Med Discoveries
An open access journal of science and medicine

Article Type: Review Article
Volume 3, Issue 1
Received: Dec 18, 2023
Accepted: Jan 22, 2024
Published Online: Jan 29, 2024

Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (TDCS) in Autism Spectrum Disorder

Leonardo Massoni*

Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy.

***Corresponding Author:** Leonardo Massoni*

Email: lmassoni700@gmail.com

Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disease characterized by deficits in social communication and the presence of restricted, repetitive behaviors or interests, as well as difficulties in emotional regulation. To date, pharmacological approaches are essentially limited to some drugs, such as aripiprazole and risperidone. Drug responses are often partial. Neuromodulation therapies, including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (TDCS) are sometimes used for cognitive, social, behavioral and affective symptoms of ASD. In fact, by targeting specific brain regions, such as the dorsolateral prefrontal cortex (DLPFC), temporoparietal junction (TPJ) and the motor cortex, these therapies can improve the main symptoms of the disease. This work examines the role of TMS and TDCS in ASD. Even though new studies need to be implemented, they have proven to be promising and precise therapeutic strategies for ASD.

Keywords: ASD; TMS; TDCS; Sociability; Cognition; Emotional regulation.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by a complex and multifaceted neurobehavioral syndrome. At the current state of research, pharmacological strategies approved for ASD are risperidone and aripiprazole, especially for irritability and aggressive symptoms, while psychostimulants could be useful for attention-deficit/hyperactivity disorders [1,2].

Other promising therapeutic strategies for ASD are non-invasive brain stimulation (NIBS). NIBS is a therapeutic strategy aimed at modulating relevant brain networks, and it is a possible candidate for the treatment of individuals with neuropsychiatric conditions. It may play a role in understanding brain network pathophysiology by expanding on traditional recording techniques of spontaneous or evoked electroencephalographic or magnetoencephalographic activity. In fact, NIBS offers the opportunity to directly interact with brain functioning in a non-invasive, safe and painless way, with a good time resolution and relatively high spatial precision [3]. In addition, NIBS is employed both in healthy subjects to investigate brain mechanisms underlying cognition, social, behavioral and emotional processes, and in psychiatric conditions to regulate neuroplasticity. This could explain the NIBS rationale in neurodevelopmental diseases, where an alteration in brain plasticity is suspected [4].

Transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS) are neurostimulation techniques that can alterate cortical excitability by inducing neural activity. Particularly, suppression of cortical excitability is obtained through low frequency stimulation (less than 1 Hz), while enhancement of cortical activity is made via high stimulation frequency (5-20 Hz) [5]. Theta Burst stimulation (TBS) is a particular form of TMS consisting of the administration of repetitive stimuli to the motor cortex that, in turn, can produce robust, self-limited physiological effects on human cortex and has been implicated in long-term depression (LTD) and long-term potentiation (LTP) in human cortex [6]. Accordingly, by investigating the effect of a single session of TBS on a subsequent session of TBS carried out 24 hours later, meta plasticity, even in ASD, may be assessed [7].

Transcranial direct current stimulation (TDCS) is a neuromodulation technique where an electric current of low inten-

Citation: Massoni L. Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (TDCS) in Autism Spectrum Disorder. Med Discoveries. 2024; 3(1): 1107.

sity is injected into the brain through electrodes placed over the scalp [8]. When it arrives in the gray matter, this current can induce excitatory or inhibitory effects on neural excitability [9].

In the last few years, several studies have focused on the possible beneficial role of somatic therapies in neuropsychiatric disturbances [10]. Starting from the consideration that an abnormal balance between excitation and inhibition of neuron pathways could be at the basis of some ASD symptoms, such as repetitive behaviors, it has been proposed that somatic therapies, by usually targeting altered cortical excitability, may play a role in the treatment of this complex disease [10,11]. However, a recent work enhanced the potential of neuromodulation techniques in ASD, concluding that there is still insufficient evidence to recommend TMS and TDCS in current clinical practice [12].

This review analyses the existing literature about rTMS and TDCS employment in ASD and evaluates the possible advantages of their use as alternatives or in combination with pharmacological, psychological, and other somatic therapies, thus shedding new light on the neurophysiological mechanisms underlying this complex disease.

Transcranial magnetic stimulation (TMS) in ASD: It is known that individuals with ASD may report alterations in the gamma-frequency oscillations detectable at the electroencephalogram (EEG). As a result, TMS, which could entrain gamma modulation oscillation as well as regulation neuron circuitry, might have a rationale for mitigating these electrophysiological abnormalities in ASD and, consequently, improving some aspects of the disease [13]. Furthermore, it has been speculated that the alteration of specific genes involved in the disease is related to abnormal synaptic connections. This highlights the role of both genes and neuron plasticity in ASD [14].

