American Journal on Intellectual and Developmental Disabilities

Combined transcranial direct current stimulation with sensory-based treatments in autism: Preliminary report

--Manuscript Draft--

Manuscript Number:	AJIDD-D-24-00004R1
Article Type:	Research Report
Keywords:	autism spectrum condition (ASC); combined intervention; transcranial direct current stimulation (tDCS); sensory-based treatments; the prefrontal cortex
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Manuscript Region of Origin:	TAIWAN
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Combined transcranial direct current stimulation with sensory-based treatments in autism: Preliminary report

Abstract: This study investigated the effects of SBT combined with active transcranial direct current stimulation (tDCS) of the left prefrontal cortex (SBT+AtDCS), and SBT combined with sham tDCS (SBT+StDCS) in autism spectrum condition (ASC). Eleven ASC children were randomly assigned to receive either SBT+AtDCS or SBT+StDCS for ten sessions over two weeks. All children exhibited significant improvement in their ability to regulate and respond to sensory stimuli after treatment. The SBT+AtDCS group showed significant reductions in autism severity and behavioral difficulties compared to SBT+StDCS group. This preliminary report is the first to suggest that SBT combined with active tDCS may alleviate symptoms associated with ASC. Future research with a larger sample, neural measures, and a longitudinal design is required for validation.

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1. Introduction

Autism spectrum condition (ASC) is a heterogeneous disorder characterized by lifelong social communication difficulties, the presence of restricted, repetitive patterns of behaviors and interests, and atypical responsiveness to sensory stimuli (American Psychiatric Association, 2013). While these core features define the condition, ASC manifests in a wide range of clinical phenotypes, leading to diverse treatment needs. Therefore, developing therapeutic approaches that effectively address this heterogeneity should be prioritized in clinical research and practice.

Recent advances in neuroscience suggest that the symptoms of ASC may be linked to an imbalance in excitation and inhibition (E-I) within critical brain regions involved in social cognition, sensory processing, and cognitive control (Robertson & Baron-Cohen, 2017; Uzunova, Pallanti, & Hollander, 2016). Consequently, there is growing interest in advanced therapeutic approaches targeting these specific brain regions (Sousa, Martins, Castelo-Branco, & Goncalves, 2022; Uzunova et al., 2016). Transcranial direct current stimulation (tDCS), a non-invasive neuromodulatory technique, modulates cortical excitability and neuronal activity via a low-intensity direct current (Lefaucheur et al., 2017; Nitsche & Paulus, 2000; Priori et al., 1998). The effects of local stimulation can influence distant brain regions through network-level changes, ultimately leading to the reorganization of dysfunctional neural circuits (Palm et al., 2016). The prefrontal cortex (PFC) has long been implicated in top-down control of behavior (Miller & Cohen, 2001) and altered frontal functioning is thought to be a potential mechanism underlying the pathophysiology of ASC (Just, Keller, Malave, Kana, & Varma, 2012; Osorio & Brunoni, 2019). Accordingly, targeting the PFC, particularly in the left hemisphere, might be critical in alleviating ASC symptoms (Finisguerra, Borgatti, & Urgesi, 2019). Previous studies have found that anodal stimulation over the left PFC reduces ASC symptom severity (Gomez et al., 2017), improves verbal fluency (Rotharmel et al., 2019; Schneider & Hopp, 2011), enhances sensory awareness, and alleviates social and behavioral difficulties (Amatachaya et al., 2014; Amatachaya et al., 2015; Gomez et al., 2017; Hadoush, Nazzal, Almasri, Khalil, & Alafeef, 2020). A recent meta-analysis further demonstrated that tDCS can significantly improve socializing behaviors, health status, and behavioral difficulties in individuals with ASC (Garcia-Gonzalez et al., 2021). However, while tDCS shows promise, it is increasingly recognized not as a stand-alone treatment but as a complementary approach that may enhance the efficacy of other therapeutic interventions. For example, in the treatment of depression, tDCS has been used in conjunction with cognitive-behavioral therapy to facilitate neuroplasticity and support the reorganization of neural circuits involved in mood regulation (Aust et al., 2022). This suggests that tDCS may enhance the efficacy of other treatments by creating a neural environment conducive to therapeutic change.

