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Heightened neural reactivity to threat in child victims of family violence

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Exposure to family violence affects a significant minority of children: estimates of physical abuse range from 4 to 16%, while intimate partner violence affects between 8 and 25% of children [1]. These maltreatment experiences represent a form of environmental stress that significantly increases risk of later psychopathology, including anxiety [1,2]. To date, no functional magnetic resonance imaging (fMRI) studies have probed the neural correlates of emotional processing in children exposed to family violence. Previous psychological and electrophysiological studies indicate a selective hypervigilance to angry cues in physically abused children, which is in turn associated with elevated levels of anxiety [3]. Functional magnetic resonance imaging (fMRI) research has demonstrated increased reactivity of the anterior insula (AI) and amygdala to angry faces in individuals with anxiety disorder [4], and in psychiatrically healthy soldiers exposed to combat [5], making these regions plausible neural candidates for adaptation to threat. We demonstrated that children exposed to family violence (with normative levels of anxiety) show increased AI and amygdala reactivity in response to angry but not sad faces. While such enhanced reactivity to a biologically salient threat cue may represent an adaptive response to sustained environmental danger, it may also constitute a latent neurobiological risk factor increasing vulnerability to psychopathology.

Using fMRI we investigated brain responses to threatening (angry) and non-threatening (sad) facial expressions relative to neutral faces (see Figure 1A and Supplemental Experimental Procedures in the Supplemental Information for paradigm description) in children who had been exposed to documented violence at home (n = 20). These children presented with normal levels of anxiety and depression. Brain responses were compared to that of a closely matched comparison group (n = 23; see Supplemental Experimental Procedures and Supplemental Table S1 for additional participant details). The emotional content of the facial stimuli was incidental to our task, which required children to decide if a series of faces were male or female (see Supplemental Results and Table S2 for reaction time and accuracy data for the two groups). Compared to our comparison group, the family violence group exhibited greater activation in the right amygdala (Figure 1B) and in the AI bilaterally (Figure 1C) when angry faces, but not sad faces, were contrasted with neutral faces. In an exploratory analysis, we also examined a possible dose-response relationship between these neural activations and violence exposure within the family violence group. The degree of activation to angry faces in the left AI was positively correlated with the severity of violence exposure ($r(20) = 0.54$, $p = 0.007$, one-tailed; Figure 1D).

Neuroimaging studies of healthy adults suggest that the amygdala and the AI are part of a larger salience network that detects threat [6] and anticipates pain [7]. The AI shares dense connections with a number of cortical and subcortical regions (including the amygdala) and is therefore well placed to integrate emotional, sensory and bodily information to guide social processing and affective decision-making [8]. This region has been implicated specifically in the anticipation of a physical stimulus, generating a predictive signal as to how the body will feel. For example, greater pre-stimulus activation in the AI bilaterally has been shown to be predictive of the perceived painfulness of that stimulus [7]. This is consistent

