Contributions of Amygdala and Striatal Activity in Emotion Regulation

Todd A. Hare, Nim Tottenham, Matthew C. Davidson, Gary H. Glover, and B.J. Casey

Background: Emotional information can facilitate or interfere with cognitive processes. In this study, we examined the influence of emotional information in biasing performance and the biological basis underlying this influence.

Methods: Ten human subjects (five female) were scanned with functional magnetic resonance imaging while performing an emotional go/nogo task.

Results: Subjects were slower to approach fearful target expressions and had more difficulty avoiding happy nontarget expressions. The amygdala was recruited most for negative emotional context, and activity in this region was positively correlated with response time when detecting negative expressions. Increased signal in the right caudate nucleus was observed when avoiding nontargets and was negatively correlated with the number of false alarms subjects made.

Conclusions: Emotional context can alter behavioral and biological responses when approaching or avoiding a stimulus. We showed that recruitment of the amygdala, a region implicated in evaluating emotional significance, was associated with longer response latencies when approaching negative information, whereas recruitment of the caudate nucleus, a structure previously implicated in reward and impulse control, was most active when avoiding positive information. Our findings have significant implications for exaggerated and inhibited emotional responses that are characteristic of a number of psychiatric disorders.

Key Words: Amygdala, striatum, emotion regulation, go/nogo, fMRI

Emotional values assigned to objects and events play an important role in cognitive processes. Interpretations of objects and events, however, can change as a function of emotional context (Kim et al. 2004; Russell and Fehr 1987). The psychologic construct of emotion regulation has been defined as the dynamic influences between emotions and other psychologic or physiologic processes (Campos et al. 1994; Cole et al. 1994; Fox 1994). As such, emotion regulation is not the simple presence of an emotion like happiness or sadness, but the manner in which an emotion facilitates or interferes with other processes (Cole et al. 1994; Frijda 1988). Processes like cognitive or attentional control (Derryberry and Rothbart 1988, 1997; Rothbart and Ahadi 1994; Rothbart et al. 1994) and delay of gratification (Mischel 1958, 1961, 1966; Mischel and Metzner 1962; Mischel and Underwood 1974; Toner and Smith 1977; Walls and Smith 1970) can modulate emotional influences and thus play an important role in emotion regulation. The objective of this study was to examine the influence of emotional information in biasing performance during a go/nogo task and the biological basis underlying this influence.

Emotional modulation of cognitive control has been reported as attentional biases to positive and negative information (Derryberry 1988; Mogg et al. 2000). Behavioral responses are faster or slower in different emotional contexts and vary as a function of subject traits (e.g., negative attention bias in affective disorders; Vasey et al. 1996). Attentional bias toward negative or threatening information is hypothesized by some to play a major role in the etiology and maintenance of anxiety and depression (Beck 1967; Bower 1981; Lonigan et al. 2004; Mathews and MacLeod 1994; Vasey and MacLeod 2001; Williams et al. 1997). This bias in the processing of negative emotional information in affective disorders has been assessed through experimental studies examining the behavioral performance of subjects on tasks such as the Emotional Stroop (Williams et al. 1996). Studies from our group have found that positive and negative emotional valence can affect cognitive control in normal populations as well (Casey and Tottenham, unpublished data).

