Neural Bases of Moderation of Cortisol Stress Responses by Psychosocial Resources

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Psychosocial resources have been tied to lower psychological and biological responses to stress. The present research replicated this relationship and extended it by examining how differences in dispositional reactivity of certain neural structures may underlie this relationship. Two hypotheses were examined: (a) psychosocial resources are tied to decreased sensitivity to threat and/or (b) psychosocial resources are associated with enhanced prefrontal inhibition of threat responses during threat regulation. Results indicated that participants with greater psychosocial resources exhibited significantly less cortisol reactivity following a stress task, as predicted. Analyses using functional magnetic resonance imaging revealed that psychosocial resources were associated with greater right ventrolateral prefrontal cortex and less amygdala activity during a threat regulation task but were not associated with less amygdala activity during a threat sensitivity task. Mediational analyses suggest that the relation of psychosocial resources to low cortisol reactivity was mediated by lower amygdala activity during threat regulation. Results suggest that psychosocial resources are associated with lower cortisol responses to stress by means of enhanced inhibition of threat responses during threat regulation, rather than by decreased sensitivity to threat.

Keywords: psychosocial resources, neural, stress

Psychosocial resources is a term used in the coping literature to refer to personal dispositions that may help people perceive potentially threatening events as less so and/or help them to manage their responses to events perceived to be threatening (Taylor & Stanton, 2007). Both laboratory and field investigations have shown that psychosocial resources are associated with reduced psychological and biological responses to stress and have mental health-protective effects (e.g., Ryff & Singer, 1996; Taylor, Lerner, Sherman, Sage, & McDowell, 2003b). Among the resources most reliably related to these beneficial outcomes are optimism, mastery, self-esteem, and extraversion.

Optimism refers to outcome expectancies that good things rather than bad things will happen to the self (Carver & Scheier, 1981). Typically measured by the Life Orientation Test–Revised (LOT-R; Scheier, Carver, & Bridges, 1994), optimism has been tied to greater psychological well-being (Kubzansky et al., 2002; Park, Moore, Turner, & Adler, 1992; Scheier & Carver, 1992; Segerstrom, Taylor, Kemeny, & Fahey, 1998) and to physical health benefits (Antoni & Goodkin, 1988; Cohen, Doyle, Turner, Alper, & Skoner, 2003a; Reed, Kemeny, Taylor, & Visscher, 1999; Reed, Kemeny, Taylor, Wang, & Visscher, 1994; Scheier et al., 1989; see Carver & Scheier, 2002 for a review).

Personal control or mastery refers to whether a person feels able to control or influence his or her outcomes (Thompson, 1981). Studies show a relationship between a sense of control and better psychological health (Rodin & Langer, 1977; Rodin, Timko, & Harris, 1985; Taylor, Helgeson, Reed, & Skokan, 1991), as well as

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better physical health outcomes (Karasek, Theorell, Schwartz, Pieper, & Alfredsson, 1982; M. Seeman & Lewis, 1995).

A positive sense of self, or self-esteem, is also protective against adverse mental and physical health outcomes. Self-esteem is consistently tied to better psychological well-being (e.g., DuBois & Flay, 2004; Paradise & Kernis, 2002; Taylor, Lerner, Sherman, Sage, & McDowell, 2003a), and research consistently ties a positive sense of self to lower reactivity to stressful events (Creswell et al., 2005; M. Seeman & Lewis, 1995; Taylor et al., 2003b).

Extraversion refers to an individual's preferences for social settings and a tendency to be outgoing, which are underpinnings of a socially engaged lifestyle (Wilson et al., 2005). Extraversion is associated with physical health benefits as well (e.g., Broadbent, Broadbent, Phillpotts, & Wallace, 1984; Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997; Cohen, Doyle, Turner, Alper, & Skoner, 2003b; Totman, Kiff, Reed, & Craig, 1980; Wilson et al., 2005).

Most of the preceding research on psychosocial resources has involved naturalistic studies of people facing a broad array of stressors. Laboratory studies show similar effects. For example, using a stress challenge paradigm, Taylor et al. (2003b) found that positive self-appraisals were associated with lower cardiovascular responses to stress, more rapid cardiovascular recovery, and lower baseline cortisol levels. The association between positive self-appraisals and cortisol levels was mediated by psychosocial resources, specifically optimism, self-esteem, mastery, extraversion, and social support. In a conceptually related experimental study, Creswell and colleagues (2005) induced participants to engage in a task involving the affirmation of important personal values (Steele, 1988) or to reflect on values that were less central to them prior to completing a laboratory stress challenge task, the Trier Social Stress Task (TSST; Kirschbaum, Pirke, & Hellhammer, 1993). Those who had affirmed important values had significantly lower cortisol responses to stress. Psychosocial resources (including trait self-esteem and optimism) moderated the relation between self-affirmation and psychological stress responses, such that high resource participants who affirmed their personal values reported the least distress.

Taken together, these findings suggest that psychosocial resources represent a meaningful construct with established relations to both psychological and biological outcomes related to stress (Taylor & Stanton, 2007). Previous research has found these resources to be moderately intercorrelated (e.g., Taylor et al., 2003a), sharing some overlapping but also distinct variance (e.g., Ryff & Singer, 1996; Scheier et al., 1994).

As the previous research implies, psychosocial resources may beneficially affect mental and physical health outcomes, in part, by attenuating biological responses to stress. An important stress-related change in biological functioning is the activation of the hypothalamic-pituitary-adrenal axis (HPA axis), which leads to the production of corticosteroids, including cortisol, which is necessary for energy mobilization (Sapolsky, 1993). Although the release of cortisol in response to real stressors is adaptive and essential for survival, heightened or prolonged activation of the HPA axis has been shown to have deleterious physical and psychological effects (McEwen, 1998; T. E. Seeman, McEwen, Rowe, & Singer, 2001). For example, excess cortisol exposure has been related to medical conditions such as hypertension, atherosclerosis, obesity, insulin resistance, bone demineralization, and impaired immunity (McEwen, 1998; Tsigos & Chrousos, 2002) The present research examined the possible buffering effect of psychosocial resources on neuroendocrine responses to stress. Accordingly, in Study 1, we tested whether high levels of psychosocial resources would be associated with low cortisol responses to laboratory stress tasks.

There are several possible mechanisms by which psychosocial resources may relate to attenuated biological stress responses. Experientially, stress responses are initiated when a threat to the self (e.g., safety, social status, comfort, etc.) is detected. In response, an individual may employ a variety of conscious and unconscious processes (e.g., distraction, reappraisal, problem solving) to deal with the threat. Compared with those with few psychosocial resources, people with greater psychosocial resources may experience diminished biological stress responses because (a) they have a higher threat-detection threshold, meaning that events are less likely to be perceived as threats, and/or (b) they are more effective at managing the threat once detected. At the neural level, there are at least two types of structures underlying these processes: neural structures involved in detecting or evaluating potential threats, such as the amygdala, and neural regions involved in regulating or inhibiting threat responses, such as regions of the prefrontal cortex (PFC).

Previous research has shown that the amygdala is involved in processing fear- or threat-related information, such as threatening facial expressions (Fitzgerald, Angstadt, Jelsone, Nathan, & Phan, 2006; Morris et al., 1996; Phillips et al., 1997; Whalen et al., 1998, 2001). The amygdala is also involved in fear conditioning (Critchley, Mathias, & Dolan, 2002; Furmark, Fischer, Wik, Larsson, & Fredrikson, 1997; LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; Morris, Öhman, & Dolan, 1998). Additionally, amygdala hyperreactivity has been reported in people who are particularly sensitive to social threats. Specifically, heightened amygdala activity has been found in people with social phobias responding to threatening facial expressions and anxiety-provoking tasks such as public speaking (Lorberbaum et al., 2004; Tillfors et al., 2001; Tillfors, Furmark, Marteinsdottir, & Fredrikson, 2002) and in people with inhibited temperament in response to novel faces (Schwartz, Wright, Shin, Kagan, & Rauch, 2003). These threat-related functions suggest a potential psychological basis for the amygdala's involvement in the initiation of physiological stress responses.

