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Asymmetry in Resting Intracortical Activity as a Buffer to Social Threat

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Abstract

Social rejection can create powerful changes in people's brains and bodies. In the study reported here, we examined brain-based individual differences associated with buffering against cardiovascular threat responses to social rejection. Using EEG source-localization techniques, we examined differences in intracortical asymmetry. We predicted that individuals with greater left relative to right dorsolateral prefrontal activity would show a more approach-motivated response to social rejection. Eighty-four female participants were randomly assigned to one of three stressful situations: social rejection, social evaluation without rejection, or self-evaluation. Among participants assigned to the social-rejection condition, greater left relative to right prefrontal intracortical activity at baseline was associated with more adaptive cardiovascular profiles and more self-reported approach-oriented emotions. Participants in the other conditions did not show these relationships. Our data are the first to show that social context matters when attempting to link individual differences in cortical asymmetry with approach-related cardiovascular and emotional outcomes.

Keywords

electrophysiology, individual differences, neuroendocrinology, social influences

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Social rejection is a common, perhaps ubiquitous, outcome for social animals. People can be rejected by a romantic interest, passed over for a job, or ignored and belittled by others. Psychological research has demonstrated the powerful effects of social rejection on people's minds, bodies, and experiences. Social rejection can result in negative emotional responses, including increased shame, sadness, and anxiety (Ayduk, Mischel, & Downey, 2002; Williams, 2001); physiological changes, such as increased and sustained catabolic hormone levels; reduced immune function; malignant cardiovascular responses (Cacioppo, Hawkley, & Berntson, 2003; Mendes, Major, McCoy, & Blascovich, 2008; Stroud, Tanofsky-Kraff, Wilfley, & Salovey, 2000); and neural responses, such as activity in the dorsal anterior cingulate cortex, a region implicated in coding the emotional component of pain (Eisenberger, Lieberman, & Williams, 2003). Although the psychological and neurobiological correlates of social rejection have been explored, few studies have investigated what enables some individuals to retain an approach motivation in the face of social scrutiny. In the study reported here, we examined whether individual differences in intracortical asymmetry act as a buffer to the psychological and physiological threats that typically follow social rejection.

Correlational research suggests that trait frontal cortical asymmetry in favor of the left hemisphere is related to approach motivation, ability to regulate negative emotions, and well-being (Davidson, 1993; Harmon-Jones, Gable, & Peterson, 2010; Jackson et al., 2003; Urry et al., 2004). More specifically, recent evidence implicates left dorsolateral prefrontal cortex (DLPFC) regions in some of these positive psychological outcomes (Berkman & Lieberman, 2010; Pizzagalli, Sherwood, Henriques, & Davidson, 2005). But how do individual differences in frontal cortical activity influence these long-term outcomes? We suggest that individuals with relatively greater left than right cortical activity might respond to acute stressful and socially evaluative situations with a more resilient response profile. Cumulative effects of this psychological mettle against life's stressors may lead to better long-term outcomes, including well-being and life satisfaction. We hypothesized that increased left relative to right DLPFC resting activity would buffer against an intense psychologically

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stressful experience, specifically social rejection. To test this hypothesis, we examined how individual differences in resting frontal activity influenced autonomic nervous system (ANS) responses to social rejection compared with ANS responses to social evaluation without rejection and self-evaluation.

Brain-to-Body Effects

As ANS functioning is largely determined by activity in the brain, it is surprising how little research has managed to bridge the divide between neural and autonomic functioning and predict ANS responses from brain activity. In this study, we examined how individual differences in cortical asymmetry influence downstream ANS changes, with a specific focus on situations that are highly stressful and will activate the body's two primary stress systems: the sympathetic-adrenal-medullary (SAM) and hypothalamic-pituitary-adrenocortical (HPA) axes.

Prior research has suggested that relative activation of these two systems can differentiate benign, positive stress states (challenge) from more damaging stress responses (threat; Blascovich & Mendes, 2010; Dienstbier, 1989; Mendes et al., 2008). Although both challenge and threat occur during stressful situations, the two states differ in the appraisals of the situation and the downstream cardiovascular reactivity with which they are associated. For example, challenge occurs when individuals appraise their resources as exceeding the demands of the task, whereas threat occurs when situational demands exceed resources. Cardiovascular responses linked to challenge are characterized by increases from baseline in cardiac output (i.e., the volume of oxygenated blood ejected from the heart) and decreases in total peripheral resistance (TPR; i.e., vasodilation). Threat is characterized by little or no increase in cardiac output and increase in TPR (i.e., vasoconstriction).

