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Vigilance, the Amygdala, and Anxiety in Youths With a History of Institutional Care

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ABSTRACT

BACKGROUND: Early adversity is commonly associated with alterations of amygdala circuitry and increased anxiety. While many theoretical and clinical accounts of early adversity suggest that it increases vigilance to threatening stimuli, the current study tested whether heightened anxiety and amygdala reactivity associated with early adversity enhanced goal-directed attention for threatening stimuli. Showing this association would provide support that these adversity-induced alterations are developmental adaptations of the individual.

METHODS: A sample of 34 children and adolescents who experienced early adversity in the form of previous institutionalization (26 girls and 8 boys; mean age = 13.49 years) and a comparison group of 33 children and adolescents who were reared by their biological parents since birth (16 girls and 17 boys; mean age = 13.40 years) underwent functional magnetic resonance imaging scanning while completing a visual search task that involved quickly locating a negative target (fearful face) or positive target (happy face) in an array of neutral distracter stimuli (neutral faces).

RESULTS: Across both groups, individual differences in vigilant behavior were positively associated with amygdala responses for negative versus positive stimuli. However, a moderation analysis revealed that the degree to which amygdala responses were greater for negative versus positive stimuli was associated with greater anxiety symptomology for previously institutionalized youths but not for comparison youths.

CONCLUSIONS: Together, these findings suggest that institutional care strengthens linkages between amygdala reactivity and anxiety, perhaps serving to enhance goal-directed attention. The findings are discussed as both adaptations and risk to the individual.

Keywords: Amygdala, Attention, Early life stress, Emotion, fMRI, Neurodevelopment

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Accumulating evidence submits that early caregiving adversity—defined as negative experiences related to the family or caregiving (1)—alters amygdala development and increases anxiety symptomology (2–9). Theoretical accounts of these associations posit that early adversity reprioritizes developmental goals such that threat vigilance is emphasized over other behaviors, perhaps to promote self-preservation, and that this vigilance confers greater anxiety (9–12). However, no prior work has examined whether adversity-induced alterations in amygdala function moderate the link between vigilance and anxiety. The current study sought to directly test whether a history of previous institutional (i.e., "orphanage") care, a significant adversity, potentiates the link between amygdala-based threat vigilance and anxiety.

The literature on attentional gating mechanisms shows that stimuli with salient bottom-up features can be prioritized when they align with our top-down goals (13). For example, threatening cues, such as a menacing snake and a fearful face, are detected more rapidly than nonthreatening stimuli (14–16), but this process is facilitated when consistent with goal states. The amygdala can support this additional attentional vigilance and orient attention toward salient emotional stimuli in one of two ways—either through a crude noncortical route or by amplifying cortical processing of such stimuli (17–21). As such, the amygdala plays a crucial role in rapidly detecting and guiding attention toward motivationally relevant stimuli (16,22).

Faster detection of threatening stimuli has been associated with trait anxiety in both clinical and nonclinical samples both during development and during adulthood (23–25). Numerous neuroimaging studies have linked anxiety to exaggerated amygdala responses to threatening stimuli in children, adolescents, and adults (26,27). These associations raise the possibility that individuals with elevated amygdala reactivity, although at greater risk for anxiety, might incur an advantage when it comes to identifying threatening information. Importantly, links between vigilance and anxiety may be bidirectional in early life stress–exposed youths—anxiety could be interpreted as a natural consequence of stress that promotes vigilance, and thus survival—just as vigilance and associated neurobiological changes may trigger anxiety.

