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Right Temporoparietal Gray Matter Predicts Accuracy of Social Perception in the Autism Spectrum

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Abstract

Individuals with an autism spectrum disorder (ASD) show hallmark deficits in social perception. These difficulties might also reflect fundamental deficits in integrating visual signals. We contrasted predictions of a social perception and a spatial-temporal integration deficit account. Participants with ASD and matched controls performed two tasks: the first required spatiotemporal integration of global motion signals without social meaning, the second required processing of socially relevant local motion. The ASD group only showed differences to controls in social motion evaluation. In addition, gray matter volume in the temporal-parietal junction (TPJ) correlated positively with accuracy in social motion perception in the ASD group. Our findings suggest that social-perceptual difficulties in ASD cannot be reduced to deficits in spatial-temporal integration.

Key words: Autism; Asperger Syndrome; motion coherence; animacy; social perception; voxel-based morphometry.

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Autism Spectrum Disorders (ASD) are characterized by pervasive deficits in the social domain, including lack of understanding others' mental states ("theory of mind"), reduced social interests and impaired social-emotional reciprocity (Langdell 1978; Baron-Cohen et al. 1985; Hobson et al. 1988; Baron-Cohen et al. 2001). Unsurprisingly, the major strategy in ASD research has thus been to investigate social deficits, which has led to a predominant social-deficit account of ASD. Over the last decade, it has been acknowledged that focusing on symptom-related social functioning in ASD may have resulted in more fundamental abnormalities in perception being overlooked (Dakin et al. 2005; Behrmann et al. 2006; Happé and Frith 2006; Mottron et al. 2006; Milne and Griffiths 2007). These fundamental abnormalities might even have implications for understanding the origin and etiology of social impairments in ASD: Fundamental problems with perceptual integration have been implicated in ASD (Spencer et al. 2000; Milne et al. 2002; Brosnan et al. 2004). As social stimuli often comprise complex configural or hierarchical elements (Behrmann et al. 2006) which must be integrated into a global whole ("gestalt"), impaired social functioning in ASD might also be attributed to perceptual deficits.

One way to investigate perceptual integration is to measure the perception of "global motion", that is, the integration of local motion signals (e.g., one flying bird) into a global motion signal (e.g., a swarm). In visual neuroscience, this is often probed by displacing a population of dots into one direction, while another population moves at random. Determining the direction of coherent motion requires the observer to analyze and integrate local motion signals in space and time. Impairment of this integration has indeed been reported in ASD (Spencer et al. 2000; Milne et al. 2002; Pellicano et al. 2005; Milne et al. 2006; Tsermentseli et al. 2008; Atkinson 2009). In addition, individuals with ASD show deficits in the discrimination of biological motion (Blake et al. 2003; Parron et al. 2008; Klin et al. 2009; Annaz et al. 2010) and in the recognition of emotions from body movements (Hubert et al. 2007; Atkinson 2009), both often tested with "point-light displays" (PLDs) of

actions (Johansson 1973). The ability to extract social information from PLDs is an indication that complex social cognition can be performed on the basis of basic perceptual input (Adolphs, 2003), and thus, reduced sensitivity to PLDs of emotions has often been taken as evidence for compromised social functioning in ASD. However, PLDs also require spatiotemporal integration of local motion signals.

Social motion perception can also be investigated without the confound of global motion: Percepts of biological or "animate" (i.e., self-propelled) motion can be evoked by just one or two moving abstract objects (Heider and Simmel 1944; Tremoulet and Feldman 2000; Schultz et al. 2005), solely by the movement dynamics and irrespective of the objects' shapes. These may even lead to highly complex mental state attributions to abstract shapes in the typical observer (Heider and Simmel 1944). Individuals with ASD, however, attributed inappropriate mental states to socially interacting shapes, while correctly perceiving non-social control animations (Castelli et al. 2002; Klin and Jones 2006). Such findings of impaired perception of interactivity make a strong case for a social-deficit account of ASD independent of deficits in the spatiotemporal integration.

Magnetic resonance imaging (MRI) studies of brain structure may contribute to elucidating the nature of ASD psychopathology. Recent studies have also shown that differences in brain anatomy can predict inter-individual variability in a variety of human behaviors (Kanai and Rees 2011), relating meaningful performance measures acquired in an ecologically valid setting (i.e. outside the MRI scanner) to brain structure. For example, a recent study of this kind showed that lonely individuals have less posterior superior temporal cortex gray matter volume and at the same time deficits in basic social perception skills; the latter two variables were themselves found to be correlated (Kanai et al. 2012a). A number of further studies have reported a positive correlation between social network size and gray matter volume in socio-emotional brain regions including the amygdala and the posterior superior temporal cortex (Bickart et al. 2011; Sallet et al. 2011; Kanai et al. 2012b).

Interestingly, morphological changes such as reduced gray matter volume have been reported in ASD in both these regions (Boddaert et al. 2004; Brieber et al. 2007; Salmond et al. 2007; Ke et al. 2009; Toal et al. 2010; Via et al. 2011; Yu et al. 2011). The question arises whether the variation of social behavior deficits and of other behavioral aspects of ASD can be related to the morphology of brain regions associated with the disorder. One of the few studies that have addressed such questions directly so far has found an association between social and communication deficits in ASD with caudate, cerebellar, and precuneus volumes, as well as with frontal and temporal lobe regional volumes (Rojas et al, 2006). Another study found abnormalities in the amygdala-fusiform system in ASD, including and an increase in cortical thickness in a fusiform region of interest in ASD compared to controls, together with a negative correlation between cortical thickness in this region and facial emotion recognition in ASD (Dziobek et al 2010). We will adopt a similar approach using visual motion tasks.

