Neuroscience Research 87 (2014) 66–76

Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: www.elsevier.com/locate/neures

Attenuation of the contingency detection effect in the extrastriate body area in autism spectrum disorder

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ARTICLE INFO

Article history:
Received 17 February 2014
Received in revised form 11 June 2014
Accepted 26 June 2014
Available online 24 July 2014

Keywords:
Being imitated
Autism spectrum disorders
Extrastriate body area

ABSTRACT

Detection of the contingency between one's own behavior and consequent social events is important for normal social development, and impaired contingency detection may be a cause of autism spectrum disorder (ASD). To depict the neural underpinnings of this contingency effect, 19 adults with ASD and 22 control participants underwent functional MRI while imitating another's actions and their actions being imitated by the other. As the extrastriate body area (EBA) receives efference copies of one's own movements, we predicted that the EBA would show an atypical response during contingency detection in ASD. We manipulated two factors: the congruency of the executed and observed actions, and the order of action execution and observation. Both groups showed the congruency effect in the bilateral EBA during imitation. When action preceded observation, the left EBA of the control group showed the congruency effect, representing the response to being imitated, indicating contingency detection. The ASD group showed a reduced contingency effect in the left EBA. These results indicate that the function of the EBA in the contingency detection is altered in ASD.

1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by difficulties in social communication and social interaction, and restricted, repetitive patterns of behavior,

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http://dx.doi.org/10.1016/j.neures.2014.06.012
0168-0102/

interests or activities (DSM-5; American Psychiatric Association, 2013). The impairments in social communication and social interaction include both verbal and nonverbal behaviors. One of the impaired nonverbal behaviors is body gesture. Individuals with ASD have a fundamental impairment in gestural interaction in terms of social cause–effect representation ("I smile, therefore another person smiles"; i.e., social contingency detection, Gergely, 2001; Nadel, 2002), which is a basic element of the development of social communication skills (Mundy and Sigman, 1989). When being imitated, typically-developing children frequently changed their actions and looked at the person they were interacting with. However, most children with ASD did not display these behaviors (Nadel, 2002).

In order to account theoretically for the deficit in social contingency detection in ASD, Gergely and Watson (1999) postulated the presence of a "contingency detection module (CDM)", which functions to establish the primary representation of the bodily self as well as the later orientation toward reactive social objects. This module is innately set to preferentially explore perfect response-contingent stimulation. Around 3 months of age, the CDM is "switched" toward a preference for less-than-perfect contingent actions of others, such as reciprocal imitation (Bahrick and Watson, 1985; Gergely and Watson, 1999). In contrast, children with ASD fail to switch their preference from perfect to less-than-perfect contingency. As a result, children with ASD become less sensitive to less-than-perfect contingency situations, such as being imitated, and spend more time in repetitive motor activity in order to seek out self-related perfect contingency (Gergely, 2001). Although this hypothesis might explain the pathological origin of ASD, the neural underpinnings of the CDM are not yet understood.

Previous neuroimaging studies suggest that the occipito-temporal region is related to the detection of the congruency between one's own and another person's actions when imitating and being imitated (Decety et al., 2002; Chaminade et al., 2005). Within the occipito-temporal region, one candidate region is the extrastriate body area (EBA), which is selectively activated when viewing the human body (Downing et al., 2001) and the movements of one's own body (Astafiev et al., 2004; Orlov et al., 2010). Previous neuroimaging studies have reported that the bilateral lateral occipito-temporal region around the EBA shows a "congruency effect": it is strongly activated when one's own and another's actions were congruent (i.e., imitating and being imitated) compared to when they were different (Decety et al., 2002; Chaminade et al., 2005). These findings suggest that the EBA may be the "comparator" of the efference copy/proprioceptive information of one's own actions and the visual information received about another's actions.

If the EBA is the neural substrate of the CDM, we can predict that activity in the EBA during contingency detection between one's own actions and the resulting actions of others should be reduced in ASD. However, to our knowledge, no previous neuroimaging study has examined the effect of ASD on the neural network underlying contingency detection. In the present study, we examined brain activation of adults with ASD when they imitated hand actions and when their hand actions were imitated. Based on a previous study on being imitated (Decety et al., 2002), we manipulated the two factors: (1) the congruency between observed and executed actions (congruent/incongruent) and (2) the order of executed and observed actions (the participants executed the action BEFORE/AFTER observing the action of another person). In this task design, we were particularly interested in whether adults with ASD have abnormal congruency effect in being imitated (BEFORE conditions). If EBA corresponds to CDM, the EBA in adults with ASD should show reduced activity in BEFORE conditions.

2. Materials and methods

2.1. Participants

Nineteen adults with ASD and twenty-two typically-developing adults participated in the present study. The protocol was approved by the ethics committee of the University of Fukui (Japan), and the study was conducted in accordance with the Declaration of Helsinki. Participants were excluded if they had a history of major medical or neurological illness including epilepsy, significant head trauma, or a lifetime history of alcohol or drug dependence. Written informed consent was obtained from each participant after a complete explanation of the study. Handedness was assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). All participants' intelligence quotient (IQ) scores were obtained using the Wechsler Adult Intelligence Scale-III (WAIS-III) (Wechsler, 1997). We also measured the autism-spectrum quotient (AQ) total score (Baron-Cohen et al., 2001), which has been validated in a clinical sample (Woodbury-Smith et al., 2005).

2.1.1. High-functioning ASD group

Eighteen males and one female (mean ± standard deviation [SD] age = 24.8 ± 4.4 years) were recruited at the Department of Neuropsychiatry of the University of Fukui Hospital (Japan) and the Department of Psychiatry and Neurobiology of Kanazawa University Hospital (Japan) (Table 1). Two psychiatrists (6th and 16th authors) diagnosed the participants as ASD based on the DSM-5 classifications (American Psychiatric Association, 2013) and standardized criteria using the Diagnostic Interview for Social and Communication Disorders (DISCO) (Wing et al., 2002). These two authors were trained in the diagnosis of ASD under T. Uchiyama and are qualified to use the DISCO Japanese edition (2007). The DISCO has good psychometric properties (Nygren et al., 2009), and it contains items on early development and activities of daily life, giving the interviewer some idea of the level of functioning in several different areas, not only social functioning and communication (Wing et al., 2002). Eight of 19 patients took medications including antipsychotics (four patients), antidepressants (four patients), anxiolytics (four patients) and hypnotics (three patients) at MRI examination day. Four of 19 patients with ASD have comorbidity with obsessive compulsive disorder (two patients), anxiety disorder (one patient) and atopic dermatitis (one patient).