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Early experiences, and particularly early adversity, alter developmental trajectories associated with emotion, threat learning, and attentional control (28–31). Given this fact and that early adversity is a risk factor for the development of anxiety (1,6,7), there are strong reasons to hypothesize that threat vigilance may moderate early adversity's influence on anxiety. Importantly, it is unknown whether all forms of early adversity evoke comparable attentional biases and anxious symptomology. On the one hand, some theoretical models propose that different forms of early adversity may have varied developmental consequences (32–34). On the other hand, various forms of early adversity (abuse, neglect, and low socioeconomic status) share common threads such as not feeling safe or agentic in one's environment and have been linked to alterations of the amygdala and associated behavior (35). Studies examining how exposure to abuse or violence affects attention for threatening versus nonthreatening stimuli have mostly done so using dot-probe paradigms, which evaluate how automatically attending to threat cues incidentally biases attention. While some evidence suggests that abuse and neglect cause a negative attentional bias (i.e., attending to threatening or sad stimuli), other evidence suggests attentional avoidance (36–39). Prior work examining attentional biases toward threat in previously institutionalized (PI) children found that children who remain in institutional care display either no biased attention or a bias toward threat, whereas children who are randomly assigned to foster care show a bias toward positive stimuli (40,41). This line of work has also revealed that attentional biases toward positive stimuli and away from threatening stimuli predict fewer social and emotional problems, suggesting that individual differences in attention may confer risk or resilience for PI youths (40,41). Importantly, most prior research has focused on narrow age bands, leaving open the possibility that early adversity differentially affects attentional biases at different ages.

Amygdala hyperactivity is common to both PI youths and individuals with elevated anxiety (2,3,26,42). Thus, the amygdala presents itself as a potential neural link between adversity exposure and enhanced attention for threat. If such is the case, we might expect that amygdala responses confer anxiety for PI youths but not for comparison youths. Here, we employed a task that assesses goal-directed attention for threats versus positive stimuli and assessed whether amygdala engagement may support threat-directed attention but also increase risk for anxiety in PI youths.

PI youths were compared with a never-institutionalized comparison youth group on a neuroimaging task that involved rapidly locating either threatening or positive facial expressions in a visual array. In addition to testing main effects, including how goal-directed attention differed for threatening and positive stimuli and how group status (PI vs. comparison) affected attention, we tested three novel hypotheses. First, we examined whether amygdala activity was associated with behavioral markers of goal-directed attention for threatening versus positive stimuli. Second, we examined whether behavioral or amygdala-based markers of attention for threatening versus positive stimuli predicted greater anxiety in PI youths but not in comparison youths (i.e., a moderation effect). This hypothesis was motivated by a growing literature suggesting that amygdala responses may interact with group categorization (e.g., genotype, diagnosis) to predict distinct functional outcomes related to anxiety and well-being (43,44). Finally, we conducted exploratory age analyses to examine whether responses to threat differentially predicted anxiety across development in PI youths.

METHODS AND MATERIALS

Participants

In total, 34 PI youths (26 girls and 8 boys; mean age = 13.49 years, SD = 2.87, range = 8.36–18.26) and 33 comparison youths (16 girls and 17 boys; mean age = 13.40 years, SD = 3.51, range = 8.10–18.99) participated in this study. There were more girls in the PI group than in the comparison group (χ^2 = 5.61, p = .02), so gender was included as a covariate in all analyses. All participants were currently residing in the United States at the time of testing, and all research was completed at the University of California, Los Angeles. Participant demographic information is reported in Table 1, and correlations between study variables are presented in Table 2. This study was approved by the university's Institutional Review Board. All participants provided informed assent, and their parents provided informed consent, prior to participation.

The current data were collected as part of a larger study examining the effects of prior institutionalization on social and emotional development. A subset of participants who participated in this larger study completed the tasks and measures described here, and only data from the age range with maximal overlap between the PI and comparison groups (8–18 years) were analyzed. Of the 91 participants within this age range, 12 were excluded from analyses (5 PI youths and 7 comparison youths; 6 girls and 6 boys; mean age = 11.68 years) for correctly responding to fewer than 50% of targets for fearful faces and/or happy faces. Among the remaining 79 participants, 10 were excluded due to excessive head motion (4 PI youths and 6

Table 1. Sample Characteristics

			Analysis		
Measure	Comparison (n = 33)	PI (n = 34)	t or χ^2	df	p
Gender, Female	16	26	χ^2 = 5.61	1	< .05
Age, Years	13.41 (3.51)	13.49 (2.87)	t = 0.10	65	n.s.
Full-Scale IQ (WASI)[a]	116.5 (16.16)	105.32 (14.16)	t = 2.98	64	< .005
Anxiety (SCARED)	6.25 (5.62)	15.19 (10.79)	t = 4.23	65	< .001

Data are mean (SD) or n.

n.s., nonsignificant (p >.05); PI, previously institutionalized; SCARED, Screen for Child Anxiety Related Disorders; WASI, Wechsler Abbreviated Scale of Intelligence.

