EEG resting-state functional connectivity: evidence for an imbalance of external/ internal information integration in Autism

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Research

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Abstract

Background

Autism spectrum disorder (ASD) is associated with atypical neural activity in resting-state. Most of the studies have focused on abnormalities in alpha-frequency, as a marker of ASD dysfunctions. However, few have explored alpha synchronization, with a specific interest in resting-state networks: the default mode network (DMN), the sensorimotor network (SMN), and the dorsal attention network (DAN). These functional connectivity analyses provide relevant insight into the neurophysiological correlates of multimodal integration in ASD.

Methods

Using the high temporal resolution of EEG, the present study investigates the functional connectivity in the alpha band within and between the DMN, SMN, and the DAN. We examined eyes-closed EEG alpha lagged phase synchronization, using standardized Low-Resolution Brain Electromagnetic Tomography (sLORETA) in 29 participants with ASD and 38 age,- sex- and IQ-matched typically developing (TD) controls.

Results

We observed reduced functional connectivity in the ASD group relative to TD controls, within and between the DMN, the SMN, and the DAN. We identified three hubs of dysconnectivity in ASD: the posterior cingulate cortex, the precuneus, and the medial frontal gyrus. These three regions also presented decreased current source density in the alpha band.

Conclusion

These results may account for impairments in multimodal - sensory and internal information - integration frequently observed in ASD. Underconnectivity potentially involves difficulties switching between this externally oriented attention and internally oriented thoughts and, more broadly, may impact embodied cognition.

1. Background

Autism spectrum disorder (ASD) refers to neurodevelopmental disorders characterized by social communication difficulties and restricted and repetitive behaviors (1). Studies using functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) at rest have consistently demonstrated atypical functional connectivity in ASD that goes some way to explaining its symptoms (see 2–4, for a review). Resting-state (RS) allows the brain to integrate and prepare for changes in external and internal

environments. Thus, atypical functional connectivity at rest in ASD may indicate disintegration of the information through the brain.

In this context, alpha oscillation is an interesting marker of dysfunctions (5). Alpha oscillation (7.5–12.5 Hz) is the main rhythm in the RS, and it decreases when tasks are being performed. These alpha rhythms seem to act as a traffic controller of information flow within the cortex (6). They are thought to be an index of cortical inhibition (7, 8) and probably reflect top-down inhibitory control through modulation of the neural excitation/inhibition balance (6). Alpha oscillation is inversely related to perception and attention, reflecting functional inhibition of sensory systems (9). Alpha suppression has been consistently linked to increased attention and vigilance (10, 11).

Studies exploring brain connectivity have reported decreased connectivity across alpha band in ASD (12–21). Mathewson and colleagues' (22) group analysis showed that reduced coherence in the posterior regions was associated with preferential attention to detail in ASD groups (as measured by the Autism spectrum Quotient, AQ). Impaired neural synchrony may be a primary pathophysiological mechanism in ASD, contributing to atypical functional connectivity (23, 24), and could represent an endophenotype that underlies the information processing impairments in ASD (25, 26). Most of the connectivity findings have been based on measurements between pairs of electrodes, which have several limitations, including volume conduction (27) and poor estimation of anatomical locations (presumption of a 2- and not 3-dimensional space). 3D analyses of EEG sources and connectivity may provide more detailed and accurate information. However, most studies in ASD have focused their EEG connectivity investigations on scalp measurements. One single case study in ASD, using correlation analyses between current source density measure (implemented by standardized Low-Resolution Brain Electromagnetic Tomography (sLORETA)), showed increased short connectivity, between regions involved in the mirror neuron system and social perceptual networks (28). Finally, one MEG study used source localization approach and focused on RS networks (RSNs) in ASD, including the default mode network (DMN) and salience network (29). Results showed lower gamma-band connectivity within the DMN and between the DMN and salience network, correlated with lower social communication and interaction abilities. The DMN is involved in self-reflection, referential thinking, perspective-taking, and autobiographical memory (30, 31). Altered activation and connectivity within the DMN in ASD observed with fMRI have emerged as a key system underlying social dysfunction (see 32 for review).

In the same way, while a growing interest over the last decade concerns atypical sensory processing - a new diagnostic criterion of ASD includes in the DSM-5 (1) – few studies have focused on the sensorimotor network (SMN). Atypical sensorimotor and perceptual processes suggest an impaired SMN (33–35) that is linked to the core symptoms of ASD (36–39).

Furthermore, although attentional atypicality is well known in ASD, very few studies have explored this population's attentional networks. The dorsal attention network (DAN) is concerned with the regulation of goal-directed top-down processing (40). Dysconnectivity in this network may explain attentional process difficulties in ASD (41, 42).

Most RS studies in ASD have been conducted using fMRI, and few have focused on the RSNs in EEG. Exploring the connectivity of the alpha band is of particular interest as it is related to the coordination of distant brain regions (6, 43, 44). The alpha band is positively related to the DMN and the somatosensory system (45–47), and negatively correlated with the DAN (44). Thus, these approaches offer new insights into the mechanisms underlying the atypical functional organization of brain networks in ASD (e.g., high temporal resolution, specific oscillatory frequency-band effects, a direct measure of brain activity) that fMRI cannot reveal (48, 49).

Atypicality has been reported within these RSNs, but data are very sparse concerning connectivity between them in ASD (29, 50, 51). Between-network connectivity reflects the integration of information between different networks, which is crucial for many functions impacted in ASD, such as perception, social interaction, and communication (52, 53).

Taken together, study RS brain communication through alpha rhythms provide a scaffold for low- and high-level cognitive processes. The present study aimed to identify functional connectivity modifications within and between RSNs in the alpha band in ASD compared to typically developing (TD) participants. We expected to observe underconnectivity both within and between the DMN, the DAN and the SMN in the ASD group, indicating poor brain communication. This reduced functional connectivity may reflect the existence of a core multimodal integration deficit affecting bottom-up processes (sensory processing) with significant consequences on internal representations.

2. Methods

2.1. Participants

We recruited 29 participants with ASD and 38 TD controls (mean 16.1 and 16.5 years respectively) *via* two autism resource centers in France. All participants were right-handed and matched for sex, age, and intellectual quotient (Table 1). Because of the difficulty in finding ASD participants, we decided to keep a large range of ages across participants. Furthermore, to keep a homogenous age range between groups, we seek to find an age-matched control for each ASD participant recruited. These participants with ASD had received a clinical diagnosis of verbally and intellectually high-functioning autism according to DSM-5 criteria (1). The diagnosis was confirmed by administering the Autism Diagnostic Interview-Revised (54) and/or the Autism Diagnostic Observation Schedule-Generic (ADOS, 55), complemented by the AQ (56), except for one participant. For all participants, exclusion criteria were a history of neurological disorders or psychiatric illness (other than ASD in the ASD group), a first-degree relative with ASD in the TD group, head trauma, medication interfering with the EEG signal, intellectual disability, and learning disabilities. All participants voluntarily took part in the study, and written consent was obtained from children and their parents after providing them with detailed information. This research was undertaken following the Declaration of Helsinki and approved by the regional ethics committee (CPP Nord Ouest III). It was supported by the French Ministry of Health (PHRC, ID-RCB: 2014-A00481-46). Each participant underwent a Wechsler Intelligence Scale: the Wechsler Intelligence Scale for Children-Fourth Edition for children aged

6–17 years and the Wechsler Adult Intelligence Scale-Fourth Edition for participants aged 18 years or above.

