Is the Human Amygdala Critical for the Subjective Experience of Emotion? Evidence of Intact Dispositional Affect in Patients with Amygdala Lesions

Adam K. Anderson[1] and Elizabeth A. Phelps[2]

Abstract

■ It is thought that the human amygdala is a critical component of the neural substrates of emotional experience, involved particularly in the generation of fear, anxiety, and general negative affectivity. Although many neuroimaging studies demonstrate findings consistent this notion, little evidence of altered emotional experience following amygdala damage has been gathered in humans. In a preliminary test of the amygdala's role in phenomenal affective states, we assessed the extent of experienced positive and negative affective states in patients with amygdala damage and age-, sex-, and education-matched controls. To assess chronic changes in experienced affect, all groups were administered the Positive and Negative Affect Schedules (PANAS, Watson, Clark, & Tellegen, 1988). In the first study, we examined the effects of amygdala lesions on affective traits in 10 left and 10 right amygdala-damaged patients, 1 patient with bilateral amygdala damage (SP), and 20 control subjects. Subjects were asked to indicate the typicality of different experiential states of positive (e.g., inspired, excited) and negative (e.g., afraid, nervous) valence. In a second study, we examined more closely the effects of bilateral amygdala damage on the day-to-day generation of affective states by administering the PANAS daily for a 30-day period to patient SP and age-, sex-, and education-matched controls. In both experiments, no differences in the magnitude and frequency of self-reported positive or negative affect were found between control subjects and patients with amygdala damage. Moreover, principal components analyses of the covariation among different affects (across individuals in Study 1 and within individuals across days in Study 2) confirmed a two-factor (positive vs. negative) description of experienced affect in controls. A highly similar two-factor description of experienced affect was found in patients with amygdala lesions. This suggests that the underlying structure of affective states was intact following amygdala damage. It is concluded that the human amygdala may be recruited during phenomenal affective states in the intact brain, but is not necessary for the production of these states. ■

INTRODUCTION

The term ''emotion'' most commonly refers to the conscious experience we undergo corresponding to a specific affective state, such as the somber feeling associated with sadness or the elation associated with joy. Human affective neuroscience has begun to make progress in defining the neuroanatomy of these elusive mental experiences. One of the brain structures often associated with emotional functioning in human and nonhuman animals is the amygdaloid complex (LeDoux, 1996; Aggleton, 1992). Amygdala lesions in humans have been shown to result in both mnemonic and perceptual impairments related to emotion. These deficits include impaired conditioned fear responses (Bechara et al., 1995; LaBar, LeDoux, Spencer, & Phelps, 1995), fear-potentiated startle (Funayama, Grillon, Davis, & Phelps, 2001), arousal-enhanced memory (Labar & Phelps, 1998; Phelps et al., 1998; Cahill, Babinsky, Markowitsch, & McGaugh, 1995; Adolphs et al., 1997), and the evaluation of nonverbal expressions related to fear (Anderson & Phelps, 2000b; Calder et al., 1996; Adolphs, Tranel, Damasio, & Damasio, 1994; Adolphs, Tranel, & Damasio, 1998). Considering the amygdala's importance for a variety of emotional functions, it is largely thought to be involved in the subjective experience of emotion as well (Davidson & Irwin, 1999; Damasio, 1994). In support of this view, evidence from neuroimaging studies have implicated the amygdala in the experience of fear, anxiety, and general negative affectivity in both clinical populations with affective disorders (e.g., Abercrombie et al., 1998; Birmbauer et al., 1998; Breiter, Rauch, Kwong, Baker, & Rosen, 1996; Rauch et al., 1996; Drevets et al., 1992) and in normal healthy subjects in various emotion-eliciting situations (e.g., Lane et al., 1997; Irwin et al., 1996; Ketter et al., 1996; Schneider et al., 1996; Zald & Pardo, 1996).

Presentation of symptom-eliciting stimuli to patients with obsessive–compulsive disorder (Breiter et al., 1996), the imagining of combat-related items/scenes in

[1]Stanford University, [2]New York University

patients with posttraumatic stress disorder (Rauch et al., 1996), and the viewing of neutral human faces in patients with social phobia (Birmbauer et al., 1998) have all revealed differential amygdala activity relative to normal observers. In normal healthy adults, presentations of highly aversive odorants (Zald & Pardo, 1996) and tastes (Zald, Lee, Fluegel, & Pardo, 1998), as well as unsolvable problem sets (Schneider et al., 1996), which are thought to induce states of anxiety, have revealed changes in blood flow in the amygdala region. The experience of global negative affect, not specific to anxious states, has also been related to activity in the amygdala. In clinical populations, differential amygdala activation has been noted in patients with depression relative to healthy volunteers during resting baseline scans (Abercrombie et al., 1998; Drevets et al., 1992). Similar activations have been demonstrated in healthy volunteers during various affective challenges, such as the induction of sad moods (Lane et al., 1997; Schneider et al., 1995) and the viewing of unpleasant relative to neutral pictures (Irwin et al., 1996).

The strongest evidence for the amygdala's role in affective experience is provided by studies demonstrating that amygdala activity correlates with the intensity of evoked subjective emotional experience. Ketter et al. (1996) have shown that the pharmacological induction of fear through the administration of the anesthetic procaine is related to amygdala cerebral blood flow changes; such that, subjects with the most robust fear responses revealed the greatest change in amygdala activation. Zald and Pardo (1996) presented similar findings in subjects presented with highly aversive odorants, where the degree of subjective aversive response correlated significantly with amygdala response. With regard to nonanxious affectivity, resting regional cerebral metabolic rate in the amygdala was found to correlate with negative affect in patients with unipolar major depression (Abercrombie et al., 1998).

