), and decreased depression (7,8) and suicidality (9). Recent models of self-transcendence focus on interpersonal values ("supportive or harmonious connections with others (10)") as a main channel to self-transcendent experience. Prioritizing self-transcendent (e.g., interpersonal) values such as family and friends more than nontranscendent values such as wealth or privilege is associated with positive health behaviors. For example, feelings of love and interpersonal connection increased receptivity to potentially threatening information about the harmful effect of smoking among smokers (11). In a follow-up study, reflecting on transcendent values (compassion, supporting others) versus nontranscendent values (wealth, power) before social exclusion led to increased self-control in the form of consuming fewer unhealthy cookies (10). We propose that holding transcendent

values may be associated with differential responses to potentially threatening health information and define threat response as affective reactivity to incoming information that could potentially undermine one's self-worth. Threat response can, in turn, trigger defensiveness (versus receptivity), likely leading to rejection of the useful information.

In this study, threat response is operationalized by the degree to which individuals show heightened activity within brain areas previously associated with threat processing when presented with potentially threatening health messages. This response can be assessed at the neural level using functional magnetic resonance imaging (fMRI). We focus on regions from an automated meta-analysis of 170 studies on threat responses (12) that showed robust bilateral amygdala activity as well as smaller

AI = anterior insula, BDI = beck depression inventory, BMI = body mass index, CI = confidence interval, fMRI = functional magnetic resonance imaging, IPAQ = International Physical Activity Questionnaire, RAND = The RAND 36-Item Health Survey, ROI = region of interest, SPM = statistical parametric mapping, T1 = time 1, T2 = time 2

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SDC Supplemental Content

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clusters in insula, anterior cingulate, periaqueductal grey, and ventromedial prefrontal cortex. The amygdala encodes salient affective stimuli (13) and is critically involved in processing of unpleasant stimuli (14,15) as well as threat detection and fear-related processing (for meta-analyses, see the studies by Zappala (16) and Ellermann and Reed (17)). The anterior insula (AI) projects to the amygdala and also is implicated in threat/fear response (18). In addition, imminent threat can elicit activity within the periaqueductal grey (19), and ventromedial prefrontal cortex is implicated in psychological regulation of threat (19–21).

In addition to prioritizing self-transcendent values, reflecting on personally important values can also make people less defensive (more receptive) to otherwise threatening information (see the study by Cohen and Sherman (22) for a review). For example, writing about one's core values preceding exposure to potential threats buffered threat-related physiological responses such as threat-potentiated startle response (23) and epinephrine response, a hormone involved in the fight-or-flight response (24). As such, actively reflecting on values may increase the strength of the link between holding self-transcendent values and reduced threat response.

Another commonly studied pathway linking transcendent values and health is perceived social connection (25,26). Holding transcendent values, however, may lead to beneficial outcomes beyond those conferred by social connection (e.g., increased receptivity to healthy behaviors). Thus, it is important to determine the unique role of transcendent values in processing health messages, accounting for social connection separately. It is also possible that individuals with high transcendent values may show generalized deactivation within the neural areas associated with threat processing regardless of the context. Therefore, it is important to determine whether holding self-transcendent values is associated with diminished threat response specifically to messages encouraging behavior change or more broadly when processing any type of self-relevant information.

The Current Study

In the current study, we propose that self-transcendent values (versus nontranscendent values) may be associated with attenuated brain responses in regions previously associated with threat in the context of health communication. We use fMRI to test whether having a greater tendency to hold and esteem transcendent values is associated with lower activity within brain regions implicated in threat processing during exposure to potentially threatening, yet beneficial, health information.

Sedentary adults were presented with health information highlighting the risk of sedentary behavior. The target population was chosen on the basis of evidence that physical inactivity is a major risk factor for a number of adverse health outcomes (27,28) and that physical activity is associated with health benefits independent of BMI (29,30). As with other health behavior contexts (31), high-risk individuals (i.e., sedentary populations) may experience threats to self-worth and react defensively when confronted with health risk messages (32,33). In turn, this may lead individuals at risk to dismiss important health information.

A self-affirmation manipulation (in which participants reflect on their core values before health message exposure) was used

to test whether reflecting on core values may further strengthen the link between holding transcendent values and decreased threat-related neural processing. In addition, the unique role of transcendent values in processing health messages was tested, accounting for social connection separately. Finally, to determine whether individuals with high transcendent values show generalized deactivation within the neural areas previously associated with threat processing regardless of the context, neural responses to processing general self-relevant information were examined.

METHODS

Participants

A community sample of sedentary adults ($N = 67$; mean [standard deviation] or M [SD] age = 33.42 [13.04] years; 41 females; 44 white, 12 black, 3 Asian, 1 Hispanic, 7 others; Table 1) was recruited for a study on “daily activities” to avoid selection bias related to physical activity. Participants responded to online advertisement and flyers by completing an online prestudy screening survey. Eligibility criteria, based on self-reports collected via survey, included the following: (1) engagement in less than 195 minutes of walking, moderate, and vigorous physical activity throughout the previous 7 days from the time of participation (using a short-form International Physical Activity Questionnaire [IPAQ]), (2) standard fMRI scanning criteria (also confirmed by research staff; no metal in body, not claustrophobic, not pregnant/nursing, right-handed), (3) no history of stroke or other neurological disorders, (4) no active coronary artery disease, significant arrhythmia, or uncontrolled hypertension, (5) no current use of psychotropic medications, and (6) no history of posttraumatic stress disorder or admission to a psychiatric hospital within the past year. Participants also reported their height and weight from which the body mass index (BMI) was calculated, but BMI was not used as an inclusion criterion; rather, it was included in statistical models as a covariate when indicated.