Compared with threat states, challenge states have been associated with better cognitive performance (Kassam, Koslov, & Mendes, 2009), more approach-oriented behavior (Mendes et al., 2008), and reduced risk of cellular aging (Mendes & Epel, 2010). Furthermore, one of the primary determinants of challenge states, increased cardiac output, has been linked to decelerated brain aging in the Framingham sample (Jefferson et al., 2010). Individuals with greater cardiac output had increased brain volume and increased cognitive processing speed in older adulthood, leading Jefferson et al. to speculate that increased levels of oxygenated blood produced by the heart can have long-term protective effects in the brain.

In the present study, we expected that individuals with greater left relative to right prefrontal activity would respond with more challenge physiological profiles to stressful situations. We anticipated that this relationship would especially emerge during situations that were associated with *social-evaluative threat*—when an aspect of the self could be negatively judged by others (Dickerson & Kemeny, 2004)—compared with situations that were self-relevant or socially evaluative but not threatening.

Method

Participants

We recruited 87 females (mean age = 22.2 years; *SD* = 1.9 years) for a 3-hr study on "physiological responses during various tasks." During an initial phone screening, we administered a portion of the Structured Clinical Inventory for the DSM-IV-TR Axis I Disorders (First, Spitzer, Gibbon, & Williams, 2002) and invited right-handed women to the laboratory who reported no personal or first-degree family history of Axis I psychopathology, learning disorders, or neurological conditions. Furthermore, we prescreened participants for general health conditions and provided instructions to reduce factors that would influence neuroendocrine variables during testing. Participants were scheduled during the follicular stage of their menstrual cycle (Symonds, Gallagher, Thompson, & Young, 2004) and compensated $10 per hour.

Procedure

On arrival at the laboratory, participants were told that the experiment's general purpose was to investigate physiological responses during rest and active tasks. To prevent anticipatory stress that might contaminate baseline assessments, we did not initially describe the stress task. We applied sensors for EEG and ANS response recording; then, participants sat for 8 min to establish a resting baseline. We obtained the first saliva sample approximately 30 min after participants' arrival (Time 1).

Next, the experimenter described the upcoming social-evaluation task, a modified Trier Social Stress task (Kirschbaum & Hellhammer, 1994), and obtained verbal consent. Participants were instructed to prepare and deliver a 5-min speech, which would be followed by a 5-min question-and-answer (Q&A) session in a mock job interview (Akinola & Mendes, 2008). Participants were randomly assigned to one of three conditions: no social evaluation (control), social evaluation with positive feedback, and social-evaluative threat with negative feedback. Social evaluation was operationalized by having interviewers either present during the speech (social-evaluation and social-evaluative-threat conditions) or absent during the speech (control condition). Evaluation was differentiated into the social-evaluation and social-evaluative-threat categories on the basis of the type of nonverbal feedback given by interviewers (positive or negative, respectively). In the control condition, participants were told that they would deliver the speech alone in the room. The control condition was designed to require similar metabolic demands associated with speaking, but without social evaluation. Prior to and following the speech, all participants completed appraisal and affect questionnaires.

In the two social-evaluation conditions, participants were informed that they would deliver the speech to two interviewers. Once the participants gave consent, two research assistants (one male, one female) entered the room to reiterate the instructions. Subsequently, participants were left alone for 5 min so they could prepare their speech.

When the interviewers reentered the room, participants began the speech. At this point, the social-evaluation and social-evaluative-threat conditions diverged. The interviewers' roles were scripted and coordinated so that all participants within a condition had a consistent experience. In the social-evaluation condition, interviewers gave positive nonverbal feedback by smiling, nodding, leaning forward, and appearing actively engaged during the speech. In contrast, in the social-evaluative-threat condition, interviewers shook their heads, frowned, leaned back, and appeared to dislike the participant's performance.

After giving their speeches, participants in all conditions completed a 5-min Q&A session, during which the interviewers asked general questions (e.g., "Are you striving to be a jack-of-all-trades or an expert in one field?"). During the Q&A session, the feedback manipulations in the social-evaluation and social-evaluative-threat conditions were maintained. In the control condition, participants were handed index cards with one question per card, and they were instructed to read each question and answer it aloud. Five minutes of cardiovascular data were collected during each of the speech and Q&A sessions.

