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

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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 within a specific interest in resting-state networks, namely 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 high temporal resolution 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 developing (TD) controls (age, sex, and IQ matched).

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 shed light on possible multimodal integration impairments affecting the communication between bottom-up and top-down information. The observed hypoconnectivity between the DMN, SMN, and DAN could also be related to difficulties in switching between externally oriented attention and internally oriented thoughts.

Keywords: Autism spectrum disorder, EEG, Alpha, DMN, DAN, SMN, Connectivity, Integration, Resting state

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 found atypical functional connectivity in ASD that goes some way to explaining its symptoms (see [2–4], for a review). Importantly, it has been proposed

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that during the so-called resting-state (RS) periods, the brain integrates and processes information in an active way [5]. Thus, atypical functional connectivity at rest in ASD may indicate disintegration of the information through the brain.

In this context, alpha oscillation appears as an interesting marker of dysfunctions [6]. Alpha oscillation (7.5–12.5 Hz) is the main rhythm during unconstrained brain activity (i.e., resting state), and it decreases when subjects are asked to perform a task [7]. These alpha rhythms seem to act as a traffic controller of information flow within the cortex and are thought to be an index of cortical inhibition [7–9] via top-down inhibitory control through modulation of the neural excitation/inhibition balance [7]. Alpha oscillation is inversely related to externally oriented attention, reflecting functional inhibition of sensory systems [10]. Alpha suppression has been consistently linked to increased attention and vigilance [11, 12].

In ASD, most resting-state studies have reported decreased connectivity in the alpha band in ASD [13–22] but some observed increased connectivity [23–25]. Many EEG studies in ASD include a large range of ages with few participants: 15 ASD participants (9–18 years, [26]); 9 ASD participants (12–53 years, [27]); 10 ASD participants (21–41 years, [28]); 10 ASD participants (16–38 years, [29]); and 19 ASD participants (7–17 years, [30]). Studies with larger sample sizes are still needed. These mixed results concerning alpha connectivity are difficult to compare due to the use of very different methods (acquisition method, condition of rest, recording durations, region of interest, connectivity metric, etc.) However, considering the literature, it is still possible to envisage a decrease in these electrophysiological indexes in most people with autism.

Mathewson and colleagues [31] showed an association between reduced coherence in posterior regions with preferential attention to detail in ASD groups (as measured by the autism spectrum quotient (AQ)). In this vein, impaired neural synchrony may be a primary pathophysiological mechanism in ASD, contributing to atypical functional connectivity [32, 33], and could represent an endophenotype that underlies the information processing impairments in ASD [34, 35].

Most of the connectivity findings in EEG have been based on measurements between pairs of electrodes, which have several limitations, including volume conduction [36] 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 on 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 [37]. One MEG study used source localization approach and focused on RS networks (RSNs) in ASD, including the default mode network (DMN) and the salience network [38]. The authors showed lower gamma-band connectivity within the DMN and between the DMN and salience network, which correlated with the severity of ASD symptomatology in social communication and interaction abilities.

The DMN is involved in top-down processes related to internal-oriented thought abilities, such as self-reflection, mental representation, perspective-taking, and autobiographical memory [39, 40]. Altered activation and connectivity within the DMN in ASD have emerged as a key system underlying social dysfunction (see [41] for review).

Furthermore, 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 [42–44] that is linked to the core symptoms of ASD [45–48].

In the same way, although attentional atypicality is well known in ASD, very few studies have explored brain functional networks underpinning attentional processes. The dorsal attention network (DAN) has been linked to the regulation of goal-directed top-down processing [49]. Dysconnectivity in this network may explain attentional process difficulties in ASD [50, 51].

Most RS studies in ASD have been conducted using fMRI, and few have focused on the previously mentioned RSN, specially. Exploring the connectivity of the alpha band is of particular interest as it is related to the coordination of distant brain regions [7, 52, 53]. The alpha band is positively related to the DMN and the somatosensory system [54–56] and negatively correlated with the DAN [53]. 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 [57, 58]. Thus, we focus on SMN, DMN, and DAN which here we refer as 3-RSNs.

