Psychological Medicine

cambridge.org/psm

Improving social cognition following theta burst stimulation over the right inferior frontal gyrus in autism spectrum: an 8-week double-blind sham-controlled trial

Hsing-Chang Ni[1,2], Yi-Lung Chen[3,4], Meng-Ying Hsieh[5,6], Chen-Te Wu[7], Rou-Shayn Chen[8], Chi-Hung Juan[9], Cheng-Ta Li[10], Susan Shur-Fen Gau[11,12,13] and Hsiang-Yuan Lin[14,15]

[1]Department of Psychiatry, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan; [2]College of Medicine, Chang Gung University, Taoyuan, Taiwan; [3]Department of Healthcare Administration, Asia University, Taichung, Taiwan; [4]Department of Psychology, Asia University, Taichung, Taiwan; [5]Deparment of Pediatrics, Chang Gung Memorial Hospital at Taipei, Taipei, Taiwan; [6]Department of Pediatric Neurology, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan; [7]Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan; [8]Department of Neurology, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan; [9]Institue of Cognitive Neuroscience, National Central University, Jhongli, Taiwan; [10]Department of Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan; [11]Graduate Institute of Brain and Mind Sciences, College of Medicine, National Taiwan University, Taipei, Taiwan; [12]Neurobiology and Cognitive Science Center, National Taiwan University, Taipei, Taiwan; [13]Department of Psychiatry, National Taiwan University Hospital and College of Medicine, Taipei, Taiwan; [14]Azrieli Adult Neurodevelopmental Centre, Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto, Ontario, Canada and [15]Department of Psychiatry, Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

Original Article

Cite this article: Ni H-C, Chen Y-L, Hsieh M-Y, Wu C-T, Chen R-S, Juan C-H, Li C-T, Gau SS-F, Lin H-Y (2024). Improving social cognition following theta burst stimulation over the right inferior frontal gyrus in autism spectrum: an 8-week double-blind sham-controlled trial. *Psychological Medicine* **54**, 3261–3272. https://doi.org/10.1017/S0033291724001387

Received: 19 September 2023
Revised: 23 April 2024
Accepted: 14 May 2024
First published online: 6 September 2024

Keywords:
autism; right inferior frontal gyrus; theta burst stimulation

Corresponding author:
Hsing-Chang Ni;
Email: alanni@cgmh.org.tw;
alanni0918@yahoo.com.tw;
Hsiang-Yuan Lin;
Email: Hsiang-Yuan.Lin@camh.ca;
hsiangyuan.lin@utoronto.ca

Abstract

Background. The right inferior frontal gyrus (RIFG) is a potential beneficial brain stimulation target for autism. This randomized, double-blind, two-arm, parallel-group, sham-controlled clinical trial assessed the efficacy of intermittent theta burst stimulation (iTBS) over the RIFG in reducing autistic symptoms (NCT04987749).

Methods. Conducted at a single medical center, the trial enrolled 60 intellectually able autistic individuals (aged 8–30 years; 30 active iTBS). The intervention comprised 16 sessions (two stimulations per week for eight weeks) of neuro-navigated iTBS or sham over the RIFG. Fifty-seven participants (28 active) completed the intervention and assessments at Week 8 (the primary endpoint) and follow-up at Week 12.

Results. Autistic symptoms (primary outcome) based on the Social Responsiveness Scale decreased in both groups (significant time effect), but there was no significant difference between groups (null time-by-treatment interaction). Likewise, there was no significant between-group difference in changes in repetitive behaviors and exploratory outcomes of adaptive function and emotion dysregulation. Changes in social cognition (secondary outcome) differed between groups in feeling scores on the Frith-Happe Animations (Week 8, $p = 0.026$; Week 12, $p = 0.025$). Post-hoc analysis showed that the active group improved better on this social cognition than the sham group. Dropout rates did not vary between groups; the most common adverse event in both groups was local pain. Notably, our findings would not survive stringent multiple comparison corrections.

Conclusions. Our findings suggest that iTBS over the RIFG is not different from sham in reducing autistic symptoms and emotion dysregulation. Nonetheless, RIFG iTBS may improve social cognition of mentalizing others' feelings in autistic individuals.

Introduction

Autism spectrum is a neurodevelopmental condition with social communication difficulties and repetitive/restricted behaviors (Lord, Elsabbagh, Baird, & Veenstra-Vanderweele, 2018). Despite the increasing prevalence (Zeidan et al., 2022), there has yet to be an effective biological intervention to reduce autistic symptoms and associated adaptive function.

In the past three decades, noninvasive brain stimulation has shown the potential to improve several psychiatric disorders (Dayan, Censor, Buch, Sandrini, & Cohen, 2013). Repetitive transcranial magnetic stimulation (rTMS), a common noninvasive brain stimulation method, can deliver various focused electromagnetic pulses to modulate brain function and neuroplasticity (Klomjai, Katz, & Lackmy-Vallee, 2015). Theta burst stimulation (TBS) is a modified variant of rTMS (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). The TBS effect may be related to long-term depression/potentiation-like aftereffects, glutamatergic/GABAergic neurotransmission,

and synaptic plasticity (Huang, Rothwell, Chen, Lu, & Chuang, 2011; Li et al., 2019). Compared to conventional rTMS, TBS is delivered faster with lower stimulation intensity (Chung, Hill, Rogasch, Hoy, & Fitzgerald, 2016; Huang et al., 2005) while achieving non-inferior efficacy in depression (Blumberger et al., 2018, 2022). Previous studies demonstrated the safety and tolerability of TBS from children to older adults (Hong et al., 2015; Rossi et al., 2021). With shorter stimulation duration and comparable therapeutic efficacy, TBS thus is a favorable protocol for clinical populations.

The previous neuroscience-informed consensus and meta-analysis suggest the dorsolateral prefrontal cortex (DLPFC), posterior superior temporal sulcus (pSTS)/temporoparietal junction and right inferior frontal gyrus (RIFG) could be a potential stimulation target for autism (Barahona-Correa, Velosa, Chainho, Lopes, & Oliveira-Maia, 2018; Cole et al., 2019). However, the published results are mixed. Most studies in the past decade applied rTMS/TBS over the DLPFC in autism. Earlier open-label trials without a sham-controlled group demonstrated that low-frequency rTMS (an inhibitory protocol) over the DLPFC might reduce autistic and inattentive symptoms in autistic individuals (Casanova et al., 2014; Sokhadze et al., 2009, 2010, 2018). However, our recent double-blind, randomized, sham-controlled trial (RCT) of an inhibitory TBS (continuous TBS, cTBS) over the DLPFC did not show group differences in changes in autistic symptoms and social cognition between the active and sham conditions in autistic people (Ni et al., 2023b). Similarly, the other double-blind RCT trial did not support the efficacy of high-frequency rTMS over the DLPFC on executive function in autistic youth (Ameis et al., 2020). On the other hand, our earlier RCT demonstrated a beneficial potential of intermittent TBS (iTBS, an excitatory protocol) over the pSTS in autistic adults (Ni et al., 2017, 2022). Likewise, our further RCT in autistic youth demonstrated the safety, feasibility, and beneficial potentials of pSTS iTBS (Ni et al., 2021). However, this pSTS iTBS cannot modulate white matter properties in autistic individuals (Ni et al., 2023a).

Based on the consensus (Cole et al., 2019), the RIFG is also a potential stimulation target for autism. RIFG is involved with a wide range of social cognition, including imitation (Hogeveen et al., 2015), response inhibition (Duque, Greenhouse, Labruna, & Ivry, 2017), empathy (Massey et al., 2017), emotion (Schurz, Radua, Aichhorn, Richlan, & Perner, 2014), social touch (Peled-Avron, Glasner, Gvirts, & Shamay-Tsoory, 2019), and perspective-taking (Kuang, 2016). One-session RIFG rTMS could modulate several neuropsychological functions in neurotypical adults, such as artificial syntax processing (Udden et al., 2008), deductive reasoning (Tsujii, Sakatani, Masuda, Akiyama, & Watanabe, 2011), action stopping (Sundby, Jana, & Aron, 2021), and emotional prosody processing (Hoekert, Vingerhoets, & Aleman, 2010). Moreover, RIFG stimulation also modulates social cognition in neurotypical adults. For example, one study demonstrated that one-session 1 Hz rTMS (inhibitory) over RIFG could disrupt behavioral responses to infant stimuli (De Carli et al., 2019). Another study found that one-session 10 Hz rTMS (inhibitory) would temporarily disrupt RIFG activity and slow the pain-related empathy processing (Li et al., 2021). The other study demonstrated that RIFG iTBS could induce a more efficient strategy of task goal activation, while RIFG cTBS led to an inefficient approach (Dippel & Beste, 2015). Clinically, excitatory RIFG rTMS may benefit attention issues in Alzheimer's disease (Eliasova, Anderkova, Marecek, & Rektorova, 2014), language performance in poststroke aphasia (Winhuisen et al., 2007), smoking behaviors (Upton, Brown, Golzy, Garland, & Froeliger, 2023), and inhibitory control (Newman-Norlund, Gibson, McConnell, & Froeliger, 2020) in nicotine dependence.

Several magnetic resonance imaging (MRI) studies found alterations of RIFG in autism, including decreased gray matter volumes (Kosaka et al., 2010), hypoactivation during response inhibition (Kana, Keller, Minshew, & Just, 2007) and socially interfered cognitive control (Dichter & Belger, 2007), functional hypoconnectivity (Villalobos, Mizuno, Dahl, Kemmotsu, & Muller, 2005), and reduced local intrinsic connectivity (Kennedy & Courchesne, 2008). Despite the evidence of RIFG 'hypo-ness' in autism, the 'enhancement' by excitatory rTMS/TBS, and the tolerability, only one double-blind RCT applied 10-session high-frequency RIFG rTMS (excitatory) in a small sample of 10 autistic children (4 active) (Kaokhieo et al., 2023). They found improving adaptive functions in the active group but did not find significant active-v.-sham-by-time interaction in any outcomes. This caveat prompts further investigations of RIFG stimulation for autism in a sufficiently powered and statistically rigorous design.

