Examining the relationship between social cognition and neural synchrony during movies in children with and without autism

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Abstract

Children who have been diagnosed with autism spectrum disorder (ASD) often show a marked deficit in measures of social cognition. In autistic adults, measures of social cognition have been shown to relate to differences in brain synchronization (as measured by fMRI) when individuals are processing naturalistic stimuli, such as movies. However, whether children with impaired social cognition, with or without a diagnosis of ASD, differ in their neural responses to movies has not yet been investigated. In the current study, neural synchrony was examined in three groups of children aged 7 to 12, who differed with respect to their social cognition scores and whether or not they had been diagnosed with ASD. While watching the movie 'Despicable Me', those diagnosed with ASD had significantly less neural synchrony in areas that have been previously shown to be associated with social cognition (e.g. areas related to 'theory of mind'), and plot following (e.g. frontoparietal cortex), than those who did not have an ASD diagnosis. In contrast, two groups who differed in their social cognition scores, but did not have a diagnosis of ASD, showed no significant differences in neural synchrony across the whole brain. These results shed some light on how social cognition contributes to our conscious experience of the world, and how, for children with ASD, that experience may differ markedly from that of those without ASD.

Keywords

Autism spectrum disorder, neural synchrony, fMRI, development, Theory of Mind, social cognition

Introduction

Autism spectrum disorder (ASD) is a complex developmental condition characterised by a variety of neurological and psychological features; however, the most prominent feature of ASD is a marked deficit in 'social cognition'. Social cognition refers to understanding what other people believe, how they will react in situations, and why they feel the way they do, and is a core element of successful human interactions. Autistic individuals perform poorly on tasks that assess social cognition, such as face perception (Spencer et al., 2011), perspective taking (Hamilton et al., 2009), and theory of mind (ToM), or the ability to attribute mental states to oneself and others (Pedreño et al., 2017). One of the most common tools to screen for deficits associated with ASD is the Social Responsiveness Scale, which measures aspects of social awareness, communication, and motivation (Constantino & Gruber, 2012).

The brains of autistic individuals often show differences when compared to those of typically-developing individuals. These include structural abnormalities (Barnea-Goraly et al., 2004; Brieber et al., 2007), functional differences during task based fMRI (Bölte et al., 2008; Gilbert et al., 2008; Just et al., 2007; Mason et al., 2008; Solomon et al., 2009) and changes in resting-state functional connectivity (Cherkassky et al., 2006; Kana et al., 2015; Monk et al., 2009; Weng et al., 2010). Many of the brain regions that show differences in autistic individuals have been linked to ToM in healthy individuals, including the temporal parietal junction (Saxe & Kanwisher, 2003; Saxe & Wexler, 2005), the medial prefrontal cortex (Hartwright et al., 2013; Krause et al., 2012; Völlm et al., 2006), and the posterior superior temporal sulcus (Otsuka et al., 2009; Yang et al., 2015).

Evidence has recently emerged that autistic adults process social information in naturalistic, or 'real-life' contexts differently than typically-developing individuals. Several studies have investigated social processing differences between those with and without ASD by examining brain activity in response to watching movies (Bolton et al., 2018; Byrge et al., 2015; Hasson et al., 2009; Salmi et al., 2013). Movie watching mimics real-world experiences by requiring the viewer to integrate perceptual and cognitive systems in order to follow the complexities of the plot. It is known that the brains of healthy individuals become highly synchronized (or correlated) when viewing the same movie (Hasson, Landesman, et al., 2008). This measure of synchronization across different brains is termed *inter-subject correlation* and high levels of synchrony suggest that individuals are experiencing the movie in much the same way. For example, Naci et al., (2014) noted a high degree of synchrony in frontoparietal regions when healthy individuals watched "Bang You're Dead!" by Alfred Hitchcock and this was shown to relate to how suspenseful and engaging viewers found the movie. The brains of autistic adults have been shown to be less synchronized than those of typically-developing adults during movie watching, and synchrony across individuals tends to be more variable (Bolton et al., 2018; Byrge et al., 2015; Hasson et al., 2009; Salmi et al., 2013). However, this has not been examined in autistic children.

Richardson et al., (2018) have shown that in typically-developing children, those with poorer social cognition have reduced synchrony during movie watching in areas known to be involved with ToM, suggesting that lower synchrony in these areas may also be a feature of autistic children. In the current study, this question was investigated in three groups of children who differed with respect to their social cognition scores and whether or not they had been diagnosed with ASD. Specifically, the differences in the

degree of inter-subject correlation was examined during movie watching in children aged 7 to 12, who had either been diagnosed with ASD, did not have ASD but had low social cognition scores as measured by Social Responsiveness Scale - revised (SRS-2), or did not have ASD and had typical social cognition scores for their age.

On the basis of the existing literature, it was predicted that group differences would emerge in inter-subject correlation within brain networks associated with social cognition. Specifically, it was hypothesized that brain activity within both frontoparietal regions (Naci et al., 2014), and the ToM networks (Richardson et al., 2018) would be less synchronised in children without ASD with low social cognition scores than those with high social cognition scores. Furthermore, it was hypothesized that the brains of children with ASD would be the least synchronised of all, based on their known impairments in many aspects of social cognition.