Previous research has also shown the amygdala to be involved in biological stress responses at a mechanistic level (Feldman & Conforti, 1981; Frankel, Jenkins, & Wright, 1978; Gallagher, Flanigin, King, & Littleton, 1987; Herman, Prewitt, & Cullinan, 1996). It is well established that stress-related cortisol secretion is the downstream result of a cascade of physiological changes triggered by activation of neurons in the neuroendocrine centers of the hypothalamus (for a review, see Herman & Cullinan, 1997). It is not as clear how these neurons in the hypothalamus are activated, although evidence suggests a key role for the amygdala both functionally (Feldman & Conforti, 1981; Frankel et al., 1978; Gallagher et al., 1987; Herman et al., 1996) and anatomically (Floyd, Price, Ferry, Keay, & Bandler, 2001; Rempel-Clower & Barbas, 1998). According to these findings, if people with high psychosocial resources are less sensitive to potential threats, they may show lower amygdala reactivity in response to threat-related

stimuli that may, in turn, translate into muted physiological stress responses. In Study 2, we used fMRI to examine this possibility.

Neural structures involved in regulating or inhibiting responses to threat-related information likely play a role in stress responses as well. Regions of PFC have been shown to be involved in the regulation of threat responses. For example, fMRI studies in which participants were instructed to decrease their negative affect or reinterpret negative emotionally evocative stimuli in a less negative way have found increased activity in bilateral ventral and dorsal lateral PFC (Levesque et al., 2003; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner et al., 2004; Phan et al., 2005; for a review, see Ochsner & Gross, 2005). Other studies have examined the neural correlates of spontaneous regulation (i.e., without explicit instruction) of threat responses. Using a social exclusion paradigm, Eisenberger and colleagues found that greater right ventral PFC activity in response to social rejection was negatively correlated with self-reported distress (Eisenberger, Lieberman, & Williams, 2003). It is important that in most of these studies, the regulation strategies that led to increased PFC activity were also associated with decreased activity in the amygdala (Ochsner et al., 2002, 2004; Phan et al., 2005), supporting the PFC's role in the down-regulation of threat responses. Interestingly, right ventral lateral PFC (RVLPFC) has also been implicated in the down-regulation of amygdala activity in response to the verbal labeling of affective stimuli (Hariri, Bookheimer, & Mazziotta, 2000; Lieberman et al., 2007; Lieberman, Hariri, Jarcho, Eisenberger, & Bookheimer, 2005), demonstrating that RVLPFC activity can also inhibit amygdala activity in the absence of any conscious intention to regulate this threat response. According to these findings, if people with greater psychosocial resources are better able to manage their responses to threatening stimuli, this may be reflected in greater activity of prefrontal regions that down-regulate threat-related processing of the amygdala, thereby resulting in attenuated physiological stress responses. We examined this possibility as well in Study 2.

To summarize, in Study 1, we tested whether high levels of psychosocial resources would be associated with low cortisol responses to laboratory stress tasks. In Study 2, we explored potential mechanisms that may underlie this relationship. Individuals with greater psychosocial resources may have lower biological stress responses as a result of lower reactivity of threat detection structures, higher reactivity of regulatory structures (associated with deactivations of threat-detecting structures), or both. Thus, in Study 2, we used fMRI to examine the relationship between psychosocial resources and the reactivity of neural regions involved in evaluating potential threats and regulating threat responses, namely, amygdala and PFC, respectively. Finally, to more directly link these findings to biological stress responses, we conducted mediation analyses to examine how they related to cortisol responses obtained in Study 1.

Study 1

Method

Participants

Members of the University of California, Los Angeles (UCLA) campus community responded to an ad offering $60 in return for participating in the study. Prospective participants with the following conditions were excluded: mental or physical health problems, use of medications affecting cardiovascular or endocrine function, current treatment from a mental health professional, diagnosis of posttraumatic stress disorder, and current use of mental health-related medications (e.g., Prozac). In addition, because the study required neuroendocrine measures, pregnant and lactating women were excluded.

One hundred twenty participants (51 males and 69 females) comprised the final sample. All were affiliated with UCLA as students, employees, or both. Participants ranged in age from 18 to 36 years, with a mean age of 21.2. The sample was 3.3% African American, 36.7% Asian American, 35.0% European American, 10.8% Latino, 7.5% Middle Eastern, and 6.7% "mixed" or other, a pattern that reflects the composition of the UCLA community.

Questionnaire Session

Participants reported to a computer laboratory and completed informed consent forms and self-report measures of psychosocial resources. Psychosocial resource measures included the LOT-R (Scheier et al., 1994), a measure of dispositional optimism; the Rosenberg Self-Esteem Scale (Rosenberg, 1965); the Pearlin Mastery Scale (Pearlin & Schooler, 1978); the Extraversion subscale of the Eysenck Personality Inventory (Eysenck & Eysenck, 1975); the Psychological Health subscales of Personal Growth, Autonomy, and Purpose in Life (Ryff, 1989; Ryff & Singer, 1996); and the How I See Myself Questionnaire (HSM; Taylor & Gollwitzer, 1995), a measure of self-perception in which participants rate themselves in comparison to peers as to how much each of 42 positive and negative characteristics describe them. Several questionnaires that addressed other research issues were also included but were not part of the present study.

Psychosocial Resources Composite

To develop a psychosocial resources composite variable, scores from the above-mentioned eight scales were entered into a principal components analysis in SPSS (SPSS 11.0, Version 11.0.4) set up to extract components with eigenvalues over 1. A single component, defined as the "psychosocial resources" component, met our criterion and was extracted, accounting for 49.39% of the variance. The individual component scores resulting from this analysis were used as psychosocial resources scores for each participant. (Cronbach's α for this psychosocial resources variable is .84.) Table 1 lists scale loadings on the psychosocial resources component, and Table 2 shows the intercorrelations of the multiple measures of psychosocial resources. There was no difference in psychosocial resources composite scores between males and females, $t(118) = 0.92$, *ns*.

Stress Challenge Tasks and Procedures

Within a week of the questionnaire session, participants reported to the laboratory for the second part of the study. Sessions were scheduled in the mid to late afternoon to control for diurnal variation in cortisol (Van Cauter, Leproult, & Kupfer, 1996). The session began with the collection of a saliva sample for cortisol analysis. Participants rolled a sterile cotton swab in their mouths for 1 min and 45 s and placed the swab in a Salivette salivary

Table 1
Factor Loadings of Personality Measures on Psychosocial Resources

Measure	Psychosocial resources factor
Self-Esteem (RSES)	.807
How I See Myself (HSM)	.755
Autonomy (PH-A)	.725
Mastery (PMS)	.699
Purpose in Life (PH-PL)	.694
Extraversion (EXT)	.673
Personal Growth (PH-PG)	.647
Optimism (LOT-R)	.602

Note. RSES = Rosenberg Self-Esteem Scale; HSM = How I See Myself Questionnaire; PH-A = Psychological Health subscale of Autonomy; PMS = Pearlin Mastery Scale; PH-PL = Psychological Health subscale of Purpose in Life; EXT = Extraversion subscale of the Eysenck Personality Inventory; PH-PG = Psychological Health subscale of Personal Growth; LOT-R = Life Orientation Test–Revised.

collection tube (Sarstedt, Inc., North Carolina). Saliva samples were immediately placed on ice and transferred within the next few minutes to a freezer. Participants then responded to a set of interview questions about their home life, friendships, romantic relationships, work, and hobbies, material that is not part of the present analyses. Participants then provided a second saliva sample. Because salivary cortisol is an index of HPA activity 20–40 min prior to sampling, "baseline cortisol" was calculated for each participant as the minimum of the two resting salivary cortisol measures; this controls for the fact that some participants' first sample was elevated due to their activities before arriving at the experimental session and others' second sample may have been elevated due to the interview. Participants were next escorted into the laboratory for the stress challenge portion of the study.