Atypicality has been reported within these 3-RSNs, but data are very sparse concerning connectivity between them in ASD [38, 59, 60]. Between-network connectivity reflects the amount of information integration between different networks, which is crucial for many functions

impacted in ASD, such as perception, social interaction, and communication [61, 62].

The present study aimed to provide a detailed description of the activity and connectivity profiles within and between the 3-RSN through alpha rhythms in ASD compared to typically developing (TD) participants. We expected to observe underconnectivity both within and between the SMN, the DAN, and the DMN in the ASD group, indicating poor brain communication. This reduced functional connectivity may reflect the existence of a core multimodal integration deficit affecting the communication between bottom-up and top-down information.

Methods

Participants

We recruited 29 participants with ASD and 38 TD controls (mean 16.1 and 16.5 years respectively, Table 1) via two autism resource centers in France. All participants were right-handed and matched for sex, age, and intellectual quotient (Table 1). This study is interested in major brain functioning abnormalities found in ASD during adolescence. We have used Sawyer et al. (2018)'s publication [63] as a reference for defining the period of adolescence, including participants aged from 10 to 25 years old. As mentioned above, there are studies covering a wide age range but none on this period specifically and with a relatively large number of participants. Furthermore, to keep a homogenous age range between groups, we matched ASD individuals and controls on a case level by age.

These participants with ASD had received a clinical diagnosis of verbally and intellectually high-functioning autism according to DSM-5 criteria [1]. All ASD participants were diagnosed by the Autism Diagnostic Interview-Revised [64] (17 ASD participants) and/or the Autism Diagnostic Observation Schedule-Generic (ADOS, [65]) (15 ASD participants). All ASD and TD participants have completed the AQ [66] except for one ASD 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 [67] for children aged 6–17 years and the Wechsler Adult Intelligence Scale-Fourth Edition [68] for participants aged 18 years or above.

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 min in an awake RS eyes-closed condition, using an EGI Hydrocel Geodesic Sensor Net (HGSN-130) dense array of 128 Ag/AgCl sensors [69] (Electrical Geodesics Inc., Eugene, OR, USA). Considering our hypothesis and interest in the alpha band, we chose to study the eyes-closed condition. Alpha waves are mainly found with eyes closed and decrease with eyes opened [7, 70, 71]. Moreover, an eyes-closed condition would provide a closer measure of resting activity than open eyes because it minimizes cognitive load, goal-directed action, and external stimulation [72, 73]. Participants were instructed to relax, remain as still as possible, and close their eyes. Impedances were kept under 100 kΩ [74], 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 are being exported (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. After processing, nonoverlapping 2.048-s epochs were extracted for

Table 1 Population description

	ASD (n = 29)			TD (n = 38)			Group comparison
	Mean	SD	Range	Mean	SD	Range	
Age (years)	16.1	3.6	11.0–25.7	16.5	4.2	10.2–25.6	0.693
FSIQ	99.1	14.0	72–128	104.8	10.2	86–126	0.060
AQ total[a]	34.3	9.4	11–48	11.4	5.0	2–22	<.0001

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)

[a] 28 ASD participants completed the AQ

analysis. The EEG was visually screened by two experts (the first authors, PW and PC). The remaining artifacts (e.g., saccades, muscle contractions, head movement, etc.) were excluded manually for the analysis epoch by epoch before re-referenced to a common average reference. All participants had a minimum of 60 s of artifact-free data available for analysis (30 epochs of 2.048 s minimum per subject, ASD: mean number of epochs: 40.7, SD 11.5, range 30–69; TD: mean number of epochs: 44.1, SD 10.9, range 30–66), respecting Pascual-Marqui et al. (2011)'s guidelines [75].

We focused our spectral analysis on the alpha frequency band (7.5–12.5 Hz, [16, 76–78]) given our hypothesis.

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 [79, 80]). 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 [81]. 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 [82, 83]. *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.

