Enhanced Visual Functioning in Autism: An ALE Meta-Analysis

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Abstract: Autistics often exhibit enhanced perceptual abilities when engaged in visual search, visual discrimination, and embedded figure detection. In similar fashion, while performing a range of perceptual or cognitive tasks, autistics display stronger physiological engagement of the visual system than do non-autistics. To account for these findings, the Enhanced Perceptual Functioning Model proposes that enhanced autistic performance in basic perceptual tasks results from stronger engagement of sensory processing mechanisms, a situation that may facilitate an atypically prominent role for perceptual mechanisms in supporting cognition. Using quantitative meta-analysis of published functional imaging studies from which Activation Likelihood Estimation maps were computed, we asked whether autism is associated with enhanced task-related activity for a broad range of visual tasks. To determine whether atypical engagement of visual processing is a general or domain-specific phenomenon, we examined three different visual processing domains: faces, objects, and words. Overall, we observed more activity in autistics compared to non-autistics in temporal, occipital, and parietal regions. In contrast, autistics exhibited less activity in frontal cortex. The spatial distribution of the observed differential between-group patterns varied across processing domains. Autism may be characterized by enhanced functional resource allocation in regions associated with visual processing and expertise. Atypical adult organizational patterns may reflect underlying differences in developmental neural plasticity that can result in aspects of the autistic phenotype, including enhanced visual skills, atypical face processing, and hyperlexia. *Hum Brain Mapp 33:1553–1581, 2012.* © **2011 Wiley Periodicals, Inc.**

Key words: hyperlexia; reading; fMRI; vision; perception; enhanced perceptual functioning model; expertise; plasticity

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INTRODUCTION

Atypical perceptual processing, often manifested as enhanced perceptual performance [Dakin and Frith, 2005], is now included as an associated feature of the autistic phenotype [Belmonte et al., 2004]. Autistic visual strengths are consistently reported for the Block Design subtest of the Wechsler Intelligence Scales [Caron et al., 2006; Shah and

Frith, 1993], the Embedded Figures Task [Jolliffe and Baron-Cohen, 1997], visual search tasks [Joseph et al., 2009; Kemner et al., 2008; O'Riordan, 2004; O'Riordan et al., 2001], and visual discrimination tasks [Bertone et al., 2005; Plaisted et al., 1998]. In addition, an increasing number of studies have demonstrated autistic early sensory processing advantages or atypicalities in stimulus dimension extraction, with examples including crowding [Baldassi et al., 2009; Keita et al., 2010], contour and texture processing [Pei et al., 2009; Vandenbroucke et al., 2008] and spatial frequency processing [Jemel et al., 2010; Milne et al., 2009]. These behavioral characteristics, along with other aspects of the autistic perceptual phenotype, have been summarized in the Enhanced Perceptual Functioning Model (EPF) [Mottron et al., 2006]. Assuming generally stronger physiological engagement of the visual system in autism, this model predicts generally superior perceptual performance and a wider role for perceptual processes in autistic cognition. It also incorporates the observation that autistics[1] display better access to information typically masked by top-down influences [Wang et al., 2007], as well as relative autonomy of perceptual processes from top-down influences [Caron et al., 2006; Soulières et al., 2009].

Several neuroimaging studies have revealed stronger task-related activity in visual cortex in autism, evidenced as either higher levels of activity associated with visual information processing, or as serendipitous findings in studies employing memory or language tasks. In association with the Embedded Figures Test, autistic brain activity is higher in right occipital cortex, left posterior parietal cortex, bilateral occipital cortex, and bilateral cerebellar cortex, and lower in frontal cortex [Lee et al., 2007; Manjaly et al., 2007; Ring et al., 1999]. Higher occipital cortex activity in autistics is seen in relation to faster and more accurate visual search [Keehn et al., 2008]. These results suggest that the autistics' behavioral advantages might arise from stronger and more pervasive engagement of visual processing mechanisms. Stronger occipital activity has also been reported in association with reduced frontal activity in autism for tasks incorporating a broad range of cognitive and perceptual components, including embedded figure detection [Ring et al., 1999], attention shifting [Belmonte and Yurgelun-Todd 2003], word learning [Hazlett et al., 2004], saccades to visual targets [Luna et al., 2002], working memory [Koshino et al., 2005], visuomotor learning [Muller et al., 2003], face processing [Hubl et al., 2003], and social attribution [Castelli et al., 2002]. The wide variety of tasks associated with higher activity in autistics' visual cortical areas suggests that the atypical physiological processing mechanisms may be related to task performance in a less straightforward way than initially posited by the EPF model.

Quantitative meta-analysis of functional neuroimaging studies is one means to characterize the role of perceptual

processes in autism. Neuroimaging meta-analysis combines results from independent experiments to achieve a quantitative summary of the state of research in a specific domain [Turkeltaub et al., 2002]. It assesses the reliability of results across imaging techniques, tasks, and laboratories by revealing consistently modulated voxel activity in a collection of studies. In addition, meta-analysis can establish the specificity of the relationship between a region or network of regions and a particular task type [Wager et al., 2009]. Voxel-wise meta-analysis of neuroimaging studies, called Activation Likelihood Estimation (ALE; Turkeltaub et al., 2002] has recently been used in autism to document between-group differences in activity related to social compared to non-social tasks [Di Martino et al., 2009].

We used ALE meta-analysis to summarize patterns of activity related to visual processing by merging activity maxima reported in experiments including both autistic and non-autistic groups, a process that resulted in group maps assessing the regions of common task-related modulation across studies. Maps revealing regions differently engaged between groups were then generated by contrasting the within-group ALE maps [Laird et al., 2005]. We included the coordinates of activity increases for each group instead of using the reported coordinates of differential activity between autistics and non-autistics, an approach used in a recent autism meta-analysis [Di Martino et al., 2009]. Our method allowed identification of processing activity without any a priori bias that might result from including only studies reporting higher or lower activity in autistics compared to non-autistics. For instance, some reports do not include tables listing coordinates related to higher activity in autistics, even when such findings are described in the body of the paper. To minimize regional selection bias, we also limited our meta-analysis to studies that reported coordinates resulting from whole-brain analysis, as contrasted with region-of-interest (ROI) analysis. Because the resource allocation proposition, stated as Principle 4 of the EPF Model [Mottron et al., 2006], was primarily based on a review of neuroimaging studies of visual perception in autistics, and because there are only a limited number of neuroimaging studies of auditory processing, we limited the current analysis to studies employing visual stimuli.

In this meta-analysis our aim was to quantitatively summarize the neuroimaging findings concerning visual processing in autism in order to test the prediction that autistics will exhibit generally stronger engagement of the visual system. Additionally, we explored the relative domain specificity of atypical visual processes in autism, by examining whether any differences between autistics and non-autistics showed specificity for face, object, or word stimulus classes.

MATERIALS AND METHODS

Literature Review and Contrast Selection

We performed a PubMed literature search (www.pubmed.org) to identify functional neuroimaging studies

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[1]Throughout the report we respectfully use the term autistics, following Sinclair, J. (1999). Why I dislike "person first" language. http://www.jimsinclair.org/person_first.htm

TABLE I. Participant characteristics for the studies included in the meta-analysis

Reference	N (nAUT)	Age M (SD) (nAUT)	N (AUT)	Age M (SD) (AUT)	AUT	AS	PDD
Bird et al., 2006	16	33.3 (11.5)	16	35.3 (12.1)	1	15	
Bookheimer et al., 2008	12	11.9 (2.4)	12	11.3 (4.0)		Unspecified	
Dapretto et al., 2006	10	12.38 (2.2)	10	12.05 (2.5)		Unspecified	
Ditcher and Belger, 2007	15	23.2 (5.7)	14	22.9 (5.2)	11	3	
Gaffey et al., 2007	10	25.3 (9.8)	10	26.1 (10.5)	8	2	
Greimel et al., 2010	15	15 (1.4)	15	14.9 (1.6)	3	12	
Harris et al., 2006	22	31 (9)	14	36 (12)	7	5	2
Hubl et al., 2003	10	25.3 (6.9)	10	27.7 (7.8)	10		
Just et al., 2004	17	N/A	17	N/A	17		
Just et al., 2007	18	24.5 (9.9)	18	27.1 (11.9)	18		
Kana et al., 2009	12	24.4 (3.7)	12	24.6 (6.9)	12		
Kennedy et al., 2006	14	26.07 (7.95)	12	25.49 (9.61)	8	3	1
Kennedy et al., 2008	12	27.5 (10.9)	13	26.9 (12.3)	6	6	1
Kleinhans et al., 2008a	14	22.41 (8.67)	14	23.79 (9.58)	8	3	3
Kleinhans et al., 2008b	21	25.1 (7.6)	19	23.5 (7.8)	8	9	2
Knaus et al., 2008	12	14.94 (2.71)	12	15.45 (2.48)		Unspecified	
Koshino et al., 2007	11	28.7 (10.9)	11	24.5 (10.2)	11		
Lee et al., 2007	14	10.85 (1.47)	17	10.37 (1.85)	8	9	
Manjaly et al., 2007	12	14.3 (2.7)	12	14.4 (2.8)	3	9	
Mason et al., 2008	18	27.4 (N/A)	18	26.5 (N/A)	18		
Schmitz et al., 2006	12	39 (6)	10	38 (9)	2	8	
Schmitz et al., 2008	10	20-50 (N/A)	10	20-50 (N/A)	3	7	
Silani et al., 2008	15	33.7 (10.3)	15	36.6 (11.7)		Unspecified	
Solomon et al., 2009	23	15.9 (2.1)	22	15.2 (1.7)	10	12	
Soulières et al., 2009	13	20.15 (3.02)	12	22.08 (4.91)	12		
Uddin et al., 2008	12	12.23 (2.10)	12	13.19 (2.61)		Unspecified	

published from 1995 to July 2009 in which visual stimuli were presented to both autistic and non-autistic groups. For this analysis, what we call the autistic group included participants with diagnostic assignments falling within what are generally referred to as autism spectrum conditions. We used the following search terms: «(Autism OR Asperger OR PDD) AND (fMRI OR PET OR Neuroimaging)» and retrieved 787 articles. Among those, 692 were excluded through an initial review of the abstracts. Studies excluded were 217 reviews, 207 reports without an autistic group, 255 reports not using PET or fMRI, and 19 reports including no visual stimuli. Of the remaining 89 studies, 22 were rejected because of small sample size ($n < 10$), 21 because of partial brain coverage or analysis, 11 because results were not reported in a standard anatomical space, and 9 because only between-group contrasts were presented. The remaining 26 peer-reviewed fMRI articles reporting within-group results using whole brain acquisition techniques in a standardized stereotaxic space were included in the meta-analysis. Coordinates reported in MNI space were converted to Talairach anatomical space using the "Convert Foci" tool of the GingerALE 1.1 program [Laird et al., 2005]. This tool uses the icbm2tal Lancaster transform [Lancaster et al., 2007]. The total number of participants included 370 typical controls and 357 individuals with an autism spectrum condition determination. Most studies were conducted on adults and all included participants with Full Scale IQ in the normal range. Seven

out of the 26 studies included only autistics, while the others included autistics, individuals with Asperger syndrome and Pervasive Developmental Disorder Not Otherwise Specified (Table I).