[a]Full-scale IQ was not available for 1 comparison participant.

Table 2. Correlations Between Study Variables

	IQ	SCARED	Fear HR	Happy HR	Fear − Happy HR	Fear RT	Happy RT	Fear − Happy RT
Age	−.25*	−.01	.33*	.28*	.15	−.47***	−.48***	−.02
IQ		−.18	.07	.13	−.02	.11	−.12	.25*
SCARED			.18	−.09	.26*	.034	.018	.02
Fear HR					.75***	−.28*	−.36**	.06
Happy HR					−.24*	−.09	−.39**	.33**
Fear − Happy HR						−.25*	−.10	−.18
Fear RT							.62***	.50***
Happy RT								−.38**

HR, hit rate; RT, response time; SCARED, Screen for Child Anxiety Related Disorders.
*$p < .05$; **$p < .005$; ***$p < .001$.

comparison youths; 6 girls and 4 boys; mean age = 11.11 years), defined as 1 mm or greater framewise displacement for 20% or more repetition times. An additional 2 participants (1 15-year-old PI girl and 1 18-year-old comparison girl) were excluded from analyses because their parents did not complete the Screen for Child Anxiety Related Disorders (SCARED) (45). The final sample comprised 67 participants.

Assessment of Anxiety

Anxiety symptomology was assessed by parent report on the SCARED, which is designed for youths aged 8 to 18 years (46). The SCARED is composed of 41 questions (e.g., "My child is nervous") that may be answered on a scale of 0 to 2 ("not true" to "very true"). The range of possible scores on the SCARED is 0 to 82, with higher scores indicating greater anxiety.

Experimental Vigilance Task

Prior to scanning, participants completed a mock scanning session. Participants subsequently completed two 138-second runs, each of which contained 20 trials, of an affective vigilance task while undergoing functional magnetic resonance imaging. On one of the task runs participants were instructed to find the "happy face," and on the other run they were instructed to find the "fearful face." Task run order was counterbalanced across participants. On each trial, six pictures of the same model were shown in a circle. For the majority of trials (17/20 in each run), five of the pictures depicted a neutral facial expression and one depicted either a happy or fearful face (Figure 1A). Participants were instructed to press a button to indicate as soon as they identified whether the target face (happy or fearful) was on the left or right side of the screen. In each run, 3 trials were "foil trials," meaning that all six pictures were neutral faces and no button press was required. Foil trials were included to maximize searching behavior and not to serve as a comparison condition. Each trial (i.e., face array) was presented for 1500 ms regardless of how quickly participants responded. Trials were separated by a jittered intertrial interval during which a fixation cross was shown (average intertrial interval length = 4251 ms).

Face stimuli were taken from the NimStim set (47). Six models were used in the paradigm, and each model was shown a total of six or seven times. Half of the faces were male and half were female. The faces were ethnically diverse, with one-third being African American, one-third being European American, and one-third being Asian American. Fearful faces were chosen as a target stimulus as opposed to another negative emotional facial expression such as anger. While angry faces confer a known threat (i.e., that the model is threatening the perceiver), fearful faces provide incomplete information about the source of the threat and thus require the perceiver to vigilantly acquire more information from the broader environment (48). Thus, fearful faces tap affective and attentional processes more akin to anxiety, including uncertainty and anticipation (49), and are the face stimulus of choice for eliciting amygdala reactivity (50).

While some other tasks examining emotion and attention employ conditions wherein neutral faces are a target, we exclusively used conditions with emotional faces (fearful or happy) as targets for two reasons. First, prior work suggests that children often do not interpret neutral faces as being neutral, and thus trials with neutral targets might not provide an ideal baseline condition (51). Second, while other paradigms such as the dot-probe task are focused on whether affective stimuli incidentally affect attentional processes, here we were focused on whether two different kinds of affective stimuli would differentially facilitate goal-directed visual search. Thus, our primary interest was in comparing goal-directed attention for fearful and happy faces rather than on comparing each condition with an objective baseline.