We reported three works dealing with rTMS role in targeting neurobiological altered circuits in ASD [15-17] one addressing the physiological deregulation [18] and five showing the usefulness of the technique in improving clinical aspects of the disease [5,10,19-21].

In line with the central aspect of neuronal plasticity in ASD, Pedapati et al. (2016) compared 9 ASD individuals (M=7, F=2, age range=13-18 years) with 9 typically developed (TD) controls (M=5, F=4, age range=11-18 years) for the assessment of motor cortex plasticity by the use of low-intensity rTMS. The authors administered intermittent theta burst stimulation (iTBS) to the dominant motor cortex 1 (M1) of these individuals to compare the amplitude of motor evoked potentials (MEP) of a target muscle and found that the MEP amplitude in the ASD group at 20 minutes following iTBS was significantly lower than the one reported in the TD. Consequently, low intensity rTMS could be a potential physiological biomarker of cortical plasticity in ASD young people [17].

To analyze the anatomical impact of these abnormalities on clinical outcome and, consequently, TMS role in improving symptoms of ASD, a work by Ni et al. (2021) examined the effects of intermittent TBS (iTBS), a particular form of rTMS, on the bilateral posterior superior temporal sulcus (pSTS) on two groups of ASD individuals: those receiving iTBS then sham (n=6, M=5, F=1) and those administered with sham and then iTBS (n=7, M=6, F=1). Wisconsin Card Sorting Test (WCST) was used to evaluate cognitive flexibility, while the Autism Spectrum Quotient (AQ) and the self-rate and parent-rate were used for clinical outcomes. Results showed that multi-session iTBS over the bilateral pSTS had good effects on parent-rated autistic symptoms in adults with ASD whereas iTBS impact on cognitive flexibility was milder [15].

Another promising brain region to be targeted by high-frequency rTMS (HF-rTMS) in ASD is the left parietal cortex. Yang et al. (2019) recruited eleven low-functioning ASD children (age range=3-12 years) who underwent two separate HF-rTMS treatment courses and were assessed through the Verbal Behavior Assessment Scale (VerBAS), the Autism Treatment Evaluation Checklist (ATEC) and daily treatment logbooks completed by parents for linguistic, social, sensory and behavioral abilities. Encouraging improvements in language, social, cognitive and imitation aspects of the participants were reported both by the authors and the caregivers [16].

Also, the dorsolateral prefrontal cortex (DLPFC) is a cortical area under investigation for rTMS employment in clinical symptoms of ASD. Enticott et al. (2014) examined 28 ASD adults who were treated with 2 weeks of daily weekday treatment of active (n=15, M=13, F=2, age range=18-59 years) or sham (n=13, M=10, F=3, age range= 19-54 years) deep rTMS. Participants were assessed through the Ritvo Autism-Asperger Diagnostic Scale (RAADS), Autism Spectrum Quotient (AQ), Interpersonal Reactivity Index (IRI), and experimental measures of mentalizing (reading the mind in the eyes test and animations metalizing test) at three times: immediately before the first deep rTMS application, immediately after the last deep rTMS and one month after the last deep rTMS. In the group receiving active deep rTMS a reduction in socially related impairment and socially related anxiety was noted [22].

With the aim of investigating rTMS employment in autonomic system deregulation in ASD, a study carried out in ASD children (n=33, M=28, F=5, mean age=12,88 years), who were administered TMS for 12 weeks and had their autonomic variables analyzed through electrocardiogram and skin conductance records, pointed out a positive effect of TMS on autonomic activity in both low and high functioning ASD. It was also demonstrated that behavioral evaluation outcomes correlate with autonomic changes during the 12-session rTMS course in children with ASD [18].

Regarding rTMS application for behavioral symptoms of ASD, a study analyzed 4 ASD (age range=11-17 years) participants who were admitted to high frequency rTMS over the inferior parietal lobe (IPL) and assessed through the autism diagnostic observation schedule (ADOS), the Social Responsiveness Scale (SRS-2), the Expressive Vocabulary Test (EVT) and the D-KEFS Verbal Fluency. At follow-up, it was noted that measures of verbal fluency and social responsiveness had improved. Additionally, the SRS-2 completed by the parents demonstrated a modest improvement in social responsiveness that was sustained after 3 months of follow-up. In summary, it was emphasized that rTMS can prove to be a valuable tool for enhancing behavioral measures in ASD, and it was suggested that such enhancements may prove beneficial even months after treatment [5].

