Autism Research

RESEARCH ARTICLE

Associations Between Brain Network Connectivity and Cognitive Measures in Autism Spectrum Disorder: A Post Hoc Analysis of a Parent Study "Evaluating the Safety and Efficacy of Transcranial Pulse Stimulation on Autism Spectrum Disorder"

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ABSTRACT

This study presents a post hoc analysis of our parent study "Evaluating the Safety and Efficacy of Transcranial Pulse Stimulation on Autism Spectrum Disorder" study which was a double-blind, sham-controlled, randomized controlled trial. In this study, we examined associations between changes in brain network connectivity and cognitive performance in young adolescents (12–17 years) with autism spectrum disorder (ASD) following the administration of transcranial pulse stimulation (TPS) which is considered non-invasive, evidenced-based brain stimulation for neurodegenerative disorders and neuropsychiatric disorders. Our findings indicate that increased connectivity in specific brain networks is associated with improvements in cognitive measures, suggesting that connectivity changes may underpin cognitive changes observed after six TPS intervention. These results highlight potential neural mechanisms underlying cognitive improvements in ASD, although causality cannot be inferred from these associations.

Trial Registration: ClinicalTrials.gov identifier: NCT05408793

1 | Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by impaired capacity for reciprocal social communication and interaction (Nazeer and Ghaziuddin 2012). Recent systematic reviews concluded that the global prevalence of ASD is 0.6% (Salari et al. 2022), with approximately 1% of children diagnosed with ASD. In particular, compared with their female counterparts, males are at greater risk for negative symptoms of ASD (Zeidan et al. 2022). Notably, individuals with ASD exhibit a range of symptoms with varying degrees of severity or dysfunctions (Lord et al. 2018) that are linked with increased risk of developing psychiatric and clinical morbidities (Howlin and Moss 2012).

Summary

- In this study, we analyzed brain scans and cognitive test results from individuals with autism spectrum disorder (ASD) who took part in a larger research project called "Evaluating the Safety and Efficacy of Transcranial Pulse Stimulation on Autism Spectrum Disorder".
- We found that when certain brain networks became more connected, participants also tended to perform better on tests of thinking and memory.
- This suggests that changes in how different parts of the brain communicate may be linked to improvements in thinking skills for people with ASD.
- However, we cannot say for certain that one causes the other—only that they are related.

Previous neuroimaging studies have elucidated the potential underlying neural mechanisms of ASD (Won et al. 2013; Allen and Courchesne 2003; Courchesne 2002), including developmental structural abnormalities in the frontal (Courchesne et al. 2011), medial-parietal (Schaer et al. 2013), and supramarginal (Libero et al. 2014) regions. Similarly, aberrant brain function has been reported extensively, linking irregular neural activities and poor working memory performance (Rahko et al. 2016) and impaired social cognition (Kim et al. 2015). Resting-state functional magnetic resonance imaging (fMRI) is an effective method to identify connectivity patterns of large-scale functional networks, and it has been previously used to examine the autistic brain (Duan et al. 2017; Hull et al. 2017). Studies suggest that resting-state functional connectivity in ASD is hallmarked by a complex pattern of network disruptions. For example, studies reported extensive whole-brain aberrant functional connectivity across several major neural networks, including the Visual Network (VN), Sensorimotor Network (SMN), Dorsal Attention Network (DAN), Frontoparietal Network (FPN), and Default Mode Network (DMN) (Xue et al. 2024; Kim et al. 2024).

Currently, there is no specific pharmacological treatment available to effectively target the core symptoms of ASD (Enticott et al. 2014). The primary treatment approach for ASD involves behavioral intervention and social skills training; however, these treatment options are time-consuming and labor-intensive. Therefore, it is imperative to develop a treatment option that is efficient and well-tolerated by children with ASD. Transcranial pulse stimulation (TPS) is a novel non-invasive brain stimulation technique that applies ultrashort ultrasound pulses to targeted brain regions (Beisteiner et al. 2020). The mechanism of action for TPS is based on the principle of mechanotransduction, where mechanical stimuli are converted into cellular biochemical responses, which promote neuroplastic effects by inducing angiogenesis, improving cerebral blood flow, cell proliferation and differentiation, nerve regeneration, and the release of beneficial growth factors (Beisteiner et al. 2020). Compared with other types of non-invasive brain stimulation, TPS can reach deeper regions of the brain (up to 8 cm). Our recent randomized, sham-controlled trial demonstrated that TPS on the right temporoparietal junction can improve the core symptoms of autism spectrum disorder in young ASD adolescents (Cheung et al. 2023). Specifically, participants who received the two-week TPS intervention showed a 24% reduction in the Childhood Autism Rating Scale score and a 53.7% reduction in the Clinical Global Impression Scale score in the treatment group immediately after intervention, as well as at 1- and 3-month follow-up assessments. However, whether improvements in core symptoms of ASD were due to changes in functional network organization remained to be determined.

Despite the potential clinical utility of TPS, to our knowledge, there is no empirical evidence on whether TPS can induce changes in brain network connectivity patterns, and whether changes in network connectivity patterns have implications for better social and cognitive functions in young adolescents with ASD. Therefore, this study aimed to examine comprehensive whole brain neuromodulatory effects of TPS by exploring the changes in functional connectivity within and between seven well-established brain networks (Yeo et al. 2011) after a two-week TPS intervention. We hypothesized that (1) compared with the sham-controlled group, the TPS treatment group would demonstrate significant changes in intra-network and inter-network connectivity in the VN, SMN, DAN, FPN, and DMN after the intervention; and (2) the observed changes in network connectivity would be associated with improvements in neurocognitive and behavioral outcomes.

2 | Methods

2.1 | Study Design

This secondary analysis included data from a two-armed, randomized, double-blinded, sham-controlled trial involving TPS and 32 young adolescents clinically diagnosed with ASD; the details of the parent study can be found in the published protocol (NCT05408793) (Cheung et al. 2022) and elsewhere (Cheung et al. 2023). The present study only included data from the subset of 28 participants (13 participants in the TPS group & 15 in the sham TPS group) who underwent fMRI scanning sessions with complete neuropsychological assessments collected at study baseline and 1 month after the 2-week TPS treatment (Figure 1). Written consents were obtained from the parents. Ethics approval of this study was obtained from the Institutional Review Board of The Hong Kong Polytechnic University (HSEARS20220228005).

2.2 | Participants Characteristics

Adolescents with ASD between 12 and 17 years old that fulfilled the eligibility criteria were recruited into the study. Status of ASD was clinically diagnosed by a psychiatrist during early childhood. Additional inclusion criteria include: (1) being of Chinese ethnicity; (2) having a diagnosis of ASD according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5); (3) reporting no changes in medication profile in the past 3 months; and (4) currently taking prescribed psychotropic medication for ≥ 3 months.