Neuroimaging and lesion studies (see Phillips et al. 2003a) have described neural substrates of affective processing, especially in the amygdala, and demonstrated its influence on behavior (Adolphs et al. 1998; Bechara et al. 2003). Patients with bilateral lesions of the amygdala are impaired in judging emotional facial expressions and make suboptimal decisions (see Bechara et al. 2003). Negatively valenced stimuli increased blood oxygen level–dependent (BOLD) signal in the amygdala, and reaction times to negative stimuli were slower compared with neutral stimuli (Monk et al. 2003; Simpson et al. 2000). Likewise, positively valenced stimuli can also increase activity in regions of the amygdala (Breiter et al. 1996; Canli et al. 2002; Garavan et al. 2001; Killgore and Yurgelun-Todd 2001; Pessoa et al. 2002; Somerville et al. 2004; Whalen et al. 1998b; Yang et al. 2002), and happy expressions (positive stimuli) have been found to speed reaction times (Casey and Tottenham, unpublished data) and bias decisions (O’Doherty et al. 2003). Thus the amygdala plays an important role in the processing of emotional information, although amygdala activity and emotional influences can be attenuated by other cognitive processes (Hariri et al. 2000). Decreases in amygdala activity are seen when subjects attempt to reduce emotional responses to affective stimuli (Beauregard et al. 2001; Levesque et al. 2003; Ochsner et al. 2002; Schaefer et al. 2002). Performing a cognitive task can also reduce the amygdala response to emotional stimuli (Hariri et al. 2000, 2003; Monk et al. 2003). Understanding the interactions between cognitive and emotional processes is important for understanding behavior in both normal and clinical populations. Therefore, the details of these cognitive and emotional interactions have become the focus of an increasing number of studies but at this point remain unclear.
In the current study, we used functional magnetic resonance imaging (fMRI) to examine the neural processes involved in approaching and avoiding positive or negative emotional stimuli, with the goal of examining the mechanisms of interaction between cognitive control processes that work to regulate behavior and emotional processes that assign value to objects and actions. Functional neuroimaging studies have found that emotional facial expressions reliably activate the amygdala and related emotion processing networks (Breiter et al 1996; Canli et al 2002; Killgore and Yurgelun-Todd 2001; Morris et al 1996; Phillips and David 1997; Phillips et al 1998; Whalen et al 1998b, 2001; Yang et al 2002). Therefore, we designed a version of the go/nogo task with emotional facial expressions as stimuli. We hypothesized that emotional valence would bias behavioral responses when approaching or avoiding stimuli. Happy faces are positive approach–related stimuli, whereas fearful faces are negative and alarming stimuli (Davidson et al 1990). Thus we predicted that subjects would respond more slowly when pressing to (approaching) fearful faces relative to happy or neutral faces and that subjects would have more difficulty withholding responses to (avoiding) nogo (nontarget) faces with happy expressions. In parallel, we predicted that successfully inhibiting responses to happy nontargets would be associated with increased BOLD signal in frontostriatal regions involved in inhibitory control (Casey et al 1997b; Vaidya et al 1998) and that processing of negative expressions would be associated with enhanced amygdala activity. Furthermore, we hypothesized that increased amygdala activation would interfere with cortical functions and be associated with impaired task performance in terms of reaction time to negative expressions.

Methods and Materials

Subjects

Subjects were 10 right-handed adults (5 female) aged 25.2 ± 1.99 years (mean ± SD). All subjects were screened for current or past psychiatric, neurologic, or medical illness. In addition, all subjects scored within the normal range on the State-Trait Anxiety Inventories (Spielberger et al 1988). All subjects provided informed written consent for participation. This investigation was conducted in accordance with the guidelines established by the institutional review board of Weill Medical College of Cornell University. Because of technical difficulties, behavioral responses were unavailable for a portion of one subject’s data.

Stimuli and Apparatus

Face stimuli consisted of gray-scaled fearful, happy, and neutral expressions from 12 individuals (6 female; The identities of the faces used were numbers: 6, 8, 11, 14, 15, 16, 27, 36, 39, 43, 44, and 45) taken from the NimStim set available at www.macbrain.org (Figure 1). Four models (two female) were used from each of the following races: African American, Asian, and Caucasian. All images were normalized for size and luminance. Subjects viewed images projected onto an overhead liquid crystal display panel with the Integrated Functional Imaging System–Stand Alone (IFIS-SA; MRI Devices, Waukesha, Wisconsin). A fiber optics response box was used for recording behavioral responses. Foam padding around the head was used to reduce motion.

