Equivalent neural responses in children and adolescents with and without autism during judgments of affect

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ABSTRACT

Previous research has noted disrupted patterns of neural activation during emotion, processing in individuals with autism spectrum disorders (ASD). However, prior research relied on, designs that may place greater cognitive load on individuals with ASD. In order to address this issue, we adapted the fMRI task of Ochsner et al. (2004a) for children by, presenting fewer stimuli, with fewer valence levels, and longer stimuli duration. A localizer sample of, typically developing children ($n = 26$) was used to construct regions of interest involved in emotional, processing. Activations in these regions during self- and other-referential emotion processing was, compared in age, IQ, gender matched groups ($n = 17$ ASD, $n = 16$ TD). Matched samples replicate, condition contrasts of the localizer, but no group differences were found in behavior measures or, neural activation. An exploratory functional connectivity analysis in a subset of the matched groups, also did not detect striking differences between the groups. These findings suggest that disruptions in activation in emotion processing neural networks in ASD is partially a function of task related cognitive load.

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1. Introduction

Autism spectrum disorders (ASD) are a set of pervasive neurodevelopmental disorders characterized by a triad of impairments that include a delay or the absence of communicative skills, restricted interests and stereotyped, repetitive behaviors, and finally, impairment in social interactions. Social impairments manifest across a variety of domains in behavior and brain function. Individuals with ASD exhibit disrupted processing of faces (Behrmann et al., 2006; Chawarska and Shic, 2009; Klin et al., 2002; Webb et al., 2010), actions and biological motion (Blake et al., 2003; Cook et al., 2009; Kaiser et al., 2010; Klin et al., 2009), and emotions (Greimel et al., 2010; Nuske et al., 2013; Sigman et al., 1997). High priority has been given to identifying the neural bases of these deficits, evidenced by the increasing amount of research dedicated to them. A specific focus, of particular relevance to the current study, has been research into the way in which typically developing individuals (TD) and individuals with an ASD represent and process emotion about themselves and others.

Although there is a general consensus that individuals with an ASD tend to have impairments in processing emotion, the pattern of results is complex (for reviews see Harms et al., 2010; Weigelt et al., 2012). So while both parents rate their children with ASD and the individuals with an ASD tend to rate themselves as having more difficulty in recognizing their own emotions and exhibiting emotional awareness (Hill et al., 2004; Hobson et al., 2006), individuals can reliably exhibit and identify emotions when tested (Hobson et al., 2006). Complexity of emotion seems to be an important dimension, since they perform better on simpler emotions such as happiness and

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fear, while struggling with more complex emotions such as shame (Heerey et al., 2003). The concepts of empathy and emotion processing are intimately linked, especially in the literature discussing ASD. Individuals with autism have generally failed cognitive empathy tasks, which possibly involve the mentalization system or higher order inferential processes (Baron-Cohen and Wheelwright, 2004; Rogers et al., 2006). But it should be noted that many of the empathy self-report measures focus on cognitive components of empathy. Thus when measures of affective empathy are used individuals with autism do not appear to be as impaired (Dziobek et al., 2008).

In an important paper, Ochsner et al. (2004a) utilized fMRI to identify both distinct and overlapping regions for processing the self-referential and other-referential affect, relative to a non-emotional control task in typically developing adults. They presented affective pictures, which included positive, negative, and neutral images, drawn from the International Affective Picture Set (IAPS; Lang et al., 2008). Participants were asked to judge the affect in the picture, again positive, negative or neutral, either with respect to their own affect in response to the picture or with respect to the person in the picture. Regions common to self and other representation included the medial prefrontal cortex (mPFC), the inferior and middle frontal gyrus (IFG and MFG), and the superior temporal gyrus and sulcus (STG and STS). Several regions were activated more strongly during self-referential processing, including more specialized regions of the mPFC, the MFG, and the middle temporal gyrus, while regions in the IFG and posterior midline structures exhibited greater activation to other-referential processing. In general, this set of finding has held up in subsequent studies (Legrand and Ruby, 2009; Northoff et al., 2006; Uddin et al., 2007).

The experimental design described in Ochsner's study has since been used in several neuroimaging studies of individuals with ASD. For example, using a novel faces set, fMRI studies of self- and other-referential processing were run in adults (Schulte-Rüther et al., 2011) and adolescents (Greimel et al., 2010). Adults were reported as having aberrant patterns of activation (sometimes ASD > TD, sometimes TD > ASD) during self- and other-referential affective processing in some of the key regions described above, including mPFC and IFG. Adolescents were reported as having lower activation in IFG relative to controls during self-referential processing. Another study of adults with ASD using a very similar paradigm as that in the Ochsner study also reported a pattern of deviant activations in these key structures in ASD relative to TD controls (Silani et al., 2008). These findings, especially when added to a literature of disrupted cognitive self-referential processing (Lombardo et al., 2010; Pfeifer et al., 2013), paint a picture of a highly disrupted representation of self-knowledge and awareness.