We excluded participants who had: (1) a diagnosis other than ASD based on the DSM-5; (2) concomitant major medical

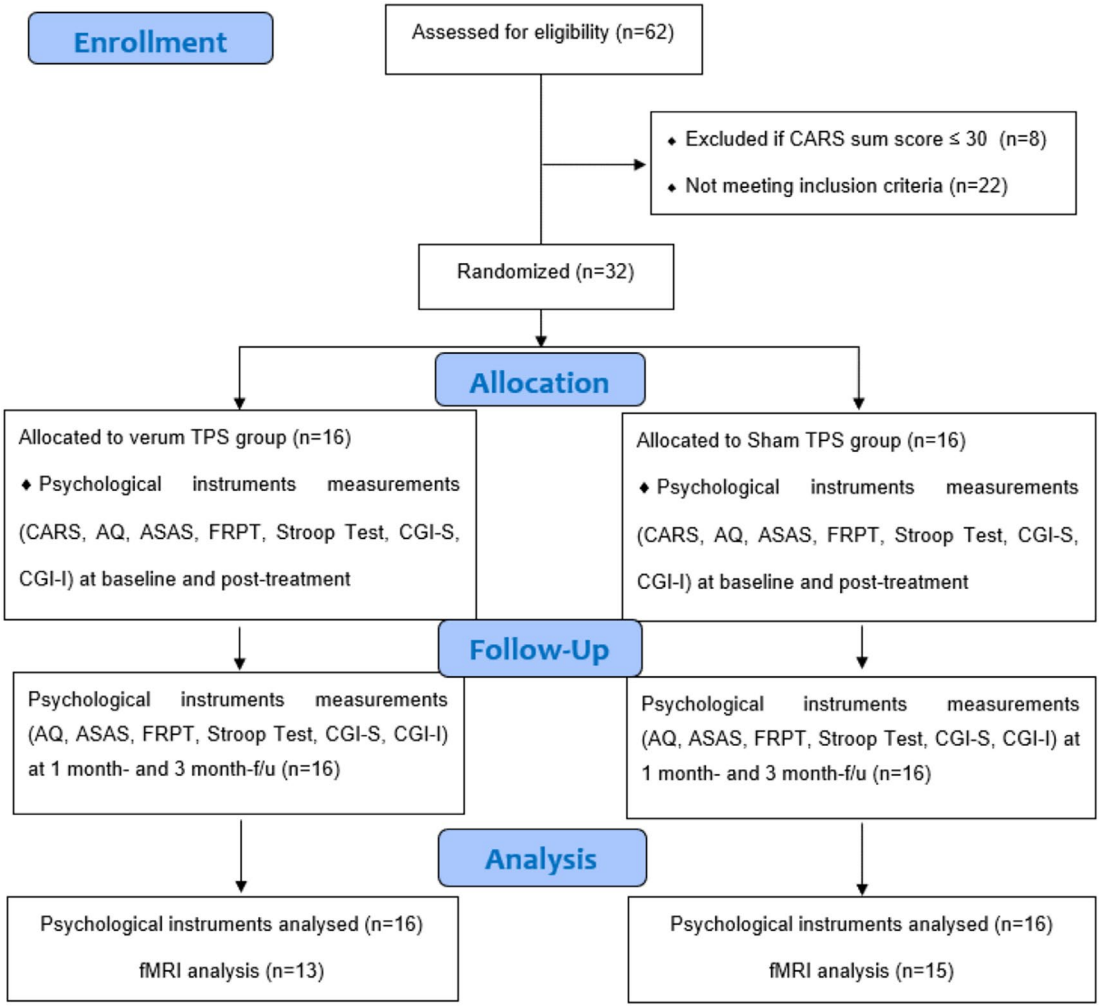

FIGURE 1 | CONSORT diagram. A total of 4 participants' post-TPS resting-state MRI (3 from TPS group) were found invalid, which left down to 13 and 15 participants in the TPS group and the sham TPS group, respectively. AQ, Autism Spectrum Quotient; ASAS, Australian Scale for Asperger's Syndrome; CARS, Childhood Autism Rating Scale; CGI, clinical global impression; TMT, Trail Making Test, Stroop test; VFT, Verbal Fluency Test.

conditions (e.g., cardiovascular disease, stroke, hypertension, sleep disorders, epilepsy); (3) neurological problems (e.g., brain tumor or brain aneurysm); (4) hemophilia or other clotting disorders or thrombosis; (5) metallic implants or other contraindications for the MRI; (6) corticosteroid treatment in the past 6 weeks before enrollment; and (7) a Childhood Autism Rating Scale (CARS) score of < 30 (i.e., no ASD).

2.2.1 | Participant Descriptors

Age and education level were recorded in units of years. Height and weight were measured in units of centimeters (cm) and kilograms (kg) respectively. Biological sex (i.e., male/female) was recorded. Medication history was collected at baseline (Table 1).

2.3 | Randomization

Eligible participants were randomized into either the real-TPS group or the sham-TPS group on a 1:1 ratio, balanced by their age, gender, and baseline score obtained from CARS. Randomization sequence commenced with every participant given a unique identification number generated by a computer. These numbers remained encrypted until the assignment of the intervention group. A statistician, who was an independent member of the team and was not involved in the enrollment, intervention, or assessments, carried out the randomization process from an offsite location. Both participants and the research assistants who performed assessments and data analysis were blinded from the group allocation (as shown in Figure 1). To assess the effectiveness of this blinding, participants were asked to guess their treatment group after finishing the 6th TPS session.

2.4 | Intervention Protocol

2.4.1 | Real TPS

The TPS intervention comprised three 30-min TPS sessions per week over 2 weeks. Each stimulation session was conducted using the TPS system (developed by NEUROLITH, Storz Medical AG, Tägerwilen, Switzerland) that applies single ultrashort (3 μs) ultrasound shockwave pulses with 0.2–0.25 energy levels (mJ/mm^2) and 2.0–4 Hz pulse frequencies (pulses per

TABLE 1 | Demographics on subjects who completed pre-post MRI scan.

Subjects	TPS ($N=13$) Mean (SD)/*n* (%)	Sham ($N=15$) Mean (SD)/*n* (%)	*p**
Age	13.38 (1.98)	12.47 (1.25)	0.56
Gender			0.88
Male	11 (84.6)	13 (86.7)	
Female	2 (15.4)	2 (13.3)	
Grade			0.29
Senior primary	4 (30.8)	9 (60.0)	
Junior secondary	7 (53.8)	5 (33.3)	
Senior secondary or above	2 (15.4)	1 (6.7)	
ASD diagnosis (age)	4.08 (2.10)	4.47 (2.85)	0.33
Prescribed medication			0.70
Yes	9 (69.2)	12 (80.0)	
No	4 (30.8)	3 (20.0)	
Medication (age of first taking)	7.78 (2.28)	7.92 (2.50)	0.58
Medication (duration in months)	76.67 (23.92)	55.27 (31.13)	0.46
Drug compliance			0.30
Good	4 (30.8)	9 (60.0)	
Fair	4 (30.8)	3 (20.0)	
Poor	5 (38.5)	3 (20.0)	
Family diagnosis of mental disorders			0.74
Yes	6 (46.2)	6 (40.0)	
No	7 (53.8)	9 (60.0)	
Parents			
Gender			0.12
Male	2 (15.4)	—	
Female	11 (84.6)	15 (100.0)	
Marital status			0.17
Married	13 (100.0)	13 (86.7)	
Separated/divorced	—	2 (13.3)	
Education level			0.66
Primary or below	1 (7.7)	1 (6.7)	
Secondary	7 (53.8)	10 (66.7)	
Vocational training/associate degree	3 (23.1)	1 (6.7)	
Undergraduate or above	2 (15.4)	3 (20.0)	

Abbreviations: ASD, autistic spectrum disorder; SD, standard deviation; TPS, transcranial pulse stimulation.
*Correlations *p*-value between the TPS and sham TPS groups.

second) to the right temporoparietal junction, identified via the participant's T_1-weighted images. The temporoparietal junction is a key node for social cognition (Lombardo et al. 2011), and the activity of the temporoparietal junction was correlated with greater social impairments (Chien et al. 2015). Within each of the three weekly TPS sessions, 800 pulses were delivered on alternate days, for a total of 4800 pulses over 6 sessions. The right temporoparietal junction was selected a priori as the target based on the notion that suggests aberrant brain activity in this region was found in those with ASD (Enticott et al. 2014).

The detailed procedure has been reported elsewhere (Cheung et al. 2023).