In this context, we conducted this double-blind, two-arm, parallel-group sham-controlled RCT to investigate the efficacy of RIFG iTBS in a sufficiently powered sample of intellectually able autistic children, adolescents and young adults. Because there has been no established rule to localize the RIFG (c.f., the '5-cm rule' of localizing the dorsolateral prefrontal cortex [Cash et al., 2021]) without a need for MRI navigation, we decided not to include autistic people with intellectual disabilities, who generally have difficulties in complying with the MRI assessment. The objectives of this paper included investigating (1) the efficacy of RIFG iTBS in reducing autistic symptoms (primary outcome), improving social cognition (secondary outcome), and improving adaptive function and emotion dysregulation (exploratory outcome) following the 8-week (two sessions per week) iTBS course (primary endpoint); (2) whether the efficacy (if there would be any) could last for four weeks after the last stimulation (Week 12, the secondary endpoint); (3) the safety and feasibility of this protocol. We hypothesized that RIFG iTBS would improve autistic symptoms and social cognition in autistic individuals without intellectual disabilities, and its effect could last four weeks. This protocol would be safe and feasible.

Methods

Design

This study was a randomized, double-blind, parallel, sham-controlled trial comparing active iTBS *v.* sham over RIFG twice per week for continuous eight weeks (16 sessions in total) in intellectually able autistic individuals. This trial was conducted at a single tertiary medical center in Taiwan (Linkou Chang Gung Memorial Hospital) from November 2019 to May 2023.

Participants were randomly assigned to the active or sham group following a computer-generated randomization list with 1:1 allocation, stratified by sex. Then, participants would receive active RIFG iTBS or sham intervention for eight consecutive weeks and be observed four weeks after the last stimulation. Considering Taiwan's tight curriculum and inflexible on-leave arrangement, participants could choose two non-fixed days for intervention per week, with at least 48 h apart between sessions. Assessments of symptoms, social cognition, MRI (including structural, diffusion, and functional MRI), and electroencephalography

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

(EEG) happened at baseline, Week 8, and Week 12. We only reported clinical and social cognition results herein. MRI and EEG data will be analyzed and reported subsequently in the future.

The blinding involved a research assistant (not involved in the enrollment) who concealed the randomization allocation. Throughout the study, only the neuromodulation technicians knew the active/sham allocation but were not involved in any assessments or analyses. All participants, parents/caregivers, and the principal investigator were blind to the allocation until Week 12. Data analysis was conducted by an independent statistician.

Our trial followed the 1964 Helsinki Declaration, its later amendments, and ethical standards of Good Clinical Practice and received ethical approval from the Research Ethics Committee at Chang Gung Medical Foundation-Institutional Review Board (CGMF-IRB 201900713A0) and Taiwan Food and Drug Administration (TFDA 1086611101). We also registered the trial on ClinicalTrials.gov (NCT04987749). Written informed consent was obtained from participants and their parents (substitute decision-makers). Whether a given participant assented or consented to the study depended on his/her/their capacity of consent to participate in the research as per the clinical assessment (Barstow, Shahan, & Roberts, 2018).

Participants

Study participants were recruited either from outpatient clinics or through online advertisements. The inclusion criteria were age 8–30 years and a clinical diagnosis of autism spectrum disorder based on DSM-5 and confirmed by the Autism Diagnosis Objective Schedule (ADOS) (Lord et al., 2000). The exclusion criteria were any lifetime major systemic or neurological illness (especially seizure), schizophrenia, bipolar disorder, current depressive disorder, substance misuse, and full-scale intelligence Quotient (FIQ) <70 based on the Wechsler Intelligence Scale-IV for children or adults. Medications remained unchanged throughout the study. Information about comorbidities and medications is detailed in online Supplementary Table S1. Because all of the participants had to comply with MRI scans to precisely localize the RIFG, the baseline functional level of autistic people was either level 1 (requiring support) or level 2 (requiring substantial support) based on the DSM-5 criteria (Table 1).

Intervention

The biphasic pulses for TBS were generated with the Magstim Super Rapid^2 system (Magstim Company, Oxford, UK) and applied with the 70-mm figure-of-eight coil. Active motor threshold (AMT) was determined based on standard methods. The stimulus intensity was 90% AMT for both groups. The sham stimulation was executed with a sham coil, producing tactile and auditory stimulation without direct brain effects.

The present iTBS protocol (Huang et al., 2005) was adopted as (1) Each iTBS train comprised a burst of 3 TMS pulses at 50 Hz at 200 ms intervals 10 times; (2) the TBS train was delivered every 10 s for 20 times to have 600 pulses for each iTBS course; (3) the total cumulative pulses were 9600 (16 sessions). Finally, iTBS was delivered when participants were in a state of rest.

Table 1. Baseline demographics and clinical characteristics

	Active ($n = 30$)	Sham ($n = 30$)	p value
Age, mean (S.D.)	19.5 (6.7)	18.2 (6.5)	0.460
Male, n (%)	28 (93.3)	27 (90.0)	0.640
Full intelligence Quotient, mean (S.D.)	81.8 (19.6)	90.2 (21.6)	0.120
Clinical symptoms			
Social Responsiveness Scale, mean (S.D.)	106.2 (28.4)	111.7 (24.1)	0.428
Repetitive Behavior Scale-Revised, mean (S.D.)	34.3 (23.1)	30.4 (21.2)	0.502
Emotion Dysregulation Inventory score, mean (S.D.)	25.1 (22.5)	21.4 (21.8)	0.516
Adaptive Behavior Assessment System –II: mean (S.D.)	79.3 (16.1)	77.4 (15.1)	0.639
Autism Diagnostic Observation Schedule (ADOS)-2			
Calibrated Severity Score (CSS), total score, mean (S.D.)	7.1 (2.2)	7.0 (2.7)	0.835
DSM-5 functional level, score 1/2	13/17	15/15	0.604
Social cognition			
Reading the Mind in the Eyes Test, mean (S.D.)	19.8 (6.6)	24.9 (7.5)	0.008**
Frith-Happe Animations, Categorization, mean (S.D.)	5.7 (1.7)	6.6 (1.7)	0.051
Frith-Happe Animations, Feeling, mean (S.D.)	2.2 (2.0)	3.6 (2.1)	0.011*
Comorbid with ADHD, n (%)	13 (43.3)	14 (46.7)	0.795
Concurrent Methylphenidate use, n (%)	2 (6.7)	7 (23.3)	0.145
Concurrent Antipsychotics use, n (%)	4 (13.3)	5 (16.7)	0.718
Psychotherapy, n (%)	5 (16.7)	5 (16.7)	1

Abbreviation: ADHD, Attention-Deficit/Hyperactivity Disorder; OCD, Obsessive-compulsive Disorder.
*$p < 0.05$, **$p < 0.01$.

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

The RIFG was localized by transforming from MNI coordinates (56, 10, 14) (Dapretto et al., 2006) to the individual's baseline T1-weighted image using the Navigated Brain Stimulation system (Nexstim®, Helsinki, Finland). Information about localization transformation is detailed elsewhere (Ni et al., 2023a). The coil was targeted at the individual's MNI coordinates and applied tangentially against the skull, with the coil handle pointing upwardly and slightly posteriorly to prevent the stimulation blockage by the ear.

Outcomes

The primary outcomes were core autistic symptoms measured by the subjective caregiver-rated Social Responsiveness Scale (SRS) (Gau, Liu, Wu, Chiu, & Tsai, 2013) and the Repetitive Behavior Scale-Revised (RBS-R) (Bodfish, Symons, Parker, & Lewis, 2000; Yang et al., 2019) and objective ADOS-2 calibrated severity scores (ADOS-2-CSS) (Hus & Lord, 2014; Lord, DiLavore, Risi, Gotham, & Bishop, 2012). Higher scores on those scales represent greater severity.

Because of the essential role of RIFG in social cognition, we used two common social tasks, the Reading the Mind in the Eye Test (RMET) (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) and Frith-Happe Animations (White, Coniston, Rogers, & Frith, 2011), as the secondary outcome. The RMET was developed to evaluate social cognition for autism (Baron-Cohen et al., 2001). The RMET requires matching visual information from photographs of a pair of eyes along with the surrounding part of a face and a pair of words describing affective or mental states (4 items). There are 36 items in the RMET. The total scores (ranging from 0 to 36) on the RMET represent how many correct answers the participant infers from the eye expressions of different emotions, which captures facial affect reading and language command (Pavlova & Sokolov, 2022). A recent meta-analysis (Penuelas-Calvo, Sareen, Sevilla-Llewellyn-Jones, & Fernandez-Berrocal, 2019) has demonstrated autistic people exhibit difficulties on the RMET in comparison to typical control ($d = 1.15$). The Frith-Happe Animations task was developed to evaluate mentalizing (theory of mind) in autistic people (Castelli, Frith, Happe, & Frith, 2002). In the Frith-Happe Animations, two triangles are presented on the screen with three different interaction patterns: perception of complex mental states involving the theory of mind (TOM; 4 questions), perception of agency for goal-directed behaviors (Goal-directed; 4 questions) or random movement with no attribution of mental states (Random; 4 questions). Participants are asked to infer whether an interaction between two triangles exists (Livingston, Shah, White, & Happe, 2021). If the participant answers correctly, they will be asked to select the words that best describe how two triangles feel during the interaction (feeling scores). The categorical scores on Frith-Happe Animations represent how participants correctly judge the interactions between two triangles; the feeling scores represent how participants select the correct words that best describe how two triangles feel during the interaction. To enhance contrast and reduce assessment time, we adopted the shortened Frith–Happe Animations that only includes TOM and Random and drops the Goal-directed. This adapted version has been used in the Human Connectome Project (Barch et al., 2013) and our previous rTMS/TBS RCTs (Ni et al., 2021, 2023b). Based on this modification, the total categorical scores of the Frith-Happe Animations Task will be 0–8. The feeling scores of the Frith-Happe Animations Task range from 0 to 8. Higher scores in the Frith-Happe Animations Task represent better mentalizing ability. A recent meta-analysis (Wilson, 2021) has demonstrated autistic people largely do not perform as well as typically developing controls in this task ($d = 0.25–0.62$).

