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RESEARCH

Atypical segregation of frontoparietal and sensorimotor networks is related to social and executive function impairments in children with ASD

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Abstract
Two possible indicators of a deficient segregation of functional networks are within-underconnectivity and between-overconnectivity. Both these processes can be observed in Autism Spectrum Disorder (ASD) to be associated with different core and co-occurring atypicalties of behavior. We focused on within- and between-network connectivity of Frontoparietal and Sensorimotor networks in ASD compared to typically developed (TD) peers and its links to social difficulties and impairments of executive and motor functions. To our knowledge, this study for the first time described between-network connectivity of Frontoparietal and Sensorimotor networks in ASD with relations to symptoms of ASD. In this study, we utilised resting-state functional MRI to investigate 121 participants with ASD and 84 TD children. We investigated between-group differences of the connectivity between Frontoparietal and Sensorimotor regions. We also conducted brain-behavior analysis for beta values of these connections and behavioral scores. Controlling for age and sex, we found a significant group difference within- Frontoparietal network (right and left posterior parietal cortices were underconnected in ASD) and between-networks (right posterior parietal and right lateral sensorimotor cortices were overconnected in ASD). In the ASD group, we also showed that within-Frontoparietal underconnectivity was related to lower scores of social and executive functions as well as between-networks overconnectivity was associated with social difficulties only. There were no significant relationships between scores of motor functions and beta values. We confirmed the hypothesis of deficient segregation for Frontoparietal and Sensorimotor networks in ASD. These findings highlight the importance of between-network connectivity investigation.

Keywords Frontoparietal network · Sensorimotor network · Autism spectrum disorder · Social deficits · Repetitive behaviors · Executive functions

Introduction

A segregation of functional networks is a process in typical neurodevelopment during which the connections between regions of canonical intrinsic connectivity networks are becoming less coordinated and synchronized despite their topographical neighborhood allowing networks to get more isolated (Dosenbach et al., 2010; Grayson & Fair, 2017). Consequences of altered functional segregation are mostly linked to the inability of the brain to transform controlled processes into automatic ones (Wang et al., 2024). Altered functional segregation is commonly reported in individuals with Autism Spectrum Disorder (ASD) across a number of networks during resting and task performing (Shih et al., 2011; Rudie et al., 2012; Nebel et al., 2014; Fishman et al., 2015). Deficient segregation may be indicated in two general ways: overconnectivity between networks and underconnectivity within them. Both these impaired processes were reported to be associated with more severe autistic traits (Chen et al., 2021) including social communication

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difficulties and repetitive behaviors (Guo et al., 2023) and co-occurring conditions such as language impairment (Gao et al., 2019) and intellectual disability (Pua et al., 2018).

Following the impaired functional segregation findings, the current study focuses on the neural correlates of executive function and motor atypicalities within and between frontoparietal and sensorimotor networks (FPN; SMN) as these two major networks are associated with these abilities. Specifically, FPN facilitates attention processing (Scolari et al., 2015; Bartolomeo & Seidel Malkinson, 2019) and cognitive control (Caldinelli & Cusack, 2022; Wood & Nee, 2023) while SMN is typically related to motor performance, coordination (Bernard et al., 2013) and general cognitive functioning (Bagarinao et al., 2019). Thus, we assume within-FPN alterations can result in attention and cognitive control deficits, within-SMN disruptions can be associated with difficulties of dealing with motor and sensory information. It has been hypothesized that FPN supports more internal processes while SMN is mostly involved in externally driven functions (Lee & Frangou, 2017). We assume that violations of the between-network connectivity of FPN and SMN may be associated with social impairments in ASD as altered switching between internal and external modes might result in inability to process external stimuli and to create adaptive social responses.

FPN, generally also known as the central executive network, comprised right and left lateral prefrontal and posterior parietal cortices according to the Human Connectome Project (https://www.humanconnectome.org/). FPN has been shown to be involved in goal-oriented and external stimuli processing (Fox & Raichle, 2007), attentional control and working memory (Gong et al., 2016; Seeley et al., 2007) and decision making (Seeley et al., 2007). In individuals with ASD, it has been shown that within-FPN connectivity is lower during the performance of inhibition tasks (Kana et al., 2007; Solomon et al., 2014). Moreover, underconnectivity of this network was linked to impaired attention in ASD (Solomon et al., 2009).

SMN generally supports voluntary movements and somatic sensation (Yeo et al., 2011) as it consists of lateral and superior motor and somatosensory regions (https://www.humanconnectome.org/). Regarding SMN connectivity in individuals with ASD, it has been hypothesized that aberrant processes of sensorimotor integration not only occur but also impact social interaction in this condition (MacDonald et al., 2013). A recent study has found that SMN is overconnected in ASD compared to typically developing peers and confirmed that its hyperconnectivity was related to social dysfunction (Wang et al., 2021).