Sensory-based treatments (SBT) are clinical interventions aimed at improving sensory and behavioral responsiveness in children with neurodevelopmental and behavioral disorders through sensory integration strategies (Ayres, 1972). Traditionally, occupational therapists create individually tailored play-based activities that incorporate specialized therapeutic modalities to provide varying levels of sensory experience and challenge (Case-Smith, Weaver, & Fristad, 2015; May-Benson & Koomar, 2010; Schoen et al., 2019). Although SBT is widely used in clinical practice and has been shown to be helpful for individuals with ASC (Case-Smith et al., 2015; Koomar & Bundy, 2002; Parham et al., 2007), much of the available evidence comes from case reports and series (Camarata, Miller, & Wallace, 2020). Few randomized controlled trials (RCTs) have demonstrated that SBT can reduce ASC symptom severity, improve sensory functioning, and alleviate social difficulties and self-care challenges (Kashefimehr, Kayihan, & Huri, 2018; Pfeiffer, Koenig, Kinnealey, Sheppard, & Henderson, 2011; Schaaf et al., 2014). Furthermore, a comprehensive study indicated that SBT enhances individualized goals related to functioning, autistic behaviors, sensory processing, and motor skills (Schaaf, Dumont, Arbesman, & May-Benson, 2018). Recent research has highlighted the potential of sensory-based interventions to positively influence early brain development. For instance, sensory-based interventions have been linked to improvements in brain growth and early developmental outcomes in preterm infants, indicating potential benefits for sensory processing and neural connectivity (Beltrán et al., 2022). Translational studies have also demonstrated that multisensory-based approaches can enhance neuroplasticity and contribute to the functional organization of neural networks in early intervention contexts (Purpura et al., 2017). Moreover, an RCT has been conducted to examine the effects of multisensory interventions on neural processing, language, and motor outcomes in preterm infants (Neel et al., 2019). These findings suggest that SBT may promote brain development and serve as a foundation for augmentative interventions that further enhance therapeutic outcomes.

Given the heterogeneous nature of ASC, a multidisciplinary or combined treatment approach may be necessary to address its diverse symptomatology (Politte, Howe, Nowinski, Palumbo, & McDougle, 2015; Delli, Polychronopoulou, Kolaitis, & Antoniou, 2018). Emerging research suggests that individuals with ASC may over-attribute salience to irrelevant sensory information while lacking the ability to down-regulate brain responses to such stimuli (Green, Hernandez, Bookheimer, & Dapretto, 2016; Green, Hernandez, Bowman, Bookheimer, & Dapretto, 2018). Therefore, normalizing sensory experiences and enhancing down-regulation processing may synergistically affect ASC symptoms. In this study, we developed a hybrid intervention combining two different yet complementary treatments: SBT and tDCS. We conducted a randomized, sham-controlled study in children with ASC to investigate the potential effects of these hybrid treatments. These treatments consisted of SBT combined with active tDCS over the left PFC (SBT+AtDCS) and SBT combined with sham tDCS over the left PFC (SBT+StDCS). We hypothesized that children with ASC receiving SBT+AtDCS would show greater improvements in autism severity, sensory functioning, and behavioral difficulties from pre-treatment to post-treatment.

2. Methods

2.1 Participants

We recruited 11 children with ASC, aged between 5 and 7 years, from a medical center in Taipei. One additional participant was excluded from the study because her parents missed several items on the questionnaires, resulting in incomplete data across all outcome measures. Eligible participants were required to be diagnosed with ASC by certified child psychiatrists according to the DSM-5 (American Psychiatric Association, 2013) and have a DSM-5 ASC severity level ranging from mild (level 1) to moderate (level 2) before entering the study. Participants were not on any medication for three months prior to the study and were required to refrain from taking any medication or participating in any other treatment experiments during the study period. The exclusion criteria were: (1) children with ASC severity level 3 (requiring very substantial support) according to DSM-5 criteria. These children may face challenges in maintaining attention and cooperation during the treatment, potentially introducing variability that could affect the study's findings and compromise both the safety and effectiveness of tDCS; (2) a history of head injury, arteriovenous malformation, brain surgery, encephalitis, or meningitis; (3) primary health problems that could limit participation (e.g., concurrent epilepsy; comorbid diagnosis of intellectual disability, other psychiatric or medical conditions); and (4) skin diseases at and near tDCS electrode application sites. Parents or caregivers of all eligible children with ASC had to complete an informed consent form before the experiments. This study was approved by the local institutional review board and conducted in accordance with the Declaration of Helsinki.