Methods

Dataset

Data was analyzed from the Healthy Brain Network Biobank collected by the Child Mind Institute (described in Alexander et al., 2017), which is an ongoing initiative to collect neuroimaging, medical, and behavioural data on 10,000 participants between the ages of 5 to 21. The Chesapeake Institutional Review Board approved this study. Detailed information on the dataset can be found at http://fcon_1000.projects.nitrc.org/indi/cmi_healthy_brain_network/

Participants and data acquisition

The Healthy Brain Network Biobank used a community-referred recruitment model to generate a heterogeneous and transdiagnostic sample. Briefly, recruitment involved advertising the study to community members, educators, local care providers, and parents who were on email lists or at events. Potential participants were screened, and were excluded if there were safety concerns, impairments that would interfere with the study procedure (such as being nonverbal or having an IQ of less than 66), and/or medical concerns that could potentially impact brain related findings (for a full description, see Alexander et al., 2017). The study protocol included, where possible, the acquisition of T1 weighted anatomical MRI scans and functional MRI data acquired while the participants watched a ten-minute clip of 'Despicable Me' (from 1:02:09 to 1:12:09). All MRI data was collected on a 3T Siemens scanner using a Siemens 32-channel head coil. Functional images were acquired with a gradient-echo planar imaging pulse sequence (TR =800 ms, TE =30 ms, Flip Angle =31 degrees, whole brain coverage 60 slices, resolution 2.4 x 2.4 mm^2). High-resolution T1-weighted MPRAGE structural images were acquired in 224 sagittal (TR = 2500 ms, TE = 3.15 ms, resolution .8 x .8 mm^2).

From this database, participants were included in the current analysis if they were between the ages of 7-12 and both anatomical and functional MRI data had been successfully acquired. Everyone included in the current study had written consent obtained from their legal guardians and written assent obtained from the participant. All participants also had scores on the Social Responsiveness Scale Revised (SRS-2), which is a measure of social reciprocity and communication associated with deficits in ASD (Constantino & Gruber, 2012). Specifically, the SRS-2 assesses deficits associated with

social awareness, social cognition, social communication, social motivation, and restrictive interests and repetitive behavior, and is rated by parents or caregivers of the child. A score of 59 or below suggests that the child does not have social difficulties associated with ASD. A score above 59 is suggestive of difficulties in social functioning. All included participants had also been assessed by a clinician using the Autism Diagnostic Observation Schedule – 2nd edition (Gotham et al., 2006), and those who met the relevant criteria were diagnosed with ASD.

Participants were divided into three groups: The "High Social Cognition" (HSC) group included those who had an SRS-2 score ≤ 59; the "Low Social Cognition (LSC)" group included participants who had an SRS-2 score of ≥ 60 (the ASD screener cut-off), but were not diagnosed with ASD; and the Autism Spectrum Group (ASD) included participants who were diagnosed with ASD by a clinician as part of the HBN protocol (for details, see Table 1).

Because the groups differed with respect to age and sex, the HSC and LSC groups were resampled to produce three demographically matched sub-groups. Specifically, for each participant in the ASD group, an HSC and an LSC individual who had the same sex and was closest in age (to the month) were selected for inclusion where possible (see Table 1). This resulted in three groups of 28 participants, ensuring sufficient power for acquiring reliable inter-subject correlation results (Pajula & Tohka, 2016).

Table 1 Participant demographics

Measure	Group		
	HSC	LSC	ASD
Full Sample:			
N	64	34	28
Mean Age (SD)	9.9 (1.74)	9.32 (1.63)	9.42 (1.68)
Sex (F/M)	27/37	13/21	2/26
SRS-2 (SD)	49.6(4.82)	67.5 (5.79)	76.6 (10.48)
Matched Sample:			
N	28	28	28
Mean Age (SD)	9.42(1.64)	9.54 (1.25)	9.42 (1.64)
Sex (F/M)	3/25	7/21	2/26
SRS-2 (SD)	48.57 (4.81)	67.20 (5.90)	76.57 (10.48)
Mean IQ (SD)	103 (18)	95.5 (14.8)	92.7 (18.1)

MRI pre-processing

For the current study, the MRI data were preprocessed and analyzed using the Automatic Analysis (AA) toolbox (Cusack et al., 2015), SPM8, and in-house Matlab scripts. Pre-processing of functional data included motion correction (using six motion parameters: left/right, anterior/posterior, superior/inferior, chin up/down, top of head left/right, nose left/right), functional and structural scans were co-registered and normalized to the Montreal Neurological Institute (MNI) template. Functional data were then spatially smoothed using a Gaussian filter (8 mm kernel), and low-frequency noise (e.g., drift) was removed by high-pass filtering with a threshold of 1/128 Hz. The data was denoised using Bandpass filter regressors, with cerebrospinal fluid, white matter

signals, motion parameters, their lag-3 2nd-order volterra expansion (Friston et al., 2000), and "spikes" (based on mean signal variance across volumes) as nuisance regressors.

Whole brain synchronization

To determine the degree of synchronization separately for each group, the degree of inter-subject correlation across the whole brain was calculated using a leave-one-out approach. That is, the pre-processed time course of every voxel was correlated (Pearson and then Fisher z-transformed) between each participant and the mean time course of every voxel from the rest of the group (N-1). A one-sample t-test was calculated on the resulting individual brain-wide correlation values. Multiple comparisons were corrected with a false discovery rate (FDR) of .05 to generate group maps of significantly correlated voxels. To identify where in the brain inter-subject correlation differences existed between the three groups, t-tests were performed on the correlation values at each voxel derived for all of the individuals within each group. Multiple comparisons were corrected with an FDR of .05.

Network of interest inter-subject correlation

The degree of synchronization within eight previously defined functional networks was calculated. To address our specific hypotheses, a map for the ToM network was used (Dufour et al., 2013) as well as the frontoparietal network from the Yeo et al., (2011) parcellation. Six additional networks (Visual, Dorsal Attention, Ventral Attention, Somatomotor, Limbic, Default Mode Network) from Yeo et al. (2011) were also included in an exploratory analysis to examine potential differences in other areas of the brain. Similar to the whole brain inter-subject correlation analysis, the within group inter-

subject correlation for each of these eight networks was calculated using a leave-one-out approach. Specifically, the time course of each network (based on the average time course of each voxel within the network) for each participant was correlated with the average time course of each network for the remaining participants in the group, minus that participant (N-1). The degree of between group inter-subject correlation was then calculated, by taking the mean time course for each individual in one group and correlating it with the mean of the two other groups. This generated a correlation value that reflected how similar each participant's time course was to the two other groups. Finally, we used a general linear model to determine if group membership was a significant predictor of both within and between group synchronization. The networks that showed a significant effect of group were followed up with Welch t-tests (all results were FDR corrected to .05). To calculate the total percentage of cortex that was synchronized, the number of voxels that were significant per group were divided by the total number of voxels in the brain. To calculate the total percentage of each network that was synchronized, the number of voxels that were significant per group were divided by the total number of voxels in the region of interest.