TABLE 1. Baseline Demographic and Health-Related Characteristics

Demographic	Mean	Mean/Sample Size	Range
Age, y	33.42	(13.04)	18–64
Female	41	(61.2%)	—
White	44	(65.7%)	—
Education, y	16.63	(3.44)	12–22
Baseline characteristics			
BMI	27.99	(6.84)	18.20–54.86
Weekly exercise minutes (IPAQ)	123.53	(49.52)	0–195
Depression (BDI)	28.16	(8.17)	21–62
Health (RAND)			
Physical functioning	91.94	(13.31)	30–100
Bodily pain	85.45	(14.60)	32.50–100
Role limitations (physical)	94.40	(14.96)	25–100
Role limitations (emotional)	94.03	(16.34)	33.33–100
Emotional wellbeing	74	(20.14)	16–100
Social functioning	79.48	(15.95)	12.50–87.50
Energy/fatigue	57.50	(17.01)	10–95
General health perceptions	70.45	(17.55)	20–100

BMI = body mass index; IPAQ = International Physical Activity Questionnaire (short-form, self-reported during the prestudy screening); BDI = Beck Depression Inventory; RAND = The RAND 36-Item Health Survey.

$N = 67$. Mean values and sample sizes are displayed with SDs and percentages, respectively, in parentheses where applicable.

Research assistants contacted eligible participants via phone to reconfirm their eligibility and schedule study visits.

Across two visits (time 1 [T1], time 2 [T2]), six participants did not complete the study, and the final sample in this report consisted of 67 participants at T1 and 61 participants at T2. In addition, three participants were excluded because of excessive movement ($n = 2$) or technical difficulties in scanning ($n = 1$), resulting in a final sample of 58 participants with both self-reports and neuroimaging data from relevant tasks.

This study was a part of a larger investigation on neural predictors of health outcome change (reported in the study by Falk et al., 2015 (34), Cascio et al., 2016 (35), Kang et al., 2016 (36)). Of these investigations, only the study by Falk et al. (34) focuses on the same neuroimaging data reported here. However, Falk et al. (34) focus on the main effects of the affirmation manipulation and do not report on any individual differences related to the types of values that participants prioritized. None of the previous reports examined self-transcendent value effects on neural activity during the message exposure.

Procedure

Participants completed a prestudy screening to verify eligibility, a baseline appointment (T1), an intervention appointment (T2), and an end-point appointment. Only the T1 and T2 data are presented in the current report. Please see the Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A354>, for a detailed study protocol. Data were collected between June 2012 and August 2013. All experimenters who worked with participants and participants themselves were blind to the study hypotheses throughout the study. During the prestudy screening, participants self-reported their level of physical activity throughout the previous week to identify individuals most likely to feel threatened in response to health risk messages. Participants also self-reported their weight and height from which BMI scores were derived. Eligible participants visited the laboratory for the baseline appointment (T1) and an fMRI appointment (T2) approximately 1 week later ($M[SD] = 9.35[6.16]$ days). At T1, participants provided informed consents and completed transcendent value ranking, self-reported perceived social connection and health status, and provided demographic information. At the T2 fMRI appointment, participants completed the self-related processing task, self-affirmation task (random assignment to either the affirmation or control condition), and health messages task, followed by self-reporting current affect outside the scanner. Once finished, participants were debriefed, paid, and thanked for their participation. All self-reports and scanner tasks were embedded among other surveys and tasks. All survey data were collected with a desktop computer using an online survey tool (Qualtrics). All scanner tasks were presented on an fMRI-compatible screen at 800×600 -pixel resolution using Presentation (NeuroBehavioral Systems). In-scanner responses were collected using a five-button response device attached to participant's right wrist. The protocol was approved by the University of Michigan Institutional Review Board.

Measures and Tasks

Self-Report Measures

Transcendent Value Ranking

Participants provided a ranking of potential values at T1. Prioritizing self-transcendent values was operationalized by the order in which people ranked their connection with family and friends by importance among seven other nontranscendent/noninterpersonally focused values (money, politics, religion, spontaneity, creativity, humor, independence). Rankings for the family/friend category (range = 1–8) were then reverse coded so that the higher scores represent greater consideration for self-transcendent values to be important in life.

Social Connection

Perceived social connection obtained at T1 was examined and adjusted for in later analysis. The eight-item subscale from the Social Connectedness

Scale (37) measures the degree of interpersonal closeness/distance individuals feel between themselves and other people and society (“Even among my friends, there is no sense of brother/sisterhood.”), rated on a 1 (*not at all true of me*) to 5 (*very true of me*) scale. All scores were coded so that the higher scores reflect greater degrees of perceived social connection. Internal consistency in the current study ($\alpha = .94$) was high.

Current Affect

To complement the neural results, self-reported positive and negative affect after the fMRI scan (that included the health message exposure) was assessed using the Positive and Negative Affect Scale (38) consisting of 15 individual positive emotion terms (interested, excited, strong, happy, relieved, enthusiastic, pleased, proud, alert, content, inspired, joyful, determined, attentive, active) and 15 negative emotion terms (frustrated, upset, distressed, guilty, miserable, scared, hostile, irritable, disappointed, ashamed, nervous, troubled, jittery, unhappy, afraid) rated on a 1 (*not at all*) to 5 (*extremely*) scale. From this, mean positive and negative affect composites were created. Internal consistency scores for positive ($\alpha = .93$) and negative ($\alpha = .87$) emotion items were high.

Health

Participants' baseline physical and psychological health was assessed at T1, including general quality of life and depression. The RAND 36-Item Health Survey measures eight health concepts, including physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. All questions were scored on a scale of 0 to 100, with 100 representing the highest level of functioning possible. Internal consistency scores across subscales in this study were adequate on average ($\alpha_{\text{mean}} = .85$, $\alpha_{\text{range}} = .44-.88$). In addition, depression was measured by the 21-item Beck Depression Inventory (39). Scores are summed to reflect current depressive symptoms, ranging from 0 to 63. Internal consistency score ($\alpha = .92$) was high.

Demographics

At the end of T1, participants reported their age, sex, ethnicity, and years of education. For detailed analyses of demographic information in relations to the main study aims, please see Supplemental Digital Content 2, <http://links.lww.com/PSYMED/A355>.

fMRI Scanner Tasks

Self-Related Processing Task

We used a well-validated self-related processing task (40,41), which was the first task performed during the T2 fMRI session, to engage general self-relevant and nonthreatening information processing. Participants were presented with positive and negative trait adjectives taken from Anderson word trait list (42) and judged the self-relevance (“Does the adjective describe you?”). Participants also judged other relevance and valence of the words. Each condition repeated in six blocks, and each block contained six trials for a total of 36 trials per condition. The same 36 words (18 negative and 18 positive) were judged in each condition, and the order of word presentation was counterbalanced. Six trials within a block consisted of three trials with positive adjectives and three with negative adjectives. Each adjective was presented for 3 seconds, and each block was preceded by a 3-second orientation screen identifying the condition participants were in, and blocks were separated by 2.5 seconds of fixation.