Behavioral Data Analysis

Accuracy. Average hit rate (the number of trials participants correctly identified the location of the target face/the number of trials where a target face was shown) for each participant was entered into a repeated-measures analysis of variance in SPSS, version 24 (IBM Corp., Armonk, NY) along with mean-centered age, group (PI vs. comparison group), gender, and the group × age interaction term. Hit rate was examined rather than a measure such as *d'*, which assesses hit rate and false alarm rate, because participants completed very few foil trials (3/20) where false alarms could be committed. The majority of participants did not commit a single false alarm for happy (83.6%) or fear (52.2%) trials. A difference score was calculated for participants between their hit rates for fearful and happy faces, and this difference was subsequently correlated with participants' SCARED total scores.

Reaction Time. Average reaction time (RT) on correct hit trials for each participant was entered into a repeated-measures analysis of variance in SPSS along with mean-centered age, group (PI vs. comparison group), gender,

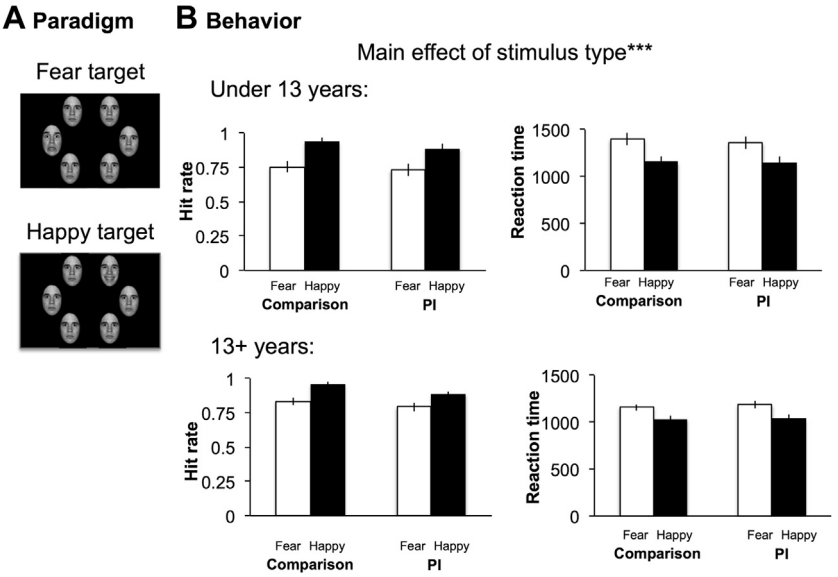

Figure 1. Functional magnetic resonance imaging task and behavior. **(A)** Participants completed blocks of trials, where they were instructed to find either a fearful or happy face. **(B)** Participants were more accurate and faster at detecting happy vs. fearful faces. Age predicted faster reaction times and better accuracy. Age is plotted categorically for illustrative purposes only. Error bars reflect between-subjects standard error. ***$p < .001$. PI, previously institutionalized.

and the group × age and group × gender interaction terms. RT variability analyses are reported in the Supplement.

Functional Magnetic Resonance Imaging Data Acquisition and Analysis

Acquisition. Whole-brain imaging data were collected on a 3T Siemens Magnetom Trio scanner (Siemens, Erlangen, Germany) using a standard radiofrequency 12-channel head coil. Participants completed a whole-brain, high-resolution, T1*-weighted anatomical scan (magnetization prepared rapid acquisition gradient-echo; 256 × 256 in-place resolution; 256-mm field of view; 192 × 1-mm sagittal slices) and two functional runs. T2*-weighted echo-planar images (interleaved) were collected at an oblique angle (ranging from ~ 10 to 30°) (154 volumes/run; repetition time, 2000 ms; echo time, 30 ms; flip angle, 90°; matrix size, 64 × 64; field of view, 192 mm; 34 slices; 4-mm-thick contiguous slices).

Preprocessing. Preprocessing was performed using SPM8 preprocessing tools (Wellcome Department of Cognitive Neurology, University College London) in NeuroElf (http://neuroelf.net). The first 4 volumes for each participant were discarded to allow for scanner signal stabilization. Preprocessing steps for the functional images included motion correction, slice-time correction, and coregistration to the first functional image for each subject. Structural images were spatially normalized, using unified segmentation, to a standard template brain (Montreal Neurological Institute avg15T1.img), and warping parameters were applied to functional images for each subject. Normalized functional images were interpolated to 3 × 3 × 3-mm voxels and spatially smoothed with a 6-mm Gaussian filter. Volumes with 1 mm or more framewise head motion were censored (removed from the time course), and their preceding volume was removed (mean percentage usable volumes = 96.8%).