2.2 Procedures

A randomized, double-blind, sham-controlled design with pre-treatment and post-treatment was conducted in this study. All participants were randomly assigned to either the SBT+AtDCS or SBT+StDCS group using a computer-generated randomization sequence in a 1:1 ratio. The tDCS setup was performed by an independent experimenter who was unaware of the study hypothesis. A second independent experimenter (a research assistant), also blinded to the stimulation conditions, administered the tDCS treatment. These procedures ensured the integrity of the double-blind design.

Before and after interventions, parents or caregivers of children with ASC were asked to complete the Chinese versions of the Autism Treatment Evaluation Checklist (Fang, Ren, Li, & Ke, 2019; Rimland & Edelson, 1999), the Child Behavior Checklist (Achenbach & Edelbrock, 1991; Chen, Huang, & Jao, 2009), and the Sensory Profile (Dunn, 1999) (Figure 1). Each participant also completed an adverse-effects questionnaire, which was verbally administered verbally by the examiner. Simplified language was used, and adjustments were made according to each child's level of understanding to assess their discomfort before and after each tDCS session. The questionnaire used a 10-point Likert scale (with 1 indicating no discomfort and 10 indicating extreme discomfort) to assess the following symptoms: headache, pain, nausea, facial/neck muscle contractions, burning and stinging sensations under the electrodes, uncomfortable feelings, and other sensations and/or adverse effects. Parents or caregivers were also asked to report whether their children had experienced any of these symptoms. If symptoms were severe (rating more than 7 points) and persisted for more than 30 minutes after cessation of stimulation, tDCS treatment would be discontinued (Charvet, Shaw, Bikson, Woods, & Knotkova, 2020).

2.3 Intervention protocols

All participants were randomized and received one of the two interventions (SBT+AtDCS or SBT+StDCS) for ten sessions [50 minutes/day (initial 20 minutes of tDCS and then 30 minutes of SBT), five days/week for two consecutive weeks]. Each session began with 20 minutes of tDCS delivered concurrently with watching kid-friendly cartoons, followed by 30 minutes of SBT. SBT and tDCS treatments were provided by a senior certified occupational therapist and a research assistant, respectively. Both were responsible for the structure of the treatment during each treatment session. This included determining the types of sensory activities, duration of each sensory task, and recording participants' responses to both tDCS and SBT. These details were reviewed by the principal investigator of this study to ensure standardization of the intervention. Outside the study, interventions and all routine interdisciplinary treatments proceeded as usual. If participants had not received any ASC-related treatments (e.g., mediations or rehabilitative programs) before entering the trial, such treatments were prohibited throughout the study.

Transcranial direct current stimulation (tDCS) protocol

Each participant received one daily session of tDCS (Neuroconn tDCS stimulator, München, Germany) for ten sessions. Participants sat comfortably during both active and sham stimulation sessions while watching kid-friendly cartoons (Gomez et al., 2017). At the beginning of each session, a pair of rubber electrodes, inserted into 35 cm^2 sponges soaked in saline solution, were attached to the heads of children with ASC. In the AtDCS group, the anodal stimulation was applied over the left PFC at the F3 site according to the 10/20 international EEG electrode system (Amatachaya et al., 2014; Amatachaya et al., 2015). The cathode was placed on the contralateral upper arm. Anodal tDCS was applied for 20 minutes, with the current gradually ramping up to 1 mA over the first 30 seconds and maintained this intensity throughout the session. Stimulation gradually ramped down during the last 30 seconds of the 19th minute.

Children with ASC in the sham stimulation group received sham stimulation on the left PFC. A ramp up phase was applied for 30 seconds in the sham condition. This was followed by a one-mA stimulation for 30 seconds and finished with a 30-second ramp down phase. This ensured that the participant experienced the typical sensations on the skin at the beginning of the condition, avoiding awareness of undergoing the sham condition (Amatachaya et al., 2014; Amatachaya et al., 2015). After the initial 2 minutes of stimulation, all participants were asked whether they experienced any discomfort or pain at the electrode sites. If the discomfort persisted, the stimulation was terminated immediately.

