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Perception of biological motion in autism spectrum disorders

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Abstract

In individuals with autism or autism-spectrum-disorder (ASD), conflicting results have been reported regarding the processing of biological motion tasks. As biological motion perception and recognition might be related to impaired imitation, gross motor skills and autism specific psychopathology in individuals with ASD, we performed a functional MRI study on biological motion perception in a sample of 15 adolescent and young adult individuals with ASD and typically developing, age, sex and IQ matched controls. Neuronal activation during biological motion perception was compared between groups, and correlation patterns of imitation, gross motor and behavioral measures with neuronal activation were explored. Differences in local gray matter volume between groups as well as correlation patterns of psychopathological measures with gray matter volume were additionally compared. On the behavioral level, recognition of biological motion was assessed by a reaction time (RT) task. Groups differed strongly with regard to neuronal activation and RT, and differential correlation patterns with behavioral as well as with imitation and gross motor abilities were elicited across and within groups. However, contrasting with the initial hypothesis, additional differences between groups were observed during perception and recognition of spatially moving point lights in general irrespective of biological motion. Results either point towards difficulties in higher-order motion perception or in the integration of complex motion information in the association cortex. This interpretation is supported by differences in gray matter volume as well as correlation with repetitive behavior bilaterally in the parietal cortex and the right medial temporal cortex. The specific correlation of neuronal activation during biological motion perception with hand-finger imitation, dynamic balance and diadochokinesis abilities emphasizes the possible relevance of difficulties in biological motion perception or impaired self-other matching for action imitation and gross motor difficulties in individuals with ASD.

Keywords: Autism spectrum disorder; Biological motion; Complex motion; Imitation; fMRI

1. Introduction

Autism spectrum disorders (ASD) are characterized by three core symptoms: difficulties in social interaction and reciprocal communication, and restrictive, stereotyped and repetitive behaviors and interests (American Psychiatric Association, 1994; World Health Organisation, 1992). In addition to these three core behavioral aspects, individuals with ASD show a wide range of neuropsychological and cognitive abilities that differ from typically developing individuals (Happe, 2003). One neuropsychological study in 8–10 years old children reported impaired biological motion recognition in children with autism employing point light displays tracking human movements at the joints of the limbs, so called Johansson-type stimuli (Blake, Turner, Smoski, Pozdol, & Stone, 2003). In contrast, a previous study in 14 years old adolescents with autism did not find differences between groups for a similar task portraying human activity by point-light animation sequences (Moore, Hobson, & Lee, 1997). However, during short, but not long exposure durations, control individuals performed consistently better than adolescents with autism in that study as well. A third study aimed to compare recognition of emotional and non-emotional biological motion in adolescents and adults with ASD and found a comparable performance for stimuli involving action and subjective states, however, point-light displays showing emotional states were less well recognized (Hubert et al., 2007).

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The three studies, however, differed in the way they operationalized the correct answers. In the Moore et al. (1997) and the Hubert et al. (2007) studies, individuals had to name the action or the emotion, whereas in the Blake et al. (2003) study, individuals simply had to choose between having seen a person or no person. In none of these studies individuals with ASD showed a complete lack of biological motion recognition, but an increased error rate or a decreased rate of correct answers. Furthermore, short exposure duration resulted in reduced performance of individuals with autism (Moore et al., 1997). It therefore might be possible that the threshold to perceive biological motion might be increased in individuals with ASD, as has been reported for tasks assessing motion coherence in individuals with ASD (Milne et al., 2002; Spencer et al., 2000). This should result in an increased reaction time to recognize moving persons from point light displays.

With regard to ASD the question of impaired perception of biological motion is interesting due to the following aspects: (1) early during development, biological motion can be differentiated from non-biological motion, as has been shown in three months old children for Johannson-type stimuli (Fox & McDaniel, 1982). ASD are predominately genetically determined developmental disorders (Freitag, 2007) showing a suspected differential development in the first year of life and obvious impairments around age 20 months regarding imitation (Williams, Whiten, & Singh, 2004) and joint attention abilities (Charman et al., 1997). It might be possible that difficulties in biological motion perception might underlie these impairments in imitation and joint attention skills, which are skills, that are strongly linked to later social and language development (Toth, Munson, Meltzoff, & Dawson, 2006). (2) Perception of biological motion, like the movement of eye gaze, body parts or the entire body, conveys social meaning and therefore is crucial to social cognition and social interaction (Clarke, Bradshaw, Field, Hampson, & Rose, 2005; Grossmann & Johnson, 2007). Interestingly, in the study by Blake et al. (2003), a positive correlation between autism severity and degree of impaired biological motion perception was observed, emphasizing the possible relevance of this paradigm in the development of ASD.

Two brain imaging studies, one functional MRI and one PET study, assessed other aspects of visual perception which are remotely related to biological motion perception: eye gaze processing (Pelphrey, Morris, & McCarthy, 2005) and processing of animated shapes (Castelli, Frith, Happe, & Frith, 2002). Both studies employed tasks which focused on the neural processing of social intentions implicated by these tasks. In the eye gaze processing task, congruent and incongruent gaze shifts were compared to elicit differences in activation due to unexpected gaze shifts inconsistent with the subject's expectation regarding the intention of the person making the eye movement. Despite correctly identifying eye movements, individuals with ASD showed a missing increase in activity in the right superior temporal sulcus (STS) during the incongruent gaze shift compared to the congruent gaze shift. Again, a negative correlation of the ADI-R social interaction score with the degree of signal change in incongruent gaze shifts was reported. The second study assessed activation during observation of animated sequences with triangles moving as interacting characters, suggesting that one triangle anticipates or manipulates the mental states of the other (i.e. a theory of mind (ToM) task), compared to random purposeless movements of the triangles. Groups differed with regard to behavioral as well as brain activation (PET) data. Bilateral basal temporal areas, the temporo-parietal junction and prefrontal areas showed less increase in cerebral blood flow during the ToM task in the ASD group.

These studies, as expected from other fMRI studies on mentalizing (Baron-Cohen et al., 1999), reported differences in brain activity between individuals with ASD and typically developing controls for biological motion tasks implying social intentions. However, it is not known, if perception of biological motion not explicitly designed to imply social intention or emotion will also elicit differential brain activity in individuals with ASD.

In this study, we therefore aimed to assess the ability to recognize and perceive biological motion of single male and female characters moving unintentionally and not expressing any emotional states (Vaina, Solomon, Chowdhury, Sinha, & Belliveau, 2001). We performed an fMRI study to compare neural activation during biological motion perception and a computer based reaction time task in 15 individuals with ASD and 15 age, IQ and sex matched controls. We hypothesized that neuronal activation during perception of biological motion would be decreased and reaction time to correctly recognize biological motion would be increased in individuals with ASD. In addition, we explored the correlation of imitation and adaptive gross motor abilities as well as autism specific psychopathological measures with neuronal activation and task performance in both comparison groups. These measures previously have been shown to differ strongly between individuals with ASD and typically developing controls (Freitag, Kleser, & Von Gontard, 2006; Freitag, Kleser, Schneider, & Von Gontard, 2007). Additionally, structural MRI data were compared to elicit possible functionally relevant local differences in gray matter volume as well as correlation with autism specific psychopathology.

2. Methods

2.1. Sample

Thirteen male and two female subjects with autism spectrum disorder (ASD; mean age 17.5, S.D. 3.5 years) and 13 male and two female control individuals, group matched with ASD subjects for age, sex and IQ (mean age 18.6, S.D. 1.2 years) were included in the study. After complete study description, informed consent was obtained from all participants or their parents if subjects were younger than 18 years. The study design was approved by the local ethics committee.

Inclusion criteria for the ASD group were as follows: The autism diagnostic interview-revised (ADI-R) (Lord, Rutter, & Le Couteur, 1994; Poustka et al., 1996) was performed with the parents. The ADI-R algorithm criteria for autism were met for the communication, social interaction and stereotyped interests/repetitive behavior domains by 13 of the 15 ASD patients. Parents of two subjects were not available for diagnosis. Mean ADI-R algorithm scores at age 4–5 years old, which are critical for diagnosis, were as follows: social interaction 26.0 (S.D. 6.6); communication 20.4 (S.D. 5.1), repetitive behavior 7.0 (S.D. 2.4). In direct observation by the autism diagnostic observation schedule-generic (ADOS-G) (Bolte & Poustka, 2004; Lord et al., 2000), all ASD subjects met the communication and social interaction domain criteria for autism or autism spectrum disorder. All participants had previously received a

clinical diagnosis of autism or Asperger's syndrome according to DSM-IV criteria (American Psychiatric Association, 1994). Additionally, a thorough review of medical records was performed. Full scale IQ was 70 or above.

