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The Action Observation System when Observing Hand Actions in Autism and Typical Development

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Social impairments in individuals with autism spectrum disorders (ASD) may be in part due to difficulty perceiving and recognizing the actions of others. Evidence from imitation studies, which involves both observation and execution of an action, suggests differences, in individuals with ASD, between the ability to imitate goal-directed actions involving objects (transitive actions) and the ability to imitate actions that do not involve objects (intransitive actions). In the present study, we examined whether there were differences in how ASD adolescents encoded transitive and intransitive actions compared to typically developing (TD) adolescents, by having participants view videos of a hand reaching across a screen toward an object or to where an object would be while functional magnetic resonance images were collected. Analyses focused on areas within the action observation network (AON), which is activated during the observation of actions performed by others. We hypothesized that the AON would differentiate transitive from intransitive actions only in the ASD group. However, results revealed that object presence modulated activity in the right inferior frontal gyrus and supramarginal gyrus of the TD group, a differentiation that was *not* seen in the ASD group. Furthermore, there were no significant group differences between the TD and ASD groups in any of the conditions. This suggests that there is not a global deficit of the AON in individuals with ASD while observing transitive and intransitive actions. *Autism Res* 2015, 8: 284–296. © 2015 International Society for Autism Research, Wiley Periodicals, Inc.

Keywords: mirror neurons; fMRI; imitation; action understanding; autism

Introduction

Understanding the actions of others is an essential aspect of human social interactions and underlies our ability to understand others' intentions. A subpopulation of visuomotor neurons in area F5 of the ventral premotor cortex (PMC) of monkeys were discovered to respond both when the monkey executed an action and when the monkey observed another individual perform the action [di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti, Fadiga, Gallese et al., 1996]. These neurons, dubbed "mirror neurons," provided a direct link between visual perception and the production of actions within the motor system. Mirror neurons offered an underlying neural mechanism for understanding others' actions by mapping those actions onto one's own motor system [Decety & Grèzes, 1999]. These neurons were initially thought to respond only when an object was present as the goal of the action [Gallese et al., 1996; Rizzolatti, Fadiga, Gallese et al., 1996;

Umiltà et al., 2001; although see Kraskov, Dancause, Quallo, Shepherd, & Lemon, 2009]. Similar neurons have been found in parietal area PF/PFG of monkeys [Gallese, Fogassi, Fadiga, & Rizzolatti, 2001; Rizzolatti, Fogassi, & Gallese, 2001; Rozzi, Ferrari, Bonini, Rizzolatti, & Fogassi, 2008]. Many studies have supported the notion that this frontoparietal network may encode motor acts or goal-related movements [Rizzolatti & Sinigaglia, 2010].

Evidence for human mirror neurons has been examined using a variety of methodologies [Buccino et al., 2001; Cochin, Barthelemy, Roux, & Martineau, 1999; Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995; Filimon, Nelson, Hagler, & Sereno, 2007; Grèzes, Armony, Rowe, & Passingham, 2003; Kilner, Neal, Weiskopf, Friston, & Frith, 2009; Maeda, Kleiner-Fisman, & Pascual-Leone, 2002; Mukamel, Ekstrom, Kaplan, Iacoboni, & Fried, 2010; Muthukumaraswamy, Johnson, & McNair, 2004; Oosterhof, Wiggett, Diedrichsen, Tipper, & Downing, 2010; Rizzolatti & Fogassi, 2014]. Neuroimaging studies have primarily used imitation tasks to identify candidate areas for the mirror network and investigate mirror

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neuron function [Buccino et al., 2004; Grèzes et al., 2003; Iacoboni, Woods, Brass, Bekkering, Mazziotta, & Rizzolatti, 1999; Tanaka & Inui, 2002] as regions that display similar activation during observation, imitation and execution of an action are hypothesized to contain mirror neurons, although this is still highly debated [Gallese, Gernsbacher, Heyes, Hickok, & Iacoboni, 2011; Hickok, 2009]. The human frontoparietal mirror network broadly includes the dorsal and ventral PMC, inferior frontal gyrus (IFG), and the superior (SPL) and inferior parietal lobules (IPL) [Caspers, Zilles, Laird, & Eickhoff, 2010; Molenberghs, Cunnington, & Mattingley, 2012; Rizzolatti & Craighero, 2004; Rizzolatti & Sinigaglia, 2010]. Similar to monkey mirror neurons, it appears that the human mirror network encodes the goal of motor actions [Rizzolatti & Sinigaglia, 2010], and may support the ability to map the behavior observed in another onto oneself, facilitating imitation. In humans, this “goal” may be more abstract and implicit, though the network is robustly active for actions that involve objects [i.e., Koski et al., 2002]. While the frontal and parietal aspects of the mirror system have similar overlapping functions, there may be some division of labor. One school of thought proposes that the frontal aspect encodes the goal of the action, while the parietal aspect encodes the motor movement and organizes the action relative to the overall intention [Bonini, Rozzi, Serventi, Simone, Ferrari, & Fogassi, 2010; Iacoboni, 2009]. Another model ascribes kinesthetic information (e.g., grasping) to the frontal area and higher level, abstract goal representation to parietal areas [Hamilton & Grafton, 2007].