Besides, rTMS was shown to improve ASD executive functions related to self-monitoring behaviors and the possibility of applying corrective actions. Specifically, when administered at low frequencies in ASD individuals, TMS has proven safe and useful to ameliorate multiple patient-oriented outcomes [20]. In line with these findings, Kang et al. (2019) analyzed 32 children (M=26, F=6, mean age=7,8 years) with low functioning ASD. Particularly, 16 of them received rTMS, while the other 16

were enrolled in the waitlist group. Cognitive preparedness was assessed through the Peak alpha frequency (PAF), a supposed neural marker of cognitive function in ASD; brain functional connectivity in ASD was specifically measured through coherence; and ASD behaviors through the Autism Behavior Checklist (ABC) score. Results showed that the rTMS group presented significant improvements in behavioral and functional outcomes compared to the waitlist group, thus enhancing the role of TMS in behavioral and functional outcomes in ASD [10]. Similar results came from a study examining the effects of rTMS administered to the dorsolateral prefrontal cortex (DLPFC) in 40 ASD individuals (M=28, F=12, mean age=16-35 years). Two groups were formed: one made up of individuals receiving real rTMS (n=20), while the second group was administered sham rTMS (n=20). Participants were assessed through the Vineland Adaptive Behavior Scale-II (VABS-II) for daily functioning, the Mini International Neuropsychiatric Interview (MINI) (≥18 years) or MINI for Children and Adolescents (MINI-KID) for co-occurring psychiatric disorders, and the Keel Transcranial Magnetic Stimulation Adult Safety Screen for potential safety problems related to TMS. Even if not significant, encouraging findings were found for the improvement of executive functions in ASD individuals with more severe adaptive functioning in the group receiving active rTMS compared to the sham group [24].

Moreover, to examine emotion recognition in ASD, a work carried out on individuals with autism-like traits investigated the role of TBS in emotion recognition improvement. Two groups were formed: the first was made by individuals receiving iTBS (n=12, M=6, F=6), the other by controls (n=15, M=6, F=9). Participants were analyzed for clinical outcomes through the Montreal Cognitive Assessment Test (MoCA), the Hamilton Depression Rating Scale (HAMD), the Hamilton Anxiety Rating Scale (HAMA), the Stroop test (color, word, and interference tests), the Trail Making Test (A and B), and the Digit Span assessment (forward, backward), while for neurophysiological aspects through eye tracking data and functional magnetic resonance imaging. Curiously, children who underwent TBS showed increased accuracy in emotion recognition. Specifically, iTBS over the right posterior superior temporal sulcus (rpSTS), could improve emotion perception in autism-like traits (ALT) individuals by modulating the associated neural network [19].

Given its role in emotional regulation, TMS has also been proposed for depressive aspects of ASD, revealing it as a well-tolerated treatment. The authors enrolled 10 individuals with moderate depression and autism symptom burden (M=9, F=1, age range=23-29 years), diagnosed through the Diagnostic and Statistical Manual of Mental Disorders-5th Edition (DSM-5). In addition, participants were evaluated through the Hamilton Rating Scale for Depression-17 (HAM-D17) for depressive symptoms and the self-reported Social Responsiveness Scale, Second Edition—Adult (SRS-2) and the Ritvo Autism Asperger Diagnostic Scale—Revised (RAADS-R), as well as informant-based questionnaires (the Aberrant Behavior Checklist (ABC) and the Repetitive Behavior Scale—Revised (RBS-R) for ASD symptoms. They were administered 25 sessions of rTMS applied to the left dorsolateral prefrontal cortex. Results showed an improvement in depressive symptoms of ASD and a potential effect in the behavioral aspects of the disease [21].

Transcranial direct current stimulation (TDCS) in ASD: The rationale of TDCS in ASD can be supported by evidence of its role in modulating motor and cognitive function in the disease. A study enrolled 26 ASD children with 26 typically developed controls (M=22, F=4, mean age=6,64±1,86 years). In addition, ASD individuals were divided into two groups based on the fact that they received or did not receive TDCS over the DLPFC: experimental group (n=13, M=11, F=2, mean age=6,52±1,76), which was administered TDCS, and the control group, which did not receive the treatment (n=13, M=11, F=2, mean age=6,38±1,79). All groups underwent evaluation through the Autism Behavior Checklist (ABC) and EEG microstates were calculated. There were significant differences in EEG microstate and ABC scale between pre- and post-TDCS in the experimental group [24].

In line with these findings, the effect of TDCS on modulating brain functional connectivity in ASD was studied. The authors examined the EEG of ASD children before and after real (n=18, M=11, F=7, mean age=6.5±1.4 years) and sham (n=18, M=11, F=7, mean age=6.7±1.3 years) tDCS. To evaluate TDCS modulation on the brain network, temporal flexibility and frequency network changes were recorded. It was found that local and global brain network dynamics could be influenced by TDCS, thus suggesting stimulation-induced differences in the manifestation of network reconfiguration [11].