2.1.2. Control group

Twenty-two age-matched typically-developing volunteers (20 males and 2 females) were recruited from the local community for the CTL group (mean ± SD age = 24.2 ± 3.7 years; Table 1). They were screened to exclude individuals who had a first-degree relative with an axis I disorder based on DSM-5 criteria. The full-scale IQ (FSIQ) scores of all participants were greater than 75, and the mean FSIQ scores of each group were over 100. Although there was a significant difference in FSIQ scores between the ASD and CTL groups ($t(39) = 2.6$, $p < .05$, two-sample t-test), there was no significant difference in verbal IQ scores between the two groups ($t(39) = 1.6$, $p > .1$, two-sample t-test). In contrast, the AQ total scores and sub-scores were significantly higher in the ASD group than in the CTL group (both $p < .01$, two-sample t-test; Table 1).

2.2. MRI parameters

All functional volumes were acquired using T2*-weighted gradient-echo echo-planar imaging (EPI) sequences with a 3 Tesla MR imager (Sigma Horizon; GE Medical Systems, Milwaukee, Wisconsin). A volume consisted of 37 oblique slices, each 3.0 mm in thickness, with a 15% gap, in order to cover the entire cerebral and cerebellar cortices. The axial slices were acquired sequentially in

Table 1
Demographic data and rating scale scores.

Subjects	CTL subjects	ASD subjects	*T* value	*P*
Number	22	19		
Males	20	18		
Females	2	1		
Handedness (right/left)	21/1	18/1		
Age	24.2 ± 3.7	24.8 ± 4.4	.48	.630
WAIS-III				
Full scale IQ	114.5 ± 8.1	104.3 ± 15.5	2.60	.015*
Verbal IQ	114.8 ± 9.6	108.2 ± 15.8	1.59	.122
Performance IQ	110.5 ± 10.4	98.3 ± 17.0	2.80	.008**
AQ				
Total scores	13.3 ± 3.5	33.5 ± 7.2	11.10	<.001***
Social skill scores	1.9 ± 1.9	7.2 ± 2.5	7.59	<.001***
Attention switching scores	3.4 ± 1.7	7.6 ± 1.7	7.90	<.001***
Attention to detail scores	3.6 ± 1.7	5.8 ± 2.9	2.98	.006**
Communication scores	1.7 ± 1.3	7.0 ± 3.0	7.23	<.001***
Imagination scores	2.7 ± 1.5	5.8 ± 2.1	5.43	<.001***

ASD, autism spectrum disorder; CTL, control; WAIS-III, Wechsler Adult Intelligence Scale Third Edition; AQ, Autism Spectrum Quotient. Handedness was assessed by the Edinburgh Handedness Inventory (Oldfield, 1971). Age, WAIS-III IQ scores, and AQ scores are shown as mean ± SD. *$p < .05$, **$p < .01$, ***$p < .001$ with independent-samples *t*-tests comparing ASD and CTL participants.

ascending order. The time interval between two successive acquisitions of the same slice (repetition time [TR]) was 2500 ms, the flip angle (FA) was 80°, the echo time (TE) was 30 ms, the field of view (FOV) was 192 mm × 192 mm, the digital in-plane resolution was 64 × 64 pixels, and each pixel was 3 mm × 3 mm. For each participant, a high-resolution anatomical T1-weighted image was also acquired using three-dimensional inversion recovery-prepared fast spoiled-gradient recalled acquisition in the steady state (SPGR) sequencing (TR = 11.3 ms; TE = 5.3 ms; FA = 10°; 320 × 192 matrix; voxel dimensions = .75 mm × 1.25 mm × 1.60 mm). Head motion was minimized by placing comfortable but tight-fitting foam padding around each participant's head.

2.3. Experimental setup

Presentation 0.90 software (Neurobehavioral Systems, CA, USA) implemented on a Windows-based desktop computer (Dimension 9200, Dell Computer Co., Round Rock, TX, USA) was used for audio-visual stimuli presentation and response collection. A liquid-crystal display (LCD) projector (TH-AE900; Matsushita Electric Industrial Co. Ltd., Osaka, Japan) projected the visual stimuli, which the participants viewed via a mirror attached to the head coil of the MRI scanner. The auditory stimuli were presented via MRI-compatible headphones (Visual Stim Controller; Resonance Technology Inc., CA, USA). For each participant, the volume of the sound was adjusted to an appropriate level for task execution in the context of the MR scanner noise. A high-definition (HD) digital video camera (HDR-XR520V, Sony, Tokyo, Japan) was used to record participants' gestures during the fMRI experiment. Each participant performed one run of the finger-gesture task as pre-scan training prior to entering the fMRI scanning room. We confirmed that all of the participants could comfortably make the finger gestures before the experiment started.

2.4. Task procedures

2.4.1. EBA localizer task

We employed a conventional block design to localize the EBA (Downing et al., 2001). Each participant was asked to observe photographs of body parts, faces, outdoor scenes, and cars (viewing angle = 10.8° × 14.4°). Each run consisted of 21 blocks, each of which lasted for 15 s. The first, sixth, eleventh, sixteenth, and twenty-first blocks were fixation-only baseline conditions. Twenty photographs from one of the four object categories were presented successively in each block. Adobe Photoshop software (Adobe Systems Inc., CA, USA) was used to transform all color photographs to grayscale images, and the luminance was adjusted so that it was matched between the different categories of objects. The matrix size of the photographs was 400 × 300 pixels. Each photograph was presented for 300 ms, and the inter-stimulus interval was 450 ms. Each object category block was repeated four times. A 10-s fixation-only baseline condition was added before the first baseline block (10 s + 15 s × 21 blocks = 325 s, 130 volumes in total). In order to maintain the participants' attention on the screen, we asked them to complete a color-detection task in which a fixation cross changed color from white to red twice during the inter-stimulus intervals in each block. Participants were asked to press a button with their right hand as soon as the fixation cross changed color. Each participant completed two runs of the localizer task.

2.4.2. Finger-gesture task

During the task, participants were required to make finger gestures to indicate the numbers from 1 to 5 (Fig. 1A) in response to an instruction cue, while observing another individual's hand gesture. Participants could not see their own hands. We employed a 2 × 2 factorial design, including the congruency of executed and observed hand gestures (congruent [C]/incongruent [I]), and the order of the participant's and the other's actions (AFTER [A]/BEFORE [B]). In "C" conditions, the executed and observed gestures were the same; in "I" conditions, the executed and observed gestures were different. In "A" conditions, the participants actively selected and executed the action after the observation of another's action; and in "B" conditions, the participants executed the action before they observed the other's action (Fig. 1B).