Individuals with autism spectrum disorders (ASD) have marked impairments with reciprocal social interactions [American Psychiatric Association 2013], which may be due to difficulty perceiving and recognizing the actions and intentions of others. One of the most universal findings in ASD is a deficit in imitation across the lifespan of an individual, regardless of overall cognitive functioning [Edwards, 2014; Rogers & Williams, 2006; Vivanti & Hamilton, 2014; Williams, Whiten, & Singh, 2004]. However, not all imitative abilities are equally impacted in autism. The ability to imitate goal-directed actions involving objects (transitive actions), such as pouring a teapot, is relatively spared compared to pantomimes or meaningless gestures [e.g., Rogers, Bennetto, McEvoy, & Pennington, 1996; Smith & Bryson, 2007; Stone, Ousley, & Littleford, 1997]. It is possible that the object itself provides cues as to what action should be performed; in situations where individuals with ASD are to imitate novel actions with familiar objects [Smith & Bryson, 1994] or imitate the style of an action [Hobson & Lee, 1999], performance is decreased relative to typically developing (TD) individuals. That said, it remains that imitative performance on

actions that do not involve objects (intransitive actions), including pantomimes, is often reported to be less accurate in individuals with ASD. This is particularly noted in paradigms that elicit sequential actions [e.g., Vanvuchelen, Roeyers, & De Weerd, 2007]. Imitation, however, involves two components: observation and execution, either of which may be disordered in children with ASD. With respect to the execution of actions, motor and coordination issues are frequently found in children with ASD [Ghaziuddin & Butler, 1998; Green, Baird, Barnett, Henderson, Huber, & Henderson, 2002], but it is unclear to what degree they contribute to deficits in imitation abilities [Colombi, Vivanti, & Rogers, 2011; Vanvuchelen et al., 2007; Zachor, Ilanit, & Itzhak, 2010]. As for the observation aspect, it is possible that children with ASD encode actions performed with objects differently than actions without objects. Further work is needed to distinguish the contribution of these two potential deficits.

As revealed through neuroimaging studies, the observation of others performing actions recruits a larger network of areas than the mirror system, although there is considerable overlap [for reviews, see: Caspers et al., 2010; Molenberghs et al., 2012]. This action observation network (AON) includes the lateral dorsal and ventral PMC along with the IFG, the inferior and superior parietal lobules, intraparietal cortex, along the postcentral gyrus, the superior and middle temporal gyri, and the fusiform face area/fusiform body area (although not for studies that only present hand actions) [Caspers et al., 2010]. Several studies have demonstrated that this network is engaged during the observation of actions and gestures that do not involve a physical object [Decety et al., 1997; Grèzes, Costes, & Decety, 1999; Villarreal et al., 2008], and even when participants are asked to imagine performing actions [Grafton, Arbib, Fadiga, & Rizzolatti, 1996; Lui et al., 2008]. This indicates that the visual presence of an object is not necessary to activate the network and instead may play a broader role during action observation. Components of the AON do appear to differentiate action types; however, such as whether the actions are familiar or novel [e.g., Liew, Han, & Aziz-Zadeh, 2011], meaningful or meaningless [e.g., Lui, et al., 2008; Newman-Norlund, van Schie, van Hoek, Cuijpers, & Bekkering, 2010], or directed toward or away from an object [e.g., Pelphrey, Morris, & McCarthy, 2004]. Few studies have directly investigated whether components of the network are modulated specifically by the presence or absence of an object [Héту, Mercier, Eugène, Michon, & Jackson, 2011; Koski et al., 2002; Turella, Tubaldi, Erb, Grodd, & Castiello, 2012]. Most examining “transitivity” tend to confound object presence with “meaning,” comparing actions performed with objects to meaningless actions [e.g., Agnew, Wise, & Leech,

2012; Menz, McNamara, Klemen, & Binkofski, 2009] or comparing pantomimed actions to communicative gestures [e.g., Corina, Chiu, Knapp, Greenwald, San Jose-Robertson, & Braun, 2007; Montgomery, Isenberg, & Haxby, 2007]. Evidence gleaned indirectly from studies that include object-directed actions and similarly matched nonobject-directed actions (i.e., pantomimes) hint that components of the AON may be sensitive to observing a person perform an action with or without an object. However, the specific contrast to directly compare object-directed versus nonobject-directed actions was not reported in these studies. The inferences drawn are also not consistent, with two suggesting increased activation to transitive actions in parietal [Buccino et al., 2001] or frontal [Newman-Norlund et al., 2010] components, and the other suggesting possible greater activation to intransitive actions in frontal areas [Grèzes et al., 2003].

A study first carried out in frontal area F5 of monkeys tested transitivity by presenting stimuli depicting a hand reaching to grasp and varied whether the hand was reaching for an object or not, allowing one to directly compare the effect of object presence [Umiltà et al., 2001]. Furthermore, they included a condition in which the final grasping action was occluded by a screen that moved in once the hand began the reaching motion. A portion of F5 mirror neurons responded in the occluded condition, although only when the subject had seen that an object was present at the beginning of the trial before the screen moved in to cover the object. This indicated that these neurons were particularly tuned to the presence of an object-goal even though the final grasping action was not observed. This finding served as the inspiration for the current study, and was recently examined in a group of TD adults [Turella et al., 2012]. Only the conditions in which the end of the action was occluded were reported in that study, and the results suggested highly similar patterns of activation within the AON for transitive and comparable intransitive actions. The only region of difference was along the somatosensory cortex, with transitive actions resulting in greater activation [Turella et al., 2012]. This is consistent with Koski et al. [2002] who only found modulation based on object presence during imitation of finger actions but not during the observation period. Therefore, one may predict similar patterns of activation in the AON of TD individuals when observing object-directed actions and their pantomimed counterpart.

With respect to individuals with ASD, thus far no studies have addressed the role of object presence during the observation of others' actions, hence the motivation for the current study. When examining group differences during observation of goal-directed actions, Marsh and Hamilton [2011] reported similar patterns of activation between TD and ASD individuals in areas of

the AON, although Grèzes, Wicker, Berthoz, and de Gelder [2009] found reduced activation in the IFG in their ASD sample. We are limited as to what can be said about possible group differences during the observation of actions that do or do not contain an object, as no study has presented similarly matched pantomimed actions. That said, Martineau, Andersson, Barthélémy, Cottier, and Destrieux [2010] found increased IFG activation in the ASD group during the observation of meaningless hand movements, while no group differences were found when observing photos of communicative hand gestures [Dinstein, Thomas, Humphreys, Minshew, Behrmann, & Heeger, 2010]. The neural activity of frontal components, particularly the IFG, has also been found to be correlated with social functioning in individuals with ASD, such that greater activation (i.e., more similar to TD individuals) is associated with better social skills [Bastiaansen et al., 2011; Dapretto et al., 2006]. Therefore, it seems that the frontal aspect of this network may be functioning differently in individuals with autism compared to TD individuals. However, it is not clear whether this component is involved in tracking the presence of an object while observing the actions of others.