Individual and Group-Level Functional Magnetic Resonance Imaging Analyses. Separate regressors were created for fearful trials, fearful foil trials, happy trials, and happy foil trials. Boxcar regressors for the different trial types were convolved with the hemodynamic response function in NeuroElf. A robust regression analysis was performed on the conditions of interest for each subject as well as estimates of global signal in gray matter, white matter, and the ventricles. Data were filtered using high-pass filters. Six motion regressors (*x, y,* and *z* displacement; pitch, roll, and yaw rotation) and their derivatives were included as covariates.

Group-level analyses were conducted in NeuroElf. Maps were first thresholded at $p < .005$ (uncorrected). Significant clusters were identified using an extent threshold that corresponded to a familywise error corrected $p < .05$, as determined by AlphaSim as implemented in NeuroElf (smoothness estimate = 8.9 mm, extent threshold = 55 voxels). The smoothness of the residuals was used to estimate how large clusters were likely to be at random given the search space, and this information was then used to estimate how large clusters need to be to maintain the specified α rate (given $\alpha = .05$; no more than 5% of maps ought to show a false positive cluster).

The following analyses were performed:

1. A random-effects analysis of covariance was performed to examine the effects of target (happy vs. fearful faces), group (PI vs. comparison group), mean-centered age, and gender.
2. To examine brain–behavior relationships, participants' accuracy difference score (fearful hit rate − happy hit rate) was correlated with the fearful > happy contrast.
3. To examine the relationship between amygdala and anxiety symptomology, β values were extracted from an amygdala cluster identified in Analysis 2. The following steps were then taken:
   a. Contrast values (fearful > happy) in the amygdala were correlated with SCARED anxiety scores.
   b. The interactive effect of group and amygdala responses on anxiety was probed using moderation analyses. Specifically, group was tested as a moderator of the relationship between amygdala responses and anxiety

4. Two analyses examined the interactive effects of age and group on relationship between amygdala and anxiety (see Supplement):
   a. A univariate general linear model examined the effects of group, mean-centered age, and the amygdala response on anxiety symptomology.
   b. Within the PI and comparison groups, age was tested as a moderator for the relationship between the amygdala response and anxiety.
5. β series analyses were used to measure amygdala connectivity (see Supplement).

RESULTS

Behavioral Results

Accuracy and RT. A repeated-measures analysis of variance revealed that participants were more accurate at detecting happy faces than fearful faces (mean fearful accuracy [adjusted for covariates] = 0.78; mean happy accuracy [adjusted for covariates] = 0.92; $F_{1,61}$ = 72.34, $p < .001$) (Figure 1B). Age predicted greater accuracy ($F_{1,61}$ = 10.78, $p = .002$). Group, gender, and interaction terms did not predict accuracy ($ps > .07$). Similar effects were observed for RTs. Specifically, participants were faster at detecting happy faces (mean RT [adjusted for covariates] = 1082.01 ms) than fearful faces (mean RT [adjusted for covariates] = 1260.73 ms) ($F_{1,61}$ = 56.43, $p < .001$) (Fig. 1B), and age predicted faster RTs ($F_{1,61}$ = 21.93, $p < .001$). No other factors or interactions significantly predicted RTs ($ps > .15$).

Accuracy, RT, and Anxiety Symptomology. Across all participants, accuracy for detecting fearful versus happy faces (fearful hit rate − happy hit rate) was correlated with SCARED anxiety scores ($r = .26$, $p = .03$). A regression analysis was performed that incorporated age (mean centered) group, gender, accuracy difference scores, group × age, group × gender, and group × accuracy difference scores as predictors. All two-way interactions involving PI group were included in this model to fully assess potential group differences, but additional interactions were not included due to concerns about insufficient power. PI participants (mean = 15.19, SD = 10.79) exhibited greater anxiety than comparison participants (mean = 6.25, SD = 5.62; t_{59} = 3.23, $p = .002$). After accounting for age, group, gender, and relevant interaction terms, the relationship between accuracy difference scores and anxiety became nonsignificant (t_{59} = 1.91, $p = .06$). No other factors significantly predicted anxiety symptomology ($ps > .16$). RTs for fearful versus happy faces (fearful RT − happy RT) were unrelated to SCARED scores ($r = .02$, $p = .87$).