The aim of the present study was to compare predictions of a social-deficit versus a spatiotemporal-integration-deficit account of ASD, using two different motion perception experiments and relating the behavioral findings to neuroanatomy. Here, we asked adult participants with ASD and matched control participants to indicate whether coherent motion moved up or down (global motion experiment), and whether two moving dots interacted or not (social motion experiment). Selective social-perceptual difficulties in ASD with intact global motion detection would provide evidence for a social deficit account, while reduced performance in both experiments would support a fundamental spatiotemporal-integration deficit account of ASD. This would be corroborated by a direct relation between anatomical variation in brain regions associated with social-emotional processing and social perception performance, together with a smaller or absent relation between anatomical variations in these regions and spatiotemporal-integration performance. Such results would suggest that social-perceptual difficulties in ASD could occur distinctly from more basic deficits in spatiotemporal integration. Therefore, using structural MRI and voxel-based morphometry

(VBM), we tested (i) for regional gray matter differences between ASD and control participants, and (ii) whether such differences could predict performance in the global motion experiment and / or the social motion experiment in the ASD group.

Methods

Participants

Fifteen right-handed participants with ASD (9 with Asperger syndrome, 6 with high-functioning autism) and 14 healthy controls participated in the experiments (Table 1). The ASD and control groups did not differ significantly from each other with respect to potentially confounding variables including: age, gender, IQ, handedness or visual attention (see Table 1).

[Please insert Table 1 about here]

Participants with ASD were recruited from the outpatient clinic at the Department of Psychiatry and Psychotherapy of the University Hospital Cologne. The sensitivity of the "gold-standard" diagnostic tools (e.g., the Autism Diagnostic Observation Schedule—Generic, ADOS-G; Lord et al. 1999) has recently been questioned for ASD in adulthood, as these tools have mostly been validated for adolescent / young adults (Bastiaansen et al. 2011; Lai et al. 2011). Those tools do therefore not seem adequate for adults in the age range of our participants (24 – 45 yrs.). At the Department of Psychiatry in Cologne, diagnoses were, thus, determined by several independent ASD-specialized physicians following a two-step procedure. This procedure began with a first interview after referral of the client from a practicing psychiatrist or neurologist. In cases in which this first interview supported a diagnosis of ASD, participants underwent a detailed neuropsychological assessment. Then in a second interview, the diagnosis was confirmed or rejected by a second psychiatrist (author K.V.) under consideration of the ICD-10 criteria and the neuropsychological profile. We included participants with the diagnostic categories F84.0 and F84.5. These participants then

underwent two additional interviews: a psychiatric anamnesis carried out by author D.S. at the Department of Psychiatry, University Medical Center Hamburg-Eppendorf, who also assessed the Structured Clinical Interview for DSM-IV axis 1 and 2 disorders, and a neurological anamnesis by author A.M. at the Department of Neurology, University Medical Center Hamburg-Eppendorf. All fulfilled the cut-off for ASD according to the Autism Spectrum Quotient (AQ; Baron-Cohen et al. 2001; Table 1). As expected, the AQ-score was significantly different between the ASD and control groups (Baron-Cohen et al. 2001).

Structural MRIs were acquired on the subsequent day. We could not obtain structural MRIs from three ASD and two control participants (remaining participants on VBM analysis: n_{ASD}=12, n_{CON}=12). All participants gave full written informed consent and were paid for their participation. The study was in accordance with the Declaration of Helsinki and approved by the ethics committee of the Hamburg Medical Association.

Stimuli and Tasks

Global Motion Experiment

Global motion perception in ASD was tested with a coarse visual motion direction discrimination task. Each motion stimulus consisted of a weighted average of a signal and a noise component. Both components consisted of normally distributed and spatiotemporally bandpass-filtered luminance noise. The mean of the luminance noise distribution was identical to the luminance of the uniform background gray. +/-3 standard deviations of the luminance distribution spanned the complete black-white dynamic range of the employed monitor. The luminance noise was spatiotemporally bandpass-filtered by multiplication in the frequency domain such that each stimulus frame contained spatial frequencies of 1.33 – 2.66 cycles/deg and that the frame sequence contained motion speeds of 2.4 – 3.0 deg/sec. Each signal component consisted of only upward or downward motion. Each noise component consisted of motion in all directions. The motion coherence of each individual stimulus was

set by adjusting the ratio of a signal and noise component, with 0 % and 100 % motion coherence corresponding to only the noise or signal component, respectively. Stimuli were presented centrally in a circular aperture (diameter: 27 deg). The stimulus was masked with the background color around the fixation dot (dot diameter 0.36 deg, mask diameter 3 deg), to rule out any stimulus interactions with the central fixation dot and to encourage monitoring of the entire stimulus field (see Figure 1A for a schematic stimulus display). Stimuli were constructed off-line using MATLAB (MathWorks Inc., Natick, MA) and presented with the software "Presentation" (Neurobehavioral systems, Albany, CA).

Each trial started with onset of a central fixation dot (.36 deg diameter). After a 500 msec delay, a motion stimulus was presented centrally for 750 msec. After another 250 msec delay the fixation dot was switched off, which served as the go-cue for the participants to indicate the perceived motion direction by pressing one of two designated keys (two-alternative forced-choice task). The participants' response was followed by presentation of a brief (50 msec) square signaling the correctness of the response (green for "correct", red for "incorrect"). This feedback served to motivate the subjects and to counteract a potential response bias. Every 48 trials, participants were given the opportunity for self-paced rest. Participants performed a total of 576 trials across six levels of motion coherence: 0, 4, 8, 16, 50, and 100 % for a total duration of 24 min. The stimulus design was fully balanced and randomized for motion coherence and motion direction.

The dependent variable was each participant's motion coherence threshold, that is, the minimum level of coherence at which participants performed 75% (established criterion) correct motion discrimination. These were determined by fitting a logistic function to each participant's motion discrimination accuracy scores obtained at the different motion coherence levels. Individual motion coherence thresholds were then submitted to a two-sample *t*-test to test for group differences (at $p<.05$ two-tailed). These motion coherence thresholds were also used for our brain-behavior correlation analysis, where we refer to these

measures as "performance in the global motion experiment". To confirm that our results are independent of the analysis method, we also ran a 2-way, repeated-measures ANOVA using SPSS (IBM, Armonk, NY) on the motion discrimination accuracy scores, with factors coherence levels and participant group.