However, it is interesting to note that in addition to using a similar method of emotional judgments, the timing of the follow-up ASD studies was also very similar to the original Ochsner study. That study was designed for, and carried out in, TD adults. Stimuli were presented for 2s followed by a rating scale for 1.5 s. The stimuli and affective judgments utilized 3 levels of emotional valence. The Greimel and Schulte-Rüther studies presented stimuli for 2.5 s, with an average ISI of 0.7 s. The Silani study presented stimuli for 2 s followed by a 4 s response window. All three studies had three levels of stimuli and judgment valence. Given that concurrent affective and cognitive processing affect one another (Blair et al., 2007; Pessoa et al., 2005) the question can be asked, without invalidating the previous results, what effect might the cognitive load of the tasks have had on this kind of emotional processing in ASD relative to TD individuals?

In face processing literature differences between ASD and TD groups are less evident in tasks with lower difficulty or cognitive load. For example, individuals with ASD tend to do worse on face recognition tasks using mismatched labels (Grossman et al., 2000) or when faces are presented very rapidly (Clark et al., 2008). However, individuals with ASD not as evidently impaired especially if the emotions expressed are basic (Baron-Cohen et al., 1997) or presentation is slower (Michelle and Rutherford, 2008). Task demands can also change the likelihood of finding differences in brain activation. For example, expression matching tasks are likely to drive differences in activation within face-processing regions between ASD and TD participants, while face labeling tasks are not (Piggot et al., 2004; Wang et al., 2004).

In order to address the issue of cognitive load, we adapted the task of Ochsner et al. (2004a) for children. Participants viewed age-appropriate emotionally salient pictures and were asked to evaluate how they felt about each picture (Self condition), how the people in the pictures felt (other condition), or where the picture was taken (control condition). Stimuli were presented for a total of 5.5 s and were present while children made ratings. The valence dimensions in the pictures and the requested responses were limited to only positive and negative (neutral was eliminated). The primary planned contrast was between emotion judgment conditions and the non-emotion judgment condition (self and other > location) with the hypothesis that with the lower processing demands, the differences between the groups would be attenuated or eliminated. A secondary comparison of interest is the contrast between self-referential processing and other-referential processing (self > other).

2. Materials and methods

2.1. Participants

Two samples of typically developing children, a localizer sample and a matched control sample and a sample of children with an ASD participated in the study. Individuals were excluded from participation in the current study if parents reported that the child had experienced neurological problems or abnormalities (unrelated to autism). In addition, if the child ever experienced seizures, epilepsy, hearing or vision loss, motor impairment, or severe allergies, then he or she was excluded from participation. Typically developing children were prescreened and excluded from participation if they had a first degree relative with an ASD, or if parent responses on the Adolescent and Child Symptom Inventories (Gadow and Sprafkin,

Table 1
Demographic information for participant samples.

	N	Age in months			Full-scale IQ			SRS		
		Max	Min	Mean	Max	Min	Mean	Max[a]	Min	Mean
TD[b]	16 (1 Female)	222	129	158	127	78	105	55	34	42
ASD	17 (1 Female)	210	114	162	136	70	108	90	52	76
Localizer	26 (16 Female)	210	85	142	140	80	109	55	37	45

[a] SRS *T*-scores cap at 90.
[b] One TD individual did not complete a DAS-II IQ test.

1994) indicated potential serious psychiatric conditions, such as major depressive disorder. Typically developing children were also required to have social responsiveness (Constantino, 2002; Constantino et al., 2003) *T*-scores < 60, which is the cut-off for clinically significant social deficits. ASD diagnosis was confirmed by expert clinical evaluations, ADOS (Lord et al., 2000) Module 13 ($n = 15$) Module 4 ($n = 2$), and ADI-R (Lord and Rutter, 1994). All participants (except for one) met cut-offs based on the revised scoring algorithm (Gotham et al., 2007). The individual who did not meet the cutoff was, nevertheless, deemed to be on the spectrum by an expert clinician with experience diagnosing autism spectrum disorders.

After further exclusions, described in Section 2.8 below, the final localizer sample consisted of 26 individuals (16 female, mean age in years = 12.1), the final matched control sample consisted of 16 individuals (1 female, mean age in years = 13.1), and the final ASD sample consisted of 17 individuals (1 female, mean age in years = 13.5).

The TD and ASD matched samples were matched on gender, age, and full scale IQ, assessed using the GCA scale of the DAS-II. The ratio of genders did not differ in the matched groups (Fischer's exact test, $p = 0.742$). The matched groups did not differ by age ($t(31) = 0.4$, $p = 0.69$), or full-scale IQ ($t(30) = 0.46$, $p = 0.65$). As expected the groups differed significantly on social responsiveness scale *T*-scores, ($t(31) = 9.95$, $p < 0.001$). Details are presented in Table 1.