Self-Affirmation Task

A scanner-adapted self-affirmation task (35), designed on the basis of standard affirmation paradigms (for a review, see the study by Cohen and Sherman (22)), was used to remind and reinforce values. During the T2 fMRI appointment, participants were randomly assigned to either reflect on their top (affirmation condition) or bottom (control condition) values ranked at T1, by completing the self-affirmation task. Those in the affirmation condition were provided with an opportunity to think about situations that allowed them to express and

connect with their highest ranked value (e.g., if family and friends were the top-ranked value, “Think of a situation when you might have fun with family and friends”), as well as value-neutral and nontranscendent control situations (e.g., “Think of a situation when you might check the weather”). Participants in the control condition were presented with a series of situations pertaining to their lowest ranked value as well as the within-subject control situations (identical to the control situations presented in the affirmation condition). The fMRI data from the self-affirmation task are not presented in the current report (35).

Health Messages Task

Although in an fMRI scanner, participants received 50 self-relevant and potentially threatening health messages targeting sedentary, high-BMI adults (e.g., “A lack of activity can be linked to a shorter life,” “Getting more activity can help you sleep better at night.”). Messages were presented across two runs (25 health messages in each run) in a randomized order. Each message block consisted of an initial suggestion (5 seconds), followed by a reason why participants should be less sedentary or more active, how participants might implement the suggestions, and messages highlighting increased risk for chronic disease due to sedentary life-style and elevated BMI (7 seconds). The end of each block included a brief reflection period (6 seconds) in which participants were encouraged to envision how they might apply the message in their own life. Blocks were separated by fixation rest periods (2.5 seconds); every seventh block contained a longer (12 seconds) block of rest. The task also included blocks with advice regarding other daily behaviors unrelated to physical activity that are not the focus of the current investigation ($n = 20$, task timing same). Detailed task descriptions and materials are available on <http://cn.asc.upenn.edu/wp-content/uploads/2013/07/Task-Description.docx.zip>.

Analysis

A series of models were computed to test the hypothesized relationships between transcendent values and reduced threat responses in the brain, with condition (affirmation, control) as a covariate when appropriate. The coefficient of determination (R^2 , $R^2_{adjusted}$), β coefficients, and 95% confidence intervals (CIs) are reported for significant results. All reported p values are two-tailed. All analyses were performed in R (v3.0.1, www.r-project.org) using the R-studio interface (v0.98.1103) and the Statistical Package for Social Science software (IBM SPSS Statistics 21).

fMRI Data

The imaging data were acquired on a 3-T GE Signa MRI scanner. Participants were self-guided through one run of self-related processing (188 volumes), one run of self-affirmation (323 volumes, not presented here), two runs of the health messages tasks (308 volumes each, 616 volumes total), and one additional task (325 volumes, not reported here). For the first six participants, slightly longer versions of the tasks were used, with two runs of 209 volumes each for self-affirmation and three runs of 257 volumes each for health messages tasks.

A spoiled gradient echo sequence recorded high-resolution T1-weighted structural images (124 slices; slice thickness, $1.02 \times 1.02 \times 1.2$ mm). In-plane T1-weighted overlay images were acquired (43 slices; slice thickness, 3 mm; voxel size, $0.86 \times 0.86 \times 3.0$ mm) to allow two-stage co-registration. The functional images were recorded using a reverse spiral sequence (repetition time, 2000 milliseconds; echo time, 30 milliseconds; flip angle, 90 degrees; 43 axial slices; field of view, 220 mm; slice thickness, 3 mm; voxel size, $3.44 \times 3.44 \times 3.0$ mm).

The anatomical and functional data were acquired and preprocessed using a standard processing stream using Statistical Parametric Mapping (SPM8; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, United Kingdom) for all stages apart from the initial despiking, which was carried out using the 3dDespik program as implemented in the AFNI toolbox. Differences in time of acquisition across the 43 slices were corrected using a sinc interpolation algorithm with the first slice as reference. Then, motion artifacts were corrected through spatial

alignment to the first slice of each volume. Next, the mean image across all blood oxygen level-dependent functional images was co-registered with the in-plane T1 image, and then the high-resolution T1 spoiled gradient echo image was co-registered to the in-plane T1 image. After co-registration, the high-resolution T1 images were segmented into white and gray matter, allowing the skull to be removed. Structural and functional images were then normalized to the MNI template (“MNI152_T1_1mm_brain.nii”) provided by the FMRIB Software Library. In the final preprocessing step, the functional images were smoothed using a Gaussian kernel (8-mm FWHM). To allow for the stabilization of the blood oxygen level-dependent signal, the first five volumes (10 seconds) of each run were discarded before analysis. Movement parameters (a total of six rigid-body parameters, three for translation and three for rotation) derived from spatial realignment were included as nuisance regressors in all first-level models. Data were high pass filtered with a cutoff of 128 seconds.

Fixed-effects models of the self-related processing task were constructed using a single boxcar function for each block. To parallel the health messages task modeling, the contrast of conditions in which participants considered the self-relevance of words versus rest was used. Fixation and condition preparation periods were considered baseline rest. Second-level random-effects models were constructed by averaging across participants and were subjected to further ROI analysis (described hereafter).

The health messages task was modeled including regressors for each message type (why to be active, why to be less sedentary, how to be active, how to be less sedentary, risk messages, why to perform other daily activities, how to perform other daily activities) and the corresponding response periods. A contrast was computed for each participant by averaging across the 50 health messages highlighting risk, being more active, and being less sedentary and comparing activity during those messages to rest. Second-level random-effects models were constructed by averaging across participants and were submitted to a further ROI analysis (described hereafter).