In order to monitor fixation, we recorded the electrooculogram (EOG) using the setup of Schlögl and colleagues (Schlögl et al. 2007). EOG artifacts were identified in a semi-automatic procedure using the EOG artifact detection function of the Fieldtrip toolbox (Oostenveld et al. 2011). EOG could not be analyzed from one control participant because of data loss.

Social Motion Experiment

This experiment was previously devised and used by Schultz and colleagues (Schultz et al. 2005). The stimuli depicted short animation sequences, in which two disks (one red and one blue, both 2° in diameter) moved across a black screen. A mathematical algorithm controlled the discs' movements through a multivariate autoregressive process which made the disks change direction and speed in a controlled but unpredictable way. One parameter in the algorithm (the cross-correlation level) controlled the degree of dependence between the disks' movements. In the experimental conditions, an increase in this parameter led to linear changes in perceived interactivity (i.e., the red disk appeared to chase the blue disk, which tried to escape). In control conditions, the same increase in the cross-correlation parameter led to smaller changes in perceived interactivity, because the trajectories of the blue disk were opposite in time and space to their trajectories in the experimental condition, which reduced the physical correlation in the movements of the two dots. In addition, changes of the cross-correlation parameter resulted in changes of disk speed, which were identical in experimental and control conditions. Four linearly spaced levels of the parameter were used in both experimental and control conditions, making for a total of eight different animation types.

Participants had to perform two tasks with these stimuli. In the first task, the interactivity-rating task, they were asked to rate by pressing one of four possible buttons "How much does the red object follow the blue object, one being the minimum and four the maximum?". This task assesses the capacity to detect basic social interactions between moving objects. In the control task, the speed-rating task, they rated "How fast do the objects move, one being the minimum and four the maximum?". This task assesses the ability to rate simple physical characteristics of the dots' motion. Performance on the two tasks was assessed in two consecutive blocks in a randomized order.

The eight animation types were repeated 10 times per task. Each trial started with an animation sequence (4.3 sec) followed by a self-paced rating phase. Stimuli were created using MATLAB and presented with the PsychToolbox (www.psychtoolbox.org). Dependent variables were the participants' rating responses, which were entered into a three-factorial ANOVA (group, level, stimulus type) and tested at $p<.05$. This analysis approach is the same as used in the original study reporting this experiment (Schultz et al. 2005). In addition, to obtain individual performance values for our brain-behavior correlation analysis, we calculated the difference between the slope of the interactivity ratings obtained in experimental and control trials, which we will refer to as the "performance in the social motion experiment". Positive values in this measure would indicate that participants perceived greater interactivity as a function of cross-correlation in the interactive trials than in the control trials, which would show that participants could correctly detect the interactivity between the moving dots. The total duration of this experiment was about 15 minutes. Performance was assessed using a repeated-measures 3-way ANOVA implemented in SPSS with factors cross-correlation level, interactive/control stimuli, and groups. This ANOVA was run separately for the speed and interactivity-rating and speed-rating tasks.

Voxel-based morphometry (VBM)

Image Acquisition

Structural T1-weighted magnetization prepared gradient-echo images (TR=2300 msec, TE=2.98 msec, FoV=256 mm, 1 mm slice thickness, TI=1100 msec, 9° flip angle) with 1x1x1 mm^3 voxel resolution were obtained on a 3T Siemens Magnetom Trio MRI scanner (Siemens Medical Systems, Erlangen, Germany) at the University Medical Center Hamburg-Eppendorf. Data were visually screened for artifacts and anatomical pathology. The duration of this scan was about 7 minutes. Careful visual inspection at the time of image acquisition and during the analysis revealed no movement-induced image blurring in any of the scans we acquired, indicating the same level of quality across scans. This excludes the possibility that anatomical differences between groups are caused by differences in data quality.

Image Preprocessing

VBM analyses were performed with the Statistical Parametric Mapping software (SPM8 Wellcome Institute of Neurology, University College London, UK) and the VBM8 toolbox for SPM (Ashburner and Friston 2000). Images were first reoriented and aligned to the anterior commissure, then segmented and normalized using default values of the VBM8 toolbox (for details see http://dbm.neuro.uni-jena.de/vbm/). These included tissue segmentation and normalization to the stereotactic space of the Montreal Neurological Institute (MNI) using the iterative "High-dimensional Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra Normalization" and light clean-up of remaining non-brain tissue to optimize overlap of normalized individual tissue maps. Tissue maps were then modulated, that is, non-linearly scaled by the amount of contraction caused by normalization so that the total amount of gray or white matter was identical to the original image. This step enables the comparison of relative differences in regional gray matter volumes, corrected for individual brain size. Modulated gray matter segments were then smoothed using a Gaussian kernel with a typical value of 12-mm full-width at half-maximum (Abell et al. 1999; Boddaert

et al. 2004; Salmond et al. 2005; Brieber et al. 2007; Salmond et al. 2007; Kanai et al. 2012a).

VBM Statistical Analysis

We were interested in testing for regional differences in gray matter in ASD relative to control participants and how variability in gray matter volume related to task performance. Each participant's smoothed gray matter images were entered into a two-sample t-test in SPM8 to investigate group differences in gray matter across the whole brain. Age and gender were included as nuisance covariates. An issue in VBM t-tests is that false positive results can be obtained if all voxels are included in the analysis. For example, non-brain voxels in the image tend to have low variability across participants and are therefore likely to appear as artefactual results in a T-test. Also, non-grey-matter voxels in the data images can have non-zero values as a consequence of the smoothing used in the preprocessing step (this leads to 'bleeding out' of grey matter into adjoining white matter or non-brain voxels). This leads to artefactual extensions of the significant clusters outside grey matter. To exclude these kinds of artefacts, we eliminated voxels with less than 20% likelihood of being grey matter (as indicated by the segmentation procedure in SPM8). This liberal threshold was chosen so as to avoid reductions in sensitivity that could result from eliminating too many voxels. 417'291 voxels were thus in for the group analysis. Statistical results were thresholded at $p<0.05$, corrected for multiple comparisons based on the spatial extent of the clusters found using a voxel-level threshold of $p<0.001$ uncorrected (threshold cluster size = 411 voxels, determined using the fMRI stat toolbox; Worsley et al. 2002). The identified regional gray matter differences were anatomically localized using (i) the SPM Anatomy Toolbox (Eickhoff et al. 2005) and (ii) a standard atlas of the human brain (Duvernoy 1999) and then used as regions-of-interest (ROI).