Functional connectivity analysis

Regions of interest

To evaluate between-group connectivity differences, we conducted analyses with different the 3-RSNs. We selected seeds from key regions within the SMN, DMN, and DAN, from the parcellations described by Wu et al. [84] and Yeo et al. [85], 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.

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 [75]). In this respect, it is considered to contain only physiological connectivity [57].

Table 2 Cortical regions of interest for RSN functional connectivity

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

SMN sensorimotor network, *DAN* dorsal attention network, *DMN* default mode network, *L* left, *R* right

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 ($t = 3.291$).

LORETA using non-parametric permutation tests, we pursued analyses by extracting connectivity values (within- and between-RSN functional connectivity) that were significantly different between groups to conduct backward stepwise regression analyses with age and ASD symptomatology (AQ) as individual predictors.

Results

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.

Functional connectivity within RSNs

We performed statistical analyses with sLORETA software to assess between-group differences in lagged phase synchronization within the 3-RSNs, namely the SMN, DAN, and DMN (Table 3, Fig. 2 and summary

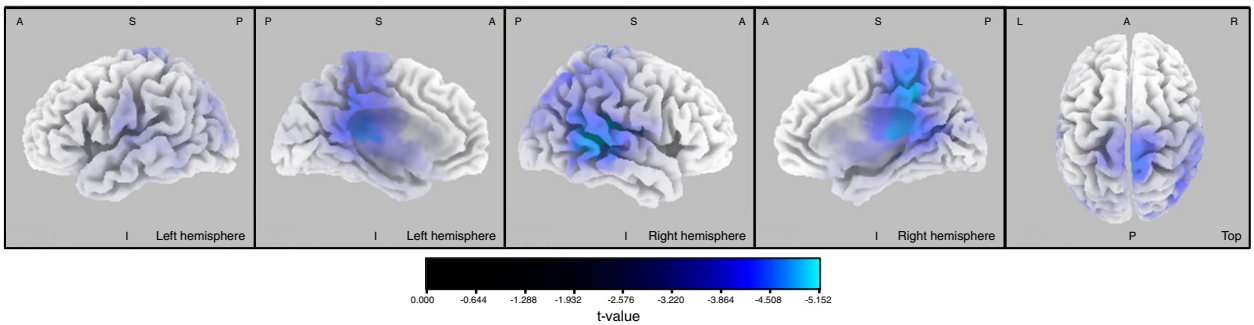

Fig. 1 Source localization differences between ASD and TD groups in the alpha frequency band. Blue areas represent the spatial extent of voxels with a significantly reduced current source density between ASD and TD groups ($p < 0.05$ corrected for multiple testing, $t < -3.426$). L left, R right, A anterior, P posterior, S superior, I inferior

Table 3 Significant differences in within-RSN functional connectivity in the ASD group relative to the TD group

Regions	MNI coordinates			Regions	MNI coordinates			*t*	*p*
	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

SMN sensorimotor network, *DAN* dorsal attention network, *DMN* default mode network, *L* left, *R* right