A total of 48 contrasts (504 foci) for the non-autistic and 44 (415 foci) for the autistic group were identified in the 26 included studies. These contrasts were categorized according to domain specificity into face, object, and word categories. The contrasts for one study [Silani et al., 2008] could not be classified, as the stimuli contained both faces and animal pictures. These contrasts were eliminated from the domain specific analysis. The face processing domain included face viewing, discrimination, matching, recognition, imitation, and identification tasks as well as one task involving facial emotional state inference and one task involving gaze direction identification. Fourteen contrasts (134 foci) for the autistic group and 14 contrasts (175 foci) for the non-autistic group were included in this domain. For the object processing domain, stimuli included pictures of houses, arrows, geometric shapes, complex figures, letters, patterns, in addition to more complex stimuli, including problems from the Tower of London task and Raven's Progressive Matrices. The tasks required matching, response inhibition, interference, identification, mental state attribution to shapes, and simple viewing. A total of 14 contrasts (123 foci) were assigned to the object processing domain for the autistic group and 15 contrasts (166 foci) for the non-autistic group. Finally, the word

processing domain included visually presented words or sentences, with participants identifying word category, making a semantic judgment, answering reading comprehension questions, counting words, or generating words in a given category (verbal fluency). The word processing domain included 14 contrasts (137 foci) for the autistic group and 17 contrasts (136 foci) for the non-autistic group. In addition, we investigated the effect of contrasting high to low level baselines across all tasks, by computing separate ALE maps using either low level baselines, such as fixation or rest, or high level baselines such as complex figure matching. Both types of maps yielded superimposable patterns for both the autistic and non-autistic groups. Therefore, in an effort to increase statistical power, contrasts with both high and low level baselines were pooled for all subsequent analyses.

ALE Meta-Analysis

ALE maps were computed using GingerALE (version 1.1 www.brainmap.org/ale) software [Laird et al., 2005], based on methods introduced by Turkeltaub et al., [2002]. The ALE technique models the uncertainty in location of task-related activity foci as Gaussian probability distributions, yielding statistical maps in which each voxel value represents an estimate of the likelihood that activity occurred in the studies included in the meta-analysis. The critical threshold for the ALE map is set using a Monte Carlo permutation analysis of sets of randomly distributed foci. A FWHM of 8 mm was selected for the Gaussian probability distributions to reflect the average smoothness of the fMRI data from which the foci were derived. The critical threshold was set using a 5,000 permutations test, corrected for multiple comparisons (False Discovery Rate (FDR); Laird et al., 2005]. The model is of the fixed-effects class and permits inferences over the studies included in the meta-analysis.

Maps reflecting regions of convergence across all reported coordinates both within- and between-groups were computed, using maxima drawn from all three processing domains. As there was an imbalance between the total number of foci included for the non-autistic (48 experiments, 504 foci) and autistic (44 experiments, 415 foci) samples, it was necessary to randomly remove experiments from the non-autistic group to equalize the number of foci between groups (44 experiments, 438 foci), increasing the possibility that the difference maps would reflect activity differences between groups rather than an imbalance in coordinate numbers between categories [Laird et al., 2005]. Second, domain specific within-group ALE maps for face, object, and word processing were computed. For each domain, the number of experiments and foci were similar enough for direct comparison. To compare activity patterns between autistics and non-autistics, the within-group ALE maps were subtracted from one another and randomization testing with 5,000 permuta-

tions was performed. This procedure tests for the presence of differences between the groups under the null hypothesis that both sets of foci are uniformly distributed [Laird et al., 2005]. The critical threshold was set at p_{FDR} (<0.05 ($k = 250$ voxels). To present results in the anatomical space most commonly used in the current literature, the ALE coordinate results were transformed into the MNI anatomical space using the Lancaster transform [Lancaster et al., 2007].

RESULTS

Behavior

Table II summarizes the behavioral findings for all studies included in the meta-analysis. In the majority of studies, autistics and non-autistics exhibited similar accuracies or response times. There were no significant between-group differences in performance in 69% of the studies (18/26), whereas autistics showed better performance in 7.6% of the studies (2/26) and poorer performance in 23% of the studies (6/26). Across domains, no between-group behavioral differences were observed in 64% of the face tasks (9/14 contrasts), 93% of the object tasks (14/15), and 71% of the word tasks (12/17 contrasts).

Five studies included information about eye movement characteristics, reporting the number or duration of fixations or saccades or the eye movement related fluctuations in the orbital BOLD-contrast signal. None of these studies found any significant between-group differences in eye movement measures acquired either during the scanning sessions [Greimel et al., 2009; Soulières et al., 2009] or in separate experimental sessions [Bird et al., 2006; Dapretto et al., 2006; Kleinhans et al., 2008b].

Combined Face, Object, and Word Processing

Within-group maps

We first analyzed the task-related activity across all processing domains within each group. ALE maxima values for the autistic and non-autistic groups are presented in Table III. Figures 1 and S1 show a broadly overlapping pattern of activity in the two groups, with large clusters in bilateral striate and extrastriate areas (BA 17, 18, 19); fusiform gyrus (BA 37); precuneus (BA 7); inferior (BA 44, 45, 47), middle (BA 46), and superior (BA 8, 9) frontal gyri; precentral (BA 6) gyrus; and the insula (BA 13).

Between-group maps

Direct comparisons between autistic and non-autistic group maps revealed differing ALE values in occipito-temporal and frontal regions (Table IV; Fig. 1 and S1). Overall higher ALE values in striate (BA 17) and extrastriate (BA 18, 19) cortex were found in autistics. Small bilateral clusters in posterior extrastriate cortex (BA 18) exhibit lower

TABLE II. A listing of: (1) studies included in the meta-analysis, (2) tasks, (3) stimuli, (4) observed performance, (5) task contrasts, (6) processing domain, and (7) number of maxima for the autistic (AUT) and non-autistic (nAUT) groups

Reference	Task	Stimuli	Performance	Contrast	Domain	nAUT	AUT
Bird et al., 2006	Look at a fixation cross in the center of each face or house picture	Photographs of houses and faces	No task	Faces vs. Houses	Faces	5	5
				Houses vs. Faces	Objects	7	7
	Indicate if two faces or two houses were the same or different (four pictures presented at same time, with attention directed to the houses or faces)		No between-group differences in RT or ACC	Attended faces vs. Unattended faces	Faces	3	2
				Attended houses vs. Unattended houses	Objects	2	0
Bookheimer et al., 2008	Select one of two choices to match a target face/target shape	Oval forms and pictures of faces (upright or inverted)	Less accurate responses in autistics for upright faces but no between-group differences in RT	Matching upright face to target vs. Form matching	Faces	10	6
				Matching inverted face to target vs. Form matching	Faces	9	8
Dapretto et al., 2006	Observe or imitate faces	Pictures of emotional faces	No between-group differences in RT or ACC	Imitation of emotional faces vs. Fixation	Faces	36	16
				Observation of emotional faces vs. Fixation	Faces	14	10
Ditcher and Belger, 2007	Reaction time flanker task: Indicate by button press whether a central stimulus (flanked by same or different direction stimuli) point to the left of to the right	Arrow flanked by arrows	No between-group differences in RT or ACC	Incongruent arrow vs. Congruent arrow	Objects	8	10
		Gaze pictures flanked by gaze pictures		Incongruent gaze vs. Congruent gaze	Faces	8	2
Gaffrey et al., 2007	Semantic: Indicate category (Tool, Color, Feeling) membership of words; Perceptual: Indicate if a target letter is present in an consonant string	Words or letters	No between-group differences in RT, but the control group was more accurate for Colors and Feeling categories	Semantic vs. perceptual	Words	14	13
Greimel et al., 2010	Empathize with the person whose face is presented and infer the emotional state (Other) or judge their own response (Self); Baseline: Judge the width of neutral faces	Happy, sad, neutral faces	No between-group differences in RT, but autistics made more errors when judging emotional state from weak expressions.	Other vs. Face width judgment	Faces	19	23
				Self vs. Face width judgment	Faces	19	14
Harris et al., 2006	Indicate if a word is positive/negative (semantic)or in upper/lower case (perceptual)	Words	No between-group differences in RT or ACC	Concrete vs. Abstract	Words	8	4
				Semantic vs. Perceptual	Words	7	3
Hubl et al., 2003	Button press to happy face or face of a woman (for the real faces blocks); No task for the scrambled faces blocks	Emotional and scrambled face pictures	No between-group differences in ACC, however RT were longer in autistics	Real vs. Scrambled	Faces	12	12
Just et al., 2004	Read a passive or active sentence and respond to a probe	Sentences and probe	No between-group differences in ACC, but autistics responded faster than controls	Sentence comprehension vs. Fixation	Words	8	10
Just et al., 2007	Tower of London task : rearrange the position of 3 balls until they match a goal configuration	Initial and goal configuration	No between-group differences in RT or ACC	Tower of London (number of steps to goal) vs. Fixation	Objects	13	19
Kana et al., 2009	Theory of mind: attributing mental state to the movement of geometrical figures	Geometrical figures	No between-group differences in RT or ACC	Theory of Mind vs. Random animations	Objects	12	5

TABLE II. (Continued)

Reference	Task	Stimuli	Performance	Contrast	Domain	nAUT	AUT
Kennedy et al., 2006	Count the number of presented words (emotional, neutral or number words) and select response (3, 4, 5 words).	Words	No between-group differences in RT or ACC	Count number of words vs. Fixation	Objects	8	8
				Count emotional vs. neutral words	Objects	3	0
Kennedy et al., 2008	Statement: Make true/false judgments for statements about themselves (self) or a close other person (other) describing psychological personality traits (internal) or observable characteristics (external); Equation: Indicate if a math equation was true or false	Statements or math equations	No between-group differences in RT or ACC	All statements vs. Equation	Words	11	8
				Internal vs.External	Words	4	0
				External vs. Internal	Words	7	12
				Other vs. Self	Words	6	4
Kleinhans et al., 2008a	Verbal fluency: Generate as many words as possible beginning with a given letter or items in given category	Letters or categories	Autistics generated less words than control group for both conditions, but no between group differences in number of errors (word repetition, non-target item, neologism)	Generate words starting with a given letter vs. repeat "nothing"	Words	1	1
				Generate words in a given category vs. repeat "nothing"	Words	3	3
				Generate words in a category vs. starting with a given letter	Words	5	0
Kleinhans et al., 2008b	Press a button whenever identical stimuli appear in succession (1-back)	Pictures of neutral faces and houses	No between-group differences in RT or ACC	Faces vs. Houses	Faces	1	3
				Houses vs. Faces	Objects	2	2
Knaus et al., 2008	Reading; select a word that best match a three-word phrase description; Letter judgment: Indicate whether letter strings were in upper or lower case	Sentences or letter strings	Autistics have better and faster responses than controls.	Reading and responding vs. Letter judgment	Words	7	8
Koshino et al., 2007	Face recognition (0-back, 1-back, 2-back): Identify a remembered target face	Grayscale pictures of faces	No between-group differences in RT or ACC	Face recognition vs. Fixation	Faces	15	9
Lee et al., 2007	Embedded Figure Task: Select one of two probe figure that contained the target shape; Matching Task: Select one of two probe figure that is identical to the target shape	Pairs of complex figures and target shapes	No between-group differences in RT or ACC	Embedded Figure Task vs. Matching Task	Objects	11	3
Manjaly et al., 2007	Embedded Figure Task: Decide if a target figure matched a subpart of a complex figure; Matching Task: Indicate if a highlighted part of a complex figure matched a target shape	Complex and target figure	No between-group differences in RT or ACC	Embedded Figure Task vs. Matching task	Objects	2	4
Mason et al., 2008	Read three-sentence stories and respond to a simple yes/no comprehension question based on a physical (direct consequence), intentional (character's goal) or emotional (character's emotion) inference	Sentence and question	N/A	Physical inference vs. Fixation	Words	12	20
				Intentional inference vs. Fixation	Words	15	17
				Emotional inference vs. Fixation	17	26	
				Words			
Schmitz et al., 2006	Motor response inhibited or executed depending on GO /no Go signal	Arrow pointing left or right	No between-group differences in RT or ACC	Go vs. No Go	Objects	11	6

TABLE II. (Continued)