When targeting a specific brain region, encouraging results also came from Qiu et al. (2021), who investigated TDCS at the DLPFC in ASD children. The authors enrolled 20 ASD participants (M=14, F=6, age range=24-79 months) who received sham TDCS and 20 who were administered real TDCS (M=16, F=4, mean age=30-81). Participants were evaluated through the CARS, ABC, RBS-R and the Repetitive Behavior Scale-Revised (RBS-R) scales. It was pointed that real TDCS can significantly improve scores in CARS and CSHQ compared to sham TDCS and does not have any significant side effects [25]. Similarly, a study analyzed the role of TDCS administration to the left DLFC in 10 ASD male individuals (mean age=6,60±0,84 years) who were evaluated through the the ATEC social subscale for social behaviors and brain concentrations of some metabolites such as N-acetylaspartate (NAA), glutamine combine glutamate (Glx), choline (Cho), myoinositol (mI), creatine (Cr) as biological indices before and after treatment. The results showed a significant decrease in the ATEC social subscale scores between pretreatment and immediately post treatment, significant increases in N-acetylaspartate/creatine (Cr) and myoinositol (mI)/Cr concentrations, and a decrease in choline (Cho)/Cr concentrations in the left DLPFC and locus coeruleus after TDCS treatment. These findings could support the hypothesis that changes in the glial activity and synaptogenesis of ASD individuals are the basis of TDCS beneficial effects [26].

A study examined the effect of TDCS on 12 high-functioning ASD individuals analyzed for working memory (WM) tasks through the administration of spatial span, backward digit span, spatial n-back and letter n-back tests, also after taking the Brief Test of Attention (ref). Left anodal/right cathodal stimulation, right anodal/left cathodal stimulation, or sham stimulation were administered to each participant in a randomized order on three different days. It was found that bifrontal TDCS administered to high-functioning ASD people involved in WM tasks could improve performance; these beneficial effects could extend also to an untrained task completed shortly after stimulation [27].

Intriguingly, it has been observed that TDCS could be a helpful tool for the rehabilitation of ASD children. Kang et al. (2018) enrolled 13 ASD individuals (M=11, F=2, mean age=6,5±1,7 years) who received TDCS over the DLPFC and 13 ASD controls (M=11, F=2, mean age=6,5±1,7 years) who waited to be admin-

istered the treatment as controls. The complexity of the EEG series was assessed through the maximum entropy ratio (MER) method. Results showed that the MER value significantly increased after TDCS thus presenting the treatment as valid for the rehabilitation of ASD children [28].

Moreover, literature reports TDCS role in high functioning ASD (HF-ASD) children. Eight children with HF-ASD were administered TDCS over the left dorsolateral prefrontal cortex for 15 minutes. Executive functions and behavioral dysexecutive syndrome were evaluated before and after the treatment, respectively, through the stroop test, trail-making tests A and B, Modified Wisconsin Card Sorting Test, Verbal fluency test for the former, and the Behavioral Dysexecutive Syndrome Inventory and the Repetitive and Restricted Behaviour scale for the latter. Results showed that TDCS could imporve initiation and cognitive flexibility in these patients, as well as hypoactivity, repetitive and restricted behaviors [29].

Also, social impairment could be mitigated by TDCS administration over the DLPFC. Han et al. (2023) enrolled ASD individuals receiving active (N=34, M=28, F=5) or sham (N=33, M=28, F=5) TDCS and a control group not receiving the treatment (N=30, M=28, F=2). TDCS stimulation was administered to the experimental group for 10 days with concurrent computerized cognitive remediation training. The Social Responsiveness Scale-2nd Edition (SRS-2) was used to detect changes in overall social functioning, social communication, and restricted, repetitive behaviors (RRB). Only the group receiving active tDCS reported significant improvements in RRB when compared to the placebo group [30].

What's more, the modulation of DLPFC through TDCS has been implicated in emotional regulation and behavioral aspects of ASD. It was investigated the effect of TDCS administration over the DLPFC in 32 ASD individuals (mean age=10,16±1,93 years, age range 7-12 years) evaluated for autism symptom severity, theory of mind, emotion regulation strategies, and emotional-behavioral functions and divided into two groups: one treated with active TDCS (n=17), the other with sham TDCS (n=15). Participants were administered 10 sessions of active or sham TDCS. At baseline, immediately after the intervention and 1 month after the intervention, the authors assessed the following aspects: autism symptom severity, theory of mind, emotion regulation strategies, and emotional-behavioral functioning. It was noted that ASD individuals had their symptom severity improved as well as specific domains of theory of mind, and emotion regulation, thus leading to speculation that treatment for ASD could target core mechanisms underlying socio-cognitive-emotional deficits in autistic children [31].