This study was conducted to add to the limited knowledge about the capacity of the AON to differentiate between object-directed and nonobject directed actions in typical individuals and those with ASD, and extend findings to an adolescent group to assess any developmental effects. Participants passively viewed short video clips that manipulated object presence, as well as visibility, adapted from Umiltà et al. [2001], while undergoing a magnetic resonance imaging (MRI) scan. We examined neural activation in several frontal and parietal components of the action observation system that was selected based on a previous study confirming activation within an adolescent population [Shaw, Grosbras, Leonard, Pike, & Paus, 2012]. Based on the adult findings [Turella et al., 2012], we did not predict differences based on object presence in our selected areas within the TD group. As for the ASD group, we hypothesized that the frontal components may differentiate object from nonobject directed actions, and that there may be reduced activation in the IFG compared to the TD group, given previous findings [i.e., Bastiaansen et al., 2011; Dapretto et al., 2006; Grèzes et al., 2009; Martineau et al., 2010].

Methods

Participants

Seventeen children and adolescents (three females) with a clinical diagnosis of an ASD and 18 age and IQ matched TD children and adolescents (four females)

Table 1. Participant Characteristics: Mean (SD., Range)

	TD group (<i>N</i> = 18)	ASD group (<i>N</i> = 17)	
Age	14 y 3 mo (2 yr 2 mo, 9 yr 1 mo–17 yr 8 mo)	14 y 7 mo (2 yr 2 mo, 10 yr 4 mo–17 yr 7 mo)	<i>t</i> (33) = 0.55, <i>P</i> = NS
Performance IQ (PIQ)	111.93 (12.85, 90–133)	105.5 (14.14, 81–126)	<i>t</i> (27) = -1.27, <i>P</i> = NS
Autism Diagnostic Observation Schedule (ADOS), Total (Reciprocal social interaction + Communication)	NA	11.13 (2.26, 7–14)	NA
Social Communication Questionnaire (SCQ)	1.7 (2.2, 0–7)	23.73 (7.23, 9–34)	<i>t</i> (16.29) = 11.35, <i>P</i> < 0.001
Developmental Coordination Disorder Questionnaire (DCDQ'07)	69.3 (7.46, 45–75)	46.31 (13.73, 27–72)	<i>t</i> (22.53) = -5.96, <i>P</i> < 0.001

participated in the current study. Autism diagnosis was confirmed by completion of the ADOS [Lord et al., 2000] for 15 of the participants with ASD. An additional 17 participants were recruited but excluded from analyses because they could not complete the protocol (TD *N* = 1, ASD *N* = 1), did not meet study criteria (ASD *N* = 5), or had excessive motion in the scanner, greater than 3.4 mm (TD *N* = 4, ASD *N* = 6). We obtained IQ measurements on 29 participants using the WISC (Wechsler Intelligence Scale for Children, TD *N* = 1) or WASI (Wechsler Abbreviated Scale of Intelligence, ASD *N* = 15, TD *N* = 13). We used performance IQ as our primary IQ measure, although verbal IQ scores were obtained for seven participants. All participants had normal or corrected to normal vision. Participant details are found in Table 1.

Participants were primarily recruited from the University of California, Davis MIND (Medical Investigation of Neurodevelopmental Disorders) Institute's Subject Tracking System. Potential participants were screened to exclude individuals with a history of seizures, head trauma, preterm birth, or who were taking any antipsychotic medications. To be included in the study, ASD participants must not have been diagnosed with any other associated disorder (e.g., fragile X), while control participants were excluded if there was a history of developmental delay or immediate family history of ASD. Prior to inclusion, participants gave assent and a parent or guardian of each participant signed an informed consent approved by the University of California at Davis Institutional Review Board. Participants received minimal financial compensation for participating in the study.

Measures

To assess motor and coordination abilities in our sample, we administered the Developmental Coordination Disorder Questionnaire (DCDQ'07) [Wilson, Crawford, Green, Roberts, Aylott, & Kaplan, 2009]. The DCDQ'07 is a 15-item parent report questionnaire designed to screen for coordination disorders in children aged 5 to 15 years. Questions fall into three groupings: control

during movement, fine motor skills, and general coordination. Responses are made on a 7-point Likert scale, the maximum score being 75 points. A score of 58 or below suggests possible developmental coordination disorder.

Some studies have noted a correlation between neural functioning and social abilities in frontal areas of the AON, with better social skills associated with more typical neural responses [Bastiaansen, et al., 2011; Dapretto, et al., 2006]. We assessed social functioning in our group by administering the Social Communication Questionnaire (SCQ) [Rutter, Bailey, & Lord, 2003] to all participants. The SCQ is a 40-item yes/no questionnaire completed by the parents or guardians and is used to screen for possible ASD by assessing communication skills and social functioning. A conservative cut-off score of 11 or greater suggests possible ASD [Wiggins, Bakeman, Adamson, & Robins, 2007].