Setting and apparatus. Participants sat at a table adjacent to cardiovascular recording equipment and directly in front of a video camera. A Critikon Dinamap Vital Signs Monitor Model 1846SX (Critikon, Inc., Tampa, FL) automatically and continuously recorded heart rate and blood pressure every 2 min throughout the laboratory session. The physiological readings were not visible to the experimenter until printed out by the Dinamap printer.

Rest and stress-challenge tasks. The laboratory session began with participants resting for 10 min and getting used to the autonomic blood pressure cuff. Each participant then participated in the TSST, a widely used laboratory stress challenge known to elicit autonomic and HPA axis stress responses (Kirschbaum et al., 1993). Participants were first asked to prepare and deliver a speech to an audience on why they would be a good administrative assistant, a popular campus job for students and employees. The speech was delivered to an unresponsive evaluative panel of two individuals who behaved as if they found the participant's speech to be lacking in quality. Participants then completed difficult mental arithmetic tasks, specifically, counting backwards by 7s and by 13s from 2,935 out loud, during which time they were urged by an apparently exasperated experimenter to try to go faster. Approximately 25 min after the commencement of the TSST, participants provided a third saliva sample (peak measure). This time lag falls within the recommended window for observing stress-related increases in cortisol (Dickerson & Kemeny, 2004; Kirschbaum et al., 1993). A 30-min recovery period then ensued, during which time participants provided self-reports of emotions experienced during the TSST and completed questionnaires assessing demographic characteristics. At the end of the recovery period, a fourth sample of saliva was taken (recovery measure); this time lag is typically associated with significant declines in cortisol levels from peak stress, although not always full return to baseline (Dickerson & Kemeny, 2004). Each participant was then debriefed and dismissed.

Salivary Cortisol Assay Procedures

Saliva samples were shipped for overnight delivery on dry ice to the Behavioral Endocrinology Laboratory at Pennsylvania State University where the cortisol assays were conducted. Salivary cortisol levels were determined from a 25-μl sample, which was assayed in duplicate by radioimmunoassay using the HS-cortisol High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit (Salimetrics LLC, State College, PA). The HS-cortisol assay allows for robust results when the saliva samples have a pH within the range of 3.5–9.0. All samples were within this pH range.

Results

As a manipulation check, we examined whether the TSST was effective as a cortisol-increasing stressor by completing a

Table 2
Intercorrelations Among Psychosocial Resources Measures

Measure	RSES	HSM	PH-A	PMS	PH-PL	EXT	PH-PG	LOT-R
RSES	—							
HSM	.534**	—						
PH-A	.523**	.464**	—					
PMS	.482**	.384**	.417**	—				
PH-PL	.441**	.399**	.321**	.388**	—			
EXT	.490**	.526**	.440**	.311**	.310**	—		
PH-PG	.387**	.344**	.380**	.307**	.481**	.233*	—	
LOT-R	.408**	.284**	.327**	.360**	.362**	.213*	.234**	—

Note. RSES = Rosenberg Self-Esteem Scale; HSM = How I See Myself Questionnaire; PH-A = Psychological Health subscale of Autonomy; PMS = Pearlin Mastery Scale; PH-PL = Psychological Health subscale of Purpose in Life; EXT = Extraversion subscale of the Eysenck Personality Inventory; PH-PG = Psychological Health subscale of Personal Growth; LOT-R = Life Orientation Test–Revised.
*$p < .05$. **$p < .01$

repeated-measures ANOVA, with one within-subjects factor of three levels (baseline, peak, and recovery cortisol). This test was significant, $F(2, 238) = 55.263$, $p = .000$, indicating a significant difference among baseline ($M = 0.162$, $SD = 0.089$), peak ($M = 0.347$, $SD = 0.247$), and recovery ($M = 0.215$, $SD = 0.154$) cortisol measures. Planned two-way comparisons revealed significant differences between baseline and peak cortisol, $F(1, 119) = 67.041$, $p = .000$, and between peak and recovery, $F(1, 119) = 65.610$, $p = .000$. Thus, the TSST was an effective stressor. Additionally, the magnitude of the observed cortisol responses is consistent with that found in other laboratories using the TSST (de Wit, Soderpalm, Nikolayev, & Young, 2003; Schommer, Hellhammer, & Kirschbaum, 2003; Takahashi et al., 2004).[1]

Cortisol reactivity was calculated as peak cortisol minus baseline cortisol. For statistical analyses, the cortisol reactivity measures were log-transformed to correct for nonnormality. (Prior to the transformation, a constant of two was added to each measure to eliminate negative reactivity measures.) Preliminary analyses revealed a significant gender difference, such that men had greater cortisol reactivity than females, $t(118) = 3.73$, $p < .001$. Accordingly, gender was entered as a covariate in all cortisol analyses (unless otherwise indicated).

We had predicted that psychosocial resources would be associated with lower cortisol reactivity to stress. As predicted and shown in Figure 1, psychosocial resources significantly predicted cortisol reactivity (pr = −.22, β = −.21, $p = .014$), such that individuals with more psychosocial resources had smaller cortisol increases following the TSST.[2] Psychosocial resources did not predict cortisol levels at baseline or recovery.[3,4]

Discussion

Consistent with predictions, higher levels of psychosocial resources were associated with lower cortisol reactivity in response to the stress tasks. As such, the results are similar to findings from previous research that has documented beneficial effects of psychosocial resources on biological stress responses (e.g., Taylor, Kemeny, Reed, Bower, & Gruenewald, 2000; Taylor et al., 2003b). In Study 2, we examined possible mechanisms underlying the relationship between psychosocial resources and cortisol stress responses by investigating how psychosocial resources moderate the reactivity of neural structures involved in processing potential threats and regulating threat responses.

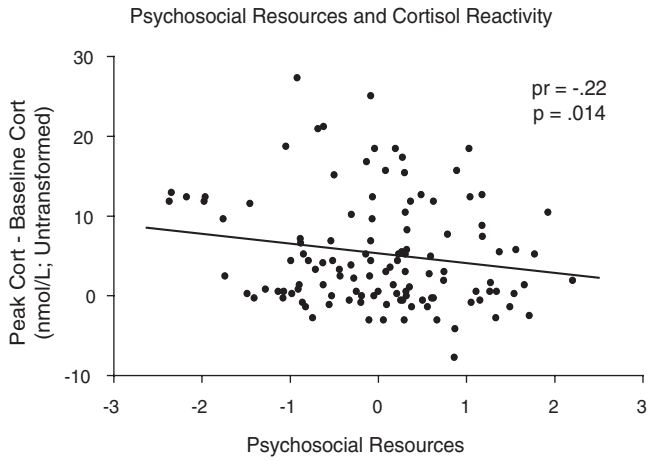

Figure 1. Scatterplot of psychosocial resources and cortisol reactivity. For presentation purposes, raw cortisol difference scores (peak–baseline) are shown here. Log-transformed cortisol difference scores were used in analyses regressing cortisol reactivity on psychosocial resources (with gender entered as a covariate; pr = −.224, β = −.213, $p = .014$). Cort = cortisol.

Study 2

The purpose of the second study was to examine potential neural mechanisms that may link psychosocial resources to reduced cortisol stress responses. Although it would have been ideal to have assessed neural activity during the TSST, it is currently not possible to complete the full TSST paradigm in the fMRI scanner (although studies have investigated the math task alone with no evaluative panel; Dedovic et al., 2005; Wang et al., 2005). Accordingly, we chose to use an approach described by Eisenberger,

[1] As shown in Figure 1, there do appear to be several data points near zero or slightly negative, suggesting that certain participants did not exhibit a cortisol increase following the TSST. In fact, approximately one quarter of participants were "nonresponders." This result is also consistent with results from other laboratories using the TSST (de Wit et al., 2003; Schommer et al., 2003; Takahashi et al., 2004).