Although neuroimaging evidence is consistent with an important role of the amygdala in generating negative affective experience, little direct evidence of the existence of emotional dysfunction following amygdala damage has been documented in humans. Neuroimaging techniques can reveal activity in brain regions associated with a particular behavior or cognitive operation, but cannot speak directly of the causal relations between discrete brain structures and their putative functions. This caveat is particularly significant in neuroimaging studies of affective functions. Affective functions are poorly defined, and thus, isolating different components of affective behavior and relating them to the constellation of observed brain activations is not often accomplished. Accordingly, although changes in amygdala activity may represent the generation of affective experience, it may also reflect other aspects of emotional processing correlated with the intensity of emotional experience. Amygdala responses accompanying the viewing of emotional materials have been shown to correlate with the post-encoding consolidation of emotional memories (Hamann, Grafton, & Kilt, 1999; Cahill et al., 1996) and the modulation of information processing in early visual and auditory processing areas (Morris, Friston, Buchel, et al., 1998; Morris, Friston, & Dolan, 1998). Consistent with this notion, it is well established that patients with damage to the amygdala have exhibited a range of emotional mnemonic (Phelps et al., 1998) and perceptual impairments (see Anderson & Phelps, 2000b, 2001). Therefore, amygdala responses to emotional events may be correlated, but not causally related, to the generation of affective experience.

Although it is widely thought that the amygdala is a critical component in network of regions supporting phenomenal affective experiences (e.g., LeDoux, 1996; Damasio, 1994), it has not been clearly demonstrated if damage to the human amygdala results in the altered magnitude, frequency, and covariance structure of affective states. In a preliminary test of the amygdala's role in mediating affective experience, we administered the Positive and Negative Affect Schedules (PANAS, Watson, Clark, & Tellegen, 1988), a well-normed questionnaire intended to measure the experience of positive and negative affective states, to patients with damage to the amygdala. To assay chronic changes in the experience of various affective states two experiments were conducted. In the first experiment, 10 left and 10 right amygdala-damaged patients, 1 patient with bilateral amygdala damage (patient SP), and age-, sex-, and education-matched controls were asked to characterize the typicality of experienced states of positive (e.g., inspired, excited) and negative (e.g., afraid, nervous) valence during the past year of their lives. That is, to indicate their dispositional affective traits. Patients with unilateral amygdala damage were examined as a more abundantly available lesion model for the effects of amygdala lesions. The validity of such a model is shown in numerous studies, which have replicated impairments following bilateral lesions of the amygdala in patients with unilateral amygdala damage (Anderson et al., 2000; LaBar & Phelps, 1998; LaBar et al., 1995). In order to examine emotional experience following bilateral amygdala damage more closely, a second experiment measured the daily fluctuations in the occurrence of positive and negative states over a 1-month period by having SP and age-, sex-, and education-matched control subjects keep a PANAS affective diary.

RESULTS

Experiment 1: Dispositional Affective Traits

Magnitude of Self-Reported Affective Traits

The PANAS are comprised of 20 affect descriptors (10 positive and 10 negative). The group means were derived by collapsing across the 10 descriptors from the

Positive (PA) and Negative Affect (NA) scales and a subset of the NA scale pertaining specifically to fear and anxiety (i.e., afraid, scared, nervous, jittery, distressed). We submitted these means to a 3 × 3 ANOVA, with group (left temporal lobectomy [LTL], right temporal lobectomy [RTL], and controls) and affect (positive affect, negative affect, and fear/anxiety) entered as separate between-subjects and within-subject factors. We compared SP's mean positive-, negative-, and fear/anxiety-related responses to controls by calculating separate Z scores for each affect type.

All groups reported experiencing more positive than negative states [$F(2,37) = 34.80$, $p < .01$]. No global differences in self-reported affect were found between controls and patients ($F < 1$), nor was there evidence of any valence-specific group differences ($F < 1$). Focused comparisons confirmed that all groups reported experiencing positive affects more than both negative- [$F(1,37) = 35.39$, $p < .01$] and fear/anxiety-related affects [$F(1,37) = 43.43$, $p < .01$]. Figure 1 illustrates the similarity in the mean ratings across LTL, RTL, and control groups, as well as SP Like the temporal lobectomy (TLP) patients, SP's affective traits were similar to controls, falling within the normal range for positive- (SP = 3.87 vs. controls = 3.69, $Z = .29$), negative- (SP = 3.03 vs. controls = 2.49, $Z = .68$), and fear/anxiety- (SP = 2.73 vs. controls = 2.54, $Z = .23$) related affects.

When we assessed each descriptor separately in the LTL, RTL, and control groups, we found only two differences between patients and controls: LTL patients rated themselves as being somewhat more strong [$t(18) = 2.33$, $p < .07$] and somewhat less irritable [$t(18) = 2.10$, $p <. 05$] than controls. However, after Bonferroni correction, it was found that such differences were expected from chance alone. When we restricted our analysis to descriptors of fear and anxiety (afraid, scared, nervous, jittery, distressed), we found no differences among RTL, LTL, and control groups (all Fs < 1). SP's responses to each descriptor fell within the normal range, with the exception of reporting feeling more hostile than controls ($z = 2.2$, $p < .05$). SP endorsed experiencing affective traits related to fear and anxiety to a similar extent as controls (all Zs < .65).

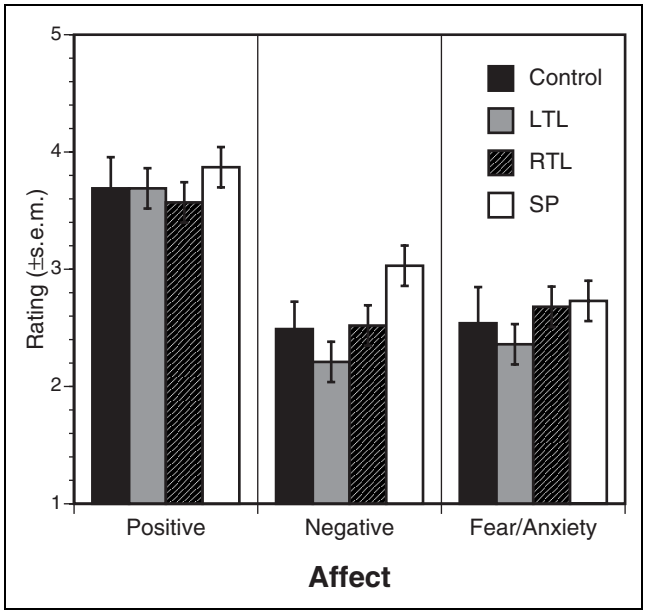

Figure 1. LTL, RTL, SP and control mean ratings (on a scale of 1–5, 1 = "very slightly or not at all"; 5 = "extremely") of the extent of experienced positive-, negative-, and anxiety/fear-related affect during the past year (i.e., affective traits). SP's means were derived from three independent administrations of the PANAS over a one-year period. The reported affective traits were similar across the four groups.