The primary a priori hypotheses focused on the amygdala and the AI, regions that have been associated with threat-related processing in a number of previous investigations (16–18,43–48). Bilateral amygdala were defined using the SPM toolbox Wake Forest University PickAtlas (49) and converted to ROIs with MarsBar. Bilateral AI was defined as all voxels within each left and right insula masks provided by PickAtlas that were anterior to the $y = 0$ plane. Parameter estimates of activity within the ROIs during nonthreatening self processing (“self > rest” trials in the self-related processing task) and during potentially threatening health messages (“health messages > rest” in the health messages task) were extracted using MarsBar (50) and converted to percent signal change.

To complement the structurally defined ROIs, a functionally defined ROI was created from the online database Neurosynth (www.neurosynth.org, 12). Neurosynth automatically synthesizes published fMRI data (413,429 activations reported in 11,406 studies as of October 2016). Using meta-analytic procedures, Neurosynth allows the users to search common activation patterns during psychological states with representational search terms. The primary analysis focused on the reverse inference map derived from the search term “threat” (using Neurosynth’s default threshold $p < .01$, corrected). This map included robust activity in the bilateral amygdala and additional voxels in the insula, anterior cingulate cortex, periaqueductal gray, and ventromedial prefrontal cortex associated with threat processing for reverse inferences.

In addition to the primary a priori hypothesized ROI analyses, whole-brain searches were performed for regions associated with self-transcendent value processing, outside of those hypothesized. For all whole-brain results, 3dClustSim was used to calculate the cluster threshold for the areas outside of the ROIs (http://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html). The estimated smoothness from each analysis was used as generated in SPM (15.5, 15.5, 13.4 for the main analysis). Based on the results from 3dClustSim, k value of 126 was applied for the whole brain outside of the ROIs and k value of 21 for the AI ($p < .005$). Given the small volume of the amygdala, uncorrected results at a p value of less than .005

are reported for amygdala. No regions outside of the ROIs survived cluster correction in this whole-brain analysis.

Associations Between Neural Responses and Self-Transcendent Values

The percent signal change results from each ROI described previously were then used in regression analyses to examine the links between prioritizing self-transcendent values and neural response to potentially threatening health information. First, five regression analyses were conducted, each with the individual difference in transcendent value ranking as a predictor variable and neural activity in the left amygdala, right amygdala, left AI, right AI, and Neurosynth “threat map” as dependent variables. Second, the value × condition interaction was tested to determine whether reinforcing core values using a self-affirmation manipulation strengthens the association between transcendent values and neural responses within the ROIs. Five regression analyses were conducted with centered value ranking, centered condition (affirmation, control), and the value × condition product term simultaneously as predictors of each of the five ROI scores. Third, to test whether this association is independent of perceived social connection, the same regressions were rerun with value ranking as a predictor and ROI scores as outcomes, including social connection as a covariate. Finally, to test the specificity of the effect, parallel regression analyses were conducted with value ranking as a predictor and ROI scores obtained while processing self-relevant but nonthreatening generic information as outcome variables.

RESULTS

The Association Between Prioritizing Self-Transcendent Values and Neural Responses to Health Messages

First, the links between self-transcendent value ranking and threat responses within the amygdala, AI, and meta-analytically defined (i.e., Neurosynth) threat mask during exposure to health messages were tested. As predicted, high transcendent value ranking was associated with attenuated activity within the bilateral amygdala,

bilateral AI and Neurosynth threat mask in response to the health messages (Fig. 1, Table 2). Linear regression analyses adjusting for randomly assigned condition revealed that higher transcendent value rankings were associated with lower activity during health messages within the left amygdala ($R^2 = .13$, $R^2_{adjusted} = .10$, $\beta = -.34$, $t(55) = -2.66$, $p = .010$, 95% CI = -0.08 to -0.01), right amygdala ($R^2 = .10$, $R^2_{adjusted} = .07$, $\beta = -.29$, $t(55) = -2.22$, $p = .031$, 95% CI = -0.06 to 0.0), left AI ($R^2 = .08$, $R^2_{adjusted} = .05$, $\beta = -.29$, $t(55) = -2.17$, $p = .034$, 95% CI = -0.04 to 0.0), and the Neurosynth threat mask ($R^2 = .11$, $R^2_{adjusted} = .07$, $\beta = -.27$, $t(55) = -2.04$, $p = .046$, 95% CI = -0.05 to 0.0). No significant effect was obtained within the right AI ($R^2 = .03$, $R^2_{adjusted} = 0$, $\beta = -.19$, $t(55) = -1.38$, $p = .17$, 95% CI = -0.04 to 0.01).

Whole-brain effects of transcendent values on decreased brain activity during exposure to health messages reinforced the effects observed in the ROI analysis. No regions survived the whole-brain cluster correction, and results in Table 3 illustrate clusters within the ROIs only. The whole-brain results for main effects of the health messages task are included in the Supplemental Digital Content 3–1, <http://links.lww.com/PSYMED/A356>. In addition, analyses examining baseline demographics and exercise-related variables as potential covariates and moderators of the relationships reported previously are reported in Supplemental Digital Content 2, <http://links.lww.com/PSYMED/A355>.

The Self-Transcendent Value and Affirmation Interaction

We tested whether making core values salient using the randomly assigned self-affirmation manipulation (reflect on highest ranked value versus lowest ranked value) further strengthens the link between of transcendent value rankings and decreased neural threat responses. A marginally significant transcendent value × affirmation (affirmed, control) interaction was observed for the activity within the right amygdala ($R^2 = .16$, $R^2_{adjusted} = .11$,

