Negative Urgency Mediates the Relationship between Amygdala and Orbitofrontal Cortex Activation to Negative Emotional Stimuli and General Risk-Taking

Melissa A. Cyders1, Mario Dzemidzic2,4, William J. Eiler2, Ayca Coskunpinar1, Kenny A. Karyadi1 and David A. Kareken2,3,4

1Indiana University Purdue University, Indianapolis, IN, USA, 2Department of Neurology, 3Department of Psychiatry, and 4Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, USA

Address correspondence to Melissa A. Cyders, Department of Psychology, Indiana University-Purdue University Indianapolis, 402 N. Blackford St. LD 124, Indianapolis, IN 46202, USA. Email: mcyders@iupui.edu

The tendency toward impulsive behavior under emotional duress (negative and positive urgency) predicts a wide range of maladaptive risk-taking and behavioral disorders. However, it remains unclear how urgency relates to limbic system activity as induced from emotional provocation. This study used functional magnetic resonance imaging to examine the relationship between brain responses to visual emotional stimuli and urgency traits. Twenty-seven social drinkers (mean age = 25.2, 14 males) viewed negative (Neg), neutral (Neu), and positive (Pos) images during 6 fMRI scans. Brain activation was extracted from a priori limbic regions previously identified in studies of emotional provocation. The right posterior orbitofrontal cortex (OFC) and left amygdala were activated in the [Neg>Neu] contrast, whereas the left posterior OFC was activated in the [Pos>Neu] contrast. Negative urgency was related to the right lateral OFC (r = 0.43, P = 0.03) and the left amygdala (r = 0.39, P = 0.04) [Neg>Neu] activation. Negative urgency also mediated the relationship between [Neg>Neu] activation and general risk-taking (regression weights = 3.42 for right OFC and 2.75 for the left amygdala). Emotional cue-induced activation in right lateral OFC and left amygdala might relate to emotion-based risk-taking through negative urgency.

Keywords: emotion, externalizing, fMRI imaging, impulsivity, risky behaviors

Introduction

Negative and positive urgency are personality traits characterized by tendencies to act rashly in the face of extreme negative or positive emotions, respectively (Cyders and Smith 2008a). These traits have been shown to be common risk factors for a wide range of risk-taking behaviors, including problematic alcohol use (see a review by Coskunpinar et al. 2013), binge eating (see a review by Fischer et al. 2008), gambling (e.g., Cyders and Smith 2008b; Fischer and Smith 2008; Michalczyk et al. 2011), sexual risk-taking (e.g., Zapolski et al. 2009; Dir et al. 2013), and drug use (e.g., Verdejo-Garcia et al. 2007; Zapolski et al. 2009). In particular, urgency has been shown to be the most important impulsivity-related trait for maladaptive and problematic levels of risk-taking (Cyders and Smith 2008a) and has been implicated in multiple clinical disorders (see Zapolski et al. 2010 for a review) such as borderline personality disorder (e.g., Peters et al. 2013), alcohol and substance dependence (e.g., Cyders et al. 2007; Verdejo-Garcia et al. 2007), bulimia (e.g., Fischer et al. 2007; Anestis et al. 2009), and antisocial personality disorder (Whiteside et al. 2005).

Despite its clinical relevance, the brain systems related to urgency traits are not yet well understood. Using functional magnetic resonance imaging (fMRI), the current study examines how urgency is related to brain responses induced by emotionally provocative stimuli, and, in turn, how both urgency and these brain responses relate to general risk-taking. Understanding how urgency and limbic activation from emotional stimuli are inter-related sheds light on the underlying mechanisms leading toward emotion-based risk-taking behaviors.

A growing body of evidence examines how urgency is related to and influenced by the frequency and intensity of emotional experiences. First, Cyders and Smith (2007) found that negative and positive urgency loaded onto the Neuroticism domain of the NEO Personality Inventory-Revised (NEO-PI-R; Costa and McCrae 1992). Although clearly overlapping with negative affectivity, much variance in urgency nevertheless remained unexplained by the additive or interactive effects of Neuroticism and lack of planning (72–85% variance remained for positive urgency and 45–61% variance remained for negative urgency). Second, we (Cyders et al. 2010) reported that, although positive urgency predicted increased alcohol consumption in response to positive mood induction, positive urgency was unrelated to baseline mood, and to mood state changes following manipulation. Third, urgency appears to be a unique predictor of risk-taking behavior, independently of emotion frequency/intensity, and it predicts risk-taking over and above the additive and interactive effects of lack of planning and the frequency/intensity of reported emotions (Cyders and Coskunpinar 2010). These cumulative data suggest that urgency shares only a small amount of variance with the experience of emotional responses, per se, and that its relationship to risk-taking persists after controlling self-reported emotional fluctuations or changes in stimulus-induced emotional states.