Frequency Distributions of Affective Traits

Considering the low mean responding to negative affective traits in both the TLP and control groups, it is possible that a floor effect could have concealed any group differences. To further establish the quantitative and qualitative similarity between the reported affective traits in TLP and controls, we next determined the frequency of occurrence of positive-, negative-, and fear/anxiety-related traits across individuals in the control and TLP groups (collapsed across hemisphere of resection, $n = 20$). Collapsing was performed due to the null finding of differences in dispositional trait magnitude between the RTL and LTL groups. The distribution of self-reported affective traits reflects how often subjects reported experiencing affects of different magnitudes over the past year (1—"very slightly or not at all"; 5—"extremely"). These distributions were derived from counting the number of responses to each increment of the five-point scale for each of the 10 positive-, 10 negative-, and 5 fear/anxiety-related descriptors for each group. These numbers were then converted to proportions. As illustrated in Figure 2, the majority of participants in the control group reported experiencing positive affects to greater extent than to a lesser extent during the past year. During the same time frame, the majority of reported negative-and fear/anxiety-related affects fell at the low end of the scale, with relatively few participants reporting experiencing such affects intensely during the past year. Importantly, these frequency distributions were highly similar across the TLP and control samples. When we considered the ratio of patient to control variability, there was substantial homogeneity of variance, falling between and F ratio of 1 and 2 for each affect type (PA = 1.46, NA = 1.33, fear/anxiety = 1.61, each nonsignificant).

Covariance Structure of Affective Traits

Previous results from large samples of the normal population reveal that PA and NA are nearly independent

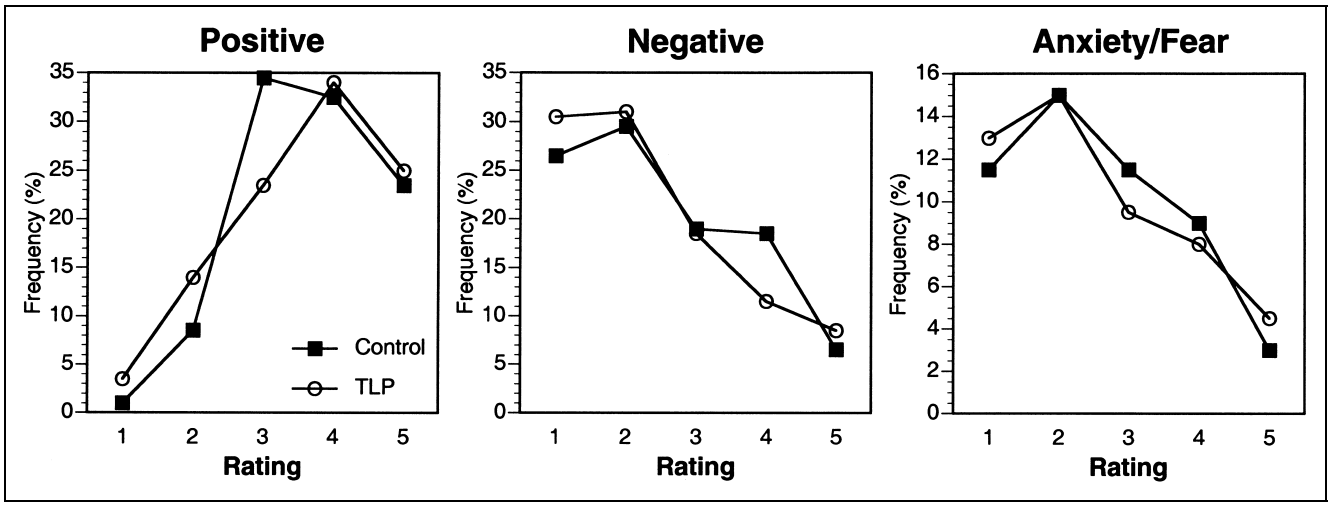

Figure 2. Frequency distribution of experienced positive-, negative-, and fear/anxiety-related affects in TLPs, collapsed across hemisphere of resection (n = 20) and controls (n = 20). The distribution of self-reported affective traits reflects how often subjects reported experiencing affects of different magnitudes over the past year (1—"very slightly or not at all"; 5—"extremely"). The frequency of occurrence of affects of differing strengths was very similar in the control and TLP samples.

measures of affect, such that the occurrence of PA and NA are minimally correlated (Watson et al., 1988). This two-factor description of affect was applied to the observed covariance structure of affective states in TLPs and controls to evaluate their similarity. We submitted the correlations among the 20 independent PANAS affect descriptors to separate principal components analyses for each the TLP and control groups. Two-factors were extracted and this solution was rotated orthogonally according to varimax criterion. This analysis allowed for a compacted representation of the 190 inter-item correlations in a two-factor space. Illustrated in Figure 3 are the factor loadings from the principal components analysis of the correlations between the 20 affect descriptors (10 positive and 10 negative) in the TLP and control groups. A two-factor solution of the control data revealed that PA and NA occupy largely independent portions of this two-factor space: positive

