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Happy and Angry Faces Elicit Atypical Neural Activation in Children With Autism Spectrum Disorder

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ABSTRACT

BACKGROUND: Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by significant impairments in social interactions and communication. The ability to accurately perceive and interpret emotional faces is critical to successful social interactions. However, few studies have investigated the spatiotemporal profile of the neural mechanisms underlying emotional face processing in ASD, particularly in children. The current study fills this important gap.

METHODS: Participants were 55 children: 28 children with ASD (mean age = 9.5 ± 1.3 years) and 27 control children (mean age = 8.5 ± 1.3 years). All children completed an implicit emotional face task while magnetoencephalography was recorded. We examined spatiotemporal differences between the groups in neural activation during implicit processing of emotional faces.

RESULTS: Within-group analyses demonstrated greater right middle temporal (300–375 ms) and superior temporal (300–400 ms) activation to angry faces than to happy faces in control children, while children with ASD showed greater activation from 250 to 500 ms to happy faces than to angry faces across frontal and temporal regions. Between-group analyses demonstrated that children with ASD showed similar patterns of late (425–500 ms) posterior cingulate and thalamic underactivity to both angry and happy faces relative to control children, suggesting general atypical processing of emotional information.

CONCLUSIONS: Atypical posterior cingulate cortex and thalamus recruitment in children with ASD to emotional faces suggests poor modulation of toggling between the default mode network and task-based processing. Increased neural activity to happy faces compared with angry faces in children with ASD suggests reduced salience or immature response to anger, which in turn could contribute to deficits in social cognition in ASD.

Keywords: Autism spectrum disorder, Children, Emotional face processing, Magnetoencephalography, Neuroimaging, Social cognition

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder exemplified by deficits in social interaction and communication as well as restricted and repetitive behaviors and/or interests. Emotional facial expressions are one of the most important visual social cues, and the ability to perceive and interpret facial emotions is integral for effective social functioning, which is markedly impaired in ASD. The biological bases of impaired social cognition in ASD, however, remain unclear. Children with ASD show deficits in face processing by 3 or 4 years of age (1) as well as difficulties in emotional awareness (2). Furthermore, individuals with ASD also have more difficulties with perception of emotional faces, which are hypothesized to reflect deficits in subcortical and cortical processing of faces and the extended face perception network, which in turn may be associated with broader social dysfunction in social processing [see (3) for a review].

Positive versus negative facial expressions also appear to be differentially salient to children with ASD, as indicated by longer looking times at negative faces than at positive faces (4). Anger processing may pose a specific difficulty to those with ASD because displays of anger are usually in response to aggravations and require complex understanding of others' mental states and social norms (5–7). In addition, there appear to be age effects in anger processing, with older children and adolescents with ASD showing greater accuracy at anger identification compared with younger counterparts (8).

The ability to perceive and interpret emotions also matures across typical development, following an extended developmental trajectory into adolescence (9–11). Because ASD is a neurodevelopmental disorder, it is important to understand how brain function underlying emotional processing develops during childhood and how this may affect the poor social skills.

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Although the global developmental trajectory of face processing in ASD appears to be similar to the trajectory observed in typical development, there are differences that may be critical (12).

Neuroimaging provides a means of obtaining insight into the mechanisms underlying affective processing in ASD throughout development. Neural responses to affective faces occur automatically and are emotion specific, varying according to the emotion presented (13). Functional magnetic resonance imaging (fMRI) has been the most commonly used neuroimaging modality to explore emotional processing in ASD, with atypical activation noted in regions implicated in emotional face processing such as the amygdalas and fusiform gyri [e.g., (14–16)]. However, discrepancies in neural activity during the early stages of affective processing between individuals with ASD and those without ASD may be missed owing to the poor temporal resolution of fMRI.