Social cognitive functions in ASD seem to be linked to another brain area: the temporoparietal junction (TPJ). It has been reported that TDCS on the TPJ may improve social cognitive functions in ASD, such as imitation-inhibition and perspective taking. Nobusako et al. (2017) carried out a study in 30 healthy individuals (M=15, F=15, mean age 21,37±1,22 years), who were divided into 3 groups: a control group (n=10), which did not receive TDCS, and two other groups receiving tDCS on TPJ (n=10) or inferior frontal cortex (IFC, n=10). Participants were examined for behavioral tasks through an imitation-inhibition task and a visual perspective-taking task and completed the AQ questionnaire for autistic traits. It was found that both the TPJ and IFC may play a role in behavioral tasks [32]. To analyze the effect of TDCS on the primary motor cortex, 18 ASD children (age range=6-14 years) were administered TDCS and selective motor training. Raven's Colored Progressive Matrices were used to assess participants' general intelligence, while the Movement Assessment Battery for Children-2 examined children's fine and gross motor skills. It was suggested that motor skills for ASD children could be improved by TDCS [33]. Accordingly, Wilson et al. (2018) examined the effectiveness of social skills' intervention in 6 ASD people (M=4, F=2, age range=18-58 years) who underwent TDCS over the right temporoparietal junction (rTPJ). Tests for verbal fluency (VF) and social skills (TASSK-M), were performed, whereas autistic traits were quantified through the AQ test. The authors concluded that TDCS could be a promising therapeutic strategy for improving skills of emotion and verbal fluency in ASD [34].

Moreover, a work investigated 53 ASD individuals (M=23, F=30, mean age=30) before and after the administration of high-definition TDCS, a particular type of TDCs that is directed to a specific brain region. Participants were evaluated through the AQ and the SRS-2 for symptoms of autism and social cognition. People with higher AQ scores showed a reduced pre-stimulation mental state attribution. These findings contributed to an understanding of how such trait-level variation might interact with the effects of tDCS as well as the potential roles of the rTPJ in both attention and social cognition and how autism-relevant traits might influence TPJ function [35]. Some years later, Parmar et al. (2021) studied the effects of active and sham (placebo) anodal high-definition transcranial direct current stimulation (aHD-tDCS) over the right vlPFC in adolescents and young ASD adults. Four indices of cognitive flexibility (behavioral, electrophysiological, cognitive, and clinical), as well as safety and tolerability of aHD-TDCS, were investigated. aHD-TDCS over the right vlPFC, even when safe and well tolerated, was not effective for cognitive flexibility difficulties in ASD [36].

Discussion

In this review, we reported promising effects of both rTMS and TDCS in ASD. Specifically, we showed that rTMS could play an important role in cognitive [15,16], behavioral [5,10], and social [22] deficits of the disease, as well as in depressive symptoms [21] and emotional deregulation [19]. Interestingly, rTMS seems to improve behavioral aspects of ASD by targeting autonomic system deregulation occurring in the disease [18]. Starting from the consideration that the DLPFC is an important region for cognitive functions in ASD, we reported promising findings for rTMS administered to the DLPFC [23] and the pSTS [15] for executive function improvements in ASD. Also, TDCS has been suggested as a good therapeutic strategy for core symptoms of ASD, including emotional deregulation, hyperactivity, irritability, and repetitive behaviors [25,30], as well as cognitive performances, executive functions [27], initiation, and cognitive flexibility in high functioning ASD [29]. Intriguingly, TDCS has allowed us to better clarify the role of specific brain regions in some autistic symptoms, such as the DLPFC for RRBs [30], emotional regulation [31], social cognition and verbal fluency [34], the TPJ for social cognitive functions [32], and the primary motor cortex for motor skills [33]. The TPJ has been implicated in attention switching and memory. In ASD, it has been suggested that an atypical function of this area is associated with a reciprocal social impairment [37]. Other recent works presented encouraging findings on non-invasive brain stimulation (NIBS) techniques employment in ASD symptoms such as repetitive behavior, sociability, and some executive and cognitive functions [8,12,38]. Accordingly, it has been recently reported that some biological factors, such as the brain-derived neurotrophic

factor (BDNF), could be used as biomarkers to evaluate the effectiveness of non-invasive brain stimulation (NIBS) in ASD [39].

Conclusion

Globally, despite the limited literature available, some interesting evidence on the efficacy of TDCS and rTMS in ASD was highlighted. However, as previously noted [12], larger, randomized controlled trials incorporating neuroimaging and neuromodulation therapies to develop predictive biomarkers of treatment response and optimize treatment parameters could be advisable. In fact, given that pharmacological approaches to ASD may not always be successful [40], NIBS could be a promising potentiating or augmentation therapeutic strategy for ASD, and it could be speculated that NIBS together with pharmacological approaches could play a synergistic role in the core symptoms of the disease.

References

1. Hirota T, King BH. Autism Spectrum Disorder: A review. JAMA. 2023; 329(2): 157-168. doi: 10.1001/jama.2022.23661. PMID: 36625807.