However, thus far the relationship between urgency and the experience of emotional responses has been based primarily on subjectively rated emotional states that are likely affected by self-report and expectancy biases. Therefore, the current study sought to examine how urgency relates to brain activation from emotionally provocative images, as derived from the International Affective Picture System (IAPS; Lang et al. 1997). Such emotionally charged scenes (positive or negative) induce activation within the visual system (occipital cortex, primarily Brodmann’s Areas 18 and 19, the calcarine cortex, the fusiform gyrus [Lan et al. 1997; Reiman et al. 1997; Lang et al. 1998; Phan et al. 2002]) and in limbic regions such as the amygdala, orbitofrontal cortex (OFC), and cingulate cortex (see meta-analyses by Sabatinelli et al. 2011).

Urgency itself has been theorized to be related to multiple brain regions, including the medial, ventromedial, dorsolateral, and orbitofrontal regions (Levesque et al. 2003, 2004; Ochsner et al. 2004; Kim and Hamann 2007; Mak et al. 2009), the anterior cingulate cortex (Levesque et al. 2004), and the amygdala (Ochsner et al. 2004) (see a review by Karyadi et al. 2012). Emerging empirical data have been somewhat inconsistent.
Joseph et al. (2009) reported reduced blood oxygen level-dependent (BOLD) responses to a mixture of positively and negatively valenced high-arousal stimuli in the anterior and medial OFC and anterior cingulate. On the other hand, Albein-Urios et al. (2013) found that negative urgency was positively related to amygdala activation during negative emotion maintenance and reappraisal. We recently reported that negative urgency is related to increased ventromedial (limbic) prefrontal cortex activation from alcoholic drink aromas and that the relationship between this activation and both alcohol cravings and problematic alcohol use is mediated by negative urgency (Cyders et al. 2013). This suggests that neural responses to alcohol cues might increase cravings and problematic alcohol use by way of tendencies to engage in risky behaviors in response to negative emotion.

As this prior report focused on the appetitive stimuli of alcoholic drink aromas, we re-analyzed data from Cyders et al. (2013) to instead examine brain responses to the emotionally charged visual stimuli used to induce mood (and in theory, states of urgent behavior). In particular, we examined how positive and negative urgency relate to BOLD responses to visual emotional stimuli in the OFC and the amygdala. We hypothesized that urgency would be related to activation in these areas to either positive or negative emotional stimuli. Finally, we hypothesized that urgency would mediate the relationship between activation in these regions and self-reported risk-taking behaviors.

**Materials and Methods**

**Participants**

Thirty-eight right-handed healthy social drinkers (drinking at least 1–3 drinks per week and 1 incidence of drunkenness over the previous month, but excluding alcohol dependence and maternal alcoholism) between the ages of 21 and 35 were recruited, and 30 completed all study procedures. The participants who completed the study did not differ from non-completers on any demographic variables (P-values ranged from 0.19 to 0.86), number of drinks per week (t = −0.58, P = 0.57), or family history of alcohol problems (χ² = 0.40, df = 1, P = 0.53). Three subjects whose head motion during functional imaging exceeded peak-to-peak translations of 2 mm, and rotations of 2° were excluded from supplementary Table for images used and developmental ratings. In verifying that the images selected were sufficiently different in their intended characteristics, a 3 (Positive, Neutral, and Negative mood condition) × 2 (valence and arousal developmental ratings) repeated measures analysis of variance on the developmental ratings indicated a main effect of mood condition (F = 502.60, P < 0.001), and an interaction between mood condition and rating (F = 448.63, P < 0.001). Follow-up paired t-test comparisons confirmed that positive image valence and arousal ratings were significantly higher than ratings of the neutral and negative images (t = 23.81, P < 0.001 and t = 42.26, P < 0.001, respectively); negative valence ratings were lower than the neutral valence ratings (t = 32.24, P < 0.001), and negative arousal ratings were higher than the neutral arousal ratings (t = 19.60, P < 0.001). Positive arousal ratings were significantly higher than neutral valence ratings (t = 23.03, P < 0.001), but there was no significant difference between positive and negative image arousal ratings (t = 1.79, P = 0.08).

**Procedure**

**Study Sessions**

All procedures were approved by the Indiana University Institutional Review Board. Participants completed 2 sessions, a screening session and an imaging session. In screening sessions, participants completed a series of self-report questionnaires, as well as a urine drug and pregnancy tests to assess eligibility for the imaging session. Upon meeting inclusion criteria, participants were scheduled for imaging (average of 32 days post-screening session) and asked to refrain from alcohol consumption for 3 days prior to imaging. On the imaging day, participants reported to the Indiana University Clinical Research Center between 8 and 10 a.m., and were provided with a light, standardized breakfast. Vitals and repeat drug and pregnancy urine screens were conducted.