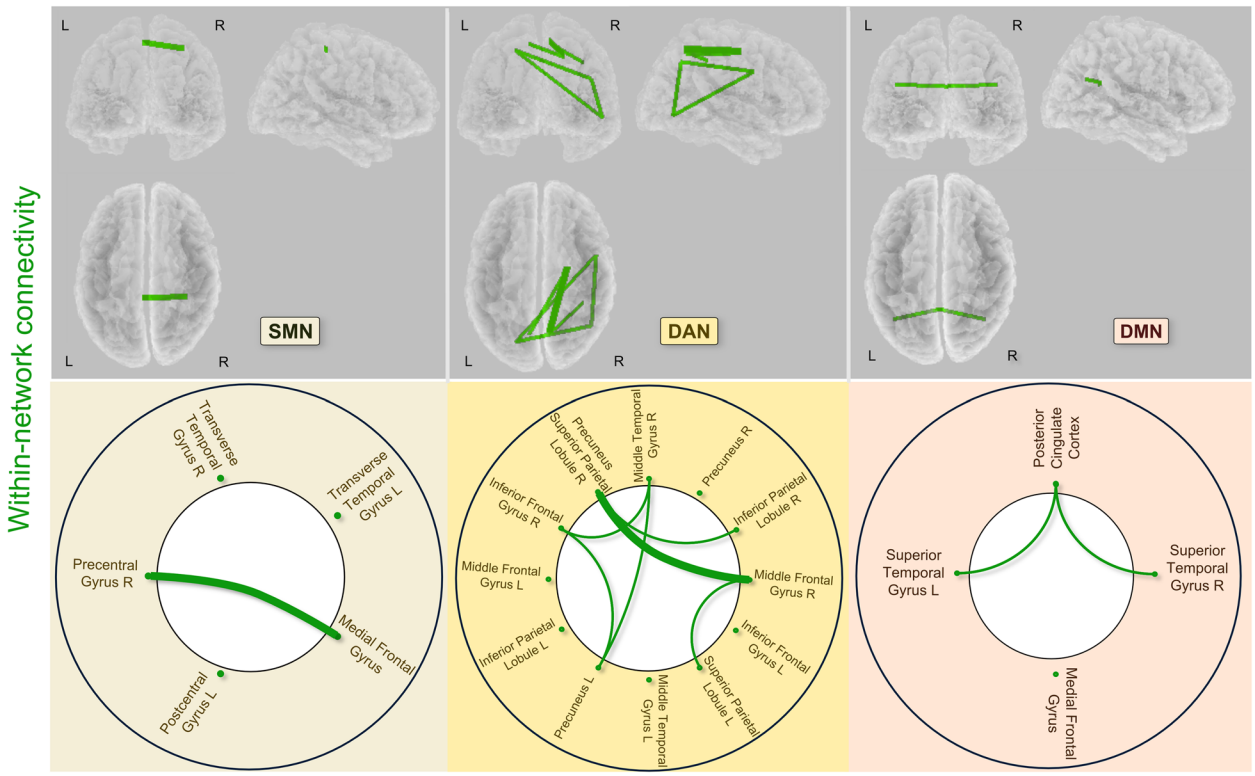

Fig. 2 Connectogram of significant differences in within-RSN connectivity in the ASD group relative to the TD group. Lines indicate significantly decreased lagged phase synchronization for the ASD group relative to the TD group within SMN, DAN, and DMN (thin line $p < 0.05$, thick line $p < 0.01$). L left, R right

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 ($t = -3.555$, $p < 0.005$). 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 ($t = -3.817$, $p < 0.009$) and the right inferior parietal lobule ($t = -3.247$, $p < 0.038$), (2) between the left precuneus and both the right middle temporal gyrus ($t = -3.764$, $p < 0.011$) and the right inferior frontal gyrus ($t = -3.503$, $p < 0.020$), (3) between the right middle temporal gyrus and the right inferior frontal gyrus ($t = -3.315$, $p < 0.032$), and (4) between the right middle frontal gyrus and the left superior parietal lobule ($t = -3.160$, $p < 0.046$). Within the DMN, we identified significantly decreased connectivity between the posterior cingulate cortex and the right and left superior temporal gyrus ($t = -2.559$, $p < 0.038$, $t = -2.892$, $p < 0.018$, respectively) in the ASD group relative to the TD group.

Functional connectivity between RSNs

The ASD and TD groups also differed on connectivity between the 3-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 ($t = -3.667$, $p < 0.025$) and the bilateral precuneus of the DAN (right precuneus: $t = -3.611$, $p < 0.028$; left precuneus: $t = -3.459$, $p < 0.038$), (2) between the left transverse temporal gyrus of the SMN and the right precuneus (superior parietal) of the DAN ($t = -3.640$, $p < 0.026$), and (3) between the right precentral gyrus of the SMN and the right inferior parietal lobule of the DAN ($t = -3.561$, $p < 0.032$). 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 ($t = -3.529$, $p < 0.015$). For DAN and DMN connectivity, results revealed significantly decreased lagged phase synchronization in the ASD group relative