Exclusion criteria for ASD and control subjects were: history of cerebral palsy; congenital anomaly of the central nervous system; history of schizophrenia; known genetic syndrome; history of focal epilepsy; tuberous sclerosis, neurofibromatosis or any other neurological or psychiatric disorder. Data on medical history were obtained by parents and/or the participating individual.

Subjects filled in the youth or young adult self report (Achenbach, 1991, 1997), a screening instrument to assess self rated psychopathology in eight domains (socially withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, delinquent behavior, aggressive behavior). Intelligence was measured by the German version of the Wechsler intelligence scale-version III, with norms from 2000, or the Wechsler adult intelligence scale-revised, with norms from 1991. Handedness was determined by the Edinburgh handedness inventory (Oldfield, 1971). All participants had corrected or normal vision and none received psychopharmacotherapy.

2.2. fMRI Stimuli

At the start of the trial, a fixation cross was shown, which represented the baseline condition. Moving point-light displays of 15 male and 15 female walkers without contours as well as 30 scrambled stimulus control conditions were shown each for 1.5 s in random order, separated by a variable (8–20 s) inter-trial interval during which the fixation cross (i. e. baseline condition) was shown.

The biological motion task consisted of moving point-light displays of male and female walkers without contours, tracking movements at the joints of the limbs. It was created using Labview version 6.0 (http://www.ni.com/labview). The presented movements portrayed persons walking in different speeds, seen from different angles. Stimuli were based on motion capture data as previously described (Troje, 2002). Walkers marked by 15 white dots at the joints against a black background were orthographically projected from viewpoints randomly sampled between −90° (left profile view) and 90° (right profile view). The size of the walkers subtended 5° of visual angle horizontally and 9° vertically. Each dot subtended 0.1°.

The scrambled (i.e. control) condition was derived from these walkers. First, the position of the 15 individual trajectories was permutated. Leaving the shape of each trajectory intact, the velocity profile along the trajectory was replaced with a constant velocity, derived by averaging the velocity over one cycle. This manipulation retains the overall frequency individually for each dot, but masks the acceleration profile indicative for biological motion.

Stimuli were presented by color video projection onto a transparent screen that could be viewed over a mirror system (Siemens AG) mounted on the head coil. Subjects were asked to assemble each point light animation to a figure for later report. Both, ASD subjects and control individuals reported the nature of the task correctly.

2.3. MRI Data acquisition

A 1.5 Tesla MRI scanner with a standard head coil (Siemens Sonata, Erlangen, Germany) was used to acquire 36 slices of T2* weighted transverse echo-planar images (TR 3.05 s, TE 60 ms) with blood oxygenation level-dependent (BOLD) contrasts for functional analysis. Structural MRI data were acquired using a T1-weighted, sagittally planned MPRAGE (magnetization-prepared rapid-acquired gradient echoes) sequence with a spatial resolution of 1 mm × 1 mm × 1 mm (TR: 1900 ms, TE 3.93 ms, TI 1100 ms, FA 15°). Anatomical abnormalities were ruled out by visual inspection of structural T1 and T2 weighted images by a trained neuroradiologist.

2.4. Statistical analysis of functional MRI-data and stimuli contrasts

fMRI Data analysis was carried out at the Department of Neuroradiology, Homburg, Germany, using SPM99 (www.fil.ion.ucl.ac.uk/spm) implemented in MatLab (Mathworks Inc., Sherborn, MA). The first four fMRI volumes were discarded to avoid transient magnetic saturation effects and to allow for the hemodynamic response function to reach a steady state. Images were sinc interpolated over time to correct for phase during data acquisition (slice-time correction), realigned to the first volume by rigid body transformation (motion correction), and normalized into standard stereotactic space with a resolution of 2 mm × 2 mm × 2 mm using the Montreal Neurological Institute (MNI) template. The normalized images were spatially smoothed by a Gaussian kernel of 8 mm × 8 mm × 8 mm. Subjects were discarded from further analysis if head movements exceeded 3 mm or 3°. The stimuli were assessed by event-related design modeled as half sine events of 3 s or 1.5 s duration, respectively, convolved with a synthetic hemodynamic response function and its first temporal deviation in the context of the general linear model implemented in SPM99. Head motion related degrees of freedom (three translations, three rotations) were added as regressors to reduce residual movement-related effects for each session (Lund, Norgaard, Rostrup, Rowe, & Paulson, 2005).

T maps of activations were computed by subject for each condition against the baseline condition. Group-average maps were computed for both conditions using the individual subject's t maps as the basis of random effects analysis. For each voxel, each group of t values was tested for a difference from zero. Differences between groups were assessed by a random effects 2 (group) × 2 (condition) ANCOVA, adjusted for full scale IQ. Height threshold for voxel level was set at $T = 3.43$ ($p < 0.001$); extend threshold was defined at $k = 5$ voxels (voxel size 2.0 mm × 2.0 mm × 2.0 mm). Correlation analyses were calculated by linear regression implemented in SPM with the activation t values as the dependent and the explanatory variable of interest as the independent variable with adjustment for IQ differences. In addition, t values at the respective correlated region of interest (ROI; see below) were extracted from SPM and Spearman correlations with the respective variable of interest were calculated.

2.5. Analysis of structural MRI-data

T1 weighted images were transferred to the IZKF research group at the University of Munster, Germany, for structural analysis which was carried out on the case-control sample (15 ASD versus 15 controls). Structural MRI data were processed using the optimized voxel-based morphometry method described by Good et al. (2001). Image analysis was performed using the SPM2 software package (www.fil.ion.ucl.ac.uk/spm).

2.5.1. Image preprocessing

To account for systematic differences in brain size between adolescents and the adult brains included in the MNI templates, a customized whole brain T1 template and prior gray, white and cerebrospinal fluid (CSF) images were created using T1 weighted MR images from all subjects included in the study as previously described (Good et al., 2001). Second, each MR image was again linearly transformed into MNI space using the customized T1 template created in step 1. The normalized images were segmented into gray matter, white matter, and CSF using own prior images. The extracted gray matter volumes were then used to estimate spatial normalization parameters using linear and nonlinear components (7 × 8 × 7 basis functions). These transformations were used to spatially normalize the original T1 images. Image volumes were resliced to isotropic voxels (1 mm × 1 mm × 1 mm) and segmented into gray matter, white matter and CSF. To compensate for possible volume changes due to the spatial normalization procedure, the segmented images were modulated by the Jacobian determinants derived from the spatial normalization step. Finally, all segments were smoothed applying a Gaussian kernel of 12 mm.

2.5.2. Statistical analysis

The normalized, segmented, modulated, and smoothed gray matter images were analyzed by SPM2. Groups were compared by ANCOVA with adjustment for global brain volume differences (total gray plus white matter volume) and full scale IQ. An absolute threshold of 0.2 was applied. Height threshold for voxel level was set at $T = 3.43$ ($p < 0.001$); extend threshold was defined at $k = 20$ voxels (voxel size 1.0 mm × 1.0 mm × 1.0 mm). Correlation analyses were calculated by linear regression implemented in SPM with local volumetric measures as dependent and the explanatory variables of interest as independent variables with adjustment for IQ and total brain volume differences. Results are displayed at $p < 0.001$ uncorrected with a cluster extend threshold of $k >= 20$ voxels.

2.6. Biological motion computer based reaction time experiment

Biological motion and scrambled motion control condition were created exactly as described above (fMRI stimuli). Participants were asked to press different buttons on a keyboard if either a coherent walking person or a scrambled version had been shown on a computer screen. Stimuli were presented in the same resolution and duration as during the fMRI experiment in which subjects had taken part before. Inter-trial interval was set to a constant time and different data sets of point light figures were used. Forty female and 40 male moving persons as well as their respective scrambled versions (80) were shown for 1.5 s with an inter-trial interval of 1 s. Reaction time (RT) to perceive biological and scrambled motion as well as error rates were assessed. Data on the RT experiment were obtained from 15 control and 13 individuals with ASD.

2.7. Assessment of imitation and adaptive motor abilities

In a subgroup of this sample ($N = 12$ cases; $N = 12$ controls), data on hand-finger imitation (Goldenberg, 1996) and adaptive gross motor abilities (i.e. diadochokinesis and dynamic balance skills from the Zurich Neuromotor assessment, ZNA) (Largo, Fischer, & Rousson, 2003) were obtained as described (Freitag et al., 2006, 2007).