Sensory-based treatment (SBT) protocol

Following each tDCS daily session, all children with ASC received 30 minutes of SBT. The SBT program was based on Ayres' theory of sensory integration (Ayres, 1972), and followed a protocol similar to that described by Schaaf et al. (Schaaf et al., 2014). Before treatment initiation, a senior certified occupational therapist evaluated each child's sensory needs with ASC through clinical observation and the Sensory Profile. Based on these assessments, the same therapist provided tailored sensory-based activities to meet each child's individual needs. The activities incorporated various modalities and exercises targeting different sensory domains. These included toys emitting different light and sound frequencies to enhance visual and auditory experiences, gentle brush strokes along the dorsal surface of the child's forearm, suspended swings (e.g., platform swings, bolster swings, rollers) for vestibular stimulation, finger painting activities for tactile experiences, and wearing a weighted vest while playing tug of war or bouncing on the space hopper for proprioceptive stimulation. The level of challenge was adjusted based on each child's abilities and progress throughout the intervention.

2.4 Outcome measures

The Autism Treatment Evaluation Checklist (ATEC) is a 77-item diagnostic assessment tool designed to evaluate the effectiveness of autism treatment (Rimland & Edelson, 1999). It is applicable to children aged 5-12 years and is completed by caregivers, providing a total score and scores for four subscales: speech/language/communication; social; sensory and cognitive awareness; and health/physical/behavior. Higher scores indicate greater difficulties in each domain, while lower scores suggest improvements. The Chinese version of ATEC has proven to be a reliable and valid scale (Fang et al., 2019).

The Child Behavior Checklist (CBCL) is a component of the Achenbach System of Empirically Based Assessment. The CBCL consists of 113 items to assess child adaptive and maladaptive behaviors in children. These behaviors are categorized into internalizing problems (e.g., anxious or depressed, withdrawn or depressed, and somatic complaints), externalizing problems (e.g., rule-breaking and aggressive behaviors), and the DSM-associated scales (e.g., affective problems, attention-deficit/hyperactivity problems, and oppositional defiant problems) (Achenbach & Edelbrock, 1991). Each item is rated on a 3-point scale from 0 (not true) to 2 (very true), with higher scores indicating more significant behavioral problems. The test-retest reliability and criterion validity of the CBCL have been confirmed (Leung et al., 2006).

The Sensory Profile (SP) is a widely used assessment tool to evaluate how children aged 3 to 10 process sensory information during their daily activities (Dunn, 1999). The SP examines sensory processing patterns across various domains, including auditory, visual, tactile, gustatory, olfactory, proprioceptive, and vestibular processing. Parents or caregivers use a 5-point Likert scale to rate the child's responses to sensory stimuli and activities. Lower scores on the SP indicate greater challenges in sensory processing. The test-retest reliability of the Chinese version of the SP in autism is optimal (Yang, Tseng, Cermak, Lu, & Shieh, 2020).

2.5 Statistical analysis

Given the small sample size, non-parametric statistical tests were used for the analyses. A paired Wilcoxon test was employed to compare pre-treatment and post-treatment raw scores for the ATEC, the CBCL, and the SP within each group. To evaluate between-group differences in change scores, the Mann-Whitney *U* test was applied. Change scores were calculated as proportional difference: (post-treatment score − pre-treatment score) / pre-treatment score. We also estimated 95% confidence interval (CI) for the difference between medians was estimated using bootstrapping procedures (Davison & Hinkley, 1997). Statistical significance was set at $p < 0.05$ and the effect size (r) was calculated for significant differences, with thresholds for small (< 0.3), medium (0.3–0.5), and large (> 0.5) effects.

3. Results

To assess the success of blinding, participants and their parents were asked after the final session whether they could determine if they were in the treatment or control group. All responded that they could not, indicating successful blinding. These procedures ensured the integrity of the double-blind design. Six children with ASC received SBT combined with active tDCS. The demographic data and results from the ATEC, the CBCL, and the SP assessments for all study participants are presented in Table 1.