Reference	Task	Stimuli	Performance	Contrast	Domain	nAUT	AUT
	Stoop: Press a button if an arrow indicating left (or right) is displayed on left (or right)	Arrow on left or right side	No between-group differences in RT or ACC	Correct stroop inhibition vs. Congruent	Objects	5	9
	Shift attention and switch response to new association patterns	Red dot and four squares	No between-group differences in RT or ACC	Switch vs. Repeat set trials	Objects	9	9
Schmitz et al., 2008	Press a button to two target letters, one of which was linked to monetary reward	Letter	No between-group differences in RT or ACC	Successful reward vs. Successful unrewarded	Objects	5	4
Silani et al., 2008	Rate (visual analogue scale) the emotional value or the ratio of black/white pixels in pleasant, unpleasant or neutral pictures	Affective pictures	No between-group differences in RT or ACC	Emotion vs. Color rating Unpleasant vs. Neutral	* *	24 3	8 13
Solomon et al., 2009	Preparing to overcome prepotency (POP) task (response inhibition): Press key on same or different side as target	Squares and arrows	No differences in RT, but autistics made more errors on trials requiring response inhibition	Inhibition vs. No Inhibition	Objects	16	4
Soulières et al., 2009	Pattern matching; Select one of 8 response that best match a pattern; Raven's standard progressive matrices (RSPM): Select one of 8 response to matrices from which the final entry is missing	Target pattern or RSPM plus 8 response choices	No between-group differences in RT or ACC	Pattern matching vs. Fixation Raven vs. Fixation	Objects Objects	33 30	23 18
Uddin et al., 2008	Press a button if the face presented looks like self and another button if it looks like another or scrambled face	Pictures of participant and another person	No between-group differences in RT or ACC	Own face vs. Fixation Other face vs. Fixation	Faces Faces	12 12	18 6

TABLE III. ALE maxima of regions showing within-group effects for combined «FACES, OBJECTS and WORDS» processing domains ($p_{FDR}< 0.05$, $k = 250vx$)

Region	BA	Left x	y	z	ALE ($\times10^{-3}$)	Right x	y	z	ALE ($\times10^{-3}$)
Non-autistic									
Occipital									
Inferior occipital gyrus	18	−18	−95	−4	39.10	14	−95	−7	30.83
Fusiform gyrus	19	−31	−87	−9	36.88	42	−74	−9	33.00
	19	−42	−81	−12	34.62				
Lingual gyrus	17	−18	−94	7	22.00				
	18	−18	−78	−10	27.02				
Temporal									
Fusiform gyrus	37	−42	−54	−19	53.51	41	−59	−13	28.54
						42	−47	−21	40.38
Middle temporal gyrus	21	−53	−35	−7	30.23	59	−37	−2	29.67
	21	−55	−32	2	21.62				
	21	−61	−47	−4	20.19				
Parietal									
Precuneus	7	−1	−59	35	30.21	32	−65	42	32.15
Superior parietal lobule	7					26	−62	50	26.13
Angular gyrus	39	−30	−58	44	26.23				
Frontal									
Precentral gyrus	6	−46	1	34	37.45	47	7	28	63.17
Middle frontal gyrus	46					42	33	12	40.01
	9	−46	15	30	31.66	42	26	21	24.04
	9	−1	57	17	29.53				
	9	−46	23	25	20.22				
Superior frontal gyrus	6	0	15	52	39.52				
	6	−5	9	57	38.34				
	8	−11	55	37	29.90				
	8	−3	29	42	28.23				
	9	−25	51	27	27.14				
Inferior frontal gyrus	47	−47	27	−4	35.11				
	45	−53	22	10	27.29				
	44	−55	14	−1	25.92	53	9	9	21.71
Insula	13	−31	23	0	24.50	31	26	−1	52.71
	13					44	14	9	24.94
Subcortical									
Cingulate gyrus	31	−1	−47	31	43.46				
Parahippocampal gyrus	37	−27	−46	−11	27.81	29	−46	−12	37.16
	27	−25	−31	−8	29.53				
Thalamus						27	−26	−3	34.68
Caudate						21	−24	18	34.23
Putamen		−23	0	3	25.61				
Autistic									
Occipital									
Fusiform gyrus	19	−48	−72	−5	24.78	38	−74	−9	46.87
	19	−40	−66	−18	48.79	29	−83	−15	23.81
	19	−20	−81	−10	24.48				
Middle occipital gyrus	18	−31	−85	−7	42.92	34	−87	10	27.23
	18	−22	−93	18	26.71	23	−98	−9	25.31
	19					32	−80	23	21.51
Cuneus	17	−12	−99	3	32.31				
Lingual gyrus	19					23	−71	−2	28.53
	18					8	−77	3	22.37
Temporal									
Fusiform gyrus	37	−44	−51	−17	34.13	31	−47	−16	51.51
	37	−33	−63	−7	29.81	46	−49	−16	36.56
	37	−33	−48	−22	26.59				

TABLE III. (Continued)

Region	BA		Left					Right		
		x	y	z	ALE ($\times 10^{-3}$)		x	y	z	ALE ($\times 10^{-3}$)
Superior temporal gyrus	39						60	−60	25	27.09
	22	−50	−55	20	23.97					
Parietal										
Precuneus	7	−26	−67	41	39.29		4	−55	37	27.34
	7						30	−65	42	27.23
Superior parietal lobule	7	−22	−64	51	15.04					
Frontal										
Inferior frontal gyrus	47	−49	22	−10	44.14					
Middle frontal gyrus	9	−48	19	26	30.82		56	23	35	32.84
	9						47	6	39	16.45
Superior frontal gyrus	6	−7	10	60	39.76					
	6	−3	15	43	19.38					
	9						3	59	18	23.42
Precentral gyrus	6						51	7	27	35.58
	6						40	11	32	26.44
Insula	13	−31	24	5	36.79		36	24	1	45.55
Subcortical										
Putamen		−25	6	4	32.22					
Globus pallidus		−25	−10	−10	29.41					
Cingulate gyrus	31						2	−51	32	27.35
	24						3	43	0	26.35
Parahippocampal gyrus	28	−25	−27	−8	25.76					
	19						27	−54	−6	23.02
	37	−27	−46	−11	21.69					
Thalamus		−12	−19	9	24.20		27	−30	0	25.57
							25	−24	−5	22.32

ALE values in autistics. While both groups showed strong activity in BA 37, lower ALE values were found in autistics bilaterally in the anterior fusiform gyrus and in the medial part of the left fusiform gyrus. Additionally, autistics had lower ALE values in left middle temporal gyrus (BA 21) and higher ALE values in the left precuneus and intraparietal sulcus (BA 7).

In the frontal cortex, lower ALE values were observed in autistics in bilateral precentral (BA 4, 6), superior frontal (BA 6, 8, 9) and inferior frontal (BA 45, 47) gyri. Higher ALE values in autistics were limited to small regions in the posterior part of the left inferior frontal gyrus (BA 47) and in right medial frontal gyrus (BA 8). Clusters of lower activity in the autistics were also observed in bilateral insula (BA 13) and in cingulate cortex (BA 24) (Fig. S1).

To better visualize the spatial pattern of the differential visual activity in both groups, we computed the number of voxels for which ALE values differed between autistics and non-autistics in the left and right hemispheres for the frontal, parietal, occipital, temporal and subcortical regions (Table V). Combining counts across all tasks, 6368 voxels had higher ALE values, and 2016 voxels had lower ALE values in the temporal, occipital and parietal lobes of the autistics compared to the non-autistics. In contrast, the frontal lobes of the autistics exhibited a reversed pattern, with higher ALE values in 1360 voxels and lower ALE values in 4808 voxels (see Fig. 2). The associated analysis of variance revealed a significant effect of Region, $F (4, 10) = 6.4$, $p = 0.008$ and a Region x Group interaction $F (4, 10) = 6.2$, $p = 0.009$. These patterns reveal an atypical spatial distribution of visual processing in autism, seen as a posterior to anterior gradient of group activity differences, with the autistics exhibiting generally higher ALE values in posterior regions and lower ALE values in frontal regions.

Face Processing

Within-group maps

We then restricted the analysis to the face processing domain (Table VI). Figures 1 and S2 show partially overlapping clusters of group activity. While both groups had high ALE values bilaterally along the fusiform gyrus (BA 19, 37), the largest overlap was observed in the anterior and middle fusiform gyrus, involving more posterior and lateral regions on the left than on the right. Additionally, both groups had high ALE values in right superior temporal gyrus (BA 22) and medial parietal cortex (BA 7). Moreover, both groups displayed activity in the posterior cingulate, the globus pallidus and at the temporo-occipital junction (BA 21, 39). Significant ALE values in frontal cortex were more numerous in non-autistics (BA 4, 6, 9, 10, 44, 45, 46) and overlap between the groups was limited to ALE values in precentral gyrus (BA 6) and insula (BA 13).
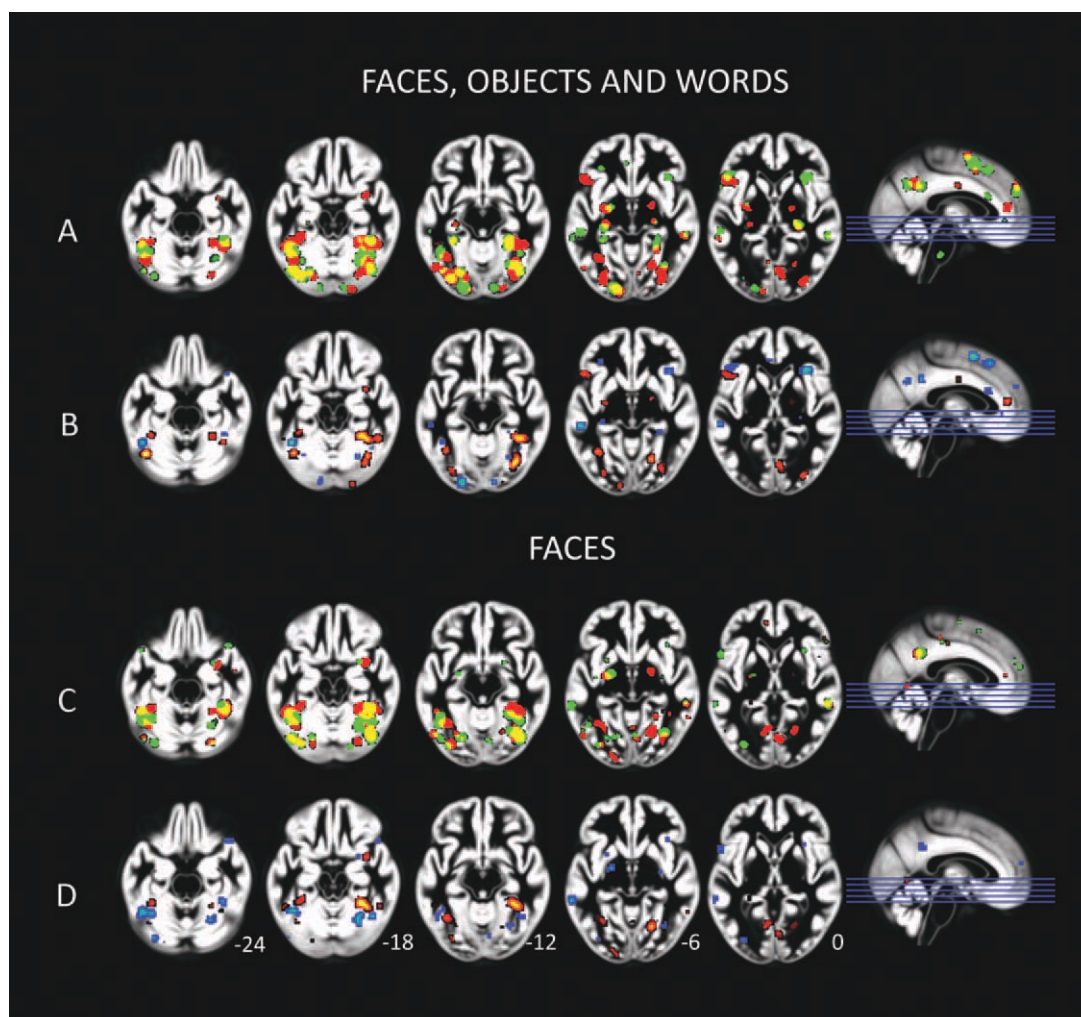
Figure 1.