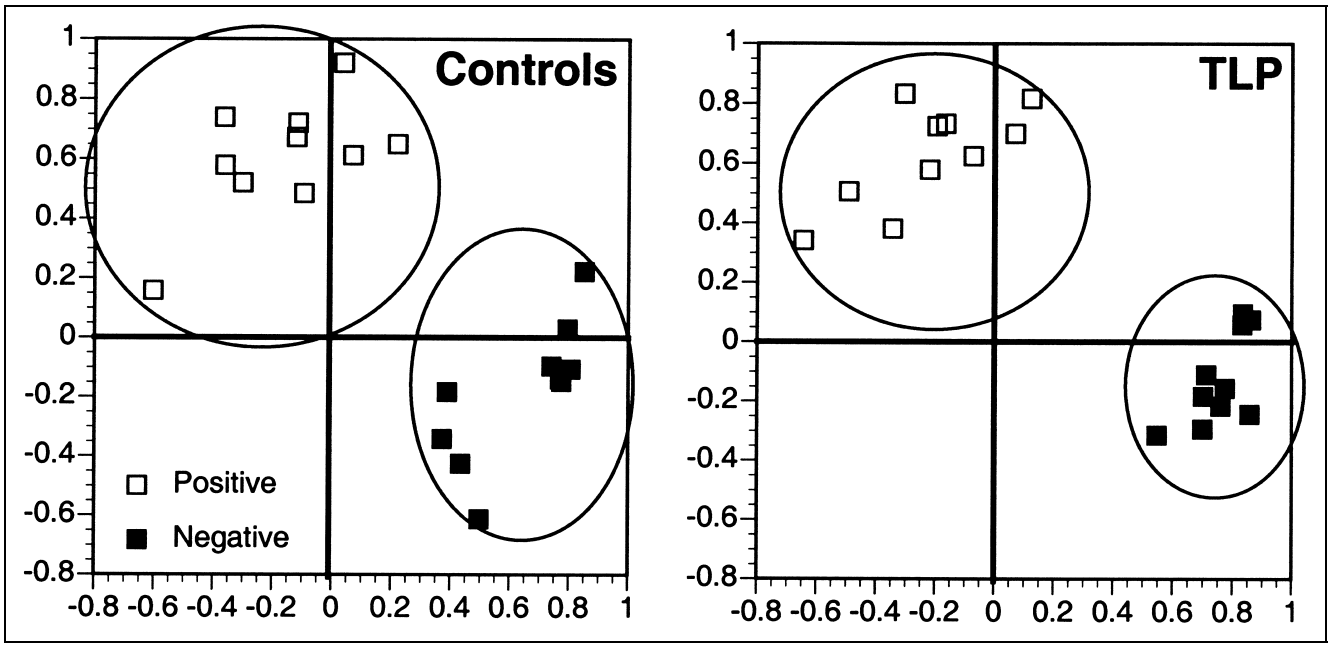

Figure 3. Factor loadings from a principal components analysis of the correlations between the 20 affect descriptors (10 PA and 10 NA) in the TLP and control groups. A two-factor solution of the control data reveals that positive affect traits covary and negative affect traits covary, suggesting the factors represent positive and negative affect; and in addition, these two dimensions of affect are largely uncorrelated, implying relative independence. A highly similar solution was found in the TLP group, suggesting that the underlying structure of affective traits is intact following unilateral amygdala damage. The two factor model accounts for 51% (48% PA and 53% NA) and 57% (52% PA and 62% NA) of the variance in the control and TLP groups, respectively.

traits tend to covary and cluster around one axis and the negative traits tend to covary and cluster around the other axis. Thus, PA and NA were found to be largely uncorrelated, suggesting relative independence. A highly similar solution was found in the TLP group, with PA and NA occupying similar positions in this two-factor space and showing similar levels of independence of positive and negative affective traits. This two-factor description accounts for 51% of control variance (48% of PA and 53% of NA) and 57% of TLP variance (52% of PA and 62% of NA). Z tests on r to Z-transformed PA factor loadings ($Z = .01$) and NA factor loadings ($Z = -.45$) revealed no significant differences between TLP and controls. Illustrating that both patient and control groups demonstrated similar levels of independence between positive and negative traits, variance common to both positive and negative factors was minimal in each group (controls = 8% vs. TLP = 7%).

Experiment 1: Discussion

When asked to indicate the extent of experienced emotional states during the past year, neither bilateral amygdala damage nor unilateral left or right amygdala damage resulted in substantial changes in the magnitude of self-reported experienced affective traits, including affects related specifically to fear and anxiety. When we analyzed the frequency of occurrence of affective traits of differing magnitudes in the 20 TLPs (collapsing across hemisphere of resection) and 20 age-, sex-, and education-matched controls, the distribution of reported affects across individuals was highly similar in both groups for each positive-, negative-, and fear/anxiety-related affects. An analysis of covariation in affective states across control participants confirmed a two-factor (positive vs. negative) description of affect, with the occurrence of positive and negative affective traits being largely independent in the control sample. A highly similar solution was found in TLPs. This analysis of the correlations among the 20 affect descriptors revealed that the resultant covariance between affective descriptors was similar in patients and controls, suggesting that the underlying structure of affectivity is intact following unilateral amygdala damage.

Experiment 2: Daily Fluctuations in Affective States

The first study focused on how patients with amygdala damage characterized their dispositional affect—their affective traits. Patients with unilateral or bilateral amygdala damage did not characterize their emotional life differently than that of demographically matched controls. It would be of interest to assess daily fluctuations in evoked affective states, which may be a more sensitive indicator of affective experience. In addition, we wished to examine more closely the effects of bilateral amygdala damage on the generation of positive and negative affective states. To achieve these aims, patient SP and two age-, sex-, and education-matched control participants were asked to keep an affective diary over a 1-month period by daily self-administering the PANAS. Six hundred affective rating data points were collected from each participant during this 30-day sampling period.

Results

Magnitude of self-reported affective states. We began by submitting each daily administration of the PANAS for SP and controls as independent measures to an ANOVA. The group means were derived by collapsing across the 10 descriptors from the PA and NA scales and a subset of the NA scale pertaining specifically to fear and anxiety (i.e., afraid, scared, nervous, jittery, distressed) across the 30-day period. We submitted these means to a 2 × 3 ANOVA, with group (SP and controls) and affect (positive, negative, and fear/anxiety) entered as separate between-subjects and within-subject factors. Day of rating was the random factor ($n = 30$ for SP; $n = 60$ for controls). Figure 4 depicts SP's and controls' (JA and BD) mean responses to the PA and NA scales and to a subset of the NA scales particular to fear and anxiety. Both SP and controls reported more positive affect than negative affect over this period [$F(2,176) = 92.73$, $p < .01$], and SP's magnitude of reported affect, irrespective of valence, tended to be greater than that of controls during this period [$F(1,88) = 3.08$, $p < .08$]. There was no evidence of valence-specific differences in self-reported affect across SP and controls ($F < 1$). When considering affects related to fear and anxiety separately, we found no difference between SP and controls ($F < 1$).