2.4.2 | Sham TPS

The sham TPS process was similar to the real TPS, with the only difference being that the silicone oil used in the actual TPS group was substituted with an air-filled cushion in the handpiece which was designed by NEUROLITH, Storz Medical AG, Tägerwilen, Switzerland. This sham device generated comparable sounds and sensations in the participant's head. All participants and their parents were instructed to maintain their regular medication schedule during the TPS treatment phase.

2.5 | Primary Outcome Measures

2.5.1 | Behavioral Outcome

The Childhood Autism Rating Scale (CARS) was the primary behavioral outcome. The CARS is a 15-item behavioral rating scale that is designed to detect and measure the severity of autism (Rellini et al. 2004). The scale covers interpersonal relations, imitation behavior, emotional reactions, usage of body and objects, adaptability to change, responses to visual/listening/perception, fear or anxiety, communication (verbal/nonverbal), activity level, consistency of intellectual relations, and overall impressions. The total score varies from 15 to 60, with scores under 30 suggesting a non-autistic range, scores between 30 and 36.5 indicating mild to moderate autism, and scores from 37 to 60 pointing to severe autism (Schopler et al. 2010). This assessment tool has been validated and extensively employed in numerous ASD studies (Amatachaya et al. 2014; Darwish et al. 2021; Gabr 2019). A previous NIBS study also used CARS scores as their primary outcomes, with parents completing the baseline and post-stimulation CARS score (Qiu et al. 2021). CARS was evaluated at baseline, immediately after post-stimulation at Week 2, and at 1- and 3-month post-stimulation follow-ups.

2.5.2 | Neuroimaging Outcome & Acquisition

Structural MRI and 5-min resting-state fMRI (rs-fMRI) were conducted using a Siemens Prisma 3 T scanner equipped with a 32-channel head coil at the University Research Facility in Behavioral and Systems Neuroscience of The Hong Kong Polytechnic University. High-resolution sagittal 3D T_1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) images of $1\times1\times1$ mm were acquired with the following parameters: repetition time (TR) = 1820 ms, echo time (TE) = 2.06 ms, FOV = 224×224 mm, flip angle (FA) = 7°, and isotropic voxel resolution of $1.0\times1.0\times1.0\,mm^3$. A T_2-weighted gradient echo planar imaging (EPI) sequence was used to acquire rs-fMRI data with the following parameters: TR = 2000 ms, TE = 32 ms, FOV = 192×192 mm, FA = 71°, and 32 slices with a voxel resolution of $3\times3\times4$ mm. During the rs-fMRI scanning, subjects were asked to keep their eyes open and were visually presented with a fixation cross ('+') in the center of the projected screen.

2.6 | Secondary Outcome Measures

The Autism Spectrum Quotient—Adolescent Version (AQ-Adolescent), Social Responsiveness Scale (SRS), Australian Scale for Asperger's Syndrome (ASAS), Clinical Global Impression (CGI), Trail Making Test (TMT), Verbal Fluency Test (VFT), Stroop Test, and Digit Span Test were the secondary outcomes.

The AQ-Adolescent is a self-report instrument for autistic traits, with scores ranging from 0 to 50. The instrument comprises 10 questions assessing: (i) social skills, (ii) attention switching, (iii) attention to detail, (iv) communication, and (v) imagination (Baron-Cohen et al. 2006).

The SRS is used to assess the severity of autism symptoms in children and adolescents aged 4 to 18 (Bölte et al. 2008). It includes 65 items that cover five areas related to social deficits: social awareness, social cognition, social communication, social motivation, and autistic mannerisms. Parents of the children/adolescents with autism symptoms were asked to rate each item on a scale of 0 to 4, with higher scores indicating greater social deficits. The SRS is reliable and valid for measuring autism symptoms in individuals under 18 years of age (Gau et al. 2013; Wigham et al. 2012).

The Chinese version of the ASAS is a 25-item instrument that is rated by parents of the children/adolescents with autism symptoms to identify behaviors and abilities associated with Asperger's syndrome in individuals who are 6 years of age and older (Attwood 1997).

The CGI is a 7-point scale that is used to evaluate core symptoms of autism, behavior, and activities of daily living over the past 7 days. The scale is based on both observed and reported symptoms, with higher scores reflecting the greater averaged severity level across the 7 days. This scale has been shown to be sensitive in detecting whether core symptoms of autism have improved or worsened after intervention (Busner and Targum 2007).

The TMT is a cognitive function assessment used to evaluate an individual's executive functions related to set-shifting (Attwood 1997). The test consists of three sub-tests (TMT1, TMT2, TMT3). TMT2 measures the speed to visually process a single-condition task by connecting numbers in sequential orders from 1 to 2 to 3, etc., in the form of digits and Chinese words. TMT3 consists of one module that measures the ability to shift mental sets within a task with two distinct conditions by, in alternating fashion, connecting numbers and the corresponding Chinese characters in sequential order (i.e., 1 to 一 to 2 to 二 to 3, etc.). The time taken to complete each module (in units of seconds) was recorded. Set-shifting is reflected by calculating the interference score by subtracting the time required to complete TMT2 from TMT3 (i.e., TMT 3–2). The TMT test has been found to have good reliability and validity (Wagner et al. 2011).

The VFT involves asking participants to generate as many words as possible within a specific time limit from both a semantic and phonemic category. Each category is given a time limit of 60 s. Participants are asked to produce words from three

categories: animals, vegetables, and fruits. The same word cannot be repeated. VFT is considered to have good reliability (Chiu et al. 1997).

The Stroop Test is a neuropsychological test that evaluates the inhibition control component of executive function. Response inhibition reflects an individual's ability to suppress cognitive interference that arises when conflicting stimuli are presented simultaneously (Jensen and Rohwer Jr 1966). The Stroop Test consists of three distinct conditions: neutral, congruent, and incongruent. In the neutral condition (Stroop 1), participants are to verbally recite words printed in black ink (e.g., Green). In the congruent condition (Stroop 2), they are asked to recite the ink color of colored-X's. In the incongruent condition (Stroop 3), participants are presented words printed in varied colored inks (e.g., "RED" written in blue ink). Participants are required to recite the color of the ink but not the word itself. Time taken to complete each task is recorded, and response inhibition is reflected by the interference score calculated by subtracting the time required to complete the congruent condition from the incongruent condition (i.e., Stroop 3−(Stroop 1 + Stroop 2)/2) (Table 2).

The Digit Span Test is a commonly used measure of working memory (WM) in which participants are asked to recall a sequence of digits in both forward and backward order. This test has been utilized in research to assess WM in school-aged children with Autism Spectrum Disorder (ASD) in Hong Kong (Chan et al. 2011). The total scores and the total duration of completion (in min/s) in both forward and backward digit span tests were collected. The mean score of the digit span test (forward and backward) is calculated for inferential statistical analysis in this study.