Table 1
Population description. Mean, standard deviation (*SD*), range, and analyses for group differences (Student’s *t*-test) for age, Full-Scale Intelligence Quotient (FSIQ), and Autistic Quotient (AQ).

	ASD (n = 29)		TD (n = 38)		Group Comparison
	Mean	SD	Mean	SD	
Age (years)	16.1	3.6	16.5	4.2	<i>ns</i>
FSIQ	99.1	14.0	104.8	10.2	<i>ns</i>
AQ total*	34.3	9.4	11.4	5.0	<.0001

2.2. EEG recording and data acquisition

Continuous EEG recording and data acquisition procedures were similar across research centers. They were performed in a faraday cage for 3 minutes in an awake RS eyes-closed condition, using an EGI Hydrocel Geodesic Sensor Net (HGSN-130) dense array of 128 Ag/AgCl sensors (57) (Electrical Geodesics Inc., Eugene, OR, USA). Participants were instructed to relax, remain as still as possible, and close their eyes. Impedances were kept under 100 kΩ (58), and the EEG channel was referenced to a vertex reference (fixed by the EGI system). EEG data were processed offline using Netstation 4.4.2 (Electrical Geodesics Inc., Eugene, OR, USA) before they were exported, given that we used EEG processing software developed in our laboratory (see the detailed method in 59). The signal was sampled at 1 kHz and filtered using a low-pass filter at 500 Hz and a high-pass filter at 1 Hz. The EEG was then visually screened by two experts (the first authors, PW and PC). The remaining artifacts (e.g., saccades, muscle contractions) were removed before re-referenced to a common average reference.

After processing, nonoverlapping 2.048-s segments were extracted for analysis, and all participants had a minimum of 40 s of artifact-free data available for analysis, respecting Pascual-Marqui et al. (2011)’s guidelines (60). We focused our spectral analysis on the alpha frequency band (7.512.5 Hz) given our hypothesis.

2.1. Source localization analysis and statistical non-parametric mapping (SNPM)

Using sLORETA, we estimated the current density recordings of source signals in a standardized brain atlas space, utilizing a restricted inverse solution (for details, see 61,62). Current source density distributions in the ASD and TD groups were compared in a voxel-by-voxel analysis of sLORETA data for the alpha frequency band. We submitted the sLORETA images to statistical non-parametric mapping (SnPM) for each contrast, applying a *t*-statistic to log-transformed data for unpaired groups. We log-transformed sLORETA images before the statistical analyses for each participant to reduce confounds

with no regional specificity (63). Correction for multiple comparisons was applied in SnPM with random permutations (5000 in the current study) and has been shown to yield results similar to those obtained from statistical parametric mapping with a general linear model and multiple comparison corrections derived from random field theory (64, 65). A t -threshold ($t = 3.426$) corresponding to a statistical significance threshold ($p < 0.05$) was calculated using the statistical tool provided by sLORETA. Only regions with at least five significant voxels were retained.

2.2. Functional Connectivity analysis

2.2.1. Regions of interest

To evaluate between-group connectivity differences, we conducted analyses with different RSNs. We selected seeds from key regions within the SMN, DMN, and DAN, from the parcellations described by Wu et al., (66) and Yeo et al. (67), resulting in five regions of interest (ROIs) for the SMN, four for the DMN, and twelve for the DAN. SMN coordinates were transformed from Talairach to MNI coordinates.

ROIs were created by including all gray-matter voxels within a 10-mm radius of the seed. The log-transformed electric current density was averaged across all voxels belonging to a given ROI. LORETA gave the names of all the regions to the corresponding coordinates (listed in Table 2). For DAN, two voxels were each labeled *precuneus right* by LORETA nomenclature. As one of them was very close to the right Superior parietal, we labeled it *precuneus-superior parietal lobule R* to differentiate it from the second voxel located more in the center of the precuneus.

Table 2

Cortical regions of interest for RSN functional connectivity. SMN: sensorimotor network; DAN: dorsal attention network; DMN: default mode network; L: left, R: right.

RSNs	Regions	MNI coordinates		
		X	Y	Z
SMN	Precentral gyrus R	34	-32	59
	Postcentral gyrus L	-44	-30	58
	Medial frontal gyrus	-4	-33	66
	Transverse temporal gyrus L	-56	-23	12
	Transverse temporal gyrus R	55	-23	12
DAN	Middle frontal gyrus R	22	-8	54
	Middle frontal gyrus L	-22	-8	54
	Inferior parietal lobule R	34	-38	44
	Inferior parietal lobule L	-34	-38	44
	Precuneus R	18	-69	51
	Precuneus L	-18	-69	51
	Middle temporal gyrus R	51	-64	-2
	Middle temporal gyrus L	-51	-64	-2
	Precuneus - Superior parietal lobule R	8	-63	57
	Superior parietal lobule L	-8	-63	57
	Inferior frontal gyrus R	49	3	34
	Inferior frontal gyrus L	-49	3	34
DMN	Superior temporal gyrus R	41	-60	29
	Superior temporal gyrus L	-41	-60	29
	Medial frontal gyrus	0	49	18
	Posterior cingulate cortex	0	-52	26

2.2.2. Functional Connectivity Analyses

The connectivity analyses were performed by computing lagged phase synchronization using sLORETA. Lagged phase synchronization provided the similarity (a corrected phase synchrony value) between signals in the frequency domain based on normalized Fourier transforms. This measure corrects the

volume conduction effects, intrinsic physics artifacts or non-physiological effects, and low spatial resolution. It represents a non-linear connectivity measure between two regions after excluding this zero-lag contribution (for more details on the sLORETA connectivity algorithm, see 60). In this respect, it is considered to contain only physiological connectivity (48).

We examined group differences on within- and between-network connectivity by comparing lagged phase synchronization between ROIs for each artifact-free EEG segment in the alpha frequency band. Analyses were conducted using a one-tailed t statistic on log-transformed data corrected for multiple comparisons with a non-parametric permutation procedure (5000 randomizations). The t thresholds corresponding to statistical significance thresholds ($p < 0.05$) were calculated for connectivity analyses within the SMN ($t = 2.604$), DAN ($t = 3.127$) and DMN ($t = 2.412$), and for differences in connectivity between the SMN and DAN ($t = 3.343$), SMN and DMN ($t = 3.019$), and DAN and DMN ($t = 3.291$).

3. Results

3.1. Source Localization

In the ASD group, relative to the TD group, source localization analyses in the alpha band showed significantly decreased current source density. Reduced current source density was localized in temporoparietal and somatosensory/medial areas, in the main regions involved in the DMN, the SMN, and the DAN (Fig. 1, see Additional file 1). No difference was found for ASD > TD.

3.2. Functional connectivity within RSNs

We performed statistical analyses with sLORETA software to assess between-group differences in lagged phase synchronization within the three RSNs, namely the SMN, DAN, and DMN (Table 3, Fig. 2 and summary Fig. 4). No difference was found for ASD > TD. Within the SMN, we identified significantly reduced connectivity between the medial frontal gyrus and right precentral gyrus in the ASD group relative to the TD group. Within the DAN, statistical analyses revealed reduced connectivity in the ASD group relative to the TD group 1) between the right precuneus- superior parietal lobule and both the right middle frontal gyrus and the right inferior parietal lobule, 2) between the left precuneus and both the right middle temporal gyrus and the right inferior frontal gyrus, 3) between the right middle temporal gyrus and the right inferior frontal gyrus, and 4) between the right middle frontal gyrus and the left superior parietal lobule. Within the DMN, we identified significantly decreased connectivity between the posterior cingulate cortex and the right and left superior temporal gyrus in the ASD group relative to the TD group.