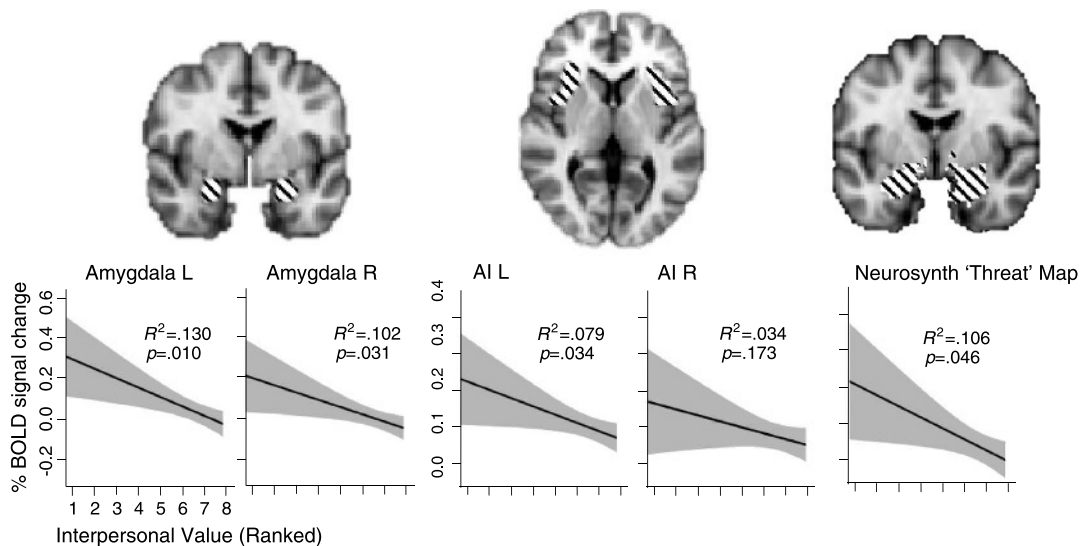


FIGURE 1. People who highly rank self-transcendent values demonstrate lower threat responses during exposure to potentially threatening health information. Brain activity within the a priori ROIs, including bilateral amygdala, bilateral AI, and the Neurosynth’s reverse inference map of threat, during exposure to health messages are shown ($n = 57$). 95% CIs are displayed in shades. Amygdala L = left amygdala; amygdala R = right amygdala; AI L = left anterior insula; AI R = right anterior insula.

TABLE 2. Separate Linear Regression Results, With Self-Transcendent Value Ranking as a Predictor Variable for Activity Within Each of the Threat-Responsive ROIs During Exposure to Health Messages

ROIs	R^2		β		t		p	
		w/SC		w/SC		w/SC		w/SC
L amygdala	.130	.131	-.340	-.338	-2.660	-2.617	.010	.012
R amygdala	.102	.102	-.288	-.289	-2.217	-2.202	.031	.032
L AI	.079	.086	-.285	-.291	-2.170	-2.194	.034	.033
R AI	.034	.055	-.186	-.195	-1.380	-1.450	.173	.153
Neurosynth threat map	.106	.106	-.265	-.267	-2.043	-2.036	.046	.047

ROI = region of interest; w/SC = values accounting for social connection; L = left; AI = anterior insula; R = right.
 $n = 57$.

$\beta = -1.16$, $t(54) = -1.93$, $p = .059$, 95% CI = -0.06 to 0.0) and Neurosynth threat mask ($R^2 = .17$, $R^2_{\text{adjusted}} = .13$, $\beta = -1.23$, $t(54) = -2.07$, $p = .043$, 95% CI = -0.06 to 0.0).

Specifically, those with greater transcendent values showed more attenuated activity within the right amygdala in response to health messages only when they were reminded of their important values ($R^2 = .19$, $\beta = -.44$, $t(28) = -2.57$, $p = .016$, 95% CI = -0.09 to -0.01) but not when the values were not affirmed ($R^2 = 0$, $\beta = .06$, $t(27) = .28$, $p = .78$, 95% CI = -0.04 to 0.05). Similarly, a greater tendency to prioritize transcendent values was associated with lower activity within the Neurosynth's reverse-inferenced map of threat only when core values were affirmed ($R^2 = .21$, $\beta = -.45$, $t(28) = -2.67$, $p = .013$, 95% CI = -0.08 to -0.01) but not when the values were not affirmed ($R^2 = .01$, $\beta = .10$, $t(27) = .50$, $p = .62$, 95% CI = -0.03 to 0.05). No significant value \times affirmation interactions were observed for the left amygdala or bilateral AI ($p > .20$).

The Unique Role of Self-Transcendent Values, Accounting for Social Connection

Next, the unique role of self-transcendent values independent of social connection was examined. Social connection was not correlated with transcendent value rankings ($r = .07$, $p = .63$) and was not associated with responses within the neural ROIs ($r = -.05$, $-.01$, $.07$, $.14$, $.01$; $p = .69$, $.99$, $.63$, $.31$, $.93$, for left amygdala, right amygdala, left AI, right AI, and the Neurosynth threat mask, respectively). After adjusting for the perceived social connection as a covariate, the association between transcendent value rankings and neural responses within the ROIs remained parallel to those obtained when not adjusting for perceived social connection (Table 2). Social connection was negatively associated with self-reported negative affect ($r = -.44$, $p = .001$) but not correlated with self-reported positive affect ($r = .19$, $p = .16$).

Specificity of the Effect

Additional analyses were performed to test whether the effects of interest were selective for activity in the specified ROIs during exposure to health messages or whether they reflect general deactivation in these regions across all self-related processing among individuals with high transcendent values. For instance, those with high transcendent values may show generalized deactivation within the specified ROIs when processing self-related information. To test this alternative possibility, activity within the target ROIs was examined during self-relevant information processing

in a separate self-related processing task (whole-brain results are included in the Supplemental Digital Content 3-1, <http://links.lww.com/PSYMED/A356>). Linear regression analyses using the same ROIs reported previously revealed no significant links between transcendent value rankings and activity within the left amygdala ($p = .98$), right amygdala ($p = .67$), left AI ($p = .99$), right AI ($p = .78$), or the threat map from Neurosynth ($p = .96$) while processing general self-relevant information. In addition, activation across the Neurosynth's reverse threat map, health messages $>$ rest, and self $>$ rest contrasts are compared in Supplemental Digital Content 3-2, <http://links.lww.com/PSYMED/A356>.