2.8. Statistical analysis of RT, imitation and adaptive motor abilities

Descriptive data were compared by independent sample T tests, non-parametric analysis of variance (ANOVA) and parametric analysis of covariance (ANCOVA) with full scale IQ, Wechsler symbol search subtest and/or repetitive dominant finger movement of the ZNA as covariates. As full scale IQ and age did show a high correlation ($\rho = 0.68$) in this sample, no additional adjustment for age was made to avoid colinearity. Bivariate correlations were assessed by the non-parametric Spearman correlation coefficient.

Exploratory linear regression models were calculated to assess the influence of the two independent variables RT to recognize (1) the biological and (2) the scrambled motion stimulus on the dependent variables hand-finger imitation, ZNA dynamic balance and diadochokinesis abilities as well as the social problems score derived from the Y(A)SR. In the ASD group only, the influence on current ADI-R algorithm scores was additionally explored. Analyses were adjusted for case-control-status, full scale IQ, performance in the symbol search subtest of the Wechsler scales, and speed of repetitive dominant finger movement of the ZNA, as both latter measures were correlated with RT to recognize the biological motion ($\rho = -0.68/\rho = -0.51$) and RT to recognize the scrambled stimulus ($\rho = -0.53/\rho = -0.36$). By inclusion of these four covariates we aimed to statistically minimize group differences in fine motor performance and visuo-motor-coordination, which might confound RT measures in individuals with ASD. Residuals of all linear regression analyses were normally distributed. Statistics were calculated by SAS (SAS/STAT, version 8.2; SAS Inc., Cary, NC, USA).

3. Results

3.1. Descriptive data

Descriptive data of the case-control sample are presented in Table 1. No differences between groups were found for full-scale IQ and age. Handedness and sex distribution were similar or equal. Current ADI-R algorithm scores were lower than the scores reported for age 4–5 (see Section 2.1. Sample), which is to be expected in high functioning individuals with ASD. Psychopathological measures as well as performance in the Wechsler symbol search subtest, imitation and gross motor abilities strongly differed between groups. Despite statistically

Table 1
Descriptive data

	ASD subjects $N = 15$	Control subjects $N = 15$	
Male/female (N/N)	13/2	13/2	
Right handed/left handed (N/N)	13/2	14/1	
	Mean (S.D.)	Mean (S.D.)	T-test/F-test/χ^2-test, $T/F/\chi^2$ value (DF) p-value
Verbal IQ	107.9 (18.1)	113.8 (17.7)	−0.9 (28) $p = 0.38$
Performance IQ	93.3 (23.5)	106.8 (17.8)	−1.8 (28) $p = 0.09$
Wechsler symbol search subtest[a]	8.7 (0.8)	11.4 (0.8)	6.1 (1) $p = 0.020$
Full scale IQ	101.2 (21.2)	112.1 (18.0)	−1.5 (28) $p = 0.14$
Age in years	17.6 (3.6)	18.6 (1.2)	−1.1 (17.1) $p = 0.27$
Psychopathology			
Y(A)SR social problems score	65.8 (11.4)	54.2 (5.3)	3.6 (19.7) $p = 0.002$
ADI-R algorithm social interaction score–current behavior	11.3 (4.3)	N/A	
ADI-R algorithm communication score–current behavior	9.8 (4.6)	N/A	
ADI-R algorithm repetitive score–current behavior	4.7 (2.7)	N/A	
RT, imitation, motor abilities			
RT biological motion (ms)[b]	790.3 (48.3)	640.9 (44.3)	4.3 (1) $p = 0.048$
RT scrambled motion (ms)[b]	972.0 (66.0)	713.9 (60.6)	6.9 (1) $p = 0.015$
Errors biological and scrambled motion[b]	3.0 (1.1)	4.3 (1.0)	0.6 (1) $p = 0.460$
Hand-finger imitation[a,c]	18.7 (1.0)	24.9 (1.0)	17.0 (1) $p = 0.0005$
Dynamic balance Z-score[a,c]	−5.7 (1.0)	−0.3 (1.0)	16.3 (1) $p = 0.0006$
Diadochokinesis Z-score[a,c]	−3.0 (0.3)	−1.4 (0.3)	12.0 (1) $p = 0.002$

ASD: Autism spectrum disorder, DF: degrees of freedom, N/A: not applicable, S.D.: standard deviation, RT: reaction time.

[a] Mean and test statistic adjusted for full scale IQ effects.

[b] Two measures missing; mean and test statistic adjusted for full scale IQ, performance in Wechsler symbol search subtest and speed of repetitive finger movements dominant side.

[c] Measures obtained in 12 cases and 12 controls; Z-score: standardized score with a mean of 0 and a S.D. of 1.

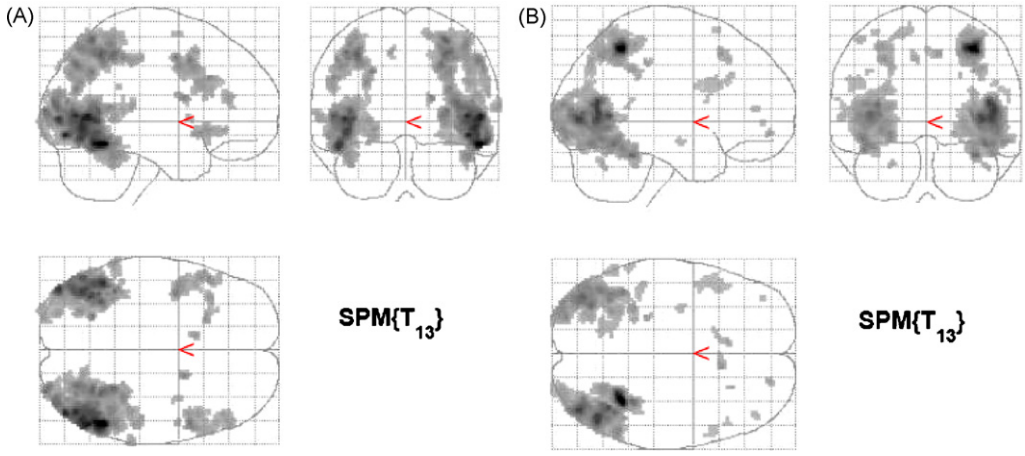

Fig. 1. Activation maps of the biological and scrambled motion condition combined.
Activation maps indicating regions with activity evoked by spacially moving point lights, i. e. biological and scrambled motion condition against the baseline fixation cross. (A) Activation in typically developing individuals (set level $p = 0.014$). Strongest activation: inferior temporal gyrus bilaterally; right: $T = 15.0$, extent = 22176 mm^3; left: $T = 10.5$, extent = 18528 mm^3. (B) Activation in ASD individuals (set level $p < 0.0001$). Strongest activation: right superior parietal lobule: $T = 17.3$, extent = 5760 mm^3; right medial temporal gyrus: $T = 11.3$, extent = 20688 mm^3.

controlling for speed of repetitive finger movements and visuo-motor-coordination abilities as possible confounding variables, RTs to recognize biological as well as scrambled motion stimuli were increased in individuals with ASD. Error rates did not differ between groups.

3.2. Analysis of functional MRI data

3.2.1. Spatially moving point lights independent of type of motion

FMRI data were first assessed in both groups individually followed by a comparison between groups. Data of one individual in each group had to be discarded due to motion artifacts. To compare regions which were activated by spatially moving point lights independent of type of motion, the biological motion and the scrambled motion condition together were compared against the baseline fixation cross. The spatially moving point lights strongly activated bilateral posterior temporal and occipital areas as well as bilateral superior parietal areas in both groups (Fig. 1). Additionally, bilateral middle frontal gyri were activated in both groups. Typically developing individuals did show more activation than ASD individuals in the right middle temporal gyrus adjacent to the superior temporal sulcus (STS; MNI coordinates 58, −34, −4; $T = 4.0$, extent = 72 mm^3). ASD individuals did show more activation than typically developing individuals bilaterally in the postcentral gyri (MNI coordinates 34, −40, 56; $T = 4.4$, extent = 120 mm^3; MNI coordinates −28, −38, 46; $T = 4.0$, extend 40 mm^3), left hippocampus (MNI coordinates −30, −40, −4; $T = 4.4$, extend 112 mm^3) as well as right middle frontal gyrus (MNI coordinates 28, 18, 60; $T = 4.2$, extent = 160 mm^3). These differences between groups, however, were not significant on the set-level ($p_{\text{both}} > 0.05$) which indicates that the number of differentially activated regions might have occurred by chance.