[2] Because of the possibility that some specific contributor makes a greater contribution to the effect than others, we completed additional analyses regressing cortisol reactivity on each of the psychosocial resources measures separately, controlling for gender. In these analyses, cortisol reactivity was significantly predicted by the How I See Myself Questionnaire (HSM; pr = −.33, $p < .001$), the Extraversion subscale of the Eysenck Personality Inventory (EXT; pr = −.27, $p < .003$), and the Psychological Health subscale of Purpose in Life (PH-PL; pr = −.24, $p < .008$), marginally predicted by the Rosenberg Self-Esteem Scale (pr = −.17, $p = .072$) and the Psychological Health subscale of Personal Growth (pr = −.16, $p = .091$), and not predicted by the Life Orientation Test–Revised (LOT-R; pr = .04, *ns*), the Pearlin Mastery Scale (pr = −.06, *ns*), or the Psychological Health subscale of Autonomy (PH-A; pr = −.03, *ns*).

[3] We also examined whether psychosocial resources would be related to lower cardiovascular responses to the stress tasks. Psychosocial resources were marginally negatively correlated with systolic blood pressure (SBP) math reactivity (i.e., SBP during the math task minus baseline SBP; $r = −.18$, $p = .056$), such that people with more psychosocial resources had a smaller increase in SBP during the math task, relative to baseline. Psychosocial resources were not significantly correlated with reactivity scores for speech SBP ($r = −.01$, *ns*), math diastolic blood pressure (DBP; $r = −.002$, *ns*), speech DBP ($r = .01$, *ns*), math heart rate (HR; $r = −.05$, *ns*), Speech HR ($r = −.01$, *ns*), or with baseline or recovery measures of HR, SBP, or DBP. There were no significant gender differences in reactivity scores for SBP, DBP, or HR, but gender did significantly predict baseline and recovery SBP, so gender was entered as a covariate in these analyses.

[4] Consistent with the idea that greater psychosocial resources are associated with less negative appraisals of threat, psychosocial resources were also inversely correlated with self-reports of several negative emotions experienced during the TSST (reported by participants immediately following the TSST), including anger ($r = −.23$, $p = .011$), fear ($r = −.22$, $p = .015$), anxiety ($r = −.34$, $p < .001$), sadness ($r = −.30$, $p = .001$), and frustration ($r = −.26$, $p = .005$). Psychosocial resources were also marginally negatively correlated with disgust ($r = −.17$, $p = .061$) but were not related to happiness ($r = .12$, *ns*) or interest ($r = .01$, *ns*).

Lieberman, and Satpute (2005), in which an fMRI task that directly taps into the computations of a specific neural structure is used to generate an index of individual dispositional reactivity of that structure. Thus, in a separate session, a subset of participants from Study 1 completed threat detection and regulation tasks while being scanned, providing indices for each participant of the activity of neural structures involved in detecting threat-related information (i.e., amygdala) and regulating these threat responses (i.e., PFC).

Several studies have found that the amygdala is activated in response to negative or threatening facial expressions (Fitzgerald et al., 2006; Morris et al., 1996; Phillips et al., 1997; Whalen et al., 1998, 2001). Furthermore, many studies have shown that the magnitude of amygdala responses to threatening facial expressions is moderated by individual difference factors reflecting threat-sensitivity such as social phobia and anxiety symptoms (Phan, Fitzgerald, Nathan, & Tancer, 2006), neuroticism and trait anxiety (Etkin et al., 2004; Stein, Simmons, Feinstein, & Paulus, 2007), and serotonergic genotype (i.e., polymorphisms in the serotonin transporter gene, 5-HTTLPR; Hariri et al., 2002, 2005; Heinz et al., 2005). Amygdala responses to threatening facial expressions have also been shown to be stable across time (Johnstone et al., 2005). As such, amygdala reactivity to threatening facial expressions may reflect dispositional responses to threat or other social emotionally evocative stimuli. Thus, we scanned participants while they viewed negative emotional facial expressions to generate an index of amygdala reactivity to social threat-related information.

There are several ways to regulate threat responses. For example, distraction can be used to focus attention away from the source of the threat, reappraisal may be used to change the meaning of the threat, and suppression may be used to hide any outward emotional response to the threat (Gross, 1998). Recent work has shown that linguistic processing can also dampen threat responses (i.e., amygdala activity) to emotional stimuli. Specifically, verbally labeling emotionally evocative facial expressions has been shown to result in increased RVLPFC activity and decreased amygdala activity (Hariri et al., 2000; Lieberman et al., 2007, 2005). In addition to its relation to psychotherapy, which is based on the idea that talking through one's feelings is beneficial, linguistic processing of emotions (i.e., writing about one's emotions) has been shown to be associated with positive mental and physical health outcomes (e.g., Hemenover, 2003; Pennebaker, 1997). Linguistic processing may also be a component of other threat regulation strategies, such as reappraisal. For example, in reappraising threatening information, one may reflect on how the information has made them feel by attaching a label (e.g., "I am scared, but there is really nothing to worry about"). Therefore, to generate an index of neural activity during the regulation of threat responses, we scanned participants while they verbally labeled the emotion depicted in several threatening facial expressions. Because verbally labeling affective stimuli has previously been shown to involve RVLPFC activation and amygdala deactivation (Hariri et al., 2000; Lieberman et al., 2007, 2005), we focused our analyses on these regions.

Results of the main effects of the threat reactivity and regulation tasks completed by the participants in the present study have previously been published elsewhere (Lieberman et al., 2007). As detailed in Lieberman et al. and referenced above, participants exhibited significant amygdala activation during the threat reactivity task and significant RVLPFC activation and amygdala deactivation during the threat regulation task, suggesting that the threat processing tasks are evoking the expected neural responses. In the present article, we re-examined these data with regression analyses to investigate potential moderation by psychosocial resources and/or cortisol reactivity.

Thus, in Study 2, we examined two potential mechanisms by which psychosocial resources may be related to reduced biological stress responses. First, we examined the hypothesis that psychosocial resources are associated with reduced threat reactivity (i.e., less amygdala activity) in response to threat-related information, and second, we examined the hypothesis that psychosocial resources are associated with enhanced down-regulation of these threat responses by RVLPFC during the processing of threat-related information (i.e., greater RVLPFC activation and amygdala deactivation). To further link psychosocial resources to cortisol stress responses, we subsequently examined how this threat-related neural reactivity related to participants' cortisol reactivity scores obtained during Study 1.

Method

To investigate potential neural underpinnings of the relationship between psychosocial resources and biological responses to stress, we scanned a subset of the Study 1 sample in the fMRI scanner at the Ahmanson-Lovelace Brainmapping Center at UCLA. Participants from Study 1 responded to an e-mail requesting participation in an additional study and were further screened for risk factors that contraindicated participating in an fMRI protocol: tendency to be claustrophobic and metal in the body other than dental fillings. The final sample consisted of 28 healthy right-handed individuals ages 18–36 years (11 men, 17 women).[5] Participants in the fMRI subsample did not significantly differ from non-fMRI participants in psychosocial resources, $t(118) = -0.56$, *ns*, or cortisol reactivity, $t(118) = 1.7$, *ns*. In the fMRI subsample, the inverse relationship between psychosocial resources and cortisol reactivity remained, although the significance level dropped slightly (pr $= -.38$, $\beta = -.33$, $p = .054$) due to the smaller sample size.

Laboratory Paradigm

Participants completed several threat-related tasks within the fMRI scanner in a within-subjects blocked design. In the "affect match" task, participants viewed emotionally expressive facial expressions and were asked to match the emotion in the target face to one of two additional emotional facial expressions presented at the bottom of the screen. In the "shape match" task, participants viewed geometric shapes and were asked to choose the shape that matched the target shape from two choices presented at the bottom of the screen. The shape matching task is a comparison task that controls for some of the processing demands of the affect match task, yet lacks any emotional or threat-related content. The use of this condition as a "baseline" minimizes the spontaneous cognitions that can occur during extended periods of blank fixation (Gusnard & Raichle, 2001). In the "affect label" and "gender

[5] Behavioral data (i.e., response times to the different tasks) are missing for 3 of the final 28 participants due to procedural errors.

label" tasks, participants viewed emotionally expressive facial expressions and were asked to choose either the appropriate label for each emotion from two choices presented at the bottom of the screen (i.e., "anger" or "fear") or the gender-appropriate name from two choices presented at the bottom of the screen (i.e., "Sally" vs. "Henry"). The gender-labeling task is a comparison condition that controls for the general processing demands required for the affect labeling task and differs solely in the affective nature of the linguistic processing.