Cluster-based inter-subject correlation analysis

To explore the potential relationship between SRS-2 scores and inter-subject correlation, pairwise correlations were also calculated between the mean time course for each participant and that of every other participant in the ToM and frontoparietal networks. These pairwise correlations were then plotted in a matrix by ranking each participant by their SRS-2 score (from low to high). Because SRS-2 scores were skewed (upwards) in the ASD and LSC groups, this analysis included all participants (N = 126),

rather than the smaller matched groups. Finally, a clustering analysis was conducted to determine whether groups of participants could be identified based solely on their neural synchronization, rather than group membership or SRS-2 scores. To do this, a k-means clustering algorithm was used to group together participants using the time series of neural activity in the ToM and frontoparietal networks. The MATLAB evalclusters function was used to identify the optimal number of clusters based on the variance in the data using the Calinski-Harabasz Index computed over 1000 iterations to minimize the fitting parameter. Based on the groupings generated from this cluster analysis, a regression analysis was computed to investigate which factors (SRS-2 total and subscale scores, age, sex, and social cognition group membership) best predicted the cluster-generated groupings.

Results

There was a total of 267 eligible participants who met the inclusion criteria (see Methods). Of this sample, 141 participants were excluded because of failed registration, excessive motion, or because 25% or more of the data contained large 'spikes' (significant fluctuations in signal intensity).

There was a significant difference between the three groups in terms of SRS-2 scores ($F_{(2,81)} = 101.76$, p < .001) and post-hoc t-tests showed that the LSC group had significantly higher scores than the HSC group ($t_{(51.9)} = 12.96$, p < .001) and had significantly lower scores than the ASD group ($t_{(42.54)} = 4.12$, p < .001). There were no significant differences between the groups on the Wechsler's Intelligence Scale for Children (WISC) full scale IQ scores ($F_{(2,80)} = 2.71$, $p = .073$), or any of the WISC subscales except for working memory; ($F_{(2,80)} = 3.29$, $p = .042$). The ASD group had

significantly lower working memory scores compared to the HSC group ($t_{(52.10)} = 2.35$, p = .023) but not the LSC group ($t_{(50.24)} = 1.05$, $p = .30$).

Differences in correlated motion within each group were examined, in order to ensure that this did not inflate the inter-subject correlation results. Correlated motion was calculated separately for each group, by taking each participant's 6 motion parameters for each frame and correlating the time course with that of the mean of the rest of the group (N-1). No significant differences were found between the groups in their degree of correlated motion ($F_{(2,81)} = .181$, p = .835).

Whole brain synchronization

Whole brain synchronization was characterized in the three different social cognition groups. All groups showed significant synchronization in the auditory and visual areas (Figure 1a). In fact, synchronization in these areas was stronger than in any other brain areas, replicating previous inter-subject correlation findings during movie watching (Hasson et al., 2008). The LSC and HSC groups also showed significant inter-subject correlation in areas associated with ToM and executive processing, including parts of the right and left temporal parietal junction, the precuneus, the intraparietal sulcus, the superior parietal lobe, and portions of the medial and lateral prefrontal cortex. In contrast, the ASD group had very little significant inter-subject correlation outside of visual and auditory areas (see Figure 1a, bottom row).

Next, whole brain contrasts were conducted (Figure 1b) to examine whether the magnitude of synchronization differed between the three groups. The HSC group showed significantly greater inter-subject correlation than the ASD group in bilateral temporal parietal junction, precuneus, right posterior superior temporal sulcus, right hippocampus,

and in regions of the lateral and medial prefrontal cortex (Figure 1b, middle row). The

LSC group had significantly greater synchronization than the ASD group in the

precuneus, right hippocampus, and in regions of the lateral and medial prefrontal cortex

(Figure 1b, bottom row). When the HSC group was contrasted to the LSC group, only

tiny areas of difference were observed after multiple comparisons corrections, in the

inferior temporal gyrus and white matter (see Figure 1b, top row).

Figure 1 Whole brain inter-subject correlation analysis. **a)** Voxels displayed in red showed significant inter-subject correlation during movie watching in the HSC group. Voxels displayed in violet showed significant inter-subject correlation in the LSC group. Voxels displayed in blue showed significant inter-subject correlation in the ASD group. All p values were FDR corrected to an alpha of .05. **b)** Whole brain contrasts were calculated by conducting one-tailed t-tests on the inter-subject correlation values between each group (p values corrected to a FDR of .05). Voxels displayed in red showed significantly greater inter-subject correlation values based on this contrast.

Network based synchronization

Group differences in the magnitude of synchronization in each network revealed a

main effect of group in the ToM (F $_{(2,81)}$ = 4.94, *p* = .009) and the limbic (F $_{(2,81)}$ = 3.93, p

= .023) networks (Figure 2), but not in any of the others examined, including the

frontoparietal network ($F_{(2,81)}$ = 2.02, p = .140, Cohen's d ranged from .037 to .476).