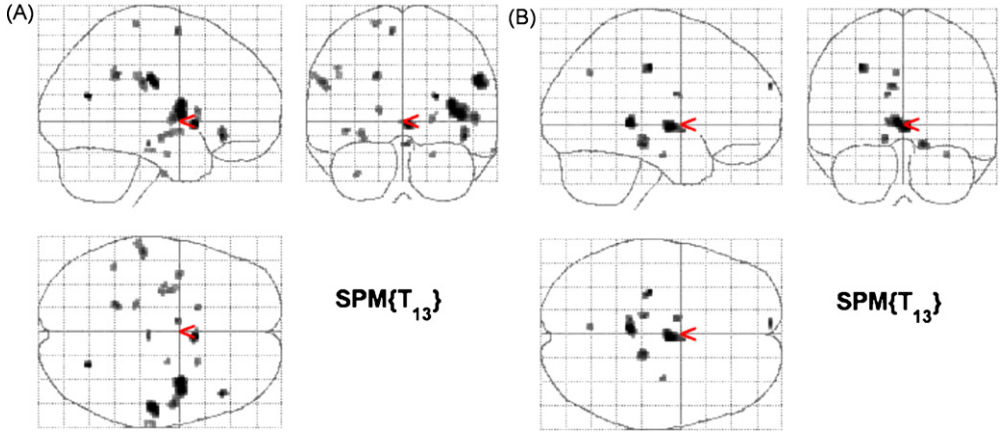

Fig. 2. Activation maps of the biological versus the scrambled motion condition.
Activation maps indicating regions with activity evoked by the biological motion but not the scrambled motion stimulus. (A) Activation in typically developing individuals (set level $p = 0.032$). Strongest activation: right postcentral gyrus: $T = 7.0$, extent = 496 mm^3; right insula/superior temporal gyrus: $T = 6.9$, extent = 1440 mm^3. (B) Activation in ASD individuals (set level $p = 0.789$). Strongest activation: posterior cingulum: $T = 6.2$, extent = 400 mm^3; right Thalamus: $T = 6.0$, extent = 488 mm^3.

Table 2
Biological motion vs. scrambled motion stimulus in typically developing and ASD individuals

Side	Region	Brodmann	MNI coordinates of peak activation (*x, y, z*)	Extent (mm^3)	*T*-Value	*Z*-Value	Uncorrected *p*-value
Typically developing (set level $p = 0.032$)							
Right	Postcentral gyrus	1–3	54, −20, 30	496	7.0	4.4	<0.001
	Parieto-occipital sulcus	17	24, −68, 18	24	6.1	4.1	<0.001
	Medial temporal gyrus/superior temporal sulcus	21	64, −20, −20	56	4.3	3.3	<0.001
	Superior temporal gyrus	22	52, −4, 2	1440	5.2	3.8	<0.001
	Insula	N/A	42, 2, 6		6.9	4.4	<0.001
	Caudate nucleus	N/A	4, 12, −2	200	6.5	4.3	<0.001
	Putamen	N/A	22, 12, 2	64	4.5	3.4	<0.001
	Inferior frontal gyrus	47	44, 30, −10	200	5.6	3.9	<0.001
Left	Inferior parietal lobule	40	−56, −26, 28	304	5.2	3.8	<0.001
	Inferior parietal lobule/intraparietal sulcus	40	−46, −46, 38	80	4.4	3.4	<0.001
	Posterior cingulate gyrus	31	−18, −44, 34	128	5.2	3.8	<0.001
	Fusiform gyrus	20	−32, −10, −38	48	4.4	3.4	<0.001
	Insula	N/A	−40, 0, −6	88	4.7	3.5	<0.001
	Caudate nucleus	N/A	−16, 12, 8	56	4.6	3.5	<0.001
	Putamen	N/A	−28, −8, −2	176	4.6	3.5	<0.001
	Superior frontal gyrus	6	−8, −2, 64	72	5.0	3.7	<0.001
ASD individuals (set level $p = 0.789$)							
Right	Posterior cingulate gyrus	35	14, −30, −14	216	5.0	3.7	<0.001
	Thalamus	N/A	4, −8, 2	488	6.0	4.1	<0.001
	Hippocampus	34	30, −12, −20	40	4.3	3.3	<0.001
Left	Postcentral gyrus	1–3	−32, −22, 44	128	5.4	3.9	<0.001
	Precuneus	7	−4, −64, 36	56	4.3	3.3	<0.001
	Posterior cingulate gyrus	29	−12, −38, 4	400	6.2	4.1	<0.001
	Posterior cingulate gyrus	35	−16, −30, −10	112	4.7	3.5	<0.001
	Caudate nucleus	N/A	−10, −4, 22	40	4.6	3.5	<0.001
	Superior frontal gyrus	10	−8, 64, 28	56	4.9	3.6	<0.001

N/A: not applicable.

3.2.2. Biological versus scrambled motion

When activation during perception of biological motion was contrasted with activation during perception of scrambled motion, both groups did show different areas of activation (Fig. 2). In typically developing individuals, activation was found bilaterally in parietal, temporal and frontal lobes as well as basal ganglia and insula (Table 2). These activation patterns in controls were significant on the set level ($p = 0.032$), indicating that the number of differentially activated regions has not occurred by chance, but activation represents a bilateral, predominately temporo-parietal network involving the basal ganglia, which seems to be relevant for the perception of unintentional biological motion. This network comprises the right superior temporal sulcus, which has been shown to be a central structure in biological motion perception (Puce & Perrett, 2003). In individuals with ASD, less activated clusters specific for biological motion perception were observed (set level $p = 0.789$). Activation was found predominately on the left hemisphere in parieto-temporal (limbic) and frontal areas as well as basal ganglia (Table 2). On the right, activation specific for biological motion perception was observed in the limbic system and Thalamus only.

When activation patterns during biological versus scrambled motion perception were compared between typically developing and ASD individuals, reduced activation was found in the ASD group, which reached significance at the set level ($p = 0.014$), indicating that the differentially activated clusters between groups have not occurred by chance. Hypoactivation in ASD individuals was found bilaterally in temporal and parietal areas as well as in the anterior cingulate gyrus (Table 3, Fig. 3). On the right, less activation was found in the middle temporal gyrus close to the superior temporal sulcus as well as in the postcentral gyrus and inferior parietal lobule. Also, right occipital as well as areas in the right medial and middle frontal gyri were underactivated in the ASD group. On the left, the anterior superior temporal and fusiform gyri, the postcentral gyrus and inferior parietal lobule as well as the claustrum did show less activation in ASD than in typically developing individuals.

When ASD and control individuals were compared with regard to higher activation in ASD individuals, only two small clusters of hyperactivation were found which did not reach significance on the set level ($p = 0.999$): right posterior cingulum (MNI coordinates 18, −44, 32; $T = 3.7$, extent = 40 mm^3) and left claustrum (MNI coordinates −28, −16, 20; $T = 4.3$, extent = 80 mm^3).

3.2.3. Correlation with neuronal activation patterns

To explore potential behavioral correlates of the differences in brain activity, correlation analyses were performed in both groups combined (negative correlation, i.e. more problems and less activation: Y(A)SR Social problems score; positive correlation, i.e. worse performance and less activation: hand-finger

Table 3
Biological motion vs. scrambled motion stimulus–higher activation in control vs. ASD subjects

Side	Region	Brodmann	MNI coordinates of peak activation (*x, y, z*)	Extent (mm^3)	*T*-value	*Z*-value	Uncorrected *p*-value
Right	Calcarine sulcus	17	16, −84, 10	104	3.9	3.4	<0.001
	Parieto-occipital sulcus	7	22, −64, 18	152	4.4	3.7	<0.001
	Central sulcus/postcentral gyrus	3	38, −16, 42	64	3.6	3.2	<0.001
	Postcentral gyrus/postcentral sulcus	1–3	54, −20, 30	464	4.8	4.0	<0.001
	Postcentral sulcus/inferior parietal lobule	40	32, −36, 44	72	4.7	4.0	<0.001
	Inferior parietal lobule	40	62, −26, 24	88	3.8	3.3	<0.001
	Middle temporal gyrus/superior temporal sulcus	37	54, −64, 6	176	4.4	3.7	<0.001
	Insula	N/A	44, 0, 4	56	3.7	3.3	<0.001
	Anterior cingulate gyrus	24/32	10, 0, 46	120	4.1	3.6	<0.001
	Medial frontal gyrus	6	10, −6, 60	280	4.5	3.8	<0.001
	Middle frontal gyrus	8	28, 34, 48	48	4.1	3.6	<0.001
Left	Central sulcus/postcentral gyrus	3	−20, −30, 70	224	5.4	4.3	<0.001
	Inferior parietal lobule	40	−54, −26, 24	88	4.2	3.6	<0.001
	Fusiform gyrus	20	−32, −10, −36	56	4.5	3.8	<0.001
	Superior temporal gyrus	22	−58, 2, 2	592	4.5	3.8	<0.001
	Claustrum	41	−38, −12, 18	64	4.2	3.6	<0.001
	Anterior cingulate gyrus	24/32	−6, 2, 48	216	4.6	3.9	<0.001

N/A: not applicable.

imitation, dynamic balance abilities, Diadochokinesis) as well as in the ASD group only (negative correlation: ADI-R algorithm current social, communication and repetitive behavior score). Correlations were calculated with activation (*t* values) of both contrasts, the biological and scrambled motion condition combined against the baseline condition as well as the biological versus the scrambled motion condition, to elicit correlation patterns for the perception of spatially moving point lights in general as well as specific correlation patterns for the perception of biological motion.