In individuals with ASD, not only within-network deficient and redundant connectivity was found for FPN and SMN but also between these connections with other large-scale brain networks. A study of Wang et al. (2021) who investigated functional connectivity in the Triple-Network Model (FPN, default mode network, DMN; salience network, SN) in ASD with co-occurring Attention deficit hyperactivity disorder revealed increased connectivity between the ventral part of DMN and left FPN indicating altered segregation of these networks. Regarding SMN, Oldehinkel et al. (2019) found decreased functional connectivity of somatosensory and lateral motor networks with visual association network and linked these atypicalities to multisensory and visual-motor impairments commonly occurring in individuals with ASD.

The current study aims to investigate, first, a segregation of FPN and SMN in individuals with ASD compared to typically developed (TD) participants, second, the relationships of within-, between-network connectivity and executive functions, repetitive behavior and social deficits. For the group comparisons, we conducted the region of interest (ROI) analysis between FPN and SMN assuming weaker within-network connectivity but stronger between-network one in individuals with ASD. Next, we hypothesized the weaker within-network connectivity deficits to be associated with difficulties of executive and motor functions for FPN and SMN, respectively, but greater between-network connectivity of FPN and SMN to be related to social impairments in individuals with ASD.

Method

Participants

This study was conducted using resting-state (*rs*-) fMRI and structural MRI data from the Autism Brain Imaging Data Exchange II (Di Martino et al., 2014). A total of 205 participants were included in the current study: 121 individuals with ASD (108 males, age range 5.1–13.9, M_{age}=9.1, SD_{age}=2.4) and 84 TD participants as a control group (56 males, age range 5.9–13.8, M_{age}=10, SD_{age}=2). As our study focused on inhibitory control and shifting attention abilities, the main inclusion criteria was the presence of Behavior Rating Inventory of Executive Function (BRIEF; Gioia et al., 2000). Five subsamples met this criterion (Georgetown University, Kennedy Krieger Institute, New York University, San Diego State University and University of Miami). Further, we decided to include subsets only with the same scanner used and scanning procedure conducted to minimize data acquisition variability. Thus, our sample resulted in Universities of Georgetown (initial N(ASD/controls)=51/55, included N(ASD/controls)=51/55) and New York (initial N(ASD/ controls)=75/30, included N(ASD/controls)=70/39) subsets (see GU scan parameters, NYU

scan parameters, for details) where 3 Tesla Siemens scanners and scanning procedures with 2 *ms* repetition time were applied. For each participant's rs-fMRI data, 154 measurements and 43 slices (the Georgetown site), 180 measurements and 34 slices (the New York site) were available. Severity of autistic traits was measured by Social Responsiveness Scale (SRS; Constantino & Gruber, 2012) and motor skills were assessed by Vineland Adaptive Behavior Scales (VABS; Sparrow & Cicchetti, 1989) in both these sites. Finally, as these subsets were age-wide, we also excluded participants above 14 years (three from the ASD group and one from TD).

Data preprocessing and processing

Preprocessing of demographic and behavioral data included scaling for continuous variables using the *MinMaxScaler* function and encoding for categorical ones with the *OneHotEncoder* transformer from the Python3 (Van Rossum & Drake, 2009) scikit-learn package (Pedregosa et al., 2011). Preprocessing of rs-fMRI data was performed using the *CONN toolbox* Version 22.a (https://www.nitrc.org/projects/conn; Whitfield-Gabrieli & Nieto-Castanon, 2012) following a flexible preprocessing pipeline (Nieto-Castanon, 2020). The steps included realignment with correction of susceptibility distortion interactions, slice timing correction, outlier detection, direct segmentation and MNI-space normalization, and smoothing. In addition, functional data were denoised using a standard denoising pipeline. The Supplementary file 1 provides the detailed processing description.

Data analysis

Regions of interest (ROIs) within FPN and SMN were defined by CONN's ICA analyses of Human Connectome Project dataset (Whitfield-Gabrieli & Nieto-Castanon, 2012). FPN included right/left lateral prefrontal (LPFC) and posterior parietal (PPC) ROIs (Fig. 1). SMN comprised lateral and (latSMN) superior (supSMN) somatosensory and motor regions bilaterally (Fig. 1).

ROI-to-ROI connectivity (RRC) analysis was performed for each pair of ROIs independently using General Linear Models (GLMs) to correlate the mean BOLD time-series at the single-subject level, resulting ROI-to-ROI functional connectivity matrices consisting of Fisher-transformed bivariate correlation coefficients (z-scored). Due to age and sex significant differences between the groups, we implemented these variables as control ones in each group-comparison model. All network nodes were used as both sources and targets, and ROI-to-ROI connections were set to a threshold by intensity of two-sided False discovery rate (FDR)-corrected $p < 0.05$.