Table 3

Significant differences within-RSN functional connectivity in the ASD group relative to the TD group.
 SMN: sensorimotor network; DAN: dorsal attention network; DMN: default mode network; L: left, R: right.

Regions	MNI Coordinates			Regions	MNI Coordinates			<i>t</i>	<i>p</i>	
	x	y	z		x	y	z			
SMN										
Medial frontal gyrus	-4	-33	66	Precentral gyrus R	34	-32	59	-3.555	<0.005	
DAN										
Precuneus-Superior parietal lobule R	8	-63	57	Middle frontal gyrus R	22	-8	54	-3.817	<0.009	
Precuneus L	-18	-69	51	Middle temporal gyrus R	51	-64	-2	-3.764	<0.011	
Precuneus L	-18	-69	51	Inferior frontal gyrus R	49	3	34	-3.503	<0.020	
Middle temporal gyrus R	51	-64	-2	Inferior frontal gyrus R	49	3	34	-3.315	<0.032	
Precuneus-Superior parietal lobule R	8	-63	57	Inferior parietal lobule R	34	-38	44	-3.247	<0.038	
Middle frontal gyrus R	22	-8	54	Superior parietal lobule L	-8	-63	57	-3.160	<0.046	
DMN										
Posterior cingulate cortex	0	-52	26	Superior temporal gyrus L	41	-60	29	-2.892	<0.018	
Posterior cingulate cortex	0	-52	26	Superior temporal gyrus R	-41	-60	29	-2.559	<0.038	

3.3. Functional connectivity between RSNs

The ASD and TD groups also differed on connectivity between RSNs (Table 4, Fig. 3 and summary in Fig. 4). No difference was found for ASD > TD. For lagged phase synchronization between SMN and DAN, we identified significantly decreased connectivity in the ASD group relative to the TD group 1) between the medial frontal gyrus of the SMN and both the left superior parietal lobule and the bilateral Precuneus of the DAN, 2) between the left transverse temporal gyrus of the SMN and the right Precuneus (Superior parietal) of the DAN, and 3) between the right precentral gyrus of the SMN and the right inferior parietal lobule of the DAN. For SMN and DMN, we identified significantly decreased connectivity in the ASD group relative to the TD group between the medial frontal gyrus of the SMN and the right superior temporal

gyrus of the DMN. For DAN and DMN connectivity, results revealed significantly decreased lagged phase synchronization in the ASD group relative to the TD group between the right Precuneus (Superior parietal) of the DAN and both the left superior temporal gyrus and the posterior cingulate cortex of the DMN.

Table 4

Significant differences between-RSN functional connectivity in the ASD group relative to the TD group. SMN: sensorimotor network; DAN: dorsal attention network; DMN: default mode network; L: left, R: right.

Regions	MNI Coordinates			Regions	MNI Coordinates			<i>t</i>	<i>p</i>
	x	y	z		x	y	z		
SMN & DAN <i>SMN</i>				DAN					
Medial frontal gyrus	-4	-33	66	Superior parietal lobule L	-8	-63	57	-3.667	<0.025
Transverse temporal gyrus L	-56	-23	12	Precuneus-Superior parietal lobule R	8	-63	57	-3.640	<0.026
Medial frontal gyrus	-4	-33	66	Precuneus R	18	-69	51	-3.611	<0.028
Precentral gyrus R	34	-32	59	Inferior parietal lobule R	34	-38	44	-3.561	<0.032
Medial frontal gyrus	-4	-33	66	Precuneus L	-18	-69	51	-3.459	<0.038
SMN & DMN <i>SMN</i>				DMN					
Medial frontal gyrus	-4	-33	66	Superior temporal gyrus R	41	-60	29	-3.529	<0.015
DAN & DMN <i>DAN</i>				DMN					
Precuneus-Superior parietal lobule R	8	-63	57	Superior temporal gyrus L	-41	-60	29	-3.460	<0.033
Precuneus-Superior parietal lobule R	8	-63	57	Posterior cingulate cortex	0	-52	26	-3.293	<0.05

4. Discussion

The present study investigated sources and functional connectivity in RSN in the alpha frequency band, comparing participants with and without ASD, using lagged phase synchronization. We observed decreased connectivity within and between the DMN, the SMN, and the DAN in the ASD group compared to the TD group. We highlighted three principal hubs of dysconnectivity: the posterior cingulate cortex, the

precuneus, and the medial frontal gyrus. We also showed reduced current source density in the alpha band mainly located in temporoparietal and somatosensory/medial areas considered as key nodes in the DMN, SMN and DAN.

4.1. Alpha band: a relevant marker for studying ASD atypicality

The alpha band is involved in controlling and regulating the information flow, both within and between brain networks, as it selectively inhibits task-irrelevant pathways (6, 68, 69). Alpha activity seems to be associated with modulating sensory input (68, 70, 71). Alpha disturbances could lead to atypical sensory processing in ASD (72, 73). Given together, this might suggest that individuals with ASD would have more difficulty integrating incoming information (bottom-up) at rest and actively inhibit their sensitivity to sensory input.

Increasing evidence also shows that alpha activity plays a role in abnormal social and emotional stimuli processing in ASD (74, 75). Given the alpha band involvement in attention and perception (lower-level processes) and social cognition (high-level process) (5, 6, 22, 76), we speculated that alpha atypicality contributes to autistic symptoms. Indeed, Shepard ((77) recently showed that children with ASD who exhibit greater reductions in alpha power have more social communication difficulties.

In their review, Wang et al. (4) proposed that decreased alpha band may be related to an imbalance of excitatory (e.g., glutamatergic) and inhibitory (e.g., GABAergic) activity in ASD (also see 75,78). In particular, alpha desynchronization may be linked to increased neural excitability/decreased neural inhibition (6). Previous studies in ASD reported abnormal cortical inhibitory interneurons (79, 80) and altered glutamatergic levels (81, 82), associated with atypical sensory processing in ASD (73, 83). The excitation/inhibition imbalance increases neural noise in ASD and may lead to atypical sensory processing and under-responsiveness to behaviorally relevant stimuli in participants with ASD (72).

Our data points out that excitation/inhibition imbalance highlighted by a decrease in alpha activity increases neural noise in ASD. This seems to impact integration difficulties affecting both low-level processes (sensory processing) and high-level processes, with an effect on the representation of oneself in the world and the shifting of mental representations (84–86).

4.2. *Functional connectivity within resting-state networks*

We revealed reduced lagged phase synchronization within and between the SMN, DAN, and DMN in the ASD group compared to the TD group, possibly reflecting an imbalance between external and internal information integration.

First, participants with ASD exhibited decreased connectivity within the DMN, involving the posterior cingulate cortex and right and left superior temporal gyrus, as previously reported in fMRI studies (32, 87–89) and MEG studies for the gamma band (29). A study revealed that underconnectivity involving the

posterior cingulate cortex, insula, and superior temporal gyrus was negatively associated with ASD symptom severity measured by ADOS (90). These DMN perturbations may profoundly modify internal information, including memory, mental simulation, or the sense of self, and act as a significant contributor to social dysfunction (see 32 for review).