Table 4 Significant differences in between-RSN functional connectivity in the ASD group relative to the TD group

Regions	MNI coordinates			Regions	MNI coordinates			*t*	*p*
	x	*y*	*z*		*x*	*y*	*z*		
SMN and DAN									
SMN				*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 and DMN									
SMN				*DMN*					
Medial frontal gyrus	−4	−33	66	Superior temporal gyrus R	41	−60	29	−3.529	<0.015
DAN and DMN									
DAN				*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

SMN sensorimotor network, *DAN* dorsal attention network, *DMN* default mode network, *L* left, *R* right

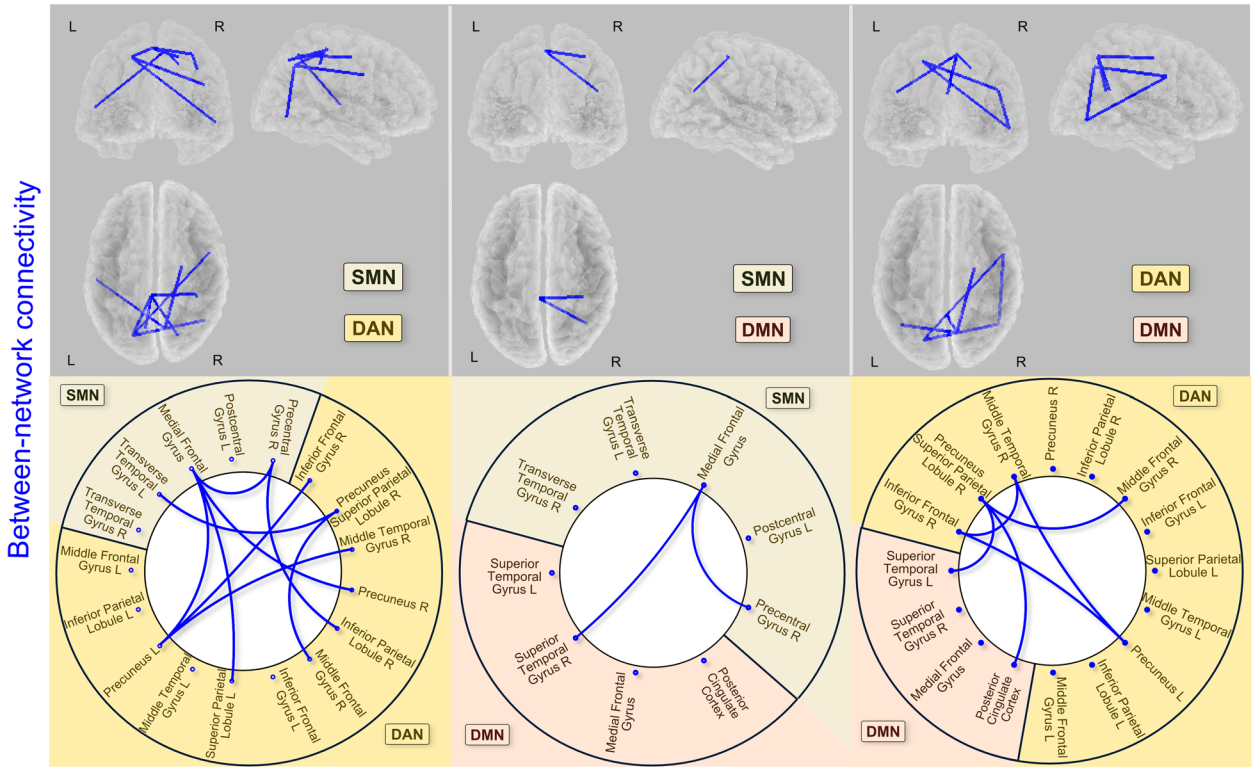

Fig. 3 Connectogram of significant differences in between-RSN connectivity in the ASD group relative to the TD group. Lines indicate significantly decreased lagged phase synchronization for the ASD group relative to the TD group between SMN and DAN, between SMN and DMN, and between DAN and DMN (thin line $p < 0.05$). L left, R right