For behavior-brain analysis, two separate GLM was built for BRIEF (T-scores of inhibitory control and shifting attention subscales), one GLM for SRS (total T-score - one model) and one GLM for VABS (raw scores of motor skills

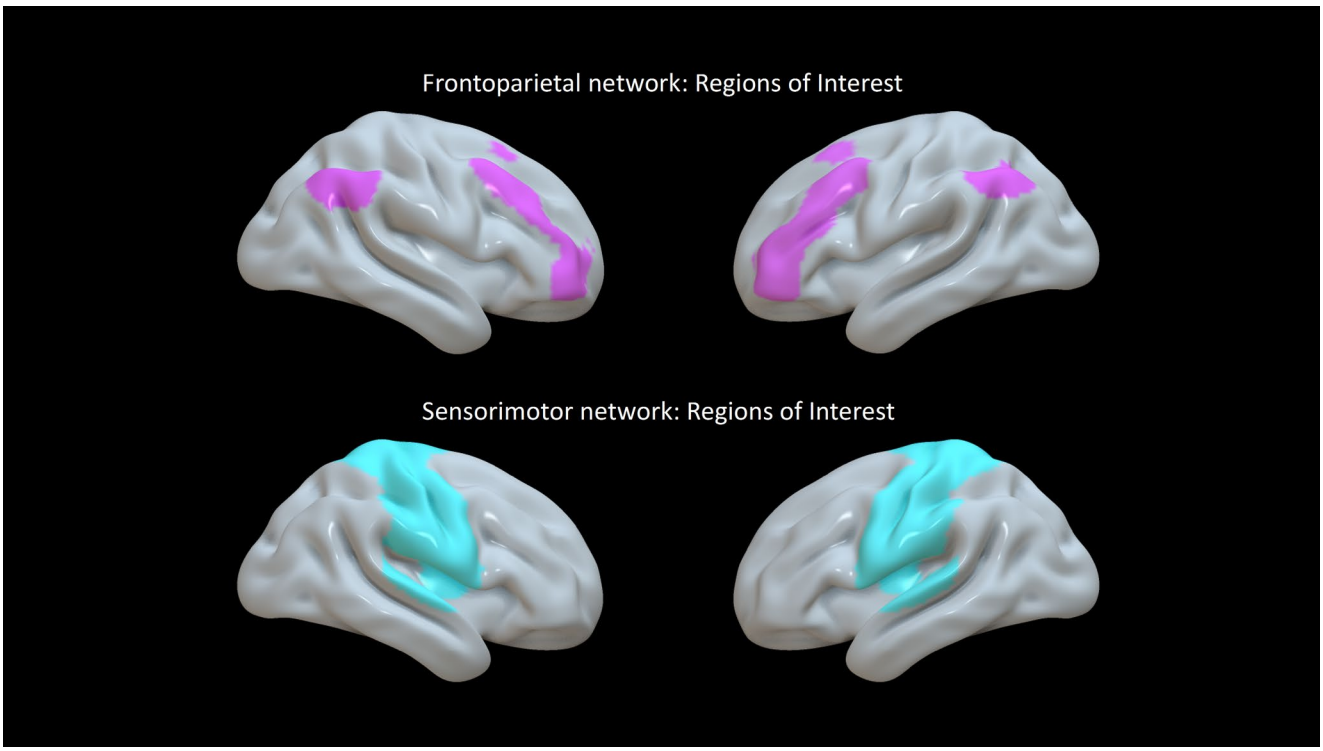

Fig. 1 Regions of interests (ROIs) within Frontoparietal and Sensorimotor networks

subscale). Age and sex were implemented as control variables in each model as well.

All reported p-values were FDR-corrected.

Results

Behavioral data

Generally, groups differed in their SRS, BRIEF and RBSR performances. Participants with ASD had greater SRS scores (more severe social impairments) M_{TD} = 44.6 (SD=6.7) vs. M_{ASD} = 76.7 (SD=15.4), U=234.5, p<0.001. Scores of BRIEF inhibitory control (M_{TD}= 46.4 (SD=7.9) vs. M_{ASD} = 60.7 (SD=11.9), U=1569, p<0.001) and BRIEF shifting attention (M_{TD}= 45.5 (SD=7.7) vs. M_{ASD} = 67.9 (SD=13.5), U=777, p<0.001) were also lower in the ASD group (more impaired abilities). Table 1 provides the descriptive statistics for the total study sample.

Between-group comparisons

ROI-to-ROI between groups analysis revealed increased connectivity in the ASD group during between-network comparisons (Fig. 2): left PPC of FPN and right latSMN ($beta$=0.08, T(201)=2.53, p=0.05). Also, within-network analysis showed decreased connectivity between left and right PPCs of FPN in the ASD group ($beta$ = -0.09, T(201) = -2.44, p=0.05).