Neuroimaging Results

Brain Activation Associated With Attention for Happy and Fearful Faces. Trials with fearful targets recruited dorsomedial and dorsolateral prefrontal cortex and the cerebellum to a greater extent than trials with happy targets (Table 3). By contrast, searching for happy targets recruited the right hippocampus and broad swaths of the posterior temporal cortex to a greater extent than fearful targets.

Interactions between age and target valence were observed in the left superior frontal gyrus and the precuneus (Supplemental Table S1). Specifically, left superior frontal gyrus responded more strongly to fearful targets than to happy targets at younger ages and responded more to happy targets than to fearful targets at older ages, whereas the opposite effect was observed in the precuneus. Interactions between group and other variables are reported in Supplemental Table S2.

Brain Activation Associated With Accurately Detecting Fearful Versus Happy Faces. Although similar main effects were observed for accuracy and RT, accuracy scores correlated with SCARED anxiety scores and, thus, brain-behavior analyses focused on accuracy rather than on RT. Greater behavioral accuracy for detecting fearful versus happy faces was correlated with greater recruitment of visual cortex (cuneus), temporal cortex (including middle and posterior insula), and subcortical regions (including the amygdala) (Table 4 and Figure 2B).

Relationship Between Amygdala and Anxiety Symptomology. Given a priori hypotheses about the amygdala, β values were extracted from an amygdala subcluster (Montreal Neurological Institute coordinates: −18, −6, −21, 11 voxels) located within a larger cluster (which encompassed the amygdala, hippocampus, and ventral striatum) identified by the above analysis examining correlations between activation and accuracy. This subcluster was identified using a higher values–first watershed searching algorithm implemented in NeuroElf ("splitclustercoords"). An independent-samples t test revealed that amygdala responses to fearful faces (t_{65} = 1.06, $p = .29$) and happy faces (t_{65} = 0.96, $p = .96$) within this amygdala cluster did not differ between PI youths and comparison youths.

Collapsing across PI and comparison participants, amygdala responses to fearful versus happy faces were not significantly associated with anxiety symptomology ($r = .22$, $p = .08$). Exploratory analyses, however, revealed that group significantly moderated the relationship between amygdala responses and anxiety symptomology (adjusted R^2 change = .05, $F_{1,63}$ = 5.40, $p = .02$) (Figure 2C). Specifically, amygdala responses to fearful versus happy faces predicted greater anxiety symptomology in PI youths ($\beta = 2.71$, $t_{32} = 2.28$, $p = .03$) but not in comparison youths ($\beta = -0.49$, $t_{31} = 0.73$, $p = .47$). Exploratory analyses examined age as a moderator of the amygdala–anxiety relationship within each group (see Supplement).

DISCUSSION

The current study examined the neural substrates of goal-directed attention for threat in PI and comparison youths. Across both groups, better detection of threatening versus positive stimuli was associated with higher trait anxiety and amygdala recruitment. Consistent with prior work, we found that PI youths on average exhibited greater anxiety symptomology than comparison youths but that the relationship