A representative summary value for gray matter volume in each ROI was obtained by averaging over the gray matter volume values of the voxels in each ROI. In order to treat each

ROI as similarly as possible despite their differences in volume and shape, and to make sure that the anatomical labels of the peak voxels apply to the voxels included in the average, we calculated this average only on the 200 voxels closest to the voxel with peak gray matter difference across participant groups. Depending on the ROI, these voxels were all within 5.6 to 8.6mm of the peak. Note that this method yielded a stable estimate: very similar results were obtained when using values only from the peak voxel or the mean across various numbers of voxels within the ROI. In order to gain insight into structure-function relationships, these values were correlated against performance on the two behavioral experiments. For each ROI and each group of participants, a stepwise regression with gray matter volume as dependent variable and the two performance measures as independent variables was carried out. Correction for multiple tests across ROIs was performed using the Bonferroni method, using an estimate (Meff) of the effective number of independent tests given the correlation in the brain data (Cheverud 2001). The threshold for significance was then calculated as $p_$corrected = 0.05/Meff. The parameter estimates from the regressions were compared in a separate regression model that included the interaction term between groups (ASD and Control) and the effect of interest.

Results

Note on statistical power

Before describing the results of our study, we feel that a discussion of statistical power is in order. A major issue of the current study is the number of participants tested (12 with ASD to 12 matched controls). These numbers appear relatively low because of our difficulty to recruit large numbers of participants with clear diagnosis, homogenous symptomatology, and good MRI data who also agreed to participate in a battery of clinical and behavioral tests and psychophysical experiments. These numbers are relatively common in neuroimaging, but low numbers can lead to overestimates of effect size and low reproducibility of results (Button et

al 2013), as indicated for example by poor positive predictive values (probability that an observed effect that passes the required threshold of claiming its discovery actually reflects a true effect). Calculating positive predictive values would be helpful, but requires knowledge about the study's power, the Type I and II errors, and the pre-study odds ratio that an effect is indeed non-null. Unfortunately, the pre-study odds ratio of our study could not be estimated, making a precise assessment of positive predictive values impossible. However, as will be described in the following paragraphs, our results are very much in accord with previous work and we thus believe that our results really reflect a true effect that is highly likely to be replicated if tested on different samples.

Global Motion Experiment

The groups' behavioral performance is displayed in Figure 1a. Motion coherence thresholds in the ASD group were not significantly different from the control group (mean±SD: ASD: 7.4%±0.43; controls: 7.2%±0.6; $t(27)=0.008$, n.s.). This was confirmed by an ANOVA performed on the motion discrimination accuracy values, which revealed changes in discrimination performance with the coherence level as expected ($F(5,65)=585.35$, $p<<0.01$), but no difference between participant groups ($F(1,13)=0.28$, $p>0.6$) and no interaction between group and coherence levels ($F(5,65)=0.33$, $p>0.8$). The ASD group did not differ significantly from the control group in the number of overall EOG artifacts (eye blinks and saccades; $t(26)=-.798$, n.s.) or the number of trials in which saccades were made ($t(26)=-1.493$, n.s.).

Social Motion Experiment

The participants' performance in the interactivity-rating task is depicted in the left panel of Figure 1b. There was a significant three-way interaction effect ("stimulus type x level x group", $F(2.1,56.8)=4.3$, $p<.05$). The origin of the effect was as follows: ratings for

experimental stimuli were more different from ratings for control stimuli at level 4 versus 2, and this effect was greater for controls than for participants with ASD ($t(22) = 2.29$, $p<.05$). These results show that participants with ASD had significantly greater difficulties in perceiving the differences in interactivity displayed in the experimental and the control trials: they tended to over-estimate the interactivity displayed in the control stimuli. In addition, the two-way interaction "stimulus type x level" reached significance ($F(2.1,56.8)=20.04$, $p<.001$), as well as the main effects "level" ($F(1.7,47.1)=162.05$, $p<.001$) and "stimulus type" ($F(1,27)=68.37$, $p<.001$). Note that the non-integer degrees of freedom reflect the application of the Greenhouse-Geisser correction for non-sphericity in the data.

In a separate control task (Schultz et al. 2005), participants rated the speed of both dots (Figure 1b, right panel). There were no group differences on speed ratings in the same tests as performed on the interactivity ratings (all $p>.60$, n.s.). Only the main effect "level" reached significance ($F(1.5, 39.1)=269.76$, $p<.001$), indicating that participants correctly considered the objects' speed to increase across levels.

[Please insert Figure 1 about here]

Voxel-based morphometry

VBM revealed seven clusters of gray matter reductions in the ASD compared to the control group (Figure 2; Table 2). There were no suprathreshold clusters in which the ASD group showed increased gray matter volume compared to controls.

We then tested for relations between gray matter in these seven clusters and behavioural measures in both groups. For the ASD group, the stepwise regression analyses yielded significant results only for one region: the right angular gyrus / ascending segment of the posterior superior temporal sulcus, also called the temporoparietal junction or TPJ (Corbetta et al. 2000; Decety and Lamm 2007; Mars et al. 2011). The regression model that could explain gray matter in this region included only performance in the interactivity task as

predictor ($F(1,9)=13.08$, $p<0.008$; $r=.75$, $r^2=.56$; Figure 3). The relation was positive: ASD participants with more gray matter within this region were better at the social motion task. In the control group, no regression analyses were significant. For the control group's TPJ data, the best regression model contained only performance in the interactivity task as predictor and yielded $F(1,10)=3.10$, $p>0.1$; $r=-.49$, $r^2=.24$ (see Figure 3). The relation between TPJ gray matter and performance in the interactivity-rating task was different between groups: a separate regression model testing this interaction (ASD / Control x interactivity performance) was significant ($F(1,22)=5.10$, $p<0.035$). As the TPJ region is quite large, we attempted to refine the localization of our cluster by referring to a recent study which identified three subdivisions of the right TPJ on the basis of structural and functional connectivity analyses (Mars et al. 2011). The TPJ cluster identified in the current study was located in the posterior and superior aspect of the "TPJ posterior" or TPJp subdivision (distance between centroids were 49 mm and 31 mm, for TPJ anterior respectively TPJ posterior subdivisions), which was coupled with areas associated with mentalizing and the default network.