Table 1 Demographic information for ASD and TD groups, M±SD (range)

Variable	*N* (ASD/TD)	ASD	TD	U	*p*
Age (years)	121/84	9.1±2.4 (5.1–13.9)	10±2 (5.9–13.8)	3910.5	<0.01
SRS total (T) [a]	121/82	76.7±15.4 (42–116)	44.6±6.7 (34–66)	234.5	<0.001
BRIEF Inhibitory (T) [b]	119/80	60.7±11.9 (36–91)	46.4±7.9 (36–73)	1569	<0.001
BRIEF shifting (T)[b]	119/80	67.9±13.5 (37–99)	45.5±7.7 (36–64)	777	<0.001
VABS motor skills [c]	26/NA	86.7±11.7 (67–111)	NA	-	-
			Chi-squared		*p*
Sex (male/female)		108/13	56/28	15.81	<0.001

NA not applicable

Mann-Whitney U-tests were conducted to compare the mean of the demographic and behavioral data in ASD and TD groups

[a]Social Responsiveness Scale – Second Edition. The result is provided in T-scores

[b]Behavior Rating Inventory of Executive Function, Shifting attention and Inhibitory control subscales. The results are provided in T-scores

[c]Vineland Adaptive Behavior of Motor Skills subscale. The results are provided in raw scores

Brain-behavior relationships

GLMs with behavioral measures as independent variables in the ASD group showed that weaker connectivity within FPN (left LPFC and right PPC) is associated with greater BRIEF scores in inhibitory control ($beta$ = -0.27, T(115) = -2.96, p=0.02) and shifting attention ($beta$ = -0.31, T(115) = -3.51, p=0.004) subscales (Fig. 3). In other words, the lower connectivity within ROIs of FPN is the more impaired executive functions in individuals with ASD.

Next, we found that increased between-network connectivity (right PPC of FPN and left latSMN; $beta$=0.25, T(117)=2.75, p=0.02) and decreased within-FPN connectivity (right PPC and left PPC of FPN; $beta$ = -0.25, T(117) = -2.47, p=0.03; right PPC and left LPFC of FPN; $beta$ = -0.28, T(117) = -3.00, p=0.02) were related to greater SRS scores (more severe social impairments; Fig. 4).

There were no significant effects for relationships between VABS and ROI-to-ROI connectivity.

Post-hoc analysis

As our sample was not balanced, we run the ROI-to-ROI connectivity between-group analysis to identify if our results are robust. Thus, we decided to subsample the groups using the R package *MatchIt* (Ho et al., 2011) according to such variables as age, sex and handedness, and re-run the same analysis for these new subsamples (ASD_1 vs. TD_1, ASD_2 vs. TD_2). Table 2 provides all the demographic information of the subsamples.

Between-group comparisons for the *Subsample 1* showed decreased within-FPN connectivity between left PPC and right LPFC ($beta$ = -0.14, T(75) = -2.87, p-unc=0.005, p-FDR-$corrected$=0.03) in the ASD group (Fig. 5). Between-group analysis for the *Subsample 2* demonstrated greater between-networks connectivity of left PPC to left latSMN ($beta$=0.12, T(80)=2.69, p-unc=0.009, p-FDR-$corrected$=0.03) and right latSMN ($beta$=0.11, T(80)=2.59, p-unc=0.01, p-FDR-$corrected$=0.03) in the ASD group (Fig. 5).

Discussion

In this study, we characterized functional segregation of two large scale networks, namely FPN and SMN, in children with ASD. Specifically, we analyzed within- and between-network connectivity of FPN and SMN in the ASD group