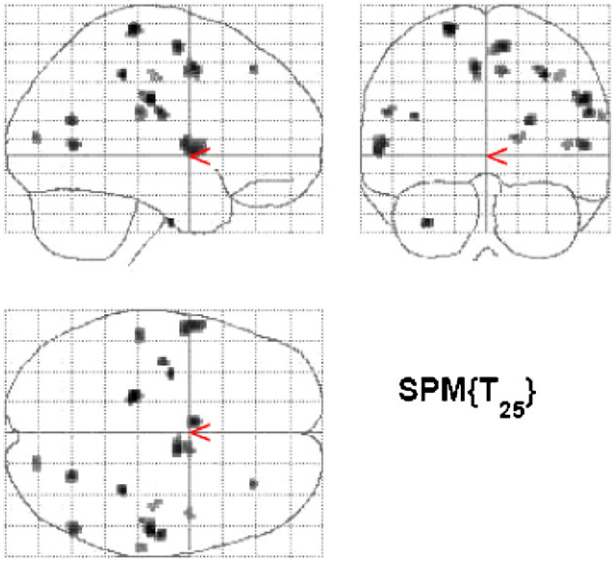

Fig. 3. Areas of stronger activation in typically developing than in ASD individuals during the biological vs. scrambled motion condition.
Activation maps indicating regions in which typically developing individuals showed more activation than ASD individuals during perception of biological motion compared to the scrambeld motion condition. Strongest hypoactivation in ASD individuals was found in the right postcentral gyrus/sulcus (MNI coordinates 54, −20, 30: $T = 4.8$, extent = 464 mm^3) and the left anterior superior temporal gyrus (MNI coordinates −58, 2, 2: $T = 4.5$, extent = 592 mm^3).

3.2.3.1. Spatially moving point lights. As typically developing individuals showed more activation than ASD individuals during the biological and scrambled motion versus the baseline condition in the right STS (MNI coordinates 58, −34, −4), this region of interest (ROI) was explored for correlation with activation during perception of both motion tasks against baseline. Despite not having found hypoactivation at the left STS for this contrast, exploratory analyses were performed for this side as well, as in the paper by Castelli et al. (2002), hypoactivation on the left was found, which might have not been picked up in our sample due to limited power. As the Castelli et al. (2002) coordinates on the left were located outside the MNI brain, the following MNI coordinates were assessed as ROI: −60, −52, 8 (Castelli et al., 2002: −66, −52, 8). Two further ROIs were assessed in the right and left intraparietal sulcus (IPS), as less volume in the right IPS was found in the VBM analysis in the present sample (see below) and the IPS is a central structure for polymodal motion processing (Lewis, Beauchamp, & DeYoe, 2000). ROIs assessed were MNI coordinates 35, −50, 49 and −41, −44, 49 (taken from Lewis et al., 2000). Search volume for each ROI analysis was set at a radius of 15 mm.

When activation during the biological and scrambled motion versus the baseline condition at the right and left STS was assessed for correlation, a strong negative correlation ($\rho = -0.85$) with activation at the left STS (MNI coordinates −48, −50, 0) was observed for the ADI-R algorithm current repetitive behavior score in the ASD group.

Activation in the right and left IPS negatively correlated with the ADI-R algorithm current social interaction score in the ASD group as well as with Y(A)SR social problems score in the full

group. The ADI-R algorithm current communication score in the ASD group negatively correlated with activation in the right IPS, and hand-finger imitation abilities showed a positive correlation with the left IPS in the full group. As – despite the positive correlation findings – correlation with activation in these four ROIs was not always located at the maximum point of activation, no Spearman correlations could be calculated for the ADI-R algorithm current social interaction and communication scores as well as hand-finger imitation abilities, because *t* values could not be extracted from SPM.

Correlation with activation of biological and scrambled motion versus baseline condition in the IPS bilaterally was

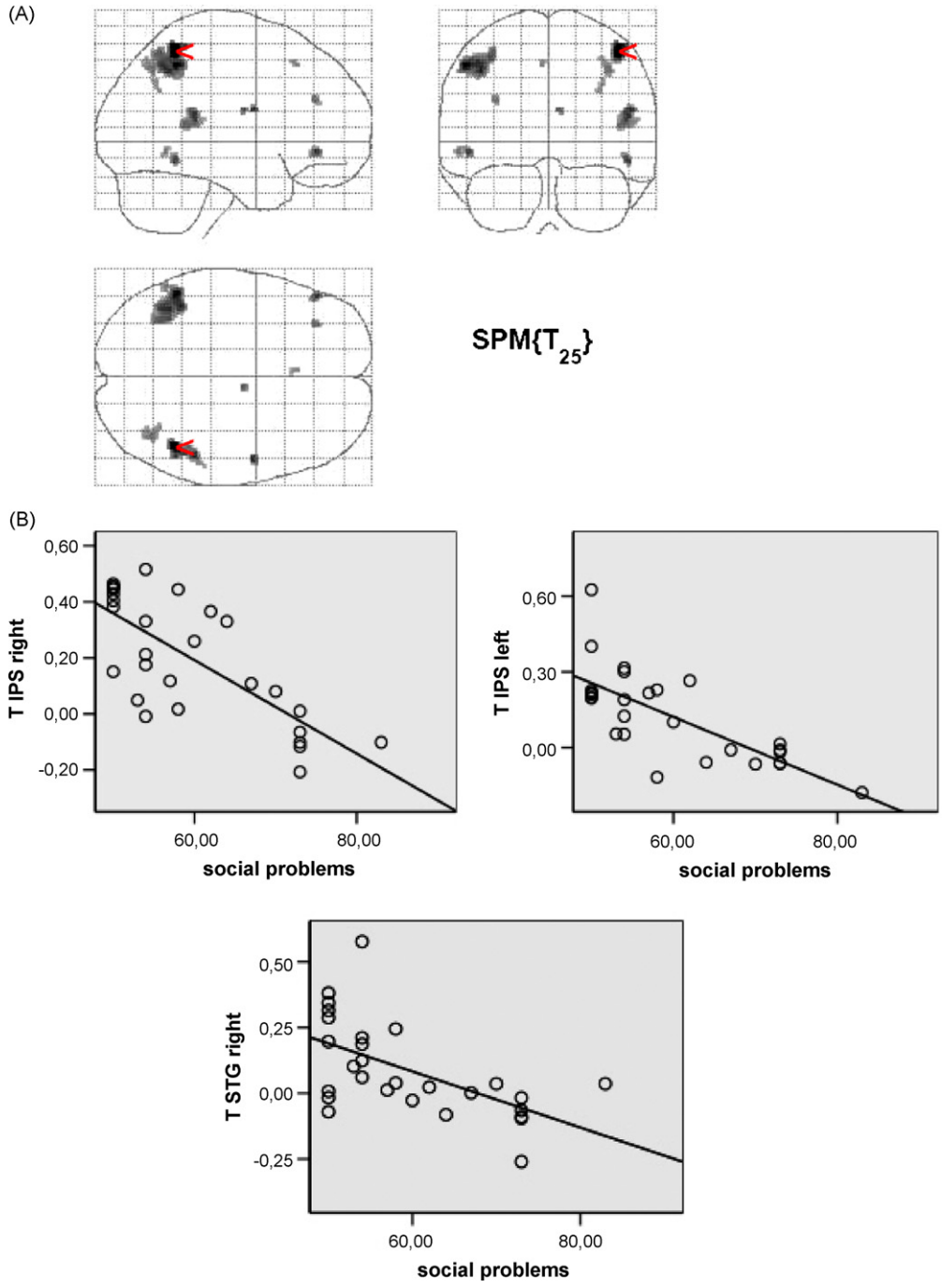

Fig. 4. Negative correlation of Y(A)SR social problems score with activation of biological and scrambled motion combined vs. baseline condition in both groups combined. (A) Activation maps indicating regions in which the Y(A)SR social problems score showed a negative correlation with activation during the biological and scrambled motion vs. baseline condition. Strongest negative correlations were found with activation in the inferior parietal lobule/intraparietal sulcus bilaterally (right MNI coordinates 44, −50, 56: $T = 6.0$, extent = 584 mm^3; left MNI coordinates −52, −50, 48: $T = 4.9$, extent = 2592 mm^3). Additionally, strong negative correlation was found with activation in the right posterior superior temporal gyrus (MNI coordinates 50, −38, 16: $T = 4.4$, extent = 616 mm^3). (B) Scatter plots of the Y(A)SR Social Problems score against *t*-values of activation in the right and left inferior parietal lobule/intraparietal sulcus (T IPS) and the right superior temporal gyrus (T STG).