Children were recruited through online and print advertisements. Parents or guardians gave written informed consent for the minors to participate in research. Assent was obtained for each minor participant by giving age-appropriate verbal and written explanations of the research protocols and their rights. Research was reviewed and approved by the Institution's Human Investigation Committee.

2.2. Stimuli and design

Experimental stimuli were present using an E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) script. Each participant was presented with a series of pictures and was required to make judgments under three conditions. In the Self condition, they were asked whether the picture made them feel good or bad. In the Other condition, they were asked whether the person or people in the picture felt good or bad. In the Location condition, they were asked whether the picture was taken inside or outside. Responses were made by pressing a corresponding button located in each hand. The left button box was used for 'good' and 'inside';

the right button box was used for 'bad' and 'outside'. All button presses were recorded with an inline E-prime script. The pictures were chosen from the International Affective Picture System (Lang et al., 2008), and balanced for valence. All pictures included people.

The experiment consisted of 20 s of initial fixation and 12 s of final fixation. Each condition (Self, Other, and Location) was presented in 5 blocks. Each block was preceded by an auditory and visual task reminder. (e.g. "Now it is time to respond to how the person in the picture feels.") Each block was 26 s long and consisted of 4 picture judgment trials. Blocks were balanced for picture valence (two positive and two negative). Each picture was presented for 5.5 s, with an auditory prompt appearing after 2 s (e.g. "Do they feel good or bad?"). Consecutive pictures were separated by 1 second of fixation. To mitigate against order effects, three versions of the task were administered using different task orders with the constraint that no condition could be presented twice in a row. To mitigate against idiosyncratic effects of specific pictures, the assignment of pictures to conditions was changed for each version. To ensure that each child understood the task, they were given a practice session prior to the experiment that familiarized them with the task using pictures not included in the experiment.

2.3. Behavioral data coding

For the self emotional judgment conditions, there is no true correct response for any given probe. A positive valence picture could plausibly induce a negative affect (e.g. the happy picture of a child with a dog might make a participant sad if they recently lost their dog). However, for the purposes of analyses both Self and Other responses were coded as correct or incorrect relative to the standard valence of a picture, i.e. positive pictures should be given a "Good" response, negative pictures should be given a "Bad" response. Location judgment responses were coded as correct relative to the most common response ("inside" or "outside") given to that picture in a pilot group of adults.

2.4. Data acquisition

Imaging data were collected on a Siemens 3T Tim Trio scanner. T1-weighted anatomical images were acquired using an MPRAGE sequence (TR = 1900 ms; TE = 2.96 ms; FOV = 256 mm; image matrix 256 × 256; 1 mm × 1 mm × 1 mm). Whole-brain functional images were acquired using a single-shot, gradient-recalled echo planar pulse sequence (TR = 2000 ms; TE = 25 ms; flip angle = 60°; FOV = 220 mm; image matrix = 64 × 64; voxel

size = 3.4 mm × 3.4 mm × 3.4 mm; 34 slices) sensitive to blood oxygenation level-dependent (BOLD) contrast.

2.5. Preprocessing

Functional data were analyzed with the BrainVoyager QX 2.6 (BrainInnovation, Maastricht, the Netherlands) software package. The first 5 functional volumes were discarded. Preprocessing of the remaining functional data included slice scan time correction using cubic spline interpolation, motion scrubbing (described below), 3D motion correction using trilinear interpolation to correct for small head movements, linear trend removal, and temporal high pass filtering to remove low-frequency non-linear drifts 2 or fewer cycles per time course (2.86×10^{-3} Hz), and Gaussian spatial smoothing using a 7 mm kernel. Functional images were co-registered to each individual's anatomical volume and transformed into Talairach space (Talairach and Tournoux, 1988).

2.6. Motion scrubbing

The functional data for each participant were subjected to the following process for motion scrubbing. First, each functional run was analyzed and an optimal volume was selected for the purpose of serving as the reference volume for motion-correction and anatomical coregistration preprocessing steps. The optimal volume was defined as the functional volume for which the sum of estimated motion parameters relative to that volume was minimized. After preprocessing, the motion estimates across all individuals were inspected. Among the subset of functional runs with no motion estimate greater than 3 (standard motion exclusion criteria), the distribution of volume-to-volume motion changes was computed. Next, the per volume motion characteristics for all functional runs was inspected. Volumes were marked for excision for excessive drifts and motion spikes. A volume exhibited excessive drift if it exceeded an absolute motion parameter greater than 3 relative to that person's optimal reference volume. A volume exhibited a motion spike if it exceeded a motion parameter that differed, absolutely, from the prior volume's motion greater than 0.26, which represents 6 standard deviations greater than what was observed in the standard sample. Entire functional runs were excluded from analysis based on the proportion of data remaining after scrubbing (described below). A set of independent samples *t*-test were computed to compare the ASD and TD groups. After motion scrubbing, they did not differ in the maximum estimated motion parameter ($t(31) = 0.49$, $p = 0.63$), the mean estimated motion parameter ($t(31) = 0.61$, $p = 0.55$), the mean estimated volume to volume motion ($t(31) = 0.76$, $p = 0.46$), or the proportion of data remaining after scrubbing ($t(31) = 0.47$, $p = 0.64$).