Self-Reported Affect

We tested the association between each of the variables described previously and self-reported positive and negative affect after message exposure. Activity within the neural ROIs was not significantly associated with average positive ($p > .20$) or negative ($p > .10$) affect composite scores. When individual emotion items were examined, however, greater activity within key regions of interest during health messages was associated with later feeling more frustrated (left amygdala: $r = .32$, $p = .022$), troubled (left amygdala, left AI, right AI, Neurosynth mask: $r = .28$, $.36$, $.32$, $.30$, $p = .051$, $.010$, $.024$, $.034$, respectively), less interested (left amygdala, right amygdala, Neurosynth mask: $r = -.30$, $-.31$, $.28$, $p = .035$, $.030$, $.052$, respectively), and less enthusiastic (right amygdala, right insula: $r = -.27$, $-.27$, $p = .060$, $.063$, respectively). Transcendent value rankings were not significantly associated with the self-reported positive or negative affect composite

TABLE 3. Decreased Activity During Health Message Exposure Associated With Self-Transcendent Value Ranking

Region	x	y	z	Size	t
L insula	-37	-16	19	31	4.38
R insula/stg	60	5	-2	94	4.01
R amygdala	29	1	-23	8	3.12
L amygdala	-23	-9	-23	4	2.79

L = left; R = right; stg = superior temporal gyrus.

$n = 57$. No regions survived the whole-brain cluster correction and the results illustrate clusters within the ROIs only. Small volume corrected results for bilateral AI ($p = .005$, $k = 21$, corresponding to $p < .05$, corrected) and uncorrected results for bilateral amygdala are reported at $p < .005$.

scores ($p > .40$), although as noted previously, perceived social connection was associated with reduced negative affect ($r = -.44$, $p = .001$).

In addition, baseline depression was not significantly associated with value rankings ($p = .99$) or with the activity within any of the neural ROIs, including left amygdala ($p = .76$), right amygdala ($p = .55$), left AI ($p = .48$), right AI ($p = .64$), or the Neurosynth threat mask ($p = .87$).

DISCUSSION

In the current study, we tested whether prioritizing self-transcendent values more than other nontranscendent values is associated with decreased neural responses to potentially threatening health information. Having high transcendent values was associated with attenuated neural responses within the bilateral amygdala and left AI during exposure to health messages. Supporting the interpretation of this neural activity in terms of threat response, having high transcendent values was also associated with attenuated neural responses within regions derived from an automated meta-analytic reverse inference map of the term threat, based on 170 studies from the Neurosynth database. This effect was reinforced within the right amygdala (marginal) and the Neurosynth threat map by explicitly cueing reflection on the core values through an affirmation task. The transcendent value effect remained significant after accounting for social connection and was specific to processing health information.

Linking Self-Transcendent Values and Threat Processing

Previous reports linked self-transcendent values and positive health behaviors (10,11). The current data are consistent with the idea that having transcendent values is associated with less defensiveness in response to health messages that challenge one's behavior but, nonetheless, contain beneficial information. The transcendent value effect was significant within a region of interest on the basis of an automated meta-analytic reverse inference map of threat. A central assumption of our study is that sedentary adults should be particularly defensive in response to health messages; however, our sample does not allow us to directly test this assumption. Although additional data are needed to establish a causal direction and tighter links to threat processes in particular, this finding may inform future efforts to localize specific neural regions associated with defensive responding to self-relevant persuasive messages.

Previous studies have focused primarily on how socially mediated emotion regulation attenuates threat responses in the presence of another person or when calling to mind specific social resources. For example, holding a spouse's hand (versus a stranger's hand or no hand) predicted decreased threat processing in the face of electric shock (51), and this effect was strengthened by high motivation to connect with a romantic partner (52). Likewise, providing social support to a loved one in close proximity has also been associated with attenuated neural responses to threat (53). Beyond physical proximity to loved ones, pictures of a romantic partner also attenuated threat reactivity (54). Together, the extant literature has demonstrated ways in which social connection is associated with reduced neural reactivity to threats.

The current results suggest an additional pathway through which holding more generalized other-directed values that transcend self-boundaries can provide benefits by diminishing neural threat responses to otherwise beneficial information. More broadly, it is possible that prioritizing self-transcendent values can preempt self-focused defensiveness through the process of psychological expansion beyond self-boundaries (1,2). Previous research supports the notion that pursuing values beyond one's self-interest may allow people to transcend concerns about self-inadequacy, which then can reduce defensiveness (11). The distinction between having social connection and prioritizing transcending values highlights one possible explanation for their distinct effects, where the latter may chronically reduce self-focus and hence the need to defend the self. Future studies that employ experimental designs to control focus on transcendent values can help better interpret the mechanisms and directionality of the current effects.

Moderation Effects by Demographics

Female participants and individuals with lower BMI in our sample were more likely to rank transcendent values higher than other values. Participants' sex, but not BMI, moderated the link between transcendent value ranking and neural responses to health messages. Please see the Supplemental Digital Content 2, <http://links.lww.com/PSYMED/A355>, for further discussions about the moderation effects by demographics.

Enhancing Self-Transcendent Value Effects Through Affirmation, Beyond Social Connection

Reminding participants of their highest values partially strengthened the link between transcendent values and brain responses in the right amygdala and the Neurosynth threat map. This suggests that the associations between transcendent values and some brain responses may be altered by motivational states. Converging with research on physical or imagined presence of close others buffering deleterious effects of threat (e.g., a partner holding hands (51), partner in the room (53), pictures of a partner (54)), reminding participants of their high values marginally enhanced the buffering effects in the right amygdala and in the Neurosynth threat mask. Conscious reflection on core values, however, may be more important for some subpathways; holding high transcendent values diminished responses in all ROIs regardless of whether the values were actively affirmed with an external task or not. This suggests at least some degree of automaticity in the link between prioritizing self-transcendent values and neural responses within key brain systems, which may ultimately suggest one source of power in such values. Indeed, we observed that consequences of prioritizing family and friends are distinct from perceiving high levels of social connection; hence, self-transcendent values may function with or without the online awareness or presence of close others.