strongest for the Y(A)SR social problems score (Fig. 4). Therefore, *t* values at the respective ROIs could be extracted from SPM and Spearman correlations were compared between groups. In the full group, correlation with activation in the right IPS was $\rho = -0.75$, in the left IPS $\rho = -0.71$. In the typically developing individuals, these correlations were less strong (right: $\rho = -0{,}43$; left: $\rho = -0.19$) than in ASD individuals (right: $\rho = -0.83$; left: $\rho = -0.83$), possibly due to lower variability of the Y(A)SR social problems score in the typically developing group.

3.2.3.2. Biological versus scrambled motion. Correlation with activation during the biological versus scrambled motion contrast was assessed at ROIs in the right STS (MNI coordinates 54, −64, 6), and bilateral inferior parietal lobule / postcentral sulcus (IPL/PCS; MNI coordinates right: 54, −20, 30 and 32, −36, 44; left: −54, −26, 24) derived from the differential activation patterns found between groups for this contrast (Table 3). As on the left, the STS was not differentially activated, correlation was assessed for the MNI coordinates reported above, derived from Castelli et al. (2002): −60, −52, 8. Additionally, activation in the left fusiform gyrus (MNI coordinates −32, −10, −36) and the left anterior superior temporal gyrus (MNI coordinates −58, 2, 2) were explored for correlation, as in both temporal lobe ROIs, differential activation was found between groups.

No correlation with activation during the biological versus scrambled motion contrast for any of these ROIs was found for the Y(A)SR social problems score and the three ADI-R algorithm derived scores. Hand-finger imitation as well as dynamic balance and diadochokinesis abilities, however, showed strong positive correlations with the two ROIs in the right IPL/PCS but not the left IPL/PCS. As dynamic balance, diadochokinesis and hand-finger imitation abilities also correlated mutually ($\rho > 0.70$) and did show very comparable correlation patterns, only hand-finger imitation abilities were assessed further to quantify correlation with activation of biological versus scrambled motion in the right IPL/PCS (Fig. 5). Correlation of hand-finger imitation abilities with both ROIs in the right IPL/PCS was high in the full group ($\rho = 0.85/\rho = 0.83$). In the typically developing group, these correlations were slightly lower for ROI 54, −20, 30 ($\rho = 0.40$) than in the ASD group ($\rho = 0.75$). For ROI 32, −36, 44, correlation in the typically developing group ($\rho = 0.76$) was slightly higher than in the ASD group ($\rho = 0.68$). Additionally, a positive correlation of

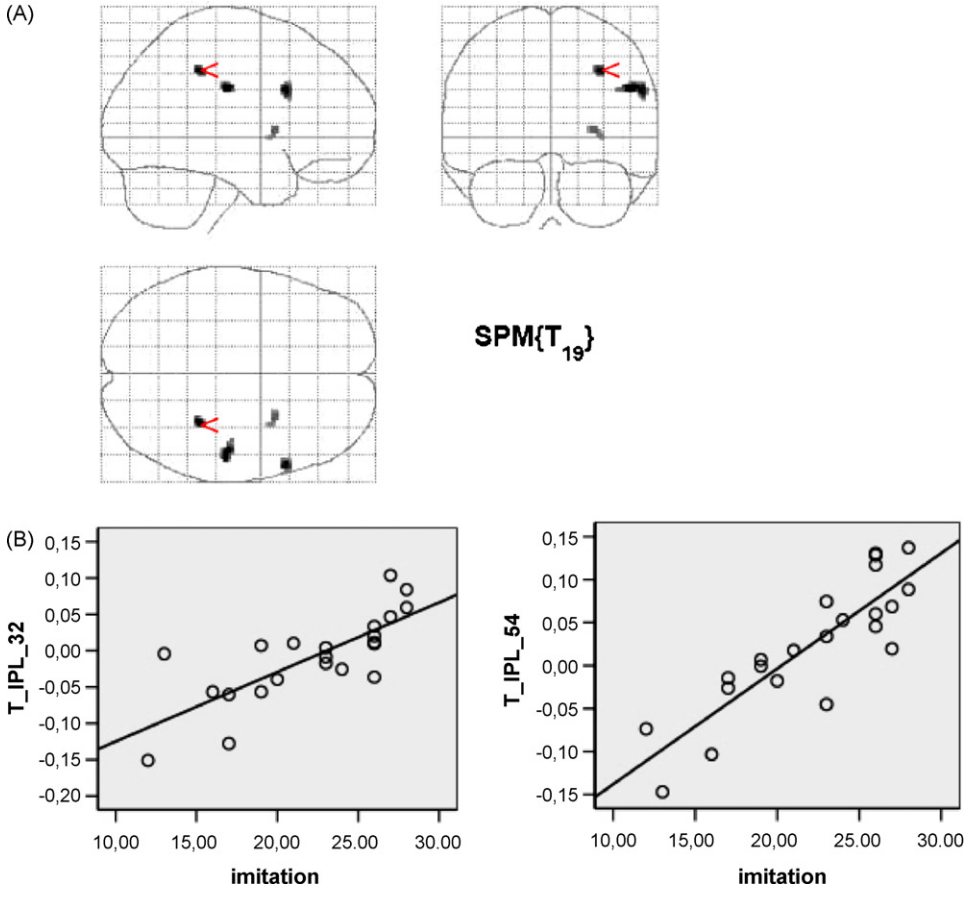

Fig. 5. Positive correlation of hand-finger imitation abilities with activation of the biological vs. scrambled motion contrast in both groups combined. (A) Activation maps indicating regions in which the hand-finger imitation score showed a positive correlation with activation during the biological vs. scrambled motion contrast. Strongest correlation was found with activation in the right inferior parietal lobule/postcentral sulcus (MNI coordinates 32, −36, 44: $T = 5.5$, extent = 136 mm^3; and 54, −22, 30: $T = 5.5$, extent = 272 mm^3). Additionally, strong positive correlation was found with activation in the right inferior frontal gyrus (MNI coordinates 56, 16, 30: $T = 5.1$, extent = 272 mm^3). (B) Scatter plots of the hand-finger imitation score against *t*-values of activation in the right inferior parietal lobule/postcentral sulcus (T_IPL_32: at MNI coordinates 32, −36, 44; T_IPL_54: at MNI-coordinates 54, −22, 30).

$\rho = 0.74$ was found with activation in the right inferior frontal gyrus, which was stronger in typically developing individuals ($\rho = 0.86$) than in the ASD group ($\rho = 0.49$).

3.3. Analysis of structural MRI data

Locally reduced gray matter volume in ASD compared to control subjects was found around the right intraparietal sulcus (MNI coordinates 36, −58, 43; $T = 4.1$, extent = 102 mm^3; $p < 0.001$). No area of locally increased gray matter in ASD individuals was observed. To explore, if longer RT to perceive the biological or scrambled motion stimulus might be associated with a reduction in temporal or parietal gray matter volume, which then might reflect an anatomical counterpart of the differential activation patterns observed in the functional analysis, correlation analyses with gray matter volumes were performed. No negative correlation of RT measures and gray matter bilaterally in temporal or parietal areas was observed. Also, no correlation with temporal or parietal gray matter volume and the Y(A)SR social problem score in the full group or the ADI-R current communication and social interaction scores in ASD individuals was elicited. However, the ADI-R current repetitive behavior score correlated negatively with gray matter volume of the right Fornix (MNI coordinates 28, −31, 1; $T = 5.2$, extent = 22 mm^3; $p < 0.001$), the right middle temporal gyrus (MNI coordinates 69, −40, −10; $T = 5.1$, extent = 178 mm^3; $p < 0.001$), as well as right and left inferior parietal lobule (MNI coordinates 39, −42, 59; $T = 4.5$, extent = 45 mm^3; $p < 0.001$; MNI coordinates −48, −34, 55; $T = 5.1$, extent = 336 mm^3; $p < 0.001$).