2.7. First-level statistical model

A general linear model (GLM) was used to compute first-level statistics on the Z-normalized BOLD signal for each individual. A model time course was constructed for condition (Self, Other, and Location) by convolving a gamma function (Boynton et al., 1996) with a boxcar function equal to 1.0 when the condition was present in the experiment and 0.0 otherwise. An emotional valence model timecourse was created for each condition by convolving a step function with the gamma function. In this case the step function was defined as 1.0 during the presentation of positively valence pictures, −1.0 during the presentation of negatively valence pictures, and 0.0 otherwise. Motion estimates derived from the motion correction were added as nuisance predictors. Experimental and nuisance predictors were Z-normalized. If a volume was marked for excision by the motion scrubbing algorithm, the corresponding timepoint in the design matrix was also removed.

2.8. Exclusions

Individuals' were excluded on the basis of issues with behavioral, motion, and functional data. They were excluded if the overall proportion of behavioral responses coded as correct was less than 0.67, this represents above chance performance ($p < 0.05$) on a binomial distribution. Individuals were excluded if the computed beta value to Self, Other, and Location in the visual cortex, defined anatomically from Brodmann's Area 17, was each less than 0.0, indicating unexplained deactivation to visual stimuli. For standard analysis they were excluded if, following motion scrubbing, less than 75% of the data remained (overall and per condition). For connectivity analyses, they were excluded if the proportion was below 95%.

A total of 20 children with ASD were excluded: 8 for failing to meet behavioral criteria, 1 for not showing an evoked response in V1, 9 for motion, and 2 for behavior and motion. A total of 13 typically developing children were excluded: 5 for behavior, 4 for motion, 1 for motion and above cutoff SRS score, 1 for motion, behavior, and SRS score, and 2 for no evoked response in V1. The behavioral data for one TD child was not collected in scanner due to technical malfunction, but task understanding was subsequently assessed outside the magnet. Their brain data was included in the analysis, but their behavioral data was not.

2.9. Event-related functional connectivity

To compute the connectivity between two ROIs, the mean time course from each was extracted and z-normalized. The first order statistical model (experimental conditions, picture valence, instruction presentation, and motion) plus a white matter nuisance predictor was regressed out of the mean time course. For ROIs, denoted R_i and R_j we denoted a window of 5 successive timepoints, as $t(R_i)$ and $t(R_j)$, respectively. The functional distance $FD(R_iR_j)$ between each window, defined as the Euclidean distance in functional space between them, is given as: $FD(R_iR_j) = \mathrm{sqrt}(\mathrm{sum}((t(R_i) - t(R_j))^2)$. Functional (Euclidean) distance has been used in a variety of contexts to operationalize similarity and connectivity (Bullmore et al., 1996; Friston, 1994; Shen et al., 2010). Here, because other sources of signal variability, such as task, motion, and scanner/biological noise, have been regressed out we interpret the value as indexing bidirectional connectivity.
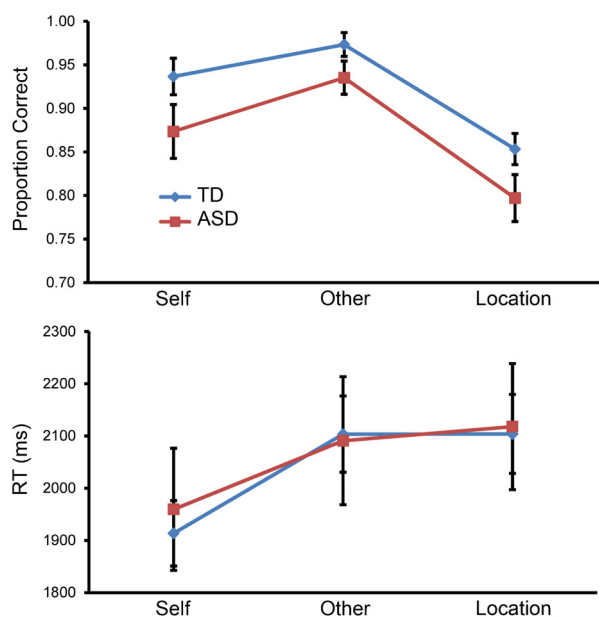
Fig. 1. Proportion correct and reaction time as a function of condition and group. Error bars denote SE.