Because the RIFG is involved in response inhibition, which may be associated with emotion regulation and adaptive function, we also included these two domains as parent/caregiver-rated exploratory outcomes. Emotion dysregulation (Mazefsky et al., 2013) and lower adaptive function (Kenworthy, Case, Harms, Martin, & Wallace, 2010) are common in autistic people. Emotion dysregulation was estimated using the caregiver-rated Emotion Dysregulation Inventory (EDI) (Mazefsky, Yu, White, Siegel, & Pilkonis, 2018b). EDI comprises 30 items in two factors (Emotion Reactivity and Dysphoria) and can capture common emotional dysregulation issues in autistic youth with good test-retest reliability and sensitivity to change. The original psychometric sample during the development of EDI aged 4–20 years (Mazefsky et al., 2018a, 2018b). Seldom published studies recruited samples of young adults aged beyond 20 years. Nonetheless, Dr Mazefsky and the team suggest that 'the EDI can be used by caregivers of adults with ASD' (Mazefsky, 2021). Higher scores of EDI represent worse emotion regulation. The adaptive function was measured with Adaptive Behavior Assessment System-II (ABAS-II) (Harrison & Oakland, 2003). The ABAS-II is a caregiver-rated measurement for adaptive function, including communication, community use, functional academics, home living, health/safety, leisure, self-care, self-direction and social (Harrison & Oakland, 2003). Higher ABAS-II scores represent better adaptive functions.

All questionnaires were assessed at baseline, Week 8 (within three days after the last iTBS) and Week 12. The social tasks were measured within one hour after the last iTBS in Week 8.

Adverse events were checked at each session using open-ended questions regarding physical discomfort, followed by close-ended questions studying the most common side effects of TBS, such as 'pain at the application site,' 'headache/dizziness,' and 'tinnitus' (Elmaghraby et al., 2022). A neurologist evaluated the EEG data of each time point to assess any neurophysiologic changes.

Sample size

The sample size and the post-hoc power estimation were calculated with G*Power 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009). A minimum sample size of 44 was estimated with 95% power and 0.05 significance to detect a standardized effect of 0.50 (based on the previous meta-analysis [Barahona-Correa et al., 2018]) from the within-between interaction of the repeated-measure analysis of the variance model. Considering dropouts (30%), the total sample size was 60. The mean attrition rate in RCTs for chronic pediatric mental health conditions is suggested to be 20% (Karlson & Rapoff, 2009). Because of the location of the RIFG, we expected that there might be a substantial proportion of participants would drop out because of the intolerable local pain induced by stimulation. When we calculated the sample size, the expected attrition rate was thus set at 30% (higher than the mean of 20%).

Statistical analysis

Demographic and clinical characteristics at baseline and adverse events between the active and sham groups were compared using an independent t test and χ^2 test. We used the

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

intent-to-treat (ITT) approach to account for dropouts. The proportion of missing data is 2% (4/180) in the SRS, RBS-R, EDI, and ABAS-II and 7% (12/180) in the RMET and Frith-Happe Animations. The Expected-Maximization algorithm was used to impute these missing data based on variables that were part of the planned analysis, comprising demographics (sex and age), intervention status, visit status, and all outcome variables (SRS, RMET, EDI, and ABAS-II). The generalized estimating equations (GEE) model was used to explore the treatment effect, time effect, and treatment-by-time effect from baseline to Week 8 and from baseline to Week 12, respectively. A working correlation matrix with a compound symmetry (exchangeable) autocorrelation was used with the robust standard error estimator to account for correlations between individuals' repeated measurements between visits. In the GEE model, baseline scores on the outcome of interest, age, and medication use were taken as covariates in our analysis. A paired t test was used as a post-hoc analysis within the active and sham groups, with the baseline as the reference. Notably, because earlier studies highlighted a possible age-dependent response to TBS in autistic people (Jannati et al., 2020; Oberman, Pascual-Leone, & Rotenberg, 2014), we did an additional age-stratified GEE as shown in online Supplementary Information.

The statistical analysis was performed using the SAS Version 9.4 software (SAS Institute, Cary, NC, USA). The results from the GEE and post-hoc analyses were considered statistically significant at p value $\leqslant 0.05$. As the first preregistered clinical trial of RIFG TBS in autistic people, we aimed to investigate all potentially relevant effects caused by RIFG iTBS extensively. Given the exploratory nature, we did not correct for multiple comparisons in our study.

Results

Feasibility

Sixty-eight participants were screened by the principal investigator (H.-C.N.) (Fig. 1). Sixty participants completed the baseline assessments and were randomly assigned to the active or sham group (30 active). Two participants in the active group withdrew (one withdrew after 13 sessions for personal reasons, and the other withdrew after 16 sessions because of refusing to complete assessments). One participant in the sham group was withdrawn because of incidental findings (right frontal encephalomalacia) in the baseline MRI. Eventually, fifty-seven participants completed the study, with a retention rate of 95%. The post-hoc power calculation achieved 98.8%, with the conditions of two-sided alpha = 0.05, effect size $d = 0.50$, nonsphericity correction $\varepsilon = 1$, and correlation among repeated measures = 0.5.

Both groups did not differ in the baseline demographic and clinical features, including age, sex, FIQ, clinical severity, psychiatric comorbidity, and concurrent treatment (Table 1). However, total scores on the RMET ($p = 0.008$) and feeling scores of Frith-Happe Animations ($p = 0.011$) were lower in the active group than in the sham. Therefore, baseline performance was adjusted in the GEE.

Adverse events during iTBS comprised local pain (63%), dizziness (10%) and eye pain (3%) in the active group, and local pain (3%), dizziness (3%), and headache (3%) in the sham group (online Supplementary Table S2). All adverse events were transitory. No seizure was reported during the intervention and at Week 12. No abnormal findings on EEG were identified. All participants could tolerate iTBS, and none withdrew due to adverse events. No participants actively mentioned or questioned their allocation status during the study.

Primary outcome

The subjective SRS, RBS-R, and objective ADOS-2 CSS outcomes are reported in Table 2 and online Supplementary Fig. S1. Although we detected a significant time effect on changes in SRS (Week 8, $Z = -2.96$, $p = 0.003$; Week 12, $Z = -3.19$, $p = 0.002$; Table 3 and online Supplementary Table S3) and ADOS-2 CSS (Week 12, $Z = -3.56$, $p < 0.001$; online Supplementary Table S3), there was no significant treatment-by-time interaction effect on SRS ($p_{\text{Week 8}} = 0.984$; $p_{\text{Week 12}} = 0.399$), RBS-R ($p_{\text{Week 8}} = 0.146$; $p_{\text{Week 12}} = 0.247$) and ADOS-2 CSS ($p_{\text{Week 8}} = 0.240$; $p_{\text{Week 12}} = 0.580$), indicating both groups

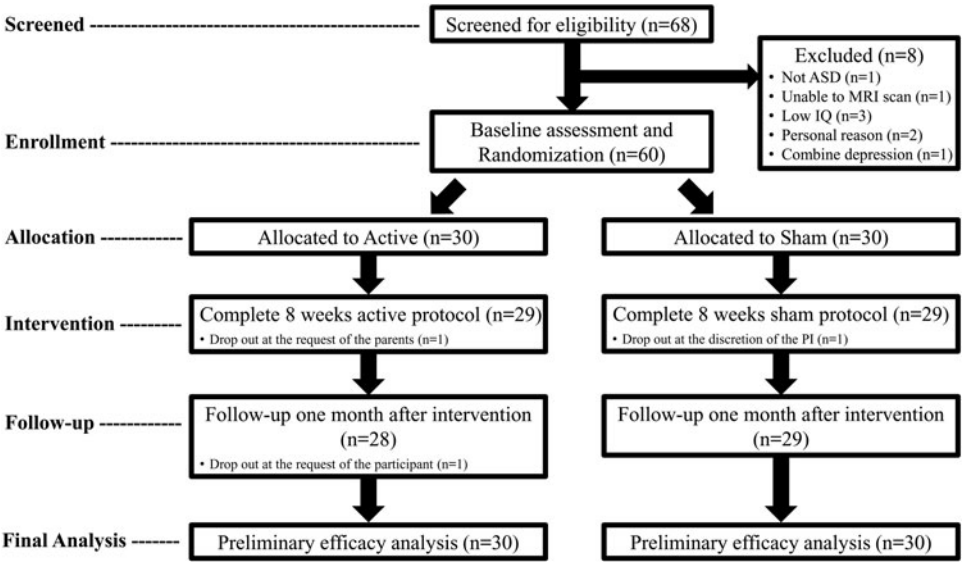

Figure 1. Flow diagram.