Within- and between-group distribution of task-related activity in inferior occipital and inferotemporal cortex. **A**: Regions showing increases in autistics (RED), non-autistics (GREEN), and their overlap (YELLOW) for «FACES, OBJECTS and WORDS» tasks combined. **B**: Regions showing more task-related activity in autistics vs. non-autistics (RED-YELLOW) and less task-related activity in autistics vs. non-autistics (BLUE-GREEN) for the combined «FACES, OBJECTS, and WORDS» tasks. **C**: Regions showing increases in autistics (RED), non-autistics (GREEN), and their overlap (YELLOW) for the «FACES» tasks. **D**: Regions showing more task-related activity in autistics vs. non-autistics (RED-YELLOW) and less task-related activity in autistics vs. non-autistics (BLUE-GREEN) for the «FACES» tasks. ALE maps ($p_{FDR} < 0.05$) are superimposed on axial slices from a gray matter template in MNI space. Anatomical left is image left.

Between-group maps

Between-group comparisons of face processing revealed areas of differential activity in occipital, temporal and frontal cortex (Table VII; Figs. 1, 3, and S2). First, higher ALE values in autistics were found in the fusiform gyrus (BA 37) bilaterally, while regions immediately posterior showed lower ALE values. Autistics also had higher ALE values in the middle portion of the left fusiform gyrus,

the right lingual gyrus (BA 18, 19) and primary visual cortex (BA 17), with below threshold clusters at −20, −95, +3; vx = 48 and −14, −99, +1; vx = 32. Maxima were also seen in left middle temporal gyrus (BA 21), with greater ALE values for autistics in the extreme anterior portion and lower values in autistics in the posterior part of the gyrus. The autistics had lower ALE values in left superior temporal gyrus (BA 39), while the corresponding region on the right had higher ALE values. The

TABLE IV. ALE maxima of regions showing between-group differences for combined «FACES, OBJECTS and WORDS» processing domains ($p_{FDR} < 0.05$, $k = 250vx$)

Region	BA	Left x	y	z	ALE ($\times 10^{-3}$)	Right x	y	z	ALE ($\times 10^{-3}$)
Non-autistic > Autistic									
Occipital									
Fusiform gyrus	19					29	−66	−17	27.25
Inferior occipital gyrus	18	−18	−95	−4	31.23				
Temporal									
Fusiform gyrus	37	−40	−56	−19	34.50				
	37	−44	−63	−25	18.35				
Middle temporal gyrus	21	−51	−35	−7	29.58				
	21	−55	−33	2	21.12				
Frontal									
Precentral gyrus	4	−44	1	34	25.73	47	7	30	38.91
Superior frontal gyrus	6					4	13	52	35.91
	9	−25	51	27	27.14				
	8	−3	29	42	27.51				
Inferior frontal gyrus	45					44	31	12	33.29
	47	−44	29	−5	26.21				
Insula	13					31	25	−3	37.00
Subcortical									
Cerebellum						18	−74	−35	31.99
Autistic > Non-autistic									
Occipital									
Fusiform gyrus	19	−29	−86	−2	25.97	38	−74	−9	35.29
						38	−68	−12	31.87
Middle occipital gyrus	18	−22	−93	18	26.27	34	−85	10	22.62
	19					32	−82	19	19.26
	19					32	−80	23	19.14
Parietal									
Precuneus	7	−28	−67	41	32.61				
Temporal									
Fusiform gyrus	37	−38	−67	−18	43.26	32	−49	−14	30.20
	37	−33	−63	−5	27.91	36	−49	−14	37.16
	37	−34	−48	−22	24.89				
Frontal									
Inferior frontal gyrus	47	−49	22	−10	37.33				
Middle frontal gyrus	8					55	23	35	29.17

between-group differences in frontal cortex all involved lower ALE values in the autism group. For instance, differences were observed in right dorsolateral cortex (BA 9, 46), right anterior prefrontal cortex (BA 10), bilateral inferior frontal cortex (BA 44), bilateral premotor cortex (BA 6) and left primary motor cortex (BA 4). The autistics also exhibited lower ALE values in right anterior insula (BA 13).

Voxel count in the fusiform gyrus for faces

To visualize the differential activity related to visual processing, we computed the number of voxels in the fusiform gyrus for which ALE values differed between autistics and non-autistics for the face, object and word processing domains in both hemispheres (Table VIII). The

TABLE V. Autistics show a rightward shift of temporal and parietal lobe visual activity when compared with non-autistics

	Autistics > Non-autistics		Non-autistics > Autistics	
	Left	Right	Left	Right
Temporal lobe	1,384	2,960	1,216	200
Occipital lobe	968	904	384	96
Parietal lobe	96	296	552	80
Frontal lobe	872	488	2,104	2,704
Subcortical	448	392	264	617

The differential between-group voxel counts for the left and right hemisphere lobes are shown for the combined «FACES, OBJECTS, and WORDS» domains ($p_{FDR} < 0.05$).

TABLE VI. ALE maxima of regions showing within-group effects for the «FACES» processing domain
($p_{FDR}< 0.05$, $k = 250vx$)

Region	BA	Left				Right			
		x	y	z	ALE ($\times 10^{-3}$)	x	y	z	ALE ($\times 10^{-3}$)
Non-autistic									
Occipital									
Fusiform gyrus	19	−42	−81	−12	26.88	42	−74	−9	32.95
	19	−29	−86	−16	22.67	29	−64	−17	22.24
	19					31	−59	−15	20.76
Middle occipital gyrus	18	−31	−84	4	16.47				
	18	−33	−87	−7	14.62				
Lingual gyrus	18	−18	−79	−10	22.79				
	18	−12	−76	−1	13.52				
Temporal									
Fusiform gyrus	37	−42	−56	−19	38.18	42	−47	−21	30.45
						42	−59	−13	28.37
Superior temporal gyrus	22	−61	−45	30	22.40	53	−45	19	17.40
Middle temporal gyrus	21	−62	−42	−4	19.84	59	−39	−2	20.53
						57	−44	8	14.18
Parietal									
Precuneus	19					34	−65	42	18.74
Frontal									
Middle frontal gyrus	46					42	33	12	35.95
	10					40	48	10	22.27
Precentral gyrus	6	−44	−2	34	13.81	47	5	28	33.36
	4	−44	−7	42	17.49				
Inferior frontal gyrus	44	−55	14	−1	25.53	53	9	9	21.70
	45					55	30	−2	23.20
Insula	13					44	14	9	24.89
	13					33	28	5	24.36
Subcortical									
Cingulate gyrus	31	−1	−47	31	31.16				
Globus Pallidus		−18	−10	−10	24.02				
Autistic									
Occipital									
Fusiform gyrus	19	−31	−85	−9	25.30	40	−74	−9	32.96
	19	−36	−61	−9	25.12	29	−83	−15	23.02
	19	−38	−62	−16	23.30				
	19	−42	−79	−14	19.35				
Lingual gyrus	18	−25	−74	−6	14.38	23	−71	−2	28.33
	17					8	−77	3	18.32
Middle occipital gyrus	19	−51	−76	−3	19.38				
Temporal									
Fusiform gyrus	37	−44	−51	−17	29.61	36	−49	−14	47.93
		−34	−48	−22	24.63				
Superior temporal gyrus	39					62	−60	23	21.50
	22	−48	−54	20	20.01	59	−39	−2	21.21
Middle temporal gyrus	21	−36	0	−42	21.04				
	38					35	2	−26	22.85
Parietal									
Precuneus	19	−28	−67	43	22.15				
Frontal									
Precentral gyrus	6					42	10	34	17.78
Insula	13					36	24	1	20.12
Subcortical									
Cerebellum		−5	−67	2	15.25	3	−67	−3	13.23
Cingulate gyrus	31	2	−51	32	22.74	12	−51	32	12.66
	31	−9	−49	30	12.77				
Globus Pallidus		−25	−10	−10	16.25				

TABLE VII. ALE maxima of regions showing between-group differences for the «FACES» processing domain ($p_{FDR} < 0.05$, $k = 250$vx)

Region	BA	Left				Right			
		x	y	z	ALE ($\times 10^{-3}$)	x	y	z	ALE ($\times 10^{-3}$)
Non-autistic > Autistic									
Occipital									
Fusiform gyrus	19					38	−69	−3	13.75
	19					34	−69	−5	13.50
	19					29	−64	−17	21.13
Temporal									
Fusiform gyrus	37	−40	−54	−19	25.06				
	37	−42	−63	−25	19.96				
	37	−42	−55	−7	13.25				
Superior temporal gyrus	39	−61	−45	30	22.40				
Middle temporal gyrus	21	−62	−42	−4	19.85				
Frontal									
Middle frontal gyrus	46					42	33	9	29.05
	10					40	48	10	22.22
	9					51	13	29	13.10
Inferior frontal gyrus	44	−55	14	−1	25.50	53	9	9	21.63
Precentral gyrus	6	−44	−2	34	13.80	47	5	28	24.78
	4	−44	−7	42	17.45				
Insula	13					44	14	9	24.70
	13					31	28	5	20.41
Autistic > Non-autistic									
Occipital									
Lingual gyrus	19					23	−71	−2	27.89
Fusiform gyrus	19	−33	−61	−7	22.15				
		−36	−66	−15	13.21				
Temporal									
Fusiform gyrus	37	−34	−47	−23	23.30	33	−46	−14	41.65
Middle temporal gyrus	21	−36	0	−42	21.04				
Superior temporal gyrus	39					62	−60	22	21.41

associated analysis of variance revealed higher ALE values for the autistics $F(1,6) = 9.12$, $p = 0.023$, such that more voxels had ALE values that were greater in the autistic vs. non-autistic groups and a trend for the largest between group differences to be associated with face processing tasks, $F(2, 6) = 4.64$, $P = 0.060$ (see Fig. 4).

Object Processing

Within-group maps

The within-group analysis for contrasts involving object processing revealed a roughly overlapping pattern of activity in both groups (Table IX; Figs. 5 and S3), including bilateral clusters in the anterior fusiform gyrus (BA 37) and posterior extrastriate cortex (BA 18, 19). In contrast, most of the activity in the occipital gyri did not exhibit overlap between groups. In the parietal cortex, overlapping ALE values were seen in medial parietal cortex (BA 7), while activity was observed in slightly different portions of the inferior parietal lobule (BA 40) in each group. Overlapping activity was also seen bilaterally in anterior insula (BA 13), and precentral and middle frontal (BA 6) gyri.

Between-group maps

Widespread between-group differences in visual object processing were seen in occipital, temporal, parietal and frontal cortex (Table X; Figs. 5, 3, and S3). In occipital regions, the autistic group had greater ALE values bilaterally in the posterior fusiform gyrus (BA 19) and the middle occipital gyrus (BA 19). Conversely, autistics had lower

TABLE VIII. Autistics exhibited relatively stronger engagement of the fusiform gyrus for face processing compared with objects and words

Domain	Autistics > Non-autistics		Non-autistics > autistics	
	LEFT FG	RIGHT FG	LEFT FG	RIGHT FG
Faces	1440	2688	592	168
Objects	1136	1616	1232	952
Words	624	520	496	8

The differential between-group voxel counts for the «FACES», «OBJECTS», and «WORDS» processing domains are shown for the left and right hemispheres ($p_{FDR} < 0.05$, $k = 250$vx).