Post-hoc analyses of neural synchronization revealed that the ASD group had

significantly lower inter-subject correlation values compared to the HSC group within the

ToM ($t_{(50.11)}$ = 3.50, $p_{corrected}$ = .006, Cohen's d = .934) and limbic networks ($t_{(50.00)}$ =

2.48, $p_{corrected}$ = .044, Cohen's d = .664). They also had significantly lower inter-subject

correlation values compared to the LSC group in the limbic network ($t_{(50.21)}$ = 2.18,

$p_{corrected}$ = .044, Cohen's d = .631), although differences in inter-subject correlation just

failed to meet the corrected alpha level in the ToM network ($t_{(52.33)}$ = 2.36, $p_{corrected}$ =

.0504, Cohen's d = .584). Moreover, no significant differences in inter-subject correlation

were observed between the HSC and LSC groups within the ToM ($t_{(45.72)}$ = .488, $p_{corrected}$

=.628, Cohen's d = .130) or limbic networks ($t_{(45.21)}$ = .417, $p_{corrected}$ =.628, Cohen's d =

.111).

Figure 2 Within group network of interest analysis. Mean inter-subject correlation, based on the leave one out correlation analysis conducted separately for each group, is displayed as dots for each participant in the eight networks. Boxplots indicate the median inter-subject correlation value and interquartile range for each group (blue = HSC, yellow = LSC, red = ASD). The ASD group had significantly lower inter-subject correlation in the limbic and ToM networks compared to the HSC group. The ASD group also had significantly lower inter-subject correlation in the limbic network compared to the LSC group, while in the ToM network this difference narrowly missed statistical significance (corrected p value = .0504). The groups did not differ significantly in any of the six other networks.

A between group network analysis was performed to investigate whether individuals in one group had significantly greater neural synchronization with their own group than that of the other two groups. The results revealed that the degree of inter-subject correlation was not significantly different between any of the groups in any of the examined networks, including the frontoparietal and ToM networks.

When looking at the percentage of synchronized voxels across the whole brain, the ASD group had nearly one-third less (38%) than the HSC (56%) and LSC (52%) groups (see Figure 3). The percentage of significant voxels in each of the eight networks of interest was also calculated (see Figure 3). The difference in percentage across the whole brain between the groups was not accounted for by less synchronization in any one network; rather, the ASD group had fewer synchronized voxels in every network, including in the ToM and frontoparietal networks.

Figure 3 Percentage of correlated voxels. Percent was calculated by dividing the number of voxels with significant inter-subject correlation by the total number of voxels in the whole brain or network for each group separately (blue = HSC, yellow = LSC, red = ASD).

Cluster-based inter-subject correlation analysis

Pairwise inter-subject correlation was calculated between each participant (N=126) in the frontoparietal and ToM networks, and the matrix of pairwise correlation values was plotted by ranking each participant by their SRS-2 score, from low to high (see Figure 4a). A k-means clustering analysis was conducted on the pairwise correlations to explore potential factors that predicted groups of participants who have the most similar degree of synchrony in these two networks. The best fit was achieved by dividing the data into two clusters in both the frontoparietal and ToM networks; cluster 1 included individuals with similar neural responses to the movie (large positive correlations) and cluster 2 included individuals with unrelated neural responses to the movie (Figure 4b). Moreover, there was also a large overlap between the participants who were in cluster 1 in the ToM and frontoparietal networks. Specifically, of the 58 participants who had high similarity in the ToM network (cluster 1), 45 of them also had high similarity in the frontoparietal network.

Figure 4 Pairwise inter-subject correlations. Yellow squares indicate a high positive correlation (i.e. high similarity in time series), blue squares indicated a low or negative correlation (i.e. low similarity in time series). **a)** Pairwise correlations in time series in the frontoparietal and ToM networks between each pair of participants are ordered by SRS-2 scores (from low to high). **b)** Pairwise correlations in time series are ordered based on the K means analysis in the frontoparietal and ToM networks. Black boxes indicate cluster 1 (the high similarity group) for each network.

Logistic regression was run to determine whether the probability of being in cluster 1 versus cluster 2 could be predicted by age, sex, full scale IQ, SRS-2 total and subscales, or social cognition group (i.e., HSC, LSC and ASD). None of these factors significantly predicted cluster membership in the frontoparietal network. However, in the ToM network, social cognition group significantly predicted cluster membership. Cluster 1 comprised 35 participants (60%) in the HSC group, 17 individuals (29%) from the LSC groups, and 6 individuals (10%) who were diagnosed with ASD. In contrast, cluster 2 consisted of 29 individuals (45%) from the HSC group, 17 individuals (20%) from the LSC group, and 22 individuals (35%) diagnosed with ASD. There were significantly

more participants from the ASD group in cluster 2 than in cluster 1 in the ToM network

($X^2 = 8.63$, p = .003).

Discussion

In the current study, a group of ASD participants had significantly less neural

synchronization when watching a movie compared to the HSC and LSC groups across

the whole brain, including in areas within the ToM, limbic, default mode, and

frontoparietal (i.e., lateral prefrontal cortex) networks. All of these networks have been

shown previously to be associated with elements of 'plot following' during movie

watching (Hasson, Furman, et al., 2008; Hasson, Landesman, et al., 2008; Naci et al.,

2014; Nguyen et al., 2019), suggesting that the children in the ASD group were

experiencing the movie qualitatively differently than the participants in the other two

groups. These results, in particular the fact that the ToM network was less synchronised

in the ASD group, are intriguing given that regions within this network are associated

with social cognition (Dufour et al., 2013; Mills et al., 2014; Richardson et al., 2018;

Rilling et al., 2004), which is known to be affected in ASD (Hamilton et al., 2009;

Pedreño et al., 2017; Spencer et al., 2011). While aspects of social cognition are usually

discussed in the context of inter-personal relationships, they are also essential

components of movie-watching, allowing one to become immersed in the plot by taking

the perspective of the characters appropriately, understanding their motives, and

following their verbal and nonverbal communication cues. Yeshurun et al., 2017 have

reported previously that manipulating an individual's understanding of a plot reduces

neural synchrony in ToM regions, including the precuneus, temporal parietal junction,

and medial prefrontal cortex. Thus, these findings support the idea that autistic children

process social stimuli in a distinct way, as they have different neural responses in the ToM network during a movie, when compared to children without ASD.