Fig. 2. Regions discovered in localizer analysis. Blue: location > emotion. Orange: Emotion > location. Regions are rendered in functional resolution on a reconstructed cortical surface. Voxels that are semi-transparent are located below the rendered cortical surface. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

The algorithm was iterated over the entire time course by moving the window from volume 5 (window over timepoints 1–5) to the final volume V (window over timepoints V−5 to V). Event-related plots were constructed by averaging subsets of the FD series, time-aligned to the onset of the block of a given condition. These plots represent temporal moving averages of the functional distance between two ROIs as a function of the presentation of different stimulus conditions.
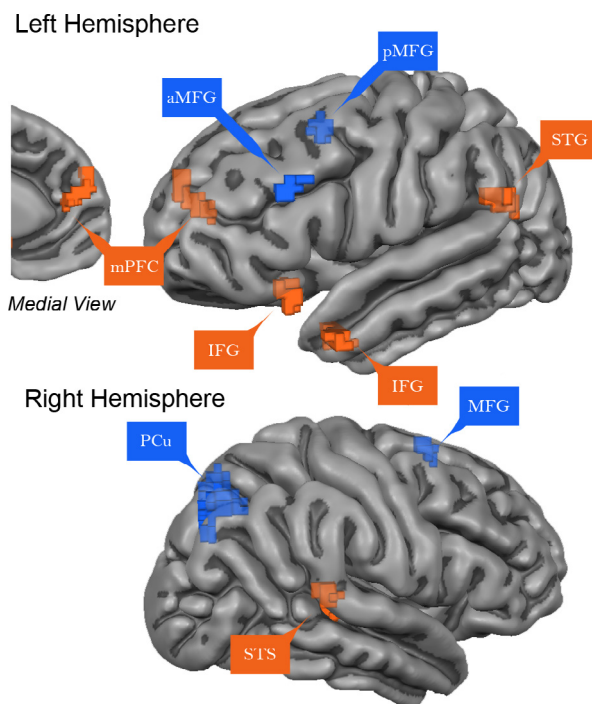
3. Results and discussion

3.1. Behavioral data

Behavioral responses during the in-scanner task were analyzed for the matched samples. Proportion correct (defined above) and reaction were used as dependent variables (Fig. 1).

3.1.1. Proportion correct

Proportion correct was analyzed using a mixed design ANOVA with a Greenhouse–Geisser correction. Condition (Self, Other, and Location) was treated as a within-subject factor and group (ASD or TD) was treated as a between-subjects factor. There was a main effect of condition, ($F(1.47,44.25) = 20.75$, $p < 0.001$, $\eta^2 = 409$) and a main effect of group, such that the ASD group was less accurate overall ($F(1,30) = 5.43$, $p < 0.05$, $\eta^2 = 153$). Post hoc tests using the Bonferroni correction method revealed that participants were significantly more accurate during the Other condition than the Self ($p < 0.05$) or Location ($p < 0.001$) conditions and that participants were significantly more accurate during Self than Location conditions ($p < 0.05$).

3.1.2. Reaction time

Reaction time (RT) was also analyzed using the same mixed design ANOVA, though correction for violations of the assumption of sphericity was unnecessary (Mauchly's test ($\chi^2(2) = 1.41$, $p = 0.495$). There was a main effect of condition, ($F(2,60) = 21.84$, $p < 0.001$, $\eta^2 = 421$), but no effect of group ($F(1,30) = 0.13$, $p = 0.912$). Post hoc tests using the Bonferroni correction method revealed that participants were significantly faster to respond during the Self condition than the Other ($p < 0.001$) or Location ($p < 0.001$) conditions.

3.2. fMRI localizer analysis

An analysis of the patterns of activation in the Localizer samples was used to construct regions of interest (ROIs). First, an antomical mask was constructed by averaging participants' Talairach normalized anatomical images to exclude voxels outside the averaged brain, white matter, or ventricles from analysis. The first-level GLM was used to compute beta values. A contrast was computed between emotion judgment conditions (Self and Other) and the non-emotion judgment condition (Location). The contrast was balanced by multiplying the Location betas by a factor of 2. First-level contrasts were entered into a second-level random effects analysis. The resulting t maps were thresholded at the voxel level, false discovery rate (FDR) $q < 0.005$ (Genovese et al., 2002), and at the cluster

Table 2
Peak Talairach coordinates for regions significant regions by contrast.

Contrast	Region	Hemisphere	TAL			mm^3
			X	Y	Z	
Emotion > Location	STS	R	46	−34	3	432
	mPFC	L	−4	50	24	1026
	aTP	L	−47	9	−23	756
	IFG	L	−44	25	−7	486
	STG	L	−57	−50	24	729
Location > Emotion	Pcu	R	30	−72	37	2052
	MFG	R	28	7	54	432
	pMFG	L	−24	7	49	351
	aMFG	L	−49	24	30	351

level, contiguous $k > 300$ mm^3. The regions are described in Table 2 and depicted in Fig. 2.