TABLE IX. ALE maxima of regions showing within-group effects for the «OBJECTS» processing domain
($p_{FDR} < 0.05$, $k = 250vx$)

| Region	BA	Left				Right			
		x	y	z	ALE ($\times 10^{-3}$)	x	y	z	ALE ($\times 10^{-3}$)
Non-autistic									
Occipital									
Inferior occipital gyrus	18	−16	−93	−2	27.07				
Cuneus	17	−18	−94	9	21.79				
Middle occipital gyrus	18	−29	−92	3	13.08				
Fusiform gyrus	19	−27	−68	−13	20.46				
	19	−29	−87	−9	12.49				
Parietal									
Precuneus	7	−18	−66	52	24.86	28	−63	39	26.33
	7	−24	−61	44	15.97				
	7	−13	−72	57	13.05				
Precuneus	31	−26	−75	30	22.48				
Superior parietal lobule	7					26	−62	50	26.09
Inferior parietal lobule	40	−35	−41	47	21.36				
	40	−50	−48	44	14.12				
	40	−44	−54	46	13.67				
Frontal									
Precentral gyrus	6					47	7	30	30.85
						60	9	23	14.31
Superior frontal gyrus	6	2	13	52	30.01	4	19	45	13.63
	6	−24	−2	54	26.45	28	0	53	21.70
Middle frontal gyrus	9					42	23	24	19.53
Insula	13	−31	25	0	20.93	31	25	−3	36.33
Subcortical									
Parahippocampal gyrus	36	−27	−46	−11	26.33	29	−44	−12	35.78
Putamen		−25	−1	−2	17.34				
Brainstem						3	−36	−41	23.45
Autistic									
Occipital									
Fusiform gyrus	19	−36	−81	−9	19.43	36	−76	−9	21.79
Middle occipital gyrus	19					32	−84	17	18.92
	19					38	−81	9	13.38
	18	−22	−93	16	24.11	32	−87	10	16.55
	18	−27	−88	−2	15.57	34	−88	1	15.91
	18	−27	−90	2	15.55				
	18	−31	−87	11	13.23				
Inferior occipital gyrus	18					38	−84	−4	15.21
	18					24	−93	−3	14.87
Cuneus	17					25	−97	0	14.31
Lingual gyrus	17	−11	−97	1	20.34				
Parietal									
Superior parietal lobule	7	−22	−64	51	14.52	32	−51	49	23.13
Inferior parietal lobule	40	−44	−26	−48	18.64	36	−39	43	19.40
	40					36	−33	56	13.64
	40					56	−26	46	14.65
Precuneus	7	−24	−63	42	15.51	23	−59	55	22.32
	7	−15	−66	51	13.99				
	31					30	−75	25	12.65
Frontal									
Precentral gyrus	6	−48	9	31	13.64	53	7	30	25.69
	6	−46	3	34	14.25				
	6	−55	2	31	13.00				
Middle frontal gyrus	6	−24	−2	54	19.13				
Insula	13	−31	23	3	22.89	38	24	1	16.74
Subcortical									
Cingulate gyrus	24	−3	−6	30	23.85				
	24	−3	5	31	13.34				
	32					8	25	40	15.49
Parahippocampal gyrus	36	−27	−46	−11	20.42				
Thalamus		−14	−19	9	19.83				
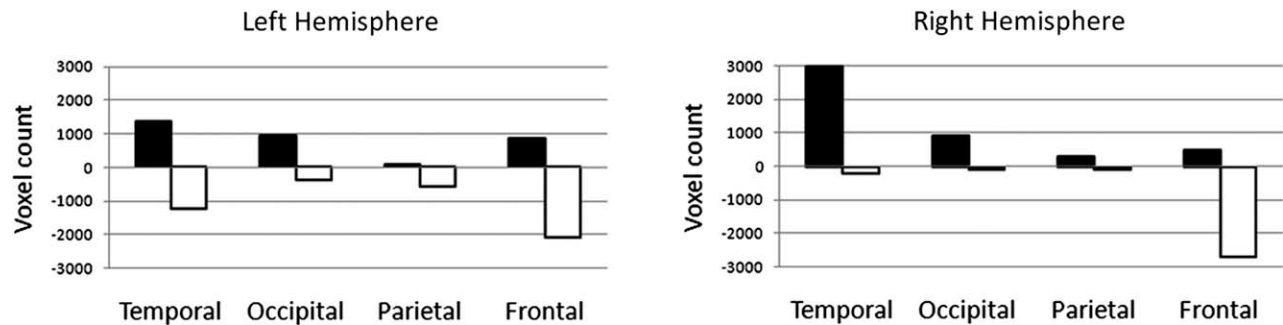
Figure 2.

In both hemispheres, autistics exhibit more activity in temporal and occipital cortex. Between-group differences in task-related effects related to the combined «FACES, OBJECTS and WORDS» processing domains are shown with individual bars representing the number of suprathreshold voxels for autistics vs. non-autistics (BLACK) and non-autistics vs. autistics (WHITE) ($p_{FDR} < 0.05$). Voxel counts are presented separately for the left and right temporal, occipital, parietal and frontal lobes.

ALE values in left lingual gyrus (BA 18) and the right anterior fusiform gyrus (BA 37). Additionally, autistics had lower values in the left mid-fusiform gyrus (BA 19; +29, −68, −14), in an area anterior and medial to the area in which autistics had higher values. Both groups had ALE value maxima in the medial (precuneus) and lateral parietal cortex. Higher ALE values in autistics were more medial than those of non-autistics in right inferior parietal cortex (BA 40) and anterior to those of controls in right lateral and medial superior parietal cortex (BA 7). As for frontal cortex, lower ALE values were observed in superior frontal gyrus (BA 6) in the autistics. Additionally, the autistic group exhibited lower ALE values in the right anterior insular cortex (BA 13) and higher ALE values in the cingulate gyrus (BA 24).

Word Processing

Within-group maps

ALE maps were computed for contrasts involving word processing (Table XI; Fig. 5 and S4). In both groups, activity was observed in striate (BA 17) and extrastriate cortex (BA 18), overlapping mostly in the right hemisphere, while left hemisphere activity was slightly more anterior in autistics. In parietal cortex, both groups showed overlapping activity in the medial parietal cortex (BA 7), while activity in left middle temporal gyrus (BA 21) was observed in a more posterior location in autistics. In frontal cortex, both groups had significant ALE values in inferior (left BA 45, 47), middle (BA 6, 46), and superior frontal (BA 6, 8, 9) gyri, with overlapping activity in the left inferior and superior frontal gyri. We observed group overlap in subcortical activity in the thalami, right cingulate gyrus (BA 31), and left parahippocampal gyrus (BA 36).

Between-group maps

Between-group ALE maps revealed differences in word processing activity (Table XII; Figs. 3, 5 and S4). First, ALE values differed between groups in occipitotemporal areas, with lower activity in bilateral striate cortex in autistics, just under the critical threshold on the right (+16, −95, −7), and higher activity in autistics in extrastriate cortex (BA 18; −14, −87, −5 and +25, −98, −9). Autistics also had higher activity in both the right fusiform gyrus (BA 19, 37) and, more ventrally, in the left ventral fusiform gyrus (BA 19). In parietal cortex, the autistics had higher ALE values in bilateral medial parietal cortex (BA 7), although the values were subthreshold on the left (−28, −68, +38; vx = 144). Between-group differences were also seen in the middle temporal gyrus, with higher ALE values found posteriorly in autistics and anteriorly in non-autistics on the left.

A more complex pattern of effects was observed in frontal and subcortical regions. For example, while autistics generally had more areas exhibiting lower ALE values in frontal cortex compared to non-autistics, the lower ALE values were seen primarily in left inferior, superior frontal, and precentral gyri (BA 4, 8, 47) and higher ALE values were found bilaterally in left posterior inferior frontal gyrus (BA 47), left superior frontal gyrus (BA 6), as well as left and right middle frontal gyri (BA 8, 9, 46). At the subcortical level, the right caudate nucleus, and bilateral thalami (sub-threshold cluster on the right; +29, −26, −2; vx = 120) exhibited lower ALE values in autistics, while the left putamen had higher ALE values in autistics.

DISCUSSION

Summary of Findings

On the basis of the behavioral, cognitive and physiological phenomena previously summarized in the enhanced perception function model, we predicted that autistics would exhibit stronger engagement of the visual system across a range of tasks. In addition, we were interested in whether any observed atypical visual activity patterns in

TABLE X. ALE maxima of regions showing between-group differences for the «OBJECTS» processing domain ($p_{FDR} < 0.05$, $k = 250$vx)

Region	BA	x	y	z	ALE (x10^{-3})	x	y	z	ALE (x10^{-3})
			Left				Right		
Non-autistic > Autistic									
Occipital									
Lingual gyrus	18	−18	−93	−4	25.07				
	18	−18	−94	7	17.91				
Temporal									
Fusiform gyrus	37					29	−44	−10	24.82
Parietal									
Precuneus	7					28	−61	39	26.12
Superior parietal lobule	7					28	−62	48	20.65
Inferior parietal lobule	40	−35	−41	47	20.89				
	40	−50	−48	−43	14.10				
	40	−43	−54	46	13.67				
Frontal									
Superior frontal gyrus	6	2	13	52	30.02				
Insula	13					31	25	−3	33.33
Subcortical									
Putamen		−25	0	0	16.75				
Autistic > Non-autistic									
Occipital									
Middle occipital gyrus	19	−24	−91	16	22.78				
Fusiform gyrus	19	−36	−79	−10	19.16	36	−76	−9	21.24
Parietal									
Superior parietal lobule	7					32	−51	49	22.99
Inferior parietal lobule	40					34	−39	43	17.32
	40					36	−32	47	14.72
Subcortical									
Cingulate gyrus	24	−3	−6	30	23.39				

autism were specific to particular processing domains. We compared the magnitude and spatial distribution of brain activity associated with visual processing in autistics and non-autistics using ALE meta-analysis, including data drawn from 26 neuroimaging studies using visual stimuli. The analysis provided information about between-group differences with respect to location and amplitude of task-related activity. Combining all visual tasks, we observed widespread effects in both groups in regions spanning temporal, occipital, parietal, and frontal cortex. However, compared to non-autistics, autistics displayed generally higher task-related activity in posterior regions, and lower task-related activity in frontal cortex. In addition, for each processing domain, we observed spatial overlap in activity in autistics and non-autistics, accompanied by an atypical functional spatial distribution of domain-specific responses in autism.

Domain-Independent Similarities and Differences

As visual stimuli were used in all studies, large clusters of activity were found in both groups in the cortical areas

involved in the first visual processing stages, namely striate (BA 17) and extrastriate (BA 18, 19) cortex. Both groups had responses in inferotemporal cortex, a region involved in recognition and identification of visually presented animate or inanimate objects [Op de Beeck et al., 2008]. Both groups also displayed posterior parietal cortex activity mainly in the medial parietal cortex (BA 7), an associative region involved in visuospatial information processing [Cavanna and Trimble 2006]. In addition, both groups exhibited activity in the dorsal (BA 6, 8, 9, 46) and ventral (BA 44-47) prefrontal cortex, regions involved in multiple aspects of sensorimotor and cognitive control [D'Esposito et al., 2000; Duncan and Owen 2000; Petrides 1996; Petrides 2005]. The high ALE values seen in both groups across a broad network comprising temporal, occipital, parietal, and frontal regions were consistent with the wide range of visual processing tasks included in the study.

Between-group comparisons using the combined face, object, and word processing tasks revealed an atypical pattern of resource allocation in autistics, with relatively higher activity in posterior visual processing regions and lower activity in frontal regions, as demonstrated by voxel
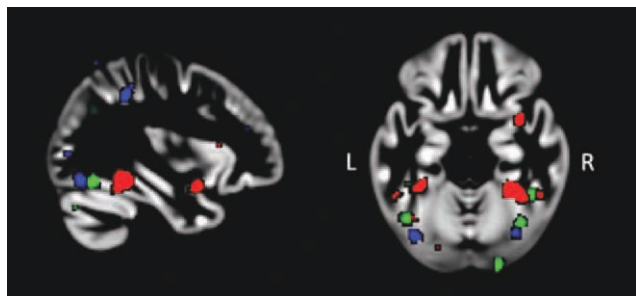
Figure 3.