It is also interesting that participants in the ASD group had significantly less synchrony in regions of the frontoparietal network when compared to those in the other two groups. Understanding a complex narrative (such as a movie's plot) requires a viewer to remember previous events, pay attention to what is currently happening, make predictions about the future consequences of current events, and integrate this information over time, all of which depends on frontoparietal executive processing (Naci et al., 2014). In previous studies, reduced synchrony in this network has been associated with 'losing the plot' during deep sedation (Naci et al., 2018), and in patients with severe brain damage (Naci et al., 2014). Thus, this decrease in inter-subject correlation in the frontoparietal network likely suggests that participants in the ASD group are also failing to grasp elements of the plot in the way that the other participants do.

Despite finding that inter-subject correlation was reduced in prefrontal regions using a whole brain analysis, no differences in the degree of inter-subject correlation were found in the frontoparietal network when a network of interest analysis was used. One potential reason is that the parcellation used for the frontoparietal network was based on adult data and may not accurately capture this network in children. Previous work has shown that the frontoparietal network continues to develop into early adulthood (Baum et al., 2017; Peters et al., 2016), and so the parcellation masks from Yeo et al., (2011) may have led us to average neural activity from regions that are not yet fully integrated in children.

While not part of our hypotheses, it is interesting that the ASD group showed less inter-subject correlation in the right hippocampus in the whole brain analysis as well as in

the limbic network, when examined using the parcellation by Yeo et al (2011). Similar findings have been reported in autistic adults watching movies (Byrge et al., 2015). Moreover, Chen et al., (2017) found that, in healthy adults, the degree of inter-subject correlation within the hippocampus during movie watching predicted events that were later recalled, although this has not been examined during development. Nevertheless, long-term memory deficits have been reported in ASD; specifically, autistic individuals perform worse on episodic, but not semantic, memory tasks (Crane & Goddard, 2008; Lind, 2010)

Contrary to our hypothesis, no meaningful differences in neural synchrony were found between the HSC and LSC groups. This contrasts with the results of Richardson et al., (2018) who found that social cognition in typically-developing children was related to the degree of inter-subject correlation within the ToM network during movie-watching. One potential reason for this difference is that Richardson et al., (2018) calculated inter-subject correlation based on how similar each child's time course was to a group of adults watching the same movie, whereas in the current study, inter-subject correlation was calculated by correlating each participant's time course to the mean of their own group. Moreover, the measure of social cognition used by Richardson et al. (2018) focused specifically on comprehension of a social narrative, which has many things in common with how people follow the plot of a movie. It is perhaps not surprising then, that the two things correlated. In the current study, a composite measure of social cognition was used – the SRS-2, which measures an individual's motivation to engage in social interactions, their use of social communication, and their ability to understand social cues (Constantino & Gruber, 2012) and this may have given a more holistic picture of social cognition. Thus, while the LSC and HSC groups differed in terms of their social

cognitive abilities as measured by the SRS-2 scale, these mechanisms may be unrelated, or only moderately related, to those that are involved in plot following. Taken together, these results suggest that it is only when social cognition is in the clinical range, as is seen in ASD, that differences in conscious processing of naturalistic stimuli emerge.

As a group, autistic participants had less inter-subject correlation compared to those without ASD, but these differences did not apply uniformly to each individual. The clustering analysis indicated that the majority of ASD participants had low similarity in their time courses compared to all other participants. However, six out of 28 of those diagnosed with ASD clustered with the 'high similarity' group (comprising about 10% of the group) according to their synchronization in the ToM network. Using a similar clustering analysis, Byrge et al., (2015) found that in a sample of 17 high functioning autistic adults, five showed idiosyncratic patterns of inter-subject correlation compared to typically-developing individuals, while the other 12 clustered with the control group. Moreover, they found that these five individuals were significantly worse than the control group and the other 12 ASD participants, when asked to explain elements of a movie plot. Together, these findings suggest that lower synchronization during movie-watching may be common, but not a uniform characteristic of either autistic children or adults. Indeed, heterogeneity in clinical features, cognitive profiles, and differing genetic and environmental risk factors has plagued research in ASD (Betancur, 2011; Jeste & Geschwind, 2014; Lenroot & Yeung, 2013). For example, within the neuroimaging literature, some studies have reported underconnectivity across the brains of autistic individuals (Cherkassky et al., 2006; Di Martino et al., 2014; von dem Hagen et al., 2013), while others find hyperconnectivity (Supekar et al., 2013; Uddin et al., 2010, 2013).

Finally, it is important to keep in mind the exploratory nature of the current study when interpreting these findings. This is a step towards a better understanding of how children with and without ASD process naturalistic stimuli, but replication and further investigation is needed to better understand the nature of the differences observed. A memory test, or some measure of how well the movie clip was understood, may help to explain the nature of the neural differences observed in this study.

Conclusion

In sum, the current results suggest that autistic children, as a group, process movies in a unique way compared to those without ASD. Interestingly, a minority of these children had time courses that were highly correlated with a group of children without ASD in the ToM network. Future research should investigate factors that underlie this heterogeneity, as this may be one avenue to better understand how autistic individuals process the world around them.

Author contributions

Conceptualization, writing–reviewing and editing, K.M.L., R.A.S, A.M.O, B.S.;

Methodology, Formal analysis, K.M.L., B.S.; writing–original draft preparation, K.M.L.,

B.S., A.M.O; funding acquisition, A.M.O.