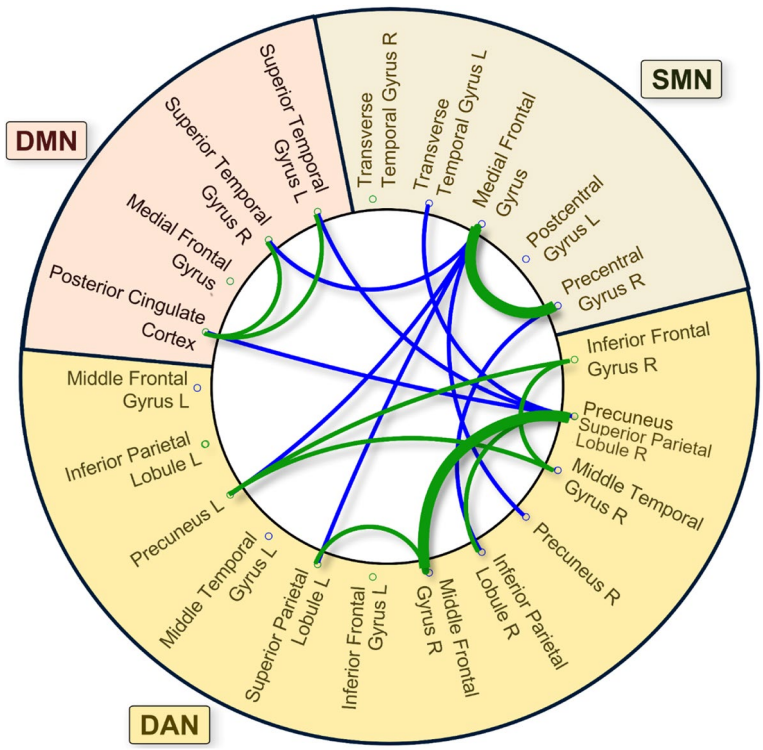

Fig. 4 Summary of decreased connectivity within and between RSN in the ASD group relative to TD. Lines indicate significant decreased lagged phase synchronization for the ASD group relative to the TD group. Green lines represent decreased connectivity within RSNs, and blue lines represent decreased connectivity between RSNs. Thin line $p < 0.05$, thick line $p < 0.01$. L, left, R right

to the TD group between the right precuneus (superior parietal) of the DAN and both the left superior temporal gyrus ($t = -3.460$, $p < 0.033$) and the posterior cingulate cortex of the DMN ($t = -3.293$, $p < 0.05$).

Backward stepwise regression analyses with age and ASD symptomatology (AQ) as individual predictors revealed no significant effect for the ASD group. However, we observed significant results in the TD group. Age was a significant predictor within the three 3-RSNs (SMN, DAN, and DMN) and between RSN functional connectivity (SMN-DAN and DAN-DMN). AQ was a significant predictor within 2-RSNs (DAN and DMN) and between RSN functional connectivity (DAN-SMN and DMN-SMN, see supplementary data for details).

Discussion

The present study investigated sources and functional connectivity in the 3-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.

Alpha band: a relevant marker for studying ASD atypicality

Our results showed decreased activity and connectivity in the alpha band in ASD participants. 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 [7, 70, 86]. Moreover, alpha activity seems to be associated with modulating sensory input [70, 87, 88], and alpha disturbances could lead to atypical sensory processing in ASD [89, 90]. Given together, this might suggest that individuals with ASD would have more difficulty integrating incoming information (bottom-up) at rest.

Increasing evidence from publications also shows that alpha activity plays a role in abnormal social and emotional stimuli processing in ASD [91, 92]. Given the alpha band involvement in attention, perception, and social cognition [6, 7, 31, 93], we speculated that alpha atypicality would participate in autistic symptoms. In this vein, Shephard et al. [94] 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 [92, 95]). In particular, alpha desynchronization may be linked to increased neural excitability/decreased neural inhibition [7]. Previous studies in ASD reported abnormal cortical inhibitory interneurons [96, 97] and altered glutamatergic levels [98, 99], associated with atypical sensory processing in ASD [90, 100]. 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 [89].

