Introduction

Extreme environments are characterized as those situations which place a high demand on the physiological, affective, cognitive, and/or social processing resources of the individual. Extreme environments strongly perturb the body and mind, which in turn initiate complex cognitive and affective response strategies. Different types of extreme environments may share some aspects but can also have unique demand characteristics. For example, exposure to the cold and isolated environment of an Antarctic expedition may result in extreme social and sensory deprivation, whereas exposure to military combat operations may entail extreme sensory overload. It is clear that there are many different types of extreme environments or situations, but it is less clear that an individual's cognitive and affective responses are as varied as the different types of extreme environments.

From a systems neuroscience perspective, optimal performance under extreme conditions can be conceptualized as goal-oriented task completion during a high demand context. This conceptualization highlights the importance of stress-related neural processing, of cognitive control, and of learning for the adaptation to extreme environments. Here we suggest that two cognitive processes which can be examined experimentally and that are critical for top-down control and learning, may be critical for optimal performance. These two cognitive processes are: (1) feedback of an adverse outcome, which is necessary for adjusting behavioral strategies in decision-making; and (2) top-down modulation of ascending sensorimotor information to predict future states, which is an important evolutionary advantage associated with the development of complex cortical circuitry. The top-down modulatory ability is fundamentally related to the cognitive appraisal notion introduced above and to learning associations between stimuli and future pleasant or aversive outcomes. For example, the rate of reward learning depends on the discrepancy between the actual occurrence of reward and the predicted occurrence of reward, the so-called ‘reward prediction error’ (Schultz, Dayan, & Montague, 1997). Below we briefly review aspects of stress, the key neural substrates in performing under stressful conditions, and the proposed role of two brain areas that may contribute to optimal performance in extreme conditions.

We have developed a preliminary model of optimal performance in extreme environments (Paulus et al, in press) that starts with the observation that these environments exert profound interoceptive effects. Interoception is: (a) sensing the physiological condition of the body (Craig, 2002), (b) representing the internal state (Craig, 2009) within the context of ongoing activities, and (c) initiating motivated action to homeostatically regulate the internal state (Craig, 2007). Interoception includes a range of sensations such as pain (LaMotte, Thalhammer, Torebjork, & Robinson, 1982), temperature (Craig & Bushnell, 1994), itch (Schmelz, Schmidt, Bickel, Handwerker, & Torebjork, 1997), tickle (Lahuerta, Bowsher, Campbell, & Lipton, 1990), sensual touch (Vallbo, Olausson, Wessberg, & Kakuda, 1995; Olausson et al., 2002), muscle tension (Light & Perl, 2003), air hunger (Banzett et al., 2000), stomach pH (Feinle, 1998), and intestinal tension (Robinson et al., 2005), which together provide an integrated sense of the body’s physiological condition (Craig, 2002). These sensations travel via small-diameter primary afferent fibers, which eventually reach the anterior insular cortex for integration (Craig, 2003b). The interoceptive system provides this information to (1) systems that monitor value and salience (orbitofrontal cortex and amygdala); (2) are important for evaluating reward (ventral striatum/extended amygdala); and (3) are critical for cognitive control processes (anterior cingulate). Moreover, the more anterior the representation of the interoceptive state within the insular cortex the more “textured”, multimodal, and complex the information that is being processed due to the diverse cortical afferents to the mid and anterior insula. We have hypothesized that the anterior insula not only receives interoceptive information but is also able to generate a predictive model (Paulus & Stein, 2006), which provides the individual with a signal of how the body will feel, similar to the “as if”
loop in the Damasio somatic marker model (Damasio, 1994). The interoceptive information is thus “contextualized”, i.e. brought in relation to other ongoing affective, cognitive, or experiential processes, in relation to the homeostatic state of the individual, and is used to initiate new or modify ongoing actions aimed at maintaining the individual’s homeostatic state. In this fashion interoceptive stimuli can generate an urge to act. Thus we propose the following process hypotheses: (1) individuals who are optimal performers have developed a well “contextualized” internal body state that is associated with an appropriate level to act. In contrast, sub-optimal performers either receive interoceptive information that is too strong or too weak to adequately plan or execute appropriate actions. As a consequence, there is a mismatch between the experienced body state and the necessary action to maintain homeostasis. Therefore, a neural systems model of optimal performance in extreme environments needs to include brain structures that are able to process cognitive conflict and perturbation of the homeostatic balance, i.e. the anterior cingulate and insular cortex. Thus, ultimately, engagement of these brain structures is likely to be predictive of performance and may also be used as an indicator of efficacy of an intervention.