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Conflict of interest

The authors have no conflicts of interest to declare.

References

Alexander, L. M., Escalera, J., Ai, L., Andreotti, C., Febre, K., Mangone, A., ... & Litke, S. (2017). The Healthy Brain Network Biobank: An open resource for transdiagnostic research in pediatric mental health and learning disorders.

Barnea-Goraly, N., Kwon, H., Menon, V., Eliez, S., Lotspeich, L., & Reiss, A. L. (2004). White matter structure in autism: Preliminary evidence from diffusion tensor imaging. *Biological Psychiatry*, *55*(3), 323–326. https://doi.org/10.1016/j.biopsych.2003.10.022

Baum, G. L., Ciric, R., Roalf, D. R., Betzel, R. F., Moore, T. M., Shinohara, R. T., Kahn, A. E., Vandekar, S. N., Rupert, P. E., Quarmley, M., Cook, P. A., Elliott, M. A., Ruparel, K., Gur, R. E., Gur, R. C., Bassett, D. S., & Satterthwaite, T. D. (2017). Modular Segregation of Structural Brain Networks Supports the Development of Executive Function in Youth. *Current Biology*, *27*(11), 1561-1572.e8. https://doi.org/10.1016/j.cub.2017.04.051

Betancur, C. (2011). Etiological heterogeneity in autism spectrum disorders: More than 100 genetic and genomic disorders and still counting. *Brain Research*, *1380*, 42–77. https://doi.org/10.1016/j.brainres.2010.11.078

Bölte, S., Hubl, D., Dierks, T., Holtmann, M., & Poustka, F. (2008). An fMRI-study of locally oriented perception in autism: Altered early visual processing of the block design test. *Journal of Neural Transmission*, *115*(3), 545–552. https://doi.org/10.1007/s00702-007-0850-1

Bolton, T. A. W., Jochaut, D., Giraud, A.-L., & Ville, D. V. D. (2018). Brain dynamics in ASD during movie-watching show idiosyncratic functional integration and

segregation. *Human Brain Mapping*, *39*(6), 2391–2404.

https://doi.org/10.1002/hbm.24009

Brieber, S., Neufang, S., Bruning, N., Kamp-Becker, I., Remschmidt, H., Herpertz-
Dahlmann, B., Fink, G. R., & Konrad, K. (2007). Structural brain abnormalities in
adolescents with autism spectrum disorder and patients with attention
deficit/hyperactivity disorder. *Journal of Child Psychology and Psychiatry*,
48(12), 1251–1258. https://doi.org/10.1111/j.1469-7610.2007.01799.x

Byrge, L., Dubois, J., Tyszka, J. M., Adolphs, R., & Kennedy, D. P. (2015). Idiosyncratic
Brain Activation Patterns Are Associated with Poor Social Comprehension in
Autism. *Journal of Neuroscience*, *35*(14), 5837–5850.

https://doi.org/10.1523/JNEUROSCI.5182-14.2015

Chen, J., Leong, Y. C., Honey, C. J., Yong, C. H., Norman, K. A., & Hasson, U. (2017).
Shared memories reveal shared structure in neural activity across individuals.
Nature Neuroscience, *20*(1), 115–125. https://doi.org/10.1038/nn.4450

Cherkassky, V. L., Kana, R. K., Keller, T. A., & Just, M. A. (2006). Functional
connectivity in a baseline resting-state network in autism. *NeuroReport*, *17*(16),
1687–1690. https://doi.org/10.1097/01.wnr.0000239956.45448.4c

Constantino, J. N., & Gruber, C. P. (2012). *Social Responsiveness Scale–Second Edition
(SRS-2)*. Western Psychological Services.

Crane, L., & Goddard, L. (2008). Episodic and Semantic Autobiographical Memory in
Adults with Autism Spectrum Disorders. *Journal of Autism and Developmental
Disorders*, *38*(3), 498–506. https://doi.org/10.1007/s10803-007-0420-2

Cusack, R., Vicente-Grabovetsky, A., Mitchell, D. J., Wild, C. J., Auer, T., Linke, A. C.,
& Peelle, J. E. (2015). Automatic analysis (aa): Efficient neuroimaging workflows

and parallel processing using Matlab and XML. *Frontiers in Neuroinformatics*, *8*.

https://doi.org/10.3389/fninf.2014.00090

Di Martino, A., Yan, C.-G., Li, Q., Denio, E., Castellanos, F. X., Alaerts, K., Anderson,

J. S., Assaf, M., Bookheimer, S. Y., Dapretto, M., Deen, B., Delmonte, S.,

Dinstein, I., Ertl-Wagner, B., Fair, D. A., Gallagher, L., Kennedy, D. P., Keown,

C. L., Keysers, C., … Milham, M. P. (2014). The autism brain imaging data

exchange: Towards a large-scale evaluation of the intrinsic brain architecture in

autism. *Molecular Psychiatry*, *19*(6), 659–667.

https://doi.org/10.1038/mp.2013.78

Dufour, N., Redcay, E., Young, L., Mavros, P. L., Moran, J. M., Triantafyllou, C.,

Gabrieli, J. D. E., & Saxe, R. (2013). Similar Brain Activation during False Belief

Tasks in a Large Sample of Adults with and without Autism. *PLoS ONE*, *8*(9).

https://doi.org/10.1371/journal.pone.0075468

Gilbert, S. J., Bird, G., Brindley, R., Frith, C. D., & Burgess, P. W. (2008). Atypical

recruitment of medial prefrontal cortex in autism spectrum disorders: An fMRI

study of two executive function tasks. *Neuropsychologia*, *46*(9), 2281–2291.

https://doi.org/10.1016/j.neuropsychologia.2008.03.025

Gotham, K., Risi, S., Pickles, A., & Lord, C. (2006). The Autism Diagnostic Observation

Schedule (ADOS). *Journal of Autism and Developmental Disorders*.