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

Table 2. Primary, secondary, and exploratory outcomes before and after intervention for Active and Sham groups

	Active group			Sham group		
Mean (s.d.)	Baseline	Week 8	Week 12	Baseline	Week 8	Week 12
Primary outcome						
SRS	106.2 (28.4)	95.1 (29.9)***	98.7 (27.1)*	111.7 (24.1)	100.6 (24.1)**	100.0 (24.3)**
RBS-R	34.3 (23.1)	26.9 (26.2)**	29.7 (26.6)*	30.4 (21.2)	28.3 (18.1)	30.1 (20.1)
ADOS-2, CSS	7.1 (2.2)	7.0 (2.2)	6.5 (2.7)	7.0 (2.7)	6.5 (2.7)	6.1 (2.8)***
Secondary outcome						
Frith-Happe animations, categorization	5.7 (1.7)	6.0 (1.7)	5.7 (2.0)	6.6 (1.7)	6.0 (1.8)*	6.1 (2.1)
Frith-Happe animations, feeling	2.2 (2.0)	2.8 (2.0)*	3.0 (2.3)*	3.6 (2.1)	3.3 (2.2)	3.4 (2.6)
RMET, total correct	19.8 (6.6)	22.7 (6.9)***	20.7 (7.9)	24.9 (7.5)	26.0 (7.3)	26.1 (6.5)
Exploratory outcome						
ABAS-II	79.3 (16.1)	83.8 (17.3)**	82.0 (17.1)	77.4 (15.1)	79.2 (17.5)	80.0 (18.8)
EDI	25.1 (22.5)	18.0 (21.5)	14.6 (12.5)**	21.4 (21.8)	16.4 (18.8)*	18.2 (19.7)

SRS, Social Responsiveness Scale; RBS-R, Repetitive Behavior Scale-Revised; EDI, Emotion Dysregulation Inventory; ABAS-II, Adaptive Behavior Assessment System-II; RMET, Reading the Mind in the Eyes Test.
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

did not differ in changes in autistic symptoms from baseline to Week 8 and Week 12. The post-hoc within-group analysis (Table 2) revealed that total SRS scores significantly reduced from baseline to Week 8 (active: $p < 0.001$, $Z = -3.60$, Cohen's $d = 0.66$; sham: $p = 0.004$, $Z = -2.90$, Cohen's $d = 0.53$) and Week 12 (active: $p = 0.025$, $Z = -2.24$, Cohen's $d = 0.41$; sham: $p = 0.002$, $Z = -3.12$, Cohen's $d = 0.57$) in both groups, respectively. Total RBS-R scores decreased from baseline to Week 8 ($p = 0.003$, $Z = -2.94$, Cohen's $d = 0.52$) and Week 12 ($p = 0.048$, $Z = -1.98$, Cohen's $d = 0.35$) in the active group. ADOS-2 CSS scores decreased from baseline to Week 12 in the sham group ($p < 0.001$, $Z = -3.52$, Cohen's $d = 0.64$).

Secondary outcome

From baseline to week 8 (Table 3 and Fig. 2), we found a significant time effect ($p = 0.020$, $Z = -2.32$) and treatment-by-time interaction effect ($p = 0.023$, $Z = 2.28$, Cohen's $d = 0.58$) on categorical scores of Frith-Happe Animations. Post-hoc analysis revealed that categorical scores significantly decreased in the sham group ($p = 0.018$, $Z = -2.36$, Cohen's $d = 0.42$) but did not change in the active group (Table 2). There was also a significant treatment-by-time interaction effect on feeling scores of Frith-Happe Animations from baseline to Week 8 ($p = 0.026$, $Z = 2.22$, Cohen's $d = 0.57$) and Week 12 ($p = 0.025$, $Z = 2.24$, Cohen's $d = 0.57$), respectively (Table 3 and Fig. 2). Post-hoc

Table 3. Adjusted estimates of primary, secondary, and exploratory outcomes based on GEE model from baseline to week 8 for Active and Sham groups

	Treatment effect		Time effect		Treatment × Time effect			
	Estimate	*p* value	Estimate	*p* value	Estimate	*p* value	*Z*	*Cohen's d*[a]
Primary outcome								
SRS	−0.02 (1.39)	0.990	−11.07 (3.74)	0.003**	−0.10 (4.82)	0.984	−0.02	<0.01
RBS-R	0.46 (0.88)	0.600	−2.12 (2.63)	0.418	−5.31 (3.65)	0.146	−1.45	0.37
ADOS-2, CSS	0.06 (0.13)	0.614	−0.54 (0.29)	0.063	0.44 (0.37)	0.240	−1.45	0.30
Secondary outcome								
Frith-Happe animations, categorization	−0.09 (0.13)	0.460	−0.55 (0.24)	0.020*	0.80 (0.35)	0.023*	2.28	0.58
Frith-Happe animations, feeling	−0.22 (0.15)	0.133	−0.34 (0.30)	0.253	0.95 (0.43)	0.026*	2.22	0.57
RMET, total correct	−0.73 (0.34)	0.033*	1.10 (0.69)	0.108	1.80 (0.98)	0.067	1.83	0.47
Exploratory outcome								
ABAS-II	−0.08 (0.36)	0.833	1.81 (1.41)	0.199	2.65 (2.14)	0.215	1.24	0.31
EDI	1.69 (2.19)	0.441	−5.02 (2.34)	0.032*	−2.14 (4.45)	0.631	−0.48	0.12

The Sham group serves as the reference group.
SRS, Social Responsiveness Scale; RBS-R, Repetitive Behavior Scale-Revised; EDI, Emotion Dysregulation Inventory; ABAS-II, Adaptive Behavior Assessment System-II; RMET, Reading the Mind in the Eyes Test.
* $p < 0.05$, ** $p < 0.01$.
[a]Cohen's d effect size was calculated using the mean difference between groups with difference score as the mean score at follow-up minus the mean score at baseline score for each group to take the difference at baseline into account.

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

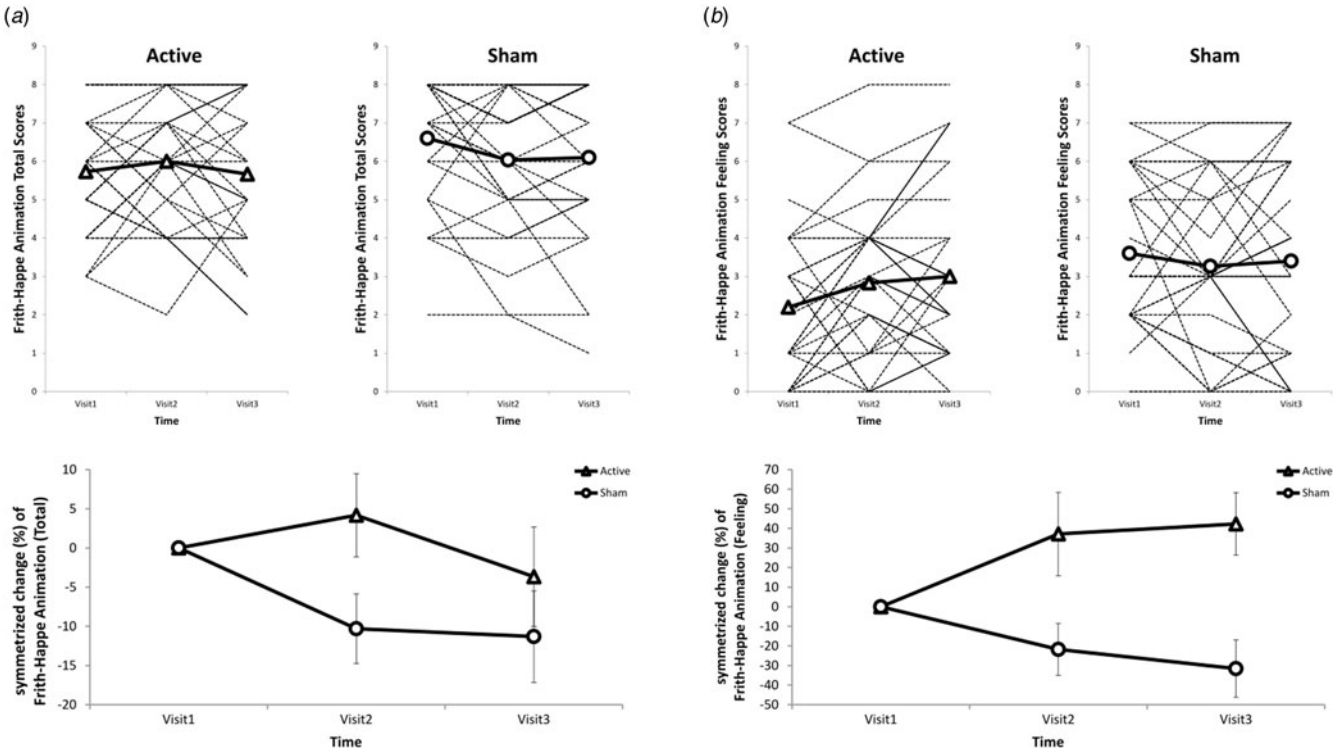

Figure 2. The individual and average scores of Frith-Happe Animations in Active and Sham groups at Baseline, Week 8, and Week 12, (a) categorical scores, (b) feeling scores. To better illustrate the trend of changes of categorical and feeling scores of Frith-Happe Animations, symmetrized percentage changes from the baseline are compared between both groups. The error bars denote standard errors.

analyses showed feeling scores increased from baseline to Week 8 ($p = 0.051$, $Z = 1.95$, Cohen's $d = 0.36$) and Week 12 ($p = 0.014$, $Z = 2.46$, Cohen's $d = 0.45$) in the active group, while there was no significant change in the sham group. As for the RMET, there was no significant time or treatment-by-time effect. Nonetheless, total scores significantly increased from baseline to Week 8 in the active group ($p < 0.001$, $Z = 4.03$, Cohen's $d = 0.75$; Table 2 and online Supplementary Fig. S2).

Exploratory outcome

There was no significant treatment-by-time interaction effect on emotion dysregulation or adaptive function from baseline to Week 8 and Week 12 (online Supplementary Figs S3 and S4), but a significant time effect existed from baseline to Week 8 on emotion dysregulation ($p = 0.032$, $Z = -2.15$; Table 3 and online Supplementary Table S3). Post-hoc analysis showed adaptive function ($p = 0.005$, $Z = 2.81$, Cohen's $d = 0.50$ from baseline to Week 8) and emotion dysregulation ($p = 0.003$, $Z = -3.02$, Cohen's $d = 0.55$ from baseline to Week 12) significantly improved in the active group. At the same time, emotion dysregulation improved in the Sham group from baseline to Week 8 (Table 2).

Discussion

This sufficiently powered clinical trial sought to address the clinical efficacy of multi-session prefrontal iTBS in reducing autistic symptoms. Sixteen sessions of neuro-navigated iTBS delivered over the RIFG had no superior effect over sham in reducing autistic symptoms, emotion dysregulation, or adaptive function difficulties. Nonetheless, active iTBS, relative to sham, was associated with significant improvement in social cognition of inferring others' feelings (estimated by the Animations task) in autistic individuals, and this benefit could still be noted four weeks following the last stimulation. Notably, these results would not survive the stringent multiple comparison corrections. Neurophysiological data and adverse event profiles suggest RIFG iTBS is safe and tolerable in autistic individuals. If replicated in another independent dataset, results from our multimodal trial provide evidence to support the beneficial potential of RIFG iTBS to improve social cognition in autistic people.