[Please insert Figures 2 and 3 and Table 2 about here]

Discussion

In the present study, we aimed at disentangling social and perceptual-integration deficits in ASD. While spatiotemporal integration in a global motion experiment was intact in ASD, these participants showed deficits compared to controls in a higher-order social motion experiment in which they determined whether two moving objects interacted or not. The ASD group showed decreased gray matter volume in several brain regions. Of these regions, only the TPJ showed a correlation between anatomy and performance: gray matter volume correlated with accuracy in the social motion experiment but not in the global motion experiment. This result was found only in the ASD group.

Patterns of Motion Perception in ASD

Our participants showed normal global motion perception as indicated by normal motion coherence thresholds in contrast to previous reports on "hallmark" deficits in global motion perception and reduced perceptual integration in ASD (Spencer et al. 2000; Milne et al. 2002; Bertone et al. 2005; Pellicano et al. 2005; Milne et al. 2006; Tsermentseli et al. 2008; Atkinson 2009). In accordance with our present finding, other psychophysical data also failed to find global motion processing deficits in ASD (Bertone et al. 2005; Del Viva et al. 2006; de Jonge et al. 2007; Sanchez-Marin and Padilla-Medina, 2008; Vandenbroucke et al. 2008; Jones et al. 2011). This discrepancy is in accordance with growing evidence that, while common in ASD, abnormalities in motion perception are not universal and may affect only sub-types of individuals with the condition (e.g. Milne et al. 2006; Annaz et al. 2010). Although the sub-type structure of ASD is not yet clear, one study has reported an association between impaired motion discrimination and history of delayed language in a sample of high-functioning adults with autism (Takarae et al. 2008). Further studies with high numbers of participants are needed to pursue this work.

Despite intact global motion perception, ASD and control participants differed in judging the degree of interactivity between the two moving objects but not in judging the objects' speed. Yet, participants with ASD were not unable to detect interactivity, but were more prone than controls to detect interactivity also in independently moving objects, yielding a higher number of false alarms. This might seem somewhat at odds with previous work which reported that ASD participants have problems understanding animations with shapes moving interactively with implied intentions, and give less frequent mentalizing-like interpretations of their movements than controls (Abell et al. 2000; Castelli et al. 2002). However, a recent study (Zwickel et al. 2011) showed that individuals with ASD can spontaneously detect social interactions in Heider & Simmel-like animations, but differ in the verbal descriptions of the story line underlying the stimuli, and over-attribute intentionality to

control animations. It has been shown that individuals with ASD can strategically overcome initial difficulties in detecting social causality in two moving squares when being explicitly prompted (Congiu et al. 2010). In our current study, we used a rating task with a simple question in order to obtain a quantitative measure of performance rather than verbal descriptions. The ASD participants' bias towards reporting interactions even when there were none might reflect an over-compensation, which was facilitated by the fact that it was easy to understand what answers were expected in our rating task. The fact that the performance of our participants with ASD was worse than controls demonstrates that their compensatory strategies were however not successful. Taken together, these findings suggest that detection of interactions between moving objects is not fundamentally lacking in ASD, but different and less accurate compared to controls.

The Social Deficit versus Spatiotemporal-Integration Deficit Account

Related studies have previously tried to link social-perceptual impairments in ASD to general motion perception deficits, for example demonstrating a relationship between high motion coherence thresholds and lower sensitivity to emotion detection in point-light displays in ASD (Atkinson 2009). Other studies did not find evidence for deficits in coherent motion perception after controlling for IQ differences (Koldewyn et al. 2010; Jones et al. 2011; Koldewyn et al. 2011), while reporting significantly reduced action recognition from PLDs in ASD. Koldewyn and colleagues' (2010; 2011)—but not Atkinson's (2009)—results suggested that deficits in biological motion perception are independent of coherent motion perception in ASD. In the present study we found decreased performance in a social perception experiment with higher-order local motion in ASD but no deficit in spatiotemporal-integrative functioning, in accordance with Koldewyn et al. (2010). A recent study revealed a significant correlation between biological motion perception and mental state ascription to moving interacting shapes in participants with and without ASD (Jones et al.

2011). The authors hypothesized a common functional basis such as shared social–cognitive requirements underpinned by the posterior temporal cortex. To look for further support of the social deficit account, we (i) searched for regional gray matter differences between ASD and controls, and (ii) within these regions, tested correlations between both kinds of motion perception and gray matter volume.

Regional Gray Matter Abnormalities and their Correlation with Performance

Our participants with ASD showed several regional gray matter reductions compared to the control group including the amygdala, superior and middle temporal cortex, the angular gyrus / TPJ, the insula, and ventromedial frontal as well as inferior frontal cortices. This is in accord with many previous VBM studies (Abell et al. 1999; Boddaert et al. 2004; Brieber et al. 2007; Salmond et al. 2007; Ke et al. 2009; Dziobek et al. 2010; Kosaka et al. 2010; Toal et al. 2010; Riva et al. 2011; Via et al. 2011; Yu et al. 2011). However, other studies have found gray matter increases in some of these and other regions in ASD, making the current picture on structural brain differences in ASD somewhat inconsistent (Amaral et al. 2008). These inconsistencies may be related to the recently often discussed heterogeneity in the spectrum, as well as between-study differences with respect to functionality and age of the ASD group (Brambilla et al. 2003; Nordahl et al. 2007; Amaral et al. 2008; Nickl-Jockschat et al. 2011).