Participants completed a total of two functional runs, each containing six blocks: one block each of the affect match, shape match, affect label, and gender label tasks, plus two other tasks not analyzed for this article, "gender match" and "observe only." Each block consisted of 10 randomized trials of one task type (e.g., 10 affect match trials). Each trial lasted 5 s, resulting in blocks that were 50 s in length. Each block was preceded by a 10-s fixation crosshair and a 3-s instruction cue indicating the task type for that block (i.e., affect match, shape match, affect label, gender label, gender match, or observe only). The order of the blocks was counterbalanced across participants. Participants responded via a button box and were told to respond as quickly as possible. The stimuli remained on the screen for the entire 5-s trial.

Eighty percent of the facial expressions depicted a negative emotion (i.e., fear or anger), and 20% depicted a positive or neutral emotion (i.e., happiness or surprise). The positive and neutral expressions were included to prevent the stimuli from becoming too predictable. Because the blocked design averaged the activity across all trials (negative and positive) within each block, the significantly greater number of negative faces biases the neural activity to reflect responses to negative expressions. Half of the faces were male and half were female. The gendered names were matched to the affect labels in total number of unique names/labels, number of letters per name/label, and first letter of name/label.

Image Acquisition

Data were acquired on a Siemens Allegra 3T scanner (Siemens, Iselin, NJ). Head movements were restrained with foam padding and surgical tape placed across participants' foreheads. High-resolution structural T2-weighted echo-planar images (spin-echo; TR = 5,000 ms; TE = 33 ms; matrix size 128 × 128; 36 axial slices; FOV = 20 cm; 3-mm thick, skip 1 mm) were acquired coplanar with the functional scans. Two functional scans were acquired (echo planar $T2^*$-weighted gradient-echo, TR = 3,000 ms, TE = 25 ms, flip angle = 90°, matrix size 64 × 64, 36 axial slices, FOV = 20 cm; 3-mm thick, skip 1 mm), each scan lasting 6 min and 18 s. Participants viewed the stimuli through goggles connected to a Macintosh G4 computer.

fMRI Analyses

The imaging data were analyzed using SPM'99 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, England). Images for each subject were realigned to correct for head motion, normalized into a standard stereotactic space, and smoothed with an 8-mm Gaussian kernel, full width at half maximum, to increase signal-to-noise ratio. The design was modeled using a boxcar function convolved with a canonical hemodynamic response function. Data from the two blocks for each task (e.g., affect match from the first and second functional runs) were combined to represent each condition. Linear contrasts were employed to assess neural activity during the affect match condition compared with the shape match condition and the affect label condition compared with the gender label condition. The affect match–shape match contrast was designed to provide a measure of threat reactivity as indexed by amygdala activation, and the affect label–gender label contrast was designed to provide a measure of threat regulation as indexed by RVLPFC activation and amygdala deactivation.

As mentioned above, results of random-effects group analyses comparing the main effects of affect match versus shape match (i.e., threat reactivity) and affect label versus gender label (i.e., threat regulation) in this dataset have previously been published elsewhere (Lieberman et al., 2007). As detailed in Lieberman et al., significant amygdala activation was found during affect matching compared with shape matching, and significant RVLPFC activation and amygdala deactivation were found during affect labeling compared with gender labeling. Accordingly, in the present manuscript, we re-examined these data to investigate potential moderation by psychosocial resources and/or cortisol reactivity, using the above findings from the main effects analyses to define our neural regions of interest (ROI).[6]

To assess the relationship between psychosocial resources and neural activity, we first completed whole-brain random-effects regression analyses with the psychosocial resources composite scores entered as a regressor for neural activity for the affect match–shape match and affect label–gender label contrasts. We then examined activity in the ROIs described above (i.e., amygdala during affect matching vs. shape matching and RVLPFC and amygdala during affect labeling vs. gender labeling; Lieberman et al., 2007). A small volume correction (SVC) of 5-mm radius was used with an uncorrected p value of .05 combined with a cluster size threshold of 10 voxels.

We used a similar procedure to assess the relationship between cortisol reactivity and neural activity. We completed whole-brain random-effects regression analyses with cortisol reactivity scores (with the effects of gender partitioned out) entered as a regressor for neural activity during the contrasts of interest and then examined activity in the amygdala and RVLPFC ROIs described above (Lieberman et al., 2007). A SVC of 5-mm radius was used with an uncorrected p value of .05 combined with a cluster size threshold of 10 voxels.

For the fMRI regression analyses, in addition to any significant activity in our primary ROIs (i.e., amygdala and RVLPFC) observed in the SVC analyses, we also report all limbic and prefrontal activations from the whole-brain analyses that survived an uncorrected p value of .005 with a 10 voxel extent threshold (Forman et al., 1995). All coordinates are reported in Montreal Neurological Institute (MNI) format.

To examine the neural regions that may link psychosocial resources to cortisol reactivity, we used two procedures (Eisenberger, Taylor, Gable, Hilmert, & Lieberman, 2007). First, we extracted the parameter estimates for regions significantly corre-

[6] The sample size reported here (N = 28) is smaller than reported in Lieberman et al. (2007; N = 30) because cortisol samples were not obtained from two of those participants.

lated with psychosocial resources as observed in the regression analyses described above and then examined whether these parameter estimates correlated with cortisol reactivity, controlling for gender, at a standard statistical threshold ($p < .05$). Second, we used the reverse procedure. We extracted the parameter estimates for regions significantly correlated with cortisol reactivity as observed in the regression analyses described above and then examined whether these parameter estimates correlated with psychosocial resources at a standard statistical threshold ($p < .05$). Using these two procedures, we thus examined whether any of the regions that were significantly correlated with psychosocial resources were also significantly correlated with cortisol reactivity. Regions that were significantly correlated with both psychosocial resources and cortisol reactivity using either approach were then tested as potential mediators of the relationship between psychosocial resources and cortisol reactivity using the Distribution of Products method (MacKinnon, Lockwood, & Hoffman, 1998; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002).

Results

Behavioral Data

Regression analyses indicated that psychosocial resources did not predict response times for the affect match task ($\beta = -.10$, *ns*), the shape match task ($\beta = -.17$, *ns*), the affect label task ($\beta = -.10$, *ns*), or the gender label task ($\beta = -.16$, *ns*). Because the fMRI data analyses examine neural activity in response to one task compared with another, we also used regression analyses to examine whether psychosocial resources predicted response time difference scores for the contrasts of interest (e.g., response time for affect match minus response time for shape match). Psychosocial resources did not predict response time difference scores for affect match–shape match ($\beta = .02$, *ns*) or affect label–gender label ($\beta = .05$, *ns*). These results significantly discount the possibility that the observed differences in neural activity between individuals high and low in psychosocial resources presented below were due to differences in behavioral responses to the tasks.

Tests of the Hypotheses—Do Psychosocial Resources Moderate Threat Reactivity?

To examine how psychosocial resources may moderate threat reactivity, we examined whether psychosocial resources predicted amygdala activity during the affect match condition compared with the shape match condition. Using an ROI small volume correction (5-mm radius, $p < .05$) on amygdala coordinates previously found to be significantly more active in the affect match condition relative to the shape match condition (MNI coordinates: $-22, -8, -20$; Lieberman et al., 2007), we did not find a significant relationship between amygdala activity and psychosocial resources. The whole-brain analysis also did not yield significant amygdala activity ($p < .005$). Table 3 lists other limbic and prefrontal regions whose activity was correlated with psychosocial resources during affect matching compared with shape matching ($p < .005$). Because psychosocial resources did not moderate threat reactivity (i.e., amygdala reactivity) during affect matching relative to shape matching, we did not complete any mediation analyses linking activity during this task to cortisol reactivity.[7]

Table 3
Regions Correlating With Psychosocial Resources During Affect Matching Compared With Shape Matching

Region	Cluster size (mm^3)	x	y	z	r	t
Positive correlations with PR						
ACC (BA 24/32)	152	−10	40	12	.53	3.16
Left PFC (BA 10)	96	−24	62	16	.53	3.21
Negative correlations with PR						
No significant activity						

Note. $p < .005$ with cluster-size threshold of 10 voxels. PR = psychosocial resources; ACC = anterior cingulate cortex; BA = Brodmann area; PFC = prefrontal cortex.