Emotion judgments activated many of the key regions marked by previous literature, including the medial prefrontal cortex (mPFC), the left inferior frontal gyrus (IFG), the left anterior temporal pole (aTP), and temporal cortex bilaterally in the left superior temporal gyrus (STG) and the right superior temporal sulcus (STS). Identifying these regions as showing robust preferential activation to emotion judgments, thereby replicating previous findings, both validates the paradigm and also provides ROIs that are used in subsequent analyses in the matched samples.

Although not our primary interest, several regions showed stronger activation to the Location judgment condition than to the emotion judgments. These included several frontal regions on the left and right side, as well as a posterior parietal region that was identified in the Talairach.org database (Lancaster et al., 1997, 2000) as the precuneus (PCu). These regions were also used in subsequent analysis, chiefly as a means of assessing the degree to which the matched samples replicated the findings of the Localizer sample.

3.3. Region of interest analysis on matched samples

The first-level GLM was computed per Localizer ROI for each participant in the matched samples. The set of beta values computed for the Self, Other, and Location conditions, which are plotted in Fig. 3. These betas were entered into two second level mixed design ANOVAs with a Greenhouse–Geisser correction, one each for emotion preferential regions and the location preferential regions, respectively. ROI and condition were treated as within-subject factors and group (ASD or TD) was treated as a between-subjects factor.

3.3.1. Emotion ROI ANOVA

The ANOVA determined that there were significant main effects of ROI ($F(2.93,90.91) = 10.69$, $p < 0.001$, $\eta^2 = 0.559$) and condition ($F(1.95,60.42) = 29.39$, $p < 0.001$, $\eta^2 = 648$) and a significant ROI by condition interaction ($F(5.70,176.58) = 6.32$, $p < 0.001$, $\eta^2 = 690$). No significant interactions with group were observed, although the ASD sample was insignificantly more active than the TD group overall ($F(1,31,) = 2.78$, $p = 0.11$, $\eta^2 = 0.082$).

Of secondary interest was the contrast between self- and other-referential processing. Collapsing across ROIs, post hoc tests using the Bonferroni correction method revealed that Self had significantly higher activation than Other ($p < 0.01$) and Location ($p < 0.001$), and the Other had significantly higher activation than Location ($p < 0.001$). To further explore differential activation specifically to Self and Other across the ROIs, a set of two-tailed paired t-tests using the Bonferroni correction method revealed that Self activation was greater than other in the mPFC ($t(32) = 5.30$, $p < 0.001$), the left IFG ($t(32) = 3.86$, $p < 0.01$), and the left STG ($t(32) = 3.19$, $p < 0.05$).

3.3.2. Location ROI ANOVA

An ANOVA determined that were significant a main effects of ROI ($F(2.41,74.65.) = 11.91$, $p < 0.001$, $\eta^2 = 277$) and condition ($F(1.79,55.39) = 34.17$, $p < 0.001$, $\eta^2 = 0.524$) and a significant ROI by condition interaction ($F(4.57,141.72) = 9.63$, $p < 0.001$, $\eta^2 = 0.237$). There was no main effect of group, but there was a marginal group by condition interaction ($F(1.79,55.39) = 2.87$, $p = 0.071$, $\eta^2 = 0.085$). Post hoc tests using the Bonferroni correction method revealed that Location had significantly higher activation than Self ($p < 0.001$) and Other ($p < 0.001$).