Procedure

Written instructions were displayed on the overhead liquid crystal display panel inside the magnet before the beginning of each run, instructing subjects to respond to the target facial expression (fearful, happy, or neutral) by pressing the right thumb whenever it appeared on the screen and not to press for any other facial expression. Each run contained one block in which subjects responded to the specified emotional expression. Subjects were reminded before each run to respond as fast as possible without making mistakes. During each 170-sec functional run, 60 stimuli were presented for 500 msec with a 2-sec interstimulus interval (ISI). During the ISI, a fixation cross was presented on an otherwise blank screen. Stimuli were presented in a pseudorandom order parametrically manipulated as in Durston et al (2002) with go trials (targets) occurring on 70% of the trials. Subjects participated in two different scan sessions and completed eight separate functional runs per scan session (for 9

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Figure 1. Temporal layout of stimulus presentations within a scan in which fearful expressions were the targets and happy expressions were the nontargets.
of the 10 subjects, the two scan sessions were on different days). One session included counterbalanced runs of responding to fearful target faces in the presence of happy or neutral nontargets (fearful target/happy nontarget and fearful target/neutral nontarget, respectively) and responding to happy or neutral target facial expressions in the presence of fearful nontargets (happy target/fearful nontarget and neutral target/fearful nontarget, respectively).

Behavioral Data Analysis

The behavioral data were analyzed with a repeated measures general linear model (GLM) with emotional context (fearful target/happy nontarget and fearful target/neutral nontarget, happy target/fearful nontarget, and neutral target/fearful nontarget) as the within-subjects factor. Post hoc t tests were performed on significant main effects.

Image Acquisition and Analysis

Subjects were scanned with a General Electric Signa 3.0-Tesla fMRI scanner (General Electric Medical Systems, Milwaukee, Wisconsin) with a quadrature head coil. A whole brain, high resolution, T1-weighted anatomic scan (three-dimensional spoiled gradient; 256 × 256 inplane resolution, 240 mm field of view [FOV]; 124 mm × 1.4 mm axial slices) was acquired for each subject for transformation and localization of functional data into Talairach space (Talairach and Tournoux 1988). A spiral in-and-out sequence (Glover and Thomason 2004) was used to collect functional data (repetition time = 2500 msec, echo time = 30 msec; FOV = 200 mm, flip angle = 90°, 64 × 64 matrix). We obtained 34 4-mm-thick coronal slices (skip 0) with an inplane resolution of 3.125 × 3.125 mm covering the entire brain except for the tip of the frontal pole and the posterior portion of occipital lobe. Inplane T1-weighted anatomic images (256 × 256 inplane resolution, FOV = 200 mm) were also acquired with the same prescription as the functional images.

The Brainvoyager QX (Brain Innovations, Maastricht, The Netherlands) software package was used to perform a random effects analysis of the functional data. Before analysis, preprocessing procedures were performed on the raw functional images, including slice scan time correction (with sinc interpolation); linear trend removal; high-pass temporal filtering to remove nonlinear drifts of three or fewer cycles per time course; spatial data smoothing with a Gaussian kernel with a 4-mm full width at half maximum; and three-dimensional motion correction to detect and correct for small head movements by spatial alignment of all volumes to the first volume by rigid body transformation. Estimated rotation and translation movements were less than 2 mm for all subjects in this analysis. Functional data were co-registered to the anatomic volume by alignment of corresponding points and manual adjustments to obtain optimal fit by visual inspection. Functional data were then transformed into Talairach space with coordinates defined on the anatomic volume. During Talairach transformation, functional voxels were interpolated to a resolution of 1 mm.

Statistical analysis of the functional data was performed with a GLM comprising 159 (16 runs × 10 subjects [data from one run was lost because of technical problems]) functional time courses. Signal values in each time course were normalized to z scores representing a change from the mean signal for that run. The signal values after presentation of the target and nontarget stimuli were considered the effects of interest. The corresponding predictors, obtained by convolution of an ideal boxcar response (assuming a value 1 for the volume of task presentation and a volume of 0 for the remaining time points) with a linear model of the hemodynamic response (Boytont al 1996), were used to build the design matrix of each time course in the experiment.