After the Q&A session in the two social-evaluation conditions, the interviewers left the room. A recovery period followed for all conditions, after which the experimenter collected a second saliva sample (25 min from the start of the stressor; Time 2); this served as a reactivity sample. The participants then completed additional tasks not relevant to this study. Forty-five minutes after the start of the stressor (Time 3), participants provided a third saliva sample; this served as a recovery sample.

Physiological and self-report measures

EEG measures. Resting EEG was recorded using a 128-channel Electrical Geodesics (Eugene, OR) system during eight alternating 1-min periods (four with eyes closed, four with eyes open; order was counterbalanced across participants). Data were sampled at 250 Hz (0.1- to 100-Hz analog filter) and referenced to the vertex. Impedances were kept below 45 kΩ.

ANS measures. Cardiac measures were recorded noninvasively using an ambulatory monitor for impedance cardiography (AMS46; Vrije University, Department of Biological Psychology, Amsterdam, The Netherlands). Cardiac impedance and ECG recordings were obtained from six electrodes placed on the neck and torso. In addition to these cardiac measures, blood pressure was measured throughout the experiment using tonometric technology (Biopac, Goleta, CA), which estimates blood pressure from the radial artery.

Data were scored in 1-min segments to calculate cardiac output as well as preejection period (PEP), a time-based measure of the force of the ventricle contractions. TPR was estimated with the standard equation: (mean arterial pressure/cardiac output) × 80.

Neuroendocrine measures. Saliva samples were obtained using the passive drool method and stored at –80 °C. On completion of the study, samples were sent to Clemens Kirschbaum's laboratory at the Dresden University of Technology to be assayed for cortisol using commercial immunoassay kits (IBL, Hamburg, Germany). Intra- and interassay coefficients were less than 10%.

Self-report measures. We used various self-report measures to assess appraisals of demands (e.g., "The upcoming task is very demanding"), appraisals of resources (e.g., "I have the abilities to perform the task successfully"), affect states, and participants' perceptions of how they were perceived by the interviewers (Akinola & Mendes, 2008). As in previous research, we averaged ratings for perceived demands and perceived resources (all $\alpha s > .75$), and then we created a threat ratio by dividing the former by the latter; higher scores indicated greater threat states.

Self-reported affect was assessed using the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). Participants rated their current feelings on 20 affect states (10 positive and 10 negative) using 5-point scales ranging from 1 (*not at all*) to 5 (*a great deal*). The positive and negative affect scales were calculated for each time point in the experiment and had high reliability ($\alpha s = .85–.91$). We also calculated an approach response by averaging four of the PANAS items: *strong*, *alert*, *determined*, and *active* ($\alpha s = .72–.76$; see Harmon-Jones et al., 2010, for a similar construct).

As a manipulation check, we asked participants assigned to the social-evaluation conditions to rate how they believed each of the interviewers thought they performed (e.g., "She thought I performed well on the task"). Responses for the male and female judges were highly correlated ($\alpha = .91$), so we averaged these responses into a single score.

Data reduction and scoring

EEG data were rereferenced off-line to an average reference. Eye movement (e.g., blinks) and ECG artifacts were removed using independent component analysis, which was performed with Brain Vision Analyzer software (Brain Products GmbH, Munich, Germany). Data were scored manually to eliminate artifacts, and all available artifact-free 2,048-ms EEG epochs were extracted. Low-resolution electromagnetic tomography (LORETA; Pascual-Marqui et al., 1999) was used to estimate current density for various EEG frequency bands; following the extensive frontal EEG asymmetry literature, analyses focused on the alpha1 band (8.5–10.0 Hz) and alpha2 band (10.5–12.0 Hz; Pizzagalli et al., 2005). The LORETA solution space included 2,394 cubic elements (voxels, 7 × 7 × 7 mm) and was restricted to cortical gray matter and hippocampi, as defined by the Montreal Neurological Institute 305 template. Before statistical analyses, the intensity of the overall current density for each band was normalized to 1.

In light of a priori hypotheses about the role of alpha activity within DLPFC regions, a region-of-interest approach was used to minimize the number of statistical tests performed. Specifically, the left and right Brodmann's areas (BAs) 9 and 46 were anatomically defined using the Talairach Daemon (Lancaster

et al., 2000) and anatomical landmarks (Petrides & Pandya, 1999; Rajkowska & Goldman-Rakic, 1995a, 1995b; Fig. 1). Areas of activation in the left and right BA 9 contained 35 voxels (12.01 cm^3) and 38 voxels (13.03 cm^3), respectively; areas of activation in the left and right BA 46 each contained 12 voxels (4.12 cm^3).