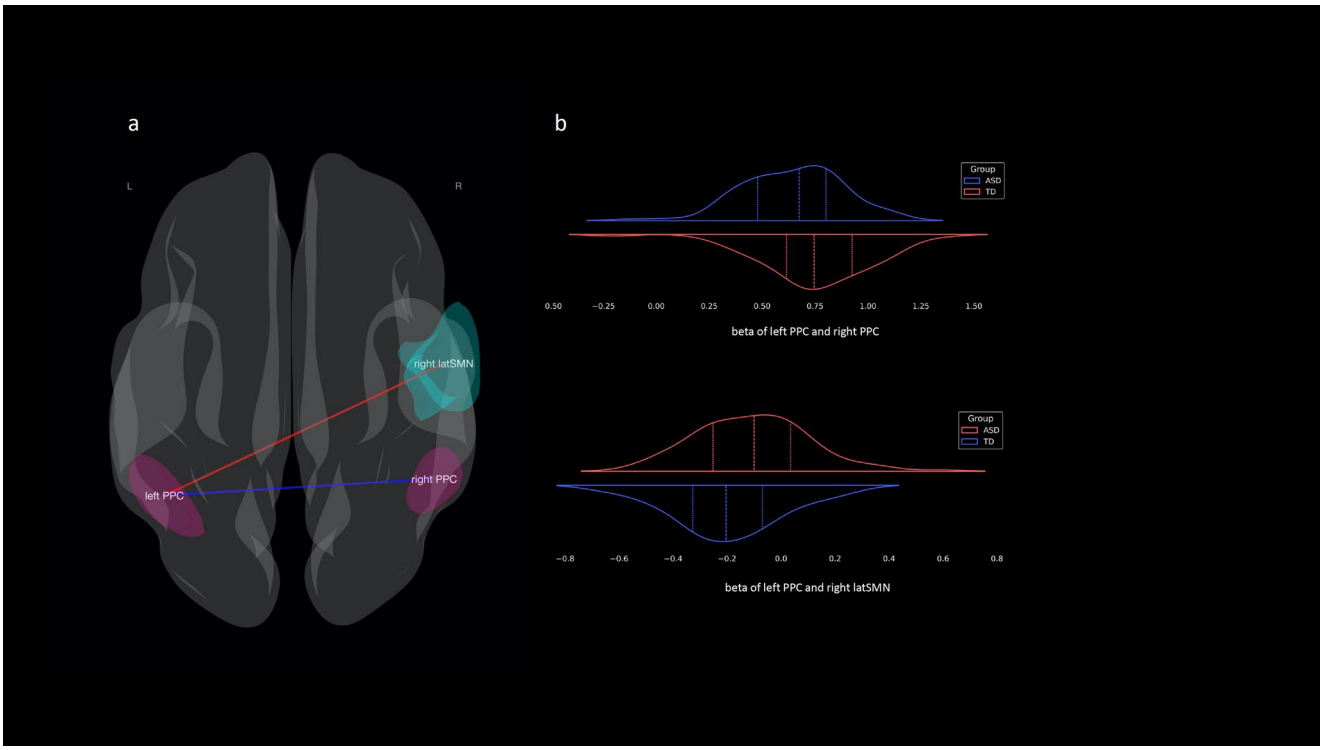

Fig. 2 Significant differences of ROI-to-ROI connectivity between ASD and TD groups of children: (**a**) overconnectivity (red line) between SMN (aquamarine nodes) and FPN (lilac nodes), underconnectivity within FPN in ASD group compared to TD children; (**b**) distributions of beta values for right left PPC - latSMN and left PPC - right PPC in each group