The use of electrophysiological modalities affords the advantage of obtaining precise temporal information regarding the patterns of neural responses during emotional face processing in ASD. Electrophysiological studies have shown slowed or reduced neural responses during face processing in adolescents and adults with ASD [(17,18); but see (19)]. Temporal differences in brain activity during emotional face processing have also been reported during early childhood. For example, 3- and 4-year-old children with ASD showed slower event-related potential responses to neutral but not fearful faces relative to typically developing control subjects and failed to distinguish between neutral and fearful faces (20). In children and adolescents with ASD, delayed or reduced event-related potential responses have been found [(21,22); but see also (23)], and event-related potential responses in youths with ASD did not differentiate between different emotions, as seen in typically developing control subjects (24,25).

Magnetoencephalography (MEG) is a noninvasive neuroimaging technique that combines the strengths of fMRI and electroencephalography, yielding high-resolution spatial and temporal measures of cognitive processes. In clinical populations such as children with ASD, MEG is better tolerated than other neuroimaging modalities because electrodes do not need to be applied and the MEG is totally silent. The advantages of using MEG have given rise to a number of studies examining the ASD population [see (26) for a review]. However, despite the importance of studying the development of affect processing in ASD, there is a considerable gap in the literature regarding children and adolescents with ASD. Only a few studies have examined emotional face processing using MEG (27–29). Reduced early emotion-specific occipital gamma-band responses were observed in children and adolescents with ASD (n = 13), relative to control subjects (27). Children with ASD also showed increased alpha-band phase synchronization to happy faces relative to control subjects (28). Lastly, atypical activity in the insula, anterior and posterior cingulate, and temporal and orbitofrontal regions during affective processing has also been shown in adolescents with ASD (n = 24) (29). The current study expanded on these findings in a young cohort, using MEG to investigate whether there are differences in the neural correlates of emotional face processing between 7- to 10-year-old high-functioning children with ASD and typically developing children. We hypothesized reduced and delayed activation in children with ASD relative to typically developing children.

METHODS AND MATERIALS

Participants

The study included 55 children 7 to 10 years of age: 28 children with ASD (6 girls; mean age = 9.5 $\pm$ 1.3 years, mean IQ = 101.2 $\pm$ 17.5; 3 left-handed) and 27 typically developing control children (6 girls; mean age = 8.5 $\pm$ 1.3 years, mean IQ = 113.8 $\pm$ 15.2; 2 left-handed). The diagnosis of ASD in our clinical sample was confirmed with a combination of the Autism Diagnostic Observation Schedule (ADOS)-Generic (30), ADOS-2 (31), and expert clinical judgment. Participants were not included if there was a history of neurological or neurodevelopment disorders (other than ASD for participants in the clinical group), acquired brain injury, IQ $\leq$ 65, or standard contraindications to MEG and MRI. Additional exclusion criteria for control children included use of psychotropic medications. Five children with ASD taking psychotropic medication (e.g., Biphentin, Dexedrine, Strattera) were included in the analyses, as this is in keeping with the proportion of youths with ASD who typically use pharmacological intervention and thus provided external validity. The study was approved by the Hospital for Sick Children Research Ethics Board. Informed assent was obtained from the children, and written informed consent was obtained from their parents.

Characterization Measures

The ADOS-Generic and ADOS-2 are semistructured clinical assessments of autistic symptomology (30,31). Module 3, appropriate for children with fluent speech, was administered to all participants with ASD. The two-subtest version (vocabulary and matrix reasoning) of the Wechsler Abbreviated Scale of Intelligence (32) was used to estimate IQ in all children.

Implicit Emotional Face Task

The stimuli were emotional (happy or angry) or neutral faces paired with a scrambled pattern that were presented on each side of a central fixation cross. Because differences in lateralization of the face presentation were not expected, left/right presentation of the emotional faces was counterbalanced across trials. The use of implicit emotion processing was based on findings that 1) different neural regions were implicated in explicit versus implicit emotional face processing, particularly with stronger limbic activity in response to implicit processing (15); 2) individuals with ASD have much greater difficulty in explicitly recognizing emotional faces, and using an explicit task would likely have produced a performance confound between the groups; and 3) using an implicit face processing task would increase the ecological validity given that in most social situations adaptive social behavior requires individuals to automatically and rapidly process affect.