Consistent with most of the published sham-controlled blind rTMS/TBS RCTs (Ameis et al., 2020; Ni et al., 2021, 2023b), we did not find significant treatment-by-time interactions on any core or associated clinical symptoms, indicating no group differences between RIFG iTBS and sham. Nonetheless, also in line with effect sizes reported in previous open-label rTMS trials (Sokhadze et al., 2018) and within-group post-pretreatment analyses in earlier blind RCTs (Kaokhieo et al., 2023), our post-hoc within-group analysis revealed that autistic symptoms, adaptive function, and emotion dysregulation improved with time in both groups. Generally, we observed a more positive extent in the active group than in the sham group (in terms of larger effect sizes, which nonetheless were not robust enough to result in significant treatment-by-time interactions), except for the pattern of the ADOS-2 CSS (i.e. more reduction from the baseline to week 12 in the sham relative to active). This within-group pattern may reconcile the ostensible discrepancy between our findings (i.e. no group differences in clinical symptoms as quantified by treatment-by-time effects) and results from an earlier RIFG rTMS RCT (Kaokhieo et al., 2023). Namely, Kaokhieo et al. (Kaokhieo et al. 2023) showed that excitatory 5 Hz RIFG rTMS

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

is associated with improving adaptive function in four autistic children in the active group, as evidenced by a significant time effect, but not by a significant treatment-by-time interaction. We cannot rule out the possibility that active RIFG iTBS/rTMS might still be superior to the sham in reducing clinical difficulties associated with autism, considering the sampling heterogeneity (Masi, Lampit, Glozier, Hickie, & Guastella, 2015). Further, despite being sufficiently powered for the whole sample analysis, the current sample size is not big enough for valid sub-group analyses stratified by severity, age, or sex, precluding the detection of hidden changes due to inter-individual variability in response (Ni et al., 2021, 2022). Given the current intellectually able sample, relatively lower severity may also affect sensitivity to detect changes in clinical trials for autism spectrum (King et al., 2013). This limitation merits more endeavors (e.g. NCT04987541) to include the autistic subpopulation with more severe symptoms and high support needs (i.e. those with minimally verbal status and/or intellectual disabilities) in the rTMS/TBS trials. Despite these possible explanations and caveats, our findings of null treatment-by-time interaction but significant time effects on changes in autistic symptoms following RIFG iTBS echo the concern that clinical rTMS/TBS studies (Burke et al., 2022) involving neurodevelopmental populations are susceptible to generalized/placebo effects (Masi et al., 2015).

We found that 16-session RIFG iTBS, relative to sham, was associated with improved social cognition (feeling scores on Frith-Happe Animations, indicating mentalizing others' feelings) in autistic individuals. This group difference in social cognition change can continue for four weeks after the last stimulation. However, this iTBS-associated change in social cognition was not meaningfully noted in category scores on the Animations task and RMET. This discrepancy could be explained as follows. The categorical score on the Animations task simply estimates whether a participant can judge the presence of an intention to interact between two agencies (i.e. two triangles in this task). On the other hand, the feeling score involves a more complex and subtle process of mental state inference, which requires a participant to correctly infer what these agencies are feeling during interactions to score (Livingston et al., 2021). Thus, the categorical score may be associated with ceiling effects, limiting sensitivity to capture sufficient variance in reflecting changes (Livingston et al., 2021). Regarding the double dissociation between changes in the Animations and RMET, this finding largely matches the theory and empirical findings of social cognition. Specifically, the RMET relies on facial affect reading, language command, and memory (Pavlova & Sokolov, 2022), which differs from the mentalizing process reflected by Frith-Happe Animations. Further, RMET performance is supported by ensembles of circuits beyond the social brain (Pavlova & Sokolov, 2022). In contrast, the RIFG is considered a gateway into a mentalizing network (Tettamanti et al., 2017). RIFG stimulation in neurotypical adults has also been shown to modulate mentalizing processes (De Carli et al., 2019; Dippel & Beste, 2015; Li et al., 2021).

Despite this preceding neurobiological endorsement, several psychometric issues are considered. Specifically, there were between-group baseline differences in the RMET and feeling scores on Frith-Happe Animations, thus included as covariates. However, this baseline difference is considered a random artifact that could exist even in perfect randomization (Altman, 1985) and is a 'ubiquitous error' in published RCTs (Austin, Manca, Zwarenstein, Juurlink, & Stanbrook, 2010). Therefore, the CONSORT recommends that 'significance testing of baseline differences in randomized controlled trials (RCTs) should not be performed because it is superfluous and can mislead investigators and their readers' (Moher et al., 2010). Including covariates of the baseline scores in the models can minimize this concern of randomization (Austin et al., 2010). Notably, we acknowledge there might be a ceiling effect on the RMET result, despite the fact that the current RMET mean and standard deviation were similar to those reported in a meta-analysis (Penuelas-Calvo et al., 2019). The other concern is whether there is a learning effect in these two social cognition tasks. Previous studies have reported good test-retest reliability of the RMET with a 4-week interval (intraclass correlation coefficient 0.833) (Vellante et al., 2013) and the Animations task with a 3-month interval (intraclass correlation coefficient 0.78) (Altschuler & Faja, 2022). The good test-retest stability suggests that the learning effect for these two tasks may be minimal. In our study, the intervals between the time points were 8 weeks and 4 weeks, respectively, similar to these test-retest investigations. Moreover, the inference of whether active *v.* sham difference exists is based on the treatment-by-time interaction effect. A learning effect is more associated with a time effect, for which we did not find any significant change from baseline to Week 8 (Table 3) and baseline to Week 12 (online Supplementary Table S3) for most RMET and Animations results. The only exception was the categorical score of Frith-Happe Animations from baseline to Week 8 ($p = 0.020$), with an average worse performance at follow-up in the whole sample. If there had been a learning effect, this change would have been better with time, and the effect should have existed evenly in the two treatment groups, given the current proper randomization. We thus consider the learning effect in these two social cognition tasks to be minimal. These preceding reasons, the objective nature of social cognitive tasks, and lasting changes at the follow-up of Week 12 endorse the robustness of this RIFG iTBS-associated improvement in inferring others' feelings in autistic people.

Notably, RIFG iTBS-associated social cognition change cannot be translated into changes in autistic symptoms. Several explanations may account for this conceivable discrepancy. First, autism-associated social-communication symptoms involve interactions between a wide range of social cognition beyond mentalizing and non-social mental processes (Leekam, 2016). Correlations between social cognition and social difficulties in autistic people are thus just small to medium (Bottema-Beutel, Kim, & Crowley, 2019). Second, social cognitive tasks may not represent ecologically valid interpersonal processes involved in real-life interactions (Konstantin, Nordgaard, & Henriksen, 2023). Third, cognition and symptoms in autism sometimes have a paradoxical relationship (Geurts, Corbett, & Solomon, 2009). Fourth, the present primary outcome measures are parent/caregiver-rated and might not be sensitive to capture changes in RCT. Lastly, the current stimulation frequency/intensity might not be sufficient to induce broad social functioning improvement in autistic people.

The last argument brings forward general methodological considerations of rTMS/TBS. Specifically, optimal stimulation intensity, frequency, and cumulative doses, which could generate clinically meaningful changes in autism spectrum (among other psychiatric disorders), are far from being conclusive. Further, although theoretical rationales and empirical evidence justify the present implementation of RIFG iTBS (excitatory) for autism, neurotypical literature suggests that there exists high inter-individual variability in behavioral and neurobiological responses to TBS paradigms (Chung et al., 2016; Corp et al., 2020). This idiosyncratic response might be even more pronounced in autistic people, evidenced by a small study showing

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press

that some autistic people had excitatory. In contrast, others had inhibitory cumulative aftereffects following cTBS (generally considered an inhibitory protocol) (Jannati et al., 2020). This inter-individual variability in cTBS aftereffects may be driven by unique genotypes (Jannati et al., 2020), idiosyncrasy in GABAergic system dysfunction in autism (Zhao et al., 2021), shared and different synaptic mechanisms between iTBS and cTBS (Lee et al., 2023), or differential regional neurobiological properties resulting in variable responses (Gollo, Roberts, & Cocchi, 2017). These methodological issues prompt extensive investigations in the future.

The feasibility and safety of RIFG iTBS for autistic youth accords with most rTMS RCT trials (Ameis et al., 2020; Enticott et al., 2014; Kaokhieo et al., 2023). The current retention rate was 95%, compatible with previous RCTs on the pSTS (91%) and DLPFC (98%) (Ni et al., 2021, 2023b). Regarding the adverse events, 63% of participants in the active group felt local pain, which is higher than our previous DLPFC (27%) and pSTS (10%) trials. Nevertheless, all these discomforts were transitory and did not lead to dropouts. Moreover, we are the first to provide EEG evidence to prove that no seizure was induced by TBS in autistic people.

This study has some other limitations. First, considering the real-world generalization, we did not exclude participants with psychiatric comorbidities and concurrent medications. However, we acknowledge that hidden complex relationships between comorbidities/medications and treatment responses might exist. Second, the sex ratio of participants was quite uneven (5 females), precluding the investigation of sex/gender effects. Third, although we tried our best to maintain the integrity of blinding, the considerably higher incidence of reported pain in the active group might partly compromise the blinding. Future studies need to formally adopt the assessment of blinding in the protocol (e.g. Bang Blinding indexes) to assess whether caregivers/participants and raters could correctly guess to which arm participants are assigned. Lastly, although the measure developer team has suggested that the EDI can be rated by caregivers of autistic adults, there has been no caregiver norm for the EDI. Self-report perspectives might be different from the informant's response (Sandercock, Lamarche, Klinger, & Klinger, 2020), while psychometrics of self-report measures for emotion dysregulation in autistic adults have not been validated yet.