Experimental Design

Stimuli consisted of 5-second movies recorded from a live presentation of four conditions [adapted from

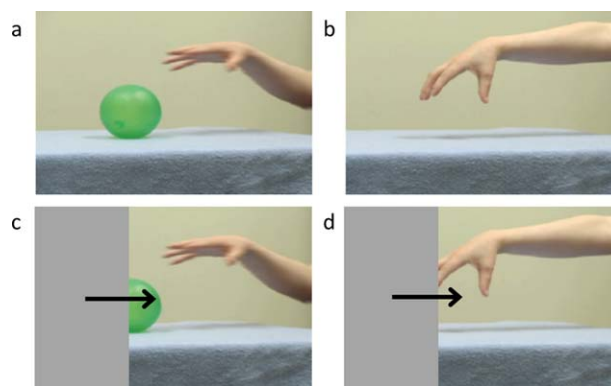


Figure 1. Example of video conditions. Still photo taken from 5-second video presentation, (a) visible transitive, (b) visible intransitive, (c) hidden transitive, and (d) hidden intransitive. In the hidden conditions, an opaque screen moved in to cover half of the display, including the object goal and final hand position.

Umiltà et al., 2001]: visible transitive (VT), visible intransitive (VI), hidden transitive (HT), and hidden intransitive (HI). In the VT condition, an object was laying on a table and a hand reached in across the display to grasp the object. There were four possible objects: ball, bead, block, and a cube. Two actors, a male and a female, were used, and videos presented the hand reaching in from either the left or the right, providing 16 unique trials. In the VI condition, the hand reached across the display, but no object was present. The hidden conditions were nearly identical to the two previous conditions, except that midway during the video presentation, an opaque screen moved in to cover the half of the visual display where the object was located, occluding the end of the hand reach and object grasp (see Fig. 1).

Each movie was presented once over two 5.36-minute runs, for a total of 64 trials, 16 per condition. Trials were separated by central fixation image of a circular rainbow, appearing for a jittered interstimulus interval ranging from 2 to 8 sec. Subjects were instructed to pay attention to the stimuli at all times.

Imaging Acquisition and Preprocessing

Data were acquired using a 3.0T Siemens Trio scanner using a standard Siemens 8-channel whole-head coil. Functional images were collected using a standard echo planar pulse sequence with TR 2,000 millisecond, TE 30 millisecond, flip angle 90 degrees, FOV 21.8 cm, 3.4 mm slice thickness, 64×64 matrix, and 32 axial slices, resulting in a voxel size of 3.4 mm^3 . A T1-weighted MPRAGE 3D MRI sequence was also acquired in the same scan session for registration (TR = 2,170 millisecond, TE = 4.86 millisecond, flip angle = 7 degrees, FOV = 256 mm, matrix = 256^2 , slice thickness = 1 mm, 192 slices). The functional task was programmed in Presentation™ and projected to a screen at the participant's feet, viewed with a head-coil mounted mirror.

Data were preprocessed and analyzed using Statistical Parametric Mapping (SPM 5; Wellcome Trust Centre for Neuroimaging, <http://www.fil.ion.ucl.ac.uk/spm>). Preprocessing of the functional data included slice-timing correction, alignment of slices (using cubic spline interpolation to the first nondiscarded scan within a scan run), coregistration of the functional data with the MNI-transformed MPRAGE structural scan using cubic spline interpolation, normalization to standard anatomical space Montreal Neurological Institute (MNI), and spatially smoothed with a 5-mm full width half maximum Gaussian kernel. All participants included in analyses moved less than 3.4 mm in x , y , or z planes. First-level analyses were performed using the general linear model in SPM5. Each trial was modeled with a standard boxcar function convolved with a canonical hemody-

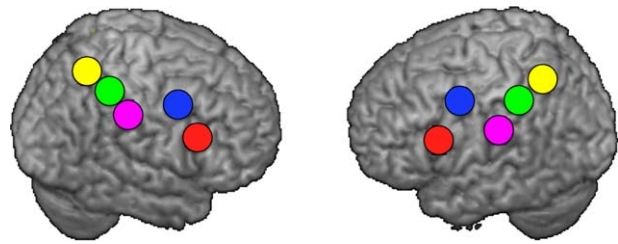


Figure 2. Location of our 10 areas of interest on rendered brain, left and right hemisphere. Center coordinates were taken from Shaw et al. [2012] and can be found in the text. Red: inferior frontal gyrus, IFG; blue: premotor cortex, PMC; magenta: supramarginal gyrus, SMG; green: inferior parietal lobule, IPL; yellow: superior parietal lobule, SPL.

amic response function over the duration of the video, and a high-pass temporal filter with a cut-off of 128 sec was applied to remove low frequency drift. Regressors were included to account for differences in global signal across scanning runs and for participant head movement.

Within-group analyses were conducted to identify areas showing similar responses across participants within each group for given contrasts. Between-group analyses were also performed to determine how the two groups differed in their response to specific contrasts of interest. Individual contrasts were entered into second-level analyses which were one- and two-sample t -tests in which participant was treated as a random effect. The four main video conditions were examined compared to baseline to observe the general pattern of activation to our stimulus conditions. To examine the effect of object presence, we compared Transitive > Intransitive regardless of visibility ((VT+HT) > (VI+HI)) as well as just in the visible condition (VT > VI). We also assessed the effect of occluding the end of the action (HT > HI; VT > HT) to see if any aspect of the AON encodes the object when the action is not visible and to compare results to Turella et al.'s [2012] findings.