The faces were selected from the NimStim Set of Facial Expressions (threshold: 80% minimum accuracy) (33). Color photographs of happy, angry, and neutral faces (25 in total: 13 male and 12 female) for each of the three expressions were selected for a total of 75 stimuli. Unique scrambled patterns

(targets) were created by modifying each of the faces using Adobe Photoshop. Face stimuli were randomly divided into 64 cells. A mosaic was applied to the image (15 cells per square) followed by a Gaussian blur (10.0°). Face-pattern pairs were luminosity and color matched. Although inclusion of neutral faces was originally planned owing to their intended use as an emotional baseline, there have been a number of studies criticizing the extent to which neutral faces truly represent an affectively neutral baseline in clinical populations [e.g., (34–36)]. In light of similar findings in individuals with ASD who have recently been shown to misinterpret neutral faces and assign negative valence to emotionally neutral faces (37), neutral faces were not included in analyses.

The task consisted of 300 trials, with 50 trials of each expression in the left and right hemifields such that each face was presented twice in each hemifield. Children were instructed to fixate on a central cross and indicate the location of a scrambled pattern (target) using a response button box; the emotional faces were irrelevant to the completion of the task. Presentation software (http://www.neurobs.com/) was used to present stimuli and record behavioral responses. To minimize saccadic eye movements, stimuli were shown for only 80 ms with a jittered interstimulus interval ranging from 1300 to 1500 ms. Stimuli were back projected onto a screen in front of the child. The viewing distance was 79 cm, and the visual angle of each stimulus was between 1.9° and 6.9°, falling within the parafoveal region. Prior to the completion of the task in the MEG, all children completed a practice session outside the MEG to ensure that they understood the task and were comfortable with the rapid presentation.

MEG Data Acquisition

MEG data were acquired using a 151-channel CTF MEG system (MEG International Services Ltd., Coquitlam, British Columbia, Canada) with a 600-Hz sampling rate, third-order spatial gradient, and recording bandpass of 0 to 150 Hz. All children lay in a supine position while completing the emotional face paradigm in the MEG in a magnetically shielded room at the Hospital for Sick Children. To monitor head position and motion within the MEG dewar, three fiducial coils were placed on the left and right preauricular points and the nasion. Radio-opaque markers replaced these fiducial coils for MRI coregistration.

MRI Data Acquisition

For all participants, a T1-weighted MR image (three-dimensional sagittal magnetization prepared rapid acquisition gradient-echo: parallel imaging techniques, generalized autocalibrating partial parallel acquisition = 2, repetition time = 2300 ms, echo time = 2.96 ms, flip angle = 9°, field of view = 28.8 × 19.2 cm, 240 × 256 matrix, 192 slices, slice thickness = 1.0 mm isotropic voxels) was also obtained using a 3T MR scanner (MAGNETOM Tim Trio; Siemens, Erlangen, Germany) and a 12-channel head coil.

Data Analyses

MEG data were preprocessed and analyzed using SPM12 (Wellcome Trust Centre of Neuroimaging, London; http://www.fil.ion.ucl.ac.uk/spm/) implemented in MATLAB R2014b (The Mathworks, Inc., Natick, MA). MEG data were first filtered using a fifth-order Butterworth filter with a bandpass at 1 to 50 Hz and epoched into 800-ms time windows, from 200-ms prestimulus onset to 600-ms poststimulus onset. Trials containing inter- and intratrial movement in excess of 10 and 5 mm, respectively, were rejected. Artifact detection by channel thresholding (bad channel threshold = 0.2, thresholded 2000 fT, excision window of 600 ms) rejected signal components from eye movements or muscle activity. Trials were then averaged within emotion for each participant. Using the three fiducial markers placed on the left and right preauricular points and the nasion from each participant's T1-weighted MR image, the SPM12 cortical mesh template in Montreal Neurological Institute standard space was coregistered to MEG sensor space. To forward compute the gain matrix of the lead field model (38), a single shell head model was used. Source activity was estimated using the Empirical Bayes Beamformer (39,40). Beamformer results for sliding time windows of 50 ms in duration, overlapping by 25 ms (e.g., 100–150 ms, 125–175 ms) from 100 to 500 ms, were obtained. A full width at half maximum Gaussian smoothing kernel of 12 mm was used to spatially smooth beamformed images. Statistical analyses were then conducted to identify areas of peak differences in neural activity for happy and angry faces both within and between groups. Group (ASD or control) by emotion (angry or happy) contrasts were first conducted to explore interactions (group 1: ASD angry = −1; group 2: control angry = 1; group 3: ASD happy = 1; group 4: control happy = −1) . Follow-up *t* tests then were conducted to determine statistical significance of differences in neural activity and were corrected for multiple comparisons ($p_{corr} < .0017$) (41,42). Images were visualized using Analysis of Functional NeuroImages (AFNI) software (43). Lastly, three-dimensional renderings of significant differences in neural activity on spatially normalized brain images were created using MRIcron software (44).