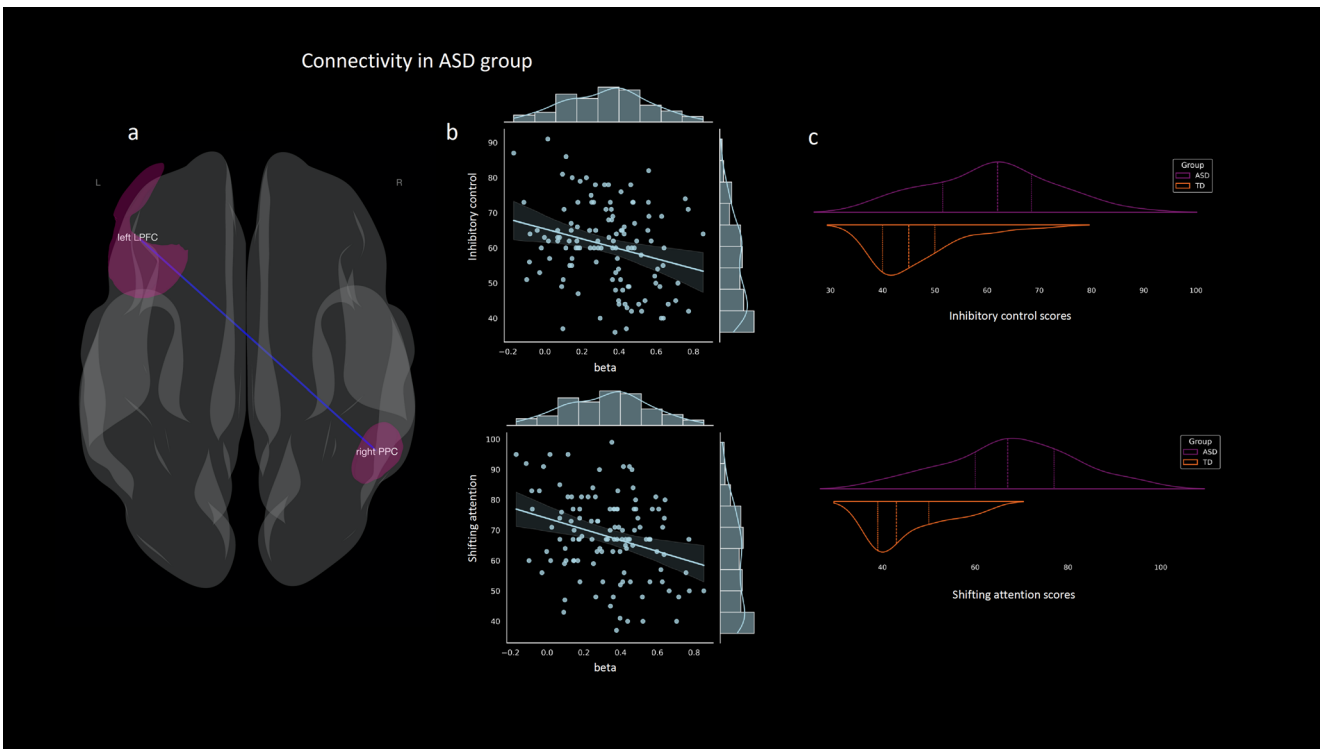

Fig. 3 The relationships between ROI-to-ROI connectivity and BRIEF scores in ASD group: (**a**) negative BRIEF-effect for both inhibitory control and shifting attention subscales on left LPFC and right PPC connection within FPN; (**b**) relationships between beta values of LPFC and right PPC connection and BRIEF scores of inhibitory control and shifting attention subscales in ASD group; (**c**) distributions of BRIEF scores of inhibitory control and shifting attention subscales in ASD and TD groups of children

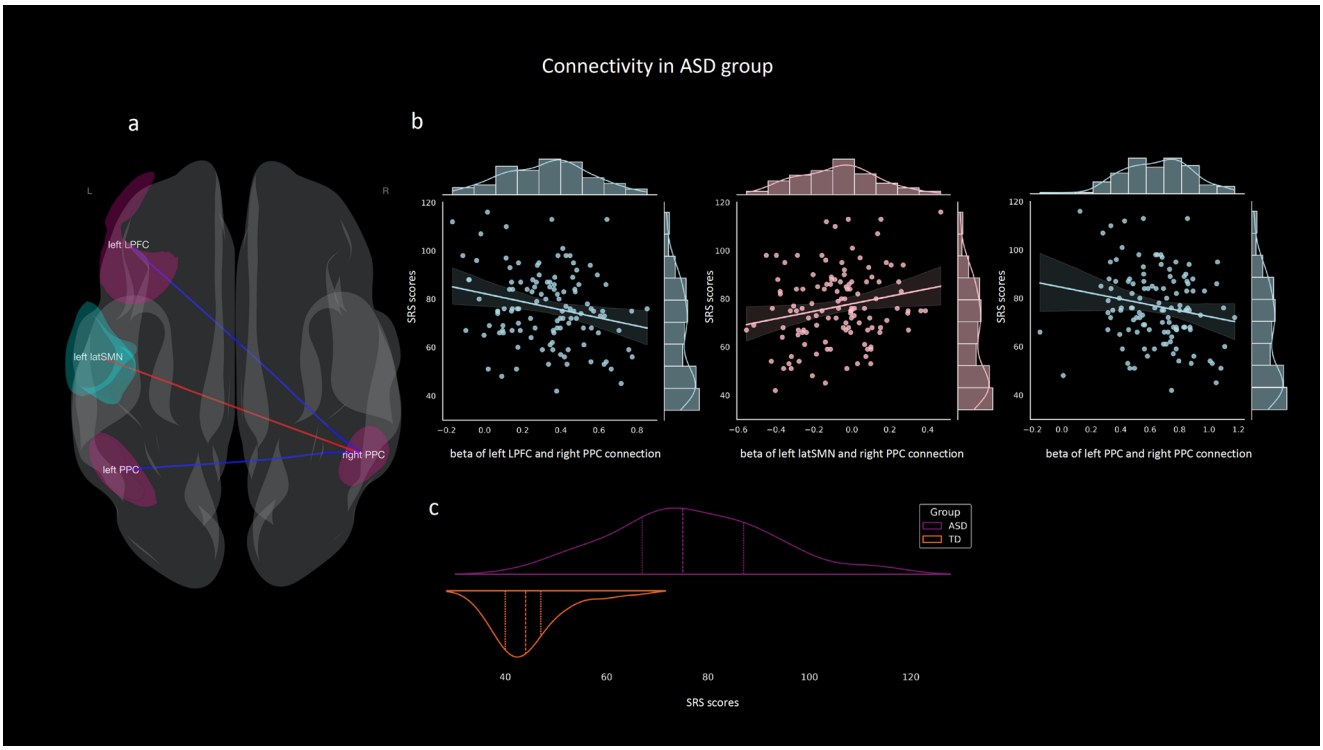

Fig. 4 The relationships between ROI-to-ROI connectivity and SRS scores in ASD group: (**a**) negative SRS-effect on left LPFC and right PPC, left PPC and right PPC connections within FPN; positive SRS-effect on right PPC of FPN and left latSMN connection; (**b**) relationships between beta values of these connections and SRS scores in ASD group; (**c**) distribution of SRS scores in ASD and TD groups of children