2.7 | Neuroimaging Analysis

Functional imaging analysis was performed with a custom pipeline that incorporated toolboxes from FSL (version 6.0.6.2), SPM12, and Matlab (R2022b). Stages within preprocessing were performed using FSL and included rigid body motion correction, spatial smoothing with a 6.0 mm Full-Width-Half-Maximum Gaussian kernel, and high-pass temporal filtering of 0.008 Hz. Participants' functional images were registered to the corresponding high-resolution T_1w images using FSL's FLIRT (FMRIB's Linear Image Registration Tool) (Jenkinson et al. 2002; Jenkinson and Smith 2001), and subsequently to the standardized 152 T_1 Montreal Neurological Institute (MNI) template through FSL's FNIRT (FMRIB's Non-linear Image Registration Tool) (Andersson et al. 2010). Motion-related signal spikes were removed via FSL's motion outlier command, followed by Independent Component Analysis based Automatic Removal of Motion Artifacts (ICA-AROMA) to remove remaining motion-related artifacts. Results from ICA-AROMA were visually inspected by CLH for quality control. Nuisance signals from the cerebral spinal fluid and white matter were regressed out from the timeseries data via a general linear model. Seed-based functional connectivity for each network was computed from correlating timeseries extracted from the preprocessed data using Yeo's 7-network templates (Yeo et al. 2011) as regions of interest (ROI). Fisher's *r*-to-*z* transformation was performed to normalize the extracted ROI-ROI correlations to construct the connectivity matrix with corrections for multiple comparisons, statistically set threshold at $Z > 3.11$ and a cluster correction p threshold of 0.05. The computed normalized functional connectivity correlation coefficients were exported to SPSS Statistics Version 28.0 for subsequent statistical analyses.

2.8 | Statistical Analyses

A significant level of 0.05 was set for all tests. Statistical tests involved functional connectivity within and between the seven established neural networks: the Visual Network (VN), SomatoMotor Network (SMN), Dorsal Attention Network (DAN), Ventral Attention Network (VAN), Limbic Network (LN), FrontoParietal Network (FPN), and Default Mode Network (DMN) (Yeo et al. 2011).

Two-way repeated measures ANCOVAs (adjusted for baseline performance) were used to examine the group, time, and group × time interaction effects on functional connectivity. False-Discovery Rate (FDR) correction was performed for multiple comparisons ($q = 0.05$). Pearson Correlation analyses with Bonferroni corrections were performed to identify potential significant associations between ASD symptoms and changes in cognitive function across the cognitive assessments in ARS, AQ, SRS, ASAS, TMT, VFT, Stroop test, Digit Span Test as well as changes in functional network connectivity.

3 | Results

3.1 | Participants

The mean age of the 28 study participants was 12.9 years. All study participants were right-handed. There were significantly more males than females across both study groups (84.6% and 86.7% males in the real-TPS and sham-TPS group respectively). We found no observable group differences in baseline socio-demographic variables between those who underwent real-TPS and sham-TPS at study baseline (all $p > 0.05$; Table 1).

3.2 | Primary Outcome Measures

3.2.1 | The Childhood Autism Rating Scale (CARS)

There was no baseline difference in the CARS between the real-TPS group and the sham-TPS group ($p = 0.79$). After intervention, a significant between-group effect was detected on the CARS ($F(1, 26) = 4.61$, $p = 0.04$; Table 2).

3.3 | Secondary Outcome Measures

Table 2 presents the results of the TPS on secondary outcomes. At baseline, there were no statistically significant differences in secondary outcomes between the real-TPS and sham-TPS groups (i.e., $p > 0.05$), with the exception of TMT 2 and 3, which revealed a significant difference favoring the sham-TPS group ($p < 0.05$).

TABLE 2 | Primary and secondary outcome measures of MRI participants at baseline and 1-month follow-up time point and the ANCOVA ($N = 28$).

Outcomes	TPS ($n = 13$)		Sham ($n = 15$)		Baseline diff	Between-group effect		
	Baseline	1-month follow-up	Baseline	1-month follow-up				
Time point	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	*p*	*F*	*p*	η^2
CARS	30.85 (6.07)	22.92 (6.28)	28.33 (7.11)	27.27 (6.35)	0.79	**4.61**	**0.04***	**0.16**
AQ	32.85 (5.96)	28.77 (6.13)	31.93 (4.80)	30.40 (6.37)	0.35	1.35	0.26	0.05
ASAS	86.38 (14.02)	71.77 (18.92)	85.93 (12.77)	85.33 (11.90)	0.59	**5.92**	**0.02***	**0.19**
SRS	100.62 (14.41)	82.08 (13.46)	92.87 (16.41)	83.73 (16.14)	0.49	0.77	0.39	0.03
Stroop test (RT; s)								
Test 1	19.47 (5.37)	16.00 (8.92)	21.37 (10.40)	16.29 (5.87)	0.09	0.36	0.56	0.01
Test 2	25.14 (14.74)	18.47 (9.86)	21.47 (7.36)	18.32 (6.77)	0.10	0.49	0.49	0.02
Test 3	35.06 (17.85)	24.62 (12.14)	34.39 (11.01)	28.57 (12.84)	0.12	1.29	0.27	0.05
Interference	12.76 (10.19)	7.39 (7.35)	12.97 (8.78)	11.26 (8.46)	0.95	1.55	0.23	0.06
Trail making test (s)								
Test 1	16.17 (17.34)	10.14 (10.53)	14.51 (9.54)	6.63 (2.18)	0.10	1.53	0.23	0.06
Test 2	18.84 (20.03)	12.32 (11.50)	12.58 (4.21)	9.35 (5.17)	**< 0.001*****	0.00	0.98	0.00
Test 3	52.96 (47.10)	33.05 (18.92)	44.36 (13.21)	30.33 (8.82)	**0.02***	0.03	0.86	0.00
Interference	34.11 (31.44)	20.73 (8.59)	31.78 (11.21)	20.98 (7.36)	0.79	0.14	0.71	0.01
Digit span test								
Score (forward)	10.85 (1.82)	12.08 (1.56)	10.27 (2.37)	11.27 (2.40)	0.47	0.56	0.47	0.02
Score (backward)	6.15 (3.13)	6.85 (3.11)	7.73 (3.26)	7.80 (4.16)	0.50	0.62	0.44	0.02
Interference (scores)	4.69 (2.87)	5.23 (3.27)	2.53 (2.64)	3.47 (3.96)	0.05	0.10	0.76	0.00
Length (forward) (s)	95.38 (23.39)	86.46 (12.77)	96.93 (40.41)	85.36 (14.50)	0.17	0.07	0.80	0.00
Length (backward) (s)	88.69 (68.47)	93.23 (49.47)	156.07 (142.18)	110.29 (85.73)	0.10	0.84	0.37	0.03
Interference (time)	−6.69 (85.15)	6.77 (50.62)	59.14 (122.36)	24.93 (82.46)	0.12	0.76	0.39	0.03

(Continues)

TABLE 2 | (Continued)

Outcomes	TPS ($n=13$)		Sham ($n=15$)		Baseline diff	Between-group effect		
	Baseline	1-month follow-up	Baseline	1-month follow-up				
Time point	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	*p*	*F*	*p*	η^2
Verbal fluency test								
Score at 30 s	26.46 (7.68)	29.46 (7.93)	26.93 (8.57)	30.00 (9.20)	0.73	0.00	0.95	0.00
Score at 60 s	38.00 (10.86)	41.00 (10.93)	38.27 (14.79)	41.93 (15.56)	0.17	0.07	0.79	0.00
CGI								
Severity	5.15 (0.99)	3.38 (1.26)	4.60 (0.99)	3.87 (0.83)	0.79	3.31	0.08	0.12
Improvement	4.00 (0.00)	1.85 (0.69)	4.00 (0.00)	4.00 (0.00)	>0.99	**147.57**	**<0.001*****	**0.85**
Efficacy	2.00 (3.92)	0.08 (0.28)	1.67 (3.68)	0.07 (0.29)	0.75	0.02	0.90	0.00
Total	11.15 (4.36)	5.31 (1.84)	10.27 (4.30)	7.93 (0.80)	0.93	**34.99**	**<0.001*****	**0.58**

Note: ANCOVA = analysis of covariance (adjusted for baseline scores). Bold values indicate $P<0.05$ (two-tailed).
Abbreviations: AQ, Autism Spectrum Quotient Adolescent Version; ASAS, Australian Scale for Asperger's Syndrome; CARS, Childhood Autism Rating Scale; RT, Reaction time; s, seconds; SRS, Social Responsiveness Scale; VFT, Verbal Fluency Test; CGI, Clinical Global Impression.
*$P<0.05$.
**$p<0.01$.
***$p<0.001$.