Participants were then escorted to the imaging suite, where they rated their current mood and were exposed to the odors and 3 sample images (1 from each mood condition—Positive, Negative, and Neutral) that they would encounter during imaging (see below). Odors included the participant’s most frequently consumed alcoholic beverage, grape juice, and sham odorant controls. The details and effects of the odorant presentations are reported elsewhere (Cyders et al. 2013) and will not be reviewed here.

Mood images from the IAPS (Lang et al. 1999) were chosen based on the developmental ratings of valence and arousal provided by Lang et al. 1997. Three image groups were formed: Neutral (mean valence = 5.11, mean arousal = 3.28), Negative (mean valence = 2.55, mean arousal = 5.55), and Positive (mean valence = 6.94, mean arousal = 5.78; see Supplementary Table for images used and developmental ratings). In verifying that the images selected were sufficiently different in their intended characteristics, a 3 (Positive, Neutral, and Negative mood condition) × 2 (valence and arousal developmental ratings) repeated measures analysis of variance on the developmental ratings indicated a main effect of mood condition (F = 502.60, P < 0.001), and an interaction between mood condition and rating (F = 448.63, P < 0.001). Follow-up paired t-test comparisons confirmed that positive image valence and arousal ratings were significantly higher than ratings of the neutral and negative images (t = 23.81, P < 0.001 and t = 42.26, P < 0.001, respectively); negative valence ratings were lower than the neutral valence ratings (t = 32.24, P < 0.001), and negative arousal ratings were higher than the neutral arousal ratings (t = 19.60, P < 0.001). Positive arousal ratings were significantly higher than neutral valence ratings (t = 23.03, P < 0.001), but there was no significant difference between positive and negative image arousal ratings (t = 1.79, P = 0.08).

**Scan Characteristics**

A total of 6 functional imaging scans of combined olfactory/visual stimuli were performed, with a short (∼ 5–10 min) break after the first 3 scans. Two scans were completed for each mood (2 positive mood scans consisting of all positive images from the IAPS [Pos], 2 negative mood scans consisting of all negative images from the IAPS [Neg], and 2 neutral mood scans consisting of all neutral images from the IAPS [Neu]; see also Supplementary Table). Mood condition order was randomly assigned across scans, but randomization was restricted so that
all 3 moods were presented prior to, and again following, the break. Participants first saw 2 s IAPS images, followed by a 2-s odorant trial (alcohol, appetitive control, or sham odorant; see full description in Cyders et al. 2013), and an interstimulus interval ranging from 3 to 10 s. Participants then saw another 2-s IAPS image, followed by another 3- to 10-s interstimulus interval. The presentation of odorant and image repeated a total of 30 times throughout the scan, for a total of 32 images and 30 odorant presentations (10 in each class: alcohol, appetitive control, and sham; see Fig. 1 from Cyders et al. 2013). Between scans, participants again rated current mood.

**Image Acquisition**

BOLD contrast sensitive functional imaging scans were conducted with a 12-channel head coil array on a Siemens 3T Magnetom Trio-Tim scanner (Erlangen). A whole-brain high-resolution anatomic image volume (1.0 × 1.0 × 1.2 mm³ voxels) was first collected using a 3D magnetization prepared rapid gradient echo sequence for anatomic registration of the functional images. For each functional scan, 189 BOLD volumes were acquired in 6:54 min using an echo-planar imaging pulse sequence (gradient echo, 2200/29 ms repetition/echo time, 78° flip angle, 88 × 88 matrix, 2.5 × 2.5 × 3.0 mm³ voxels, 39 slices, GRAPPA acceleration factor 2) that incorporated a 3D prospective acquisition correction to minimize effects of the head motion (Thesen et al. 2000).

**Data Analysis**

Data were analyzed using SPM8 (Wellcome Department of Imaging Neuroscience, University College, London) and PASW Statistics v. 18.0 (SPSS, Inc.). Functional volumes were corrected for differences in slice acquisition timing and rigid-body realigned to the initial volume of the first functional imaging scan to account for residual movement after prospective motion correction. Each subject’s high-resolution anatomic image was co-registered to the reference functional volume (first volume of the first functional scan) and segmented into tissue classes. Nonlinear spatial transformation from native to Montreal Neurological Institute (MNI) space was performed during the segmentation stage, and then those transformation parameters were applied to all BOLD volumes, which were subsequently re-sampled to isotropic (2 mm per side) voxels and smoothed by a 6-mm full-width at half-maximum isotropic Gaussian Kernel. Within-subjects general linear model used SPM’s canonical hemodynamic response function and included both

### Table 1

BOLD activation to positive and negative images contrasted to the neutral image baseline