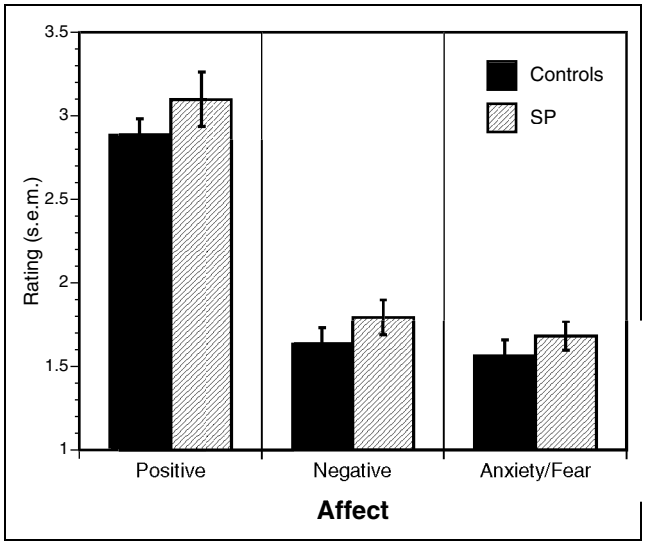

Figure 4. SP's and controls' average rating of the extent of experienced positive-, negative-, and anxiety/fear-related affective states during a 30-day period. SP and controls report experiencing affective states of different varieties to a similar degree.

We further compared SP's mean positive-, negative-, and fear/anxiety-related responses to controls for each of the 20 PANAS affect descriptors. During this period SP reported being more distressed [2.60 vs. 1.95, $F(1,88) = 5.24$, $p < .03$], proud [3.40 vs. 2.58, $F(1,88) = 7.63$, $p < .007$], alert [3.43 vs. 2.95, $F(1,88) = 7.31$, $p < .01$], ashamed [1.80 vs. 1.20, $F(1,88) = 12.57$, $p < .01$], determined [3.97 vs. 3.25, $F(1,88) = 8.20$, $p < .01$], attentive [3.63 vs. 3.23, $F(1,88) = 3.45$, $p < .07$], and less interested [2.50 vs. 3.05, $F(1,88) = 5.01$, $p < .03$] than controls. In general, the magnitudes of SP's self-reported affective states were largely equal to or greater than that reported from controls.

Frequency of experienced affective states. We next compared the frequency of occurrence of positive-, negative-, and fear/anxiety-related states in SP and controls during the 30-day sampling period. These distributions were derived from counting the number of responses to each increment of the five-point scale for each of the 10 positive-, 10 negative-, and 5 fear/anxiety-related descriptors across the 30-day sampling period, converting these counts to proportions for SP and controls. The distribution of self-reported affective states reflects how often SP and controls reported experiencing affects of different magnitudes (1—"very slightly or not at all"; 5—"extremely") over the 30-day sampling period. The control participants reported experiencing positive affects to a greater extent most frequently. The majority of reported negative- and fear/anxiety-related affects fell at the low end of the scale, with control participants reporting feeling these affects intensely relatively rarely during the 30-day period. As illustrated in Figure 5, these frequency distributions were highly similar across SP and controls. When we considered the F ratio of control to patient variance, there was substantial homogeneity of variance across SP and controls for positive (controls = .43 vs. SP = .79, ratio = 1.84), negative (controls = .31 vs. SP = .33, ratio = 1.08), and fear/anxiety (controls = .38 vs. SP = .23, ratio = 0.61) descriptors.

Covariance structure of affective states. The two-factor (positive/negative) description of affect (Watson et al., 1988) was applied to the observed covariance structure of affective states during the 30-day sampling period in SP and two controls to evaluate their similarity. We submitted the correlations among the 20 independent PANAS affect descriptors to a principal components analysis for each participant. Two-factors were extracted and then this solution was rotated orthogonally according to varimax criterion. This analysis allowed for a compacted representation of the 190 inter-item correlations derived from responses during the 30-day sampling period for each SP and controls. Figure 6 presents the factor loadings from a principal components analysis of the correlations between the 20 affect descriptors (10 positive and 10 negative) in SP and controls (BD and JA) derived from fluctuations in experienced affect over the 30-day period. Although not as tightly clustered as affective traits revealed from correlations across people, correlations in affective states derived from fluctuations across days revealed a relatively clear covariance structure within an individual. We found that for both controls (JA and BD), positive and negative affects occupied relatively independent portions of a two-factor (positive/negative) space. A very similar solution was derived from SP's observed correlated affective states. This two-factor description of experienced affective states accounted for 41% (46% PA and 35% NA) of control BD's, 50% (53% PA and 47% NA) of control JA's, and 48% (59% PA

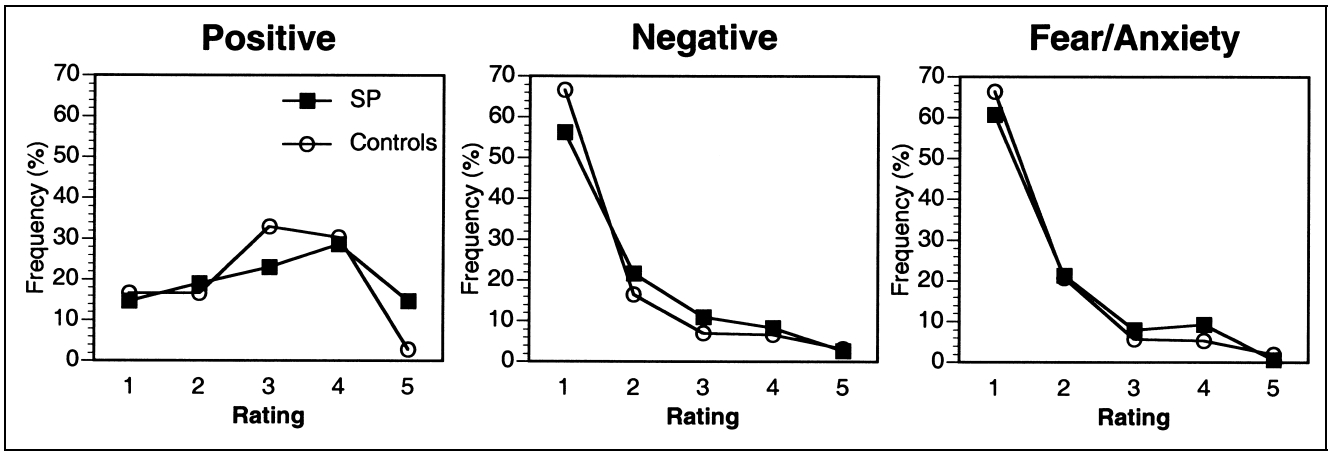

Figure 5. Frequency distribution of experienced positive-, negative-, and fear/anxiety-related affects in SP and controls. The distribution of self-reported affective states reflects how often subjects reported experiencing affects of different magnitudes daily over a 30-day period (1—"very slightly or not at all"; 5—"extremely"). The frequency of reported affects of differing strengths was very similar in SP and controls during this period.