Most of the regions in which we found gray matter reductions have consistently been implicated in socio-emotional processing and communication abilities that are deficient in ASD, such as (i) theory of mind (Di Martino et al. 2009; Van Overwalle, 2009; Sugranyes et al. 2011), (ii) mirror neuron functioning and language (Lai et al. 2012; Molenberghs et al. 2012), and (iii) limbic system functions (Sugranyes et al. 2011). However, some of the aforementioned regions have also been associated with functions other than social ones. One of these regions that is particularly important for the current study is the TPJ region, which has also been involved in attention (Shulman et al. 2009). One indication about which

function our TPJ cluster might be related to could be drawn from its location: As described in the Results section, our cluster is located in the "TPJp" subdivision, which was defined by being coupled with areas associated with mentalizing and the default network (Mars et al. 2011). While TPJ activations vary tremendously between studies of social cognition (Van Overwalle 2009), our cluster is very close (10.4 mm) to the TPJ activation cluster found in a study on the processing of action statements on causality, in the comparison intentional causality > physical causality (Ouden et al. 2005). We are not aware of functional neuroimaging studies of ASD using simple object-interaction stimuli similar to ours.

Given the inconsistent morphological findings in ASD and the ambiguity of some of the associations between functions and the brain regions involved, we aimed at gaining insight into the functional implications of the morphological changes we found, following the idea that inter-individual differences in task performance can be used as source of information to link anatomy to cognition (Kanai and Rees 2011). Thus, we tested for correlations between performance in both our experiments (global motion and social motion) and gray matter volume in the clusters of gray matter differences we identified. We hypothesized that a relation between the structure of these brain regions and performance in the social experiment, together with a smaller or absent relation between anatomy and spatiotemporal-integration performance, would support the social-deficit account. In line with this idea, we show for the first time that in individuals with ASD, gray matter volume in the right TPJ predicted accuracy of social motion perception—but not coherent motion perception. The higher the TPJ gray matter volume, the more ASD individuals performed like control participants in the interactivity-detection task. This brain-behavior correlation in the ASD group is in accordance with the proposal that the right TPJ is implicated in the uniquely human capacity of social cognition, including the ability to reason and empathize with other people's mental and affective states (Frith and Frith 1999; Saxe and Kanwisher 2003; Saxe 2006; Decety and Lamm 2007) and to take others' perspectives (Blanke 2005). The present

correlation is in line with recent findings: (i) posterior superior temporal volume can be linked to loneliness and the ability to recognize social signals (i.e., eye gaze; Kanai et al. 2012); and (ii) enhanced social ability (i.e., imitation and perspective talking) can be obtained by stimulating right temporoparietal junction via transcranial direct current stimulation (Santiesteban et al. 2012). Our findings thus nicely complement previous studies relating brain structure abnormalities in ASD to behavioral measures (Rojas et al, 2006; Dziobek et al, 2010), and show similar relations in the domain of motion perception.

The TPJ has been shown to be recruited during the viewing of animated shapes that trigger mental state attributions (Castelli et al. 2000), but only in control participants without ASD and not with ASD (Castelli et al. 2002). We found that participants with ASD had worse performance at the social perception task and less gray matter in TPJ than controls. Together with the relation we found in ASD between more gray matter in TPJ and better performance (i.e., less overcompensation of their perceptual deficits), this could indicate that an intact TPJ allows adequate perception of (basic) social interactions. When this is not warranted, participants with ASD seem to attempt to compensate the deficits. This compensation mechanism raises many interesting questions: is this is a voluntary, controllable process or not, what kind of stimuli does it apply to, how is it instantiated in the brain? Given our current data, we feel uncomfortable to speculate more, but this aspect of our findings could develop into interesting future studies. However, an interesting comparison can be made with the study by Dziobek and colleagues (2010), who found an *increase* in cortical thickness in the fusiform gyrus, a *deficit* in recognizing face expressions in ASD, and a *negative* correlation between these two variables. Note that this study also reported an abnormal amygdala-fusiform connectivity, which we will not focus on here. Thus, the increase in cortical thickness described by Dziobek and colleagues appears to have rather dysfunctional effects as it was associated with worse face expression recognition performance. This is in contrast to our findings, where less gray matter reductions were associated with better performance.

Future studies will be needed to clarify the causes and mechanisms leading to these differences.

Together, the former functional and the present anatomical evidence support (i) a functionally relevant abnormality in the temporoparietal region with possible pathophysiological significance for ASD, and (ii) a distinction between social perception and spatiotemporal integration capacities in ASD.

Alternative accounts

Spatial attention impairments in the ASD group together with systematic differences in the spatial attentional requirements of the two tasks might also account for our results. The TPJ region has indeed also been implicated in spatial attention, including attention to motion and reorienting of attention (Corbetta et al. 1991; Luks and Simpson, 2004; Shulman et al. 2009). Impairments in high-level dynamic attentional processes (Koldewyn et al. 2010), and particularly deficits in disengaging or shifting of attention have also been described in autism spectrum disorders (Courchesne et al. 1994; Wainwright and Bryson 1996; Goldstein et al. 2001). While such aspects of spatial attention are certainly involved in our social motion paradigm, only an extremely specific deficit in spatial attention could explain the present pattern of results. In addition, eye movements (as potential indicators as to where attention had been allocated) have previously been shown to be similar in the speed and interactivity rating tasks, as well as in control and experimental stimuli in typical participants (Schultz et al. 2005). Moreover, both our groups did not differ in the Trail Making Test (TMT), a test of visuospatial attention, which also involves mental flexibility and attentional set-shifting abilities (Reitan 1958; Sánchez-Cubillo et al. 2009). Performance on the TMT did not show a significant correlation with the social motion experiment, nor did it account for TPJ gray matter in the ASD or control group.