Tests of the Hypotheses—Do Psychosocial Resources Moderate Threat Regulation?

Next, we examined whether psychosocial resources moderated threat regulation by examining whether psychosocial resources predicted RVLPFC activation and amygdala deactivation to the affect label task compared with the gender label task. As shown in Table 4 and Figure 2, using an ROI small volume correction (5-mm radius) on coordinates previously found to be significantly more active in the affect label condition relative to the gender label condition (RVLPFC, Brodmann's area [BA] 47; 54, 24, −10; Lieberman et al., 2007), we found that psychosocial resources were significantly positively correlated with activity in RVLPFC (BA 47; 52, 26, −12, $r = .43$), $t(27) = 2.42$, $p < .05$.

As shown in Table 4 and Figure 3, an ROI small volume correction (5-mm radius) on coordinates previously found to be significantly less active in the affect label condition relative to the gender label condition (left amygdala: −24, 0, −24; Lieberman et al., 2007) revealed that psychosocial resources were significantly negatively correlated with a large cluster of activity in left amygdala during the affect label condition relative to the gender label condition ($-26, -2, -20$, $r = -.55$), $t(27) = 3.32$, $p < .005$. Additional foci of activity within this cluster (that were also significantly negatively correlated with psychosocial resources) include ($-28, -8, -16$, $r = -.59$), $t(27) = 3.72$, $p < .005$, and ($-26, 0, -18$, $r = -.56$), $t(27) = 3.48$, $p < .005$. Thus, to the extent that participants had greater psychosocial resources, they also exhibited greater activity in RVLPFC and less activity in left amygdala (i.e., greater amygdala deactivation) during the affect label condition relative to the gender label condition. As shown in Table 4, psychosocial resources were also negatively correlated with activity in other limbic regions during the affect label condition relative to the gender label condition, including anterior cingulate cortex and the parahippocampal gyrus ($p < .005$).

[7] In additional fMRI analyses with cortisol reactivity scores entered as a regressor for activity during the affect matching–shape matching contrast, cortisol reactivity was not significantly correlated with amygdala reactivity using either an ROI analysis based on previously published main effects (Lieberman et al., 2007; $p < .05$, 10 voxels) or a whole-brain analysis ($p < .005$, 10 voxels).

Table 4
Regions Correlating With Psychosocial Resources During Affect Labeling Compared With Gender Labeling

Region	Cluster size (mm^3)	x	y	z	r	t
Positive correlations with PR						
RVLPFC (BA 47)	400	52	26	−12	.43	2.42†
Negative correlations with PR						
Left amygdala	2904	−26	−2	−20	−.55	3.32
		−28	−8	−16	−.59	3.72*
		−26	0	−18	−.56	3.48
Subgenual ACC (BA 25)	560	2	24	−10	−.58	3.66
ACC (BA 24)	104	−10	14	28	−.54	3.25
Parahippocampal gyrus	1112	36	−34	−2	−.53	3.21
		30	−30	0	−.56	3.43

Note. $p < .005$ with cluster-size threshold of 10 voxels except †small volume correction of 5-mm radius at $p < .05$. PR = psychosocial resources; RVLPFC = right ventral lateral prefrontal cortex; ACC = anterior cingulate cortex; BA = Brodmann area. *Indicates activations also positively correlated with cortisol reactivity at $p < .05$.

Tests of the Hypotheses—Does Cortisol Reactivity Moderate Threat Regulation?

To examine the relationship between cortisol reactivity and threat regulation, we examined whether cortisol reactivity (with gender effects partitioned out) also predicted RVLPFC activation and amygdala deactivation to the affect label task compared with the gender label task. Somewhat unexpectedly, an ROI small volume correction (5-mm radius) on RVLPFC coordinates previously found to be more active in the affect label condition relative to the gender label condition (BA 47; 48, 46, −6; Lieberman et al., 2007) revealed that cortisol reactivity was significantly positively correlated with activity in RVLPFC (BA 47/10; 44, 44, −4, r = .47), $t(27) = 2.73$, $p < .05$. As shown in Table 5, the whole-brain analysis revealed additional clusters of activity that were positively correlated with cortisol reactivity in RVLPFC (BA 47), left ventral lateral prefrontal cortex (LVLPFC; BA 10/11), dorsal medial prefrontal cortex (DMPFC; BA 9), dorsal lateral prefrontal cortex (DLPFC; BA 9), and lateral prefrontal cortex (LPFC; BA 10) at $p < .005$.

An ROI small volume correction (5-mm radius) on amygdala coordinates previously found to be less active in the affect label condition relative to the gender label condition (−24, 0, −24; Lieberman et al., 2007) did not reveal any activity that was significantly correlated with cortisol reactivity ($p < .05$). However, the whole brain analysis revealed that activity in a nearby region of the left amygdala was significantly positively correlated with cortisol reactivity (−26, −6, −12), $t(27) = 3.08$, $p < .005$. It should be noted that this left amygdala region is very close to the left amygdala region whose activity was negatively correlated with psychosocial resources. Thus, to the extent that participants exhibited higher cortisol reactivity in response to the TSST, they also exhibited greater RVLPFC activation and greater amygdala activation (i.e., less amygdala deactivation) during affect labeling relative to gender labeling. There were no limbic or prefrontal regions negatively correlated with cortisol reactivity.

Tests of the Hypotheses—Does Neural Activity During Threat Regulation Link Psychosocial Resources to Cortisol Reactivity?

To examine which neural regions may mediate the relationship between psychosocial resources and cortisol reactivity, we completed two sets of analyses (for a discussion of this method, see Eisenberger et al., 2007). First, we extracted the parameter estimates for all regions that were significantly correlated with psychosocial resources during affect labeling relative to gender labeling (see Table 4) and then correlated them with cortisol reactivity, controlling for gender, at a standard statistical threshold ($p < .05$). Of all regions either positively or negatively correlated with psychosocial resources during affect labeling relative to gender labeling, only one of these regions, left amygdala, was also significantly

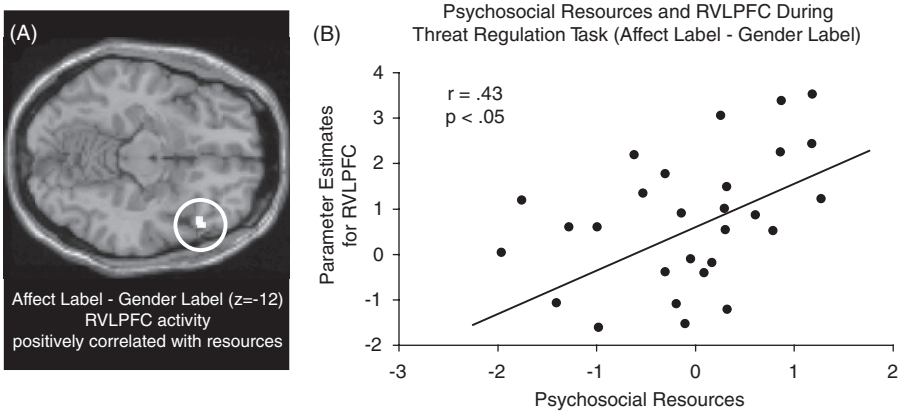

Figure 2. (A) Magnetic resonance image showing right ventral lateral prefrontal cortex (RVLPFC) activation (centered at 52, 26, −12) that was positively correlated with psychosocial resources during the affect label condition relative to the gender label condition (r = .43, $p < .05$, 10 voxel threshold) on an axial slice at z = −12, and (B) scatterplot of parameter estimates extracted from RVLPFC (52, 26, −12) from the affect label–gender label contrast and psychosocial resources.