Resilience refers to (1) the ability to cope effectively with stress and adversity and (2) the positive growth following homeostatic disruption (Richardson, 2002) and is an important psychological construct to examine how individuals respond to challenging situations and stay mentally and physically healthy in the process (Tugade, Fredrickson, & Barrett, 2004c). The ability to regulate and generate positive emotions plays an important role in the development of coping strategies when confronted with a negative event (Bonanno, 2004b). In particular, resilient individuals often generate positive emotions in order to rebound from stressful encounters (Tugade, Fredrickson, & Barrett, 2004b). Nevertheless, the experimental assessment of resilience is challenging and requires novel behavioral and neural systems techniques (Charney, 2006).

Resilience is a complex and possibly multi-dimensional construct (Luthar, Cicchetti, & Becker, 2000). It includes trait variables such as temperament and personality as well as cognitive functions such as problem-solving that may work together for an individual to adequately cope with traumatic events (Campbell-Sills, Cohan, & Stein, 2006b). Here, we focus on resilience in terms of a process through which individuals successfully cope with (and bounce back from) stress (e.g., after being fired from a job, an individual adopts a proactive style improving his job hunting and work performance), rather than a simple recovery from insult (e.g., job loss causes a period of initial depressive mood followed by a return to affective baseline without attempting to modify habitual coping mechanisms to prevent its reoccurrence).

The current study was aimed to show that resilience, which is a critical characteristic to perform optimally in extreme environments, has significant effects on brain structures that are thought to be important for optimal performance. We used an emotion face assessment task that we have previously shown to be sensitive to levels of trait anxiety (Stein, Simmons, Feinstein, & Paulus, 2007), can be modulated by anti-anxiety drugs (Paulus, Feinstein, Castillo, Simmons, & Stein, 2005a), and is well known to be sensitive to genetic differences across individuals (Hariri et al., 2002a). As elaborated above, we hypothesize that limbic and paralimbic structures play an important role in helping individuals adjust to extreme conditions. Thus, we hypothesized that activation in amygdala and insular cortex are critically modulated by the level of resilience. In particular, if the anterior insular plays an important role in helping to predict perturbations in the internal body state, one would hypothesize that greater activation in this structure is associated with better resilience. Moreover, if one assumes that the amygdala is important in assessing salience in general and the potential of an aversive impact in particular, one would hypothesize that greater resilience is associated with relatively less activation in the amygdala during emotion face processing.

**Methods**

**Participants:** This study was approved by the University of California San Diego (UCSD) and the San Diego State University (SDSU) Institutional Review Boards and all subjects signed informed consent. Initially, a sample of SDSU undergraduate psychology students participated in mass screening using the Spielberger Trait Anxiety Questionnaire (Spielberger, 1983). All subjects were subsequently interviewed with a structured diagnostic interview (SCID) (First, Spitzer, Gibbon, & Williams, 1995), modified to enable us to document the presence of subthreshold anxiety and mood disorders. Only subjects who did not have a DSM-IV(American Psychiatric
Association, 1994) diagnosis were included in this study. Twenty-six subjects were studied, 17 females and 9 males. These subjects were 19. (18-26) years old and had an average of 12.8 (11 – 15) years of education. All subjects were trained to perform the emotion face processing task prior to testing during fMRI scanning and received $50 for participation. No restrictions were placed on the consumption of caffeine-containing beverages; none of the subjects were smokers.