Conclusions

It has been suggested that individuals with ASD are impaired at social perception because of a primary deficit in global perception or spatiotemporal integration. Here, we disentangled perception of global non-social and local social motion, providing evidence that spatiotemporal integration deficits cannot necessarily explain atypical social perception in ASD. Moreover, our data provide the first anatomical evidence of a compromised structure of the temporoparietal cortex predicting social dysfunctions in ASD, highlighting the behavioral significance of ASD-related structural changes. Regional gray matter changes in ASD, however, might vary, for example as a function of age or diagnostic subgroup (Brambilla et al. 2003; Nordahl et al. 2007; Amaral et al. 2008). Here we only investigated adult high-functioning individuals with ASD, and our conclusions are limited by a rather small sample size. Future, possibly longitudinal, studies will be necessary to determine the altered trajectory of temporoparietal cortex development and its relationship to ASD social psychopathology.

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Figure Captions

Fig. 1 Behavioral results

A. Results of the global motion experiment. Curves represent logistic functions fitted to the average motion detection performance of the ASD (Autism Spectrum Disorder) and control (CON) groups. Bar graphs illustrate the mean motion coherence thresholds of the ASD and CON groups (i.e., at which coherence level 75% of their answers were correct), evaluated on the basis of logistic functions fitted to the individual data. Error bars in all sub-panels represent the standard error of the mean. **B**. Results of the social motion experiment. On the X-axes of both panels are reported the different levels of the parameter that controlled the interactivity between (and speed of) the objects' movements from 1 (minimum) to 4 (maximum). The Y-axis shows participants' average ratings from 1 (minimum interactivity or speed) to 4 (maximum). Broken and unbroken lines show, respectively, the results obtained in the interactive conditions (where the dots' movements were correlated and the dots should appear to interact; a steep slope indicates good performance) and in the control conditions (where the correlation between the dots' movements was removed and the dots should appear to interact much less; a gentler slope indicates good performance). Separate panels are shown for interactivity ratings (the social motion perception task) and speed ratings (the control task).

Fig. 2 Results of the gray matter volume analysis

Statistical map for the gray matter analysis showing brain regions with less gray matter volume in participants with ASD compared to control participants, overlaid on a single subject's inflated structural image (see Table 2 for abbreviations). Note that the cortical reconstruction in this image was chosen for better visualization of the VBM results only and does not represent a surface-based analysis. Lateral and medial views (lower panel) are shown. Results are displayed thresholded at a $p<.001$ (uncorrected for multiple comparisons),

with an extent threshold of 411 voxels. Note that due to the inflation process some bigger clusters appear split into separate clusters.

Fig. 3 Relationship between gray matter volume and task performance

ASD participants generally showed less gray matter in the right TPJ compared to controls (CON). In the ASD group, the volume of gray matter in this region was significantly and positively correlated with performance in the social motion experiment. This correlation in the ASD group was higher than in the control group, where it was not significant. Participants with ASD with higher gray matter volume within this area were better at assessing the interactivity of the two moving dots in the social motion experiment. The panel on the left shows the right TPJ cluster also presented in Figure 2, rendered on an inflated template brain for better visualization. The gray matter volume – performance correlation is shown in the right panel where the Y-axis shows performance in the social motion experiment (positive values indicate better performance), assessed as the difference between the slopes of interactivity ratings obtained for experimental and non-interactive control stimuli. The dotted lines indicating 95% confidence intervals about the regression line.

Figure 1

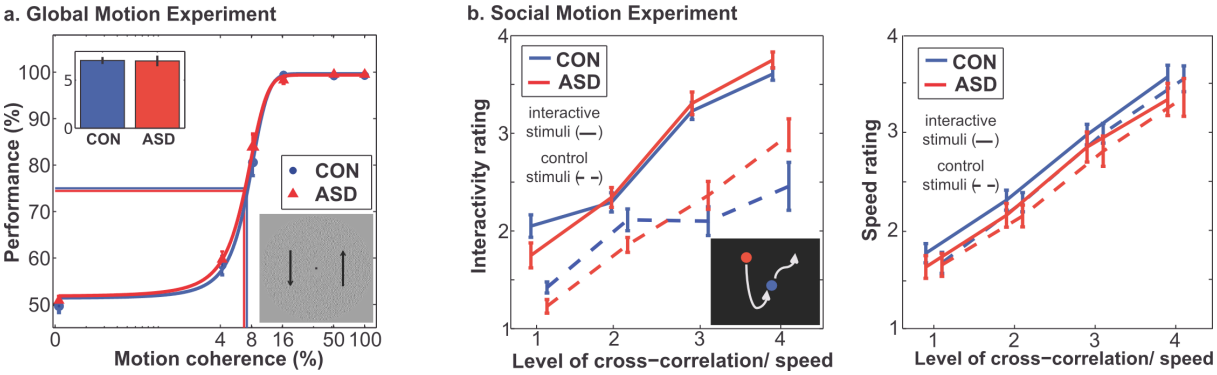
a. Global Motion Experiment
Performance (%)
Motion coherence (%)
CON
ASD
b. Social Motion Experiment
Interactivity rating
Level of cross−correlation/ speed
interactive stimuli (—)
control stimuli (- -)
Speed rating