2.4.2.1. Stimulus preparation. We recorded an actress making the five finger gestures shown in Fig. 1A with her left hand using a video camera (Handycam, HDR-SR1; Sony, Tokyo, Japan) with a matrix size of 352 × 240 pixels, a digitization rate of 30.0 frames/s (1 frame = 33.3 ms), and a viewing angle of 16.8° × 9.4°. Each movie clip started when the actress closed her fist, and ended after she made one of the five finger gestures and then closed her fist again. The duration of each movie clip was 700 ms. In order to ensure that all stimuli were 2200 ms in duration, we used Adobe-Premiere software (Adobe Systems Inc., CA, USA) to insert a static picture before and after the movie clip. Two types of stimulus were produced: video clip A, which consisted of the presentation of a static image of a fist for 1200 ms, followed by a motion picture showing a finger gesture for 700 ms, and a static image of a fist for 300 ms; and video clip B, which consisted of the presentation of a static image of a fist

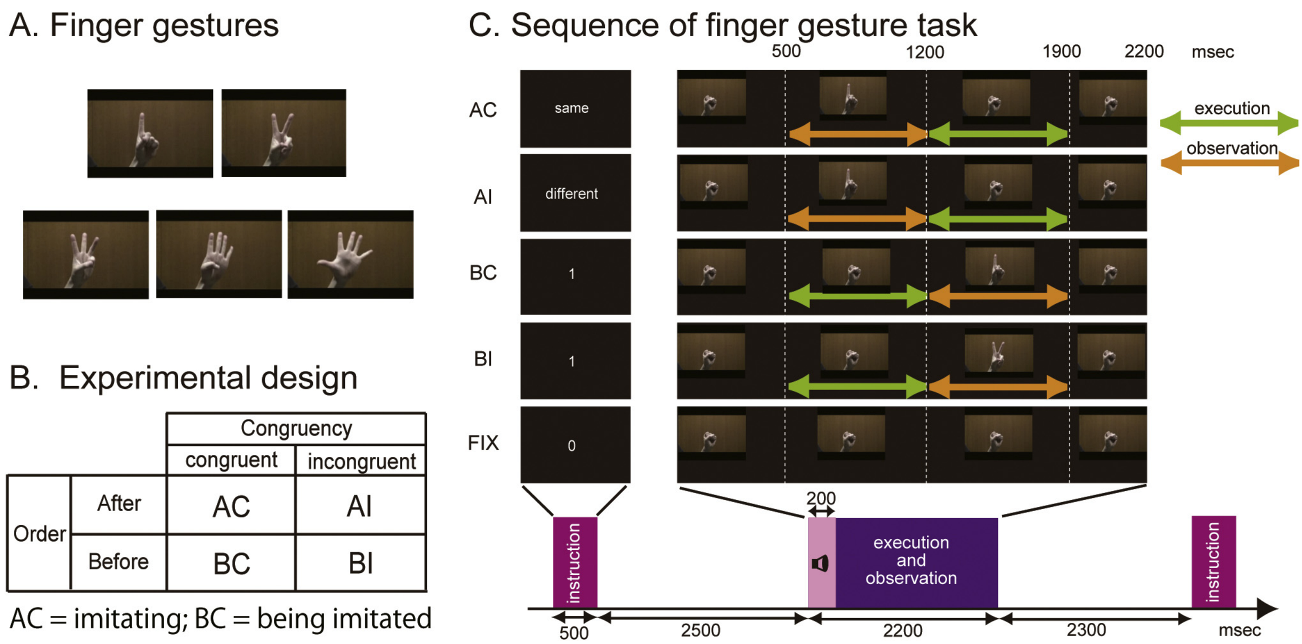

Fig. 1. Finger gesture task. (A) Finger gestures: Five finger gestures expressing five numbers were used for the task. (B) Experimental design: 2 × 2 factorial design which manipulated congruency and order. (C) Sequence of finger gesture task: Sequence of each condition (AC, AI, BC, BI and FIX). Participants executed the finger gestures around the time indicated by green arrows. Note that participants could not see their own hands.

for 500 ms, followed by a motion picture showing a finger gesture for 700 ms, and a static image of a fist for 1000 ms. The two video clips were used as stimuli for different conditions, as explained in the following sections.

2.4.2.2. Conditions. In the AFTER-congruent (AC) condition, the participants observed the actress's finger gesture and then performed the same gesture, imitating the actress's movement (Fig. 1C, first row). The instruction for the condition ("same") was visually presented for 500 ms. A 200-ms auditory cue was presented 2500 ms after the offset of the visual instruction. At the same time as the auditory cue, video clip B was presented for 2200 ms. Participants were asked to execute the same finger gesture as soon as they observed it. Although the participants were required to match the final hand gesture in the imitating condition, they did not have to conduct the observed actions with the same kinematics (i.e., trajectory, acceleration, and velocity). Before the experiment, we confirmed that each participant could execute the finger gestures within 2200 ms (the time-span of the video clip). We included a 2300-ms interval before the next trial. In total, it took 7500 ms to complete each trial.

The AFTER-incongruent (AI) condition was identical to the AC condition, except that the participant was required to make a finger gesture that differed from that presented on the screen (Fig. 1C, second row). Thus, the participant had to select and execute one of four finger gestures. We instructed the participants to choose each of the four finger gestures equally often.

In the BEFORE-congruent (BC) condition, the participants initially executed a finger gesture and then observed the same gesture, as though they were being imitated (Fig. 1C, third row). In each trial, a number from 1 to 5 was visually presented for 500 ms as the instruction cue. A 200-ms auditory cue was presented 2500 ms after the offset of the visual instructions. The participants were asked to make a finger gesture that expressed the same number as that in the instructions as soon as the auditory cue was presented. At the same time as the auditory cue, video clip A was presented for 2200 ms. There was a 2300-ms interval before the next trial.

The BEFORE-incongruent (BI) condition was identical to the BC condition, except that the observed finger gesture differed from the gesture that was executed by the participants (Fig. 1C, fourth row).

In addition to the four conditions mentioned above, we included a control condition (FIX) in our task design. This served as a control for the instruction cue, the auditory cue, and the visual input of the images of the human hand. The instruction "0" was visually presented for 500 ms (Fig. 1C, fifth row). The auditory cue was presented for the same duration and at the same time as in the other four conditions. Instead of the video clip, the participant observed a static image of a fist for 2200 ms. The participants were instructed to observe the static image of the closed fist and not to execute any movements during the FIX condition.

Each run consisted of 10 trials of each condition, with each trial lasting 7500 ms (10 trials × 5 conditions × 3 volumes = 150 volumes). The order of the trials was pseudo-randomized to optimize the efficiency of the design (Dale, 1999; Friston et al., 1999). The first trial was preceded by 10 s (4 volumes) of the baseline condition, and the last trial was followed by 12.5 s (5 volumes) of the baseline condition (159 volumes in total). Each participant completed four runs.

2.5. Data analysis

2.5.1. Behavioral data

We calculated participants' behavioral performance based on the recorded video data. We classified trials as "correct" if the participants accurately performed the instructed action. We also calculated the response time (RT) of the executed actions. For the AFTER conditions, during which the participants imitated the action, the RT was defined as the length of time between the onset of the observed action and the participant's movement. For the BEFORE conditions, during which the participants performed the action first, the RT was defined as the length of time between the onset of the auditory cue (instructing the participants to execute a finger gesture) and the onset of the participant's action.