In the SBT+AtDCS group, the ATEC total score significantly improved from pre-treatment to post-treatment (95% CI: -19–-3.5, $Z = -2.207$, $p = 0.027$, effect size $r = 0.637$) (Figure 2A). Significant improvements were also observed in the ATEC subscales for speech/language/communication (95% CI: 1–9.5, $Z = -2.032$, $p = 0.042$, effect size $r = 0.587$) and health/physical/behavior (95% CI: -14.5–-1.5, $Z = -2.214$, $p = 0.041$, effect size $r = 0.639$). However, no significant improvements were found in the SBT+StDCS group for the ATEC total score or any subscales. Between-group comparison using the Mann–Whitney *U* test did not reveal significant difference in change scores for the ATEC total scale (95% CI: -0.67–0.13, $Z = -1.643$, $p = 0.1$, effect size $r = 0.495$). A power analysis estimated that a total of 44 participants (n=22 per group) would be required to achieve significant between-group differences. However, significant differences were observed in the change scores for the ATEC health/physical/behavior subscale between groups (95% CI: 4.5–25.5, $Z = -2.470$, $p =$

0.013, effect size *r* = 0.743).

For the CBCL, significant reductions were noted in the SBT+AtDCS group for the total score (95% CI: -26–-1.5, *Z* = -2.201, *p* = 0.028, effect size *r* = 0.635) and externalizing problems subscale scores (95% CI: -13–-3, *Z* = -2.027, *p* = 0.027, effect size *r* = 0.637). No significant within-group improvements were observed in the SBT+StDCS group for the CBCL total score or any subscales (Figure 2B). For between-group comparisons, the Mann–Whitney *U* test did not show significant differences in change scores for the CBCL total scale (95% CI: -0.38–0.41, *Z* =-1.826, *p* = 0.068, effect size *r* = 0.551). A power analysis estimated that a total of 32 participants (n=16 per group) would be required to achieve significant between-group differences. Nevertheless, significant between-group differences were observed in change scores for the CBCL externalizing problems subscale (95% CI: -0.88–-0.04, *Z* = -2.470, *p* = 0.013, effect size *r* = 0.743).

Regardless of the groups, children with ASC showed significant improvements in sensory modulation subscale scores following intervention (SBT+AtDCS: 95% CI: 1–13, *Z* = -2.201, *p* = 0.028, effect size *r* = 0.635; SBT+StDCS: 95% CI: 3–15, *Z* = -2.023, *p* = 0.043, effect size r = 0.639) (Figure 2C). Furthermore, in the SBT+AtDCS group, the SP total score significantly improved from pre-treatment to post-treatment (95% CI: 15–35, *Z* = -1.992, *p* = 0.046, effect size *r* = 0.575) (Figure 2D). However, no significant between-group differences were found in change scores for the SP total scale or any SP subscales (all *p* > 0.4, with small effect sizes ranging from $r = 0.032$ to $r = 0.219$). The estimated sample size required to achieve significant between-group differences in the SP total scale was 1,068 participants in total (n=534 per group).

Importantly, parents or caregivers of all eligible children with ASC did not report or notice any adverse events in either the SBT+AtDCS or SBT+StDCS groups (Table S1).

4. Discussion

This pilot study is the first to examine the combined effects of SBT and tDCS in children with ASC. The findings indicate that all participants demonstrated significant improvements in their ability to regulate and respond to sensory stimuli after treatment, irrespective of whether they received active or sham tDCS. This suggests that the SBT protocol alone is beneficial for enhancing sensory processing in ASC. Furthermore, children with ASC who received SBT+AtDCS intervention showed greater reductions in autism severity and behavioral difficulties compared to those who receive SBT+StDCS. Although the small sample size limits the generalizability of these findings, the results are encouraging and provide valuable insights for future research and larger-scale investigations.