3.4. Exploratory connectivity analysis in low motion subsets of matched samples

Deficits in functional connectivity are a frequently reported feature of the neural functioning of individuals with ASD. Since our groups exhibited such similarity in activation patterns, we hypothesized that functional connectivity patterns in this sample may also be similar. Due to the susceptibility of connectivity analyses to motion artifacts (Power et al., 2012), they were performed on only a restricted subset of individuals in the matched samples with very low levels of motion. Specifically, 95% or more of an individual's data had to remain after motion scrubbing. This left a sample of 10 TD individuals and 9 individuals with ASD. Due to the small sample size these analyses should be considered exploratory. We restricted connectivity analyses by only computing connections between the mPFC and left IFG ROIs and between the mPFC and the left STS ROI. The mPFC and IFG ROIs were chosen because they each exhibited strong preferential responses to emotion conditions in both groups. The connection between the
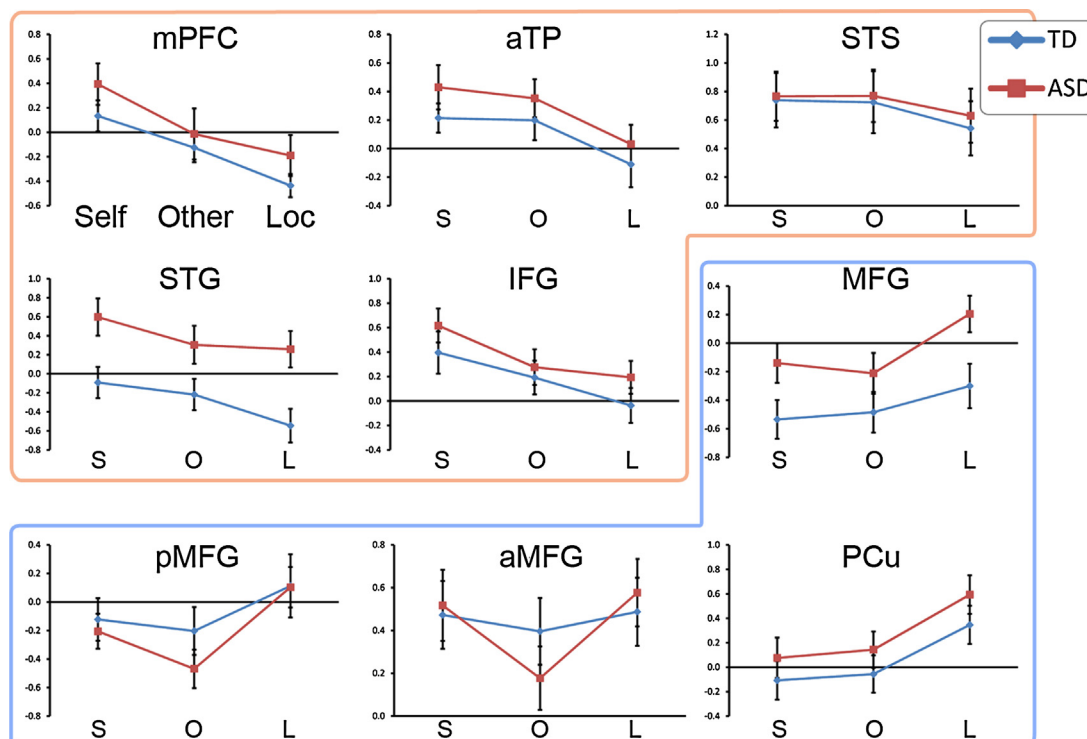
Fig. 3. Beta values as a function of condition from matched samples extracted from localizer ROIS. Plots are grouped according to contrast. Regions bounded by blue: location > emotion. Orange: emotion > location. The three plots on the right are located right hemisphere, others are located in the left. Note differences on the *y*-axis scale. Error bars denote SE. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

mPFC and STG ROIs affords the opportunity to explore long range fronto-temporal connections that previous research has indicated is disrupted in ASD. The STG ROI did not show as strong a preferential response to emotion conditions. However, a post hoc test using the Bonferroni correction did indicate that the difference between Self and Location was significant ($p < 0.001$), while the difference between Other and Location was nearly so ($p = 0.057$). Since we were interested in connectivity during emotion processing, the Self and Other conditions were collapsed for the purposes of this analysis. Results are displayed in Fig. 4.

4. Discussion

In the current study brain activation was recorded in samples of TD and ASD children while they made emotional and non-emotional judgments of pictures. Despite prior research suggesting that individuals with ASD have altered activation during emotion processing we found no effect of group, in either the emotion or non-emotion conditions within regions localized in an independent group of TD participants. Crucially, the task used in this study was much simpler than those used in previously, utilizing longer stimulus latencies and fewer levels of emotion valence in both the pictures themselves and in the responses the participants' were asked to make. These differences were intended to reduce the difficulty of the task and cognitive load on the participants. The ASD and TD groups

exhibited comparable, above chance, performance the task suggesting the changes were successful in equating difficulty across the groups.

In the localizer sample several regions of interest were found to preferentially respond during non-emotion judgments, including the precuneus and bilateral regions of the middle frontal gyrus. Emotion judgments also preferentially activated a network of both frontal regions such as the medial prefrontal cortex and left inferior frontal gyrus, as well as temporal regions including the left anterior temporal pole, and bilateral superior temporal gyrus/sulcus. Both the matched TD and ASD groups replicated the preferential responses to non-emotional judgments the results of the Localizer sample, i.e. Location was significantly more active in the respective regions relative to the emotion conditions. Conversely, the matched samples also replicated the preferential responses to emotion processing in the emotion ROI. Critically, there were no significant differences between the ASD and TD groups in indicating equivalent neural activation during emotion processing. This suggests that, with a sufficiently low cognitive load, individuals with ASD may not exhibit emotion process deficits in cortical activation. This finding contrasts with prior studies of the neural correlates of emotion processing in ASD.