2. Salazar de Pablo G, Pastor Jordá C, Vaquerizo-Serrano J, Moreno C, Cabras A, et al. Systematic review and meta-analysis: Efficacy of pharmacological interventions for irritability and emotional dysregulation in autism spectrum disorder and predictors of response. J Am Acad Child Adolesc Psychiatry. 2023; 62(2): 151-168. doi: 10.1016/j.jaac.2022.03.033. Epub 2022 Apr 22. PMID: 35470032.

3. Menardi A, Rossi S, Koch G, Hampel H, Vergallo A, et al. Toward noninvasive brain stimulation 2.0 in Alzheimer's disease. Ageing Res Rev. 2022; 75: 101555. doi: 10.1016/j.arr.2021.101555. Epub 2021 Dec 30. PMID: 34973457; PMCID: PMC8858588.

4. Finisguerra A, Borgatti R, Urgesi C. Non-invasive Brain Stimulation for the rehabilitation of children and adolescents with neurodevelopmental disorders: A systematic review. Front Psychol. 2019; 10: 135. doi: 10.3389/fpsyg.2019.00135. PMID: 30787895; PMCID: PMC6373438.

5. Assadi M, Dave J, Leone P, Redjal N, Curtin A. Enhancement of behavioral and linguistic outcome measures in autism spectrum disorder through neuro-navigated transcranial magnetic stimulation: A pilot study. J Clin Neurosci. 2020; 74: 151-154. doi: 10.1016/j.jocn.2020.02.005. Epub 2020 Feb 20. PMID: 32089385.

6. Huang YZ, Edwards MJ, Rounis E, Bhatia KP, Rothwell JC. Theta burst stimulation of the human motor cortex. Neuron. 2005; 45(2): 201-6. doi: 10.1016/j.neuron.2004.12.033. PMID: 15664172.

7. Oberman L, Ifert-Miller F, Najib U, Bashir S, Woollacott I, et al. Transcranial magnetic stimulation provides means to assess cortical plasticity and excitability in humans with fragile x syndrome and autism spectrum disorder. Front Synaptic Neurosci. 2010; 2: 26. doi: 10.3389/fnsyn.2010.00026. PMID: 21423512; PMCID: PMC3059673.

8. Osório AAC, Brunoni AR. Transcranial direct current stimulation in children with autism spectrum disorder: a systematic scoping review. Dev Med Child Neurol. 2019; 61(3): 298-304. doi: 10.1111/dmcn.14104. Epub 2018 Nov 19. PMID: 30451290.

9. Yamada Y, Sumiyoshi T. Neurobiological mechanisms of transcranial direct current stimulation for psychiatric disorders; Neurophysiological, chemical, and anatomical considerations. Front Hum Neurosci. 2021; 15: 631838. doi: 10.3389/fnhum.2021.631838. PMID: 33613218; PMCID: PMC7890188.

10. Kang JN, Song JJ, Casanova MF, Sokhadze EM, Li XL. Effects of repetitive Transcranial Magnetic Stimulation on children with low-function autism. CNS Neurosci Ther. 2019; 25(11): 1254-1261. doi: 10.1111/cns.13150. Epub 2019 Jun 22. PMID: 31228356; PMCID: PMC6834922.

11. Zhou T, Kang J, Li Z, Chen H, Li X. Transcranial direct current stimulation modulates brain functional connectivity in autism. Neuroimage Clin. 2020; 28: 102500. doi: 10.1016/j.nicl.2020.102500. Epub 2020 Nov 19. PMID: 33395990; PMCID: PMC7695891.

12. Oberman LM, Francis SM, Lisanby SH. The use of noninvasive brain stimulation techniques in autism spectrum disorder. Autism Res. 2023; 10. 1002/aur.3041. Epub ahead of print. PMID: 37873560.

13. Kayarian FB, Jannati A, Rotenberg A, Santarnecchi E. Targeting Gamma-Related pathophysiology in autism spectrum disorder using Transcranial Electrical Stimulation: Opportunities and challenges. Autism Res. 2020; 13(7): 1051-1071. doi: 10.1002/aur.2312. Epub 2020 May 28. PMID: 32468731; PMCID: PMC7387209.

14. Belmonte MK, Allen G, Beckel-Mitchener A, Boulanger LM, Carper RA, et al. Autism and abnormal development of brain connectivity. J Neurosci. 2004; 24(42): 9228-31. doi: 10.1523/JNEUROSCI.3340-04.2004. PMID: 15496656; PMCID: PMC6730085.

15. Ni HC, Lin HY, Chen YL, Hung J, Wu CT, et al. 5-day multi-session intermittent theta burst stimulation over bilateral posterior superior temporal sulci in adults with autism-a pilot study. Biomed J. 2022; 45(4): 696-707. doi: 10.1016/j.bj.2021.07.008. Epub 2021 Aug 3. PMID: 34358713; PMCID: PMC9486126.