Table 2 Ratio information for ASD and TD subsamples

	Sex (m: f)	Hand (*r*: l:amb)	Age (M ± SD)
Subsample 1: ASD/TD	35:6 / 27:14	38:2:1 / 39:2:0	9.8 ± 1.9 / 9.8 ± 1.9
Subsample 2: ASD/TD	36:6 / 28:14	33:7:2 / 40:1:1	10.2 ± 2 / 10.3 ± 1.9

m = males, f = females

r = right-, l = left-handed, amb = ambidextrous

M = Mean, SD = Standard Deviation

ASD = Autism Spectrum Disorder, TD = Typically Developing

compared to TD peers linking this variability to executive functions, social interactions and motor skills in the ASD group. Confirming the hypothesis of the segregation deficiency, we demonstrated that children with ASD exhibited weaker within-network but stronger between-network connectivity. Moreover, weaker within-FPN connectivity was associated with impairments in inhibitory control and shifting attention and more severe social deficits in individuals with ASD. As well, increased between-network connectivity was related to more severe social difficulties in ASD. A segregation of functional networks plays a crucial role during neurodevelopment tailing higher modularity of the brain and maturing of more specified neural subsystems (Wang et al., 2024). As we found increased between- but decreased within-network connectivity of FPN and SMN, in line with Wang et al. (2021) and Oldehinkel et al. (2019), we may conclude that sensorimotor and executive subsystems are less segregated and less isolated in children with ASD. Moreover, we showed that the greater between FPN and SMN and the weaker within-FPN connectivity is associated with the more severe social difficulties of the core autistic symptoms. Putting previous studies' and our findings together, we believe that apart from the within-network underconnectivity, the between-network overconnectivity, i.e. impaired network differentiation and specification, is also a possible marker of ASD (Shih et al., 2011; Rudie et al., 2012; Nebel et al., 2014; Fishman et al., 2015). Conceptually, our results are in line with Nomi and Uddin's theory as we also showed that children with ASD exhibit atypical within- and between-network functional connectivity (Nomi & Uddin, 2015). Moreover, we complemented this assumption by the details on lower within- but greater between-network connectivity in children with ASD compared to TD. This finding may be important for understanding the nature of connectivity alterations in ASD.

Our post-hoc analysis on balanced subsamples showed the same patterns of the group differences as the initial one did. Specifically, once again we demonstrated between-network over- and within-network underconnectivity but with