Thus, our data point out that excitation/inhibition imbalance highlighted by a decrease in alpha activity increases neural noise in ASD. This may result in integration difficulties affecting both external information (sensory processing, bottom-up) and internal information (mental representations, top-down) with an effect on the representation of oneself in the world and the shifting of mental representations [101–103].

Functional connectivity within resting-state networks

We found reduced lagged phase synchronization within the SMN, DAN, and DMN in the ASD group compared to the TD group, possibly reflecting an imbalance between bottom-up and top-down information integration explained as follows. This reduction is correlated with neither age nor symptom severity in the ASD group. However, we observed mainly an age effect on connectivity within the DAN, SMN, and DMN in the TD group supporting a developmental effect on RSNs. The same pattern is observed for between RSNs. We can hypothesis particularities in connectivity observed in autism are stable over time.

First, we highlighted underconnectivity within the SMN, between the medial frontal gyrus and the right precentral gyrus. A recent fMRI study also showed reduced functional connectivity among visual association, somatosensory, and motor networks [104]. This decreased functional connectivity between somatosensory and motor networks seems to be consistent with the atypical multisensory and motor integration observed in individuals with ASD and could participate in the core symptoms of ASD [105, 106]. Dysconnectivity within the SMN may result in an atypical integration of the external sensory environment and might be interpreted as an index of increased sensitivity to sensory information, which is in line with the enhanced perceptual functioning theory [107]. Therefore, aberrant functional connectivity in the SMN may explain multisensory and motor integration deficits, which play a crucial role in developing imitation, motor communication, and social skills [108, 109], all impaired in ASD.

Second, in line with previously findings reported in fMRI studies [41, 110–112] and MEG studies for the gamma band [38], participants with ASD exhibited decreased connectivity within the DMN, particularly involving the posterior cingulate cortex and right and left superior temporal gyrus. Li et al. showed that underconnectivity involving the posterior cingulate cortex, insula, and superior temporal gyrus was negatively associated with ASD symptom severity measured by ADOS [113]. These DMN perturbations may profoundly modify internal information, including memory, mental scene construction, or the sense of self, and act as a significant contributor to social dysfunction (see [41] for review).

Finally, in agreement with previously reported results in fMRI by Bi et al. [50] and Farrant and Uddin [51], 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 difficulties 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 [49], it would be possible that this atypical connectivity might participate in shifting difficulties associated with autistic symptoms [114].

Functional connectivity between resting-state networks

We showed decrease between-network connectivity between SMN, DAN, and DMN in the ASD group relative to the TD group. Importantly, the communication among brain regions belonging to the SMN, DAN, and DMN could be related to the ability to switch between external and internal information sources.

The underconnectivity observed in the ASD group between the SMN and DAN may generate delays in perceptual input and information transmission, thereby compromising the integration of information from the environment [40, 115]. In ASD, the attentional focus seems to be less oriented to the external information, especially when directly related to own's body representation. Therefore, these results shed light on the atypical perception that may focus on details in ASD [107, 116].

Moreover, the underconnectivity we observed between the right superior temporal gyrus in the DMN and the medial frontal gyrus in the SMN could participate in the atypical integration of external sensory information (SMN) and bind this external information to internal information (DMN), which may modify the perception

of environmental stimuli related to the self [117]. Hence, an atypical representation of the body and its location in space provided by the SMN may participate in an atypical sense of self [118, 119].

Finally, the underconnectivity we observed between DAN (precuneus-superior parietal lobule) and DMN (superior temporal gyrus and posterior cingulate cortex) provides additional arguments pointing to a communication deficit in ASD. This decreased connectivity suggests difficulties switching between externally oriented attention (the world) and internally oriented thoughts (representations of the world and the self). Furthermore, studies have shown that decreased connectivity between the precuneus and temporal gyrus is correlated with the ADOS social score [101], highlighting the importance of these regions in ASD symptomatology.