Table 2
Predefined contrasts for the finger-gesture tasks.

Regressors	AFTER		BEFORE		Baseline task
	Congruent AC (Imitating)	Incongruent AI	Congruent BC (Being imitated)	Incongruent BI	FIX
Activity greater than baseline					
c01. AC vs. FIX	1	0	0	0	−1
c02. BC vs. FIX	0	0	1	0	−1
Congruency effect					
c03. AC vs. AI	1	−1	0	0	0
c04. BC vs. BI	0	0	1	−1	0

Note that the design matrix included other regressors of no interest: a single regressor for missed responses and incorrect trials (if any), and 6 regressors for head motion.

2.5.2. fMRI analysis

2.5.2.1. Pre-processing. The first four volumes of each run were discarded because of unsteady magnetization. The remaining 155 volumes per run for the finger-gesture task (620 volumes per participant) and 126 volumes per run for the EBA localizer task (252 volumes per participant) were used for the following analyses. The data were analyzed with Statistical Parametric Mapping software (SPM8; Wellcome Department of Imaging Neuroscience, London, UK) implemented in MATLAB (MathWorks, Natick, MA, USA). After realignment of all functional images, slice timing correction was conducted. Then, the high-resolution anatomical image was coregistered to the functional images. The coregistered anatomical image was normalized to a template T1 image that was already fitted to Montreal Neurological Institute [MNI] space (Evans et al., 1994). The parameters from this normalization process were then applied to all functional images, which were resampled to a final resolution of 2 mm × 2 mm × 2 mm. The normalized fMRI images were filtered using a Gaussian kernel of 8 mm (full-width at half-maximum) in the x, y, and z axes.

2.5.2.2. Statistical analysis.

2.5.2.2.1. EBA localizer task. In the individual analyses, we fitted a general linear model to the fMRI data from each participant (Friston et al., 1994; Worsley and Friston, 1995). Neural activity was modeled with delta functions convolved with the canonical hemodynamic response function (HRF). Each run of the localizer task included 11 regressors. Four regressors (faces, body, scenes, and cars) were modeled at the onsets of each block, and the duration was 15 s. A fifth regressor was modeled for the participant's response to the color-detection task. Motion-related artifacts were modeled as regressors of no interest using the six parameters (three displacements and three rotations) obtained by the rigid-body realignment procedure. The time series for each voxel was high-pass filtered at 1/128 Hz. Assuming a first-order autoregressive model, the serial autocorrelation was estimated from the pooled active voxels with the restricted maximum likelihood (ReML) procedure, and was used to whiten the data (Friston et al., 2002). Global signal changes were utilized to remove global confounding factors such as scanner gain. The parameter estimates for each condition in each individual were compared using linear contrasts.

Contrast images from the individual analyses were then used for the group analysis, with between-participants variance modeled as a random factor. The contrast images obtained from the individual analyses represent the normalized task-related increment of the MR signal of each participant. To define the EBA at the group level, a two-sample t-test was conducted on the contrast images of non-face body parts versus the mean of the other three categories in the ASD and CTL groups. The resulting set of voxel values for each contrast constituted the SPM$\{t\}$, which was transformed to normal distribution units [SPM$\{z\}$]. The statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons at the cluster level over the whole brain (family-wise error [FWE]), with a height threshold of $Z > 3.09$ (Friston et al., 1996). Brain regions were anatomically defined and labeled according to a probabilistic atlas (Shattuck et al., 2008).

2.5.2.2.2. Finger-gesture task. In the individual analyses, one regressor was modeled for the instructions for all conditions, which lasted for 500 ms (Fig. 1C). The trials for each condition (AC, AI, BC, BI, and FIX) were then modeled. Each regressor was modeled from the onset of the video clip for 2200 ms (Fig. 1C). The visual and motor components were similar between the regressors of the four conditions (AC, AI, BC, and BI), with the exception of the timing of the execution and observation of finger gestures between the AFTER and BEFORE conditions, which differed by 1400 ms (Fig. 1C). The five regressors were modeled only for trials in which the participant gave correct answers. If there was a missed response or an incorrect trial in a run, we added another regressor to the design matrix in order to model these trials as effects of no interest. Six regressors modeled motion artifacts in the same way as for the EBA localizer task. Therefore, each run contained 12 or 13 regressors.

In order to implement the group analysis in a random-effects model, we obtained contrast images for each predefined contrast (AC − FIX, BC − FIX, AC − AI and BC − BI; Table 2). For each predefined contrast, we performed a two-sample t-test to compare the two groups. In other words, the design matrix for the two-sample t-tests included the two regressors, each of which contained the contrast images of a predefined contrast in each group. The statistical thresholds were the same as those used for the EBA localizer task: the statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons at the cluster level over the whole brain (FWE), with a height threshold of $Z > 3.09$ (Friston et al., 1996).

We evaluated the effect of congruency (congruent vs. incongruent) in each group (Table 2). The brain regions which showed greater activation in AC than AI were assessed by the overlap of activation between the AC − AI and AC − FIX contrasts. It was necessary to include AC − FIX, because the negative response of the AC condition below the baseline task can make the interpretation of data difficult. As we conducted a two-sample t-test on the AC − AI contrast between the two groups, we evaluated the conjunction between AC − AI and AC − FIX using the inclusive-masking procedure. This approach is identical to the standard conjunction analysis (with the conjunction null, Friston et al., 2005; Nichols et al., 2005), because the whole brain was used as the search volume for the overlap of activation. Thus, this analysis should not bias the statistical inference ("double dipping", Kriegeskorte et al., 2009). Similarly, we evaluated the overlap of activation revealed by the contrasts of BC − BI and BC − FIX. Then, we compared the congruency effect between the ASD group and the CTL group.