To analyze the effect of conditions compared with one another, predictors were created specifying the sequence of conditions across all runs. Only correct trials were included in these conditions, and separate predictors were created for error trials. After creating predictors, three-dimensional group statistical maps were generated by assigning an F value to each voxel corresponding to the specific set of predictors and calculated on the basis of the least mean squares solution of the GLM. Contrast analyses were then performed based on t test differences between the β weights of predictors to identify regions that showed greater activity for targets versus nontargets or between target and nontargets in different emotional contexts. Contrasts were conducted with a random effects analysis, and a contiguity threshold of 50 voxels was used to correct for multiple comparisons (Forman et al 1995). Percent changes in the BOLD signal were calculated for selected regions of interest defined from clusters of significantly active voxels obtained from the contrast analyses. Percent signal changes shown for each condition represent the average for voxels in the region of interest across all subjects and runs.

Results

Behavioral Results

A repeated measures GLM demonstrated a main effect of target emotion (fearful, happy, or neutral) on reaction time \( F(3,27) = 4.451, p < .05 \) (Figure 2). To test our hypothesis that subjects would be slower to approach fearful targets, we com-
pared responses to fearful targets versus happy and neutral targets. Because response times to happy and neutral targets did not differ, they were combined \((p = .55)\). Mean reaction times were slower when subjects had to respond to (approach) fearful targets \((500 \text{ msec})\) than when they had to approach happy and neutral targets \((448 \text{ msec})\) \(t(9) = 2.301, p < .05\).

There was also a main effect of nontarget emotion (fearful, happy, or neutral) on the number of false alarms (FA) made to nontarget trials \(F(3,27) = 3.116, p < .05\) (Figure 3). To test our hypothesis that subjects would make more FA to happy expressions we compared accuracy for happy nontargets with that of fearful and neutral nontargets. Again, because FA to fearful and neutral nontargets did not differ they were combined \((p = .49)\). Mean accuracy was worse when withholding responses to happy nontarget trials \((89\%)\), compared with fearful and neutral nontarget trials \((93\%)\) \(t(9) = 2.516, p < .05\).

To determine the effects of emotion on the relationship between response time and accuracy, correlations between these two variables were examined in each of the four conditions (fearful target/happy nontarget, fearful target/neutral nontarget, happy target/fearful nontarget, and neutral target/fearful nontarget). For fearful target/happy nontarget blocks there was a negative correlation between reaction time to fearful target trials and the number of FA made to happy nontarget trials \((r = - .658, p < .04)\).

**Imaging Results**

Blood oxygen level–dependent signal in the amygdala varied as a function of target and nontarget valence. Figure 4 shows greater increases in BOLD signal in the right ventral amygdala and cingulate cortex \((p < .01)\) for go trials in blocks that included negative valence (fearful target/neutral nontargets and neutral target/fearful nontargets) versus blocks that included positive and negative valence (happy target/fearful nontarget and fearful target/happy nontarget; at less stringent statistical thresholds, a similar pattern of activation was observed in the left amygdala as well). Blood oxygen level–dependent signal levels in the amygdala were related to behavioral performance. Percent signal increase in the right amygdala for fearful and neutral target trials correlated with mean reaction time \((r = .464, p < .05)\), with more amygdala activity associated with slower responses (Figure 5).

Consistent with previous imaging studies using go/nogo tasks, target trials relative to nontarget trials were associated with increased BOLD signal in the contralateral motor cortex and ipsilateral cerebellum \((p < .0032)\) (Table 1). The contrast of nontarget relative to target trials showed increased BOLD signal in the inferior frontal gyrus and anterior cingulate cortex \((p < .01)\) regardless of emotional context (Table 1; see Supplementary Figures 1 and 2, online only). Increased signal in the right caudate nucleus \((p < .02)\) was seen for nontarget trials relative to target trials in fearful target/happy nontarget and fearful target/fearful nontarget blocks (Figure 6). Figure 7 shows that the percent of FA made to nontarget trials in blocks with fearful and happy stimuli was negatively correlated with the percent signal increase in the right caudate \((r = -.504, p < .04)\). Finally, increased BOLD signal in the ventral striatum \((p < .02)\) was seen in response to happy expressions relative to fearful expressions, regardless of stimulus type (i.e., target or nontarget) (Figure 8).