Self-transcendent values and perceived social connection also diverged in their relationships to key outcome variables. Higher social connection was associated with lower self-reported negative affect generally, but social connection was not robustly associated with the specific processing of health messages in the target brain regions. By contrast, transcendent value ranking was a stronger predictor of attenuated responses in key brain regions but not robustly associated with self-reported negative affect. These findings

are also consistent with the idea that high levels of perceived social connection can influence conscious perception and management of emotion, whereas transcendent values may operate outside of conscious awareness or regulation. It is also possible that transcendent values may buffer more specific threats, such as self-relevant health information. For example, actively pursuing self-transcendent values may bring additional benefits to having social connection by providing motivation and direction to persevere through potentially threatening challenges.

The current study did not collect state affect at baseline, leaving ambiguity in the link between transcendent values and changes in affect after health message exposure. However, transcendent values were not associated with the baseline depression scores, suggesting that the self-reported negative affect after health messages is likely state negative affect (versus generalized negative affectivity). Future studies may collect state affect at multiple time points to examine temporal relationships among these variables.

Finally, our operationalization of self-transcendence focused on interpersonal values; inherent in this operationalization is prioritizing social and interpersonal values more than material rewards, which may be a key component of the type of self-transcendence under study. This may also include altruistic over selfish motivations or other key ingredients that cannot be distinguished from the current intervention. As such, we encourage future studies to examine distinct types of transcendence that may or may not involve interpersonal values, to test potentially divergent neural pathways and associated outcomes.

Specificity of the Effect

The self-transcendent value effect was specific to processing self-relevant, potentially threatening health (versus general self-related) information. Having high transcendent values may therefore be distinct from other traits also linked to healthy emotion processing, such as mindfulness associated with generalized deactivation within the amygdala (55). This specificity suggests that transcendent value effects may be particularly beneficial in potentially threatening contexts, and interventions that encourage cultivating self-transcendent values may complement existing intervention strategies that target problems associated with processing psychological threat.

CONCLUSIONS

The current research offers direct, novel evidence that prioritizing self-transcendent values is associated with lower amygdala and AI response, as well as lower response in a set of brain regions associated with threat in a large-scale, automated meta-analysis, to potentially threatening information. These findings suggest that one way through which transcendent values benefit health may be by reducing neural indicators of threat in response to health messaging. These data add to a growing body of literature on the benefits of interpersonal, transcendent values. Self-transcendent values should also be considered as an active individual difference variable in future intervention strategies and theories of affective processing and health communication.

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REFERENCES

- Levenson MR, Jennings PA, Aldwin CM, Shiraishi RW. Self-transcendence: conceptualization and measurement. *Int J Aging Hum Dev* 2005;60:127–43.
- Reed PG. Self-transcendence and mental health in oldest-old adults. *Nurs Res* 1991;40:5–11.
- Coward DD. Facilitation of self-transcendence in a breast cancer support group: II. *Oncol Nurs Forum* 2003;30:291–300.
- Coward DD, Kahn DL. Transcending breast cancer: making meaning from diagnosis and treatment. *J Holist Nurs* 2005;23:264–83.
- Coward DD, Reed PG. Self-transcendence: a resource for healing at the end of life. *Issues Ment Health Nurs* 1996;17:275–88.
- Zappala CR. Well-being: The Correlation Between Self-Transcendence and Psychological and Subjective Well-being. Palo Alto, CA: Institute of Transpersonal Psychology; 2007.
- Ellemann CR, Reed PG. Self-transcendence and depression in middle-age adults. *West J Nurs Res* 2001;23:698–713.
- Klaas D. Testing two elements of spirituality in depressed and non-depressed elders. *Int J Psychiatr Nurs Res* 1998;4:452–62.
- Buchanan D, Farran C, Clark D. Suicidal thought and self-transcendence in older adults. *J Psychosoc Nurs Ment Health Serv* 1995;33:31–4.
- Burson A, Crocker J, Mischkowski D. Two types of value-affirmation implications for self-control following social exclusion. *Soc Psychol Pers Sci* 2012;3:510–6.
- Crocker J, Niiya Y, Mischkowski D. Why does writing about important values reduce defensiveness? Self-affirmation and the role of positive other-directed feelings. *Psychol Sci* 2008;19:740–7.
- Yarkoni T, Poldrack RA, Nichols TE, Van Essen DC, Wager TD. Large-scale automated synthesis of human functional neuroimaging data. *Nat Methods* 2011;8:665–70.
- Cunningham WA, Brosch T. Motivational salience amygdala tuning from traits, needs, values, and goals. *Curr Dir Psychol Sci* 2012;21:54–9.
- Lloyd DM, Findlay G, Roberts N, Nummikko T. Illness behavior in patients with chronic low back pain and activation of the affective circuitry of the brain. *Psychosom Med* 2014;76:413–21.
- Zunhammer M, Geis S, Busch V, Greenlee MW, Eichhammer P. Effects of intranasal oxytocin on thermal pain in healthy men: a randomized functional magnetic resonance imaging study. *Psychosom Med* 2015;77:156–66.
- Sergerie K, Chochol C, Armony JL. The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. *Neurosci Biobehav Rev* 2008;32:811–30.
- Phan KL, Wager T, Taylor SF, Liberzon I. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage* 2002;16:331–48.
- Critchley H. Emotion and its disorders. *Br Med Bull* 2003;65:35–47.
- Mobbs D, Marchant JL, Hassabis D, Seymour B, Tan G, Gray M, Petrovic P, Dolan RJ, Frith CD. From threat to fear: the neural organization of defensive fear systems in humans. *J Neurosci* 2009;29:12236–43.
- Goldin PR, Gross JJ. Effects of mindfulness-based stress reduction (MBSR) on emotion regulation in social anxiety disorder. *Emotion* 2010;10:83–91.
- Mobbs D, Petrovic P, Marchant JL, Hassabis D, Weiskopf N, Seymour B, Dolan RJ, Frith CD. When fear is near: threat imminence elicits prefrontal-periaqueductal gray shifts in humans. *Science* 2007;317:1079–83.
- Cohen GL, Sherman DK. The psychology of change: self-affirmation and social psychological intervention. *Annu Rev Psychol* 2014;65:333–71.
- Crowell A, Page-Gould E, Schmeichel BJ. Self-affirmation breaks the link between the behavioral inhibition system and the threat-potentiated startle response. *Emotion* 2015;15:146–50.
- Sherman DK, Bunyan DP, Creswell JD, Jaremka LM. Psychological vulnerability and stress: the effects of self-affirmation on sympathetic nervous system responses to naturalistic stressors. *Health Psychol* 2009;28:554.
- Cohen S, Wills TA. Stress, social support, and the buffering hypothesis. *Psychol Bull* 1985;98:310.