Spatial distribution of regions showing more task-related activity in autistics than non-autistics for the three processing domains: «FACES» in RED, «OBJECTS» in GREEN, and «WORDS» in BLUE. ALE maps ($p_{FDR} < 0.05$) are superimposed on slices from a gray matter template in MNI space. LEFT, a right hemisphere sagittal slice at $x = +35$; RIGHT, an axial slice at $z = -18$.

count lobar distributions (see Fig. 2). In inferotemporal, occipital, and inferior parietal regions, more voxels showed higher ALE values in autistics than in non-autistics in areas subserving integration of local visual features, manipulation of visual features, object recognition and object identification [Wandell et al., 2007]. Moreover, autistics displayed higher activity bilaterally in the precuneus (BA 7), a region subserving visual imagery [Suchan et al., 2002], visual search and detection [Brown et al., 2006; Hufner et al., 2008; Patel and Sathian, 2000], and the maintenance of visual information in working memory [Owen, 2004; Suchan et al., 2006; Yeh et al., 2007].

Conversely, ALE values in more anterior frontal regions (BA 4, 6, 8, 9, 45, and 47) were mostly lower in autistics. These areas include a range of regions with specialization for movement execution, movement planning, and cognitive control. The most posterior frontal region (BA 4) in the precentral gyrus is involved in fine motor control and sensorimotor transformations [He et al., 1993; Rizzolatti and Luppino 2001]. The posterior part of the dorsolateral prefrontal cortex (DLPFC; BA 6, 8) is responsible for response selection, attention shifting between alternative stimuli or responses in visuomotor tasks [Petrides, 1994, 2005]. The mid-DLPFC (BA 9) is involved in planning and monitoring of behavior in accordance with internal goals [Petrides, 1991, 2000]. The adjacent mid-ventrolateral prefrontal cortex (VLPFC; BA 45, 47) plays an important role in decision making [Petrides, 2002], response comparison, selection and inhibition based on stored stimulus representations [Badre and Wagner, 2007; Petrides, 2005]. Finally, BA 6 and 9 are believed to be involved in cognitive control, mainly through the activation of task representations to adjust behavior to changing contexts [Brass et al., 2005].

Our principal finding resulting from the examination of results from the pooled face, object and word domains is that, in performing predominantly visual tasks, autistics

exhibit a consistent pattern of stronger engagement of posterior cortical regions known to support visual processes of varying complexity. In addition, autistics exhibit lower activity in frontal regions subserving motor and cognitive control functions across a wide range of stimulus and task types.

Domain-Specific Similarities and Differences

Although our results are largely consistent across the three visual processing categories, examining the domain-specific patterns of differential activity informs the understanding of specific atypical functional resource allocation patterns in autism. The decision to classify the included tasks broadly by stimulus type rather than by specific cognitive operation was dictated by our difficulty in identifying sufficient numbers of studies utilizing tasks employing comparable cognitive operations. As the number of papers using functional neuroimaging to explore the neural mechanisms of perception and cognition in autism is expanding rapidly, it may soon be possible to attempt meta-analysis of particular cognitive processes in autism.

Face processing

Much effort has been directed towards identifying the nature of face processing in autism. Our meta-analysis of face processing tasks revealed strong, and partially overlapping, occipital and temporal activity in both groups. Face processing involves occipital and temporal cortical areas that show selectivity for face versus nonface stimuli in typical groups [Haxby et al., 2000; Kanwisher et al., 1997]. Consistent identification of preferential activity for face stimuli have been observed in the middle and lateral fusiform gyri, sometimes referred to as the Fusiform Face Area (FFA). This region generally shows stronger responses to faces compared to objects. Activity in the FFA correlates with successful face detection [Andrews and Schluppeck 2004; Grill-Spector et al., 2004]. A region in the lateral inferior occipital gyrus, referred to as the occipital face area (OFA), also shows selectivity for faces [Gauthier et al., 2000]. While the OFA is mostly sensitive to the individual physical features of faces, the FFA shows strong responses to both face parts and configurations [Liu et al., 2010; Rotshtein et al., 2005]. The third face-selective region is found in the posterior superior temporal sulcus and is called fSTS, showing stronger responses to more complex aspects of face processing, such as eye-gaze direction [Hoffman and Haxby 2000] and emotional expression [Haxby et al., 2000].

With regards to face processing, spatial overlap in activity for autistics and non-autistics was observed in the FFA [Kanwisher et al., 1997; Lehmann et al., 2004; Rhodes et al., 2009; Scherf et al., 2010]. Activity was also seen in the OFA [Rhodes et al., 2009; Rotshtein et al., 2005]. In addition, activity in fSTS was seen in both groups on the right, but only in non-autistics on the left. Therefore, the results of our meta-

TABLE XI. ALE maxima of regions showing within-group effects for the «WORDS» processing domain ($p_{FDR} < 0.05$, $k = 250$vx)

Region	BA	x	y	z	ALE (x10^{-3})	x	y	z	ALE (x10^{-3})
			Left				Right		
Non-autistic									
Occipital									
Inferior occipital gyrus	17	−18	−97	−4	20.85	14	−96	−7	30.74
Lingual gyrus	18	−10	−96	−11	19.55				
Temporal									
Middle temporal gyrus	21	−51	−35	−5	24.30				
	21	−55	−33	2	21.16				
	39					56	−66	26	17.94
Parietal									
Precuneus	7	2	−59	37	18.08				
Frontal									
Superior frontal gyrus	8	−18	28	47	25.57				
	8	−12	55	37	21.17				
	8	−7	47	45	16.68				
	8	−13	33	53	13.59				
	9	−1	60	19	20.53				
	8	−1	34	44	18.88				
	6	−5	9	57	26.20				
Inferior frontal gyrus	45	−49	24	12	20.48				
	47	−47	27	−6	23.50				
	47	−40	29	−5	19.21				
	47	−32	33	−12	13.18				
Middle frontal gyrus	46	−46	21	23	13.18				
	6	−44	8	49	13.95				
Precentral gyrus	4	−55	−3	46	24.87				
	6	−50	6	45	14.62				
	6	−44	0	50	13.59				
Subcortical									
Parahippocampal gyrus	27	−25	−31	−8	29.49				
	36	−21	−42	−9	13.71				
Caudate						21	−24	18	33.27
Thalamus		−18	−47	5	21.50	27	−27	7	31.97
Cingulate	29	−5	−51	10	17.58				
	30	−3	−62	8	13.10				
Autistic									
Occipital									
Fusiform gyrus	19	−40	−69	−17	37.16	38	−68	−12	25.65
Inferior occipital gyrus	17					23	−98	−9	23.84
Lingual gyrus	18	−14	−87	−7	16.75				
Temporal									
Middle temporal gyrus	21	−57	−42	−2	17.79				
	21	−61	−47	8	13.87				
Fusiform gyrus	37					46	−49	−14	23.50
Parietal									
Precuneus	7	−5	−59	37	13.96	4	−57	37	20.54
	7	−9	−54	41	13.62	30	−65	42	22.02
Frontal									
Inferior frontal gyrus	47	−49	22	−10	42.79				
	45	−49	24	5	13.28				
Superior frontal gyrus	6	−7	10	60	36.64				
	8	−9	50	38	20.25	12	45	49	17.32
	9	1	58	26	18.25				
Middle frontal gyrus	46	−44	21	21	26.65				
	9					56	23	35	20.67
	8					28	28	44	19.59

TABLE XI. (Continued)

Region	BA	Left x	y	z	ALE (x10^{-3})	Right x	y	z	ALE (x10^{-3})
Subcortical									
Putamen		−25	6	4	32.21				
		−25	−8	−8	13.34				
Thalamus		−5	−12	12	15.07	27	−30	0	25.37
		−7	−16	13	14.99				
Parahippocampal gyrus	35	−25	−27	−10	24.76	12	−51	5	13.20
Insula	13	−31	24	5	13.82				
	13	−40	23	3	13.81				
	13	−31	27	0	13.05				
Amygdala		−23	−10	−12	14.30				
		−29	−8	−14	13.41				
Cingulate	30					4	−53	7	15.25

TABLE XII. ALE maxima of regions showing between-group differences for the «WORDS» processing domain (p_{FDR} < 0.05, k = 250vx)

Region	BA	Left x	y	z	ALE (x10^{-3})	Right x	y	z	ALE (x10^{-3})
Non-autistic > Autistic									
Occipital									
Inferior occipital gyrus	17	−18	−97	−4	20.28				
Lingual gyrus	18	−10	−96	−11	19.32				
Temporal									
Middle temporal gyrus	21	−51	−36	−7	23.83				
	21	−55	−33	2	20.66				
	39					56	−66	26	17.94
Frontal									
Precentral gyrus	4	−55	−3	46	24.85				
Superior frontal gyrus	8	−18	26	47	22.24				
	8	−1	34	44	18.88				
Inferior frontal gyrus	47	−40	31	−5	18.21				
Subcortical									
Caudate						21	−24	18	24.97
Thalamus		−27	−33	−5	19.14				
Parahippocampal gyrus	36	−21	−42	−9	13.67				
	36	−18	−36	−14	13.61				
Autistic > Non−autistic									
Occipital									
Fusiform	19	−40	−69	−17	36.82				
Temporal									
Middle temporal gyrus	21	−59	−44	−2	17.03				
Fusiform gyrus	37					46	−49	−14	23.50
Parietal									
Precuneus	7					30	−65	42	22.02
Frontal									
Inferior frontal gyrus	44	−49	22	−10	36.82				
Superior frontal gyrus	6	−7	81	55	23.15				
Middle frontal gyrus	46	−42	29	18	13.09				
	8					56	23	35	20.66
	9	−51	17	26	19.91				
	9	−42	21	21	17.23				
Subcortical									
Putamen		−25	6	4	30.20				
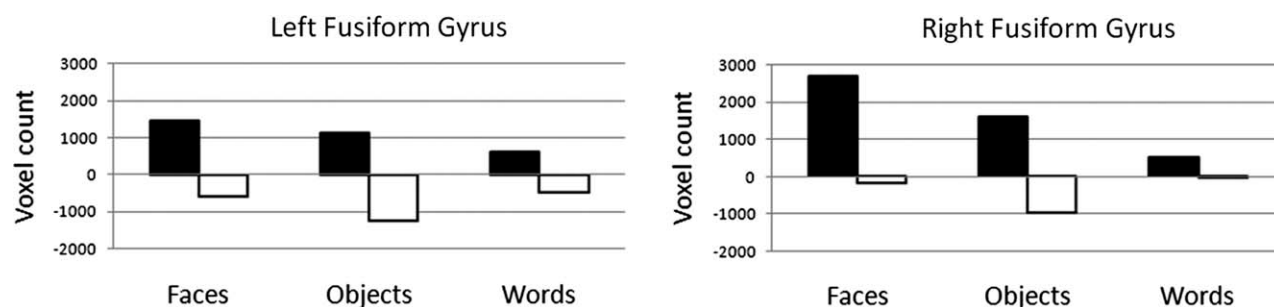
Figure 4.

In the fusiform gyrus, more suprathreshold voxels are found for the autistic vs. non-autistic than the non-autistic vs. autistic contrasts. Between-group differences in effects related to the «FACES», «OBJECTS», and «WORDS» processing domains are shown with bars representing the number of suprathreshold voxels for autistics vs. non-autistics (BLACK) and non-autistics vs. autistics (WHITE) ($p_{FDR} < 0.05$). The voxel counts are presented separately for the left and right hemispheres.

analysis do not support the notion that autism is characterized by an overall hypoactivation in face-selective areas. We believe that the reported reduction of FFA activity in autism in response to face images [Dalton et al., 2005; Pierce et al., 2001; Schultz et al., 2000] could be dependent on specific task properties, rather than related to a generalized dysfunction of fusiform gyrus mechanisms or stemming from a lack of face expertise [Hadjikhani et al., 2004; Hadjikhani et al., 2007; Pierce et al., 2004].