After the intervention, there was a significant between-group effect in ASAS (F (1, 26) = 5.92, $p=0.02$) and in the CGI improvement subscale ($p<0.001$) and CGI Total ($p<0.001$). The effects of TPS in other secondary outcomes including AQ, SRS, Stroop Test, TMT, Digit Span Test, and VFT were not statistically significant after intervention ($p>0.05$).

3.4 | Neuroimaging

3.4.1 | Effects of TPS on Network Connectivity

We performed a 2×2 (time×group) repeated measures ANCOVA adjusted for baseline observations on functional connectivity of resting-state fMRI in the seven aforementioned networks. The pre- and post-TPS means and standard deviations in functional connectivity for each of the seven networks were reported in Table 3.

We found significant interaction effects for functional connectivity within the VN (F (1, 26) = 5.52, $p=0.03$); and between VN-DAN (F (1, 26) = 6.83, $p=0.02$) (Table 4). The results also indicated a significant main group effect, F (1, 26) = 6.73, $p=0.02$; and a significant time effect, F (1, 26) = 6.67, $p=0.02$, for the connection between DAN-LN. However, there was no significant time×group interaction for the connectivity between the DAN and LN. The reported statistics did not reach statistical significance after FDR correction.

Next, to investigate changes in network connectivity after the two-week intervention, we performed a post hoc ANOVA and found a trend-level significance for TPS-induced change in the inter-network connectivity for DAN-LN only in the real-TPS group (t (13) = 2.08, $p=0.06$; Table 4). We also observed significant change in the intra-network connectivity of VN (t (15) = −2.45, $p=0.03$; Table 4), and the inter-network connectivity of VN-DAN (t (15) = 2.69, $p=0.02$; Table 4), in the sham-TPS group. The reported statistics did not reach statistical significance after FDR correction for multiple comparison.

3.4.2 | Correlations Between Neural Connectivity Networks and Secondary Outcomes

All statistical analyses were performed using IBM SPSS Statistics Version 28.0 (SPSS Inc., Chicago, IL, USA) with statistical significance defined as $\alpha<0.05$. To examine associations between connectivity of networks and secondary outcomes, we performed a Pearson's correlation on those significant between-group neurocognitive measures, that is, CARS, ASAS, CGI-Improvement and CGI Total with the seven pre-defined networks adjusted for multiple comparisons via FDR correction (Table 5).

Focusing on the primary outcome, we found that CARS interference score was negatively correlated with the intra-network connectivity of DMN, SMN-DAN, SMN-DMN, DAN-VAN, DAN-DMN, and positively correlated with LN-FPN in the real-TPS group (non-significant after FDR corrections). Further, there was a negative correlation ($r=-0.60$, p-$unc=0.03$) between the CGI Total score and the LN-FPN connectivity for the real-TPS group. On the contrary, a negative correlation ($r=-0.52$, p-$unc=0.05$) was also found between the ASAS score and the inter-network connectivity of VAN-LN for the sham-TPS group. There was also a negative correlation ($r=-0.61$, p-$unc=0.02$) between the CGI Total score and the DMN for the sham-TPS group.

TABLE 3 | Descriptive statistics for connectivity changes between TPS group and sham TPS group.

		Pre-intervention		Post-intervention			
Group ($N=28$)	**Networks**	**Mean**	**SD**	**Mean**	**SD**	***t***	***p*-unc**
TPS ($N=13$)	VN	2.35	0.59	2.53	0.39	1.14	0.28
	VN-DAN	0.88	0.53	0.75	0.54	−0.89	0.39
	DAN-LN	−0.05	0.24	0.11	0.18	**2.08**	**0.06**
Sham ($N=15$)	VN	2.36	0.47	2.09	0.45	**−2.45**	**0.03***
	VN-DAN	0.33	0.50	0.82	0.56	**2.69**	**0.02***
	DAN-LN	−0.14	0.17	−0.06	0.13	1.46	0.17

Note: Functional connectivity represented in *z*-correlational matrices. Non-statistically significant results are not reported in this table. Bold values indicate $P<0.05$ (two-tailed).
Abbreviations: DAN, Dorsal Attention Network; LN, Limbic Network; SD, standard deviation; VN, Visual Network.
*p-unc <0.05.

TABLE 4 | Repeated measures ANCOVAs on functional connectivity of resting-state fMRI conditions using seven pre-defined networks ($N=28$).

Source network	Target network	Main effect		Interaction
		Group	**Time**	**Group × time**
VN	—	0.18	0.69	**0.03**
VN	DAN	0.15	0.13	**0.03**
DAN	LN	**0.02**	**0.02**	0.42

Note: Uncorrected *p*-values were in display. Non-significant results were not shown. Bold values indicate $P<0.05$ (two-tailed).
Abbreviations: DAN, Dorsal Attention Network; LN, Limbic Network; VN, Visual Network.

4 | Discussion

In this secondary analysis of a two-week, double-blind, sham controlled TPS randomized controlled trial, we investigated the effect of a novel NIBS on connectivity patterns of seven well-established functional neural networks among young adolescents who were clinically diagnosed with ASD. To our knowledge, this is the first study that utilized TPS to modulate neural networks and examined the association between TPS-induced intra- and internetwork connectivity changes and the associated neurocognitive outcomes. We found that TPS to the right temporoparietal junction elicited significant changes to the connectivity of the VN and VN-DAN. However, TPS-related changes to VN and VN-DAN connectivity were not significantly associated with behavioral improvements in ASD symptoms or cognitive function. Nevertheless, we attempted to offer insight on the potential neural correlates of clinical symptoms of ASD. We found distinct intra- and inter-network connectivity patterns of the seven networks were significantly associated with CARS, ASAS, and CGI performance. More work will be necessary to delineate the effects of TPS on functional organization of neural networks, as well as to elucidate the optimal targets for TPS specific to treating core symptoms of ASD.

In line with the results from the parent study (Cheung et al. 2023), we found that TPS significantly improved CARS, ASAS, and the CGI. But to our surprise, TPS to the right temporoparietal junction did not significantly alter functional connections of the FPN and DMN, for which the right temporoparietal junction is considered a key hub functionally assigned to both networks (Igelstrom and Graziano 2017). However, as hypothesized, we observed TPS induced changes to connectivity patterns of the VN and DAN. It is plausible that the selected stimulation intensity of single ultrashort (3 μs) ultrasound shockwaves pulses at 0.2–0.25 mJ/mm^2 and 2.0–4 Hz pulse frequencies may be restrictive and less optimal for modulating connectivity of large neural networks with extensive interhemispheric connections (e.g., FPN and DMN). Previous study reported that the effect of TPS on interhemispheric connectivity may be intensity-dependent (Morales-Quezada et al. 2014). Additionally, given that the targeted brain region (i.e., right temporoparietal junction) is not part of the DMN or FPN, the extend of the effects may be spatially restricted. Further research is necessary to uncover the underlying mechanisms pertaining to the behavioral benefits of TPS among young adolescents with ASD.