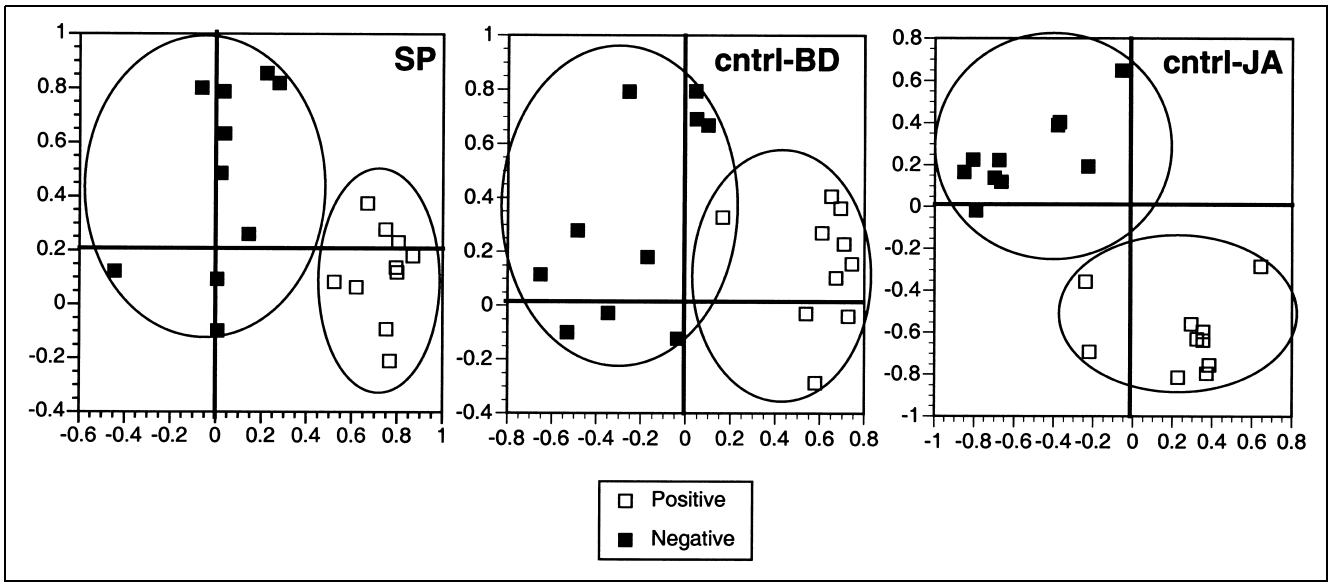

Figure 6. Factor loadings from a principal components analysis of the correlations between the 20 affect descriptors (10 positive affect and 10 negative affect) in SP and controls (BD and JA) derived from fluctuations in experienced affect over a 30-day period. Similar solutions were found in SP and controls, suggesting that the underlying structure of affective states is intact following bilateral amygdala damage. The two factor model accounts for 48% (59% PA and 38% NA) of SP's, 41% (46% PA and 35% NA) of BD's, and 50% (53% PA and 47% NA) of JA's variance.

and 38% NA) of SP's response variance. Z tests on r to Z-transformed positive affect factor loadings of PA (SP vs. control BD, $Z = .81$, vs. control JA, $Z = .81$), NA (SP vs. control BD, $Z = .66$, vs. control JA, $Z = -.35$) revealed no significant differences between SP and controls. This suggests that a two-factor model of affect was an equally appropriate description of SP's and controls' affective experience. Further, the degree of independence in occurrence of positive and negative affects was low in both SP and controls, as evidenced by similar levels of common variance across the positive and negative factors (SP = 4%, control BD = 9%, control JA = 11%).

Experiment 2: Discussion

When asked to monitor her daily affective states for a 1-month period, SP's self-reported affective experiences were highly similar to that of normal controls. SP's bilateral amygdala damage did not result in substantial decrease in the magnitude of experienced positive and negative affective states, including affects related specifically to fear and anxiety. In fact, SP expressed affective states of even greater magnitude than controls on average. We also found the frequency distribution of reported affects was highly similar in both SP and controls. This suggests that the frequency of occurrence of positive and negative affective states of varying intensity following bilateral amygdala damage was similar to what would be expected from the normal population. When we analyzed the covariation in experienced emotional states over a 30-day period, SP and controls revealed a highly similar covariance structure. Affective states within the normal population have been argued to vary along proposed fundamental independent dimensions of positive and negative affect (Watson et al., 1988). We confirmed this two-factor description of affect in normal controls by showing that negative states tended to co-occur and positive states tended to co-occur, with the occurrence of negative and positive affective states being largely independent of each other. Importantly, SP revealed a highly similar solution to that of controls. This similar covariance structure of affective states in SP and controls suggests that the underlying structure of fluctuations in affective states is largely intact following bilateral amygdala damage.

DISCUSSION

The findings of the present study suggest that neither patients with unilateral nor bilateral amygdala damage characterize their emotional life differently than that of normal, healthy controls. In addition to evidence of intact chronic affective traits, bilateral amygdala damage does not appear to result in the altered day-to-day production of positive and negative affective states. These findings are contrary to evidence from functional neuroimaging studies that suggest the human amygdala is a critical component of the neural substrates supporting the subjective experience of emotion (for a review, see Davidson & Irwin, 1999). Although observed neural responses in the amygdala region covary with occurrence of negative affective states, such evidence by itself cannot demonstrate directly that the amygdala is causally related to their generation. Although impairments noted following selective brain damage are also

correlational in nature (due to failure of random assignment), the lack of impairment, as evidenced in the present study, does provide evidence that the brain structure in question is not necessary for normal phenomenal affectivity. The discrepancy between neuroimaging and lesion evidence may be attributable to a variety of factors. First, our results are restricted to the analysis of self-reported affective experience, and hence rely solely on introspection. Although this argument concerns the generalizability of our findings, it cannot account for the discrepancy with neuroimaging studies because such studies are largely dependent on the correspondence between evoked amygdala activity and self-reported affect. Thus, self-reported affect is a critical measure of emotional experience, characterizing the essential dimension of emotion—one's subjective experience. The present study demonstrates that patients with amygdala lesions provide reports of affective experience of normal magnitude, frequency, and underlying covariance structure. Thus, we argue that the human amygdala may be recruited during phenomenal affective states in the intact brain but is not necessary for the production of these states.