However, our results do suggest that face stimuli are processed in an atypical fashion in autism, such that stronger, but less category-specific, occipital and temporal activity may underlie face processing in this population. Specifically, compared with non-autistics, autistics showed bilateral clusters of higher ALE values in the anterior fusiform gyrus, extending into the posterior part of the parahippocampal gyrus (see Fig. 3). In typical individuals, these areas are thought to be important for face recognition [Hudson and Grace, 2000], perceptual expertise [Gauthier et al., 1999], and object processing [Grill-Spector, 2003]. Moreover, previous studies have identified functional response selectivity for places and spatial layout in the posterior parahippocampal cortex [Epstein and Kanwisher, 1998]. In our results, autistics showed greater activity bilaterally in extrastriate (BA 18, 19) and striate (BA 17) cortex compared to non-autistics. Therefore, face processing in autistics seems to rely on a large network of occipital and temporal areas specifically responsive to other visual categories in non-autistics. Interestingly, the more anterior inferotemporal areas were more responsive to nonface objects in non-autistics. A recent fMRI study looking at response specificity to faces, objects, and places in autism reported a similar atypical distribution of activity, in the form of bilateral displacement of the face-specific response to the postero-ventral fusiform gyrus in autistics, while non-autistics showed greater object-related responses in the same region [Scherf et al., 2010]. These findings are consistent with the results of our meta-analy-

sis, indicating a general pattern of atypical facial response selectivity in autism, with a corresponding atypical spatial distribution of place- and object-specific responses.

The differential activity we observed in autistics could reflect an atypical processing strategy for facial stimuli. Langdell [1978] first reported superior performance in judging face identity based on the presentation of elementary facial features such as the eye or mouth in autistic children compared with non-autistics. More recent studies confirmed that autistics rely to a greater extent on individual features to process faces [Deruelle et al., 2004; Lahaie et al., 2006; Pelphrey et al., 2002]. However, these atypical processing strategies are not necessarily detrimental to performance, as autistics and non-autistics exhibited similar performance in 9 out of 14 contrasts included in the meta-analysis.

We observed generally lower activity in prefrontal cortex in autistics during face processing, consistent with previous reports [Di Martino et al., 2009; Scherf et al., 2010]. It is known that frontal top-down mechanisms may modulate extrastriate and inferotemporal activity during "deep" processing of faces, facilitating facial feature recognition [Haxby et al., 2000; Johnson et al., 2007; Li et al., 2009; Mechelli et al., 2004] and visual category determination [Jiang et al., 2007; Jiang et al., 2006]. Our findings suggest that, although frontal processes are consistently engaged for face processing in non-autistics, the perceptual mechanisms in temporal, occipital, and parietal regions may be sufficient to allow for successful face processing in autistics. Although it is possible that the lack of task-related frontal activity in autistics could result from localized dysfunction of the frontal cortex, suggested by some current models [e.g. Courchesne and Pierce 2005], an alternative account is that utilization of frontal processing mechanisms may not be mandatory under some circumstances in autistics due to the existence of more efficient perceptual processing resources available in posterior cortical structures [Soulières et al., 2009]. Finally, the reduced engagement of frontal regions may reflect atypical connectivity between anterior and posterior regions, resulting in reduced functional coupling
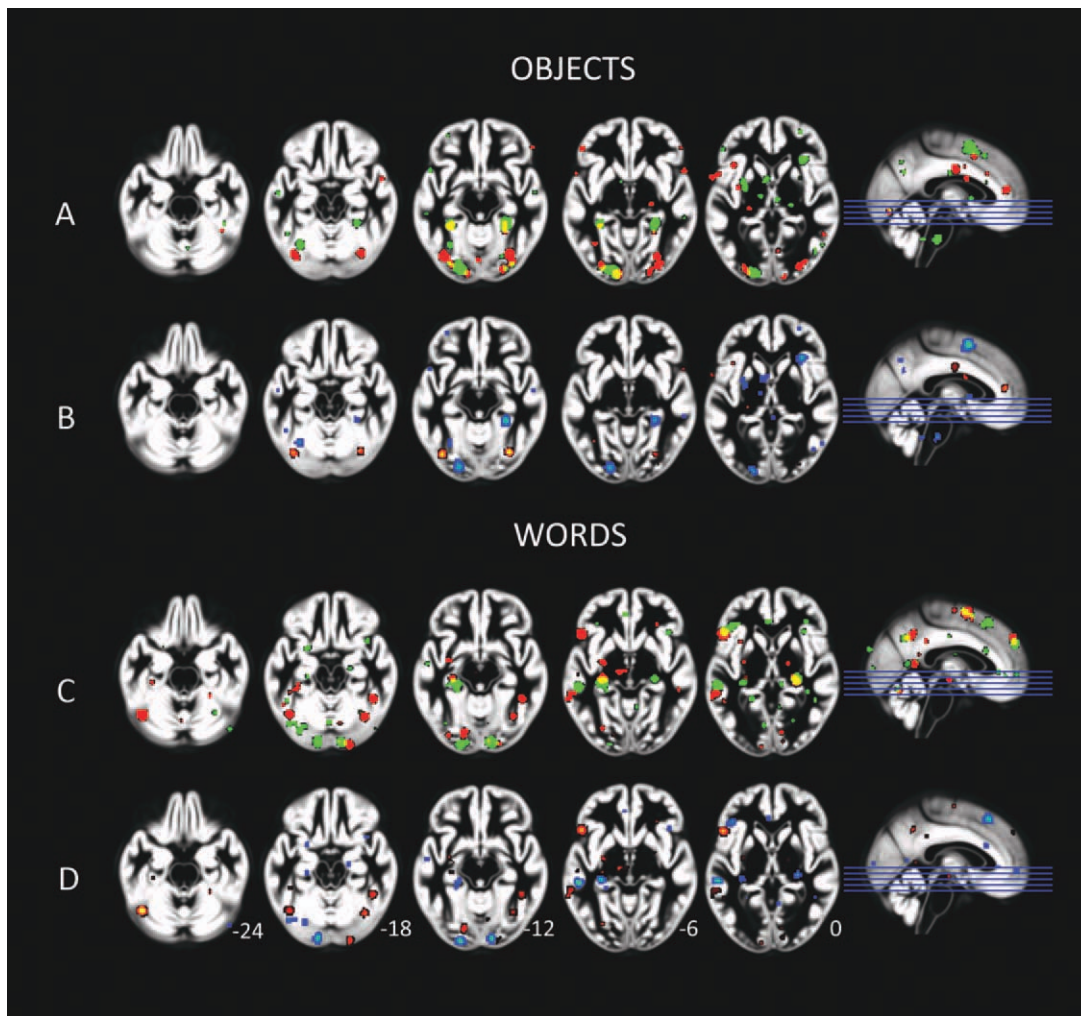
Figure 5.

Within- and between-group distribution of task-related activity in inferior occipital and inferotemporal cortex. **A**: Regions showing increases in autistics (RED), non-autistics (GREEN), and their overlap (YELLOW) for the «OBJECTS» tasks. **B**: Regions showing more task-related activity in autistics vs. non-autistics (RED-YELLOW) and less task-related activity in autistics vs. non-autistics (BLUE-GREEN) for the «OBJECTS» tasks. **C**: Regions showing increases in autistics (RED), non-autistics (GREEN), and their spatial overlap (YELLOW) for the «WORDS» tasks. **D:** Regions showing more task-related activity in autistics vs. non-autistics (RED-YELLOW) and less task-related activity in autistics vs. non-autistics (BLUE-GREEN) for the «WORDS» tasks. ALE maps ($p_{FDR} < 0.05$) are superimposed on axial slices from a gray matter template in MNI space. Anatomical left is image left.

and regional interaction during visual processing. As our results are consistent with all of these hypothetical mechanisms, further studies are warranted to better delineate the physiological basis of the generalized frontal cortical hypoactivity commonly seen in autism.

Object processing

Autistics often exhibit unexpectedly strong and atypical abilities in visual tasks involving object detection or manipulation. For object processing, we observed activity in both groups in occipital (BA 17, 18, 19), temporal (BA 37), medial and lateral superior parietal (BA 7), inferior parietal (BA 40), and dorsal and ventral lateral prefrontal cortex (BA 6, 9 46, 47). Object processing is typically associated with activity in occipital and temporal cortex, with previous studies identifying responses in lateral occipital cortex to pictures of common objects [Malach et al., 1995], line drawings of objects [Kanwisher et al., 1996] and shapes [Hayworth and Biederman 2006]. We observed activity in both groups that was located more medially

than previously reported, possibly due to the heterogeneity of stimuli and tasks combined in the current analysis. While the lateral occipital region plays a specific role in object recognition [Grill-Spector et al., 2001], object recognition as such was not a prominent component of all the tasks included in the meta-analysis. Activity common to both groups was also observed in the anterior fusiform gyrus, another area involved in object processing [Grill-Spector, 2003] and spatial relations [Epstein and Kanwisher, 1998]. Overall, both groups showed occipital and temporal activity in brain regions typically recruited by material-independent visual information processing, such as integration of local visual features and manipulation of visual properties [Wandell et al., 2007].

Both groups also showed responses in prefrontal cortical regions, consistent with cognitive control requirements of the object processing tasks. For instance, lateral prefrontal cortex activity has been reported in relation to set shifting [Rogers et al., 2000], inhibitory control [Konishi et al., 1999], and category discrimination [Jiang et al., 2007; Jiang et al., 2006], processes common in object processing tasks [Dichter and Belger, 2007; Schmitz et al., 2006; Schmitz et al., 2008; Solomon et al., 2009]. The observed prefrontal activity could also be related to planning and categorization [Petrides 2005], processes critical to tasks such as the Embedded Figure Test [Lee et al., 2007; Manjaly et al., 2007], the Tower of London task [Just et al., 2007], spatial reasoning, and pattern matching [Soulières et al., 2009].

Both groups showed activity in superior parietal cortical areas involved in visuospatial attention [Corbetta et al., 1993; Nobre et al., 1997] and manipulation of information in working memory [Cabeza, 2008; Cabeza et al., 2008]. Despite the variability of the tasks and stimuli combined within the object category, we observed a pattern concordant with the previous literature.

Regarding between-group differences in activity related to object processing, autistics had higher ALE values in occipital (BA 19) and parietal (BA 7, 40) areas and lower values in the fusiform gyri (BA 37). The clusters of between-group differential activity were smaller for the object than the face domains, which may be explained by greater task and stimulus variability for the object vs. face domain. Greater task variability within each domain might be expected to lead to a greater degree of spatial variability and consequently weaker constructive interference among the local maxima. As with face processing, autistics performed similarly to non-autistics while displaying lower ALE values in the superior frontal gyrus (BA 6). Enhanced autistic performance has been reported in a broad range of visual perceptual tasks based on pattern detection, matching, and manipulation of objects, aspects encompassed here in the very general object processing domain. Therefore, we tentatively relate the atypical functional allocation of activity in visual perceptive regions in autism to enhanced performance in object processing.

Word processing

Some autistics acquire reading skills at an unexpectedly early age, a phenomenon known as hyperlexia. It is possible that these atypical reading skills result from differential organization in the visual areas responsible for processing letters or words. In our meta-analysis results, group activity distributions related to word processing corresponded well to the known functional neuroanatomy of reading systems. A first level of word analysis in the occipito-temporal junction supports word identification; a second level at the parieto-temporal junction supports phonological processing; and a third level in the inferior frontal cortex supports semantics, phonology, and articulation [Shaywitz and Shaywitz, 2008]. Both groups displayed bilateral posterior fusiform and lingual activity, presumably associated with word form analysis [Fiez and Petersen, 1998; Price, 2000]. Also consistent with this finding are the previous studies that have reported occipito-temporal and lateral occipital sensitivity to letter strings [Puce et al., 1996] and written words [Baker et al., 2007]. In addition, both groups displayed activity in regions typically associated with semantic processing [Howard et al., 1992; Martin and Chao, 2001; Petersen et al., 1988; Poldrack et al., 1999], verbal fluency [Abrahams et al., 2003; Gaillard et al., 2000], and sentence comprehension [Just et al., 1996; Roder et al., 2002], including the left middle temporal gyrus, the left superior temporal gyrus, the left inferior frontal gyrus and multiple lateral prefrontal regions. The word processing tasks included semantic decision [Gaffrey et al., 2007; Harris et al., 2006], sentence judgment and comprehension [Just et al., 2004; Kennedy and Courchesne, 2008; Mason et al., 2008], word counting [Kennedy et al., 2006], and verbal fluency [Kleinhans et al., 2008a], for which we observed the expected activity in a number of left hemisphere language regions.