<table>
<thead>
<tr>
<th>Region</th>
<th>MNI coordinates x, y, z (mm)</th>
<th>Peak significance (unc.)</th>
<th>Cluster size k</th>
<th>Peak voxel Z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>[Neg&gt;Neu] contrast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R Middle occipital gyrus</td>
<td>50, −74, 4</td>
<td>&lt;0.001</td>
<td>10 831</td>
<td>6.05</td>
</tr>
<tr>
<td>R precentral gyrus</td>
<td>44, 6, 30</td>
<td>&lt;0.001</td>
<td>336</td>
<td>4.50</td>
</tr>
<tr>
<td>R OFC</td>
<td>40, 30, −16</td>
<td>&lt;0.001</td>
<td>146</td>
<td>4.41†</td>
</tr>
<tr>
<td>L parahippocampal gyrus</td>
<td>−22, −26, −6</td>
<td>&lt;0.001</td>
<td>76</td>
<td>4.36</td>
</tr>
<tr>
<td>R ventromedial prefrontal cortex</td>
<td>8, 50, −14</td>
<td>&lt;0.001</td>
<td>5</td>
<td>4.32</td>
</tr>
<tr>
<td>R middle temporal gyrus</td>
<td>50, −10, −16</td>
<td>&lt;0.001</td>
<td>71</td>
<td>4.06</td>
</tr>
<tr>
<td>R parahippocampal gyrus</td>
<td>18, −32, −10</td>
<td>&lt;0.001</td>
<td>5</td>
<td>3.96</td>
</tr>
<tr>
<td>R superior frontal gyrus</td>
<td>12, 6, 68</td>
<td>&lt;0.001</td>
<td>7</td>
<td>4.06</td>
</tr>
<tr>
<td>R inferior frontal gyrus</td>
<td>54, 34, −2</td>
<td>&lt;0.001</td>
<td>5</td>
<td>3.69</td>
</tr>
<tr>
<td>R postcentral gyrus</td>
<td>−42, −16, 56</td>
<td>&lt;0.001</td>
<td>5</td>
<td>3.69</td>
</tr>
<tr>
<td>L precentral gyrus</td>
<td>−40, 6, 40</td>
<td>&lt;0.001</td>
<td>19</td>
<td>3.55</td>
</tr>
<tr>
<td>L middle temporal gyrus</td>
<td>−62, −6, −14</td>
<td>&lt;0.001</td>
<td>16</td>
<td>3.45</td>
</tr>
<tr>
<td>R amygdala</td>
<td>16, −8, −12</td>
<td>&lt;0.001</td>
<td>6</td>
<td>3.45*</td>
</tr>
<tr>
<td>R caudate/lateral gyrus</td>
<td>−2, 68, 4</td>
<td>&lt;0.001</td>
<td>6</td>
<td>3.39</td>
</tr>
<tr>
<td>R middle frontal gyrus</td>
<td>38, −2, 58</td>
<td>0.001</td>
<td>10</td>
<td>3.25</td>
</tr>
<tr>
<td><strong>[Pos&gt;Neu] contrast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R middle occipital gyrus</td>
<td>48, −74, 4</td>
<td>&lt;0.001</td>
<td>14 544</td>
<td>6.49</td>
</tr>
<tr>
<td>R inferior frontal gyrus</td>
<td>46, 6, 28</td>
<td>&lt;0.001</td>
<td>222</td>
<td>4.52</td>
</tr>
<tr>
<td>R ventromedial prefrontal cortex</td>
<td>8, 48, −14</td>
<td>&lt;0.001</td>
<td>33</td>
<td>4.51</td>
</tr>
<tr>
<td>L inferior parietal lobule</td>
<td>−28, −56, 52</td>
<td>&lt;0.001</td>
<td>108</td>
<td>4.50</td>
</tr>
<tr>
<td>R OFC</td>
<td>34, 26, −18</td>
<td>&lt;0.001</td>
<td>55</td>
<td>4.29*</td>
</tr>
<tr>
<td>L frontal operculum/insula</td>
<td>−34, 24, −12</td>
<td>&lt;0.001</td>
<td>79</td>
<td>4.14**</td>
</tr>
<tr>
<td>L anterior putamen</td>
<td>−30, 6, −6</td>
<td>&lt;0.001</td>
<td>8</td>
<td>3.93</td>
</tr>
<tr>
<td>R ventromedial prefrontal cortex</td>
<td>10, 60, −8</td>
<td>&lt;0.001</td>
<td>10</td>
<td>3.88</td>
</tr>
<tr>
<td>R middle temporal gyrus</td>
<td>50, −14, −18</td>
<td>&lt;0.001</td>
<td>18</td>
<td>3.73</td>
</tr>
<tr>
<td>L middle temporal gyrus</td>
<td>−64, −12, −16</td>
<td>&lt;0.001</td>
<td>10</td>
<td>3.69</td>
</tr>
<tr>
<td>R ventral anterior thalamus</td>
<td>14, −6, −2</td>
<td>&lt;0.001</td>
<td>10</td>
<td>3.69</td>
</tr>
<tr>
<td>R precentral gyrus</td>
<td>40, 0, 40</td>
<td>&lt;0.001</td>
<td>27</td>
<td>3.65</td>
</tr>
<tr>
<td>L superior frontal gyrus</td>
<td>−34, −2, 42</td>
<td>&lt;0.001</td>
<td>32</td>
<td>3.60</td>
</tr>
<tr>
<td>R inferior parietal lobule</td>
<td>60, −30, 28</td>
<td>&lt;0.001</td>
<td>13</td>
<td>3.52</td>
</tr>
<tr>
<td>L precentral gyrus</td>
<td>−10, 40, 48</td>
<td>&lt;0.001</td>
<td>28</td>
<td>3.51</td>
</tr>
<tr>
<td>L medial prefrontal cortex</td>
<td>−6, 62, 0</td>
<td>&lt;0.001</td>
<td>11</td>
<td>3.49</td>
</tr>
<tr>
<td>L ventromedial prefrontal cortex</td>
<td>−4, 54, −16</td>
<td>&lt;0.001</td>
<td>5</td>
<td>3.43</td>
</tr>
<tr>
<td>R medial Frontal gyrus/SMA</td>
<td>8, 14, 58</td>
<td>&lt;0.001</td>
<td>6</td>
<td>3.34</td>
</tr>
</tbody>
</table>