16. Yang Y, Wang H, Xue Q, Huang Z, Wang Y. High-frequency repetitive Transcranial Magnetic Stimulation applied to the Parietal Cortex for low-functioning children with autism spectrum disorder: A Case Series. Front Psychiatry. 2019; 10: 293. doi: 10.3389/fpsyt.2019.00293. PMID: 31143132; PMCID: PMC6520602.

17. Pedapati EV, Gilbert DL, Erickson CA, Horn PS, Shaffer RC, et al. Abnormal cortical plasticity in youth with autism spectrum disorder: A Transcranial Magnetic Stimulation case-control pilot study. J Child Adolesc Psychopharmacol. 2016; 26(7): 625-31. doi: 10.1089/cap.2015.0183. Epub 2016 Mar 23. PMID: 27007257; PMCID: PMC5035833.

18. Wang Y, Hensley MK, Tasman A, Sears L, Casanova MF, et al. Heart rate variability and skin Conductance during repetitive TMS course in children with autism. Appl Psychophysiol Biofeedback. 2016; 41(1): 47-60. doi: 10.1007/s10484-015-9311-z. PMID: 26341093.

19. Liu P, Xiao G, He K, Zhang L, Wu X, et al. Increased Accuracy of Emotion Recognition in Individuals with Autism-Like Traits after Five Days of Magnetic Stimulations. Neural Plast. 2020; 2020: 9857987. doi: 10.1155/2020/9857987. PMID: 32714385; PMCID: PMC7355343.

20. Casanova MF, Sokhadze EM, Casanova EL, Li X. Transcranial Magnetic Stimulation in Autism Spectrum Disorders: Neuropathological underpinnings and clinical correlations. Semin Pediatr Neurol. 2020; 35: 100832. doi: 10.1016/j.spen.2020.100832. Epub 2020 Jun 24. PMID: 32892959; PMCID: PMC7477302.

21. Gwynette MF, Lowe DW, Henneberry EA, Sahlem GL, Wiley MG, et al. Treatment of adults with autism and Major Depressive Disorder using Transcranial Magnetic Stimulation: An open label pilot study. Autism Res. 2020; 13(3): 346-351. doi: 10.1002/aur.2266. Epub 2020 Jan 15. PMID: 31944611; PMCID: PMC10150802.

22. Enticott PG, Fitzgibbon BM, Kennedy HA, Arnold SL, Elliot D, et

al. A double-blind, randomized trial of deep repetitive transcranial magnetic stimulation (rTMS) for autism spectrum disorder. Brain Stimulation. 2014; 7(2): 206-211.

23. Ameis SH, Blumberger DM, Croarkin PE, Mabbott DJ, Lai MC, et al. Treatment of Executive Function Deficits in autism spectrum disorder with repetitive transcranial magnetic stimulation: A double-blind, sham-controlled, pilot trial. Brain Stimul. 2020; 13(3): 539-547. doi: 10.1016/j.brs.2020.01.007. Epub 2020 Jan 15. PMID: 32289673; PMCID: PMC8129776.

24. Kang J, Fan X, Zhong Y, Casanova MF, Sokhadze EM, et al. Transcranial Direct Current Stimulation modulates EEG microstates in low-functioning autism: A pilot study. Bioengineering (Basel). 2023; 10(1): 98. doi: 10.3390/bioengineering10010098. PMID: 36671670; PMCID: PMC9855011.

25. Qiu J, Kong X, Li J, Yang J, Huang Y, et al. Transcranial Direct Current Stimulation (tDCS) over the Left Dorsal Lateral Prefrontal Cortex in children with autism spectrum disorder (ASD). Neural Plast. 2021; 2021: 6627507. doi: 10.1155/2021/6627507. PMID: 34257640; PMCID: PMC8245257.

26. Auvichayapat N, Patjanasoontorn N, Phuttharak W, Suphakunpinyo C, Keeratitanont K, et al. Brain metabolite changes after anodal Transcranial Direct Current Stimulation in Autism Spectrum Disorder. Front Mol Neurosci. 2020; 13: 70. doi: 10.3389/fnmol.2020.00070. PMID: 32581703; PMCID: PMC7287211.

27. van Steenburgh JJ, Varvaris M, Schretlen DJ, Vannorsdall TD, Gordon B. Balanced bifrontal transcranial direct current stimulation enhances working memory in adults with high-functioning autism: a sham-controlled crossover study. Mol Autism. 2017; 8: 40. doi: 10.1186/s13229-017-0152-x. PMID: 28775825; PMCID: PMC5534041.

28. Kang J, Cai E, Han J, Tong Z, Li X, et al. Transcranial direct current stimulation (tDCS) can modulate EEG complexity of children with autism spectrum disorder. Front Neurosci. 2018; 12: 201. doi: 10.3389/fnins.2018.00201. PMID: 29713261; PMCID: PMC5911939.