The reduced connectivity between these 3-RSNs seems to imply an atypical integration of both information from the external environment via the sensory organs (bottom-up) and top-down mental representations of the environment (memories, beliefs or expectations, top-down) but also to switch between these external and internal information [5]. The difficulty in integrating incoming sensory information to previously stored information could be linked to the weak central coherence theory [120]. The sensory over-responsivity may lead to a chronic state of hyperarousal at rest [121] that would impact the internal organization.

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 the 3-RSNs, suggesting atypical multisensory integration, feeling of body ownership [122], and imitation skills, which play a role in social skills [108, 109]. 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 [118, 119]. 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 [123, 124]). The precuneus associated with the posterior cingulate cortex contributes to self/other referential processing [125, 126] and the monitoring of the environment [127]. 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 [128], arousal and awareness [129], and self-referential thought [130] and affect the stability of the brain network over time (*whole-brain metastability* [131];). Given their involvement, abnormalities in these brain regions may significantly impact social disabilities in autism.

Beyond, from a broader perspective, our results might be better understood though the lens of the embodied cognition framework. Embodied cognition refers to the theory that the environment and the body (e.g., sensorimotor information) influence cognition (e.g., memory, mental simulation, representation, and attention) with a *bottom-up* process and, reversely, how cognition influences the body through a *top-down* process. Specifically, the SMN and its relationship to the DMN and DAN may be an important brain correlate of the perception-action loop [132]. In the case of ASD individuals, an impairment in the communication between and within the SMN may be responsible to poor integration of sensorimotor information [133–135]. Reduced functional connectivity may modify the conscious perception of the external world in relation to self-referential processes, with possible consequences on social skills [40, 136–138].

Limitations

We used sLORETA to measure cerebral activity and identify brain regions, but this technique has spatial limitations. As such, other methods would be needed to precise the spatial characteristics of our results. Second, we have chosen a wide period of adolescence, from 10 to 25 years, and it would be relevant to examine specific neurodevelopmental changes between early and late adolescence. Such a study would enable the results to be replicated with a larger sample size. Hypotheses have been formulated on the cognitive difficulties observed in autism but it would be very interesting to confirm them by directly analyzing the relation between connectivity deficits and ASD symptoms, especially social difficulties. High heterogeneity was described in ASD and other studies would be needed to precise for example the relation between hypo- or hyper-sensitivity to sensory stimuli and connectivity. Finally, our population was composed of high-functioning participants, limiting generalization to adolescents across the spectrum.

Conclusion

We report reduced functional connectivity within and between DMN, SMN, and DAN in the ASD group relative to the TD group in the alpha band. Impaired neural communication within and between the 3-RSN may lead to altered integration and switching between externally oriented information and internally oriented thoughts. Indeed, hypoconnectivity analyses revealed atypicality in integrative brain regions that may account for difficulties in (1) perception (external): somatosensory integration of the environment, (2) cognition (memory, mental representation, attention, etc.) integration of internal representations, and (3) reciprocal influence between external environmental stimuli to internal

representations (bottom-up process) and, reversely, between cognition and the body through a *top-down* process. These possible impairments in the embodiment are interesting to consider and might participate in 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.

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; ROIs: 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.

Supplementary Information

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Additional file 1. Significant differences in current source density in alpha band for ASD and TD groups ($p < 0.05$). For each region that showed significant decrease in current source density, the number of voxels, the localization of the maximum statistical peak difference, and the involvement in a RSN of interest for this region were indicated. The names of the regions are the labels given by sLORETA for the corresponding coordinates.

Additional file 2. Backward stepwise regression analyses with age and ASD symptomatology (AQ) as individual predictors on connectivity values (within and between-RSN functional connectivity) that were significantly different between groups. Significant results were obtained only for the TD group. SMN: sensorimotor network; DAN: dorsal attention network; DMN: default mode network; L: left, R: right. RSNs: Resting State Networks.

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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 and 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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Availability of data and materials

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

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the French ethics 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.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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