Areas of interest were chosen using the frontal and parietal coordinates reported by Shaw et al. [2012] from an activation likelihood estimation (ALE) meta-analysis of regions involved in the AON, specifically when viewing hand actions. These 10 areas included the following (bilaterally): inferior frontal gyrus (IFG: $-50, 12, 22$; $50, 16, 24$), premotor cortex (PMC: $-40, -2, 45$; $42, 2, 44$), inferior parietal lobule (IPL: $-42, -41, 47$; $37, -42, 49$), supramarginal gyrus/angular gyrus (SMG/AG: $-58, -28, 34$; $50, -30, 42$), and superior parietal lobule (SPL: $-28, -56, 56$; $26, -56, 60$). Masks were created using MarsBaR [Brett, Anton, Valabregue, & Poline, 2002] by building a 5-mm sphere around the peak coordinate of each of the 10 areas (Fig. 2). All 10 locations were included in 1 mask and results were thresholded

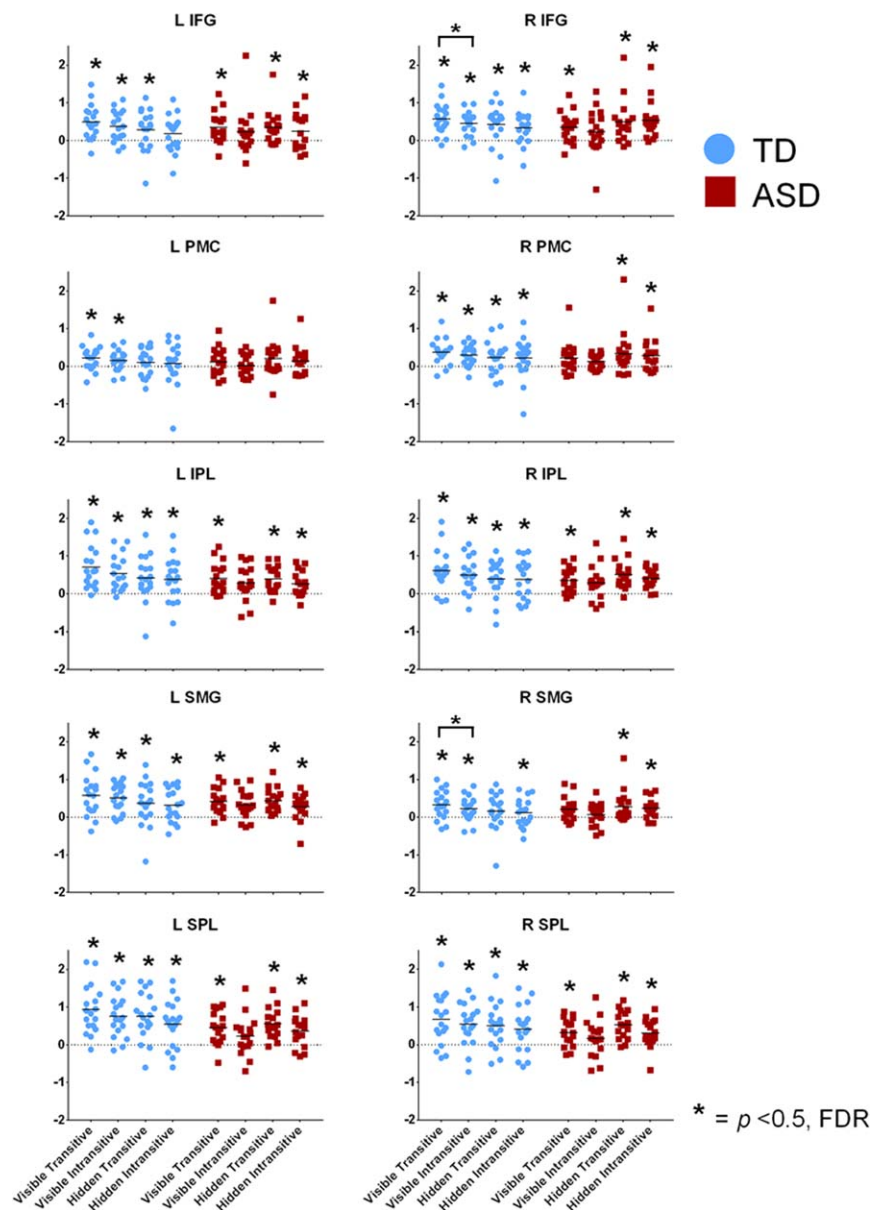


Figure 3. Individual level activation in each of the 10 areas of interest for the TD group (blue) and the autism spectrum group (red) in each of the four video conditions compared to baseline. Each point is one individual and the line indicates mean level of activation. Asterisks indicate activation significantly above threshold ($P < 0.05$, FDR).

at $P < 0.005$, $k \geq 0$, surviving FDR $P < 0.05$ correction [Genovese, Lazar, & Nichols, 2002]. Mean parameter estimates (beta) were extracted from each region using MarsBar.

Results

Behavioral Measures

Scores on the SCQ were significantly higher in the ASD group compared to the TD group (Table 1, $t(16.35) = 11.35$, $P < 0.001$), indicating impaired social functioning in the ASD group. The DCDQ'07 scores

assessing motor abilities in our sample also were significantly different between groups, with poorer motor skills reported in the ASD group (Table 1, $t(22.53) = -5.96$, $P < 0.001$).

Neural Response to Each Video Condition

To get an overview of the pattern of activation in the AON under different stimulus conditions, we assessed activation in 10 areas (bilateral: IFG, PMC, IPL, SMG, SPL) of the AON while participants viewed each of the four video conditions (VT; VI; HT; HI) compared to baseline (Table 2, Fig. 3). For TD adolescents, all areas

Table 2. Results of Video Condition Type: (1) Visible Transitive, (2) Visible Intransitive, (3) Hidden Transitive, and (4) Hidden Intransitive