Critically, while we found several significant correlations between TPS-related behavioral/clinical improvements and functional network connectivity, it is imperative to point out that these networks were not the ones that we observed to have changed after TPS (i.e., not VN, DAN, or LN). For instance, among those who received real-TPS, the DMN showed a strong negative correlation with CARS ($r=-0.74$, *p-unc* <0.01), suggesting that greater DMN connectivity is associated with lower autism severity as measured by CARS. This finding aligns with previous review indicating that disruptions in DMN connectivity were linked to ASD (Uddin et al. 2013; Peterson et al. 2024; Xie et al. 2022). The review reported that disruptions in DMN connectivity were linked to impairments in social cognition and self-awareness—the core symptoms in ASD. Similar finding was observed in another study that demonstrated intra-network functional connectivity of the DMN in ASD was inversely associated with the severity of autistic traits (Wang et al. 2019). The observed relationship between DMN and CARS may be indicative of impaired cognitive processes involved in in self-referential thoughts (Buckner et al. 2008). More specifically, neuroimaging evidence regarding ASD have placed emphasis on specific regions within the DMN, including the dorsal posterior cingulate cortex (Lau et al. 2019), where results from a meta-analysis concluded that lower functional connectivity in the dorsal posterior

TABLE 5 | Pearson's correlations in pre- and post-TPS comparison between changes on cognitive measures and functional network connectivity.

	CARS			ASAS			CGI – improvement			CGI – total		
***Z* scores**	***r***	***p-unc***	***p-FDR***	***r***	***p-unc***	***p-FDR***	***r***	***p-unc***	***p-FDR***	***r***	***p-unc***	***p-FDR***
TPS												
DMN	**−0.74**	**< 0.01****	**0.11**	−0.52	0.07	0.85	0.01	0.97	1.00	0.35	0.24	0.84
SMN-DAN	**−0.58**	**0.04***	**0.18**	−0.29	0.34	0.85	0.00	1.00	1.00	0.06	0.85	0.95
SMN-DMN	**−0.59**	**0.03***	**0.18**	−0.12	0.71	0.89	−0.09	0.78	1.00	0.11	0.72	0.88
DAN-VAN	**−0.62**	**0.02***	**0.18**	−0.35	0.25	0.85	−0.13	0.68	1.00	0.04	0.89	0.95
DAN-DMN	**−0.58**	**0.04***	**0.18**	−0.12	0.70	0.89	−0.07	0.83	1.00	0.11	0.72	0.88
VAN-LN	0.27	0.38	0.53	0.27	0.38	0.85	0.02	0.95	1.00	−0.30	0.32	0.88
LN-FPN	**0.61**	**0.03***	**0.18**	0.53	0.06	0.85	0.19	0.54	1.00	**−0.60**	**0.03***	**0.71**
Sham												
DMN	0.10	0.97	0.99	0.29	0.29	0.83	—	—	—	**−0.61**	**0.02***	**0.45**
SMN-DAN	0.00	0.99	0.99	0.18	0.51	0.85	—	—	—	0.19	0.51	0.96
SMN-DMN	−0.19	0.49	0.99	0.14	0.61	0.85	—	—	—	−0.25	0.38	0.96
DAN-VAN	0.14	0.63	0.99	0.16	0.57	0.85	—	—	—	0.13	0.65	0.96
DAN-DMN	0.11	0.70	0.99	0.38	0.16	0.83	—	—	—	−0.11	0.69	0.96
VAN-LN	0.02	0.95	0.99	**−0.52**	**0.05***	**0.77**	—	—	—	−0.10	0.74	0.96
LN-FPN	0.27	0.33	0.99	0.19	0.49	0.85	—	—	—	0.03	0.92	0.96

Note: Non-significant results were not reported in this table. No correlations were calculated for CGI-Improvement for the Sham group due to the overall unchanged score in the pre-post measure. Bold values indicate $P < 0.05$ (two-tailed).
Abbreviations: ASAS, Australian Scale for Asperger's Syndrome; CARS, Childhood Autism Rating Scale; CGI, Clinical Global Impression; DAN, Dorsal Attention Network; DMN, Default Mode Network; FPN, Frontoparietal Network; LN, Limbic Network; *p-FDR*, False-Discovery Rate *p*-values; *p-unc*, uncorrected *p*-values; SMN, SomatoMotor Network; VAN, Ventral Attention Network.
*$p\text{-}unc < 0.05$.
**$p\text{-}unc < 0.01$.
***$p\text{-}unc < 0.001$.

cingulate cortex is observed among individuals with ASD, such that their ability to attend and be cognitively flexible is hindered. Due to the small sample size, this secondary analysis did not further investigate region-to-region connectivity of particular areas within the DMN. Future studies with TPS may want to consider targeting the dorsal posterior cingulate cortex as the primary region of interest.

At the trial endpoint, we found that SMN and DAN showed significant negative correlations with CARS among those who received real TPS. Whereas for those who received sham-TPS, ASAS was negatively correlated with inter-network connectivity of VAN-LN, and CGI was negatively correlated with the DMN connectivity. It may be plausible that the two-week TPS had led to altered allocation of neural resources for interpersonal and emotional regulations that were absent among those who did not receive TPS. Additionally, these results suggest that greater SMN and DAN intra-network connectivity were associated with lower autism severity, which aligned with the findings that demonstrated lower DMN, SMN, and DAN connectivity in the ASD group compared to the controls (Wantzen et al. 2022). Seminal study by Geurts and colleagues (Geurts et al. 2009) suggests that there may be an inherent disparity among individuals with ASD to exhibit signs of behavioral inflexibility and deficits in cognitive flexibility, in which literature findings remain equivocal. Nevertheless, the DAN is established as a network that plays a significant role in cognitive flexibility by integrating sensory inputs and exerting top-down cognitive control of relevant responses (Dajani and Uddin 2015). The DAN-VAN connectivity is crucial for sensorimotor integration and attentional control, whereas the temporoparietal junction is believed to be involved in the interaction and communication between

the dorsal and ventral attention streams. However, as we did not observe significant SMN, DAN, or VAN changes after TPS, our findings should be taken cautiously. Future studies may also consider targeting major hubs of the SMN, DAN, and VAN to elicit increases in SMN, DAN, and VAN connectivity to investigate whether it could provide beneficial effects in enhancing the underlying neural mechanisms of deficiencies in social/behavioral flexibility among individuals with ASD.

Our data showed that in the real-TPS group, the LN and FPN exhibited a positive correlation with CARS scores and a negative correlation with CGI total scores. Again, this may be reflective of an altered neural resource allocation strategy induced by 2 weeks of TPS sessions. The LN is considered to be associated with emotional processing, while the FPN is essential for executive functions (Menon 2011). These findings are consistent with neuroimaging study that reported significantly greater LN-FPN inter-connectivity in individuals with ASD compared to controls (Zhou et al. 2024). However, given that we did not find any TPS-related changes to LN-FPN connectivity, further investigation is needed to delineate the relationship between the LN-FPN network flexibility and strength of intra-network connectivity on clinical traits among the ASD population.

5 | Limitations

There are several limitations which needs to be addressed in this study. First, this pilot study was limited by its small sample size that may affect the overall generalizability of our findings; due to our small sample, none of the results reached significance after adjustment for multiple comparison (FDR-correction). Given the small sample size for the neuroimaging component ($n = 28$), the generalizability of the findings may be limited, and the study should be interpreted within the context of its pilot nature. Second, all participants underwent post-TPS neuroimaging 1 month after the last TPS session, and hence, the effects of TPS may have been attenuated. Additionally, the long-term effects of TPS on treating core symptoms of ASD need to be further explored. Future trials with larger sample size should consider post-TPS follow-up assessments and neuroimaging to evaluate the long-term effects of TPS on ASD. Third, four out of 13 participants in the TPS group reported that they had not been prescribed any medications in the enrolment stage but when these participants were asked whether they had taken the prescribed medications regularly, they changed their verdicts to being granted a 'drug free holiday' by the prescribing doctor. Upon enquiry, we found that these participants and their parents withheld this information intentionally for fear of ineligibility for the study. Although medication history/status was not a significant predictor in this study, we cannot rule out potential impact of variations in medication intake on our findings. Fourth, in this study we did not collect data on the intelligence levels (IQ) of the participants. These factors can significantly influence cognitive processing, adaptive behavior, and neurological differences, potentially affecting how participants respond to interventions or assessments. Future studies should include IQ assessments to better understand their impact on the outcomes.