Table 3. Age-Independent Effects of Target Valence on Brain Recruitment

Region	Hemisphere	No. Voxels	*F*	MNI Coordinates		
				x	*y*	*z*
Fearful > Happy						
Middle frontal gyrus	L	87	17.25	−30	48	0
Middle frontal gyrus	L	33	13.30	−24	45	15
Middle frontal gyrus	L	14	11.33	−33	39	12
Middle frontal gyrus	R	56	14.88	42	36	24
Inferior frontal gyrus	R	17	11.55	42	27	15
Inferior frontal gyrus	R	68	17.31	48	48	−15
Middle frontal gyrus	R	38	14.05	36	45	−6
dmPFC	M	75	21.08	0	15	54
Superior frontal gyrus	L	35	15.65	−12	12	57
Cerebellum	L	166	19.65	−6	−75	−27
Cerebellum	L	30	15.48	−36	−69	−48
Cerebellum	L	38	14.66	−18	−78	−45
Cerebellum	L	22	13.89	−15	−69	−30
Cerebellum	L	17	10.91	−42	−72	−39
Happy > Fearful						
Hippocampus	R	56	27.12	24	−21	−18
Superior temporal gyrus	L	496	26.20	−63	−15	6
Temporoparietal junction	L	49	17.35	−54	−15	15
Posterior insula	L	31	17.04	−45	−12	−3
Temporoparietal junction	L	72	16.25	−51	−27	12
Precentral gyrus	L	75	15.57	−63	−12	30
Superior temporal gyrus	L	62	15.48	−66	−30	15
Posterior insula	L	42	14.49	−45	−36	24
Superior temporal gyrus	L	23	14.10	−63	0	3
Posterior insula	L	11	13.82	−39	−6	6
Posterior insula	L	9	13.15	−36	−9	18
Posterior insula	L	18	11.28	−39	−15	6
Posterior insula	L	14	11.13	−39	−33	12
Superior temporal gyrus	R	245	22.94	54	−6	−3
Superior temporal gyrus	R	93	20.17	60	−27	9
Superior temporal gyrus	R	70	20.14	54	−15	3
Superior temporal gyrus	R	35	13.80	66	−15	6
Superior temporal gyrus	R	5	11.44	72	−30	3

Brain regions are identified by the main effect of target valence. Subclusters are reported under their supracluster.
dmPFC, dorsolateral prefrontal cortex; *F*, maximum *F* statistic for a given cluster; L, left; M, medial; MNI, Montreal Neurological Institute; R, right.

between adversity exposure and anxiety was not one to one (2,30). Amygdala recruitment for threatening versus positive stimuli was associated with greater anxiety among PI youths but not among comparison youths. These results preliminarily indicate that amygdala-supported attention for threat may be an endophenotype for anxiety in PI youths, which has both basic and translational significance for neurodevelopmental models of anxiety and early adversity.

Across our sample, participants were faster and more accurate at detecting happy faces than fearful faces. At first blush, this contradicts prior evidence that children possess superior attention for threatening versus positive cues (52–54), yet this discrepancy might be reconciled by three facts. First, many, although not all (52), other paradigms have examined responses to threatening targets amid positive distracters or vice versa, whereas our participants identified threatening targets or positive targets amid neutral distracters. Given that happy faces are more easily identified than fearful faces, particularly during childhood (55), it is not entirely surprising that they "popped out" against a sea of neutral faces (56,57). Second, our task required participants to make a button press, consistent with an "approach" response, that may have been incongruent with aversive stimuli (fearful faces) (58,59). Third, there were substantial and consequential individual differences with regard to attention for happy versus fearful faces.

While prior studies have examined whether behavioral correlates of threat vigilance or early adversity exposure predict trait anxiety, little work has examined how these factors interact to predict anxiety during development (1,60–62). We found that behavioral correlates of threat vigilance predicted anxiety for both PI and comparison youths,

Table 4. Brain Activation Correlated With Accurate Detection of Fearful Versus Happy Faces

Region	Hemisphere	No. Voxels	*r*	MNI Coordinates *x*	*y*	*z*
Posterior Amygdala	L	57	.46	−18	−12	−12
Ventral striatum	L	19	.41	−18	3	−18
Hippocampus	L	9	.40	−30	−12	−12
Amygdala	L	11	.40	−18	−6	−21
Superior Temporal Gyrus	L	67	.46	−51	−6	3
Midinsula	L	16	.41	−36	3	6
Cuneus	R	92	.47	18	−60	15
Cuneus	R	17	.38	9	−57	0
Cuneus	R	8	.37	15	−66	30
Cuneus	R	8	.40	21	−54	3
Precuneus	R	8	.37	24	−63	24

Brain regions identified by the main effect of target valence. Subclusters are reported under their supracluster.