Note: unc. Uncorrected. Brain regions showing increased BOLD response to negative [Neg>Neu] and positive [Pos>Neu] emotional images when compared with baseline neutral images ($P = 0.001$, $k = 5$). Family-wise error-corrected peak significance ($P_{FWE} < 0.05$) within assessed volume of a priori regions of interest is reached in the OFC (right*, left**) and left amygdala (†). For the [Pos>Neu] contrast, left OFC activation is part of the left frontal operculum/insula cluster. SMA, supplementary motor area; MNI, Montreal Neurological Institute; L, left; R, right.

---

![Figure 1](Image)  
**Figure 1.** Brain regions showing significant [Neg>Neu] and [Pos>Neu] BOLD activation to IAPS images, with a priori regions of interest denoted by circles (blue: left amygdala, yellow and red: left and right OFC, respectively). Display height $P = 0.001$, $k = 5$. For more details see Table 1. No activation was found for [Neu>Neg] and [Neg>Pos] contrasts. Color bar scale represents the $t$-statistic.
image and odorant presentations with events modeled to have 2- and 3-s durations, respectively. However, odorant presentations were treated as events of no interest. Movement parameters from realignment were included as regressors whereas a high-pass filter with a cutoff of 1/128 Hz was applied to each voxel’s time series to remove low-frequency noise.

As prior research suggests the activation of particular limbic brain regions in response to emotionally provocative images (Sabatinelli et al. 2011), we targeted 4 a priori defined regions of interest (ROIs; see Supplementary Figure) in the left and right amygdala and the right and left lateral OFC. ROIs were constructed as 8-mm-radius spheres with MarsBaR utility (Brett et al. 2002; http://marsbar.sourceforge.net/) using OFC (right: [40, 32, 12], left: [−40, 32, −14]) and amygdala (right: [22, −4, −18], left: [−20, −6, −18]) coordinates derived from a meta-analysis by Sabatinelli et al. (2011). The mean BOLD contrasts of [Pos>Neu] and [Neg>Neu] images were first assessed for significant peak effects using voxel-wise analyses, and correcting for family-wise error (FWE) based on the ROI volume. For those ROIs in which peak effects surpassed $p_{FWE} < 0.05$, the mean BOLD contrast values were extracted and then analyzed with SPSS for their relationships with urgency traits, as well as for how urgency might mediate the relationship between brain response and risk-taking.

Results

Self-Report Mood Responses to Images

There were no significant differences between mood ratings across scans of the same mood condition. Valence ratings following the first and the second scan of the same mood condition did not differ from each other and were averaged to create 1 rating for each mood condition. As analyzed in a Mood Condition (3: positive, negative, neutral) × Response Type (2: self-reported valence and arousal) linear-mixed-effects model, there was a significant main effect for Mood Condition ($P < 0.001$) and Response Type ($P = 0.03$), as well as a significant interaction between these 2 factors ($P = 0.001$; also reported in Cyders et al. 2013). Valence ratings following the negative mood condition were significantly lower than following either the neutral ($t = −7.14, P < 0.001$) or positive ($t = −7.46, P < 0.001$) mood conditions; valence ratings following the positive mood condition were also significantly higher than those following the neutral mood condition ($t = 2.53, P = 0.02$). Arousal ratings following both negative and positive mood conditions were higher than those for the neutral mood condition ($t = 2.85, P = 0.01$ and $t = 6.44, P < 0.001$, respectively). Contrary to expectations, arousal ratings following the positive mood condition were significantly higher than arousal ratings following the negative mood condition ($t = 2.60, P = 0.02$).