We observed group differences for the word processing tasks, with higher task-related ALE values in autistics in the fusiform gyrus (mostly on the right; BA 19, 37), medial parietal cortex (BA 7), middle posterior temporal gyrus (BA 21), left inferior frontal gyrus (BA 44), and bilateral lateral prefrontal cortex (BA 6, 8, 9, 46). Many of these areas are also part of the reading network seen in non-autistics. However, predominantly left lateralization, expected based on previous studies of language in typical samples, was not seen here in autism, in line with reports of reduced leftward hemispheric response lateralization for speech processing in autism [Boddaert et al., 2003; Boddaert et al., 2004; Lepisto et al., 2005]. Higher activity for words in the fusiform gyrus and medial parietal cortex supports the hypothesis that autistics more strongly engage mental imagery and visualization to process written sentences [Just et al., 2004] and words [Gaffrey et al., 2007; Toichi and Kamio, 2001]. In addition, we observed lower activity in the autistic group in many reading regions, including occipital (BA 17, 18), left parieto-temporal (BA 21, 39) and left inferior frontal (BA 47) cortex. In

summary, the regional functional allocation of word related activity is clearly atypical in autism, as we observed more right-lateralized activity in autistics related to reading as well as stronger involvement of regions typically involved in broader aspects of perceptual expertise (BA 19, 37).

This atypical activity pattern could explain the emergence of hyperlexic abilities in some autistics. Hyperlexia is defined as reading skills exceeding those predicted by an individual's general intelligence or language comprehension capacities [Grigorenko et al., 2003]. Hyperlexia occurs in about 5–10% of autistic children [Burd et al., 1985]. While it has been suggested that enhanced visual pattern recognition may underlie hyperlexia [Cobrinik, 1982], heightened phonological and orthographic abilities may also contribute to precocious reading skills [Goldberg and Rothermel, 1984]. Although hyperlexic children could engage typical reading strategies to attain superior word recognition abilities, word recognition mechanisms could operate more autonomously from more abstract word comprehension mechanisms in this group [Newman et al., 2007]. The atypical pattern of occipital and temporal word processing activity seen in our meta-analysis might underlie this autonomy, a phenomenon that we called functional independence in a different cognitive context [Soulières et al., 2009].

Alternative Interpretations of the Between-Group Differences

Could atypical saccades cause the observed atypical occipital and parietal activity?

Differences in brain activity apparently associated with visual processing might trivially result from differences in eye movements used to explore the stimuli, rather than from differences in perceptual processing per se. We argue that this is not the case for the following reasons. First, all studies included in the meta-analysis that reported eye movement data found no differences between the autistic and non-autistic groups [Bird et al., 2006; Dapretto et al., 2006; Greimel et al., 2009; Kleinhans et al., 2008b; Soulières et al., 2009], in line with other studies reporting no differences in visual saccade or fixation properties between autistics and non-autistics [Dalton et al., 2005; Kemner et al., 2004; Luna et al., 2007; Luna et al., 2002; Takarae et al., 2004; Takarae et al., 2007]. Second, the spatial pattern of activity across tasks for the between-group differences reported here does not overlap with the network thought to control visual search and saccades. For instance, both groups exhibited activity in lateral prefrontal cortex in the frontal eye fields [FEF; Amiez and Petrides 2009; Grosbras et al., 2005]. This area is consistently involved in controlling saccade and pursuit eye movements [Astafiev et al., 2003; Ettinger et al., 2008; Grosbras et al., 2005]. It is also active in tasks requiring changes in visuospatial attention, even in the absence of saccades

[Armstrong et al., 2009]. Nevertheless, no significant between-group differences were observed in this region. Similarly, regions previously reported as less active in autism in association with visually-guided saccades [Takarae et al., 2007] do not correspond to the areas of lower activity reported here in autistics across all visual tasks. Lower ALE values in non-autistics were observed in the dorsal part of the medial frontal gyrus, anterior to the supplementary eye fields [Grosbras et al., 1999]. However, this region is known to be less active in autism well beyond the context of saccade generation, specifically during executive and working memory tasks [Gilbert et al., 2008; Silk et al., 2006]. Therefore, the pattern of between-group differences reported here is unlikely to be related to oculomotor effects.

Are the observed activity patterns explained by differences in task complexity?

Another interpretation of the differential engagement of cortical regions in autistics across a range of visual tasks could be that these differences are driven mainly by tasks incorporating more substantial perceptual complexity. However, the autistic pattern of relative posterior hyperactivity was consistently found for a range of tasks involving visual information ranging from simple to complex, and cognitive complexity ranging from low to high. For instance, our meta-analysis included stimuli varying from simple shapes (i.e. letters in Keehn et al., 2008] to more complex visual patterns (i.e. facial stimuli in Hall et al., 2003; Raven's Progressive Matrices in Soulières et al., 2009]. Tasks of varying complexity were included as well, ranging from passive viewing of faces (e.g. Bird et al., 2006] and stimulus matching (e.g. Bookheimer et al., 2008; Lee et al., 2007] to sentence comprehension (e.g. Mason et al., 2008], mental state inference (e.g. Kana et al., 2009] and abstract reasoning [Soulières et al., 2009]. In sum, more strongly engaged perceptual processing regions engaged across a disparate collection of tasks indicates a greater role for perceptual processes in autism for tasks not necessarily incorporating complex perceptual or cognitive components.

Does differential between-group performance explain the observed activity patterns?

It is possible that performance differences could be responsible for atypical neural activity patterns in autistics. However, autistics and non-autistics exhibited similar performance levels in 18 of the 26 included studies, compared to two studies with enhanced and six studies with diminished performance in autistics. While enhanced autistic performance was seen in the form of faster responses for sentence comprehension tasks [Just et al., 2004; Knaus et al., 2008], diminished performance was mainly observed in the form of reduced accuracy. Even in studies where accuracy was significantly reduced, the autistics still

performed fairly well. While one study reported 93% correct responses in autistics compared with 100% in non-autistics [Bookheimer et al., 2008], another observed reduced but significantly greater than chance (81.9% and 73.8%) accuracy for a semantic decision task in autistics [Gaffrey et al., 2007]. Kleinhans et al. [2008a] reported that autistics generated fewer words than non-autistics in a verbal fluency task, while no group differences in error number were seen. One study [Hubl et al., 2003] reported longer response times for autistics detecting the sex of real and scrambled faces, but the task instructions did not explicitly require participants to respond as quickly as possible. Other studies reported more errors when autistics were asked to judge emotional states from weak facial expressions [Greimel et al., 2009] or when they had to overcome an automatic response tendency [Solomon et al., 2009]. Given that atypical visual processing is observed in association with mostly typical performance levels in autism, we suggest that autistics make more use of perceptual processes than do non-autistics in executing cognitive tasks involving complex operations.

Is Hemispheric Asymmetry for Visual Processing Atypical in Autism?

Face processing was associated with generally similar hemispheric effects in autistics and non-autistics, with both groups showing bilateral activity in the FFA and the OFA. However, while activity increases were seen in posterior fSTS in both groups on the right, it was observed only in non-autistics on the left. For face processing in autistics, some have hypothesized atypical regional allocation of activity, not necessarily reflecting reduced lateralization of the face-specific activity compared to non-autistics [Pierce et al., 2001]. In addition, recent studies have demonstrated displacement of the face-specific response in autism to regions typically responsive to non-face visual stimuli in non-autistics in both hemispheres [Humphreys et al., 2008; Scherf et al., 2010]. One other meta-analysis of functional neuroimaging studies looking at social vs. non social tasks did not report activity lateralization differences between autistics and non-autistics [Di Martino et al., 2009]. For object processing, hemispheric activity was similarly distributed in both groups. The laterality of word processing is atypical in autism, as evidenced by more symmetric activity in autistics related to reading. Predominantly left lateralization, expected based on previous studies of language in typical samples, does not appear to characterize autism. With respect to language tasks in general, some studies have suggested that atypical hemispheric specialization might be related to the communication difficulties observed in autistics. Atypical leftward lateralization in autism has been most consistently observed at the structural level in frontal language areas [Herbert et al., 2005] and in temporal regions such as planum temporale, middle and inferior temporal gyri [Her-

bert et al., 2005; Rojas et al., 2002]. Some functional imaging studies have reported reduced left frontal activity associated with language tasks [Gaffrey et al., 2007; Just et al., 2004; Kana et al., 2006] and others have reported reduced leftward temporal response lateralization for auditory language tasks in autism [Boddaert et al., 2003; Boddaert et al., 2004; Lepisto et al., 2005]. It is possible that the lateralization effects related to language might be task-dependent, as the hemispheric differences between autistics and non-autistics were not the same for two language tasks examined in a study in which autistics showed reduced leftward asymmetry for one task (fluency) and typical lateralization for the other (categorization) [Kleinhans et al., 2008a].

In summary, while we observed a trend for decreased hemispheric asymmetry in autism for word processing, the left/right differences in associated ALE values were more subtle than the more consistent finding of higher ALE values across all three task domains in posterior compared to frontal cortical regions.

Are the Results Consistent With the Predictions of the EPF Model?

Our ALE meta-analysis results both confirm and extend the original EPF Model, demonstrating that: (1) perceptual processing in autistic individuals plays an enhanced role across a wide range of visual tasks and (2) that the neural organization of perceptual processing is atypically organized, extending to areas involved in the development of perceptual expertise. The first major finding of this study consists of evidence for generally stronger engagement of visual processing regions in autism across a range of tasks, consistent with our previous non-quantitative review of brain imaging results [Mottron et al., 2006]. In addition, the observed stronger engagement of visual areas emerges despite multiple sources of noise introduced by variations in matching strategies, participant age and general intelligence, and whether group assignment was defined using a specific diagnosis of autism versus the broader classification of autism spectrum condition. Our findings are consistent with the hypothesis that autistics rely more heavily on visual processing mechanisms regardless of the stimulus domain, particularly for language functions [Gaffrey et al., 2007; Just et al., 2004; Lambert et al., 2004]. Enhanced activity in brain regions related to visual processing may therefore represent a core atypicality in autistic neural organization.

However, while behavioral evidence for visuospatial strengths in autism is now strong, it is not possible to simply associate higher levels of neural activity with superior behavioral performance, a relationship that has been clearly demonstrated in only a limited number of studies. For instance, we recently reported increased extrastriate (BA 18) combined with reduced prefrontal (BA 9) and parietal (BA 7) activity during performance of a matrix

reasoning task in a group of autistics who had been matched with a non-autistic group on both accuracy and response time [Soulières et al., 2009]. In this study, an autistic behavioral advantage, as evidenced by faster performance, and enhanced occipital activity both increased as task complexity increased. The relative independence of the observed occipital findings with respect to task performance in the present study indicates that higher levels of neural activity may be associated with more efficient task performance in only some circumstances.

The second main finding of this meta-analysis is that atypical regional functional resource allocation, involving both primary and associative cortical areas across a range of visual processing tasks, engages mechanisms responsible for the development of perceptual expertise in areas such as the fusiform gyrus. This important finding allows an extension of the original EPF Model that suggests that the overall process of perceptual expertise development, as well as the specific nature of related category-specific responses, may be atypical in autism. Material-independent variations in the acquisition of autistic perceptual expertise, their reciprocal interactions with low-level perceptual processes, and their involvement in a broad range of both social and non-social atypical behaviors characteristic of autism, may all represent promising fields for future investigation.

Lastly, considering that atypical spatial allocation of brain resources may be an indication of developmental functional plasticity, our results indicate that enhanced cortical plasticity may be beneficial to visual perception in autism, in the light of preliminary findings of greater cortical plasticity, including enhanced long-term potentiation of synaptic strength in an animal model of autism [Rinaldi et al., 2008], and more lasting changes in cortical excitability following in vivo theta burst stimulation in a few autistics [Oberman et al., 2010].

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