Figure 2

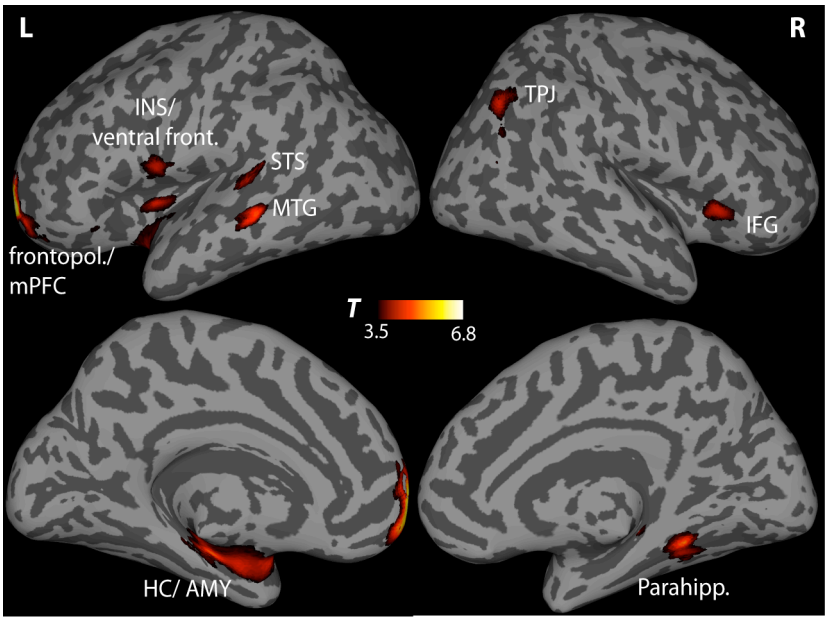
L
R
INS/
ventral front.
STS
MTG
frontopol./
mPFC
TPJ
IFG
T
3.5
6.8
HC/ AMY
Parahipp.

Figure 3

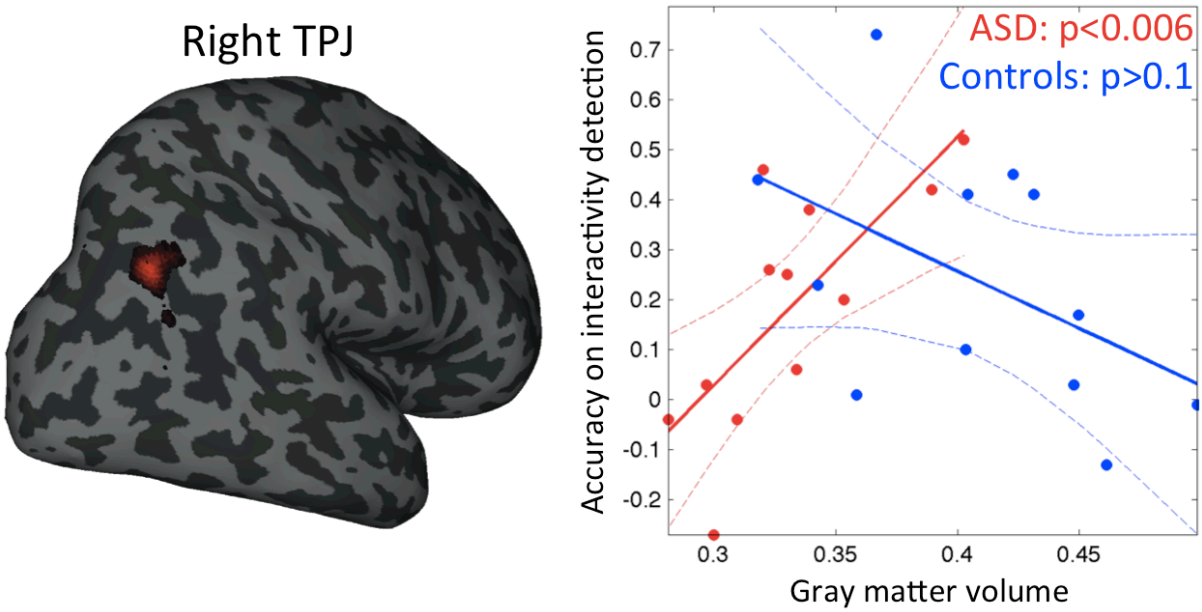
Right TPJ
ASD: p<0.006
Controls: p>0.1
Accuracy on interactivity detection
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
-0.2
0.3
0.35
0.4
0.45
Gray matter volume

Table 1. Sample characteristics (means and standard deviations)

	ASD	CON	
Age (yrs.)	33.2 (7.4)	32.9 (7.6)	F(1,27)=0.01, n.s.
Gender (m:f)	7:8	7:7	$\chi 2$ =0.03, n.s.
Mean verbal IQ[1]	112.7 (13.9)	111.4 (15.1)	F(1,27)=0.002, n.s.
Handedness[2]	67 (31)	82 (22)	F(1,27)=2.52, n.s.
AQ[3]	39.3 (5.5)	15.4 (5.3)	F(1,27)=141.81, p<.001
Visual Scanning [4]	54.3 (30.1)	57.1 (20.1)	F(1,27)=0.09, n.s.
Divided attention [4]	50.7 (36.5)	55.4 (30)	F(1,27)=0.14, n.s.

[1] Estimated using the German verbal "Mehrfach-Wortschatz-Intelligenz-Test" (Lehrl 1995); [2] laterality Quotient assessed with the Edinburgh Handedness Inventory (Oldfield 1971): a score >40 reflects right-handedness, between -40 and +40 ambidexterity, <-40 left-handedness; [3] Autism Spectrum Quotient (Baron-Cohen et al. 2001): a (raw) score of ≥ 32 indicates the probability of an ASD; [4] performance (percentile rank) in Trail Making Test A and B (Reitan 1958). *Abbrev.*: ASD = Autism Spectrum Disorder, CON = control group.

Table 2. Regional gray matter reductions in ASD compared to control participants (at p<0.001 uncorrected, cluster size threshold=411 voxels)

Region	Cluster Extent	Cluster Peak (MNI)			Peak Statistic
	k	X	Y	Z	T (20)
L. Frontopolar Gyrus, extending medially (L FPG)	1425	-20	66	0	6.84
R. Parahippocampal Gyrus (R PHG)	542	36	-43	-5	6.19
R. Inferior Frontal Gyrus extending into insula (R IFG/INS)	579	33	34	-3	5.30
L. Hippocampus, extending to Amygdala (L HC/AMY)	2256	-36	-16	-15	5.17
L. Superior Temporal Sulcus, extending to Middle Temporal Gyrus (L STS)	651	-68	-40	6	5.15
R. Angular Gyrus, extending to the ascending Superior Temporal Sulcus (R TPJ)	430	40	-75	45	4.63
L. Insula extending into inferior frontal gyrus (L INS/INF)	958	-44	6	-2	4.46