Second, we highlighted underconnectivity within the SMN, between the medial frontal gyrus and right precentral gyrus. A recent fMRI study also showed reduced functional connectivity among visual association, somatosensory, and motor networks (91). This decreased functional connectivity between somatosensory and motor networks is consistent with the atypical multisensory and motor integration observed in individuals with ASD and participate in the core symptoms of ASD (92, 93). Dysconnectivity within the SMN may participate in an atypical integration of the sensory environment and might be interpreted as an index of increased sensitivity to sensory information according to the Enhanced Perceptual Functioning theory (94). Individuals with ASD may have more difficulty gate incoming information (bottom-up processing) at rest. Therefore, multisensory and motor integration plays a crucial role in developing imitation, motor communication, and social skills (95, 96), all impaired in ASD.

Finally, as previously reported in fMRI by Bi et al. (41) and Farrant & Uddin (42), we found dysconnectivity within several DAN regions for participants with ASD relative to the TD group. We observed the main underconnectivity between the right precuneus-superior parietal lobule and right middle frontal gyrus, consistent with deficits in attention regulation and shifting between external and internal stimuli that may directly impact self-information integration. More broadly, as the DAN is involved in regulating exogenous goal-directed top-down processing (40), we hypothesized that this atypical connectivity might contribute to the difficulties in arousal regulation and shifting associated with autistic symptoms (97).

4.3. Functional connectivity between resting-state networks

The underconnectivity observed in the ASD group between the SMN and DAN may generate delays in perceptual input and information transmission to systems downstream, thereby compromising information integration (31, 98). The attentional focus seems to be less oriented to the external information, especially when directly related to own's body representation. It may help to explain atypical functioning in the form of detail-focused perception (99).

Moreover, the underconnectivity we observed between DAN (precuneus-superior parietal lobule) and DMN (superior temporal gyrus and posterior cingulate cortex) provides additional arguments. This decreased connectivity suggests difficulties switching between externally oriented attention and internally oriented thoughts. Furthermore, studies have shown that decreased connectivity between the precuneus and temporal gyrus is correlated with the ADOS social score (84), highlighting the importance of these regions in ASD symptomatology.

Finally, the underconnectivity we observed between the right superior temporal gyrus in the DMN and the medial frontal gyrus in the SMN may modify the perception of somatosensory stimuli (100). Hence, an atypical representation of the body and its location in space provided by the SMN may participate in an

atypical sense of self (101, 102). The decreased connectivity between the SMN and the DMN could participate in the atypical integration of external sensory information (SMN) and bind this external information to internal information (DMN).

Reduced connectivity between RSN may involve a blurring integration between external and internal information that would impact thought contents at rest (103). This difficulty integrating sensory details to a self-information, with a more global level, could be linked to the theory of the weak central coherence (104). The sensory over-responsivity may lead to a chronic state of hyperarousal at rest (105) that impacts the internal organization. Beyond, these results of atypical communication between external and internal information may be related to a weakened embodied cognition. Embodied cognition refers to the theory that the environment and the body (e.g., sensorimotor information) influence cognition (e.g., memory, mental simulation, attention, etc.) with a *bottom-up* process and, reversely, how cognition influences the body through a *top-down* process. Some studies report a decrease or lack of embodiment effect in ASD with poor integration of sensorimotor information (106–108). Reduced functional connectivity may modify the conscious perception of the external world in relation to self-referential processes, leading to social difficulties (31, 109–111).

The present study also highlighted three key nodes, which presented decreased current source density. First, the medial frontal gyrus was associated with reduced connectivity within and between RSNs, suggesting atypical multisensory integration, feeling of body ownership (112), and imitation skills, which play a role in social skills (95, 96). Second, the precuneus is involved in spatial functions of self and the spatial environment and may contribute to the altered sense of self and agency in ASD (101, 102). The precuneus, with a more lateral cortex, is also involved in attentional shifting from low- (e.g., simple stimulus) to high-level processing (shifting mental representations; e.g., theory of mind; 113,114). The precuneus associated with the posterior cingulate cortex contributes to self/other referential processing (115, 116) and the monitoring of the environment (117). Third, the posterior cingulate cortex's underconnectivity with the superior temporal gyrus and precuneus may account for difficulty regulating and balancing the focus of attention on internal or external thoughts (118), arousal, and awareness (119), self-referential thought (120), and affect the stability of the brain network over time (*whole-brain metastability*, 121). Given their involvement, abnormalities in these brain regions may significantly impact social disabilities in autism.

5. Limitations

The study had three main limitations. First, although EEG directly measures cerebral activity and identifies some brain regions using sLORETA, this technique has spatial limitations. As such, other methods would be useful for determining spatial topographies. Second, we focused on adolescence as defined by Sawyer et al. (122) (participants aged 10–25 years in the present study), but it would be relevant to go further by examining neurodevelopmental changes during this period. Finally, our population was composed of high-functioning participants, limiting generalization to adolescents across the spectrum.

6. Conclusion

We report reduced functional connectivity within and between DMN, SMN, and DAN in the ASD group relative to the TD group. We hypothesize that the ASD group was less effective in modulating communication between brain regions in the alpha band and may lead to altered integration and switching between externally oriented information and internally oriented thoughts that may account for a “disembodied” cognition. Atypical alpha synchronization at rest in ASD may be linked to neural excitation/inhibition imbalance, impacting integration difficulties that affect low and high cognitive processes. Indeed, connectivity analyses revealed atypicality in integrative brain regions that may account for difficulties in 1) perception (external): somatosensory integration of environment, 2) cognitive (internal) integration, and 3) reciprocal influence between the external environment and self-endogenous stimuli. These impairments in the embodiment may contribute to social abilities: high-level integration required for related self-processing, notably interaction (e.g., nonverbal communication such as gestures, facial expressions, and modulation of timing and intonation of speech) and theory of mind, which requires individuals to switch from a self-perspective to another perspective. Further studies could be relevant to test the direct impact of these atypical brain functioning on embodied processes in ASD.

Abbreviations

ADOS: Autism Diagnostic Observation Schedule

AQ: Autism spectrum Quotient

ASD: Autism spectrum disorder

DAN: dorsal attention network

DMN: default mode network

DSM: Diagnostic and Statistical Manual of Mental Disorders

EEG: electroencephalography

fMRI: functional magnetic resonance imaging

MEG: magnetoencephalography

MNI: Montreal Neurological Institute

ROI: regions of interest

RS: resting-state

RSN: resting-state network

sLORETA: standardized Low-Resolution Brain Electromagnetic Tomography

SMN: sensorimotor network

SnPM: statistical non-parametric mapping

TD: typically developing

Declarations

8.1 Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the French ethic committee (CPP Nord Ouest III, N° 2014-02). Written informed consent to participate in this study was provided by the participant's legal guardian/next of kin for minor participants and directly by the participant for major participants.

8.2 Consent for publication

Not applicable

8.3 Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

8.4 Competing Interest

The authors declare that they have no competing interests.

8.5 Funding

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8.6 Authors' contributions

PW collected all the data and participated in the analysis and writing. PC participated in the collection of the data, methods, and analysis. FD collected the data, directed the EEG recording, and made it possible to collect the EEG data. FW, PD, CM, JMG, and FG worked on including patients and their clinical exploration. MM and FW participated in the methods and relecture. BGG designed the study participated in writing. PC, FD, FW, MM, PD, CM, JMG, FG, FE, and JMB provided substantial modifications to the manuscript. All authors read and approved the final manuscript.