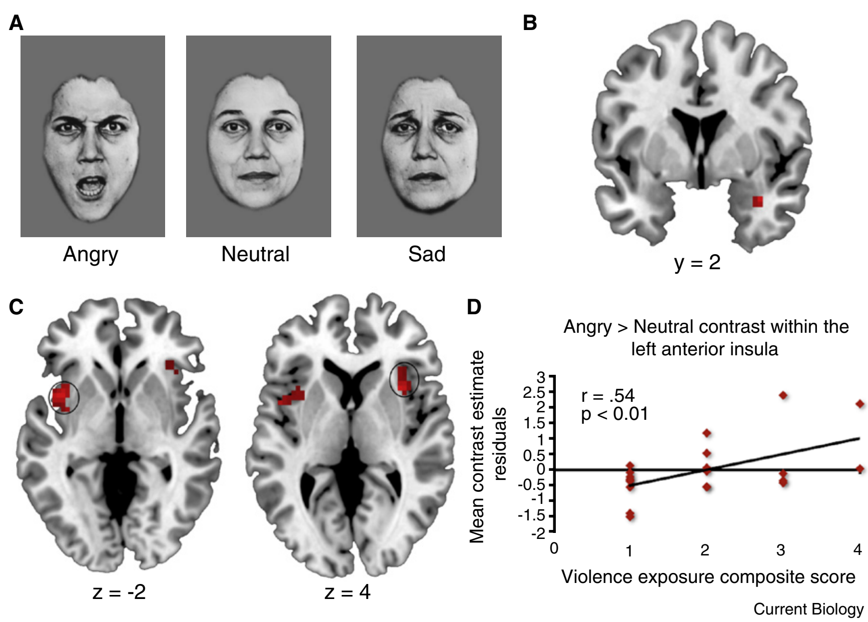

Figure 1. Example stimuli and functional magnetic resonance imaging activation.
(A) Participants viewed blocks of angry, neutral and sad faces in a pseudorandom order while indicating the gender of the target. (B) Statistical parametric map (SPM) showing increased right amygdala activation in children exposed to family violence for the contrast angry > neutral (36, 2, -23, $z = 3.31$, $p = .0014$, Family-Wise Error (FWE) corrected). (C) Increased bilateral AI activation in children exposed to family violence for the contrast angry > neutral (left AI: –42, 8, -2, $z = 3.52$, $p = 0.033$, FWE corrected; right AI: 33, 14, 4, $z = 3.75$, $p = 0.014$, FWE corrected). All coordinates reference the coordinate system of the Montreal Neurological Institute. SPM thresholded at $p < 0.005$ (uncorrected) for visualization purposes. (D) Scatter plot depicting the correlation between the contrast estimates (angry > neutral) from the left anterior insula (y axis) and degree of family violence exposure (x axis) after accounting for variance explained by age and gender.

with the proposal that the insula supports the interaction between perceived threat signals and bodily states of arousal leading to emotional experiences [7]. The role of the amygdala in detecting threat is widely recognized [6], with recent evidence suggesting that, in the context of face processing, it predominantly signals salience independent of level of threat or degree of emotionality [9].

Recently it has been shown that children exposed to early stress in the form of institutionalisation and removal from their families show heightened activation of the amygdala when viewing fearful faces; this suggests that poor caregiving may alter functional development of limbic structures [10]. In adults, studies of soldiers exposed to combat have been used to study prolonged experience of stress, and specifically exposure to environmental threat. In a recent longitudinal study [5], both the AI and amgygdala demonstrated functional adaptation in soldiers exposed to a combat zone: combat stress increased AI and amygdala reactivity to angry and fearful faces, even in the absence of self-reported changes in post-traumatic stress symptoms or other measures of psychopathology. This suggests that sustained exposure to environmental danger and potential physical harm recalibrates the neural responsiveness of these regions, which are densely interconnected [4]. Functionally, this may augment vigilance to threat, but it is thought that heightened neural reactivity in the AI and amygdala is not adaptive in safe environments and may serve as a latent risk factor for subsequent anxiety disorders [5]. A meta-analysis of functional imaging studies found increased reactivity of both the AI and amygdala to threat to be reliably associated with several anxiety disorders, including post-traumatic stress disorder [4]. While disorder-specific activations in other brain areas were also reported, atypical activations of these two structures represented a neural signature associated with anxiety-disordered processing.

Clinically, these findings indicate that even sub-threshold trauma symptoms may conceal significantly heightened neural responsiveness to threat. We suggest that such threat hypervigilance may compromise a child's development in at least three ways. First, it could limit attentional resources for mastering age-appropriate skills in social and cognitive domains [3]. Second, it may serve to increase future vulnerability to later stressors, increasing risk of anxiety. Finally, it may predispose to reactive aggression. Our findings are consistent with a pattern of amplified emotional reactivity to anger that may underpin inappropriate behavioural responses to such cues from peers and adults.

While exposure to family violence has been reliably associated with an increased life-time risk of psychopathology [2], little is known about how this association manifests at the neurobiological level. We found that angry faces, a biologically salient threat cue, elicited increased activation in bilateral AI and the amygdala in maltreated children exposed to family violence. This pattern of brain reactivity has been previously associated with combat exposure and with a range of anxiety disorders in adults. The increased AI response is consistent with heightened anticipation of pain, and our exploratory analyses suggested that it was stronger in those children exposed to higher levels of family violence. The increased amygdala response to angry faces, but not sad faces, is consistent with the proposal that prolonged exposure to violence selectively heightens the salience of threat cues such as angry faces [3]. We suggest that these findings constitute neurobiological correlates of heightened threat sensitivity in children who have been exposed to family violence. This apparent neural adaptation in AI and amygdala responsiveness may arguably confer a short-term functional advantage in enhancing a child's vigilance to threat in a chaotic and dangerous family environment. However, heightened functional responsiveness of both structures could also constitute a latent neural risk factor that predisposes to an increased likelihood of psychopathology in adult life.

Supplemental information

Supplemental information includes two Supplemental Tables and Supplemental Experimental Procedures, and can be found with this article online at doi: 10.1016/j.cub.2011.10.015.

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