29. Rothärmel M, Moulier V, Vasse M, Isaac C, Faerber M, et al. A prospective open-label pilot study of Transcranial Direct Current Stimulation in high-functioning autistic patients with a dysexecutive syndrome. Neuropsychobiology. 2019; 78(4): 189-199. doi: 10.1159/000501025. Epub 2019 Jul 2. PMID: 31266030.

30. Han YM, Chan MM, Shea CK, Mo FY, Yiu KW, et al. Effects of prefrontal transcranial direct current stimulation on social functioning in autism spectrum disorder: A randomized clinical trial. Autism. 2023; 27(8): 2465-2482. doi: 10.1177/13623613231169547. Epub 2023 May 8. PMID: 37151094.

31. Zemestani M, Hoseinpanahi O, Salehinejad MA, Nitsche MA. The impact of prefrontal transcranial direct current stimulation (tDCS) on theory of mind, emotion regulation and emotional-behavioral functions in children with autism disorder: A randomized, sham-controlled, and parallel-group study. Autism Res. 2022; 15(10): 1985-2003. doi: 10.1002/aur.2803. Epub 2022 Sep 7. PMID: 36069668.

32. Nobusako S, Nishi Y, Shuto T, Asano D, Osumi M. Transcranial Direct Current Stimulation of the Temporoparietal Junction and Inferior Frontal Cortex improves Imitation-Inhibition and Perspective-Taking with no effect on the Autism-Spectrum Quotient Score. Front Behav Neurosci. 2017; 11: 84. doi: 10.3389/fnbeh.2017.00084. PMID: 28536512; PMCID: PMC5422472.

33. Mahmoodifar E, Sotoodeh MS. Combined Transcranial Direct Current Stimulation and Selective Motor Training enhances balance in children with autism spectrum disorder. Percept Mot Skills. 2020; 127(1): 113-125. doi: 10.1177/0031512519888072. Epub 2019 Nov 19. PMID: 31744385.

34. Esse Wilson J, Trumbo MC, Wilson JK, Tesche CD. Transcranial direct current stimulation (tDCS) over right temporoparietal junction (rTPJ) for social cognition and social skills in adults with autism spectrum disorder (ASD). J Neural Transm (Vienna). 2018; 125(12): 1857-1866. doi: 10.1007/s00702-018-1938-5. Epub 2018 Oct 19. PMID: 30341695.

35. Donaldson PH, Kirkovski M, Rinehart NJ, Enticott PG. Autism-relevant traits interact with temporoparietal junction stimulation effects on social cognition: a high-definition transcranial direct current stimulation and electroencephalography study. Eur J Neurosci. 2018; 47(6): 669-681. doi: 10.1111/ejn.13675. Epub 2017 Sep 27. PMID: 28960573.

36. Parmar D, Enticott PG, Albein-Urios N. Anodal HD-tDCS for cognitive inflexibility in autism spectrum disorder: A pilot study. Brain Stimul. 2021; 14(5): 1298-1300. doi: 10.1016/j.brs.2021.08.020. Epub 2021 Aug 24. PMID: 34450360.

37. Lombardo MV, Chakrabarti B, Bullmore ET; MRC AIMS Consortium; Baron-Cohen S. Specialization of right temporo-parietal junction for mentalizing and its relation to social impairments in autism. Neuroimage. 2011; 56(3): 1832-8. doi: 10.1016/j.neuroimage.2011.02.067. Epub 2011 Feb 26. PMID: 21356316.

38. Khaleghi A, Zarafshan H, Vand SR, Mohammadi MR. Effects of Non-invasive Neurostimulation on Autism Spectrum Disorder: A systematic review. Clin Psychopharmacol Neurosci. 2020; 18(4): 527-552. doi: 10.9758/cpn.2020.18.4.527. PMID: 33124586; PMCID: PMC7609207.

39. Robinson-Agramonte MLA, Michalski B, Fernández LG, Vidal-Martinez B, Cuesta HV, et al. Effect of non-invasive brain stimulation on behavior and serum brain-derived neurotrophic factor and insulin-like growth factor-1 levels in autistic patients. Drug Dev Res. 2021; 82(5): 716-723. doi: 10.1002/ddr.21808. Epub 2021 Mar 18. PMID: 33734467.

40. Noda Y, Fujii K, Mimura Y, Taniguchi K, Nakajima S, et al. A case series of intermittent Theta Burst Stimulation treatment for depressive symptoms in individuals with Autistic Spectrum Disorder: Real world TMS study in the Tokyo Metropolitan Area. J Pers Med. 2023; 13(1): 145. doi: 10.3390/jpm13010145. PMID: 36675806; PMCID: PMC9867406.