The extracted alpha1 and alpha2 current density were averaged across voxels and log transformed, and then frontal asymmetry was calculated by taking the current density in the right hemisphere and subtracting the current density in the left hemisphere. Because alpha activity is inversely correlated with brain activation (Coan & Allen, 2004; Davidson, Jackson, & Larson, 2000; Oakes et al., 2004), a positive frontal intracortical asymmetry index reflects relatively higher activity in the left DLPFC than in the right DLPFC. The four variables (two subbands, two regions of interest) were highly related ($\alpha = .89$); accordingly, analyses focused on a composite of alpha1 and alpha2 bands extracted from BA 9. BA 9 was prioritized because it was closer than BA 46 to the location of F3 and F4, the scalp electrodes most widely probed in frontal EEG studies, whereas BA 46 is closer to F5 and F6 (Figs. 1c and 1d). Similar, albeit statistically less robust, findings emerged when considering BA 46.

Results

Participant attrition

Of the original 87 participants, 1 was lost because of illness, and 2 were excluded because of protocol deviations. Data from the remaining 84 participants were used in all analyses, and the varying degrees of freedom reported resulted from missing values for physiological or self-report data.

Sympathetic nervous system responses

To assess responses in the sympathetic nervous system, we first compared the control condition (no evaluation) with the average of the two evaluation conditions with respect to changes in sympathetic activation, PEP, during the stress task. Average changes in PEP from the speech task yielded a significant difference by evaluation condition, $F(1, 73) = 17.34$, $p < .0001$. As expected, the control condition showed significantly less sympathetic activation (ΔPEP: $M = –2.0$, $SD = 7.0$) than the evaluation conditions did (ΔPEP: $M = –10.2$, $SD = 8.5$). It is important to note that only the evaluation conditions showed a significant decrease from baseline—evaluation: $t(50) = –8.47$, $p < .0001$; no evaluation: $t(25) = –1.41$, n.s.

Subjective experience

Next, we examined whether the manipulations were experienced as intended. We operationalized social-evaluative threat as the extent to which participants believed that they were performing poorly and experienced the interview task as more threatening. To confirm this manipulation, we first examined participants' responses to how they believed the interviewers perceived their speech. As intended, participants in the social-evaluative-threat