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References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders [Internet]. Fifth Edition. Arlington, VA: American Psychiatric Association; 2013 [cited 2016 Nov 2]. Available from: <http://psychiatryonline.org/doi/book/10.1176/appi.books.9780890425596>
2. Hull L, Petrides KV, Allison C, Smith P, Baron-Cohen S, Lai M-C, et al. "Putting on My Best Normal": Social Camouflaging in Adults with Autism Spectrum Conditions. *J Autism Dev Disord*. 2017;47(8):2519–34.
3. O'Reilly C, Lewis JD, Elsabbagh M. Is functional brain connectivity atypical in autism? A systematic review of EEG and MEG studies. *PloS One*. 2017;12(5):e0175870.
4. Wang J, Barstein J, Ethridge LE, Mosconi MW, Takarae Y, Sweeney JA. Resting state EEG abnormalities in autism spectrum disorders. *J Neurodev Disord*. 2013;5(1):24.
5. Edgar JC, Heiken K, Chen Y-H, Herrington JD, Chow V, Liu S, et al. Resting-state alpha in autism spectrum disorder and alpha associations with thalamic volume. *J Autism Dev Disord*. 2015 Mar;45(3):795–804.
6. Klimesch W, Sauseng P, Hanslmayr S. EEG alpha oscillations: the inhibition-timing hypothesis. *Brain Res Rev*. 2007 Jan;53(1):63–88.
7. Neuper C, Pfurtscheller G. Event-related dynamics of cortical rhythms: frequency-specific features and functional correlates. *Int J Psychophysiol Off J Int Organ Psychophysiol*. 2001 Dec;43(1):41–58.
8. Pfurtscheller G, Stancák A, Neuper C. Event-related synchronization (ERS) in the alpha band—an electrophysiological correlate of cortical idling: a review. *Int J Psychophysiol Off J Int Organ Psychophysiol*. 1996 Nov;24(1–2):39–46.
9. Jokisch D, Jensen O. Modulation of gamma and alpha activity during a working memory task engaging the dorsal or ventral stream. *J Neurosci Off J Soc Neurosci*. 2007 Mar 21;27(12):3244–51.
10. Boiten F, Sergeant J, Geuze R. Event-related desynchronization: The effects of energetic and computational demands. *Electroencephalogr Clin Neurophysiol*. 1992;82(4):302–9.
11. Klimesch W. EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Res Rev*. 1999 Apr;29(2–3):169–95.

12. Boersma M, Kemner C, de Reus MA, Collin G, Snijders TM, Hofman D, et al. Disrupted functional brain networks in autistic toddlers. *Brain Connect*. 2013;3(1):41–9.
13. Carson AM, Salowitz NMG, Scheidt RA, Dolan BK, Van Hecke AV. Electroencephalogram coherence in children with and without autism spectrum disorders: decreased interhemispheric connectivity in autism. *Autism Res Off J Int Soc Autism Res*. 2014 Jun;7(3):334–43.
14. Clarke AR, Barry RJ, Indraratna A, Dupuy FE, McCarthy R, Selikowitz M. EEG activity in children with Asperger's Syndrome. *Clin Neurophysiol Off J Int Fed Clin Neurophysiol*. 2016 Jan;127(1):442–51.
15. Coben R, Clarke AR, Hudspeth W, Barry RJ. EEG power and coherence in autistic spectrum disorder. *Clin Neurophysiol*. 2008 May;119(5):1002–9.
16. Duffy FH, Als H. A stable pattern of EEG spectral coherence distinguishes children with autism from neuro-typical controls - a large case control study. *BMC Med*. 2012;10:64.
17. Elhabashy H, Raafat O, Afifi L, Raafat H, Abdullah K. Quantitative EEG in autistic children. *Egypt J Neurol Psychiatry Neurosurg*. 2015;52(3):176–82.
18. Jaime M, McMahon CM, Davidson BC, Newell LC, Mundy PC, Henderson HA. Brief Report: Reduced Temporal-Central EEG Alpha Coherence During Joint Attention Perception in Adolescents with Autism Spectrum Disorder. *J Autism Dev Disord*. 2016 Apr;46(4):1477–89.
19. Lushchekina EA, Podreznaya ED, Lushchekin VS, Strelets VB. A Comparative EEG Study in Normal and Autistic Children. *Neurosci Behav Physiol*. 2012 Mar 1;42(3):236–43.
20. Matlis S, Boric K, Chu CJ, Kramer MA. Robust disruptions in electroencephalogram cortical oscillations and large-scale functional networks in autism. *BMC Neurol*. 2015;15:97.
21. Murias M, Webb SJ, Greenson J, Dawson G. Resting State Cortical Connectivity Reflected in EEG Coherence in Individuals With Autism. *Biol Psychiatry*. 2007 Aug 1;62(3):270–3.
22. Mathewson KJ, Jetha MK, Drmic IE, Bryson SE, Goldberg JO, Schmidt LA. Regional EEG alpha power, coherence, and behavioral symptomatology in autism spectrum disorder. *Clin Neurophysiol*. 2012 Sep;123(9):1798–809.
23. Khan S, Gramfort A, Shetty NR, Kitzbichler MG, Ganesan S, Moran JM, et al. Local and long-range functional connectivity is reduced in concert in autism spectrum disorders. *Proc Natl Acad Sci U S A*. 2013 Feb 19;110(8):3107–12.
24. Wass S. Distortions and disconnections: disrupted brain connectivity in autism. *Brain Cogn*. 2011 Feb;75(1):18–28.

25. Gandal MJ, Edgar JC, Ehrlichman RS, Mehta M, Roberts TPL, Siegel SJ. Validating γ oscillations and delayed auditory responses as translational biomarkers of autism. *Biol Psychiatry*. 2010 Dec 15;68(12):1100–6.
26. Rojas DC, Maharajh K, Teale P, Rogers SJ. Reduced neural synchronization of gamma-band MEG oscillations in first-degree relatives of children with autism. *BMC Psychiatry*. 2008 Aug 1;8:66.
27. Nunez PL, Silberstein RB, Cadusch PJ, Wijesinghe RS, Westdorp AF, Srinivasan R. A theoretical and experimental study of high resolution EEG based on surface Laplacians and cortical imaging. *Electroencephalogr Clin Neurophysiol*. 1994 Jan;90(1):40–57.
28. Coben R, Mohammad-Rezazadeh I, Cannon RL. Using quantitative and analytic EEG methods in the understanding of connectivity in autism spectrum disorders: a theory of mixed over- and under-connectivity. *Front Hum Neurosci* [Internet]. 2014 Feb 26 [cited 2015 Apr 21];8. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3935255/>
29. Lajiness-O'Neill R, Brennan JR, Moran JE, Richard AE, Flores A-M, Swick C, et al. Patterns of altered neural synchrony in the default mode network in autism spectrum disorder revealed with magnetoencephalography (MEG): Relationship to clinical symptomatology. *Autism Res Off J Int Soc Autism Res*. 2018 Mar;11(3):434–49.
30. Gusnard DA, Akbudak E, Shulman GL, Raichle ME. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc Natl Acad Sci U S A*. 2001 Mar 27;98(7):4259–64.
31. Weng S-J, Wiggins JL, Peltier SJ, Carrasco M, Risi S, Lord C, et al. Alterations of resting state functional connectivity in the default network in adolescents with autism spectrum disorders. *Brain Res*. 2010 Feb 8;1313:202–14.
32. Padmanabhan A, Lynch CJ, Schaer M, Menon V. The Default Mode Network in Autism. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2017 Sep;2(6):476–86.
33. Perry W, Minassian A, Lopez B, Maron L, Lincoln A. Sensorimotor Gating Deficits in Adults with Autism. *Biol Psychiatry*. 2007 Feb 15;61(4):482–6.
34. Takarae Y, Minshew NJ, Luna B, Sweeney JA. Atypical involvement of frontostriatal systems during sensorimotor control in autism. *Psychiatry Res Neuroimaging*. 2007 Nov 15;156(2):117–27.
35. Travers BG, Kana RK, Klinger LG, Klein CL, Klinger MR. Motor learning in individuals with autism spectrum disorder: activation in superior parietal lobule related to learning and repetitive behaviors. *Autism Res Off J Int Soc Autism Res*. 2015 Feb;8(1):38–51.
36. Boyd BA, Baranek GT, Sideris J, Poe MD, Watson LR, Patten E, et al. Sensory features and repetitive behaviors in children with autism and developmental delays. *Autism Res Off J Int Soc Autism*