A primary finding of the study is the significant reduction in ASC severity and the improvement in externalizing problems such as rule-breaking and aggressive behaviors, following SBT+AtDCS intervention. In contrast, SBT+StDCS intervention did not yield similar effects. These differences in ASC severity and behavioral difficulties may be specifically linked to the active tDCS treatment. Previous research has shown that anodal tDCS applied over the left PFC can enhance behavioral and social outcomes in individuals with ASC (Amatachaya et al., 2014; Amatachaya et al., 2015; Garcia-Gonzalez et al., 2021; Hadoush et al., 2020; Toscano et al., 2019). Notably, the interaction between excitation and inhibition is critical for neural circuitry function in the brain (Sukenik et al., 2021). Emerging evidence suggests that disruptions in the E–I balance, specifically hyperglutamatergic-hypoGABAergic alterations in specific brain areas such as the prefrontal cortex, are linked to the social and behavioral abnormalities of ASC (Robertson & Baron-Cohen, 2017; Rubenstein & Merzenich, 2003; Uzunova et al., 2016; Yizhar et al., 2011). Thus, the improvements observed in children with ASC, including reduced ASC severity and fewer behavioral challenges, following SBT combined with active tDCS over the left PFC may be attributed to this E–I mechanism. Given that this study primarily focuses on clinical behavioral efficacy, further investigation is required to support this assumption.

Additionally, we observed significant improvements in sensory modulatory behaviors among all children with ASC following interventions of SBT+AtDCS and SBT+StDCS. These findings are consistent with prior evidence indicating that SBT can improve sensory responsiveness in ASC (Kashefimehr et al., 2018; Pfeiffer et al., 2011; Schaaf et al., 2014). Altered sensory modulation has been reported since the earliest descriptions of ASC (Kanner, 1943), with individuals often exhibiting difficulties in regulating their responses to sensory stimuli (Ben-Sasson et al., 2009; Case-Smith et al., 2015; Kern et al., 2007; Tavassoli et al., 2016). SBT emphasizes sensory stimulation and active participation of the child, focusing on providing planned, controlled sensory inputs based on the child's needs to help enhance their ability to self-regulate sensory demands and improve sensory experiences (Case-Smith et al., 2015; Koomar & Bundy, 2002; Parham et al., 2007; Pfeiffer et al., 2011). In this study, we followed these principles and applied individually customized sensory-motor activities at an appropriate level of challenge. The results indicated that all children with ASC responded more effectively to daily sensory experiences. Future research should investigate the significance of this individualization strategy, as it may play a critical role in achieving positive outcomes in sensory modulation.

Another notable finding of our study was the significant improvement in the SP total score following SBT+AtDCS interventions, suggesting that the additional benefit of active tDCS on overall sensory processing is highly promising. Atypical sensory processing in ASC has been observed across all age groups and levels of symptom severity, adversely affecting social behaviors and daily functioning (Baum, Stevenson, & Wallace, 2015; Leekam, 2016; Marco, Hinkley, Hill, & Nagarajan, 2011). Green and colleagues conducted a series of studies suggesting that ASC symptoms are associated with an over-attribution of salience to extraneous sensory information, accompanied by insufficient down-regulation in the brain's responses, such as reduced activation of the PFC. This results in excessive attention to sensory inputs, leading to social-communication difficulties (Green et al., 2016; Green et al., 2018). In this study, we used two different yet complementary treatments—SBT to normalize sensory experiences in individuals with ASC, and active tDCS applied to the left PFC to enhance their capacity for processing downregulation. This combined approach demonstrated synergistic effects on the overall sensory functioning in ASC.

However, direct comparisons of between-group effects revealed a more substantial effect on the ATEC and CBCL compared to the SP. Power analyses indicated that achieving significant between-group differences in SP change scores would require a larger sample size than that needed for the ABC and CBCL. This finding suggests a potential ceiling effect, where the effectiveness of the SBT protocol alone may have reached its maximum impact on sensory processing, resulting in less significant differences caused by AtDCS. Future research should consider several avenues to address these findings. Firstly, during stimulation should specifically engage the left PFC to maximize efficacy. For instance, anodal tDCS over the left PFC could potentially enhance working memory in individuals with ASC when they are instructed to maintain a calm and quiet state during the stimulation session (Hadoush et al., 2020). Alternatively, applying cathodal tDCS over the left PFC in conjunction with cognitive remediation training could improve information processing speed during executive function tasks in ASC (Chan et al., 2023).