3.4. Analysis of behavioral data

Despite the original hypothesis of specific difficulties in biological motion perception, RT was increased during the perception of biological as well as scrambled motion in ASD individuals. In addition, error rates did not differ between groups, pointing towards an intact ability to perceive biological motion (Table 1). However, the increase in RT in both tasks might point towards a higher cognitive effort to differentiate both stimuli. To explore, if RT to recognize biological motion specifically might show an influence on imitation or gross motor abilities as well as autistic symptoms, exploratory linear regression analyses were performed with RT to recognize biological or scrambled motion as well as mean RT as independent variables (Table 4). The only association which seemed to be specific for biological motion recognition RT was the association with dynamic balance abilities. No specific association with measures of autistic symptoms was observed.

4. Discussion

In this study, we hypothesized that neuronal activation during perception of biological motion would be decreased and reaction time to correctly recognize biological motion would be increased in individuals with ASD. Both hypotheses were con-

Table 4
Association of biological and scrambled motion recognition reaction time with imitation, adaptive motor abilities and autism specific behavior scores

Dependent variables	Independent variables		
	RT biological motion β-estimate (S.E.) *t*-value, *p*-value[a] (R^2)	RT scrambled motion β-estimate (S.E.) *t*-value, *p*-value[a] (R^2)	Mean RT of biological and scrambled motion β-estimate (S.E.) *t*-value, *p*-value[a] (R^2)
ASD and controls			
Hand-finger imitation score[b] $N = 23$	−0.013 (0.004) −3.5 $p = 0.003$ (0.79)	−0.005 (0.002) −2.1 $p = 0.048$ (0.72)	−0.009 (0.003) −3.0 $p = 0.007$ (0.77)
Dynamic balance *Z*-score[b] $N = 23$	−0.012 (0.005) −2.6 $p = 0.018$ (0.62)	n.s.	n.s.
Diadochokinesis *Z*-score[b] $N = 23$	−0.004 (0.002) −2.3 $p = 0.032$ (0.62)	−0.002 (0.001) −1.8 $p = 0.086$ (0.58)	−0.003 (0.001) −2.3 $p = 0.033$ (0.62)
Y(A)SR social problems score[c] $N = 28$	0.019 (0.011) 1.7 $p = 0.095$ (0.53)	n.s.	n.s.
ASD only			
ADI-R algorithm social inter-action score–current behavior[c] $N = 13$	n.s.	n.s.	n.s.
ADI-R algorithm communication score–current behavior[c] $N = 13$	n.s.	0.008 (0.004) 2.3 $p = 0.052$ (0.41)	0.011 (0.005) 2.1 $p = 0.060$ (0.39)
ADI-R algorithm repetitive score–current behavior[c] $N = 13$	n.s.	n.s.	n.s.

DF: degrees of freedom, n.s.: not significant; *p*-value > 0.10, S.E.: standard error, RT: reaction time.
[a] Statistics adjusted for case-control-status, full scale IQ, performance in the Wechsler symbol search subtest and speed of repetitive dominant finger movement.
[b] Dependent variable: higher values correspond to better performance.
[c] Dependent variable: higher values correspond to more impairment; *Z*-score: standardised measure with a mean value of 0 and a standard deviation of 1.

firmed, as the null hypotheses of no differences between groups had to be rejected for the neuronal activation patterns obtained by the BOLD response during fMRI as well as the RT data. Findings strongly support the notion of differences in biological motion processing in ASD compared to typically developing individuals by eliciting a different network of activation during the biological motion task.

However, on the behavioral level, no differences in error rates were observed, showing an intact ability to recognize biological motion in ASD individuals. In addition, RT to recognize the scrambled motion stimulus also was increased in ASD individuals. As no behavioral control task was assessed in the study, it cannot be excluded that the increase in RT might be due to slow visuo-motor-processing in ASD individuals and not specifically to impaired motion processing. As we controlled for individual differences in fine-motor and visuo-motor performance during statistical analysis, however, the remaining increase in RT in both tasks might also point towards a higher cognitive effort to differentiate both stimuli in ASD individuals. Findings, therefore, might also indicate differences in the processing of spatially moving point lights in ASD individuals in addition to differential biological motion processing. This view is supported by the distinct correlation patterns observed for phenotypic measures and neuronal activation during both fMRI contrasts.

Autism specific psychopathology (social problems score, ADI-R subscores) was specifically correlated with neuronal activation during observation of spatially moving point lights, but not biological motion processing. Imitation, dynamic balance as well as diadochokinesis abilities, which also differed strongly between groups, most strongly correlated with neuronal activation during biological motion perception, indicating a specific influence of biological motion perception abilities on these complex motor tasks. The correlation patterns of the behavioral data are also supportive of this view, as dynamic balance abilities were only influenced by RT to recognize the biological but not by RT to recognize the scrambled motion stimulus, and imitation as well as diadochokinesis abilities correlated more strongly with RT to recognize biological motion than scrambled motion.

4.1. Complex motion processing

The association of autism specific psychopathology with neuronal activation during perception of spatially moving point lights might be related to previously observed differences in the perception of moving stimuli in individuals with ASD (Dakin & Frith, 2005). In studies assessing motion coherence thresholds (Milne et al., 2006; Milne et al., 2002; Spencer et al., 2000) observers have to discriminate the overall direction of a field of coherently moving dots where some proportion of them has been replaced by randomly moving elements (Milne, Swettenham, & Campbell, 2005). ASD individuals showed an about 10% increased motion coherence threshold whereas no impairment of coherent form detection was found in one study (Spencer et al., 2000). These findings were interpreted as indicative of a dorsal visual stream deficit in ASD. The parieto-occipital dorsal visual stream analyzes motion and detects peripheral stimuli for guiding actions in space, whereas the ventral temporal visual stream is specialized in object discrimination and recognition (Devinsky & D'Esposito, 2004). Other studies have challenged the assumption of a global dorsal visual stream deficiency in ASD, but argued in favor of only a high-level dorsal cortical stream deficiency, as ASD individuals were impaired in a higher-level global dot motion task but not in a lower-level flicker contrast sensitivity task or a low-level optic flow motion stimulus (Bertone, Mottron, Jelenic, & Faubert, 2005; Del Viva, Igliozzi, Tancredi, & Brizzolara, 2006; Pellicano, Gibson, Maybery, Durkin, & Badcock, 2005). Another differentiation was made with regard to the complexity of the assessed motion task (Bertone, Mottron, Jelenic, & Faubert, 2003). For first order, luminance defined radial motion stimuli, performance between ASD and control individuals did not differ in their study, but for second order, texture or contrast defined radial motion stimuli. The authors interpreted their data with regard to difficulties in the integrative processing of complex visual motion tasks in individuals with ASD but not as indicative of a specific dorsal visual stream dysfunction.

Our data are not directly comparable to these studies as our study was designed to assess biological motion perception and not motion perception in general. The dot pattern of our two motion tasks, however, were complex in the sense that they contained information at many spatial scales (Dakin & Frith, 2005). The strong negative correlation of Y(A)SR social problems and ADI-R algorithm current social interaction and communication scores with activation in the right and left IPS might point towards an influence of higher-level or complex motion processing abilities on autistic symptomatology, as more autistic symptoms were present in individuals with less neuronal activation in this polymodal motion processing area (Bremmer et al., 2001; Lewis et al., 2000). Reduced gray matter in the right IPS in the ASD individuals of our study supports this interpretation.

The involvement of the right IPS in ASD has been shown previously in several brain imaging studies. A PET-study in individuals with ASD also found a negative correlation of the ADI-R algorithm social interaction score with activation in the right parietal region close to the hypoactivated right IPS of our study (Gendry Meresse et al., 2005). Two fMRI studies, one assessing the embedded figures test, which is a test of local processing and visual search in which ASD individuals show superior performance (Ring et al., 1999), the other assessing visually driven motor sequence learning (Muller, Kleinhans, Kemmotsu, Pierce, & Courchesne, 2003), further found hypoactivation in ASD individuals in the right superior parietal lobule close to the right IPS.