Res. 2010 Apr;3(2):78–87.

37. Cascio CJ, Woynaroski T, Baranek GT, Wallace MT. Toward an interdisciplinary approach to understanding sensory function in autism spectrum disorder. *Autism Res.* 2016;9(9):920–5.
38. Foss-Feig JH, Heacock JL, Cascio CJ. TACTILE RESPONSIVENESS PATTERNS AND THEIR ASSOCIATION WITH CORE FEATURES IN AUTISM SPECTRUM DISORDERS. *Res Autism Spectr Disord.* 2012;6(1):337–44.
39. Lim YH, Partridge K, Girdler S, Morris SL. Standing Postural Control in Individuals with Autism Spectrum Disorder: Systematic Review and Meta-analysis. *J Autism Dev Disord.* 2017 Jul 1;47(7):2238–53.
40. Corbetta M, Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci.* 2002 Mar;3(3):201–15.
41. Bi X, Zhao J, Xu Q, Sun Q, Wang Z. Abnormal Functional Connectivity of Resting State Network Detection Based on Linear ICA Analysis in Autism Spectrum Disorder. *Front Physiol* [Internet]. 2018 [cited 2019 Jul 31];9. Available from: <https://www.frontiersin.org/articles/10.3389/fphys.2018.00475/full>
42. Farrant K, Uddin LQ. Atypical developmental of dorsal and ventral attention networks in autism. *Dev Sci.* 2016;19(4):550–63.
43. Palva S, Palva JM. Functional roles of alpha-band phase synchronization in local and large-scale cortical networks. *Front Psychol.* 2011;2:204.
44. Sadaghiani S, Scheeringa R, Lehongre K, Morillon B, Giraud A-L, Kleinschmidt A. Intrinsic connectivity networks, alpha oscillations, and tonic alertness: a simultaneous electroencephalography/functional magnetic resonance imaging study. *J Neurosci Off J Soc Neurosci.* 2010 Jul 28;30(30):10243–50.
45. Ede F van, Lange F de, Jensen O, Maris E. Orienting Attention to an Upcoming Tactile Event Involves a Spatially and Temporally Specific Modulation of Sensorimotor Alpha- and Beta-Band Oscillations. *J Neurosci.* 2011 Feb 9;31(6):2016–24.
46. Haegens S, Nácher V, Luna R, Romo R, Jensen O. α -Oscillations in the monkey sensorimotor network influence discrimination performance by rhythmical inhibition of neuronal spiking. *Proc Natl Acad Sci.* 2011 Nov 29;108(48):19377–82.
47. Jones SR, Kerr CE, Wan Q, Pritchett DL, Hämäläinen M, Moore CI. Cued Spatial Attention Drives Functionally Relevant Modulation of the Mu Rhythm in Primary Somatosensory Cortex. *J Neurosci.* 2010 Oct 13;30(41):13760–5.

48. Canuet L, Ishii R, Pascual-Marqui RD, Iwase M, Kurimoto R, Aoki Y, et al. Resting-State EEG Source Localization and Functional Connectivity in Schizophrenia-Like Psychosis of Epilepsy. *PLOS ONE*. 2011 Nov 18;6(11):e27863.
49. Logothetis NK. What we can do and what we cannot do with fMRI. *Nature*. 2008 Jun 12;453(7197):869–78.
50. Cerliani L, Mennes M, Thomas RM, Martino AD, Thioux M, Keyzers C. Increased Functional Connectivity Between Subcortical and Cortical Resting-State Networks in Autism Spectrum Disorder. *JAMA Psychiatry*. 2015 Aug 1;72(8):767–77.
51. Nomi JS, Uddin LQ. Developmental changes in large-scale network connectivity in autism. *NeuroImage Clin*. 2015;7:732–41.
52. Barber AD, Caffo BS, Pekar JJ, Mostofsky SH. Developmental changes in within- and between-network connectivity between late childhood and adulthood. *Neuropsychologia*. 2013 Jan;51(1):156–67.
53. Bassett DS, Yang M, Wymbs NF, Grafton ST. Learning-induced autonomy of sensorimotor systems. *Nat Neurosci*. 2015 May;18(5):744–51.
54. Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord*. 1994 Oct;24(5):659–85.
55. Lord C, Risi S, Lambrecht L, Cook EH, Leventhal BL, DiLavore PC, et al. The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J Autism Dev Disord*. 2000 Jun;30(3):205–23.
56. Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E. The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *J Autism Dev Disord*. 2001 Feb;31(1):5–17.
57. Tucker DM. Spatial sampling of head electrical fields: the geodesic sensor net. *Electroencephalogr Clin Neurophysiol*. 1993 Sep 1;87(3):154–63.
58. Ferree TC, Luu P, Russell GS, Tucker DM. Scalp electrode impedance, infection risk, and EEG data quality. *Clin Neurophysiol Off J Int Fed Clin Neurophysiol*. 2001 Mar;112(3):536–44.
59. Desautay P, Clochon P, Doidy F, Lambrechts A, Bowler DM, Gérardin P, et al. Impact of Semantic Relatedness on Associative Memory: An ERP Study. *Front Hum Neurosci*. 2017;11:335.
60. Pascual-Marqui RD, Lehmann D, Koukkou M, Kochi K, Anderer P, Saletu B, et al. Assessing interactions in the brain with exact low-resolution electromagnetic tomography. *Philos Transact A Math Phys Eng Sci*. 2011 Oct 13;369(1952):3768–84.