RESULTS

Behavioral Results

Analyses of variance (2 [emotion] × 2 [group]) revealed no significant main effects of group or emotion or a significant

Table 1. Summary of Implicit Emotional Face Task Performance

	Emotion			
	Happy		Angry	
Group	Accuracy	Response Latency	Accuracy	Response Latency
Children With ASD	80.87 ± 16.00	565.52 ± 94.71	81.73 ± 17.76	564.07 ± 90.71
Typically Developing Children	82.87 ± 15.37	575.13 ± 114.30	82.85 ± 15.93	572.62 ± 104.07

Task accuracy (out of 100%) and response latencies (ms) in children both with and without autism spectrum disorder (ASD) are listed. There were no significant differences in accuracy or response latency between groups.

Table 2. MNI Coordinates and Pseudo-*Z* Values for Locations of Significant Differences in Peak Activations Between Happy and Angry Faces in Typically Developing Children

Time, ms	Directionality	Laterality	Region	*Z*	*p*	MNI (x, y, z)
300–350	A>H	R	Superior temporal gyrus	3.25	<.001	64, −20, 4
325–375	A>H	R	Superior temporal gyrus	3.49	<.001	64, −18, 8
		R	Middle temporal gyrus	2.95	<.0016	60, −52, 16
350–400	A>H	R	Superior temporal gyrus	2.97	.001	66, −20, 4

A>H denotes less activation in response to happy faces. Only time windows with significant differences are presented.
MNI, Montreal Neurological Institute; R, right.

interaction in reaction time or accuracy for detecting the target (see Table 1).

Neuroimaging Results

Within-group contrasts showed significant differences in neural activity to angry versus happy faces in children both with and without ASD. In typically developing children, angry faces elicited greater right middle temporal (300–375 ms) and superior temporal (300–400 ms) activation than happy faces (Table 2 and Figure 1A). In contrast, in children with ASD, the only significant between-emotion contrasts were greater activation to happy faces than to angry faces, including greater