		L IFG	R IFG	L PMC	R PMC	L IPL	R IPL	L SMG	R SMG	L SPL	R SPL
Visible transitive > Baseline											
TD	<i>P</i>	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.002	<0.001	<0.001
	FDR	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	0.003	<0.001	<0.001
	<i>T</i>	6.07	7.15	4.47	7.45	6.38	6.75	7.45	3.37	7.48	5.74
	<i>Z</i>	4.37	4.80	3.59	4.90	4.50	4.64	4.90	2.91	4.91	4.23
	peak	-50,8,28	44,12,26	-42,12,46	46,6,40	-42,-36,44	34,-48,46	-64,-24,38	54,-24,38	-30,-52,54	24,-62,56
ASD	<i>P</i>	<0.001	<0.001	—	—	<0.001	<0.001	<0.001	—	<0.001	<0.001
	FDR	0.002	0.005	—	—	0.003	0.002	0.002	—	0.002	0.004
	<i>T</i>	6.42	4.37	—	—	4.92	5.72	6.88	—	5.42	4.53
	<i>Z</i>	4.45	3.49	—	—	3.78	4.16	4.63	—	4.02	3.58
	peak	-50,8,24	50,12,24	—	—	-38,-36,50	40,-40,54	-56,-24,36	—	-32,-50,52	32,-54,58
Visible intransitive > Baseline											
TD	<i>P</i>	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
	FDR	<0.001	0.001	0.001	<0.001	<0.001	<0.001	<0.001	0.003	<0.001	0.001
	<i>T</i>	6.45	6.14	4.64	7.39	6.30	6.50	9.58	3.62	6.47	5.01
	<i>Z</i>	4.52	4.40	3.68	4.88	4.47	4.55	5.55	3.07	4.54	3.87
	peak	-48,6,26	50,14,24	-46,2,48	44,6,40	-38,-42,48	36,-44,46	-64,-24,38	56,-28,46	-24,-60,56	32,-60,60
ASD	<i>P</i>	—	—	—	—	—	0.001	0.001	—	0.001	—
	FDR	—	—	—	—	—	0.052	0.052	—	0.052	—
	<i>T</i>	—	—	—	—	—	4.13	4.59	—	3.64	—
	<i>Z</i>	—	—	—	—	—	3.36	3.61	—	3.06	—
	peak	—	—	—	—	—	38,-42,52	-60,-24,34	—	-32,-54,62	—
Hidden transitive > Baseline											
TD	<i>P</i>	<0.001	<0.001	—	<0.001	<0.001	<0.001	<0.001	—	<0.001	<0.001
	FDR	0.007	0.005	—	0.003	0.005	0.003	0.004	—	0.003	0.003
	<i>T</i>	3.97	4.25	—	5.74	4.54	5.86	4.80	—	6.54	6.35
	<i>Z</i>	3.29	3.46	—	4.22	3.62	4.28	3.77	—	4.56	4.48
	peak	-50,8,28	52,20,24	—	46,6,38	-38,-44,44	38,-46,50	-64,-26,38	—	-32,-54,52	32,-60,60
ASD	<i>P</i>	<0.001	<0.001	—	0.002	<0.001	<0.001	<0.001	0.002	<0.001	<0.001
	FDR	0.001	0.002	—	0.005	0.001	0.001	0.001	0.005	0.001	0.001
	<i>T</i>	5.12	4.62	—	3.42	6.01	7.31	6.59	3.40	7.28	5.87
	<i>Z</i>	3.88	3.63	—	2.92	4.29	4.78	4.52	2.90	4.77	4.23
	peak	-50,6,24	50,12,26	—	48,-2,44	-44,-36,42	42,-42,52	-58,-28,38	52,-24,38	-30,-52,52	30,-52,54
Hidden intransitive > Baseline											
TD	<i>P</i>	—	<0.001	—	0.001	<0.001	0.001	<0.001	0.002	<0.001	<0.001
	FDR	—	0.019	—	0.019	0.015	0.019	0.019	0.019	0.015	0.019
	<i>T</i>	—	4.97	—	3.55	5.68	3.72	4.29	3.34	5.60	4.72
	<i>Z</i>	—	3.85	—	3.03	4.20	3.14	3.48	2.89	4.16	3.72
	peak	—	54,16,26	—	44,4,40	-40,-44,44	40,-40,44	-56,-28,38	54,-28,36	-32,-60,60	32,-52,50
ASD	<i>P</i>	0.001	<0.001	—	0.002	<0.001	<0.001	0.001	0.002	<0.001	<0.001
	FDR	0.007	0.001	—	0.01	0.003	0.001	0.005	0.009	0.001	0.001
	<i>T</i>	3.68	5.56	—	3.40	4.37	7.28	3.93	3.42	5.09	5.77
	<i>Z</i>	3.09	4.09	—	2.90	3.50	4.77	3.24	2.92	3.87	4.18
	peak	54,8,28	52,10,28	—	42,-2,38	-40,-44,44	38,-44,50	-58,-30,38	52,-24,38	-26,-54,50	26,-62,56

Results are shown for each of the 10 regions of the action observation network, threshold $P < 0.005$, $k \geq 0$, FDR < 0.05 . Only areas of significance are reported, and the following information provided: *P*-value, FDR value, *T*-value, *Z*-score, and coordinate of peak activation in MNI coordinates.

were robustly engaged in both visible conditions, transitive (VT) and intransitive (VI). In the ASD group, there was also significant activation in all areas of the AON, except for bilateral PMC and the right SMG in the VT condition. When no object was present (VI), no areas of the AON in the ASD group survived correction, although right IPL, left SMG and left SPL neared significance ($P = 0.052$). Between group comparisons (tdVT>asdVT; asdVT>tdVT; tdVI>asdVI; asdVI>tdVI) however, revealed no significant differences between the two groups in any of the 10 regions.

In the hidden conditions, in which a screen occluded the final part of the action, the TD group still demonstrated significant activation although most of the AON, with the exception of the left PMC and right SMG, when the object was present as the goal of the action (HT). When the object was not present (HI), the TD group had significant activation in all areas except for the left IFG and PMC. For the ASD group, the pattern of activation did not differentiate between the two video conditions (HT and HI), with significant activation in all areas of the AON except for the left PMC. As was found

Table 3. Effect of Object Presence in the Visible Condition (Visible Transitive > Visible Intransitive)

Visible transitive > Visible intransitive (VT > VI)		L IFG	R IFG	L PMC	R PMC	L IPL	R IPL	L SMG	R SMG	L SPL	R SPL
TD	<i>P</i>	—	<0.001	—	—	—	—	—	<0.001	—	—
	FDR		0.044						0.02		
	<i>T</i>		4.16						5.87		
	<i>Z</i>		3.41						4.28		
	peak		50,12,28						44,-26,42		
ASD	<i>P</i>	—	—	—	—	—	—	—	—	—	—
	FWE										
	<i>T</i>										
	<i>Z</i>										
	peak										

Results are shown for each of the 10 regions of the action observation network, threshold $P < 0.005$, $k \geq 0$, FDR < 0.05. Only areas of significance are reported, and the following information provided: *P*-value, FDR value, *T*-value, *Z*-score, and coordinate of peak activation in MNI coordinates.

in the visible conditions, there were no between group differences (TD > ASD or ASD > TD) in either the transitive or intransitive hidden conditions.