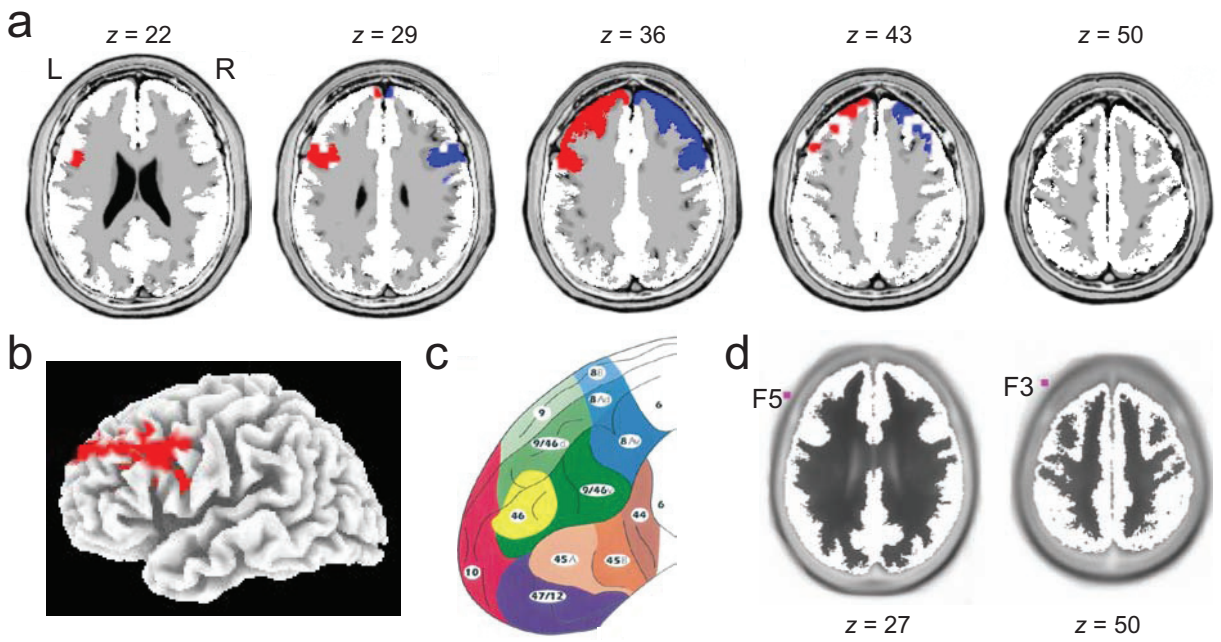

Fig. 1. Dorsolateral prefrontal cortex regions of interest. The axial slices in (a), shown in 7-mm increments, depict the location and spatial extent of the left (L; red) and right (R; blue) Brodmann's area 9. Alpha current density was extracted from these regions and entered into statistical analyses. A three-dimensional cortical-surface rendering of Brodmann's area 9 is shown in (b), and a cytoarchitectonic map illustrates the location of this area (c; reprinted from Petrides & Pandya, 1999, with permission of the authors). In (c), Brodmann's area 9 is shown in shades of green. The axial slices in (d) depict the three-dimensional location of the scalp electrodes F3 and F5 with respect to the underlying neuroanatomy of our regions of interest. All coordinates are in Montreal Neurological Institute space.

condition, compared with participants in the social-evaluation condition, perceived the evaluators as disliking their performance, $F(1, 51) = 19.50$, $p < .0001$ (Table 1).

We then compared appraisals and changes in affect in all conditions. In the social-evaluative-threat condition, participants appraised the interview situation as more threatening than participants in the social-evaluation or control conditions did, $F(2, 81) = 3.82$, $p < .02$. Next, we examined negative and positive affect and observed significant differences by condition. Controlling for pretask affect, negative affect was significantly greater in the social-evaluative-threat condition than in the other conditions, $F(2, 81) = 6.50$, $p < .01$. In contrast, positive affect was higher in the social-evaluation condition than in the other conditions, $F(2, 81) = 4.69$, $p < .02$; this effect was driven primarily by higher positive affect in the social-evaluation condition than the social-evaluative-threat condition. Altogether, these findings indicate that we successfully manipulated the subjective experience of different types of social evaluation.

Neuroendocrine responses

To evaluate neuroendocrine data, we conducted a mixed-model ANOVA with condition as a between-subjects factor, time (baseline, reactivity, and recovery) as a within-subjects factor, and number of hours since waking as the covariate. This model produced a significant effect for condition, $F(2, 79) = 4.48$, $p < .014$, which was qualified by a significant time-by-condition interaction, $F(4, 158) = 2.58$, $p < .04$ (Fig. 2). Simple-effects tests within each time period showed that there were no differences between conditions at Time 1 (baseline), $F(2, 79) = 0.48$, n.s., but there were significant condition effects at Time 2 (reactivity), $F(2, 79) = 4.29$, $p < .02$, and at Time 3 (recovery), $F(2, 79) = 4.77$, $p < .01$. Orthogonal simple comparisons confirmed that cortisol reactivity was greater at Time 2 in the social-evaluative-threat condition than in the social-evaluation condition, $F(1, 79) = 3.91$, $p < .05$, which in turn elicited greater cortisol reactivity at that time point than the control condition did, $F(1, 79) = 4.67$, $p < .04$. Simple comparisons between the conditions at Time 3 yielded similar findings; specifically, the social-evaluative-threat condition showed greater cortisol reactivity than did the social-evaluation condition, $F(1, 79) = 4.05$, $p < .05$.

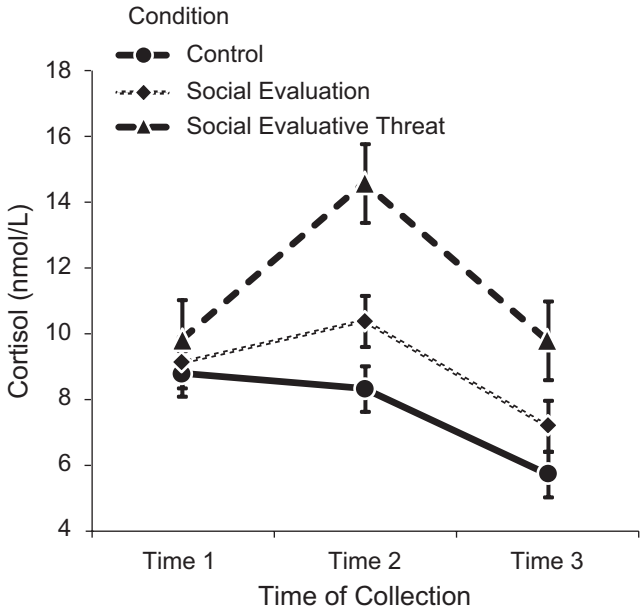

Fig. 2. Mean cortisol levels in the three conditions at baseline (Time 1), reactivity (Time 2), and recovery (Time 3). Error bars show standard errors, which were averaged across time within each condition.