One possible concern in interpreting the present results is that the low mean responding to negative affects in the control samples may have obscured any existing differences with the patient groups. Although the presence of a floor effect is of some concern, in Experiment 1 we showed that patients with unilateral amygdala damage experienced both mild and intense negative affects with highly similar frequency to that of controls. Further, both TLPs and controls revealed intercorrelations among experienced negative affects, suggesting that when an individual reported experiencing a particular negative affective descriptor intensely (e.g., hostile), they tended to report experiencing similarly valenced affects (e.g., distressed) to a greater degree as well. In Experiment 2, we found that across a 30-day sampling period, a patient with bilateral amygdala damage (patient SP) reported experiencing both positive and negative affects with similar magnitude as controls. During this period, SP also experienced both mild and intense negative affects with highly similar frequency to that of controls and revealed similar covariance in experienced negative affects as well. Such qualitative and quantitative similarities between patients and controls suggests the underlying structure of affective states is intact following amygdala damage and argues against an interpretation of intact negative affective experience as artifactual, due to floor-level responding.

Beyond Self-Reported Affect: Role of the Amygdala in Other Channels of Affective Expression

It can be argued that patients with amygdala lesions may report normal affect, but really do not experience affective states like neurologically intact individuals. Borrowing from Damasio (1994)'s concept of the ''as-if'' affective loop, the consistent pairing of particular scenarios with an affective response may allow for the affective response to be co-opted by other higher order cortical structures related to the representation of complex body states, such as the somatosensory-related cortices, including the insular region. These regions may then be sufficient to support the experience of ''virtual'' affective states in place of the amygdala's more primary contributions. Accordingly, patients with amygdala lesions may report normal phenomenal affective states, but other measures not dependent on self-report may yet indicate impaired affectivity. Evidence of intact emotional responses would then not generalize to other measures of affective experience.

Arguing against this notion, studies utilizing physiological and affective behavioral indices have revealed normal subjective and autonomic responses to affect eliciting stimuli in patients with lesions of the amygdala (LaBar & Phelps, 1998; Phelps et al., 1998; Tranel & Damasio, 1989). Amygdala lesions do not impair the normal affective evaluation of negative emotional scenes (Hamann, Cahill, & Squire, 1997; Cahill et al., 1995) and words (LaBar & Phelps, 1998; Tranel & Damasio, 1989) and do not disrupt unconditioned autonomic responses (e.g., galvanic skin responses) to aversive stimulation (LaBar et al., 1995), suggesting that amygdala damage can leave emotional responses largely unimpaired even when affect is directly manipulated. Other evidence consistent with intact emotional responses following amygdala damage comes from the study of affective facial efference. Although amygdala lesions have been shown to impair the appraisal of fearful facial expressions (Anderson & Phelps, 2000a; Broks et al., 1998; Calder et al., 1996; Adolphs et al., 1994), it leaves the generation of such expressions intact (Anderson & Phelps, 2000a). In contrast with frontal lobe lesions that result in blunted affect, amygdala lesions do not appear to mute affective efference (for a visual example, see Anderson & Phelps, 2000a). Therefore, evidence of intact emotional states following amygdala damage is not restricted to self-reported affect but extends to other modes of affective expression as well.

The Amygdala and Affective Modulatory Influences on Information Processing

At first glance, the present results appear to be at odds with studies that have demonstrated correlations between amygdala response and the intensity of experienced negative affective states. Although the magnitude of amygdala activity has been shown to vary with the degree of subjective emotional experience (e.g., Abercrombie et al., 1998; Zald & Pardo, 1996), such correlations have also been demonstrated with memory retrieval for emotional materials, with greater amygdala

activity during the viewing/encoding of emotional stimuli associated with subsequent greater retrieval success (Hamann et al., 1999; Cahill et al., 1996). Amygdala responses associated with the presentation of affectively significant visual and auditory stimuli have also been shown to covary with activity in extrastriate regions and tonotopically organized auditory cortices, respectively (Morris, Friston, Buchel, et al., 1998; Morris, Friston, & Dolan, 1998). Thus, amygdala activity revealed in neuroimaging studies during elicited affective experience may be correlated but not causally related to the generation of affective states.

In particular, we suggest that amygdala activation revealed during affective challenges may be indicative of its more general neuromodulatory role in information processing (Cahill & McGaugh, 1998; Whalen, 1998; Packard, Cahil, & McGaugh, 1994; Kapp, Wilson, Pascoe, Supple, & Whalen, 1990). This perspective is consistent with substantial evidence demonstrating that patients with amygdala lesions do not show normal enhanced memory for emotionally arousing events (LaBar & Phelps, 1998; Phelps et al., 1998; Adolphs, Cahill, Schul, & Babinsky, 1997; Hamann et al., 1997; Cahill et al., 1995). Recent evidence from our laboratory suggests that lesions of the amygdala also disrupt enhanced perceptual awareness of aversive and arousing stimulus events typically found in normal subjects (Anderson & Phelps, 2001). In a review of neuroimaging studies revealing amygdala activation, Whalen (1998) has persuasively argued that the amygdala's role is most accurately construed as a neuromodulator of information processing, whether that be mnemonic or perceptual, and is not simply tied to the generation of affective states (see also Drevets & Raichle, 1998; Servan-Schreiber, Perlstein, Cohen, & Mintun, 1998, for other contrary evidence). Thus, correlations between the amygdala and degree of subjective emotional response may reflect the benefits arousal bestows on perceptual encoding and later memory retrieval, suggesting the amygdala's role in humans is more related to affective influences on the efficacy of information processing.