Effect of Object Presence

To examine whether components of the AON were modulated by the presence or absence of an object, we compared (a) transitive versus intransitive regardless of visibility ((VT+HT)>(VI+HI)), (b) transitive versus intransitive specifically in the visible condition (VT>VI), and (c) transitive versus intransitive actions in the hidden condition (HT>HI). No areas of interest showed significant activation above threshold in either participant group when comparing transitive to intransitive conditions. Between groups comparisons (TD>ASD: [(tdVT+tdHT)-(tdVI+tdHI)] > [(asdVT+asdHT)-(asdVI+asdHI)]; ASD>TD: [(asdVT+asdHT)-(asdVI+asdHI)] > [(tdVT+tdHT)-(tdVI+tdHI)]) also revealed no significant differences. The reverse, intransitive greater than transitive, was similar, with no regions showing significant activation in either group and no between group differences. Focusing on the visible condition (VT>VI), the TD group showed significant activation (Table 3) in the right IFG ($t(1,17) = 4.16$, $P = 0.004$ FDR) and SMG ($t(1,17) = 5.87$, $P = 0.02$ FDR). Again, there was no difference between groups (TD>ASD: [tdVT-tdVI]>[asdVT-asdVI]; ASD>TD: [asdVT-asdVI]>[tdVT-tdVI]). To assess whether occluding the final grasping action modulated the AON when an object was present, we examined object-presence in the hidden condition (HT>HI). Neither the within nor between group (TD>ASD: [tdHT-tdHI]>[asdHT-asdHI]; ASD>TD: [asdHT-asdHI]>[tdHT-tdHI]) analyses revealed any significant interactions.

Effects of Social Functioning, Motor Coordination, and Age on Brain Activity

As there were no differences between the TD and ASD groups in any of the experimental conditions of interest, we did not assess whether there was a relationship

between neural activity and social or motor functioning in the ASD group. Given that there was a significant between group difference of scores on the SCQ and the DCDQ'07, yet no significant difference in neural activation, this suggests that social and motor functioning were not related to neural activation. We did assess whether there were any developmental effects in either the TD or ASD groups by examining the relationship of age, measured in months, and neural activation in our areas of interest and found no relationship in any condition.

Discussion

Overall Engagement of the AON While Viewing Hand Reaching Actions

In the current study, we examined the role of the AON in individuals with autism and in typically developing individuals when observing matched transitive and intransitive actions to assess the effect of object presence. In TD adolescents, all frontal and parietal areas examined were significantly more active when observing fully visible object-directed and nonobject directed hand actions (VT, VI) as compared to baseline. This confirms the role of these areas during action observation previously reported both in adults [Caspers et al., 2010] and recently in an adolescent sample [Shaw et al., 2012]. In the ASD group, activation in several regions did not significantly pass threshold. Most notably no AON regions survived correction in the VI condition, nor did the left PMC across all video conditions. That said, there were no significant differences between the TD group and the ASD group in any of the 10 regions in any of the video conditions.

When the end of the action was hidden, regardless of whether an object was present or not, the TD group also did not show significant activation in the left PMC. Thus, it may be that the left PMC aspect of the AON is sensitive to whether there is input from a visual stimulus. A meta-analysis examining areas involved in

action observation and imitation noted that of the frontal areas, the ventral PMC is more commonly reported in action observation tasks and the IFG is more commonly reported during imitation tasks [Caspers et al., 2010]. However, the TD group in the current study showed significant activation of bilateral IFG to all of our visual stimuli, except for the left IFG in the HI condition, even though this was a passive viewing paradigm and imitation was not required. The PMC has been shown to respond to actions in a somatotopic manner, such that observing hand, foot and mouth actions engage different areas along the PMC [Buccino et al., 2001]. These areas were similar, however, whether an object was used or the action was pantomimed. Our PMC area of interest was selected based on a meta-analysis of hand reaching action observation, similar to the stimuli in the current study. Therefore, we expected the PMC to be significantly active in all of our video conditions for the TD group. However, activation did not pass threshold when the end of the action was occluded. In individuals with ASD, activation of the left PMC never reached above threshold, regardless of whether or not the action was object-directed. In general, the PMC may not be as robustly engaged as other components of the AON when observing the actions of others [e.g., Dinstein et al., 2010].

Areas that Code for Object Presence During Object-Directed Actions in Typical Development

One goal of the present study was to identify whether any areas of the AON were modulated by object presence. We did not expect to find differences in any of our areas of interest based on object presence in our TD adolescent group based on findings from a similar study performed with adults [Turella et al., 2012] and the fact that the AON in adolescents is similar to that in adults [Shaw et al., 2012]. In the current study, we examined the effect of object presence in three different ways, one of which was similar to Turella et al. [2012], focusing on the comparison between object and no object when the final action of the reach was not visible. They concluded that activity in the AON is not modulated by object presence, as results revealed modulation only in the somatosensory cortex, which is not typically included as part of the AON. Our results corroborate their findings, as we also did not find a significant difference in any AON region for this specific contrast. However, we argue that being able to see the action being performed is important given that we found an effect of object presence in the right IFG and SMG when the action was fully visible.