Negative urgency was significantly related to valence following only the negative mood image condition ($r = −0.42, P = 0.03$); negative and positive urgency were unrelated to the remaining valence and arousal ratings (all $ps > 0.05$). As in previous studies, negative and positive urgency were highly related ($r = 0.56, P = 0.002$).

BOLD Responses to Emotional Images

Using the a priori ROIs to perform small volume corrections ($P_{FWE} < 0.05$), the [Neg>Neu] contrast elicited peak voxel effects in the right lateral OFC ([40, 30, −16], $p_{FWE} = 0.001$) and left amygdala ([−20, −6, −14], $p_{FWE} = 0.022$) (multiple comparison correction across all ROIs was performed by including all voxels within our 4 8-mm-radius spherical ROIs. Peak voxel effects remained significant for the right lateral OFC for the [Neg>Neu] contrast ($p_{FWE} = 0.004$), whereas effects in the left amygdala showed a trend toward significance ($p_{FWE} = 0.087$).

Effects in the right ($p_{FWE} = 0.068$) and left lateral OFC ($p_{FWE} = 0.069$) also showed a trend toward significance (see Fig. 1), whereas left OFC and the right amygdala failed to reach corrected significance. For the [Pos>Neu] contrast, significant peak effects were present in right ([38, 28, −18], $p_{FWE} = 0.017$) and left OFC ([−36, 26, −12], $p_{FWE} = 0.018$). Neither left nor right amygdala nor another potentially interesting limbic region, the anterior cingulate cortex, (a priori hypothesis, we also examined the anterior cingulate as a limbic region of potential interest (Karyadi et al. 2012; Sabatinelli et al. 2013). There were no significant peak effects ($P < 0.001, k = 5$) in this region in [Neg>Neu] or [Pos>Neu] contrasts [using an 8-mm-radius sphere constructed around the MNI coordinate [2, 19, 25], as suggested by Sabatinelli et al. 2013] reached corrected peak significance. Brain activations are depicted in Figure 1 and listed in Table 1.

Relationship of Urgency and BOLD Activation

Mean BOLD contrast in the a priori regions was unrelated to either self-reported valence/arousal ratings or to positive urgency; however, negative urgency was significantly related to the mean [Neg>Neu] BOLD contrast in the right OFC ($r = 0.39, P = 0.04$, Fig. 2) and left amygdala ($r = 0.43, P = 0.03$; Fig. 3).

Relationships with General Risk-Taking

We next conducted a series of 3 separate mediation analyses using the INDIRECT SPSS macro provided by Preacher and Hayes (2008), which uses the product of coefficient approach and bootstrapping to examine the indirect effect. Confidence intervals (95%) that do not contain zero are considered significant indirect effects. Here, we tested negative urgency’s mediation of: (1) mood valence ratings following the negative mood condition on risk-taking, and (2) brain activation on risk-taking. We also tested alternative reverse mediation models for each analysis (i.e., negative urgency as the independent variable and negative mood and brain activation as the mediator).

As hypothesized, negative urgency was a significant mediator of the relationship between mood valence ratings following the negative mood condition and general risk-taking (Fig. 4; regression weight, $b = −2.48, SE = 2.02, 95\% CI [−9.50, −0.12]$, controlling for sex and valence ratings following the neutral mood condition). The reverse mediation model (mood valence ratings following the negative mood condition as a mediator in the relationship between negative urgency and risk-taking) was not significant, nor were mediation analyses with arousal ratings following the negative mood condition (both as the independent variable and as a mediator). Conversely, positive urgency did not mediate the relationship between mood valence ratings following the positive mood condition and general risk-taking (controlling for sex and valence ratings following the neutral mood condition). The reverse mediation (with valence ratings following the positive mood condition as the mediator in the relationship between positive urgency and risk-taking) was also not significant.

Also as hypothesized, negative urgency mediated the relationship between left amygdala activation in the [Neg>Neu] contrast and risk-taking ($b = 2.75, SE = 1.71, 95\% CI [0.20, 7.40]$, controlling for sex), as well as the relationship between right lateral OFC activation in the [Neg>Neu] contrast and risk-taking ($b = 3.42, SE = 2.58, 95\% CI [0.02, 11.68]$, controlling for sex; see Fig. 5). The reverse mediation models (where BOLD...
activation in the left amygdala and the right lateral OFC mediated the relationship between negative urgency and general risk-taking) were not significant. There were no significant mediations using positive urgency and activation in response to [Pos>Neu] contrasts.