In addition to methodological differences built into the study related to task difficulty, several other factors may contribute to the discrepant results. First, the groups used here were children somewhat younger than those
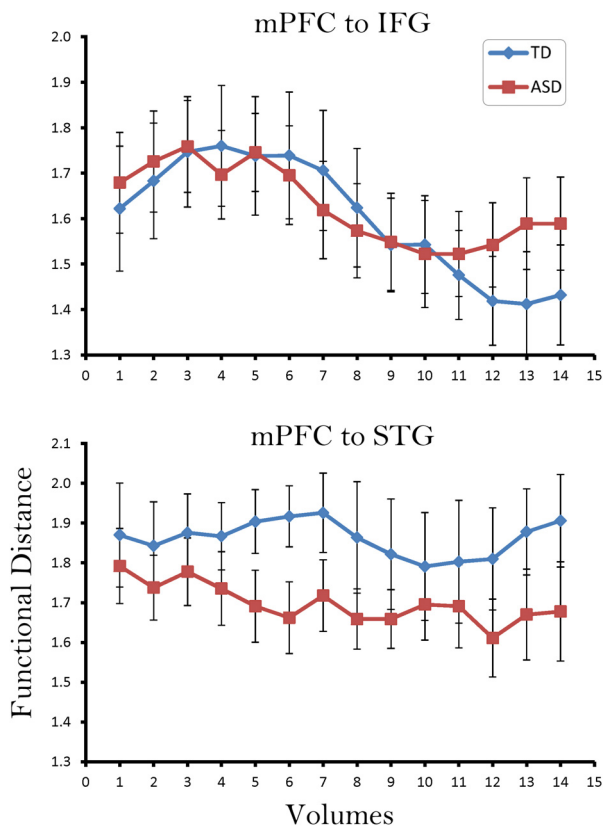
Fig. 4. Event-related function distance (*FD*) values as a function of group during emotion processing. Emotion blocks start at volume 1. Error bars denote SE.

previously studied. This certainly is not the first study to examine emotion processing in children with ASD, but many of the prior studies have focused on adults. Developmental processes, both biological and psychological, make direct cross-sectional comparisons between children and adults challenging. Additionally, there is the real possibility that cohort effects may be influencing the results. Individuals with ASD are more likely to be identified and start treatment earlier now than in the past. Thus, adult participants from several years ago may have different developmental trajectories than individuals that are children now. The TD and ASD samples were also quite homogenous, being matched on age, gender, IQ, and not differing on behavioral performance or in-scanner motion. While this represents strength of the study in terms of experimental control, it may also mean that the ASD sample is not generally representative of children with ASD. Another potential concern in interpreting the results might be that differences in activation between the groups are being obscured by noise. However, it is important to note that both groups performed the behavioral task above chance with equivalent levels of accuracy and latency. Most critically, brain activation was not simply equivalent across the TD and ASD, but it is also the case that both groups replicated the condition contrasts of the localizer group in both the emotion and location ROIs.

More specific patterns of activation within emotion processing regions were also observed. Consistent with previous studies, the mPFC showed stronger activation during self-referential processing compared to other referential process. The mPFC has been shown to be consistently active during a broad range of mentalizing tasks (Gusnard et al., 2001; Mitchell et al., 2005a) about other individuals. However, it is also consistently active during self-referential processing (Heatherton et al., 2006; Mitchell et al., 2005b, 2006), leading some researchers to theorize that it serves a dual role in social cognition. The results of the current study are broadly consistent with this theory. However, it appears to play this role in both the TD and ASD groups.

In an exploratory connectivity analysis, two intriguing patterns emerged. First, temporal changes in the degree of functional connectivity during emotion processing differ between pairs of regions. The connectivity between mPFC and IFG seems to increase sharply as processing continues, while the connectivity between mPFC and STG exhibits very weak temporal changes. We speculate that these differences arise from the differential function of the involved ROI pairs. The IFG is often implicated in emotion regulation (Goldin et al., 2008; Ochsner et al., 2004b) and may be called on to increase the degree of regulation over the mPFC as a block of emotional stimuli is presented in succession. However, the STG may be more involved in extracting information from the images and passing it to frontal regions which may not change as much in time. A second notable pattern is that the groups do not exhibit striking differences in connectivity. If anything the ASD group shows stronger long-range connections between mPFC and STG. However, given the limitations of sample size these interpretations cannot be considered anything other than preliminary.

5. Conclusions

The equivalent activation we observed between ASD and TD individuals in regions involved in emotion processing is generally inconsistent with the current consensus view. However, although a report of disrupted activation is consistent across studies, the specific disruptions are usually not. This inconsistency suggests that there are crucial dimensions that mediate whether normative or disrupted activations will be observed that are, as of yet, unaccounted for. We hypothesized that cognitive load is such a dimension. The current study was designed to require a relatively lower cognitive load than previous similar studies by presenting fewer stimuli, with fewer valence levels, and longer durations. The findings presented here suggest that while individuals with ASD may be particularly vulnerable to disruptions of emotional processing, certain contexts may support preserved functions. Future studies that refine our understanding of the contribution of cognitive load on socio-emotional processing in ASD could have profound implications for scaffolding approaches in treatment.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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