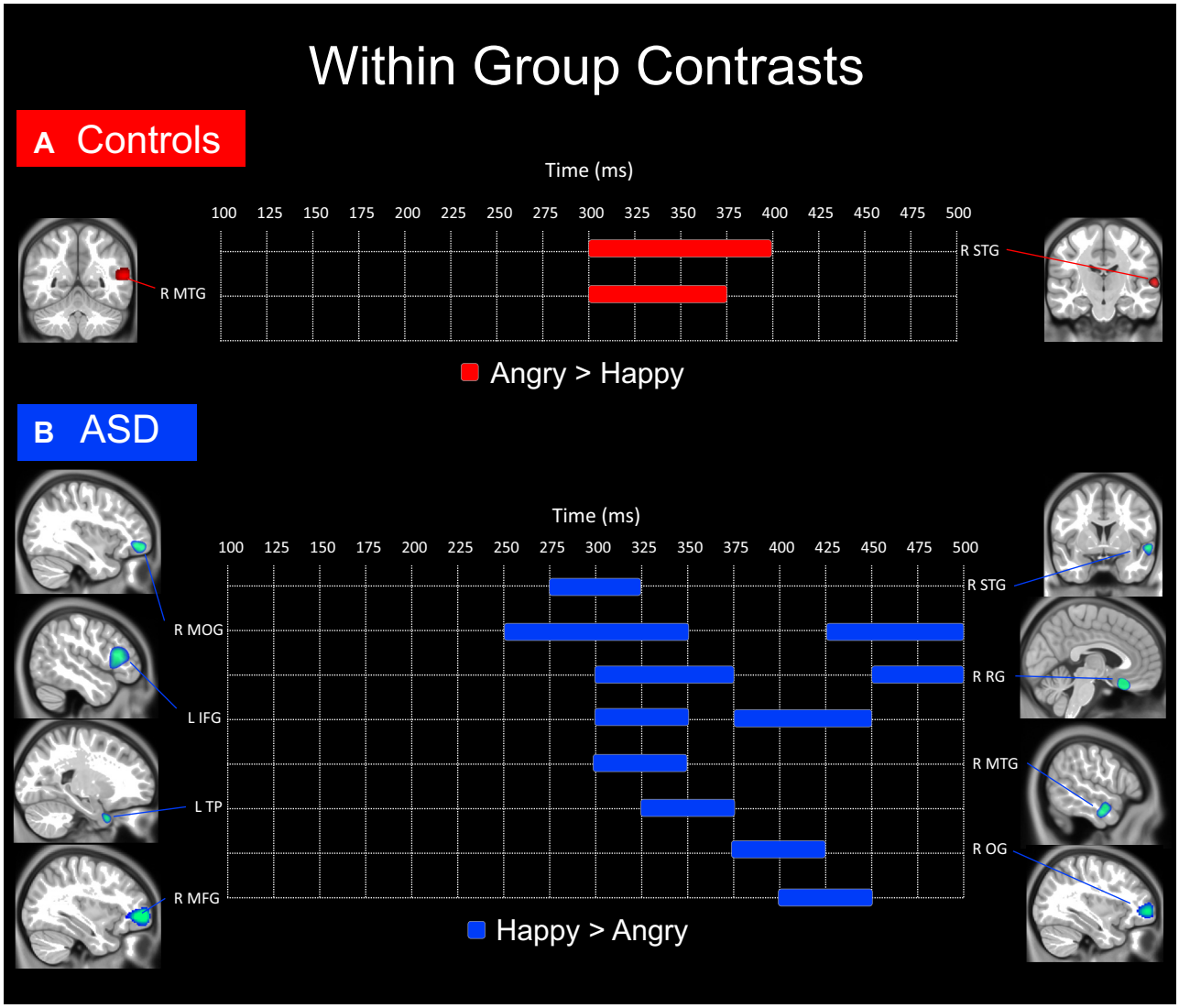

Figure 1. Summary of the spatiotemporal profile of significant differences between happy and angry processing within typically developing children **(A)** and children with autism spectrum disorder (ASD) **(B)**. IFG, inferior frontal gyrus; L, left; MFG, middle frontal gyrus; MOG, middle orbital gyrus; MTG, middle temporal gyrus; OG, orbital gyrus; R, right; RG, rectal gyrus; STG, superior temporal gyrus; TP, temporal pole.

Table 3. MNI Coordinates and Pseudo-*Z* Values for Locations of Significant Differences in Peak Activations Between Happy and Angry Faces in Children With ASD