Hamilton, A. F., Brindley, R., & Frith, U. (2009). Visual perspective taking impairment

in children with autistic spectrum disorder. *Cognition*, *113*(1), 37–44.

https://doi.org/10.1016/j.cognition.2009.07.007

Hartwright, C. E., Apperly, I. A., & Hansen, P. C. (2013). Representation, Control, or

Reasoning? Distinct Functions for Theory of Mind within the Medial Prefrontal

Cortex. *Journal of Cognitive Neuroscience*, *26*(4), 683–698.

https://doi.org/10.1162/jocn_a_00520

Hasson, U., Avidan, G., Gelbard, H., Vallines, I., Harel, M., Minshew, N., & Behrmann,

M. (2009). Shared and idiosyncratic cortical activation patterns in autism revealed

under continuous real-life viewing conditions. *Autism Research*, *2*(4), 220–231.

https://doi.org/10.1002/aur.89

Hasson, U., Furman, O., Clark, D., Dudai, Y., & Davachi, L. (2008). Enhanced

Intersubject Correlations during Movie Viewing Correlate with Successful

Episodic Encoding. *Neuron*, *57*(3), 452–462.

https://doi.org/10.1016/j.neuron.2007.12.009

Hasson, U., Landesman, O., Knappmeyer, B., Vallines, I., Rubin, N., & Heeger, D. J.

(2008). Neurocinematics: The Neuroscience of Film. *Projections*, *2*(1), 1–26.

https://doi.org/10.3167/proj.2008.020102

Jeste, S. S., & Geschwind, D. H. (2014). Disentangling the heterogeneity of autism

spectrum disorder through genetic findings. *Nature Reviews. Neurology*, *10*(2),

74–81. https://doi.org/10.1038/nrneurol.2013.278

Just, M. A., Cherkassky, V. L., Keller, T. A., Kana, R. K., & Minshew, N. J. (2007).

Functional and Anatomical Cortical Underconnectivity in Autism: Evidence from

an fMRI Study of an Executive Function Task and Corpus Callosum

Morphometry. *Cerebral Cortex*, *17*(4), 951–961.

https://doi.org/10.1093/cercor/bhl006

Kana, R. K., Maximo, J. O., Williams, D. L., Keller, T. A., Schipul, S. E., Cherkassky, V.

L., Minshew, N. J., & Just, M. A. (2015). Aberrant functioning of the theory-of-

mind network in children and adolescents with autism. *Molecular Autism*, *6*(1),

    59. https://doi.org/10.1186/s13229-015-0052-x

Krause, L., Enticott, P. G., Zangen, A., & Fitzgerald, P. B. (2012). The role of medial

    prefrontal cortex in theory of mind: A deep rTMS study. *Behavioural Brain*

    Research, *228*(1), 87–90. https://doi.org/10.1016/j.bbr.2011.11.037

Lenroot, R. K., & Yeung, P. K. (2013). Heterogeneity within Autism Spectrum

    Disorders: What have We Learned from Neuroimaging Studies? *Frontiers in*

    Human Neuroscience, *7*, 733. https://doi.org/10.3389/fnhum.2013.00733

Lind, S. E. (2010). Memory and the self in autism: A review and theoretical framework.

    Autism, *14*(5), 430–456. https://doi.org/10.1177/1362361309358700

Mason, R. A., Williams, D. L., Kana, R. K., Minshew, N., & Just, M. A. (2008). Theory

    of Mind disruption and recruitment of the right hemisphere during narrative

    comprehension in autism. *Neuropsychologia*, *46*(1), 269–280.

    https://doi.org/10.1016/j.neuropsychologia.2007.07.018

Mills, K. L., Lalonde, F., Clasen, L. S., Giedd, J. N., & Blakemore, S.J. (2014).

    Developmental changes in the structure of the social brain in late childhood and

    adolescence. *Social Cognitive and Affective Neuroscience*, *9*(1), 123–131.

    https://doi.org/10.1093/scan/nss113

Monk, C. S., Peltier, S. J., Wiggins, J. L., Weng, S.-J., Carrasco, M., Risi, S., & Lord, C.

    (2009). Abnormalities of intrinsic functional connectivity in autism spectrum

    disorders,. *NeuroImage*, *47*(2), 764–772.

    https://doi.org/10.1016/j.neuroimage.2009.04.069

Naci, L., Cusack, R., Anello, M., & Owen, A. M. (2014). A common neural code for

    similar conscious experiences in different individuals. *Proceedings of the*

National Academy of Sciences, *111*(39), 14277–14282.

https://doi.org/10.1073/pnas.1407007111

Naci, L., Haugg, A., MacDonald, A., Anello, M., Houldin, E., Naqshbandi, S., Gonzalez-

Lara, L. E., Arango, M., Harle, C., Cusack, R., & Owen, A. M. (2018). Functional

diversity of brain networks supports consciousness and verbal intelligence.

Scientific Reports, *8*. https://doi.org/10.1038/s41598-018-31525-z

Nguyen, M., Vanderwal, T., & Hasson, U. (2019). Shared understanding of narratives is

correlated with shared neural responses. *NeuroImage*, *184*, 161–170.

https://doi.org/10.1016/j.neuroimage.2018.09.010

Otsuka, Y., Osaka, N., Ikeda, T., & Osaka, M. (2009). Individual differences in the

theory of mind and superior temporal sulcus. *Neuroscience Letters*, *463*(2), 150–

153. https://doi.org/10.1016/j.neulet.2009.07.064

Pajula, J., & Tohka, J. (2016). How Many Is Enough? Effect of Sample Size in Inter-

Subject Correlation Analysis of fMRI. *Computational Intelligence and*

Neuroscience. https://doi.org/10.1155/2016/2094601

Pedreño, C., Pousa, E., Navarro, J. B., Pàmias, M., & Obiols, J. E. (2017). Exploring the

Components of Advanced Theory of Mind in Autism Spectrum Disorder. *Journal*

of Autism and Developmental Disorders, *47*(8), 2401–2409.

https://doi.org/10.1007/s10803-017-3156-7

Peters, S., Van Duijvenvoorde, A. C. K., Koolschijn, P. C. M. P., & Crone, E. A. (2016).