As cortisol increases tend to be psychologically nonspecific—many distinct psychological states are associated with increased cortisol responses—we did not expect cortisol reactivity to be associated with resting BA 9 activity. We examined correlations among cortisol reactivity and resting BA 9 responses. Even though the direction of the relationship was consistent with our hypothesis that increased left relative to right DLPFC resting activity would buffer against psychological stress (lower cortisol reactivity was associated with greater intracortical asymmetry), none of the correlations were significant in any of the conditions—control: $r = -.16$; social evaluation: $r = -.15$; social evaluative threat: $r = -.36$.

Table 1. Mean Self-Report Ratings by Condition

Measure	Social-evaluation condition	Social-evaluative-threat condition	Control condition
"[Judges] thought I performed well"	4.77 (1.0)$_a$	3.34 (1.4)$_b$	—
Negative affect	1.6 (0.5)$_b$	1.9 (0.9)$_a$	1.4 (0.4)$_b$
Positive affect	2.7 (0.9)$_a$	2.3 (0.8)$_b$	2.4 (1.0)$_{ab}$
Threat ratio	.73 (.3)$_a$	.91 (.4)$_b$	.73 (.2)$_a$

Note: Standard deviations are shown in parentheses. Within a row, values with different subscripts are significantly different ($p < .05$). Ratings on the "[Judges] thought I performed well" measure ranged from 1 to 7, and ratings for male and female judges were averaged. Negative- and positive-affect ratings ranged from 1 to 5. Means are adjusted for prespeech affect ratings. The threat ratio was calculated by dividing the average of the demand appraisals by the average of the resource appraisals.

Greater left relative to right intracortical activity as a buffer to social threat

Our primary prediction was context-specific and suggested relations between EEG asymmetry and autonomic activation only in the social-evaluative-threat condition. Before testing this prediction, we examined whether asymmetric activation was related to any of the cardiovascular responses at rest. We tested the bivariate correlation between our asymmetry variable and resting cardiovascular responses, specifically cardiac output, PEP, and TPR. None of the cardiovascular responses at baseline were significantly correlated with asymmetric activity, all rs $< |.12|$.

We then tested the primary prediction that greater left relative to right activity would be associated with buffered cardiovascular reactivity to the social-evaluative-threat condition but not to the social-evaluation or self-evaluation conditions. We first calculated bivariate correlations between asymmetric activity and cardiovascular reactivity data by condition. As shown in Table 2, significant correlations emerged between relative left frontal cortical activity and cardiovascular and emotional indicators of threat and challenge, but only in the social-evaluative-threat condition. These correlations show that greater left relative to right frontal activity at rest was associated with higher cardiac output, lower TPR reactivity, and greater approach affect; taken together, these associations suggest greater challenge than threat responses.

Using regression analyses, we then formally tested whether the effects we observed in the social-evaluative-threat condition were significantly different from those in the other conditions. To predict cardiac output, we included the asymmetry variable and effect-coded main effects of condition in our first step, which produced a nonsignificant model, R^2 = .11, n.s. The second step included the initial predictors plus the interaction terms (condition-by-asymmetry interactions). As expected, the inclusion of the interaction terms significantly increased model fit, ΔR^2 = .07, p < .02. Supporting the threat-buffering hypothesis, our results showed that greater left relative to right intracortical activity during rest was associated with greater cardiac output during the social-evaluative-threat task (b = 2.60, p < .01; Fig. 3a). The relations between asymmetry and cardiac output changes were not significant in the social-evaluation condition (b = 1.50, n.s.) or in the control condition (b = –0.65, n.s.).