**Discussion**

In this study, we examined the influence of emotional context on approaching or avoiding stimuli in a go/nogo task. We showed that subjects were slower to approach fearful target expressions and had more difficulty avoiding happy nontarget expressions. Activation in regions of the brain involved in emotion regulation corresponded with these behavioral effects. Negative emotional context recruited greater amygdala activation, and this activity correlated with reaction time to negative expressions, such that increased amygdala activity was associated with slower responses. Increased BOLD signal in the caudate nucleus was observed for avoiding happy nontargets. Furthermore, percent BOLD signal increase in the right caudate was negatively correlated with the number of FA subjects made, with those subjects making the fewest FA having more caudate activity, consistent with its role in behavioral inhibition or impulse control (Casey et al. 1997a; Durston et al. 2002b; Vaidya et al. 1998).

Behavioral performance and BOLD signal change in the amygdala were influenced by emotional context. Slower reaction times to fearful facial expressions indicate that approaching a negative stimulus interferes with task performance. A fearful face can be seen as a sign of possible harm due to some as yet unknown danger in the environment (Gray 1987; LeDoux 1998; Whalen et al. 2001). As noted earlier, numerous studies have reported increased activity in the amygdala, a structure involved in directing attention to stimuli signifying potential danger, in response to fearful faces (Breiter et al. 1996; Morris et al. 1996; Phillips and David 1997; Phillips et al. 1998; Whalen et al. 1998b, 2001). We had hypothesized that we would see an increased amygdala response to negative valence, especially fearful faces, and that the level of this response would be related to performance measures like reaction time. Consistent with this hypothesis, increased amygdala activity was seen for fearful and neutral targets, and this activity was associated with slower responses. It might be that signals from the amygdala interfere with cortical activity.
regions involved in task performance. Electrophysiologic studies of fear conditioning in rats (Garcia et al 1999) and recent neuroimaging findings (Kim et al 2003, 2004) have demonstrated inverse relationships between activity in the amygdala and regions of prefrontal cortex, although in the present study we did not find any correlation between activity in cortical regions and reaction time or amygdala activity. This might be due to limitations in our design, discussed further in subsequent sections.

Environmental context affects the emotional interpretation of objects and events (Kim et al, in press; Russell and Fehr 1987). Patterns of neural activity have been shown to differ in response to passive viewing of emotionally ambiguous surprised faces when preceded by negatively valenced versus positively valenced contextual sentences, with negative context producing greater amygdala activation (Kim et al, in press). Furthermore, the pattern of activity in the amygdala was shown to correlate with activity in prefrontal regions, suggesting that prefrontal regions might exhibit context-dependent regulation of the amygdala (Kim et al, in press). Russell and Fehr (1987) showed that the presence of fearful expressions could influence the interpretation of neutral facial expressions. In the current study, the response of the ventral amygdala to the primary expressions of fearful and happy as well as to neutral expressions seems to be modulated by the experimental context. Blood oxygen level–dependent signal in the amygdala increased for all emotional expressions when they were presented as targets compared with presentation of the same stimuli as nontargets.

Differences in the amygdala response to emotional expressions as target and nontarget might reflect the engagement of prefrontal regions involved in suppressing responses to nontargets. In several previous studies, task demands have influenced levels of activity in the amygdala (Bush et al 1998, 2000; Hariri et al 2000, 2003; Lange et al 2003; Simpson et al 2001a, 2001b; Whalen et al 1998a). This interpretation could also explain the differential response of the amygdala to fearful targets in neutral versus happy nontargets. Within the right ventral amygdala, fearful target expressions embedded in neutral nontargets were associated with the greatest signal increase, whereas when the same fearful targets were embedded in happy nontarget faces there was no significant signal increase. These fearful target/happy nontarget blocks were also more difficult than other blocks, as indicated by lower accuracy and increased frontostriatal recruitment on correct trials. Greater recruitment of frontostriatal regions might have served to suppress amygdala activation on target trials in addition to nontarget trials. Figures 4 and 6 show a pattern of decreased amygdala activation in blocks with increased frontostriatal activity. A caveat to the interpretation of decreased amygdala activity in fearful target/happy nontarget versus fearful target/neutral nontarget blocks is that this decreased signal change could be due to increased amygdala activation for happy compared with neutral nontargets. Increased amygdala

Figure 4. Increased activation in the right amygdala for fearful and neutral faces compared with fearful and happy faces. The graph shows mean (± SEM) percent signal change in the right amygdala for target trials in each emotional context. The target (T) expression is labeled on the x-axis, and the y-axis represents the percent blood oxygen level–dependent (BOLD) signal increase. NT, nontarget.