Measures: Prior analyses of the original CD-RISC in general population, primary care, psychiatric outpatient, and clinical trial samples support its internal consistency, test-retest reliability, and convergent and divergent validity (Connor & Davidson, 2003). The CD-RISC also was shown to moderate the relationship between retrospective reports of childhood maltreatment and current psychiatric symptoms (Campbell-Sills, Cohan, & Stein, 2006a) and CD-RISC scores have been suggested to increase following treatments hypothesized to enhance resilience (Davidson et al., 2005).

Task: During fMRI, each subject was tested on a slightly modified (Paulus, Feinstein, Castillo, Simmons, & Stein, 2005b) version of the emotion face assessment task (Hariri et al., 2002b; Hariri et al., 2005). During each 5 second trial, a subject is presented with a target face (on the top of the computer screen) and two probe faces (on the bottom of the screen) and is instructed to match the probe with the same emotional expression to the target by pressing the left or right key on a button box. A block consists of six consecutive trials where the target face is angry, fearful, or happy. During the sensorimotor control task subjects were presented with 5-second trials of either wide or tall ovals or circles in an analogous configuration and instructed to match the shape of the probe to the target. Each block of faces and of the sensorimotor control task was presented three times in a pseudo-randomized order. A fixation cross lasting 8 seconds was interspersed between each block presented at the beginning and end of the task (resulting in 14 fixation periods). For each trial, response accuracy and reaction time data were obtained. There were 18 trials (3 blocks of 6 trials) for each face set as well as for shapes. The whole task lasted 512 seconds (matching the scan length).

Analysis

Acquisition of images: All scans were performed on a 3T GE CXX4 Magnet at the UCSD Keck Imaging Center, which is equipped with 8 high bandwidth receivers that allow for shorter read-out times and reduced signal distortions and ventromedial signal dropout. Each one hour session consisted of a three-plane scout scan (10 seconds), a standard anatomical protocol, i.e. a sagittally acquired spoiled gradient recalled (SPGR) sequence (FOV 25 cm; matrix: 192x256; 172 sagittally acquired slices thickness: 1 mm; TR: 8ms; TE: 3 msec; flip angle =12°). We used an 8-channel brain array coil to axially acquire T2*-weighted echo-planar images (EPI) with the following parameters: FOV 230mm, 64X64 matrix; 30 2.6 mm thick slices; 1.4 mm gap; TR=2000ms, TE=32 ms, flip angle = 90°.

Image analysis pathway: The basic structural and functional image processing were conducted with the Analysis of Functional Neuroimages (AFNI) software package (Cox, 1996). A multivariate regressor approach detailed below was used to relate changes in EPI intensity to differences in task characteristics (Haxby, Hoffman, & Ida Gobbini, 2000). EPI images were co-registered using a 3D-coregistration algorithm (Eddy, Fitzgerald, & Noll, 1996) that has been developed to minimize the amount of image translation and rotation relative to all other images. Six motion parameters were obtained across the time series for each subject. These motion parameters will be used as regressors to adjust EPI intensity changes due to motion artifacts. All slices of the EPI scans were temporally aligned following registration to ensure different relationships with the regressors are not due to the acquisition of different slices at different times during the repetition interval.

Multiple regressor analyses: Four orthogonal regressors of interest were: (1) happy, (2) angry, (3) fearful, (4) circle/oval (i.e., shape) sensorimotor condition These 0-1 regressors were convolved with a gamma variate function (Boynton, Engel, Glover, & Heeger, 1996) modeling a prototypical hemodynamic response (6-8 second delay (Friston, Frith, Turner, & Frackowiak, 1995)) and to account for the temporal dynamics of the hemodynamic response (typically 12-16 seconds) (Cohen, 1997). The convolved time series was normalized and used as a regressor of interest. A series of regressors of interest and the motion regressors were entered into the AFNI program 3dDeconvolve to determine the height of each regressor for each subject. The key measure is the voxel-wise normalized relative signal change (or % signal change for short), which is obtained by dividing the regressor coefficient by the sum of the zero-
order regressor and the mean first-order regressor. Spatially smoothed % signal change data were transformed into Talairach coordinates based on the anatomical MR image, which is transformed manually in AFNI.