Discussion

The current study examined the relationship between urgency and BOLD responses to emotional stimuli, as well as how these variables relate to risk-taking behavior. As predicted from meta-analyses (Sabatinelli et al. 2011), emotional images (when compared with neutral images) provoked significant BOLD responses in the lateral OFC and amygdala. Moreover, right lateral OFC and left amygdala responses to negative images (when compared with neutral images) were related to negative urgency. Although positive images (when compared with neutral images) also activated both right and left lateral OFC, positive urgency was unrelated to this activation. Finally, negative urgency mediated the relationships between (1)

Figure 2. Positive correlation between negative urgency and [Neg>Neu] BOLD activation in 8-mm-radius spherical region centered ([40, 32, -12]) in the right lateral OFC. For reference, voxel-wise map of the correlation between [Neg>Neu] BOLD contrast and negative urgency is illustrated by inset (display threshold $P = 0.01, k = 30$, masked for [Neg>Neu] BOLD activation).

Figure 3. Positive correlation between negative urgency and [Neg>Neu] BOLD activation in 8-mm-radius spherical region centered ([−20, −6, −18]) in the left amygdala. For reference, voxel-wise map of the correlation between [Neg>Neu] BOLD contrast and negative urgency is illustrated by inset (display threshold $P = 0.01, k = 30$, masked for [Neg>Neu] BOLD activation).
negative image-induced mood ratings and (2) negative image-
provoked activation in right lateral OFC and left amygdala and
general risk-taking. Importantly, alternative mediation models
were not significant. Collectively, the results suggest that the
tendency to behave rashly in negative mood states is a key per-
sonality trait that mediates relationships between both (1) the
report of negative emotions and (2) limbic brain activity during
emotionally charged experiences and subsequent general
risk-taking.

Negative urgency has previously been associated with in-
creased ventromedial prefrontal cortex activation to alcoholic
drink aromas (Cyders et al. 2013), reduced BOLD responses in
the anterior and medial OFC and anterior cingulate to positively
and negatively valenced high-arousal stimuli (Joseph et al.
2009; both of which were outside our regions of interest,
and neither of which activated in our study), and increased
amygdala activation during negative emotion maintenance and
reappraisal (Albein-Urios et al. 2013), although this latter work
used a clinical population with cocaine use and personality dis-
orders. The current study sampled healthy, young adults and
found similar patterns of activation to negative emotional
stimuli that are related to both negative urgency and to risk-
taking behavioral outcomes (except in the case of Joseph et al.
2009, which found reduced activation to a combination of both
negatively and positively valenced high-arousal stimuli). This
suggests that links between emotionally provoked brain activa-
tion and negative urgency are likely not limited to clinical con-
texts, but rather represent more of a general vulnerability to
risk-taking and its subsequent problems.

The amygdala has long been acknowledged for its role in
emotional processing. The amygdala responds to both nega-
tive and positive emotional stimuli, although findings are less
robust with positive stimuli, related in part to the general lower
arousal level of positive emotional stimuli (see Zald 2003).
Additionally, negative stimuli tend to be lateralized to the left
amygdala; there is less consistent lateralization of amygdala re-
sponding to positive stimuli (see Wager et al. 2003). The
current study corroborates these patterns, showing responses
in the left amygdala only to negative emotional stimuli, and no
significant amygdala response to positive stimuli when com-
pared with neutral stimuli. Responses in the amygdala were
unrelated to self-reported valence and arousal, but this is not
surprising since amygdala activation to emotional stimuli often
occurs independently of conscious mood appraisal (see Zald
2003). Left amygdala responses to negative emotional stimuli
were also related to negative urgency, further implicating the

Figure 4. Mediation of negative mood valence and risk-taking through negative urgency. For clarity, only pathways with significant (*P < 0.05) regression weight (b) are depicted. Mediation was examined with the SPSS INDIRECT macro provided by Preacher and Hayes (2008) using the 95% confidence intervals. Risk-taking was assessed by total score on the Risky Behavior Scale.

Figure 5. The relationship of BOLD response to [Neg>Neu] images and risk-taking as mediated by negative urgency. For clarity, only pathways with significant (*P < 0.05) regression weights (b) are depicted. Two separate mediation models were examined with the SPSS INDIRECT macro provided by Preacher and Hayes (2008) using the 95% confidence intervals. OFC, orbitofrontal cortex. Risk-taking assessed as total score on the Risky Behavior Scale.
The right lateral OFC, also related to negative urgency and risk-taking in the current study, receives direct inputs from the amygdala, which has reciprocal connections with the prefrontal cortex (see Ongur and Price 2000). In fact, Ongur and Price (2000) describe connections between area 12 (closest to our region of interest in the current study) and nuclei of the amygdala. Given previous work linking negative urgency with ventromedial prefrontal cortex activation to alcohol cues in these same subjects (Cyders et al. 2013), the current findings implicate a set of emotionally related brain regions that are responsive to negative emotional mood states and which, in turn, might influence negative mood-based rash action.