Figure 5. Scatter plot depicting the correlation between percent signal change in the amygdala for target trials in blocks in which subjects responded to fearful targets in neutral nontargets and neutral targets in fearful nontargets and reaction time for target trials in these blocks (r = .464, p < .05). The x-axis represents percent signal change in the right amygdala, and the y-axis represents reaction time in milliseconds.
Differences in the response of the ventral amygdala to happy characteristics as well as the emotional valence of a stimulus. Happy and fearful facial expressions. The percent signal change in the right caudate was also increased when successfully inhibiting a response to happy nontargets and was negatively correlated with the number of FA committed. These results suggest that avoiding a positively valenced facial expression, like happy, is more difficult and requires more inhibitory control, than avoiding facial expressions with neutral or negative valence in normal adults. Given that accuracy in blocks of avoiding fearful nontarget expressions embedded in happy target expressions did not differ from blocks that mixed fearful and neutral expressions, it is unlikely that the difference in performance for avoiding happy nontargets embedded in fearful targets was due solely to perceptual similarity. Rather, we suggest that the positive nature of happy facial expressions might be the reason it is more difficult to inhibit responses to them. Happy faces are associated with positive affect and reward (O’Doherty et al. 2003). Increased activity in the ventral striatum is associated with reward processing (see Montague and Berns 2002 for review) and was found here in response to happy expressions, indicating that subjects might have interpreted happy faces as rewarding. Situations and stimuli that are viewed as rewarding are instinctively approached. Thus, having to overcome the natural tendency to approach a rewarding stimulus might make inhibiting responses to happy faces more difficult than to nonrewarding expressions like fearful or neutral. Responding to happy targets might also make inhibiting responses to nontargets more difficult. The greatest caudate activity was seen when subjects inhibited responses to fearful nontarget expressions in the context of happy targets, whereas no increase in caudate activation was seen when inhibiting responses to fearful nontargets embedded in neutral targets. Thus, the increase in caudate activity is not specific to withholding responses to fearful faces, but might instead be related to responding to happy targets. As we discussed above, approaching positive stimuli is a natural tendency, and responding to happy targets on the majority of trials could serve to strengthen the tendency to respond. Therefore, it would become more difficult to suppress this prepotent response tendency when infrequent nontarget trials are presented. The correlation between caudate activity and accuracy in happy target/fearful nontarget blocks supports the idea that the caudate is involved in overcoming the prepotent response to happy targets. Future work on whether this pattern holds in populations with affective disorders such as anxiety and depression would be informative as to how which emotional information might differentially bias behavior in these populations.

Table 1. Localization of Regions of Interest for Contrasts of Go Versus Nogo Trials and for Contrasts of Fear, Neutral, and Happy Emotional Stimuli