Second order analyses: The voxel-wise Talairach-transformed % signal change data was the main dependent measure and was subjected to a multivariate regression analysis to determine the effect of resiliency on brain activation during the emotion processing task. A threshold adjustment method based on Monte-Carlo simulations was used to guard against identifying false positive areas of activation (Forman et al., 1995). Based on previous studies and simulations implemented in the AFNI program AlphaSim, it was determined that a voxel-wise a-priori probability of 0.05 will result in a whole-brain corrected cluster-wise activation probability of 0.05 if a minimum volume of 1024ul and a connectivity radius of 4.0 mm is considered.

Anatomically-constrained functional regions of Interest: We have developed and extended an anatomically-constrained functional region of interest (ROI) approach to test the proposed hypothesis about amygdala and insular cortex functioning. This approach was derived from our work showing amygdala activation attenuation with a benzodiazepine anxiolytic drug (Paulus et al., 2005a). Moreover, this approach is supported by findings by other groups showing greatest test-retest reliability using this approach relative to using a pure anatomical ROI or a voxel-by-voxel approach (Johnstone et al., 2005). We have extended this approach to use a probability mask of the insular cortex. The estimated individual insula data were normalized to Talairach coordinates and reprocessed in AFNI. Finally, a group insula probability mask was created in Talairach space using the AFNI program 3dcalc.

Statistics: All behavioral analyses were carried out with SPSS 10.0 (Norusis, 1990). A repeated measures multivariate ANOVA, with face type (angry, fearful, happy) as the within-subjects factor, was used to analyze the behavioral measures and neural activation patterns. To relate resiliency to the activation patterns during the emotion face processing task, we conducted voxelwise multiple linear regression analyses using the lm module of the statistical programming language R (http://cran.r-project.org/).

Results

Task-related activation: Activation during the emotion face assessment task included both limbic and paralimbic structures including bilateral insula, amygdala, but also the fusiform gyrus (data not shown).

Resiliency related activation: Three main areas showed resiliency-related activation during the emotion face assessment task. First, the ventromedial prefrontal cortex showed a significant inverse relationship between the amount of activation during emotion face processing and levels of resilience (F(2,23) = 5.39, p = 0.012, r² = 0.319). There was no significant effect of gender (p = 0.58) on this degree of activation in this area. Moreover, when examining the different face types (anger, fear or happy), there was no significant resiliency by face-type interaction (Figure 1, F(2,22) = 0.526, p = 0.59). Thus, processing greater level of resilience was associated similarly with less activation in this area when presented with all face types. Second, the right anterior insular cortex showed a significant positive relationship between the amount of activation during emotion face processing and levels of resilience (Figure 2, F(2,23) = 6.16, p = 0.007, r² = 0.349). Similarly, there was no significant effect of gender (p = 0.71). Moreover, when examining the different face types (anger, fear or happy), there was a trend a resiliency by face-type interaction (F(2,22) = 3.365, p = 0.053). Specifically, processing greater level of resilience was associated with greater activation in this area when presented with angry faces in particular. Third, the right amygdala showed a significant positive relationship between the amount of activation during emotion face processing and levels of resilience (Figure 3, F(2,23) = 4.79, p = 0.018, r² = 0.294). Similarly, there was no significant effect of gender (p = 0.85). Moreover, when examining the different face types (anger, fear or happy), there was no resiliency by face-type interaction (F(2,22) = 1.852, p = 0.181). Thus, similar to the findings in the ventromedial prefrontal cortex, greater resiliency was associated with attenuated activation in the amygdala irrespective of the face type.

Discussion

This investigation yielded one main result: activation in limbic and paralimbic areas of the brain during face emotion processing are modulated by the level of resilience. In particular
greater resilience is associated with less activation in the ventromedial prefrontal cortex and the amygdala but more activation in the right anterior insular cortex. Given the notion that resilience is important for optimal performance in extreme environments and given the finding that resilience is related to activation in brain areas that we had hypothesized to be important for optimal performance, we offer this result as a first step to linking brain activation to optimal performance. Moreover, the involvement of the insular cortex supports our general notion that this brain structure may be critically involved in assessing ongoing internal body states as they relate to challenges in the outside world.