There are some limitations worth noting in the current study. Firstly, the sample size was small and included both boys and girls. Practical challenges, such as trial non-completion and poor treatment compliance, limit recruitment to children with mild to moderate ASC. Given the heterogeneous nature of ASC, the variability in our relatively small sample may have influenced for treatment outcomes. Using power analyses, we have estimated the number of participants required to achieve significant results between SBT+AtDCS and SBT+StDCS groups in the ATEC, CBCL, and SP. The small effect size for improvement in the SP may be attributed to a ceiling effect in the sham control group, where a validated SBT was applied to fulfill ethical considerations for clinical populations. When testing a new intervention, it is essential to ensure that participants' rights are not compromised. Even in the control group, participants should not be deprived of access to proven effective treatments (Emanuel, Wendler, & Grady, 2000; Freedman, Glass, & Weijer, 1996). Future studies testing various combinations of tDCS intervention with different levels of task engagement, such as an active task related to the dependent variable versus a passive task unrelated to the dependent variable, could form different intervention packages that affect the outcome differently (e.g., in our study, passive viewing of videos unrelated to sensory functions) are warranted.

Secondly, regarding the reliability of ASC diagnosis, the conventional approach has involved a combination of a semi-structured clinical interview with parents and individual observations. However, a new DSM-5 ASC severity rating system has emerged and is gaining recognition for its validity and utility in confirming ASC diagnoses (Mazurek, Lu, Macklin, & Handen, 2019). Therefore, despite the preliminary and inconclusive nature of the present findings, they can serve as an initial point for further research emphasizing well-defined sample groups and sufficient statistical power. Thirdly, although SBT and tDCS are widely used in ASC, there remains limited understanding of their impact on network-level brain activity and the underlying mechanisms, especially within the brain's domains of excitation and inhibition related to ASC symptoms. Fourthly, the study only examined immediate effects and did not explore long-term or delayed impacts. Furthermore, uncontrolled variables, such as the type and frequency of treatments administered beyond the study period (as outlined in Table 1), must be considered as potential confounding factors.

5. Conclusions

In summary, this randomized, double-blind, sham-controlled pilot study suggests that combining SBT with active tDCS over the left PFC shows potential in reducing symptoms and atypical behaviors associated with ASC. These findings provide initial support for the effectiveness of combined therapies in children with ASC. Validation of these results through further research is crucial, particularly for gaining insights into the underlying neurobiological mechanisms.

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Figure Legends

Figure 1. Illustration of the study procedures.

Figure 2. Differences between pre-treatment and post-treatment raw scores on (A) the ATEC-Chinese, (B) the CBCL-Chinese, and (C and D) the SP-Chinese for each intervention group.

Table 1. Demographic characteristics, clinical outcome scores, and treatment history of study participants

Subject ID	Age	Gender	Intervention	Autism severity	Before treatment			After treatment			Current treatment
					ATEC	CBCL	SP	ATEC	CBCL	SP	
1	6	Boy	SBT+AtDCS	Level I	43	19	530	38	13	521	OT, PT, ST
2	7	Girl	SBT+StDCS	Level I	41	94	326	35	92	355	OT
3	5	Boy	SBT+StDCS	Level II	74	53	394	50	45	421	OT, PT, ST
4	5	Boy	SBT+AtDCS	Level II	98	76	426	80	62	453	OT, PT, ST
5	5	Girl	SBT+AtDCS	Level I	39	37	500	21	15	528	OT, PT, ST
6	7	Boy	SBT+AtDCS	Level I	62	69	397	42	32	499	OT, PT, ST
7	5	Boy	SBT+StDCS	Level I	58	37	370	57	22	390	OT, PT, ST
8	7	Girl	SBT+StDCS	Level II	58	41	368	84	75	341	OT, ST
9	6	Boy	SBT+AtDCS	Level II	88	90	321	72	83	340	OT, PT
10	5	Boy	SBT+StDCS	Level I	18	19	525	23	19	503	OT, PT, ST
11	6	Girl	SBT+AtDCS	Level I	10	43	497	8	34	518	OT, PT

SBT+AtDCS, sensory-based treatment combined with active tDCS; SBT+StDCS, sensory-based treatment combined with sham tDCS; ATEC, the Autism Treatment Evaluation Checklist; CBCL, the Child Behavior Checklist; SP, the Sensory Profile; OT, occupational therapy; PT, physical therapy; ST, speech therapy