Previous work has yet to determine how negative urgency affects a wide range of risk-taking behaviors. This study suggests that BOLD activation to negative emotionally provocative content in the left amygdala and right lateral OFC is related to negative urgency, although not to self-reported mood changes. Additionally, negative urgency was itself largely unrelated to self-reported mood changes (as consistent with other work by Cyders et al. 2010). Such self-reported mood changes are often unrelated to amygdala function (Zald 2003) and are likely influenced by self-report and expectancy biases, making them only indirect proxies for neural responses to emotional stimuli. Therefore, other work that has reported no relationship between negative urgency and emotional responses may be limited by self-report methods in the assessment of mood responses (e.g., Cyders et al. 2010), with central nervous system physiological responses being a more direct and sensitive reflection of trait urgency's antecedent effects on behavior. As suggested by our models of mediation, negative urgency does not appear to impart risk for general risk-taking by increasing the limbic responses to emotional stimuli. Rather, increased left amygdala and lateral OFC activation from negative emotional stimuli would instead appear to engage negatively urgent impulses, which then lead to risky behavior.

Impulsivity is one of the most frequent criteria across disorders in the Diagnostic and Statistical Manual of Mental Disorders—5 (American Psychiatric Association 2013) and is a behavioral facet of borderline personality disorder, antisocial personality disorder, bulimia nervosa, attention deficit/hyperactivity disorder, mania, dementia, substance use disorders, paraphilias, and multiple other impulse-control disorders (Zapolski et al. 2010). Negative urgency may be the most clinically relevant impulsivity trait (see Smith et al. 2007), as it is related to many of these diagnoses (see Zapolski et al. 2010). Several lines of evidence have begun to indicate that negative urgency is related to multiple biological aspects, including genetic predispositions (Carver et al. 2011; Villafuerte et al. 2013) and brain responses (Joseph et al. 2009; Albein-Urios et al. 2013; Cyders et al. 2013). As our understanding of the cerebral foundations for this personality trait grows, we may then be able to determine some common mechanisms that underlie these disparate diagnostic entities. In addition, understanding the unique contribution of negative urgency to risk allows more targeted and effective prevention and treatment programs for vulnerable individuals. For example, Zapolski et al. 2010 propose that treatment approaches such as distress tolerance (such as found in Dialectical Behavior Therapy for Borderline Personality Disorder; Linehan 1987), experiencing emotions without externalizing action, and evaluating behavioral choices in terms of long-term goals might all be effective in reducing emotion-based risk-taking and the incidence of psychiatric illness.

There are limitations to the current study. First, the sample consists of social drinking, relatively young participants, which potentially limits generalizability of the findings to populations with more problematic behaviors. Second, the sample was modest, so null or trend-level results should be interpreted with caution, and the findings replicated in larger cohorts. In that vein, we could not compare responses across males and females, especially in regard to emotional reactions to positive emotional images, some of which were sexual in nature. The discrepant laterality of our effects (left amygdala, right OFC) is somewhat puzzling. This said, some research suggests a cerebral laterality in activation for externalizing behaviors (e.g., Berkman and Lieberman 2010; Spielberg et al. 2011), and this work further supports left lateralization of impulsive action at least in terms of the amygdala. The right lateral OFC activation was also related to negative urgency, further corroborating findings in the field relating activation in this region to emotional reactivity (Sabatinelli et al. 2011). Finally, the cross-sectional nature of the current study prevents a purely causal determination, and future research should seek to examine this model prospectively.

In summary, data in this study suggest that brain responses in regions known to respond to emotionally provocative stimuli are related to trait negative urgency and that negative urgency may mediate the relationship between these brain responses and the propensity to engage in risky behavior. This study provides further support for the role of negative urgency in multiple risk-taking behaviors and disorders, and it suggests a cerebral foundation for emotion-based rash action tendencies.

Supplementary Material
Supplementary Material can be found at http://www.cercor.oxfordjournals.org/online.

Funding
This work was supported by the NH (grant: K01AA020102 to MAC), The Indiana Alcohol Research Center (grant: P60 AA007611-26), and the Indiana Clinical Research Center (grant: M01 RR00750). DAK and MD were also supported in part by R01AA017661.

Notes
We also acknowledge the support of Michele Beal, Courtney Robbins and Rose Case. Conflict of Interest: None declared.

References