Conclusion

In a sufficiently powered and rigorously conducted RCT, our MRI-guided RIFG iTBS intervention failed to reduce autistic symptoms more than the sham. Nonetheless, we showed that RIFG iTBS, relative to sham, could improve social cognition of inferring others' feelings in autistic people. Future studies are required to verify if the present promising results are robust to differences in the neuromodulation parameters. Our results also prompt investigations if protocol optimization (such as stimulation intensities and doses), together with other intervention modalities, could confer additional clinical benefits.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291724001387

Acknowledgements. The authors would like to thank all of our participants and their family members for partaking in this study, Ms. Chiu-Fen Lin, Ms. Yi-Chun Liu, Mr. Wei-Cheng Lin, and Mr. Hung Chien for carrying out the recruitment and data management, CGMH for equipment support, and the anonymous reviewers for comments that significantly improved the manuscript. We would like to pay tribute to the late Professor Ying-Zu Huang, who guided and inspired this study with wisdom, insight, and tenacity.

Author contributions. Hsing-Chang Ni: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing-original draft, Writing-review & editing, Visualization, Supervision, Project administration, Funding acquisition; Yi-Lung Chen: Formal analysis, Writing-review & editing; Meng-Ying Hsieh: Resources; Yi-Ping Chao: Resources; Chen-Te Wu: Resources; Rao-Shayn Chen: Resources; Chi-Hung Juan: Conceptualization; Cheng-Ta Li: Conceptualization; Susan Shur-Fen Gau: Resources, Conceptualization, Writing-editing; Hsiang-Yuan Lin: Conceptualization, Methodology, Software, Validation, Writing-original draft, Writing-review & editing, Visualization, Supervision.

Funding statement. This study was supported by the Ministry of Science and Technology of Taiwan (108-2321-B-075-004-MY2) and Chang Gung Memorial Hospital (CMRPG3L0681-2). H-YL is supported by the Azrieli Adult Neurodevelopmental Centre, Centre for Addiction and Mental Health, and an Academic Scholar Award from the Department of Psychiatry, University of Toronto. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

Competing interests. The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

Altman, D. G. (1985). Comparability of randomised groups. *Journal of the Royal Statistical Society. Series D* (*The Statistician*), *34*(1), 125–136.

Altschuler, M. R., & Faja, S. (2022). Brief report: Test-retest reliability of cognitive, affective, and spontaneous theory of mind tasks among school-aged children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *52*(4), 1890–1895. doi: 10.1007/s10803-021-05040-6

Ameis, S. H., Blumberger, D. M., Croarkin, P. E., Mabbott, D. J., Lai, M. C., Desarkar, P., … Daskalakis, Z. J. (2020). Treatment of executive function deficits in autism spectrum disorder with repetitive transcranial magnetic stimulation: A double-blind, sham-controlled, pilot trial. *Brain Stimulation*, *13*(3), 539–547. doi: 10.1016/j.brs.2020.01.007

Austin, P. C., Manca, A., Zwarenstein, M., Juurlink, D. N., & Stanbrook, M. B. (2010). A substantial and confusing variation exists in handling of baseline covariates in randomized controlled trials: A review of trials published in leading medical journals. *Journal of Clinical Epidemiology*, *63*(2), 142–153. doi: 10.1016/j.jclinepi.2009.06.002

Barahona-Correa, J. B., Velosa, A., Chainho, A., Lopes, R., & Oliveira-Maia, A. J. (2018). Repetitive transcranial magnetic stimulation for treatment of autism spectrum disorder: A systematic review and meta-analysis. *Frontiers in Integrative Neuroscience*, *12*, 27. doi: 10.3389/fnint.2018.00027

Barch, D. M., Burgess, G. C., Harms, M. P., Petersen, S. E., Schlaggar, B. L., Corbetta, M., ... Consortium, W. U.-M. H. (2013). Function in the human connectome: task-fMRI and individual differences in behavior. *Neuroimage*, *80*, 169–189. doi: 10.1016/j.neuroimage.2013.05.033

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "Reading the Mind in the Eyes" test revised version: A study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry*, *42*(2), 241–251.

Barstow, C., Shahan, B., & Roberts, M. (2018). Evaluating medical decision-making capacity in practice. *American Family Physician*, *98*(1), 40–46.

Blumberger, D. M., Mulsant, B. H., Thorpe, K. E., McClintock, S. M., Konstantinou, G. N., Lee, H. H., … Downar, J. (2022). Effectiveness of standard sequential bilateral repetitive transcranial magnetic stimulation vs bilateral theta burst stimulation in older adults with depression: The

FOUR-D randomized noninferiority clinical trial. *JAMA Psychiatry*, *79*(11), 1065–1073. doi: 10.1001/jamapsychiatry.2022.2862

Blumberger, D. M., Vila-Rodriguez, F., Thorpe, K. E., Feffer, K., Noda, Y., Giacobbe, P., … Downar, J. (2018). Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): A randomised non-inferiority trial. *Lancet (London, England)*, *391*(10131), 1683–1692. doi: 10.1016/S0140-6736(18)30295-2

Bodfish, J. W., Symons, F. J., Parker, D. E., & Lewis, M. H. (2000). Varieties of repetitive behavior in autism: Comparisons to mental retardation. *Journal of Autism and Developmental Disorders*, *30*(3), 237–243. doi: 10.1023/a:1005596502855

Bottema-Beutel, K., Kim, S. Y., & Crowley, S. (2019). A systematic review and meta-regression analysis of social functioning correlates in autism and typical development. *Autism Research*, *12*(2), 152–175. doi: 10.1002/aur.2055

Burke, M. J., Romanella, S. M., Mencarelli, L., Greben, R., Fox, M. D., Kaptchuk, T. J., … Santarnecchi, E. (2022). Placebo effects and neuromodulation for depression: A meta-analysis and evaluation of shared mechanisms. *Molecular Psychiatry*, *27*(3), 1658–1666. doi: 10.1038/s41380-021-01397-3

Casanova, M. F., Hensley, M. K., Sokhadze, E. M., El-Baz, A. S., Wang, Y., Li, X., & Sears, L. (2014). Effects of weekly low-frequency rTMS on autonomic measures in children with autism spectrum disorder. *Frontiers in Human Neuroscience*, *8*, 851. doi: 10.3389/fnhum.2014.00851

Cash, R. F. H., Weigand, A., Zalesky, A., Siddiqi, S. H., Downar, J., Fitzgerald, P. B., & Fox, M. D. (2021). Using brain imaging to improve spatial targeting of transcranial magnetic stimulation for depression. *Biological Psychiatry*, *90*(10), 689–700. doi: 10.1016/j.biopsych.2020.05.033

Castelli, F., Frith, C., Happe, F., & Frith, U. (2002). Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain*, *125*(Pt 8), 1839–1849. doi: 10.1093/brain/awf189

Chung, S. W., Hill, A. T., Rogasch, N. C., Hoy, K. E., & Fitzgerald, P. B. (2016). Use of theta-burst stimulation in changing excitability of motor cortex: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *63*, 43–64. doi: 10.1016/j.neubiorev.2016.01.008

Cole, E. J., Enticott, P. G., Oberman, L. M., Gwynette, M. F., Casanova, M. F., Jackson, S. L. J., … r, T. M. S. i. A. S. D. C. G. (2019). The potential of repetitive transcranial magnetic stimulation for autism spectrum disorder: A consensus statement. *Biological Psychiatry*, *85*(4), e21–e22. doi: 10.1016/j.biopsych.2018.06.003

Corp, D. T., Bereznicki, H. G. K., Clark, G. M., Youssef, G. J., Fried, P. J., Jannati, A., … Big, T. M. S. D. C. (2020). Large-scale analysis of interindividual variability in theta-burst stimulation data: Results from the 'Big TMS Data Collaboration'. *Brain Stimulation*, *13*(5), 1476–1488. doi: 10.1016/j.brs.2020.07.018

Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., & Iacoboni, M. (2006). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience*, *9*(1), 28–30. doi: 10.1038/nn1611

Dayan, E., Censor, N., Buch, E. R., Sandrini, M., & Cohen, L. G. (2013). Noninvasive brain stimulation: From physiology to network dynamics and back. *Nature Neuroscience*, *16*(7), 838–844. doi: 10.1038/nn.3422

De Carli, P., Bakermans-Kranenburg, M. J., Parolin, L., Lega, C., Zanardo, B., Cattaneo, Z., & Riem, M. M. E. (2019). A walk on the dark side: TMS over the right inferior frontal gyrus (rIFG) disrupts behavioral responses to infant stimuli. *Social Neuroscience*, *14*(6), 697–704. doi: 10.1080/17470919.2019.1574891

Dichter, G. S., & Belger, A. (2007). Social stimuli interfere with cognitive control in autism. *Neuroimage*, *35*(3), 1219–1230. doi: 10.1016/j.neuroimage.2006.12.038

Dippel, G., & Beste, C. (2015). A causal role of the right inferior frontal cortex in implementing strategies for multi-component behaviour. *Nature Communications*, *6*, 6587. doi: 10.1038/ncomms7587

Duque, J., Greenhouse, I., Labruna, L., & Ivry, R. B. (2017). Physiological markers of motor inhibition during human behavior. *Trends in Neurosciences*, *40*(4), 219–236. doi: 10.1016/j.tins.2017.02.006

Eliasova, I., Anderkova, L., Marecek, R., & Rektorova, I. (2014). Non-invasive brain stimulation of the right inferior frontal gyrus may improve attention in early Alzheimer's disease: A pilot study. *Journal of the Neurological Sciences*, *346*(1-2), 318–322. doi: 10.1016/j.jns.2014.08.036

Elmaghraby, R., Sun, Q., Ozger, C., Shekunov, J., Romanowicz, M., & Croarkin, P. E. (2022). A systematic review of the safety and tolerability of theta burst stimulation in children and adolescents. *Neuromodulation*, *25*(4), 494–503. doi: 10.1111/ner.13455

Enticott, P. G., Fitzgibbon, B. M., Kennedy, H. A., Arnold, S. L., Elliot, D., Peachey, A., … Fitzgerald, P. B. (2014). A double-blind, randomized trial of deep repetitive transcranial magnetic stimulation (rTMS) for autism spectrum disorder. *Brain Stimulation*, *7*(2), 206–211. doi: 10.1016/j.brs.2013.10.004

Faul, F., Erdfelder, E., Buchner, A., & Lang, A. G. (2009). Statistical power analyses using G*power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, *41*(4), 1149–1160. doi: 10.3758/BRM.41.4.1149

Gau, S. S. F., Liu, L. T., Wu, Y. Y., Chiu, Y. N., & Tsai, W. C. (2013). Psychometric properties of the Chinese version of the Social Responsiveness Scale. *Research in Autism Spectrum Disorders*, *7*(2), 349–360. doi: 10.1016/j.rasd.2012.10.004

Geurts, H. M., Corbett, B., & Solomon, M. (2009). The paradox of cognitive flexibility in autism. *Trends in Cognitive Sciences*, *13*(2), 74–82. doi: 10.1016/j.tics.2008.11.006

Gollo, L. L., Roberts, J. A., & Cocchi, L. (2017). Mapping how local perturbations influence systems-level brain dynamics. *Neuroimage*, *160*, 97–112. doi: 10.1016/j.neuroimage.2017.01.057

Harrison, P. L., & Oakland, T. (2003). *Adaptive behavior assessment system® second edition ABAS®-II*. San Antonio: Harcourt.