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Region of Interest</th>
<th>Brodmann</th>
<th>Side</th>
<th>Cluster Sizea</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>(t) (df = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Go Versus Nogo</td>
<td>Cerebellum</td>
<td></td>
<td>R</td>
<td>6,269</td>
<td>16</td>
<td>-53</td>
<td>-21</td>
<td>7.849</td>
</tr>
<tr>
<td></td>
<td>Motor/sensory cortex</td>
<td>2-4</td>
<td>L</td>
<td>13,115</td>
<td>-42</td>
<td>-27</td>
<td>39</td>
<td>10.548</td>
</tr>
<tr>
<td>Nogo Versus Go</td>
<td>IFG</td>
<td>47</td>
<td>R</td>
<td>103</td>
<td>25</td>
<td>33</td>
<td>-2</td>
<td>4.503</td>
</tr>
<tr>
<td></td>
<td>IFG</td>
<td>47</td>
<td>L</td>
<td>101</td>
<td>-27</td>
<td>35</td>
<td>-1</td>
<td>4.757</td>
</tr>
<tr>
<td></td>
<td>ACC</td>
<td>32</td>
<td>R</td>
<td>209</td>
<td>11</td>
<td>35</td>
<td>18</td>
<td>5.350</td>
</tr>
<tr>
<td>Nogo Versus Go(^{b})</td>
<td>Caudate Nucleus</td>
<td></td>
<td>R</td>
<td>64</td>
<td>11</td>
<td>11</td>
<td>-1</td>
<td>2.144</td>
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<tr>
<td></td>
<td>IFG</td>
<td>47</td>
<td>R</td>
<td>245</td>
<td>26</td>
<td>30</td>
<td>-3</td>
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<tr>
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<td>35</td>
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<td>Fear and Neutral Targets Versus</td>
<td>Amygdala</td>
<td></td>
<td>R</td>
<td>145</td>
<td>22</td>
<td>0</td>
<td>-16</td>
<td>5.196</td>
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<tr>
<td>Fear and Happy Targets</td>
<td>Cingulate</td>
<td>24</td>
<td>L</td>
<td>670</td>
<td>-7</td>
<td>-1</td>
<td>49</td>
<td>6.597</td>
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<tr>
<td>Happy Versus Fear</td>
<td>Ventral striatum</td>
<td></td>
<td>R</td>
<td>157</td>
<td>12</td>
<td>8</td>
<td>-6</td>
<td>4.493</td>
</tr>
</tbody>
</table>

* Taalairach coordinates listed are center-of-mass for that ROI. R, right; L, left; IFG, inferior frontal gyrus; ACC, anterior cingulate cortex.
* Voxel size is 1 mm³.
* Fearful target/happy nontarget and happy target/fearful nontarget blocks only.
Limitations

One limitation of this study is that there were no blocks that included only positive valence. Therefore, behavioral performance and frontostriatal activity when avoiding happy nontargets embedded in neutral targets or vice versa could not be assessed. In addition, this limitation prevented us from examining the amygdala response to happy expressions relative to neutral expressions, which would have aided in our interpretations of the differences in amygdala activation. It will be important for future studies to determine how both positive and negative emotional contexts modulate behavior and activity in the amygdala. A related limitation is the absence of sufficient fixation for use as a baseline comparison. Finally, the present design does not permit us to deconvolve the hemodynamic response to individual trials. Future studies using long event-related or variable ISI designs might have more sensitivity to examine the effects of amygdala activity on neural activity in cortical regions.

In sum, emotional context can alter behavioral and biological responses when approach and avoidance decisions are made. We have shown that the amygdala response depends on the valence of the stimulus and context and that increased amygdala activity in response to negative valence impairs behavioral performance. Our results also suggest that positive, rewarding stimuli can provoke impulsive behavior. Finally, frontostriatal regions previously shown to play a role in behavioral regulation are shown here to facilitate emotion regulation as well.

Clinical Implications

Dysfunctions in the amygdala and frontostriatal networks have been implicated in numerous psychiatric disorders (see Phillips et al 2003b for review). Studies with fMRI have been instrumental in ascertaining the neurobiology of psychiatric disorders. For example, facial expressions have been used to show exaggerated amygdala responses to negative stimuli in patients with posttraumatic stress disorder (Rauch et al 2000). This exaggerated amygdala response in posttraumatic stress...
disorder is hypothesized to occur because of insufficient regulation of subcortical systems by prefrontal regions (Bremner 1999; Rauch et al 2000; Shin et al 1999, 2004). It is important to determine how emotional cues or contexts can trigger behavioral and neural responses that seem dysregulated in affective disorders (Thomas et al 2001) and also implicated in addiction (Breiter et al 2001). Imaging studies, like the one reported here, can aid our understanding of the role of the amygdala and frontal striatal networks in emotion regulation during normal cognitive processes and establish a point of reference for determining the perturbations that underlie psychiatric disorders.

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