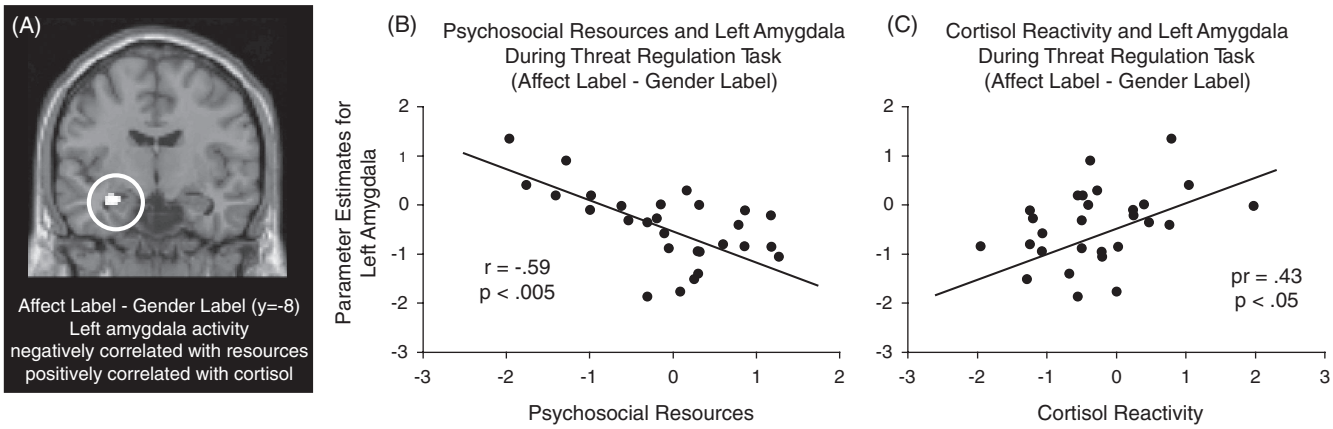

Figure 3. (A) Magnetic resonance image showing left amygdala activation (centered at −28, −8, −16) that was negatively correlated with psychosocial resources ($r = -.59$, $p < .005$, 10 voxel threshold) and positively correlated with cortisol reactivity (with gender effects partitioned out; pr = .43, $p < .05$, 10 voxel threshold) on a coronal slice at $y = -8$. Scatterplots show parameter estimates extracted from left amygdala (−28, −8, −16) plotted against (B) psychosocial resources and (C) cortisol reactivity (transformed, with gender effects partitioned out). Parameter estimates were extracted from the affect label versus gender label contrast.

correlated with cortisol reactivity (−28, −8, −16; $r = .386$, $p < .05$). Thus, psychosocial resources were associated with greater amygdala deactivation during threat regulation that was, in turn, associated with lower cortisol reactivity scores from Study 1.

Next, parameter estimates of all regions significantly correlated with cortisol reactivity (with gender effects partitioned out; see Table 5) were extracted from the contrast comparing affect labeling with gender labeling and correlated with psychosocial resources ($p < .05$). Of all regions in the affect labeling versus gender labeling contrast that significantly correlated with cortisol reactivity, only one of these regions, left amygdala, was also significantly correlated with psychosocial resources (−26, −6, −12, $r = -.40$, $p < .05$). Activity in DLPFC was marginally correlated with psychosocial resources (30, 52, 22, $r = -.364$, $p = .057$). Thus, when this reverse procedure was used, lower cortisol reactivity scores from Study 1 were associated with greater amygdala deactivation during threat regulation that was associated with greater psychosocial resources.

Table 5
Regions Correlating With Cortisol Reactivity Scores From Study 1 During Affect Labeling Compared With Gender Labeling

Region	Cluster size (mm^3)	*x*	y	z	r	*t*
Positive correlations with cortisol						
Left amygdala	208	−26	−6	−12	.52	3.08*
RVLPFC (BA 47/10)	144	42	42	0	.55	3.31
		44	44	−4	.47	2.73†
LVLPFC (BA 10/11)	184	−26	48	−8	.57	3.54
Anterior temporal /RVLPFC (BA 47)	448	34	20	−22	.56	3.48
		46	18	−18	.58	3.64
Anterior temporal/LVLPFC (BA 47)	88	−42	18	−28	.54	3.25
RLPFC (BA 10)	1032[a]	32	52	22	.58	3.61
		34	48	18	.52	3.08
RDLPFC (BA 9)	1032[a]	30	52	32	.58	3.64
LDLPFC (BA 9)	520[b]	−22	50	36	.54	3.30
DMPFC (BA 9)	520[b]	−10	46	34	.51	3.06
Negative correlations with cortisol						
No significant activity						

Note. $p < .005$ with cluster-size threshold of 10 voxels except †small volume correction of 5-mm radius at $p < .05$. *Indicates activations also negatively correlated with psychosocial resources at $p < .05$. BA = Brodmann area; RVLPFC = right ventral lateral prefrontal cortex; LVLPFC = left ventral lateral prefrontal cortex; RLPFC = right lateral prefrontal cortex; RDLPFC = right dorsolateral prefrontal cortex; LDLPFC = left dorsolateral prefrontal cortex; DMPFC = dorsal medial prefrontal cortex.
[a]Indicates a single cluster extends across RLPFC (BA 10) and RDLPFC (BA 9). [b]Indicates a single cluster extends across LDLPFC (BA 9) and DMPFC (BA 9).

Mediation Analyses

Both psychosocial resources and cortisol reactivity were significantly correlated with left amygdala activity during affect labeling relative to gender labeling, such that individuals with greater psychosocial resources exhibited less amygdala activity during the threat regulation task and a smaller cortisol increase in response to the laboratory stress task. We therefore examined amygdala activity during threat regulation as a potential mediator of the relationship between psychosocial resources and cortisol reactivity. Using the Distribution of Products method (MacKinnon et al., 1998, 2002), we found that amygdala activity significantly mediated the relationship between psychosocial resources and cortisol reactivity ($-28, -8, -16$, $Z_\alpha Z_\beta = 4.43$, $p < .05$; $-26, -6, -12$, $Z_\alpha Z_\beta = 5.42$, $p < .05$).

Discussion

We considered two possible neural mechanisms that might account for the beneficial effects of psychosocial resources on HPA axis responses to stress. The first is that resources may affect threat sensitivity directly, as reflected by reduced amygdala responses to threat. This explanation was not supported by the data. Psychosocial resources were not significantly correlated with amygdala reactivity in response to the affect match condition relative to the shape match condition. Thus, psychosocial resources may not ameliorate stress responses by making individuals more or less sensitive to potential threats.

A second possibility is that psychosocial resources enhance prefrontal inhibition of threat responses during threat regulation. Consistent with this hypothesis, we found that higher levels of psychosocial resources were associated with greater RVLPFC activation and amygdala deactivation in response to an affect labeling task. It is important that functional connectivity analyses completed for the entire sample (and published with the main effects for this dataset; Lieberman et al., 2007) indicate that activity in these two regions is negatively correlated.[8] These findings suggest that people with more psychosocial resources may have an enhanced ability to effectively inhibit negative threat responses relative to people with fewer psychosocial resources.

This possibility was supported by analyses relating cortisol reactivity directly to neural activity. Specifically, we found that the amygdala activity that was negatively correlated with psychosocial resources during the affect labeling task was also positively correlated with cortisol reactivity (as measured in Study 1). This suggests that enhanced down-regulation of amygdala activity (i.e., amygdala deactivation) during threat regulation may be the specific mechanism that links psychosocial resources to attenuated biological stress responses. In fact, amygdala activity during threat regulation was found to mediate the relationship between psychosocial resources and cortisol reactivity. These findings converge with conceptually related work by Urry et al. (2006), which found that intentional regulation of negative affect that was associated with amygdala deactivation predicted greater diurnal declines in cortisol.