Table 2. Bivariate Correlations Between Asymmetry in Frontal Cortical Activation and Measures of Challenge, Threat, and Approach

Condition	ΔCO	ΔTPR	Approach state
Control (no social evaluation)	−.30	.31	.22
Social evaluation	.21	−.05	.24
Social evaluative threat	.56**	−.45*	.42*

Note: Asymmetry was measured by subtracting current density in the left hemisphere from current density in the right hemisphere. Challenge and threat were measured by changes in cardiac output (ΔCO) and in total peripheral resistance (ΔTPR). Approach states were measured by self-report. *p < .05. **p < .01.

We reran this model predicting changes in TPR. The initial model was not significant, R^2 = .11, n.s.; however, the addition of the asymmetry-by-condition terms significantly increased model fit, ΔR^2 = .06, p < .022 (Fig. 3b). Similar to the cardiac output analyses, results showed that among participants assigned to the social-evaluative-threat condition, greater left than right frontal activation was associated with lower TPR (b = –0.88, p < .05). Asymmetric activity was not related to TPR changes in the social-evaluation condition (b = –35.0, n.s.) or in the control condition (b = 55.4, n.s.).

We then used this model to predict self-reported approach emotions. Although the bivariate correlations showed significant relations between asymmetry and self-reported approach affect in the social-evaluative-threat condition and not in the other conditions, the effects in the social-evaluative-threat condition were not significantly different than in the other conditions.

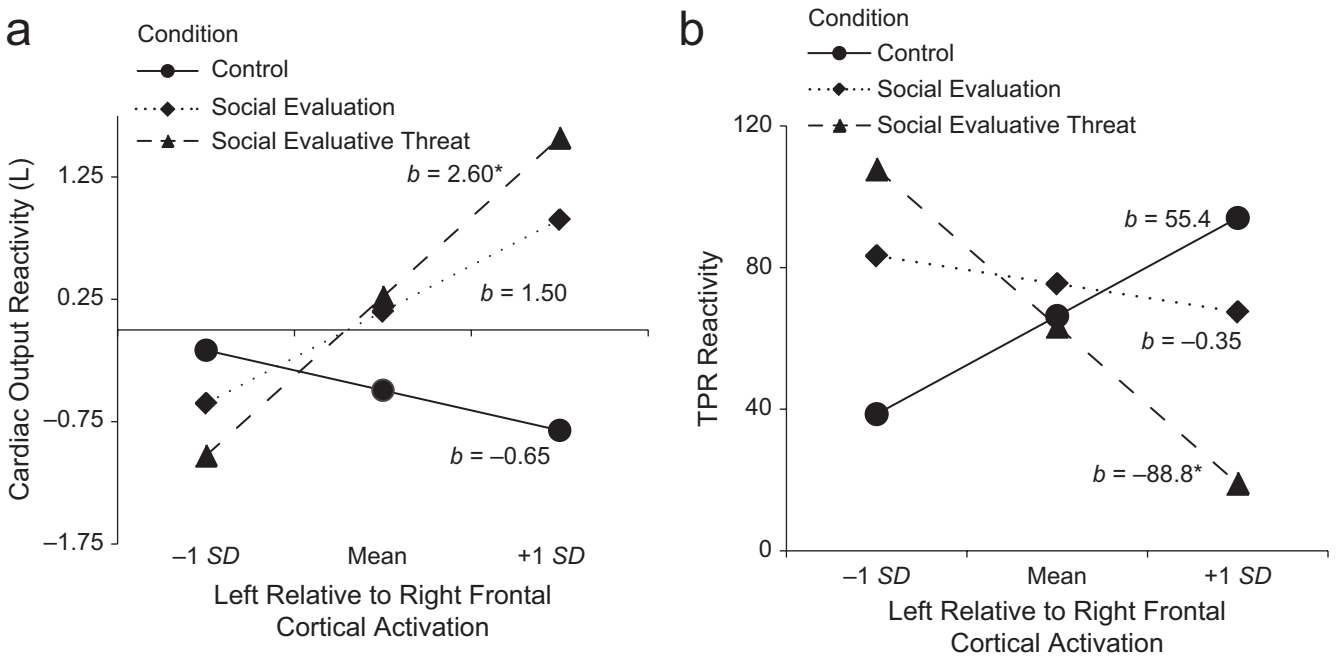

Fig. 3. Results from regression analyses predicting cardiovascular reactivity from frontal cortical asymmetry (greater left than right activation) in each of the three conditions. Results are shown for (a) cardiac output and (b) total peripheral resistance (TPR). Predicted regression values are plotted at the mean of asymmetry and 1 standard deviation above and below the mean. Asterisks indicate slopes that are significantly different from 0 (p < .05).