Longitudinal development of frontoparietal activity during feedback learning:

Contributions of age, performance, working memory and cortical thickness.

Developmental Cognitive Neuroscience, *19*, 211–222.

https://doi.org/10.1016/j.dcn.2016.04.004

Richardson, H., Lisandrelli, G., Riobueno-Naylor, A., & Saxe, R. (2018). Development

of the social brain from age three to twelve years. *Nature Communications*, *9*(1),

1027. https://doi.org/10.1038/s41467-018-03399-2

Rilling, J. K., Sanfey, A. G., Aronson, J. A., Nystrom, L. E., & Cohen, J. D. (2004). The

neural correlates of theory of mind within interpersonal interactions. *NeuroImage*,

22(4), 1694–1703. https://doi.org/10.1016/j.neuroimage.2004.04.015

Salmi, J., Roine, U., Glerean, E., Lahnakoski, J., Nieminen-von Wendt, T., Tani, P.,

Leppämäki, S., Nummenmaa, L., Jääskeläinen, I. P., Carlson, S., Rintahaka, P., &

Sams, M. (2013). The brains of high functioning autistic individuals do not

synchronize with those of others. *NeuroImage: Clinical*, *3*, 489–497.

https://doi.org/10.1016/j.nicl.2013.10.011

Saxe, R, & Kanwisher, N. (2003). People thinking about thinking people: The role of the

temporo-parietal junction in "theory of mind." *NeuroImage*, *19*(4), 1835–1842.

https://doi.org/10.1016/S1053-8119(03)00230-1

Saxe, R., & Wexler, A. (2005). Making sense of another mind: The role of the right

temporo-parietal junction. *Neuropsychologia*, *43*(10), 1391–1399.

https://doi.org/10.1016/j.neuropsychologia.2005.02.013

Solomon, M., Ozonoff, S. J., Ursu, S., Ravizza, S., Cummings, N., Ly, S., & Carter, C. S.

(2009). The neural substrates of cognitive control deficits in autism spectrum

disorders. *Neuropsychologia*, *47*(12), 2515–2526.

https://doi.org/10.1016/j.neuropsychologia.2009.04.019

Spencer, M. D., Holt, R. J., Chura, L. R., Suckling, J., Calder, A. J., Bullmore, E. T., &

Baron-Cohen, S. (2011). A novel functional brain imaging endophenotype of

autism: The neural response to facial expression of emotion. *Translational Psychiatry*, *1*(7), e19–e19. https://doi.org/10.1038/tp.2011.18

Supekar, K., Uddin, L. Q., Khouzam, A., Phillips, J., Gaillard, W. D., Kenworthy, L. E., Yerys, B. E., Vaidya, C. J., & Menon, V. (2013). Brain Hyperconnectivity in Children with Autism and its Links to Social Deficits. *Cell Reports*, *5*(3), 738–747. https://doi.org/10.1016/j.celrep.2013.10.001

Yeo, T. H., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., Roffman, J. L., Smoller, J. W., Zöllei, L., Polimeni, J. R., Fischl, B., Liu, H., & Buckner, R. L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, *106*(3), 1125–1165. https://doi.org/10.1152/jn.00338.2011

Uddin, L. Q., Supekar, K., & Menon, V. (2010). Typical and atypical development of functional human brain networks: Insights from resting-state fMRI. *Frontiers in Systems Neuroscience*, *4*. https://doi.org/10.3389/fnsys.2010.00021

Uddin, L. Q., Supekar, K., & Menon, V. (2013). Reconceptualizing functional brain connectivity in autism from a developmental perspective. *Frontiers in Human Neuroscience*, *7*. https://doi.org/10.3389/fnhum.2013.00458

Völlm, B. A., Taylor, A. N. W., Richardson, P., Corcoran, R., Stirling, J., McKie, S., Deakin, J. F. W., & Elliott, R. (2006). Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task. *NeuroImage*, *29*(1), 90–98. https://doi.org/10.1016/j.neuroimage.2005.07.022

von dem Hagen, E. A. H., Stoyanova, R. S., Baron-Cohen, S., & Calder, A. J. (2013). Reduced functional connectivity within and between 'social' resting state

networks in autism spectrum conditions. *Social Cognitive and Affective Neuroscience*, *8*(6), 694–701. https://doi.org/10.1093/scan/nss053

Weng, S.-J., Wiggins, J. L., Peltier, S. J., Carrasco, M., Risi, S., Lord, C., & Monk, C. S. (2010). Alterations of resting state functional connectivity in the default network in adolescents with autism spectrum disorders. *Brain Research*, *1313*, 202–214. https://doi.org/10.1016/j.brainres.2009.11.057

Yang, D. Y.-J., Rosenblau, G., Keifer, C., & Pelphrey, K. A. (2015). An integrative neural model of social perception, action observation, and theory of mind. *Neuroscience & Biobehavioral Reviews*, *51*, 263–275. https://doi.org/10.1016/j.neubiorev.2015.01.020

Yeshurun, Y., Swanson, S., Simony, E., Chen, J., Lazaridi, C., Honey, C. J., & Hasson, U. (2017). Same Story, Different Story: The Neural Representation of Interpretive Frameworks. *Psychological Science*, *28*(3), 307–319. https://doi.org/10.1177/0956797616682029