61. Pascual-Marqui RD, Esslen M, Kochi K, Lehmann D. Functional imaging with low-resolution brain electromagnetic tomography (LORETA): a review. *Methods Find Exp Clin Pharmacol*. 2002;24 Suppl C:91–5.
62. Pascual-Marqui RD, Michel CM, Lehmann D. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *Int J Psychophysiol Off J Int Organ Psychophysiol*. 1994 Oct;18(1):49–65.
63. Gianotti LRR, Dahinden FM, Baumgartner T, Knoch D. Understanding Individual Differences in Domain-General Prosociality: A Resting EEG Study. *Brain Topogr*. 2019;32(1):118–26.
64. Holmes AP, Blair RC, Watson JD, Ford I. Non-parametric analysis of statistic images from functional mapping experiments. *J Cereb Blood Flow Metab Off J Int Soc Cereb Blood Flow Metab*. 1996 Jan;16(1):7–22.
65. Nichols TE, Holmes AP. Non-parametric permutation tests for functional neuroimaging: a primer with examples. *Hum Brain Mapp*. 2002 Jan;15(1):1–25.
66. Wu CW, Gu H, Lu H, Stein EA, Chen J-H, Yang Y. Frequency specificity of functional connectivity in brain networks. *NeuroImage*. 2008 Sep 1;42(3):1047–55.
67. Yeo BTT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J Neurophysiol*. 2011 Sep;106(3):1125–65.
68. Jensen O, Mazaheri A. Shaping Functional Architecture by Oscillatory Alpha Activity: Gating by Inhibition. *Front Hum Neurosci* [Internet]. 2010 Nov 4 [cited 2019 Sep 21];4. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2990626/>
69. Zumer JM, Scheeringa R, Schoffelen J-M, Norris DG, Jensen O. Occipital Alpha Activity during Stimulus Processing Gates the Information Flow to Object-Selective Cortex. *PLOS Biol*. 2014 Oct 21;12(10):e1001965.
70. Klimesch W. Alpha-band oscillations, attention, and controlled access to stored information. *Trends Cogn Sci*. 2012 Dec 1;16(12):606–17.
71. Mathewson KE, Lleras A, Beck DM, Fabiani M, Ro T, Gratton G. Pulsed Out of Awareness: EEG Alpha Oscillations Represent a Pulsed-Inhibition of Ongoing Cortical Processing. *Front Psychol*. 2011 May 19;2:99.
72. Keehn B, Westerfield M, Müller R-A, Townsend J. Autism, Attention, and Alpha Oscillations: An Electrophysiological Study of Attentional Capture. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2017 Sep 1;2(6):528–36.

73. Pierce S, Kadlaskar G, Edmondson DA, McNally Keehn R, Dydak U, Keehn B. Associations between sensory processing and electrophysiological and neurochemical measures in children with ASD: an EEG-MRS study. *J Neurodev Disord*. 2021 Jan 6;13(1):5.
74. Rippon G, Brock J, Brown C, Boucher J. Disordered connectivity in the autistic brain: challenges for the “new psychophysiology.” *Int J Psychophysiol Off J Int Organ Psychophysiol*. 2007 Feb;63(2):164–72.
75. Rubenstein JLR, Merzenich MM. Model of autism: increased ratio of excitation/inhibition in key neural systems. *Genes Brain Behav*. 2003 Oct;2(5):255–67.
76. Dickinson A, DiStefano C, Senturk D, Jeste SS. Peak alpha frequency is a neural marker of cognitive function across the autism spectrum. *Eur J Neurosci*. 2018 Mar;47(6):643–51.
77. Shephard E, Tye C, Ashwood KL, Azadi B, Asherson P, Bolton PF, et al. Resting-State Neurophysiological Activity Patterns in Young People with ASD, ADHD, and ASD + ADHD. *J Autism Dev Disord*. 2018;48(1):110–22.
78. Sohal VS, Rubenstein JLR. Excitation-inhibition balance as a framework for investigating mechanisms in neuropsychiatric disorders. *Mol Psychiatry*. 2019 Sep;24(9):1248–57.
79. Casanova MF, Buxhoeveden DP, Switala AE, Roy E. Minicolumnar pathology in autism. *Neurology*. 2002 Feb 12;58(3):428–32.
80. Levitt P, Eagleson KL, Powell EM. Regulation of neocortical interneuron development and the implications for neurodevelopmental disorders. *Trends Neurosci*. 2004 Jul;27(7):400–6.
81. Tebartz van Elst L, Maier S, Fangmeier T, Endres D, Mueller GT, Nickel K, et al. Disturbed cingulate glutamate metabolism in adults with high-functioning autism spectrum disorder: evidence in support of the excitatory/inhibitory imbalance hypothesis. *Mol Psychiatry*. 2014 Dec;19(12):1314–25.
82. Zheng Z, Zhu T, Qu Y, Mu D. Blood Glutamate Levels in Autism Spectrum Disorder: A Systematic Review and Meta-Analysis. *PLOS ONE*. 2016 Jul 8;11(7):e0158688.
83. He JL, Oeltzschner G, Mikkelsen M, Deronda A, Harris AD, Crocetti D, et al. Region-specific elevations of glutamate + glutamine correlate with the sensory symptoms of autism spectrum disorders. *Transl Psychiatry*. 2021 Jul 29;11(1):1–10.
84. Cheng W, Rolls ET, Gu H, Zhang J, Feng J. Autism: reduced connectivity between cortical areas involved in face expression, theory of mind, and the sense of self. *Brain J Neurol*. 2015 May;138(Pt 5):1382–93.
85. Lau WKW, Leung M-K, Lau BWM. Resting-state abnormalities in Autism Spectrum Disorders: A meta-analysis. *Sci Rep*. 2019 Mar 7;9(1):3892.

86. Lombardo MV, Chakrabarti B, Bullmore ET, Sadek SA, Pasco G, Wheelwright SJ, et al. Atypical neural self-representation in autism. *Brain J Neurol*. 2010 Feb;133(Pt 2):611–24.
87. Kennedy DP, Courchesne E. The intrinsic functional organization of the brain is altered in autism. *NeuroImage*. 2008 Feb 15;39(4):1877–85.
88. Uddin LQ. The self in autism: an emerging view from neuroimaging. *Neurocase*. 2011 Jun;17(3):201–8.
89. Washington SD, Gordon EM, Brar J, Warburton S, Sawyer AT, Wolfe A, et al. Dysmaturation of the default mode network in autism. *Hum Brain Mapp*. 2014 Apr;35(4):1284–96.
90. Li Q, Becker B, Jiang X, Zhao Z, Zhang Q, Yao S, et al. Decreased interhemispheric functional connectivity rather than corpus callosum volume as a potential biomarker for autism spectrum disorder. *Cortex*. 2019 Oct 1;119:258–66.
91. Oldehinkel M, Mennes M, Marquand A, Charman T, Tillmann J, Ecker C, et al. Altered Connectivity Between Cerebellum, Visual, and Sensory-Motor Networks in Autism Spectrum Disorder: Results from the EU-AIMS Longitudinal European Autism Project. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2019 Mar 1;4(3):260–70.
92. Ben-Sasson A, Hen L, Fluss R, Cermak SA, Engel-Yeger B, Gal E. A meta-analysis of sensory modulation symptoms in individuals with autism spectrum disorders. *J Autism Dev Disord*. 2009 Jan;39(1):1–11.
93. Marco EJ, Hinkley LBN, Hill SS, Nagarajan SS. Sensory processing in autism: a review of neurophysiologic findings. *Pediatr Res*. 2011 May;69(5 Pt 2):48R-54R.
94. Mottron L, Dawson M, Soulières I, Hubert B, Burack J. Enhanced perceptual functioning in autism: an update, and eight principles of autistic perception. *J Autism Dev Disord*. 2006 Jan;36(1):27–43.
95. Edwards LA. A Meta-Analysis of Imitation Abilities in Individuals With Autism Spectrum Disorders. *Autism Res*. 2014;7(3):363–80.
96. Williams JHG, Whiten A, Singh T. A systematic review of action imitation in autistic spectrum disorder. *J Autism Dev Disord*. 2004 Jun;34(3):285–99.
97. Keehn B, Müller R-A, Townsend J. Atypical attentional networks and the emergence of autism. *Neurosci Biobehav Rev*. 2013 Feb;37(2):164–83.
98. Belmonte MK, Allen G, Beckel-Mitchener A, Boulanger LM, Carper RA, Webb SJ. Autism and abnormal development of brain connectivity. *J Neurosci Off J Soc Neurosci*. 2004 Oct 20;24(42):9228–31.