Several studies have reported the engagement of the IFG when observing hand reaching and grasping actions [e.g., Grafton et al., 1996; Rizzolatti, Fadiga, Matelli, 1996]. Hamilton and Grafton [2007] propose

that frontal areas of the AON encode kinesthetic information about actions, such as grasping. Others propose that frontal areas encode the “goal” of the action, meaning the overall intention of the action, not the specific object [e.g., Iacoboni, 2009]. Our findings here are more in line with the former proposal, given that we only found a significant difference in the IFG when participants could see the entire action of reaching and grasping the object.

Some have suggested that areas within the parietal lobe may differentiate among action types, with the SMG responding to nonobject directed actions and the IPL involved in object-directed actions [Bonda, Petrides, Ostry, & Evans, 1996; Buccino et al., 2001]. From neuroimaging work, the intraparietal sulcus (IPS) in the IPL is commonly activated during the observation of reaching to grasp actions and encodes movements of the body in relation to object-goals [Hamilton & Grafton, 2006, 2007; Tunik, Rice, Hamilton, & Grafton, 2007]. Furthermore, Buccino et al. [2001] reported activity in the IPL only when observing object-directed hand actions, not pantomimed actions. However, results from a direct comparison of object and nonobject directed actions were not reported in that study. Studies that have varied the meaning of hand actions within an experiment have also demonstrated variability within the parietal lobe when the meaning of the action varied. For instance, Newman-Norlund et al. [2010] presented object-directed actions, some of which were meaningful, such as a hand pressing a stapler, or meaningless, that is, a foot pressing a stapler. While the IPL responded in both of these cases, as these were object-directed actions, the SMG differentiated the meaning of the action. In all areas examined (IPL, SMG, IFG), however, it appeared there was greater activation to object-directed actions compared to their pantomimed counterpoint. Our findings are somewhat consistent with this latter point, in that we also found greater activation when the object was present than when it was absent in the right SMG. However, from this line of reasoning we may have also expected a significant difference in IPL activation when comparing object versus nonobject actions, when in fact we found no difference.

AON in ASD

The second goal of this study was to compare the AON of individuals with ASD with TD individuals. We had hypothesized that individuals with ASD may encode actions performed with objects differently than those performed without and that this would be reflected in the AON. This was based on findings indicating poorer imitative abilities, particularly for intransitive actions, in individuals with ASD [e.g., Rogers et al., 1996; Smith & Bryson, 2007; Stone et al., 1997]. While some of the

observed difference in performance could be due to a deficit in motor abilities [Ghaziuddin & Butler, 1998; Green et al., 2002], it could also be due to a difference in encoding of the action to be imitated, with actions involving objects encoded differently than actions without objects.

In the current study, the ASD group did not demonstrate activation above threshold throughout most of the AON during the VI condition, nor did they exhibit significant activation of the PMC in any condition. Also, in the specific contrasts assessing differences between transitive and intransitive actions, we did not find any areas in the AON that were modulated by object presence in the ASD group. Furthermore, while the ASD group did have lower motor performance than the TD group, there were no significant group differences in neural activity of any regions of the AON between the ASD and TD groups in any of our comparisons. This indicates that there are not global differences or deficits of the AON in individuals with autism. Several studies examining the mirror neuron system in individuals ASD, which has significant overlap with the AON, had initially reported MN dysfunction [Iacoboni & Dapretto, 2006; Oberman & Ramachandran, 2007; Rizzolatti & Fabbri-Destro, 2010]. However, our study adds to the mounting evidence of no between group differences [Bastiaansen et al., 2011; Dinstein et al., 2010; Enticott et al., 2013; Fan, Decety, Yang, Liu, & Cheng, 2010; Marsh & Hamilton, 2011; Raymaekers, Wiersma, & Roeyers, 2009].

Similarity of the AON in Adolescents and Adults

In the current study, we did not find any association between age of participants and the level of neural activity in any of our areas of interest under any viewing condition. We did see that the TD group showed significant activation of all areas in the VT and intransitive conditions, the conditions most likely to recruit the AON, reflecting that our sample had activation similar to what has been reported in the adult literature [Caspers, et al., 2010]. A recent study conducted an ALE meta-analysis of 44 action observation experiments that passively presented various hand actions, to identify all regions that respond to hand actions [Shaw et al., 2012]. This was then used to assess developmental trajectories of action observation of angry and neutral hand actions longitudinally in an adolescent sample. That study reported age-related decreases in the right PMC and IFG, and a quadratic relationship in the left SMG/AG. Our areas of interest were selected based on these previous findings and, accordingly we used the same coordinates in our current study. However, we did not see this same relationship. It is possible this discrepancy is due to the slightly younger group used in the

Shaw et al. study, the oldest being 14 years of age compared to 17 years in this study, although the frontal and parietal lobes are continuing to undergo structural developmental changes throughout adolescence [Lenroot & Giedd, 2006]. We also examined age effects cross-sectionally while Shaw et al. [2012] employed a longitudinal approach. It seems likely that we may not have had the power to detect potential developmental changes in our sample compared to a longitudinal approach.

Summary

This study examined the capacity of the AON, in both typical development and in individuals with ASD, to differentiate between actions that included an object as a goal of the action or actions that did not have an object present. Findings from our TD adolescents support previous work indicating the engagement of this network when observing object and nonobject directed actions that are fully visible [Caspers, et al., 2010; Shaw et al., 2012]. We did see that certain components of the network, namely the right IFG and SMG, were modulated by object presence. This difference was not found in the ASD group. Furthermore, there were no significant differences between our two groups in any condition, indicating that there is no global deficit of the AON in individuals with ASD compared to TD individuals. Adolescents with ASD were consistently lacking activation of the bilateral PMC in any condition. Given that this area was also not active in the TD group when no object was present and the action was hidden, we speculate that the PMC is in general less engaged during action observation than other components of the AON and may depend on a visual input.

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