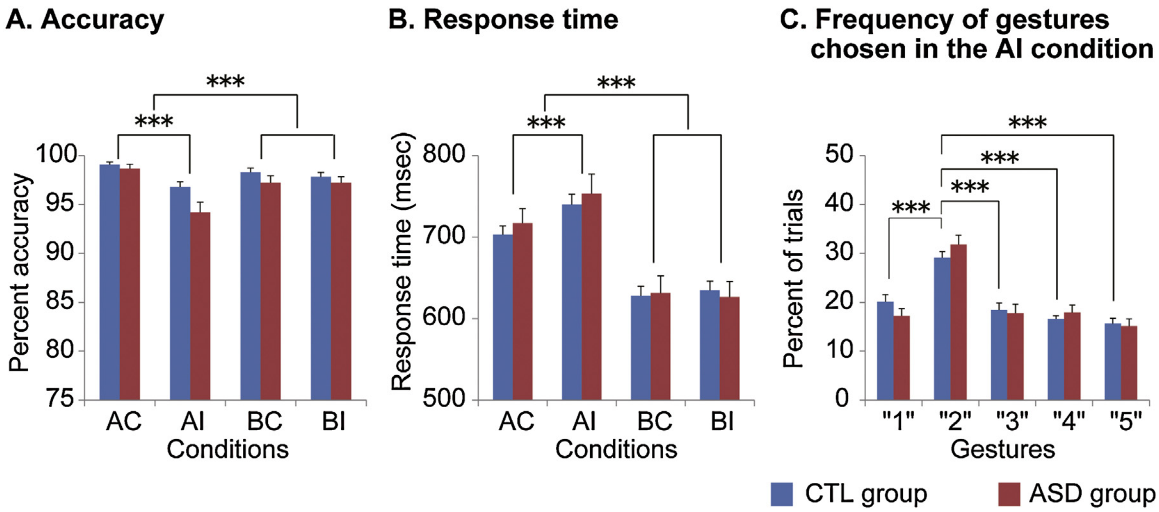

Fig. 2. Behavioral results. These data are presented as the mean ± standard error of the mean (SEM). (A) Accuracy for each condition for the CTL and ASD groups. (B) Response times for each condition for the CTL and ASD groups. (C) Frequency of gestures chosen in the AI condition. Blue: control (CTL) group. Red: ASD group. Asterisks between the AFTER and BEFORE conditions indicate a significant interaction between congruency and order; asterisks between the AC and AI conditions, and between other conditions indicate the result of post hoc pair-wise comparisons with Bonferroni correction (***p < .001).

We first evaluated these contrasts by defining the search volume as the whole brain. Subsequently, we conducted a region-of-interest (ROI) analysis by limiting the search volume to the EBA in each hemisphere.

3. Results

3.1. Behavioral results

3.1.1. Performance accuracy

The accuracy of both groups exceeded 90% in all conditions (Fig. 2A). A three-way analysis of variance (ANOVA) (2 levels of order × 2 levels of congruency × 2 groups) on the percent correct data revealed a significant interaction of order and congruency ($F(1, 39) = 19.8$, $p < .001$) and a main effect of congruency ($F(1, 39) = 16.4$, $p < .001$). In contrast, neither the main effect of group nor the interaction involving group was significant ($p > .05$ for each). Post hoc pair-wise comparisons revealed that accuracy during the AC (imitating) condition was significantly higher than during the AI condition ($p < .001$), whereas there was no significant difference between the BC and BI conditions ($p > .9$) (with Bonferroni corrections).

3.1.2. Response time (RT)

The same three-way ANOVA (order × congruency × group) on the RT data revealed a significant interaction of order and congruency ($F(1,39) = 13.9$, $p < .001$), a main effect of order ($F(1, 39) = 23.1$, $p < .001$), and a main effect of congruency ($F(1, 39) = 11.1$, $p < .01$) (Fig. 2B). We observed neither a significant main effect of group nor an interaction involving group ($p > .5$ for both). Multiple pair-wise comparisons (Bonferroni-corrected) showed that the RTs were significantly longer in the AI condition than in the AC (imitating) condition ($p < .001$), whereas there was no difference between the BC (being imitated) and BI conditions ($p > .9$).

3.1.3. The frequency of gestures executed in the AI condition

We examined the frequency of gestures executed during the AI condition (Fig. 2C). A two-way ANOVA (number × group) on the frequency data revealed a significant main effect of number ($F(4, 156) = 12.3$, $p < .001$), whereas there was no significant interaction of number and group ($F(4, 156) = 0.49$, $p > .7$). Regardless of the group, the "2" gesture was more frequently chosen than the rest of the gestures (p values < .001 with Bonferroni correction). Collectively, the behavioral performances of the CTL group and the ASD group were similar.

In sum, the behavioral performance between the two groups was comparable. In both groups, the BC and BI conditions showed similar behavioral performance, whereas the AI condition was more difficult than the AC condition.

3.2. fMRI results

3.2.1. Whole brain analyses

3.2.1.1. Congruency effect in imitating (AC – AI and AC – FIX). We examined the overlap of activation between the contrasts of AC – AI and AC – FIX to reveal the brain regions involved in congruency effects in imitation. In both groups, this analysis revealed significant activation in the bilateral lateral occipito-temporal region (Fig. 3 and Table 3). More specifically, regions of activation in the CTL group included the bilateral middle occipital gyrus, bilateral fusiform gyrus and right inferior occipital gyrus. In the ASD group, the bilateral middle occipital gyrus, bilateral middle temporal gyrus and right inferior occipital gyrus were activated. No group differences were observed in the whole brain analysis.

3.2.1.2. Congruency effect in the BEFORE conditions (BC – BI and BC – FIX). We examined the congruency effect in the BEFORE condition (BC – BI) by evaluating the overlap of activation between the contrasts of BC – BI and BC – FIX. Neither of the groups showed significant activation across the whole brain.

3.2.2. EBA region of interest (ROI) analysis

In this analysis, we examined the congruency effects in the extrastriate body area (EBA) for imitating and being imitated. The EBA was defined by the independent localizer task. As we found no significant difference between the two groups in EBA activation, the ROI was defined as the intersection of the EBAs identified in the two groups. The conjunction analysis revealed that peak activity in both hemispheres was located in the middle occipital gyrus ($x = -52$, $y = -74$, $z = 2$, Z value = 6.8, cluster size 6944 mm^3 in the left hemisphere; $x = 48$, $y = -68$, $z = 2$, Z value = 5.8, cluster size 8184 mm^3 in the right hemisphere).