The insula (for review see (Augustine, 1996; Augustine, 1985)) is a paralimbic structure which constitutes the invaginated portion of the cerebral cortex, forming the base of the sylvian fissure, considered limbic sensory cortex by some investigators (Craig, 2003a). A central insular sulcus divides the insula into two portions, the anterior and posterior insula. The anterior insula is strongly connected to different parts of the frontal lobe, whereas the posterior insula is connected to both the parietal and temporal lobes (Ture, Yasargil, Al Mefty, & Yasargil, 1999). The columnar organization of the insular cortex shows a highly organized anterior inferior to posterior superior gradient (for example see (Mesulam & Mufson, 1982)). Specifically, whereas posterior insular is characterized by a granular cortical architecture, the anterior inferior insula has an agranular columnar organization, i.e. lacks layer 4 granular cells. This type of transition is found in other parts of the brain whenever cortical representations are based on modulatory or selective feedback circuits (Shipp, 2005). Spindle cells within the anterior insular – orbitofrontal transition region (Nimchinsky et al., 1999) may be the cellular substrate underlying the possibility of widespread cortical integration. Activation of insular cortex has been reported in a number of processes including pain (Tracey et al., 2000), interoceptive (Critchley, Wiens, Rotshstein, Ohman, & Dolan, 2004), emotion-related (Phan, Wager, Taylor, & Liberonz, 2002), cognitive (Huettel, Misiurek, Jurkowski, & McCarthy, 2004), and social processes (Eisenberger, Lieberman, & Williams, 2003). In reward-related processes the insular cortex is important for subjective feeling states and interoceptive awareness (Craig, 2002; Critchley et al., 2004) and has been identified as taking part in inhibitory processing with the middle and inferior frontal gyri, frontal limbic areas, and the inferior parietal lobe (Garavan, Ross, & Stein, 1999).

Resilient individuals are able to generate positive emotions to help them cope with extreme situations (Tugade, Fredrickson, & Barrett, 2004a). According to Fredrickson’s broaden-and-build theory, positive emotions facilitate enduring personal resources and broaden one’s momentary thought of action repertoire (Fredrickson, 2004). That is, positive emotions broaden one’s awareness and encourage novel, varied, and exploratory thoughts and actions which, in turn, build skills and resources. For example, experiencing a pleasant interaction with a person you asked for directions turns, over time, into a supportive friendship. Furthermore, positive emotions help resilient individuals to achieve effective coping (Werner & Smith, 1992) serving to moderate stress reactivity and mediate stress recovery (Ong, Bergeman, Bisconti, & Wallace, 2006). We suggest individuals that score high on self-reported resilience may be more likely to engage the insular cortex when processing salient information and are able to generate a body prediction error that enables them to adjust more quickly to different external demand characteristics. In turn, a more adapt adjustment is thought to result in a more positive view of the world, and that this capacity helps maintain their homeostasis. This positive bias during emotion perception may provide the rose-colored glasses that resilient individuals use to interpret the world and achieve effective ways to bounce back from adversity (Bonanno, 2004a) and maintain wellness.