Discussion

The goal of the present study was to examine individual differences in frontal resting asymmetry as a predictor of approach motivation in stressful situations involving social rejection. We hypothesized that during socially evaluative situations, greater resting left relative to right DLPFC activation would buffer against threat responses and that such activation would be indexed by cardiovascular reactivity. We observed significant associations between left relative to right frontal activity and cardiovascular stress responses, but only when participants were exposed to social rejection. Specifically, under social-threat conditions, left relative to right frontal activity (measured as an average of the current density of alpha1 and alpha2 bands in BA 9) predicted increased cardiac output—a sign of cardiac efficiency—and decreased total peripheral pressure—an indication of dilation in the arterioles. Both of these responses have been linked to a challenge stress state. Conversely, decreased left relative to right frontal activity was associated with maladaptive, or threat, cardiovascular response. Collectively, these findings indicate that participants with higher resting activity in the left relative to right prefrontal cortex exhibited more adaptive, approach-oriented cardiovascular stress responses when confronted with social-evaluative threats.

These data highlight the importance of taking into account environmental and contextual factors when seeking the putative impact of brain-based traits on physiological and emotional outcomes. We know of no previous studies that have examined relationships between frontal cortical asymmetry and cardiovascular responses, and the work reported here indicates that such relationships may emerge only when examined in relevant contexts. In this study, that context was social evaluation operationalized as a motivated performance situation with two interviewers, in which either the interviewers gave positive feedback—itself a protective factor—or negative feedback—which led to social-evaluative threat. The beneficial effects of left relative to right prefrontal activity emerged only in the social-evaluative-threat condition, in which participants were without environmental protective factors, in short, when they were most vulnerable to experiencing social stress.

Despite these findings, it is important to emphasize that it is unclear from our data what affective states are associated with approach-motivated physiology. Although challenge states are often associated with positive affect, these states have also been associated with anger (Mendes et al., 2008). Furthermore, prefrontal activity favoring the left hemisphere has been associated with anger (Harmon-Jones, 2003; Harmon-Jones & Allen, 1998), a negatively valenced, approach-related emotion. Given these prior data highlighting both positive and negative affective correlates of greater left relative to right frontal activity, we must be cautious in interpreting these left relative to right prefrontal activity relationships in a purely positive light. Individuals with higher left relative to right frontal activity possibly experienced a blend of affective responses in the social-threat condition—anger and challenge. It is important to note that we did not find any evidence on PANAS items that participants in the social-evaluative-threat condition who had greater left than right frontal activity were angrier, but we consider this an open question. The careful conclusion to draw from this work is that left relative to right frontal activity was associated with approach motivation, and future research should attempt to disambiguate the valence components of this response.

Parallels could be drawn between our work and research highlighting associations between specific genetic traits and emotional disorders emerging exclusively when considering life stressors (e.g., Caspi et al., 2003). In an acute setting, we found that right relative to left prefrontal activity might represent a disposition toward experiencing exacerbated threat in response to social rejection. Researchers continue to search for biological differences in the etiology of physical and mental diseases, and we argue that context needs to be considered in this endeavor. The present findings represent a simple but powerful example that context matters—reactions to an acute stressor can reveal relationships that do not exist during resting states or benign stress experiences.

There may be important physical and psychological health outcomes that are dependent on both an individual's trait frontal asymmetry and the types of social stressors that he or she encounters in life. Individuals with greater right relative to left prefrontal activity demonstrated malignant acute reactivity to a social threat, and this reactivity may accumulate over time to produce vulnerabilities such as coronary disease or hypertension. In addition, increased sensitivity to and vigilance for social threat could contribute to the development and maintenance of social anxiety or depression. Within this framework, it is interesting to note that both depression (Pizzagalli et al., 2002) and social anxiety disorders (Davidson, Marshall, Tomarken, & Henriques, 2000) have been associated with increased right relative to left frontal activity. In sum, our findings demonstrate that resting prefrontal activity favoring the left hemisphere can act as a protective factor for individuals in a threatening situational context, and prefrontal activity favoring the right hemisphere may be an important vulnerability factor to consider in stress-diathesis models of disease etiology and progression.

Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article. Diego A. Pizzagalli has received research support and consulting fees from ANT Inc. and honoraria and consulting fees from AstraZeneca for projects unrelated to the current study.

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