Hoekert, M., Vingerhoets, G., & Aleman, A. (2010). Results of a pilot study on the involvement of bilateral inferior frontal gyri in emotional prosody perception: An rTMS study. *BMC Neuroscience*, *11*, 93. doi: 10.1186/1471-2202-11-93

Hogeveen, J., Obhi, S. S., Banissy, M. J., Santiesteban, I., Press, C., Catmur, C., & Bird, G. (2015). Task-dependent and distinct roles of the temporoparietal junction and inferior frontal cortex in the control of imitation. *Social Cognitive and Affective Neuroscience*, *10*(7), 1003–1009. doi: 10.1093/scan/nsu148

Hong, Y. H., Wu, S. W., Pedapati, E. V., Horn, P. S., Huddleston, D. A., Laue, C. S., & Gilbert, D. L. (2015). Safety and tolerability of theta burst stimulation vs. single and paired pulse transcranial magnetic stimulation: A comparative study of 165 pediatric subjects. *Frontiers in Human Neuroscience*, *9*, 29. doi: 10.3389/fnhum.2015.00029

Huang, Y. Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta burst stimulation of the human motor cortex. *Neuron*, *45*(2), 201–206. doi: 10.1016/j.neuron.2004.12.033

Huang, Y. Z., Rothwell, J. C., Chen, R. S., Lu, C. S., & Chuang, W. L. (2011). The theoretical model of theta burst form of repetitive transcranial magnetic stimulation. *Clinical Neurophysiology*, *122*(5), 1011–1018. doi: 10.1016/j.clinph.2010.08.016

Hus, V., & Lord, C. (2014). The autism diagnostic observation schedule, module 4: Revised algorithm and standardized severity scores. *Journal of Autism and Developmental Disorders*, *44*(8), 1996–2012. doi: 10.1007/s10803-014-2080-3

Jannati, A., Block, G., Ryan, M. A., Kaye, H. L., Kayarian, F. B., Bashir, S., … Rotenberg, A. (2020). Continuous theta-burst stimulation in children with high-functioning autism spectrum disorder and typically developing children. *Frontiers in Integrative Neuroscience*, *14*, 13. doi: 10.3389/fnint.2020.00013

Kana, R. K., Keller, T. A., Minshew, N. J., & Just, M. A. (2007). Inhibitory control in high-functioning autism: Decreased activation and underconnectivity in inhibition networks. *Biological Psychiatry*, *62*(3), 198–206. doi: 10.1016/j.biopsych.2006.08.004

Kaokhieo, J., Tretriluxana, J., Chaiyawat, P., Siripornpanich, V., Permpoonputtana, K., Tretriluxana, S., & Nanbancha, A. (2023). Effects of repetitive transcranial magnetic stimulation combined with action-observation-execution on social interaction and communication in autism spectrum disorder: Feasibility study. *Brain Research*, *1804*, 148258. doi: 10.1016/j.brainres.2023.148258

Karlson, C. W., & Rapoff, M. A. (2009). Attrition in randomized controlled trials for pediatric chronic conditions. *Journal of Pediatric Psychology*, *34*(7), 782–793. doi: 10.1093/jpepsy/jsn122

Kennedy, D. P., & Courchesne, E. (2008). The intrinsic functional organization of the brain is altered in autism. *Neuroimage*, *39*(4), 1877–1885. doi: 10.1016/j.neuroimage.2007.10.052

Kenworthy, L., Case, L., Harms, M. B., Martin, A., & Wallace, G. L. (2010). Adaptive behavior ratings correlate with symptomatology and IQ among individuals with high-functioning autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *40*(4), 416–423. doi: 10.1007/s10803-009-0911-4

King, B. H., Dukes, K., Donnelly, C. L., Sikich, L., McCracken, J. T., Scahill, L., … Hirtz, D. (2013). Baseline factors predicting placebo response to treatment in children and adolescents with autism spectrum disorders: A multisite randomized clinical trial. *JAMA Pediatrics*, *167*(11), 1045–1052. doi: 10.1001/jamapediatrics.2013.2698

Klomjai, W., Katz, R., & Lackmy-Vallee, A. (2015). Basic principles of transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS). *Annals of Physical and Rehabilitation Medicine*, *58*(4), 208–213. doi: 10.1016/j.rehab.2015.05.005

Konstantin, G. E., Nordgaard, J., & Henriksen, M. G. (2023). Methodological issues in social cognition research in autism spectrum disorder and schizophrenia spectrum disorder: A systematic review. *Psychological Medicine*, *53*(8), 3281–3292. doi: 10.1017/S0033291723001095

Kosaka, H., Omori, M., Munesue, T., Ishitobi, M., Matsumura, Y., Takahashi, T., … Wada, Y. (2010). Smaller insula and inferior frontal volumes in young adults with pervasive developmental disorders. *Neuroimage*, *50*(4), 1357–1363. doi: 10.1016/j.neuroimage.2010.01.085

Kuang, S. (2016). Two polarities of attention in social contexts: From attending-to-others to attending-to-self. *Frontiers in Psychology*, *7*, 63. doi: 10.3389/fpsyg.2016.00063

Lee, C. W., Chu, M. C., Wu, H. F., Chung, Y. J., Hsieh, T. H., Chang, C. Y., … Lin, H. C. (2023). Different synaptic mechanisms of intermittent and continuous theta-burst stimulations in a severe foot-shock induced and treatment-resistant depression in a rat model. *Experimental Neurology*, *362*, 114338. doi: 10.1016/j.expneurol.2023.114338

Leekam, S. (2016). Social cognitive impairment and autism: What are we trying to explain? *Philosophical Transactions of the Royal Society B*, *371*(1686), 20150082. doi: 10.1098/rstb.2015.0082

Li, C. T., Huang, Y. Z., Bai, Y. M., Tsai, S. J., Su, T. P., & Cheng, C. M. (2019). Critical role of glutamatergic and GABAergic neurotransmission in the central mechanisms of theta-burst stimulation. *Human Brain Mapping*, *40*(6), 2001–2009. doi: 10.1002/hbm.24485

Li, Y., Li, W., Zhang, T., Zhang, J., Jin, Z., & Li, L. (2021). Probing the role of the right inferior frontal gyrus during pain-related empathy processing: Evidence from fMRI and TMS. *Human Brain Mapping*, *42*(5), 1518–1531. doi: 10.1002/hbm.25310

Livingston, L. A., Shah, P., White, S. J., & Happe, F. (2021). Further developing the frith-happe animations: A quicker, more objective, and web-based test of theory of mind for autistic and neurotypical adults. *Autism Research*, *14*(9), 1905–1912. doi: 10.1002/aur.2575

Lord, C., Elsabbagh, M., Baird, G., & Veenstra-Vanderweele, J. (2018). Autism spectrum disorder. *Lancet (London, England)*, *392*(10146), 508–520. doi: 10.1016/S0140-6736(18)31129-2

Lord, C., Risi, S., Lambrecht, L., Cook, Jr. E. H., Leventhal, B. L., DiLavore, P. C., … Rutter, M. (2000). The autism diagnostic observation schedule-generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders*, *30*(3), 205–223.

Lord, C. R. M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, S. L. (2012). *Autism diagnostic observation schedule, second edition* (*ADOS-2*) *manual* (*part I*): *Modules 1–4*. Torrance, CA: Western Psychological Services.

Masi, A., Lampit, A., Glozier, N., Hickie, I. B., & Guastella, A. J. (2015). Predictors of placebo response in pharmacological and dietary supplement treatment trials in pediatric autism spectrum disorder: A meta-analysis. *Translational Psychiatry*, *5*(9), e640. doi: 10.1038/tp.2015.143

Massey, S. H., Stern, D., Alden, E. C., Petersen, J. E., Cobia, D. J., Wang, L., … Smith, M. J. (2017). Cortical thickness of neural substrates supporting cognitive empathy in individuals with schizophrenia. *Schizophrenia Research*, *179*, 119–124. doi: 10.1016/j.schres.2016.09.025

Mazefsky, C. A. (2021). *Encyclopedia of autism Spectrum disorders*. Cham, Switzerland: SpringerLink.