6 | Conclusion

In summary, our findings provided preliminary evidence on the efficacy of TPS among young adolescents clinically diagnosed with ASD. Particularly, TPS altered connection patterns of large-scale neural networks and reduced the core social communication deficits and behavioral flexibility in ASD. While we did not find TPS-induced functional network changes were associated with the observed behavioral improvements, we identified several neural correlates of improved ASD symptoms. These findings illustrated that TPS may be considered as an adjunct treatment for neurodevelopmental disorder in ASD, if more rigorous RCTs have similar findings emerge that fully elucidate the mechanisms of the short-term, and long-term effects TPS.

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Ethics Statement

Written consents were obtained from the parents. Ethics approval of this study was obtained from the Institutional Review Board of The Hong Kong Polytechnic University (HSEARS20220228005).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Anonymized data are available on reasonable request from the corresponding author.

References

Allen, G., and E. Courchesne. 2003. "Differential Effects of Developmental Cerebellar Abnormality on Cognitive and Motor Functions in the Cerebellum: An fMRI Study of Autism." *American Journal of Psychiatry* 160, no. 2: 262–273.

Amatachaya, A., N. Auvichayapat, N. Patjanasoontorn, et al. 2014. "Effect of Anodal Transcranial Direct Current Stimulation on Autism: A Randomized Double-Blind Crossover Trial." *Behavioural Neurology* 2014: 1–7.

Andersson, J. L. R., J. Mark, and S. Smith. 2010. "Non-Linear Registration, Aka Spatial Normalisation," FMRIB technical report TR07JA2.

Attwood, A. 1997. *Asperger's Syndrome: A Guide for Parents and Professionals*. Jessica Kingsley Publishers.

Baron-Cohen, S., R. A. Hoekstra, R. Knickmeyer, and S. Wheelwright. 2006. "The Autism-Spectrum Quotient (AQ)—Adolescent Version." *Journal of Autism and Developmental Disorders* 36: 343–350.

Beisteiner, R., E. Matt, C. Fan, et al. 2020. "Transcranial Pulse Stimulation With Ultrasound in Alzheimer's Disease—A New Navigated Focal Brain Therapy." *Advanced Science* 7, no. 3: 1902583.

Bölte, S., F. Poustka, and J. N. Constantino. 2008. "Assessing Autistic Traits: Cross-Cultural Validation of the Social Responsiveness Scale (SRS)." *Autism Research* 1, no. 6: 354–363.

Buckner, R. L., J. R. Andrews-Hanna, and D. L. Schacter. 2008. "The Brain's Default Network: Anatomy, Function, and Relevance to Disease." *Annals of the New York Academy of Sciences* 1124, no. 1: 1–38.

Busner, J., and S. D. Targum. 2007. "The Clinical Global Impressions Scale: Applying a Research Tool in Clinical Practice." *Psychiatry (Edgmont)* 4, no. 7: 28–37.

Chan, A. S., Y. M. Y. Han, S. L. Sze, et al. 2011. "Disordered Connectivity Associated With Memory Deficits in Children With Autism Spectrum Disorders." *Research in Autism Spectrum Disorders* 5, no. 1: 237–245.

Cheung, T., Y. S. Ho, K. H. Fong, et al. 2022. "Evaluating the Safety and Efficacy of Transcranial Pulse Stimulation on Autism Spectrum Disorder: A Double-Blinded, Randomized, Sham-Controlled Trial Protocol." *International Journal of Environmental Research and Public Health* 19, no. 23: 15614.

Cheung, T., T. M. H. Li, J. Y. T. Lam, et al. 2023. "Effects of Transcranial Pulse Stimulation on Autism Spectrum Disorder: A Double-Blind, Randomized, Sham-Controlled Trial." *Brain Communications* 5, no. 5: fcad226.

Chien, H. Y., H. Y. Lin, M. C. Lai, S. S. F. Gau, and W. Y. I. Tseng. 2015. "Hyperconnectivity of the Right Posterior Temporo-Parietal Junction Predicts Social Difficulties in Boys With Autism Spectrum Disorder." *Autism Research* 8, no. 4: 427–441.

Chiu, H. F., C. K. Chan, L. C. Lam, et al. 1997. "The Modified Fuld Verbal Fluency Test: A Validation Study in Hong Kong." *Journals of Gerontology Series B: Psychological Sciences and Social Sciences* 52, no. 5: P247–P250.

Courchesne, E. 2002. "Abnormal Early Brain Development in Autism." *Molecular Psychiatry* 7, no. Suppl 2: S21–S23.

Courchesne, E., K. Campbell, and S. Solso. 2011. "Brain Growth Across the Life Span in Autism: Age-Specific Changes in Anatomical Pathology." *Brain Research* 1380: 138–145.

Dajani, D. R., and L. Q. Uddin. 2015. "Demystifying Cognitive Flexibility: Implications for Clinical and Developmental Neuroscience." *Trends in Neurosciences* 38, no. 9: 571–578.

Darwish, M. E., H. W. El-Beshlawy, E. S. Ramadan, et al. 2021. "Study of the Role of the Transcranial Magnetic Stimulation on Language Progress in Autism Spectrum Disorder." *Egyptian Journal of Otolaryngology* 37, no. 1: 1–7.

Duan, X., H. Chen, C. He, et al. 2017. "Resting-State Functional Under-Connectivity Within and Between Large-Scale Cortical Networks Across Three Low-Frequency Bands in Adolescents With Autism." *Progress in Neuro-Psychopharmacology and Biological Psychiatry* 79: 434–441.

Enticott, P. G., B. M. Fitzgibbon, H. A. Kennedy, et al. 2014. "A Double-Blind, Randomized Trial of Deep Repetitive Transcranial Magnetic Stimulation (rTMS) for Autism Spectrum Disorder." *Brain Stimulation* 7, no. 2: 206–211.

Gabr, A. A. M. 2019. "Long-Term Effects of Repetitive Transcranial Magnetic Stimulation on a Sample of Children With Autism Spectrum Disorder." *Scientific Journal of Al-Azhar Medical Faculty, Girls* 3, no. 3: 681–686.

Gau, S. S.-F., L. T. Liu, Y. Y. Wu, Y. N. Chiu, and W. C. Tsai. 2013. "Psychometric Properties of the Chinese Version of the Social Responsiveness Scale." *Research in Autism Spectrum Disorders* 7, no. 2: 349–360.

Geurts, H. M., B. Corbett, and M. Solomon. 2009. "The Paradox of Cognitive Flexibility in Autism." *Trends in Cognitive Sciences* 13, no. 2: 74–82.

Howlin, P., and P. Moss. 2012. "Adults With Autism Spectrum Disorders." *Canadian Journal of Psychiatry* 57, no. 5: 275–283.

Hull, J. V., L. B. Dokovna, Z. J. Jacokes, C. M. Torgerson, A. Irimia, and J. D. van Horn. 2017. "Resting-State Functional Connectivity in Autism Spectrum Disorders: A Review." *Frontiers in Psychiatry* 7: 205.

Igelstrom, K. M., and M. S. A. Graziano. 2017. "The Inferior Parietal Lobule and Temporoparietal Junction: A Network Perspective." *Neuropsychologia* 105: 70–83.