Time, ms	Directionality	Laterality	Region	*Z*	*p*	MNI (x, y, z)
250–300	H>A	R	Middle orbital gyrus	3.03	.001	36, 50, −8
275–325	H>A	R	Middle orbital gyrus	3.41	<.001	38, 46, −8
		R	Superior temporal gyrus	3.00	.001	58, 0, −6
300–350	H>A	R	Rectal gyrus	3.20	.001	4, 24, −22
	H>A	R	Middle orbital gyrus	3.02	.001	40, 48, −8
	H>A	L	Inferior frontal gyrus	3.06	.001	−48, 26, 16
	H>A	R	Middle temporal gyrus	2.95	.001	56, −4, −20
325–375	H>A	R	Rectal gyrus	2.97	<.0015	2, 26, −18
	H>A	L	Temporal pole	2.93	<.0017	−22, 12, −38
375–425	H>A	L	Inferior frontal gyrus	3.45	<.001	−50, 28, −2
	H>A	R	Orbital gyrus	2.94	<.0017	34, 56, −2
400–450	H>A	L	Inferior frontal gyrus	3.22	.001	−48, 24, −2
	H>A	R	Middle frontal gyrus	3.19	.001	34, 54, −2
425–475	H>A	R	Middle orbital gyrus	3.52	<.001	34, 54, −4
450–500	H>A	R	Middle orbital gyrus	3.54	<.001	34, 54, −4
	H>A	R	Rectal gyrus	3.02	.001	4, 14, −22

H>A denotes less activation in response to angry faces. Only time windows with significant differences are presented.
ASD, autism spectrum disorder; L, left; MNI, Montreal Neurological Institute; R, right.

right middle orbital (250–350 and 425–500 ms), orbital (375–425 ms), middle frontal (400–450 ms), rectal (300–375 and 450–500 ms), superior (275–325 ms) and middle temporal (300–350 ms), and left inferior frontal (300–350 and 375–450 ms) and temporal pole (325–375 ms) (Table 3 and Figure 1B).

In between-group analyses, where we contrasted the ASD and typically developing groups for happy and angry faces separately, both angry and happy faces elicited late (425–475/500 ms) left thalamus and right posterior cingulate gyrus underactivity in children with ASD compared with typically developing children (Tables 4 and 5 and Figure 2).

Between-group and between-emotion contrasts showed interaction differences in neural activity for a number of frontal and temporal areas, including the right orbital, superior and middle temporal, and left inferior frontal regions, reinforcing the results from the within-group analyses (Supplemental Table S1).

DISCUSSION

Differences in neural activity during angry and happy face processing were found in children with ASD compared with typically developing children. Behavioral results indicated that neither emotion nor group influenced response latency for target detection, suggesting that discrepancies in neural activity were not attributable to differences in task performance. When comparing angry faces with happy faces within groups (i.e., within typically developing children only and children with ASD only), MEG analyses showed that a number of temporal and frontal areas demonstrated greater activation to happy faces than to angry faces in children with ASD, but no areas showed greater activity in response to angry faces. In contrast, typically developing children showed the reverse finding, whereby angry faces elicited greater activity, relative to happy faces, in right temporal areas. Between-group contrasts confirmed our study hypothesis that children with ASD showed reduced and delayed activation compared with typically developing children, specifically that control children had greater activation in thalamus and posterior cingulate cortex (PCC) compared with children with ASD for both angry and happy faces. Furthermore, these between-group differences occurred late after stimulus presentation, at approximately 425 to 475/500 ms, indicating atypical later evaluation of emotional faces in children with ASD. These findings are discussed in detail below.

Late Posterior Cingulate and Thalamic Underactivity in Children With ASD to Emotional Faces

Between-group analyses showed late posterior cingulate and thalamic underactivity in children with ASD, regardless of

Table 4. MNI Coordinates and Pseudo-*Z* Values for Locations of Significant Differences in Peak Activations Between Children With ASD and Those Without ASD in Response to Angry Faces

Time, ms	Directionality	Laterality	Region	*Z*	*p*	MNI (x, y, z)
425–475	C>A	L	Thalamus	3.33	<.001	−2, 0, 8
		R	Posterior cingulate gyrus	3.27	<.001	10, −40, 10
450–500	C>A	L	Thalamus	2.92	.0017	−2, 2, 8

C>A denotes less activation in the ASD group. Only time windows with significant differences are presented.
ASD, autism spectrum disorder; L, left; MNI, Montreal Neurological Institute; R, right.