Possible Differing Roles of the Amygdala in Human and Nonhuman Animals

In conclusion, the present results contrast with a growing body of functional neuroimaging evidence that implicates the human amygdala in emotional experience. It is often tacitly assumed that damage to the amygdala in humans results in substantial alterations in emotional behavior and affective experience. This view is likely due in part to evidence of drastic changes in emotional behavior following amygdala damage in nonhuman animals, where there are reports of substantial changes in emotional reactivity, such as a loss of fear for previously fear-evoking stimuli (e.g., Zola-Morgan, Squire, Alvarez-Royo, & Clower, 1991; Blanchard & Blanchard, 1972; Weiskrantz, 1956; Kluver & Bucy, 1937). The results of the present study regard introspective emotional experiences that are associated with complex internal and external factors and are not easily tied to simple perceptual evaluations. Unlike lower animals whose affective responses may be more tied to environmental input, human affective experiences are likely more dependent on internal representations of perceived threats and rewards in the absence of direct stimulation. This difference may reflect the evolution of neocortical propositional representations, which allow for the abstract representation of affective contingencies and associated production of phenomenal affective states. Whether patients with amygdala damage use such internal affective representations to respond to their environment optimally may be another matter (see Bechara, Damasio, Damasio, & Lee, 1999). Nonetheless, due to the ability to represent affective schema without direct perceptual stimulation, the complexity and richness of human emotional life do not appear to be supported by the amygdala alone.

METHODS

Experiment 1: Dispositional Affective Traits

Participants

Unilateral TLP. Twenty patients (age = 38.1 ± 9.8, education = 14.0 ± 3.2, 7 men and 13 women) with refractory complex partial seizures of medial temporal lobe origin were studied 2–8 years following en bloc temporal lobe resection (10 left hemisphere [LTL] and 10 right hemisphere [RTL]). Prior to their surgery, these patients had sustained unilateral damage to the amygdala and hippocampus associated with their seizure activity. Their surgical procedure involved an approximate 3.5-cm resection of the anterior middle and inferior temporal gyri, allowing access to the temporal horn. This was followed by a severing of the occipito-temporal fasciculus and subsequent removal of 70–80% of the amygdala and all of the hippocampus, parahippocampus, and projection fibers to their posterior extent. Twenty nonepileptic healthy subjects age- (40.3 ± 9.4), education- (14.4 ± 2.6), and sex-matched (7 men and 13 women) to the TLPs served as controls.

Patient SP. SP is a 56-year-old, right-handed woman whose seizures began approximately at 3–4 years of age. Her seizures were well controlled until mid-age, allowing SP to live a normal life until her early 40s, raising two children and pursuing a successful career. When her condition worsened, at the age of 48, SP underwent en bloc temporal lobe resection for medically intractable complex partial seizures of right medial temporal lobe origin. The surgical procedure is identical

to that described above for patients with unilateral TLP. Prior to undergoing right medial TLP, SP was diagnosed as having a lesion in her left amygdala. Two separate biopsies in independent locations indicated reactive gliosis extending through a significant portion of her left amygdala. For a more detailed description of this patient, see Phelps et al. (1998).

SP's neuropsychological profile suggests she is within the normal range on measures of general intelligence (WAIS-R, 100 V, 92 P, 97 FS) as well as language and memory functions. Although SP exhibits no evidence of global dysfunction, she has been shown to be impaired on a number of measures of emotional processing attributed to her bilateral amygdala damage. She is impaired on measures of facial affect identification, including expressions of fear (Anderson & Phelps, 2000a), is unable to acquire fear-conditioned responses and does not show normal enhanced memory for emotionally arousing materials (Phelps et al., 1998).

Materials and Procedure

The PANAS developed by Watson et al. (1988) consists of two 10-item mood scales intended to assess positive and negative affective experience, respectively. The PANAS demonstrates sensitivity to changes in both positive and negative affective states accompanying events such as social interaction and perceived stress. Responses to the PA and NA scales have been shown to be largely uncorrelated, and therefore have been interpreted to represent largely independent dimensions of affective experience (Watson et al., 1988). The scales can be administered to assess affective experience over varying time ranges (e.g., at the moment, day, week, over the past year). Assessments of long-term affective traits (i.e., over the past year) have been shown to be highly internally consistent over a 2-month period (Watson et al., 1988).

Participants were presented with the list of 20 affect-related descriptors in a random order fixed for all participants. The positive affect descriptors included: interested, alert, excited, inspired, strong, determined, attentive, enthusiastic, active, and proud. The negative affect descriptors included: irritable, distressed, ashamed, upset, nervous, guilty, scared, hostile, jittery, and afraid. Participants were told that the words described different feelings and emotions and were asked to indicate to what extent they have felt this way during the past year. This time scale was used to assess relatively chronic affective traits. Participants were asked to respond on a scale from 1 (''very slightly or not at all'') to 5 (''extremely'').

In order to obtain a more accurate estimate of SP's dispositional affective traits, SP's responses were acquired from three independent administrations of the PANAS over a 1-year period, each separated by approximately 4 months.

Experiment 2: Daily Fluctuations in Affective States

Participants

SP's PANAS ratings were compared with two female subjects (BD and JA) of similar age (SP = 56 vs. BD = 55 and JA = 56) and education (SP = 14 vs. BD = 12 and JA = 12). Control JA had undergone brain surgery related to an aneurysm in her right occipital lobe in her late 40s.

Materials and Procedure

In order to examine more closely the magnitude and frequency of positive and negative affective states, subjects were asked to keep an affective diary. Each participant was asked to self-administer the PANAS daily, over a 30-day period. Each participant administered the PANAS each evening, surveying the feelings and emotions that they had experienced over the course of that day. In order to maintain some degree of independence across measurements from the 30-day period, participants were asked to not look back over their responses from the preceding days. SP e-mailed her responses to author A. K. A. each evening. During this period, all three participants had reported similar significant events from their lives. For instance, within this 4-week sampling period, each participant had an appointment with a medical doctor and each had attended a funeral of a distant family member.

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Reprint requests should be sent to Elizabeth A. Phelps, Department of Psychology, New York University, 6 Washington Square, New York, NY 10003, USA, or via e-mail: liz.phelps@nyu.edu.

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