Jenkinson, M., P. Bannister, M. Brady, and S. Smith. 2002. "Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images." *NeuroImage* 17, no. 2: 825–841.

Jenkinson, M., and S. Smith. 2001. "A Global Optimisation Method for Robust Affine Registration of Brain Images." *Medical Image Analysis* 5, no. 2: 143–156.

Jensen, A. R., and W. D. Rohwer Jr. 1966. "The Stroop Color-Word Test: A Review." *Acta Psychologica* 25: 36–93.

Kim, S. Y., U. S. Choi, S. Y. Park, et al. 2015. "Abnormal Activation of the Social Brain Network in Children With Autism Spectrum Disorder: An FMRI Study." *Psychiatry Investigation* 12, no. 1: 37–45.

Kim, Y. G., O. Ravid, X. Zhang, et al. 2024. "Explaining Deep Learning-Based Representations of Resting State Functional Connectivity Data: Focusing on Interpreting Nonlinear Patterns in Autism Spectrum Disorder." *Frontiers in Psychiatry* 15: 1397093. https://doi.org/10.3389/fpsyt.2024.1397093.

Lau, W. K. W., M. K. Leung, and B. W. M. Lau. 2019. "Resting-State Abnormalities in Autism Spectrum Disorders: A Meta-Analysis." *Scientific Reports* 9, no. 1: 3892.

Libero, L. E., T. DeRamus, H. D. Deshpande, and R. K. Kana. 2014. "Surface-Based Morphometry of the Cortical Architecture of Autism Spectrum Disorders: Volume, Thickness, Area, and Gyrification." *Neuropsychologia* 62: 1–10.

Lombardo, M. V., B. Chakrabarti, E. T. Bullmore, MRC AIMS Consortium, and S. Baron-Cohen. 2011. "Specialization of Right Temporo-Parietal Junction for Mentalizing and Its Relation to Social Impairments in Autism." *NeuroImage* 56, no. 3: 1832–1838.

Lord, C., M. Elsabbagh, G. Baird, and J. Veenstra-Vanderweele. 2018. "Autism Spectrum Disorder." *Lancet* 392, no. 10146: 508–520.

Menon, V. 2011. "Large-Scale Brain Networks and Psychopathology: A Unifying Triple Network Model." *Trends in Cognitive Sciences* 15, no. 10: 483–506.

Morales-Quezada, L., L. C. Saavedra, J. Rozisky, L. Hadlington, and F. Fregni. 2014. "Intensity-Dependent Effects of Transcranial Pulsed Current Stimulation on Interhemispheric Connectivity: A High-Resolution qEEG, Sham-Controlled Study." *Neuroreport* 25, no. 13: 1054–1058.

Nazeer, A., and M. Ghaziuddin. 2012. "Autism Spectrum Disorders: Clinical Features and Diagnosis." *Pediatric Clinics of North America* 59, no. 1: 19–25.

Peterson, M., M. B. D. Prigge, D. L. Floris, et al. 2024. "Reduced Lateralization of Multiple Functional Brain Networks in Autistic Males." *Journal of Neurodevelopmental Disorders* 16, no. 1: 23. https://doi.org/10.1186/s11689-024-09529-w.

Qiu, J., X. Kong, J. Li, et al. 2021. "Transcranial Direct Current Stimulation (tDCS) Over the Left Dorsal Lateral Prefrontal Cortex in Children With Autism Spectrum Disorder (ASD)." *Neural Plasticity* 2021: 1–11.

Rahko, J. S., V. A. Vuontela, S. Carlson, et al. 2016. "Attention and Working Memory in Adolescents With Autism Spectrum Disorder: A

Functional MRI Study." *Child Psychiatry and Human Development* 47, no. 3: 503–517.

Rellini, E., D. Tortolani, S. Trillo, S. Carbone, and F. Montecchi. 2004. "Childhood Autism Rating Scale (CARS) and Autism Behavior Checklist (ABC) Correspondence and Conflicts With DSM-IV Criteria in Diagnosis of Autism." *Journal of Autism and Developmental Disorders* 34: 703–708.

Salari, N., S. Rasoulpoor, S. Rasoulpoor, et al. 2022. "The Global Prevalence of Autism Spectrum Disorder: A Comprehensive Systematic Review and Meta-Analysis." *Italian Journal of Pediatrics* 48, no. 1: 1–16.

Schaer, M., M. C. Ottet, E. Scariati, et al. 2013. "Decreased Frontal Gyrification Correlates With Altered Connectivity in Children With Autism." *Frontiers in Human Neuroscience* 7: 750.

Schopler, E., R. J. Reichler, and B. R. Renner. 2010. *The Childhood Autism Rating Scale (CARS)*. Western Psychological Services.

Uddin, L. Q., K. Supekar, and V. Menon. 2013. "Reconceptualizing Functional Brain Connectivity in Autism From a Developmental Perspective." *Frontiers in Human Neuroscience* 7: 458.

Wagner, S., I. Helmreich, N. Dahmen, K. Lieb, and A. Tadic. 2011. "Reliability of Three Alternate Forms of the Trail Making Tests a and B." *Archives of Clinical Neuropsychology* 26, no. 4: 314–321.

Wang, K., M. Xu, Y. Ji, et al. 2019. "Altered Social Cognition and Connectivity of Default Mode Networks in the Co-Occurrence of Autistic Spectrum Disorder and Attention Deficit Hyperactivity Disorder." *Australian and New Zealand Journal of Psychiatry* 53, no. 8: 760–771.

Wantzen, P., P. Clochon, F. Doidy, et al. 2022. "EEG Resting-State Functional Connectivity: Evidence for an Imbalance of External/Internal Information Integration in Autism." *Journal of Neurodevelopmental Disorders* 14, no. 1: 47.

Wigham, S., H. McConachie, J. Tandos, A. S. le Couteur, and Gateshead Millennium Study core team. 2012. "The Reliability and Validity of the Social Responsiveness Scale in a UK General Child Population." *Research in Developmental Disabilities* 33, no. 3: 944–950.

Won, H., W. Mah, and E. Kim. 2013. "Autism Spectrum Disorder Causes, Mechanisms, and Treatments: Focus on Neuronal Synapses." *Frontiers in Molecular Neuroscience* 6: 19.

Xie, Y., Z. Xu, M. Xia, et al. 2022. "Alterations in Connectome Dynamics in Autism Spectrum Disorder: A Harmonized Mega- and Meta-Analysis Study Using the Autism Brain Imaging Data Exchange Dataset." *Biological Psychiatry* 91, no. 11: 945–955.

Xue, Y., M. S. Bai, H. Y. Dong, T. T. Wang, Z. A. Mohamed, and F. Y. Jia. 2024. "Altered Intra- and Inter-Network Brain Functional Connectivity Associated With Prolonged Screen Time in Pre-School Children With Autism Spectrum Disorder." *European Journal of Pediatrics* 183, no. 5: 2391–2399.

Yeo, B. T., F. M. Krienen, J. Sepulcre, et al. 2011. "The Organization of the Human Cerebral Cortex Estimated by Intrinsic Functional Connectivity." *Journal of Neurophysiology* 106, no. 3: 1125–1165.

Zeidan, J., E. Fombonne, J. Scorah, et al. 2022. "Global Prevalence of Autism: A Systematic Review Update." *Autism Research* 15, no. 5: 778–790.

Zhou, R., C. Sun, M. Sun, Y. Ruan, W. Li, and X. Gao. 2024. "Altered Intra-and Inter-Network Connectivity in Autism Spectrum Disorder." *Aging (Albany NY)* 16, no. 11: 10004–10015.