99. Martínez K, Martínez-García M, Marcos-Vidal L, Janssen J, Castellanos FX, Pretus C, et al. Sensory-to-Cognitive Systems Integration Is Associated With Clinical Severity in Autism Spectrum Disorder. *J Am Acad Child Adolesc Psychiatry*. 2019 Jun 28;
100. Boly M, Balteau E, Schnakers C, Degueldre C, Moonen G, Luxen A, et al. Baseline brain activity fluctuations predict somatosensory perception in humans. *Proc Natl Acad Sci U S A*. 2007 Jul 17;104(29):12187–92.
101. Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain*. 2006 Mar 1;129(3):564–83.
102. Lyons V, Fitzgerald M. Atypical Sense of Self in Autism Spectrum Disorders: A Neuro- Cognitive Perspective. *Recent Adv Autism Spectr Disord - Vol I* [Internet]. 2013 Mar 6 [cited 2019 Aug 13]; Available from: <https://www.intechopen.com/books/recent-advances-in-autism-spectrum-disorders-volume-i/atypical-sense-of-self-in-autism-spectrum-disorders-a-neuro-cognitive-perspective>
103. Christoff K, Irving ZC, Fox KCR, Spreng RN, Andrews-Hanna JR. Mind-wandering as spontaneous thought: a dynamic framework. *Nat Rev Neurosci*. 2016 Nov;17(11):718–31.
104. Happé F, Frith U. The weak coherence account: detail-focused cognitive style in autism spectrum disorders. *J Autism Dev Disord*. 2006 Jan;36(1):5–25.
105. Arora I, Bellato A, Ropar D, Hollis C, Groom MJ. Is autonomic function during resting-state atypical in Autism: A systematic review of evidence. *Neurosci Biobehav Rev*. 2021 Jun;125:417–41.
106. De Jaegher H. Embodiment and sense-making in autism. *Front Integr Neurosci*. 2013;7:15.
107. Eigsti I-M. A Review of Embodiment in Autism Spectrum Disorders. *Front Psychol*. 2013;4:224.
108. Frith U, Hill EL, Klin A, Jones W, Schultz R, Volkmar F. The enactive mind, or from actions to cognition: lessons from autism. *Philos Trans R Soc Lond B Biol Sci*. 2003 Feb 28;358(1430):345–60.
109. Assaf M, Jagannathan K, Calhoun VD, Miller L, Stevens MC, Sahl R, et al. Abnormal functional connectivity of default mode sub-networks in autism spectrum disorder patients. *NeuroImage*. 2010 Oct 15;53(1):247–56.
110. Monk CS, Peltier SJ, Wiggins JL, Weng S-J, Carrasco M, Risi S, et al. Abnormalities of intrinsic functional connectivity in autism spectrum disorders. *NeuroImage*. 2009 Aug 15;47(2):764–72.
111. von dem Hagen EAH, Stoyanova RS, Baron-Cohen S, Calder AJ. Reduced functional connectivity within and between ‘social’ resting state networks in autism spectrum conditions. *Soc Cogn Affect Neurosci*. 2013 Aug;8(6):694–701.

112. Ehrsson HH, Holmes NP, Passingham RE. Touching a rubber hand: feeling of body ownership is associated with activity in multisensory brain areas. *J Neurosci Off J Soc Neurosci*. 2005 Nov 9;25(45):10564–73.
113. Le TH, Pardo JV, Hu X. 4 T-fMRI study of nonspatial shifting of selective attention: cerebellar and parietal contributions. *J Neurophysiol*. 1998 Mar;79(3):1535–48.
114. Nagahama Y, Okada T, Katsumi Y, Hayashi T, Yamauchi H, Sawamoto N, et al. Transient Neural Activity in the Medial Superior Frontal Gyrus and Precuneus Time Locked with Attention Shift between Object Features. *NeuroImage*. 1999 Aug 1;10(2):193–9.
115. Burrows CA, Laird AR, Uddin LQ. Functional connectivity of brain regions for self- and other-evaluation in children, adolescents and adults with autism. *Dev Sci*. 2016;19(4):564–80.
116. Zhao W, Luo L, Li Q, Kendrick KM. What Can Psychiatric Disorders Tell Us about Neural Processing of the Self? *Front Hum Neurosci* [Internet]. 2013 Aug 15 [cited 2019 Aug 5];7. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3744079/>
117. Qin P, Northoff G. How is our self related to midline regions and the default-mode network? *NeuroImage*. 2011 Aug 1;57(3):1221–33.
118. Leech R, Kamourieh S, Beckmann CF, Sharp DJ. Fractionating the default mode network: distinct contributions of the ventral and dorsal posterior cingulate cortex to cognitive control. *J Neurosci Off J Soc Neurosci*. 2011 Mar 2;31(9):3217–24.
119. Vogt BA, Laureys S. Posterior cingulate, precuneal and retrosplenial cortices: cytology and components of the neural network correlates of consciousness. *Prog Brain Res*. 2005;150:205–17.
120. Brewer JA, Garrison KA, Whitfield-Gabrieli S. What about the “Self” is Processed in the Posterior Cingulate Cortex? *Front Hum Neurosci* [Internet]. 2013 Oct 2 [cited 2019 Sep 21];7. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3788347/>
121. Leech R, Sharp DJ. The role of the posterior cingulate cortex in cognition and disease. *Brain J Neurol*. 2014 Jan;137(Pt 1):12–32.
122. Sawyer SM, Azzopardi PS, Wickremaratne D, Patton GC. The age of adolescence. *Lancet Child Adolesc Health*. 2018;2(3):223–8.

Figures

Figure 1

Source localization differences between ASD and TD groups in the alpha frequency band. Blue areas represent the spatial extent of voxels with a significantly reduced current source density between ASD and TD groups ($p < 0.05$ corrected for multiple testing, $t < -3.426$). L left, R right, A anterior, P posterior.

Figure 2

Connectogram of significant differences within-RSN connectivity in the ASD group relative to the TD group. Lines indicate significantly decreased lagged phase synchronization for the ASD group relative to the TD group within SMN, DAN, and DMN (thin line $p < 0.05$, thick line $p < 0.01$). L left, R right.

Figure 3

Connectogram of significant differences between-RSN connectivity in the ASD group relative to the TD group. Lines indicate significantly decreased lagged phase synchronization for the ASD group relative to the TD group between SMN and DAN, between SMN and DMN, and between DAN and DMN (thin line $p < 0.05$). L left, R right.

Figure 4

Summary of decreased connectivity within- and between-RSN in the ASD group relative to TD. Lines indicate significant decreased lagged phase synchronization for the ASD group relative to the TD group. Green lines represent decreased connectivity within RSNs, and blue lines represent decreased connectivity between RSNs. Thin line $p < 0.05$, thick line $p < 0.01$. L, left, R right.

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