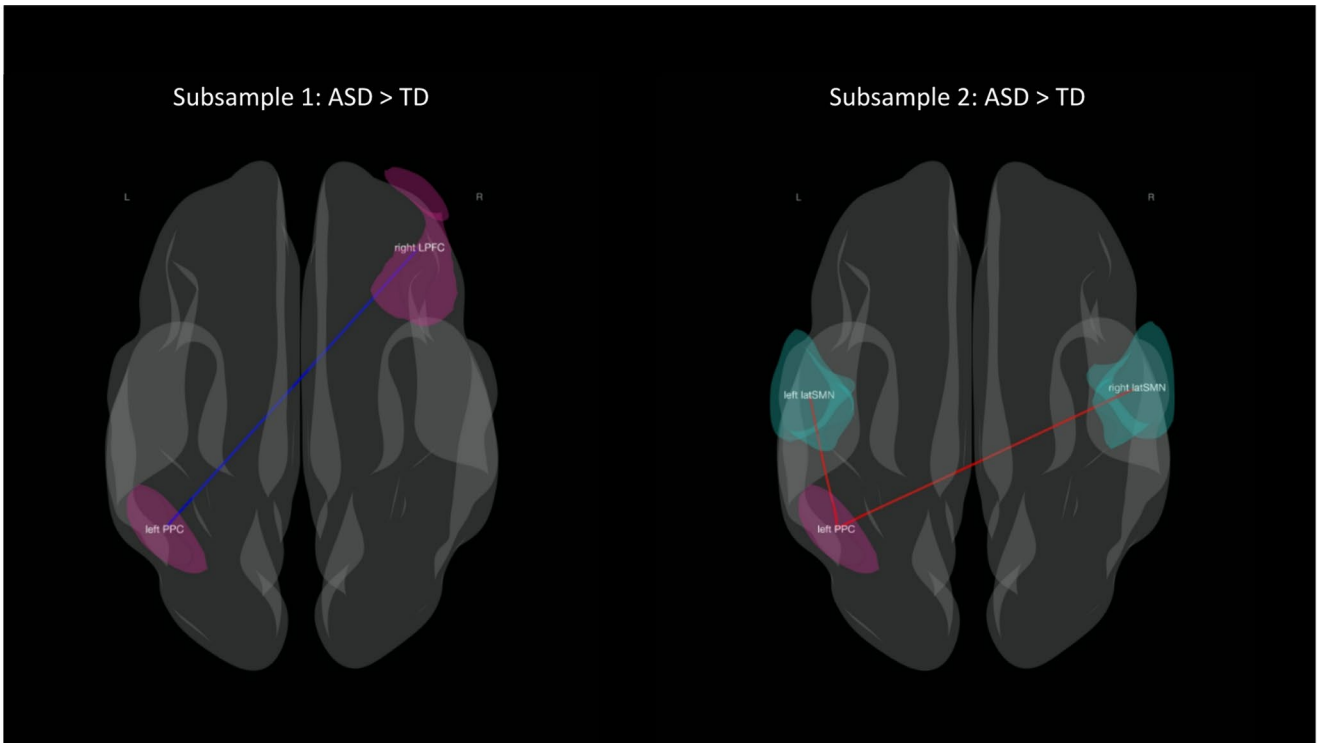

Fig. 5 Significant differences of ROI-to-ROI connectivity between ASD and TD groups of children in each subsample: overconnectivity (red line) between SMN (aquamarine nodes) and FPN (lilac nodes), underconnectivity within FPN in ASD group compared to TD children

other regions of SMN and FPN in individuals with ASD compared to TD peers. It also plays to the hypothesis of deficient segregation. These networks mature atypically in ASD meaning different trajectories or delays of development.

Aside from the social deficits, most children with ASD experience the executive function difficulties (Craig et al., 2016; Henry et al., 2010). In this study, we focused on inhibitory control and shifting attention as they are thought to underlie other core autistic traits such as restricted and repetitive interests (Faja & Nelson, 2019). According to BRIEF (Gioia et al., 2000), our participants with ASD had greater scores in inhibitory control and shifting attention subscales compared to TD peers indicating more impaired skills of these executive functions. Moreover, the more impaired inhibitory control and shifting attention abilities were related to decreased within-FPN connectivity, specifically, to weaker connectivity between left LPFC and right PPC. As the previous meta-analysis of May and Kana (2020) proposed, it could be due to the deficiency of wider activation of parietal regions within-FPN in individuals with ASD. This underconnectivity between prefrontal and posterior parietal regions may result in disruption of generating motor plans directed to cognitive tasks' performance (Katsuki & Constantinidis, 2012).

Despite our expectations and contrary to the study of Wang et al. (2021), the current results have not shown significant differences of SMN connectivity between ASD and TD groups nor associations of within-SMN connectivity and motor skills or social deficits in ASD. Regarding Wang's et al. (2021) research, the distinction of the findings could be due to the different age-range and sex of the samples. While Wang et al. (2021) have been focusing on young males with ASD only, we additionally included young adolescents to expand developmental differences. Thus, overconnectivity of SMN could be a specific marker for only 3–7-year-old boys with ASD. One more potential explanation is methodologically different approaches as the previous study used independent component analysis to identify SMN regions (Wang et al., 2021), whereas we stuck to the HPC atlas-based labeling (https://www.humanconnectome.org/). Future studies may benefit from the comparisons of various FPN- and SMN-labeling methods, specifically, with the help of independent component analysis, and dividing participants with ASD into subsamples according to phenotypes and demography.

Conclusion

This study focused on connectivity within and between FPN and SMN in children with ASD. We showed that these networks are deficiently segregated in children with ASD, thus, we concluded that executive and sensorimotor systems are less differentiated in ASD compared to typical

neurodevelopment. Moreover, their within-underconnectivity and between-overconnectivity are connected to more severe autistic traits and impairments of inhibitory control and shifting attention.

Limitations

Several limitations of this study need to be considered. First, our groups were not balanced in sex, thus, any interpretations of this work have to be taken with caution. As our study investigated network segregation only in children with ASD, it would be important to track these changes longitudinally for understanding maturation and aging of this process. Also, despite our great initial sample size, the subsample for the motor skills and SMN connectivity experiment was quite small which should be addressed in future research. Also, our data differed between groups in some of the quality fMRI metrics. One more limitation and future direction of the research is ICA-based connectivity study. For this purpose, bigger data are needed to find such components that would describe more than 80% of the sample to capture the same functional units across participants. Finally, task-based research with shifting attention, inhibitory control and motor performance are needed to verify our resting-state findings.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11682-025-01016-7.

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Author contributions AM: methodology, investigation, data curation, formal analysis, writing—original draft, and writing—review and editing. OD: writing—review and editing, resources. VA: writing—review and editing, and project administration. All authors read and approved the final manuscript.

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Data availability No datasets were generated or analysed during the current study.

Code availability The code for data analysis and processing is available from the corresponding author upon a reasonable request.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication All authors read and approved the final manuscript.

Competing interests The authors declare no competing interests.

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