Mazefsky, C. A., Day, T. N., Siegel, M., White, S. W., Yu, L., Pilkonis, P. A., … Developmental Disabilities Inpatient Research, C. (2018a). Development of the emotion dysregulation inventory: A PROMIS(R)ing method for creating sensitive and unbiased questionnaires for autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *48*(11), 3736–3746. doi: 10.1007/s10803-016-2907-1

Mazefsky, C. A., Herrington, J., Siegel, M., Scarpa, A., Maddox, B. B., Scahill, L., & White, S. W. (2013). The role of emotion regulation in autism spectrum disorder. *Journal of the American Academy of Child Psychiatry*, *52*(7), 679–688. doi: 10.1016/j.jaac.2013.05.006

Mazefsky, C. A., Yu, L., White, S. W., Siegel, M., & Pilkonis, P. A. (2018b). The emotion dysregulation inventory: Psychometric properties and item response theory calibration in an autism spectrum disorder sample. *Autism Research*, *11*(6), 928–941. doi: 10.1002/aur.1947

Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gotzsche, P. C., Devereaux, P. J., … Consolidated Standards of Reporting Trials, G. (2010). CONSORT 2010 Explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *Journal of Clinical Epidemiology*, *63*(8), e1–37. doi:10.1016/j.jclinepi.2010.03.004

Newman-Norlund, R. D., Gibson, M., McConnell, P. A., & Froeliger, B. (2020). Dissociable effects of theta-burst repeated transcranial magnetic stimulation to the inferior frontal gyrus on inhibitory control in nicotine addiction. *Frontiers in Psychiatry*, *11*, 260. doi: 10.3389/fpsyt.2020.00260

Ni, H. C., Chao, Y. P., Tseng, R. Y., Wu, C. T., Cocchi, L., Chou, T. L., … Lin, H. Y. (2023a). Lack of effects of four-week theta burst stimulation on white matter macro/microstructure in children and adolescents with autism. *NeuroImage: Clinical*, *37*, 103324. doi: 10.1016/j.nicl.2023.103324

Ni, H. C., Chen, Y. L., Chao, Y. P., Wu, C. T., Chen, R. S., Chou, T. L., … Lin, H. Y. (2023b). A lack of efficacy of continuous theta burst stimulation over the left dorsolateral prefrontal cortex in autism: A double blind randomized sham-controlled trial. *Autism Research*, *16*(6), 1247–1262. doi: 10.1002/aur.2954

Ni, H. C., Chen, Y. L., Chao, Y. P., Wu, C. T., Wu, Y. Y., Liang, S. H., … Lin, H. Y. (2021). Intermittent theta burst stimulation over the posterior superior temporal sulcus for children with autism spectrum disorder: A 4-week randomized blinded controlled trial followed by another 4-week open-label intervention. *Autism*, *25*(5), 1279–1294. doi: 10.1177/1362361321990534

Ni, H. C., Hung, J., Wu, C. T., Wu, Y. Y., Chang, C. J., Chen, R. S., & Huang, Y. Z. (2017). The impact of single session intermittent theta-burst stimulation over the dorsolateral prefrontal cortex and posterior superior temporal sulcus on adults with autism spectrum disorder. *Frontiers in Neuroscience*, *11*, 255. doi: 10.3389/fnins.2017.00255

Ni, H. C., Lin, H. Y., Chen, Y. L., Hung, J., Wu, C. T., Wu, Y. Y., … Huang, Y. Z. (2022). 5-day multi-session intermittent theta burst stimulation over bilateral posterior superior temporal sulci in adults with autism-a pilot study. *Biomedical Journal*, *45*(4), 696–707. doi: 10.1016/j.bj.2021.07.008

Oberman, L. M., Pascual-Leone, A., & Rotenberg, A. (2014). Modulation of corticospinal excitability by transcranial magnetic stimulation in children and adolescents with autism spectrum disorder. *Frontiers in Human Neuroscience*, *8*, 627. doi: 10.3389/fnhum.2014.00627

Pavlova, M. A., & Sokolov, A. A. (2022). Reading language of the eyes. *Neuroscience & Biobehavioral Reviews*, *140*, 104755. doi: 10.1016/j.neubiorev.2022.104755

Peled-Avron, L., Glasner, L., Gvirts, H. Z., & Shamay-Tsoory, S. G. (2019). The role of the inferior frontal gyrus in vicarious social touch: A transcranial direct current stimulation (tDCS) study. *Developmental Cognitive Neuroscience*, *35*, 115–121. doi: 10.1016/j.dcn.2018.04.010

Penuelas-Calvo, I., Sareen, A., Sevilla-Llewellyn-Jones, J., & Fernandez-Berrocal, P. (2019). The "Reading the Mind in the Eyes" test in autism-spectrum disorders comparison with healthy controls: A systematic review and meta-analysis. *Journal of Autism and Developmental Disorders*, *49*(3), 1048–1061. doi: 10.1007/s10803-018-3814-4

Rossi, S., Antal, A., Bestmann, S., Bikson, M., Brewer, C., Brockmoller, J., … basis of this article began with a Consensus Statement from the Ifcn Workshop on "Present, F. o. T. M. S. S. E. G. S. O. u. t. A. (2021). Safety and recommendations for TMS use in healthy subjects and patient

populations, with updates on training, ethical and regulatory issues: Expert guidelines. *Clinical Neurophysiology*, *132*(1), 269–306. doi: 10.1016/j.clinph.2020.10.003

Sandercock, R. K., Lamarche, E. M., Klinger, M. R., & Klinger, L. G. (2020). Assessing the convergence of self-report and informant measures for adults with autism spectrum disorder. *Autism*, *24*(8), 2256–2268. doi: 10.1177/1362361320942981

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: A meta-analysis of functional brain imaging studies. *Neuroscience & Biobehavioral Reviews*, *42*, 9–34. doi: 10.1016/j.neubiorev.2014.01.009

Sokhadze, E., Baruth, J., Tasman, A., Mansoor, M., Ramaswamy, R., Sears, L., … Casanova, M. F. (2010). Low-frequency repetitive transcranial magnetic stimulation (rTMS) affects event-related potential measures of novelty processing in autism. *Applied Psychophysiology and Biofeedback*, *35*(2), 147–161. doi: 10.1007/s10484-009-9121-2

Sokhadze, E. M., El-Baz, A., Baruth, J., Mathai, G., Sears, L., & Casanova, M. F. (2009). Effects of low frequency repetitive transcranial magnetic stimulation (rTMS) on gamma frequency oscillations and event-related potentials during processing of illusory figures in autism. *Journal of Autism and Developmental Disorders*, *39*(4), 619–634. doi: 10.1007/s10803-008-0662-7

Sokhadze, E. M., Lamina, E. V., Casanova, E. L., Kelly, D. P., Opris, I., Tasman, A., & Casanova, M. F. (2018). Exploratory study of rTMS neuromodulation effects on electrocortical functional measures of performance in an oddball test and behavioral symptoms in autism. *Frontiers in Systems Neuroscience*, *12*, 20. doi: 10.3389/fnsys.2018.00020

Sundby, K. K., Jana, S., & Aron, A. R. (2021). Double-blind disruption of right inferior frontal cortex with TMS reduces right frontal beta power for action stopping. *Journal of Neurophysiology*, *125*(1), 140–153. doi: 10.1152/jn.00459.2020

Tettamanti, M., Vaghi, M. M., Bara, B. G., Cappa, S. F., Enrici, I., & Adenzato, M. (2017). Effective connectivity gateways to the theory of mind network in processing communicative intention. *Neuroimage*, *155*, 169–176. doi: 10.1016/j.neuroimage.2017.04.050

Tsujii, T., Sakatani, K., Masuda, S., Akiyama, T., & Watanabe, S. (2011). Evaluating the roles of the inferior frontal gyrus and superior parietal lobule in deductive reasoning: An rTMS study. *Neuroimage*, *58*(2), 640–646. doi: 10.1016/j.neuroimage.2011.06.076

Udden, J., Folia, V., Forkstam, C., Ingvar, M., Fernandez, G., Overeem, S., … Petersson, K. M. (2008). The inferior frontal cortex in artificial syntax processing: An rTMS study. *Brain Research*, *1224*, 69–78. doi: 10.1016/j.brainres.2008.05.070

Upton, S., Brown, A. A., Golzy, M., Garland, E. L., & Froeliger, B. (2023). Right inferior frontal gyrus theta-burst stimulation reduces smoking behaviors and strengthens fronto-striatal-limbic resting-state functional connectivity: A randomized crossover trial. *Frontiers in Psychiatry*, *14*, 1166912. doi: 10.3389/fpsyt.2023.1166912

Vellante, M., Baron-Cohen, S., Melis, M., Marrone, M., Petretto, D. R., Masala, C., & Preti, A. (2013). The "Reading the Mind in the Eyes" test: Systematic review of psychometric properties and a validation study in Italy. *Cognitive Neuropsychiatry*, *18*(4), 326–354. doi: 10.1080/13546805.2012.721728

Villalobos, M. E., Mizuno, A., Dahl, B. C., Kemmotsu, N., & Muller, R. A. (2005). Reduced functional connectivity between V1 and inferior frontal cortex associated with visuomotor performance in autism. *Neuroimage*, *25*(3), 916–925. doi: 10.1016/j.neuroimage.2004.12.022

White, S. J., Coniston, D., Rogers, R., & Frith, U. (2011). Developing the frith-happe animations: A quick and objective test of theory of mind for adults with autism. *Autism Research*, *4*(2), 149–154. doi: 10.1002/aur.174

Wilson, A. C. (2021). Do animated triangles reveal a marked difficulty among autistic people with reading minds? *Autism*, *25*(5), 1175–1186. doi: 10.1177/1362361321989152

Winhuisen, L., Thiel, A., Schumacher, B., Kessler, J., Rudolf, J., Haupt, W. F., & Heiss, W. D. (2007). The right inferior frontal gyrus and poststroke aphasia: A follow-up investigation. *Stroke*, *38*(4), 1286–1292. doi: 10.1161/01.STR.0000259632.04324.6c

Yang, Y. C., Lu, L., Jeng, S. F., Tsao, P. N., Cheong, P. L., Li, Y. J., … Wu, Y. T. (2019). Multidimensional developments and free-play movement tracking in 30- to 36-month-old toddlers with autism spectrum disorder who were full term. *Physical Therapy*, *99*(11), 1535–1550. doi: 10.1093/ptj/pzz114

Zeidan, J., Fombonne, E., Scorah, J., Ibrahim, A., Durkin, M. S., Saxena, S., … Elsabbagh, M. (2022). Global prevalence of autism: A systematic review update. *Autism Research*, *15*(5), 778–790. doi: 10.1002/aur.2696

Zhao, H., Mao, X., Zhu, C., Zou, X., Peng, F., Yang, W., … Cui, R. (2021). GABAergic system dysfunction in autism Spectrum disorders. *Frontiers in Cell and Developmental Biology*, *9*, 781327. doi: 10.3389/fcell.2021.781327

https://doi.org/10.1017/S0033291724001387 Published online by Cambridge University Press