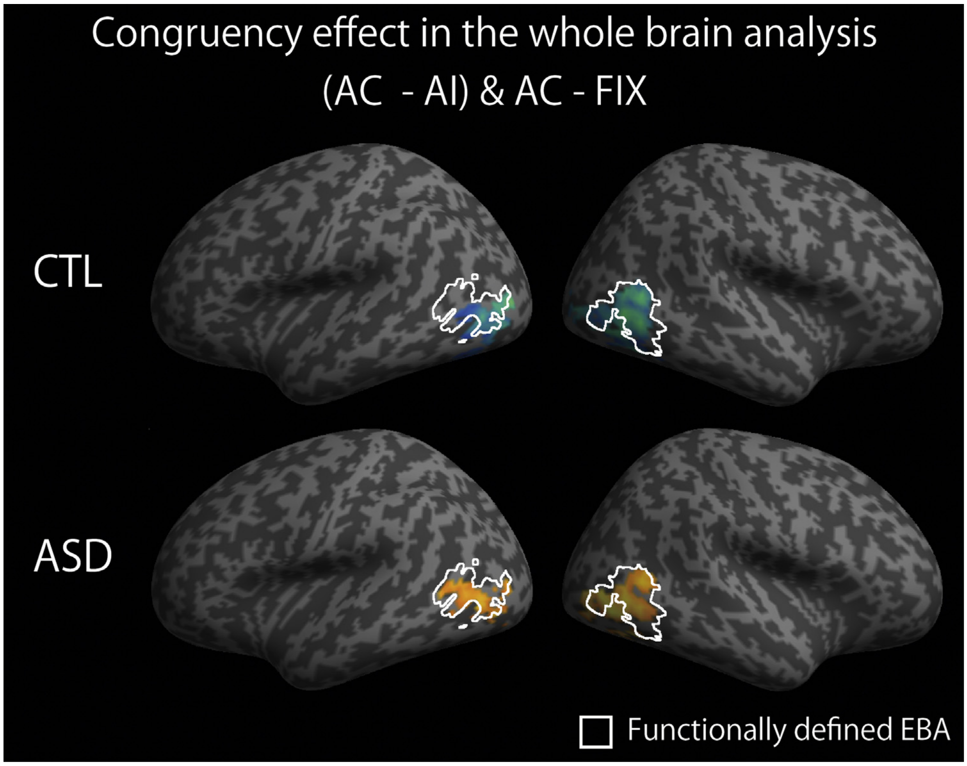

Fig. 3. Congruency effects in the whole-brain analysis. The congruency effect in the AFTER condition (AC – AI and AC – FIX) was superimposed on a surface-rendered T1-weighted MRI. There was no significant congruency effect in the BEFORE conditions in the whole brain analysis. CTL shows activation in the control group and ASD indicates activation in individuals with ASD. Regions within the white line indicate the overlap of the EBA between the CTL and ASD groups. The EBA was defined by the independent localizer task. As we found no significant difference between the EBA activation in the two groups, we defined the EBA as the intersection of the EBA between the two groups. The size of activation was thresholded at $p < 0.05$, corrected for multiple comparisons over the whole brain, with the height threshold set at $Z > 3.09$.

We confirmed a congruency effect in the AFTER conditions within the bilateral EBA for both groups. However, no significant group difference was observed (Fig. 4A and Table 4).

A congruency effect in the BEFORE conditions, revealed as the overlap of activation between BC – BI and BC – FIX, was found in the left EBA in the CTL group (Fig. 4A). In the left EBA, the ASD group showed a reduced congruency effect in the BEFORE condition (BC – BI) relative to the CTL group (Fig. 4B, Table 5). In order to examine the patterns of activity in the left EBA, we extracted the contrast estimates (i.e., activity relative to the FIX condition) at the peak coordinate of the left EBA ($x = -50$, $y = -68$, $z = -6$). A two-way ANOVA (congruency × group) on the contrast estimates in the BEFORE conditions revealed a significant interaction of congruency and group ($F(1, 39) = 12.6$, $p < .01$), and a main effect of congruency ($F(1, 39) = 5.8$, $p < .05$). The CTL group showed a significant congruency effect ($p < .001$, post hoc pair-wise comparison with Bonferroni correction), while the ASD group did not show a significant congruency effect ($p > .8$).

Table 3
Whole brain analysis: Congruency effects in AFTER conditions.

Spatial extent test	*P* values	MNI coordinate			*Z* value	Hem	Anatomical region
Cluster size (mm^3)		*x*	*y*	*z*			
AC – AI and AC – FIX							
CTL							
6752	$p < 0.001$	−36	−88	4	6.53	L	Middle occipital gyrus
		−38	−64	−18	4.48	L	Fusiform gyrus
8888	$p < 0.001$	48	−64	0	6.46	R	Middle occipital gyrus
		42	−78	−8	6.12	R	Inferior occipital gyrus
		34	−46	−22	4.41	R	Fusiform gyrus
ASD							
7104	$p < 0.001$	38	−76	−8	5.99	R	Inferior occipital gyrus
		44	−72	2	5.3	R	Middle occipital gyrus
		44	−58	6	4.51	R	Middle temporal gyrus
3920	$p < 0.01$	−38	−74	2	4.82	L	Middle occipital gyrus
		−54	−60	2	4.37	L	Middle temporal gyrus
CTL – ASD							
n.s.							
ASD – CTL							
n.s.							

The statistical threshold was $p < .05$, corrected for multiple comparisons at the cluster level over the whole brain. The statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons. Hem, hemisphere; R, right; L, left. Note that neither the CTL nor the ASD group showed significant activation in the same contrasts in the BEFORE conditions (i.e., BC – BI and BC–FIX). n.s. indicates no significant activation.