We have recently proposed a neuroanatomical processing model as a heuristic guide to understand how one can link optimal performance to how the individual "feels inside". This model focuses on the notion of a body prediction error, i.e. the difference between the value of the anticipated/predicted and value of the current interoceptive state, and consists of four components. First, information from peripheral receptors ascends via two different pathways, the A-beta-fiber discriminative pathway that conveys precise information about the “what” and “where” of the stimulus impinging on the body, and the C-fiber pathway that conveys spatially- and time-integrated affective information (Craig, 2007). These afferents converge via several way stations to the sensory cortex and the posterior insular cortex to provide a sense of the current body state. Second, centrally generated interoceptive states, e.g. via contextual associations from memory, reach the insular cortex via temporal and parietal cortex to
generate body states based on conditioned associations (Gray & Critchley, 2007; Yaguez et al., 2005). Third, within the insular cortex there is a dorsal-posterior to inferior-anterior organization from granular to agranular, which provides an increasingly “contextualized” representation of the interoceptive state (Shipp, 2005), irrespective of whether it is generated internally or via the periphery. These interoceptive states are made available to the orbitofrontal cortex for context-dependent valuation (Rolls, 2004; Kringelbach, 2005) and to the anterior cingulate cortex for error processing (Critchley, Tang, Glaser, Butterworth, & Dolan, 2005; Carter et al., 1998) and action valuation (Rushworth & Behrens, 2008; Goldstein et al., 2007). Fourth, bidirectional connections to the basolateral amygdala (Augustine, 1985; Jasmin, Burkey, Granato, & Ohara, 2004; Reynolds & Zahm, 2005) and the striatum (Chikama, McFarland, Amaral, & Haber, 1997), particularly ventral striatum (Fudge, Breitbart, Danish, & Pannoni, 2005), provide the circuitry to calculate a body prediction error (similar to reward prediction error (Pessiglione, Seymour, Flandin, Dolan, & Frith, 2006; Preuschoff, Quartz, & Bossaerts, 2008; Schultz & Dickinson, 2000)), and provide a neural signal for salience and learning. The insular cortex relays information to other brain systems to initiate motivated action to achieve a steady state (Craig, 2007) by minimizing the body state prediction error. Thus the insular cortex is centrally located in a network of structures that are important for modulating processing according to internal and external demands.

The neuroscience approach to understanding optimal performance in extreme environments has several advantages over traditional descriptive approaches. First, once the role of specific neural substrates is identified, they can be targeted for interventions. Second, studies of specific neural substrates involved in performance in extreme environments can be used to determine what cognitive and affective processes are important for modulating optimal performance. Third, quantitative assessment of the contribution of different neural systems to performance in extreme environments could be used as indicators of training status or preparedness. The observation that the insular cortex and amygdala are modulated by levels of resilience is a first step in bringing neuroscience approaches to a better understanding of what makes individuals perform differently when exposed to extreme environments. The application of this systems neuroscience approach will help to extend findings from specific studies with individuals exposed to extreme environments to develop a more general theory. As a consequence, one can begin to develop a rational approach to develop strategies to improve performance in these environments.
Figure Captions:

Figure 1: Top – scatter plot of levels of resilience (x-axis) and % signal difference in the ventromedial prefrontal cortex during the face processing relative to the sensorimotor control condition. More resilience was associated with relatively less activation in this area. Bottom – average activation for different target faces for male and female participants, respectively.

Figure 2: Top – scatter plot of resilience versus % signal difference in right anterior insular cortex. More resilience was associated with relatively greater activation in the insula. Bottom – average activation for different target faces for male and female participants, respectively.

Figure 3: Top – scatter plot of resilience versus % signal difference in right amygdala. More resilience was associated with relatively less activation in the amygdala. Bottom – average activation for different target faces for male and female participants, respectively.


Lahuerta, J., Bowsher, D., Campbell, J., & Lipton, S. (1990). Clinical and instrumental evaluation of sensory function before and after


Ventromedial Prefrontal Cortex: All Faces - Shapes

Gender

R Sq Linear = 0.317

CDRISC - Resilience

Ventromedial Prefrontal Cortex

% Signal Difference

Anger | Fear | Happy | Anger | Fear | Happy

Male | Female
Right Anterior Insula: All Faces - Shapes

Gender

R Sq Linear = 0.345

% Signal Difference

Right Anterior Insula

% Signal Difference

Anger | Fear | Happy | Anger | Fear | Happy
Male | Female|
Amygdala: All Faces - Shapes

Gender

R Sq Linear = 0.293

CDRISC - Resilience

Right Amygdala

% Signal Difference

Anger Male

Fear Male

Happy Male

Anger Female

Fear Female

Happy Female