Table 5. MNI Coordinates and Pseudo-*Z* Values for Locations of Significant Differences in Peak Activations Between Children With ASD and Those Without ASD in Response to Happy Faces

Time, ms	Directionality	Laterality	Region	*Z*	*p*	MNI (x, y, z)
425–475	C>A	L	Thalamus	3.18	<.001	−2, 0, 8
		R	Posterior cingulate gyrus	3.08	.001	10, −40, 10

C>A denotes less activation in the ASD group. The only time window with a significant difference is presented.
ASD, autism spectrum disorder; L, left; MNI, Montreal Neurological Institute; R, right.

emotion, compared with typically developing children. This similar pattern of underactivity in children with ASD to both angry and happy faces suggests a general emotion processing atypicality rather than an emotion-specific effect; that is, children with ASD may differ from their typically developing peers in terms of general affect processing. The late differences in activation further suggest differences in terms of evaluation of emotional faces. Our findings contrast with those of previous studies reporting early between-group differences in subcortical or visual processing of emotional faces [(14–16,45–47); see (48) for a review]; however, our sample differs from these studies in various sample parameters such as modality, age (e.g., preschool children, adolescents), sex (e.g., male only), and task type (e.g., passive viewing). Other studies have also documented no between-group differences (24,49). Furthermore, the M170 component does not appear reliably in children (12,50). Nevertheless, it is possible that, in contrast to previous studies documenting early atypical amygdala and fusiform activity in ASD, our groups did not differ in terms of early stages of visual processing or visual perception of emotional faces, as noted in previous studies. Our groups do, however, differ in the subsequent general evaluation of the affective faces, as evident by late posterior cingulate and thalamic underactivity in our clinical sample relative to control children.

That there are similar findings in between-group differences in neural activity to both happy and angry faces is consistent with Maddock *et al.*'s (51) suggestion that posterior cingulate activity is sensitive to emotionally salient stimuli generally rather than being valence specific. Recent research has noted increasing evidence of a dysfunctional PCC in ASD (52). A number of studies have shown metabolic and functional abnormalities in the posterior cingulate of individuals with ASD; specifically, adults with ASD show reduced posterior cingulate metabolism (53) and reduced or atypical functional connectivity between the PCC and other neural regions (e.g., 54–56).

There are, however, few studies that have noted PCC involvement in the pediatric ASD population during social cognitive tasks. Adolescents and adults with ASD showed significantly greater PCC activity to familiar faces than to strangers' faces in a similar pattern to typically developing control subjects (57). Similarly, Vogan *et al.* (58) found

Figure 2. Source localization of significant between-group differences to angry **(A)** and happy **(B)** faces. Areas highlighted in orange show regions where children with autism spectrum disorder (ASD) showed reduced activation relative to typically developing children. L Thal, left thalamus; R PCC, right posterior cingulate cortex.

comparable deactivation of the PCC in children both with and without ASD with increasing working memory load. A decrease in PCC activity with increasing cognitive load is consistent with the characterization of one of the PCC's key functional roles as a hub in the default mode network (DMN), a system of neural structures that show highly correlated and increased activity during wakeful rest or when attention is directed to internal stimuli (e.g., episodic memory retrieval, daydreaming) and are deactivated when attention is focused on external stimuli or tasks (59). Individuals with ASD have been shown to demonstrate atypical deactivation of the PCC (60). The late onset of this activity in the control children suggests activation of the DMN following affective stimuli presentation; children with ASD may fail to show this shift to default mode processing, consistent with other reports of poor DMN modulation in ASD (61).

The PCC has also been suggested to be an evaluative region that is implicated in monitoring and interpreting the external environment as well as memory-related functions and mediating interactions between emotion and facial memory (51,62). This region is responsive to both emotional faces and nonemotional stimuli and thus appears to play a general role in visuospatial processing and not uniquely for emotion regulation (63). This perspective postulates that the PCC acts as an intermediary between visual and emotional processing in the visual and anterior cingulate cortices, respectively, and facilitates differentiation between emotion and nonemotional stimuli as well as memory storage for this information (64). Thus, PCC hypoactivation is consistent with other social cognition studies in ASD (65) and indicates that a disruption between visual and emotional processing may contribute to affective processing difficulties in children with ASD.