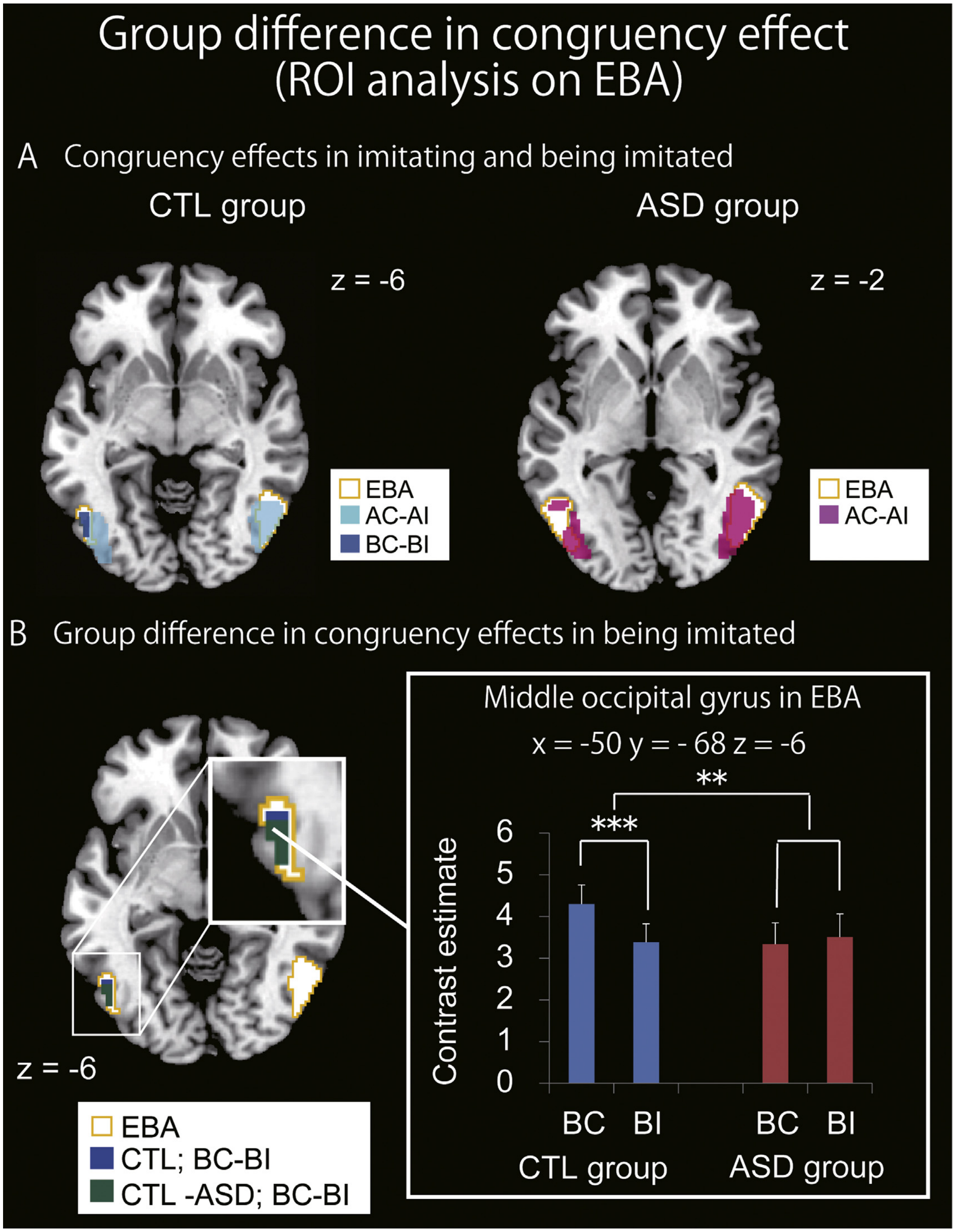

Fig. 4. Region of interest (ROI) analysis: congruency effect of AFTER (AC – AI) and BEFORE (BC – BI) conditions. White areas (surrounded by orange line) indicate the EBA, which was localized by an independent localizer task. As we found no significant difference between the two groups in EBA activation, we defined the intersection of the EBA between the two groups as the ROI. The height threshold was set at $Z > 3.09$. The threshold $p < .05$, corrected for multiple comparisons over the EBA. (A) Congruency effect in the AFTER conditions was depicted as the overlap of AC – AI and AC – FIX in the EBA. The red area indicates activation in the ASD group and the light blue area indicates activation in the control (CTL) group. (B) Group difference in the congruency effect in BEFORE conditions. The dark blue area shows the region where there was a congruency effect in BEFORE conditions in the CTL group (BC – BI and BC – FIX). The green area shows the region where there was a greater congruency effect in the CTL group than the ASD group. The inset graph shows activity relative to the FIX condition (i.e., the contrast estimates). Asterisks between the CTL and ASD groups indicate a significant interaction between congruency in the BEFORE condition and group (** $p < 01$); the asterisks between BC and BI show the result of the post hoc pair-wise comparison with Bonferroni correction (***$p < .001$).

As we included a small number of the female participants, we examined if the same result can be obtained without the female participants. The analyses on the contrast estimates of male participants showed the same results: a significant interaction of two-way ANOVA ($F(1, 36) = 11.6$, $p < .01$) and a significant congruency effect only in CTL group ($p < .01$).

3.2.3. *Does the difference in IQ explain the attenuated congruency effect in being imitated?*

The IQ differed between CTL and ASD groups (Table 1). Does this difference explain the reduced congruency effect in ASD during the BEFORE condition (BC – BI)? In order to address this point, we conducted the same analyses as Section 3.2.2 by including the FSIQ

Table 4
ROI analysis on EBA: congruency effect between AC (imitating) and AI conditions.

Spatial extent test	*P* values	MNI coordinate			*Z* value	Hem	Anatomical region
Cluster size (mm^3)		*x*	*y*	*z*			
AC – AI and AC – FIX							
CTL							
2928	$p < 0.001$	−38	−84	4	5.97	L	Middle occipital gyrus
5480	$p < 0.001$	48	−64	0	6.46	R	Middle occipital gyrus
ASD							
3048	$p < 0.001$	−38	−76	2	4.66	L	Middle occipital gyrus
		−54	−60	2	4.37	L	Middle temporal gyrus
4424	$p < 0.001$	44	−72	2	5.3	R	Middle occipital gyrus
		46	−62	−8	4.78	R	Inferior temporal gyrus
CTL – ASD							
n.s.							
ASD – CTL							
n.s.							

The statistical threshold was $p < .05$, corrected for multiple comparisons at the cluster level over the EBA in each hemisphere (6944 mm^3 for the left hemisphere and 8184 mm^3 for the right hemisphere). The statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons. Hem, hemisphere; R, right; L, left. n.s. indicates no significant activation.

Table 5
EBA ROI analysis: congruency effect between BC (being imitated) and BI conditions.

Spatial extent test	*P* values	MNI coordinate			*Z* value	Hem	Anatomical region
Cluster size (mm^3)		*x*	*y*	*z*			
BC – BI and BC – FIX							
CTL							
192	$p < 0.05$	−50	−68	−6	3.79	L	Middle occipital gyrus
ASD							
n.s.							
CTL – ASD							
96	$p < 0.05$	−50	−68	−6	3.28	L	Middle occipital gyrus

The statistical threshold was $p < .05$, corrected for multiple comparisons at the cluster level over the EBA in each hemisphere (6944 mm^3 for the left hemisphere and 8184 mm^3 for the right hemisphere). The statistical threshold for the spatial extent test on the clusters was set at $p < .05$ and corrected for multiple comparisons. Hem, hemisphere; R, right; L, left. n.s. indicates no significant activation.

score for each participant as a covariate of no interest. Nevertheless, we replicated the same patterns of activation. More specifically, the contrast of AC – AI revealed significant activation in the bilateral EBA in both groups, whereas the congruency effect of (BC – BI) was significantly lower in ASD than in CTL in the left EBA (Table S1 and S2). Collectively, it is unlikely that the reduced congruency effect was merely explained by the difference in FSIQ.

4. Discussion

4.1. Behavior

During the AI condition, both ASD and CTL groups showed longer response times (RTs) compared with the AC condition. There was no significant difference between the two groups. As compared to the AC condition, the AI condition involves the two components: inhibiting automatic imitation of observed gestures and selecting one of the other actions. Comparable response time in AI condition (relative to AC condition) indicates that these two components are processed similarly between CTL and ASD groups. This is consistent with previous behavioral studies that suggest intact automatic imitation in ASD individuals (Bird et al., 2007).

4.2. Congruency effect in the bilateral EBA in typically developing participants

In the control group, the EBA was more strongly activated when the participant's own actions were congruent with another person's actions than when they were different (Fig. 4A left). This observation confirms previous reports (Decety et al., 2002; Chaminade et al., 2005) suggesting that the EBA may be involved in congruency detection during gestural interaction. Recently, it has been debated whether the functions of the EBA can be extended to social cognition, or if they are limited to the efficient processing of body parts (Downing and Peelen, 2011). In particular, Downing and his colleagues argue that activation in the EBA in the context of social cognition may be related to differences in the degree of attention to the observed actions. However, in the present study, the task requirements were identical for the congruent and incongruent conditions. For instance, there was no need for increased attention to the visually-observed actions in the BI condition compared to the BC condition. In the imitation task, the participant was instructed to match the final hand gesture in the imitating condition, without needing to attend to the kinematics of the movement. Therefore, it is unlikely that activation in the EBA is merely due to the difference in attentional demands between the conditions.