26. Uchino BN, Cacioppo JT, Kiecolt-Glaser JK. The relationship between social support and physiological processes: a review with emphasis on underlying mechanisms and implications for health. *Psychol Bull* 1996;119:488.
27. World Health Organization. *The World Health Report 2002: Reducing Risks, Promoting Healthy Life*. Geneva: World Health Organization; 2002.
28. US Department of Health & Human Services. *Physical Activity and Health: A Report of the Surgeon General*. Atlanta: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Promotion, International Medical Publishing; 1996.
29. Bianchini F, Kaaks R, Vainio H. Weight control and physical activity in cancer prevention. *Obes Rev* 2002;3:5–8.
30. Manson JE, Greenland P, LaCroix AZ, Stefanick ML, Mouton CP, Oberman A, Perri MG, Sheps DS, Pettinger MB, Siscovick DS. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med* 2002;347:716–25.
31. Dillard AJ, McCaul KD, Magnan RE. Why is such a smart person like you smoking? Using self-affirmation to reduce defensiveness to cigarette warning labels. *J Appl Biobehav Res* 2005;10:165–82.
32. Vanden Auweele Y, Rzewnicki R, van Mele V. Reasons for not exercising and exercise intentions: a study of middle-aged sedentary adults. *J Sports Sci* 1997;15: 151–65.
33. Young DR, King AC, Oka RK. Determinants of exercise level in the sedentary versus underactive older adult: implications for physical activity program development. *J Aging Phys Act* 1995;3:4–25.
34. Falk EB, O'Donnell MB, Cascio CN, Tinney F, Kang Y, Lieberman MD, Taylor SE, An L, Resnicow K, Strecher VJ. Self-affirmation alters the brain's response to health messages and subsequent behavior change. *Proc Natl Acad Sci* 2015;112: 1977–82.
35. Cascio CN, O'Donnell MB, Tinney FJ, Lieberman MD, Taylor SE, Strecher VJ, Falk EB. Self-affirmation activates brain systems associated with self-related processing and reward and is reinforced by future orientation. *Soc Cogn Affect Neurosci* 2016;11:621–9.
36. Kang Y, O'Donnell MB, Strecher VJ, Falk EB. Dispositional mindfulness predicts adaptive affective responses to health messages and increased exercise motivation. *Mindfulness* 2016. doi: 10.1007/s12671-016-0608-7.
37. Lee RM, Robbins SB. Measuring belongingness: The Social Connectedness and the Social Assurance scales. *J Couns Psychol* 1995;42:232.
38. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988;54: 1063–70.
39. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:561–71.
40. Chua HF, Ho SS, Jasinska AJ, Polk TA, Welsh RC, Liberzon I, Strecher VJ. Self-related neural response to tailored smoking-cessation messages predicts quitting. *Nat Neurosci* 2011;14:426–7.
41. Schmitz TW, Johnson SC. Self-appraisal decisions evoke dissociated dorsal—ventral mPFC networks. *Neuroimage* 2006;30:1050–8.
42. Anderson NH. Likableness ratings of 555 personality-trait words. *J Pers Soc Psychol* 1968;9:272.
43. Derntl B, Habel U, Windischberger C, Robinson S, Kryspin-Exner I, Gur RC, Moser E. General and specific responsiveness of the amygdala during explicit emotion recognition in females and males. *BMC Neurosci* 2009;10:91.
44. Felmingham K, Kemp A, Williams L, Falconer E, Olivieri G, Peduto A, Bryant R. Dissociative responses to conscious and non-conscious fear impact underlying brain function in post-traumatic stress disorder. *Psychol Med* 2008;38:1771–80.
45. Fonzo GA, Flagan TM, Sullivan S, Allard CB, Grimes EM, Simmons AN, Paulus MP, Stein MB. Neural functional and structural correlates of childhood maltreatment in women with intimate-partner violence-related posttraumatic stress disorder. *Psychiatry Res* 2013;211:93–103.
46. Grosbras MH, Paus T. Brain networks involved in viewing angry hands or faces. *Cereb Cortex* 2006;16:1087–96.
47. Kemp AH, Felmingham KL, Falconer E, Liddell BJ, Bryant RA, Williams LM. Heterogeneity of non-conscious fear perception in posttraumatic stress disorder as a function of physiological arousal: an fMRI study. *Psychiatry Res* 2009;174:158–61.
48. Stein MB, Simmons AN, Feinstein JS, Paulus MP. Increased amygdala and insula activation during emotion processing in anxiety-prone subjects. *Am J Psychiatry* 2007;164:318–27.
49. Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage* 2003;19:1233–9.
50. Brett M, Anton JL, Valabregue R, Poline JB. Region of interest analysis using the MarsBar toolbox for SPM 99. *Neuroimage* 2002;16:S497.
51. Coan JA, Schaefer HS, Davidson RJ. Lending a hand social regulation of the neural response to threat. *Psychol Sci* 2006;17:1032–9.
52. Coan JA, Kastle S, Jackson A, Schaefer HS, Davidson RJ. Mutuality and the social regulation of neural threat responding. *Attach Hum Dev* 2013;15:303–15.
53. Inagaki TK, Eisenberger NI. Neural correlates of giving support to a loved one. *Psychosom Med* 2012;74:3–7.
54. Eisenberger NI, Master SL, Inagaki TK, Taylor SE, Shirinyan D, Lieberman MD, Naliboff BD. Attachment figures activate a safety signal-related neural region and reduce pain experience. *Proc Natl Acad Sci* 2011;108:11721–6.
55. Way BM, Creswell JD, Eisenberger NI, Lieberman MD. Dispositional mindfulness and depressive symptomatology: correlations with limbic and self-referential neural activity during rest. *Emotion* 2010;10:12–24.