We also found that cortisol reactivity was positively correlated with activity in a number of prefrontal regions, including RVLPFC. These results are not surprising because the self-regulatory efforts supported by the prefrontal cortex may be involved in both the activation and inhibition of the HPA axis (Gross & Levenson, 1993; Radley, Arias, & Sawchenko, 2006; for a review, see Sullivan & Gratton, 2002). The seemingly contradictory relationships of cortisol reactivity with psychosocial resources and RVLPFC can partially be explained by the fact that the RVLPFC regions positively correlated with cortisol reactivity are located in a different part of RVLPFC than the region that was positively correlated with psychosocial resources, with no overlap. The closest RVLPFC activation (that is clearly in PFC) that correlated with cortisol reactivity was approximately 21 mm from the region that correlated with psychosocial resources. Another region correlated with cortisol reactivity that cannot clearly be classified as either PFC or anterior temporal lobe was at least 11 mm from the region of RVLPFC correlated with resources. Despite these differences, it is not immediately clear why these two regions of RVLPFC would play different roles.

General Discussion

The results of these investigations revealed that psychosocial resources are inversely related to cortisol responses to stress. Additionally, we found that differences in RVLPFC and amygdala functioning during threat regulation may underlie these relationships. Analyses assessing mediation of the relation between psychosocial resources and cortisol reactivity to stress suggest that amygdala deactivation during threat regulation may mediate this link. Our findings run counter to a model that maintains that psychosocial resources achieve their beneficial effects on stress responses primarily via decreased threat sensitivity. Instead, these findings support a model of enhanced inhibition of threat responses during threat regulation.

This pattern may have adaptive significance for effective responses to stress. If psychosocial resources were to confer decreased threat sensitivity, people high in these resources might fail to respond to threat-relevant cues appropriately, leaving themselves vulnerable to adverse outcomes. To the extent that psychosocial resources instead confer enhanced regulatory abilities to dampen responses to threat cues, the advantage of threat detection would not be lost; rather, people with more psychosocial resources would be better able to effectively manage threat.

Previous studies have found RVLPFC activation and accompanying amygdala deactivation during the reappraisal of negative emotional stimuli (Ochsner et al., 2004; Phan et al., 2005). The enhanced RVLPFC reactivity exhibited by individuals high in psychosocial resources during affect labeling may extend to an enhanced ability to reappraise threatening stimuli in a less threatening way. This ability represents an invaluable tool for dealing with stressful situations. Indeed, the less threatening a situation is, the less stressful it is (Lazarus & Folkman, 1984). Furthermore, without the capacity to effectively down-regulate threat responses, a person could be overwhelmed by intense emotional reactions, such as fear, anxiety, or rumination (Nolen-Hoeksema, 2000). In contrast, the enhanced ability to down-regulate threat responses might provide a buffer against these negative outcomes.

[8] Unfortunately, current data analysis tools do not allow us to examine how functional connectivity between amygdala and PFC may vary as a function of psychosocial resources or cortisol reactivity.

The positive correlation between cortisol reactivity and RVLPFC during the threat regulation task may seem somewhat contradictory given that cortisol reactivity was negatively correlated with psychosocial resources, which was itself positively correlated with RVLPFC. Thus, although our results indicate that amygdala deactivation during threat regulation is a key component linking psychosocial resources and cortisol reactivity, the precise role of RVLPFC in this relationship is less clear. We did not find that RVLPFC mediated the relationship between psychosocial resources and cortisol reactivity. Psychosocial resources did predict RVLPFC activation, but RVLPFC activation did not, in turn, predict cortisol reactivity. One possible explanation is that the relationship between psychosocial resources and cortisol reactivity may depend more on the efficiency of the relationship between RVLPFC and amygdala rather than the level of RVLPFC activation per se. Unfortunately, our current data analysis tools did not allow us to examine how functional connectivity between amygdala and PFC may have varied as a function of psychosocial resources or cortisol reactivity. It may also be the case that the greater RVLPFC activity associated with psychosocial resources provides a buffer against stress by acting as a "backup" to RVLPFC-amygdala efficiency.

Limitations

One potential criticism of the present study is that the physiological and neural data were measured in different sessions using different tasks. Although neural activity in response to the fMRI tasks may provide an index for dispositional neural reactivity, these tasks are obviously different from real stressful or emotional situations. For example, viewing threatening facial expressions presented on a computer screen likely did not represent a personal threat or evoke a strong emotional response in participants, whereas making a speech to an audience of socially threatening individuals does both. Accordingly, there was not as great a need to spontaneously regulate one's responses during the fMRI tasks as there was during the laboratory stress task or as there would be in most other stressful situations. Furthermore, the fMRI tasks did not involve intentional threat regulation, whereas real-life stressful situations would be more likely to engage intentional regulation strategies. Thus, in future studies, the simultaneous collection of physiological and neural responses to a single, personally threatening stressor would provide useful converging evidence.

Nevertheless, the fact that we assessed physiological and neural activity using different tasks should not discount the findings presented here. First, several previous studies have shown that differences in neural reactivity, assessed using fMRI paradigms that share conceptual underpinnings with real-world experiences such as those we used, predict important, real-world individual differences such as anxiety and depression (Etkin et al., 2004; Phan et al., 2006; Stein et al., 2007). Second, many threat regulation processes are, in fact, unintentional. For example, participants shown a disturbing stimulus (e.g., a film showing a circumcision) that was merely framed in a less negative way (e.g., with a narration conveying a detached, analytical attitude), exhibited lower skin conductance responses compared with participants who were not given the less-threatening interpretation (Dandoy & Goldstein, 1990; Lazarus & Alfert, 1964; Lazarus & Opton, 1966). In this case, threat responses were down-regulated even though there was no clear indication that participants were intentionally or effortfully changing their reactions. Third, we would argue that our use of a more subtle threat, presented in a separate experimental session, actually made it more difficult to find any meaningful results. Thus, the paradigm we used provided a more stringent test of our hypotheses.

A second limitation is that the results are correlational. For example, although we presented the RVLPFC as a structure involved in dampening amygdala responses, it is possible that the relationship runs in the opposite direction such that diminished amygdala activity during affect labeling "releases" RVLPFC to be more active (for a discussion of this issue, see Lieberman et al., 2007). Likewise, although we suggest that psychosocial resources lead to a lower physiological stress response, it is possible that lower physiological stress reactivity may facilitate the development of psychosocial resources. Even without evidence indicating the direction of the relationship, the results presented here still make a contribution to our understanding of how neural mechanisms link psychosocial resources to attenuated biological stress responses.

Also, it is important to note that the fMRI labeling task used in this study reflected one type of threat regulation process, one that has primarily been shown to involve RVLPFC (Hariri et al., 2000; Lieberman et al., 2007). There are a variety of coping strategies that can be used to deal with threats in everyday life. Thus, future studies can extend these results by using threat regulation tasks other than verbal labeling to examine how psychosocial resources moderate neural reactivity during different regulation strategies, presumably involving other regions of PFC.

Finally, our current data analysis tools did not allow us to examine individual differences in functional connectivity between our key ROIs, amygdala and RVLPFC. Newer fMRI data analysis tools will likely allow for an examination of these differences in subsequent studies.

Conclusions

The present study integrates psychological, biological, and neural levels of analysis, revealing that psychosocial resources are associated with lower cortisol responses to an acute laboratory stressor and that differences in neural reactivity may underlie this relationship. Greater psychosocial resources were associated with lower cortisol reactivity, as well as with higher RVLPFC and lower amygdala activity during a threat regulation task. Lower amygdala activity during the threat regulation task mediated the link between psychosocial resources and lower cortisol reactivity. Results are consistent with a model that maintains that psychosocial resources achieve their stress-reducing effects by enhancing prefrontal inhibition of threat responses during threat regulation, rather than by decreasing threat sensitivity.

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