As we demonstrated (Fig. 4), the EBA extends over different gyri within the lateral occipito-temporal cortex (Spiridon et al., 2006; Downing et al., 2007; Weiner and Grill-Spector, 2011). It is known that regions around the most body-selective point in the EBA are sensitive to executed actions, suggesting that these regions receive an efference copy of the self-action (Astafiev et al., 2004; Peelen and Downing, 2005; Orlov et al., 2010). Oosterhof et al. (2010) used multi-voxel pattern analysis to demonstrate that the lateral occipito-temporal cortex encodes the same type of observed and executed actions. Therefore, the visual input of another's body parts and the efference copy of the self-action may interact with each other in the EBA to detect congruency with the visually-observed action of another person. The EBA may act as a "comparator" of the self and other's actions.

4.3. Attenuated contingency effect in the left EBA in ASD

In individuals with ASD, there was a reduced congruency effect in the left EBA between the participant's own and another's actions when the self-action was imitated. Previous neuroimaging studies mainly focused on the neural network involved in imitating of ASD (Dapretto et al., 2006; Williams et al., 2006), whereas no previous study on ASD has examined the congruency effect in being imitated (i.e., the contingency effect). Our results provide novel evidence that the contingency effect is attenuated in EBA of the ASD group. This result supports the hypothesis that EBA corresponds to the CDM.

It is unlikely that the reduced effect can be explained merely by the possibility that the ASD group paid less attention to the observed actions than the control group; even if the individuals with ASD paid less attention to the observed action, this factor should be subtracted out in comparing BC (being imitated) with BI (observing a different action after observing an action). Rather, the results indicate that the attenuated contingency effect may be related to atypical response to being imitated in the ASD population (Gergely, 2001; Nadel, 2002).

4.4. Possible neural mechanisms underlying dysfunction in ASD during gestural interactions

Unlike being imitated, the congruency effect during imitating was comparable between ASD and CTL in the EBA (Fig. 4). This result indicates that the attenuation of congruency effect in EBA is not simply extended from being imitated to imitating. In the following section, we propose that the internal model, represented in the EBA and other cortical regions, may underlie the difference between imitating and being imitated.

It has been suggested that the fronto-parietal network and the middle temporal gyrus (MTG) support the forward and inverse models that work together to allow interpersonal interaction as well as motor control (Keysers and Perrett, 2004; Gazzola and Keysers, 2009). The fronto-parietal network involves the premotor cortices (PMC) and inferior parietal lobule (IPL). A recent neuroimaging study demonstrated that patterns of activation in the fronto-parietal network between adults with ASD and typically-developed adults are highly similar during action observation and execution (Dinstein et al., 2007). The fronto-parietal network is closely linked to the MTG, which includes the posterior portion of the STS (pSTS) (Schippers and Keysers, 2011) and the EBA (Astafiev et al., 2004; Jeannerod, 2004; David et al., 2007; Orlov et al., 2010).

The visuo-motor transformation corresponds to the inverse internal model which converts the visual representation into a motor plan. The forward internal model represents the conversion of the motor plan into the sensory outcomes of the action. In an fMRI study with tasks that required no intentional imitation or action understanding, Sasaki et al. (2012) showed that the direct effective connectivity from the MTG to the PMC formed an inverse internal model, and that the reverse connectivity formed a forward internal model.

The present results indicate that the forward model is related to the congruency effect in the EBA, where the visual input of another's movement is compared with the efference copy of the self-action. When being imitated, the response of the EBA should reflect the forward model: the efference copy that is "issued" as a result of the self-action, without reference to another's action. The contingency effect, represented by the congruency effect when being imitated, should therefore reflect this forward model. The contingency effect in the left EBA was attenuated in the ASD group. This was not caused by an attenuated response of the EBA to the other person's action, because ASD and CTL participants revealed a similar congruency effect in the EBA when they voluntarily imitated another's action. Therefore, this attenuated contingency effect may be related to a less-automatic generation of the forward model in the ASD group.

4.5. Issues affecting data interpretation

There are three possible interpretational issues related to the task design. First, the AI condition (executing an action different from the observed action) was different from the other conditions in that the participant needed to select an action that differed from the observed action. As shown in Fig. 2, this action selection requirement made the AI condition more difficult than the AC condition. These additional components may reduce brain activation in the congruency detection component during imitation, revealed by the contrast of AC – AI. Nevertheless, both groups showed common activation in the EBA. Therefore, action selection (and its related task difficulty) in the AI condition should not alter the interpretation of the data in the present study. Second, we designed the task so that we could dissociate the cognitive components pertaining to imitating and being imitated. For this purpose, it was inevitable that we had to include instructions to the participant in the BEFORE conditions. However, it is unlikely that this factor produced the group difference in the left EBA, because the instruction-related activation would have been subtracted out by comparing the BC (being imitated) and BI (not being imitated) conditions. Third, the timing of observation and execution was different between BEFORE and AFTER conditions. However, we designed the task so that action observation and execution occurred within a short time period (1.4 s). Therefore, it is unlikely that the difference in the onset of the motor and visual components produced activation in the comparison between the BC and AC conditions.

4.6. Future direction

Teaching imitating other's behavior is frequently used in behavioral intervention of children with ASD (e.g., Vismara and Rogers, 2010), whereas little attention is paid to the recognition of being imitated. Several behavioral studies also suggest that the training of recognizing being imitated can alleviate such symptoms by promoting social behaviors (Escalona et al., 2002; Field et al., 2001). Thus, in the future, it is worth investigating whether early intervention involving reciprocal interaction of gestures may recover the reduced contingency effect in the left EBA of ASD.

5. Conclusion

The present study demonstrated that ASD participants showed a reduced congruency effect in the left EBA when being imitated, thus revealing a decreased contingency effect. We propose that this reduced contingency effect in ASD may be related to an attenuated automatic transition from the motor to perceptual representations when being imitated. This attenuated contingency effect may explain why individuals with ASD have difficulty with the recognition of being imitated during gestural interaction.

Acknowledgments

This work was partly supported by Grants-in-Aid for Scientific Research from the Japan Society for the Promotion of Science to N. Sadato (21220005), T. Munesue (21591509), H. Kosaka (21791120) and R. Kitada (25871059). Part of this study was the result of the project "Development of biomarker candidates for social behavior" and "Integrated research on neuropsychiatric disorders" carried out under the Strategic Research Program for Brain Sciences by the Ministry of Education, Culture, Sports, Science, and Technology of Japan (MEXT). H. Kosaka was also supported by the Takeda

Science Foundation, the Japan Research Foundation for Clinical Pharmacology, and the SENSHIN Medical Research Foundation. M.J. Hayashi was supported by Brain Research at Aalto University and University of Helsinki consortium postdoctoral program.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neures.2014.06.012.

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