L, left; MNI, Montreal Neurological Institute; *r*, maximum *r* statistic for a given cluster; R, right.

suggesting that negative attentional biases are a transdiagnostic risk factor (63). However, we also found that interindividual variability in amygdala responses to threats plays a crucial role in determining anxiety behavior among PI youths (2,30). The flip side of this observation is that PI youths who orient amygdala responses toward positive emotional stimuli are less likely to exhibit elevated anxiety. As such, future intervention work ought to examine whether training PI youths to direct attention toward positive stimuli might have anxiolytic consequences. Our current findings are consistent with prior behavioral work and suggest that amygdala-based attentional gating mechanisms may link basic cognitive processes to anxiety outcomes in PI youths (23,40,64). That amygdala–anxiety associations were not observed in comparison youths suggests that individual differences in threat vigilance might be an anxiety risk factor only for individuals who are already vulnerable to anxiety, although additional research is needed to fully test this hypothesis. This possibility is consistent with temperament research showing that the link between behavioral inhibition, another factor that is associated with amygdala reactivity and anxiety, and negative outcomes is moderated by attentional biases to threat (65–67).

It is worth noting that there may have been insufficient variability in anxiety among comparison youths to relate to amygdala responses; only 3% of comparison youths had SCARED scores that could be deemed clinically significant (≥ 25), whereas 17.6% of PI youths did. Future work might seek to compare samples such as ours with others who are at risk for developing anxiety (e.g., behaviorally inhibited youths) to examine whether or not links between amygdala reactivity and trait anxiety are unique to PI youths. In the current study, we found that adversity exposure moderated the link between amygdala responses and anxiety but did not exert a main effect on goal-directed attention for threat. This stands in contrast to prior work conducted in abused children, who show enhanced incidental attention for threat cues (68,69). As such, future work ought to compare attention for threat across different paradigms and different stress-exposed samples (34).

The current study has several limitations that ought to be addressed in future studies. First, while prior work in adults has shown that attention for threat increases anxiety (70), it is unknown whether attention for threat in PI youths would attenuate anxiety symptomology (40). Second, prior institutionalization is just one form of early adversity, and additional work is needed to determine whether the neural bases of attention for threat differ for other adversity-exposed youths. Third, a larger sample size would likely be needed to adequately test whether amygdala–anxiety links depend in part on developmental stage in PI youths (2,3,31,71).

The current results suggest that the amygdala prioritizes affective information to enhance goal-directed attention in PI youths. On the one hand, amygdala recruitment and anxiety symptomology was associated with better attentional performance, suggesting an adaptive value to heightened anxiety and amygdala reactivity. On the other hand, PI individuals are at an increased risk for anxiety, highlighting the need to consider the trade-offs associated with developmental adaptations.

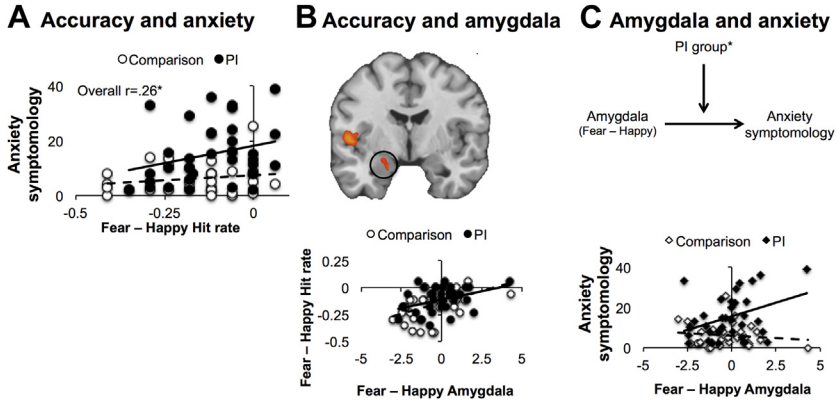

Figure 2. Relationships among task accuracy, anxiety, and amygdala responses. **(A)** Better accuracy for fearful vs. happy trials was associated with more anxiety symptomology. **(B)** Better accuracy for fearful vs. happy trials correlated with greater amygdala responses for fearful vs. happy trials. **(C)** Top: A moderation analysis revealed that greater amygdala responses for fearful vs. happy trials predicted higher anxiety symptomology in previously institutionalized (PI) youths but not in comparison youths. Bottom: Greater amygdala responses for fearful vs. happy trials predicted higher anxiety symptomology in PI youths but not in comparison youths. *$p < .05$.

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