The thalamic hypoactivation in children with ASD, concurrent with PCC hypoactivity, may reflect the reciprocal connections between the two regions and is concordant with findings of reduced intrinsic functional connectivity within both the left thalamus and right posterior cingulate (55,64). The thalamus is a key relay center for incoming information, which is then routed to the cortex (66). In primates, the mediodorsal nucleus is reciprocally linked to the prefrontal cortices and amygdala via the anterior thalamic and inferior thalamic peduncles, respectively, and research has shown that neural organization is similar in the human brain (66). In humans, the thalamus plays a key role in information processing (67), and cognitive deficits in ASD have been linked to atypical information processing (68). While no studies linking thalamic activity to social impairments in ASD have been reported, sensory features have been correlated to various aspects of social development (69,70).

Thalamic involvement in emotional processing was first suggested in Papez's circuit theory of functional neuroanatomy of emotion, which suggested that the thalamus has a role in diverting sensory information about emotional stimuli to the cortex. Facial information is rapidly conveyed (in < 100 ms) via a subcortical route, including the superior colliculus, the pulvinar in the thalamus, and then the amygdalae (71,72), which are thought to be involved with processing low-spatial frequency information regarding faces and social orienting to faces. Deficits in connectivity between the fusiform gyri and subcortical structures in ASD support the hypothesis that disrupted subcortical face processing may contribute to social impairments in ASD (71,73). Consistent with this notion, Hall *et al.* (74) also found reduced thalamic activity in individuals with ASD during emotional face processing. Thus, the current findings of thalamic underactivity in children with ASD support the model that facial affective information is abnormally processed in this population; importantly, we also showed that this is present even early in development and when faces are not processed explicitly.

Within-Group Contrasts Reveal Distinct Effects of Emotion on Neural Activity in Typically Developing Children and Children With ASD

We found greater temporal and frontal activity to happy faces in children with ASD and a reversed pattern of greater temporal activity only to angry faces in typically developing children. That differences in neural activity in response to specific emotions did not emerge until 250 ms is concordant with findings that the face-sensitive N170 component does not discriminate between different facial expressions in children (9,75).

Because facial emotions elicit distinct neural activity without explicit attention (76), our within-group results suggest that happy and angry faces differ in their salience to typically developing children and children with ASD. Our findings of increased superior temporal and middle temporal activity to angry faces relative to happy faces in control children are consistent with previous findings of an anger bias in typically developing children (77), and of neural responses to negative emotions being stronger than those to positive ones in control children. Because there is a positivity bias in young children, as well as greater ease with the detection of happy faces, the increased activity to happy faces in the children with ASD may reflect less mature emotional processing. Alternatively, because the recognition of anger is poor in those with ASD (77) and this skill increases through adolescence (8), it may be that the young children with ASD are simply not discriminating the angry faces as different from neutral (as seen in younger children) (20). Thus, the children with ASD may have recruited the network of frontal and temporal regions known to be involved in emotional face processing [e.g., (17)] to a greater extent when processing happy faces because the angry faces were not perceived as emotional. The inadequate recognition of angry faces would certainly contribute to the poor social interactions seen in these children with their family, potential friends, and teachers. These results suggest that this may be an important area to strengthen in early training programs.

Conclusions

The current study demonstrated atypical neural activation in young children with ASD during happy and angry face processing. Our data showed a unique pattern of discrepant recruitment of the right PCC and thalamus in the children with ASD, to both angry and happy faces, likely reflecting poor modulation of toggling between the DMN and task-based processing. In contrast, the children with ASD showed earlier, more extensive, and greater activity to happy faces than to angry faces, suggesting that they were not processing angry faces as salient, in contrast to what was seen in their age-matched peers. Given that emotional face processing is integral to

successful social interaction, understanding the neural mechanisms underlying this process offers a basis for understanding impaired social impairment in children with ASD.

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The authors report no biomedical financial interests or potential conflicts of interest.

ARTICLE INFORMATION

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