When typically developing individuals were directly compared to ASD individuals regarding activation during perception of spatially moving point lights (biological and scrambled motion versus baseline fixation cross condition), hypoactivation of the right STS was observed, which, however, did not reach significance on the set level. A strong negative correlation was observed with the ADI-R current repetitive behavior score and activation in the left STS. These findings argue against an isolated dorsal stream deficiency but also imply the ventral visual stream in ASD.

An involvement of the STS region in individuals with ASD has also been found in fMRI studies assessing incongruent gaze shifts (Pelphrey et al., 2005) and a theory of mind task based on animated sequences (Castelli et al., 2002) as well as in a voxel based morphometry (Boddaert et al., 2004) and two PET studies on resting brain activity in children with autism (Ohnishi et al., 2000; Zilbovicius et al., 2000). Another PET study similarly observed a negative correlation of the ADI-R algorithm repetitive behavior score with resting activation in the left STS close to the location of the maximum negative correlation of this score in our study (Gendry Meresse et al., 2005).

Our findings of a differential activation during observation of spatially moving point lights therefore point towards an involvement of structures previously interpreted in the light of the "social brain" in autism (Zilbovicius et al., 2006). Some of the above mentioned studies have assessed tasks which involved social aspects as intentions (Castelli et al., 2002; Pelphrey et al., 2005). However, most studies did employ tasks without any explicit social meaning as it was also the case in our study. Therefore, the reported hypoactivation as well as the correlation with autistic symptoms in the bilateral IPS and STS point more towards the interpretation of ASD as disorders of the association cortex, resulting in impairments in the processing of tasks placing high demands on integration of information and coordination of neural systems, as is the case with social but also with complex non-social stimuli (Minshew & Williams, 2007). This is underscored by studies emphasizing the role of the STS region not only in the processing of movements of specific body parts, but as a region possibly processing high-level information of moving stimuli and providing input into lateral temporal and inferior parietal cortices (Thompson, Hardee, Panayiotou, Crewther, & Puce, 2007). Repetitive behavior might originate from this difficulty integrating complex information, as in our study higher ADI-R current repetitive behavior symptom scores were associated with reduced activation during the perception of spatially moving point lights as well as with reduced gray matter volume in temporal and inferior parietal cortical areas.

4.2. Biological motion processing

Beyond activation differences during perception of spatially moving point lights, strong differences in activation during biological motion perception between groups were found predominately in the bilateral somatosensory cortex as well as the inferior parietal lobules (IPL), with stronger differences on the right. Also, a positive correlation of hand-finger imitation, dynamic balance and diadochokinesis abilities with ROIs in the right postcentral gyrus and IPL in the full group as well as in ASD individuals was observed. In addition, the right middle temporal gyrus (MTG) adjacent to the STS was less activated in ASD individuals specifically during biological motion processing.

Regions of hypoactivation in the IPL and MTG overlap with findings from an fMRI study designed to assess imitation abilities in individuals with ASD (Williams et al., 2006). Hypoactivation in the right IPL in that study was reported for all assessed execution, not only for imitation tasks. In our study, hypoactivation was found during mere observation of moving person point light animations, i.e. biological motion perception. This points towards the possibility that the well known impairment of action imitation in ASD (Freitag et al., 2006; Williams et al., 2004) as well as of dynamic balance and diadochokinesis (Freitag et al., 2007) might be the result either of impaired biological motion processing or of impaired self-other matching, which also relies on intact right IPL function (Uddin, Molnar-Szakacs, Zaidel, & Iacoboni, 2006). In controls only, additionally a strong correlation of hand-finger imitation with activation during the biological motion task in the right inferior frontal gyrus (IFG) was observed. Recently, less activation in this region during imitation of emotional expressions was reported in ASD individuals (Dapretto et al., 2006). As no differential activation in this region was found between groups in our study and as hand-finger imitation abilities in ASD individuals were not strongly related to activation in the right IFG, this area might not be as relevant for action imitation abilities in ASD individuals than the strongly hypoactivated parietal regions observed in our study. In the study by Williams et al. (2006), activation in right MTG differed between groups specifically during imitation but not execution tasks. Their reported MNI coordinates are located very close to the hypoactivated MTG region in the ASD individuals of our study during biological motion perception. It has been proposed previously that processing of observed actions and reafferent motor-related copies of actions made by the imitator might interact in the MTG/STS region (Iacoboni et al., 2001). Taken together, these findings point towards a possible involvement of the right MTG/STS region in action observation (biological motion perception) as well as in imitation, whereas the right IPL seems to be predominately implicated in biological motion perception and action execution, independent of concurrent imitation.

In addition to complex motion processing, processing of biological motion information relies on the integration of form and motion (Thompson, Clarke, Stewart, & Puce, 2005) and therefore places even higher demands on integration of information and coordination of neural systems than processing of spatially moving point lights. In typically developing individuals the fusiform gyrus processes structure-from-motion information of body movements (Peelen, Wiggett, & Downing, 2006). Therefore, hypoactivation in the left fusiform gyrus in our study as well as in the study assessing animated shapes (Castelli et al., 2002) indicates differential neuronal activation and coordination with respect to the integration of form and motion information in individuals with ASD. Similarly, the left anterior STG was strongly underactivated in ASD individuals during the biological motion contrast in our study. The STG also is involved in the integration of form and motion (Vaina et al., 2001) and, predominately on the left side, in semantic processing and naming of people (Devinsky & D'Esposito, 2004). In rhesus monkeys, the anterior part of the STS has been shown to contain cells that use an object centered frame of reference to code for animate objects and their actions (Jellema & Perrett, 2006). The strong hypoactivation in ASD, therefore, might imply differences in form and motion integration as well as in semantic processing of action implied by the biological motion stimulus. The latter view is supported by studies showing impairments in attributing

social meaning to moving ambiguous visual form stimuli, the so called Social Attribution Task (SAT), in adults with ASD (Klin & Jones, 2006). Given the strong connections of the left STG and the limbic system (Zilbovicius et al., 2006), hypoactivation of the left STG might indicate that difficulties in social and emotional perception could at least partially be caused by reduced abilities to integrate form and motion information or by reduced semantic processing of biological motion information in ASD.

Additional underactivation of frontal, anterior cingulate and occipital regions in ASD individuals during biological motion perception might be explained by group differences either in bottom-up or top-down attentional processing (Castelli et al., 2002). Several studies employing tasks which rely on attention processes like working memory tasks have shown under activation in the anterior cingulate cortex as well as in medial frontal areas in individuals with ASD (Belmonte & Yurgelun-Todd, 2003; Pierce, Muller, Ambrose, Allen, & Courchesne, 2001; Silk et al., 2006). These findings might either be interpreted in light of genuine problems in attention function in ASD individuals, which seem to be unlikely from our study, as the anterior cingulate gyrus as well as prefrontal regions were not under activated during observation of spatially moving point lights. Also, neuropsychological studies have not confirmed a general attention deficit in individuals with ASD (Johnson et al., 2007). Alternatively, these areas might have been hypoactivated in our study due to reduced parieto-frontal connectivity in individuals with ASD. Unfortunately, this hypothesis has not been assessed here, however, reduced connectivity of parietal and frontal areas has been found in a recent study on visuomotor coordination in adult men with autism (Villalobos, Mizuno, Dahl, Kemmotsu, & Muller, 2005).

Underscoring the relevance of our findings on biological motion perception, a structural MRI study on cortical thickness found decreased gray matter in the somatosensory cortex and IPL bilaterally as well as in the right STS and the anterior cingulate cortex in individuals with ASD, strongly corresponding to the hypoactivated areas in ASD individuals reported in our study (Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006). From the results of their study, it is to be expected, that neuronal processing of any neuropsychological task relying on these reduced gray matter structures might result in hypoactivation during fMRI in ASD individuals.

In conclusion, we reported strongly differing neuronal processing of biological motion in individuals with ASD, and additional differences in the processing of spatially moving point lights independent of biological motion. Severity of autistic symptoms was correlated with less activation in the IPS and STS during perception of spatially moving point lights, implying that either difficulties in higher-order motion perception or in the integration of complex motion information in the association cortex might be related to autistic symptoms. A specific correlation of neuronal activation during biological motion perception with hand-finger (action) imitation, dynamic balance and diadochokinesis abilities was observed, underscoring the possible relevance of differences in biological motion perception and/or self-other matching for action imitation and gross motor difficulties in individuals with ASD. Results of the structural analysis additionally emphasize the relevance of right intraparietal sulcus abnormalities in ASD.

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