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Transcranial Direct Current Stimulation (tDCS) Improves Empathy and Recognition of Facial Emotions Conveying Threat in Adults with Autism Spectrum Disorder (ASD): A Randomized Controlled Pilot Study

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Abstract

Introduction: Empathy is critical for human interactions to become shared and meaningful, and it is facilitated by the expression and processing of facial emotions. Deficits in empathy and facial emotion recognition are associated with individuals with autism spectrum disorder (ASD), with specific concerns over inaccurate recognition of facial emotion expressions conveying a threat. Yet, the number of evidenced interventions for facial emotion recognition and processing (FERP), emotion, and empathy remains limited, particularly for adults with ASD. Transcranial direct current stimulation (tDCS), a noninvasive brain stimulation, may be a promising treatment modality to safely accelerate or enhance treatment interventions to increase their efficacy. **Methods:** This study investigates the effectiveness of FERP, emotion, and empathy treatment interventions paired with tDCS for adults with ASD. Verum or sham tDCS was randomly assigned in a within-subjects, double-blinded design with seven adults with ASD without intellectual disability. Outcomes were measured using scores from the Empathy Quotient (EQ) and a FERP test for both verum and sham tDCS. **Results:** Verum tDCS significantly improved EQ scores and FERP scores for emotions that conveyed threat. **Conclusions:** These results suggest the potential for increasing the efficacy of treatment interventions by pairing them with tDCS for individuals with ASD.

Keywords: transcranial direct current stimulation; autism spectrum disorder; right temporoparietal junction; empathy; threat; facial emotion recognition; randomized controlled pilot study

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Introduction

Empathy refers to a group of socioemotional competencies that allow for perception, understanding, and affective response to the thoughts, desires, beliefs, intentions, emotions, and knowledge of other individuals (Decety & Svetlova, 2012). Empathy is critical for human interactions to become shared and meaningful (Batson, 2011), and it is often facilitated through the expression and processing of facial emotions (Clark et al., 2008). Deficits in both empathy (Blair, 2005; Reichow & Volkmar, 2010) and facial emotion recognition are associated with individuals with autism spectrum disorder (ASD; Baron-Cohen et al., 2009), with specific safety concerns over inaccurate recognition of facial emotion expressions conveying a threat (Ashwin et al., 2007; Krysko & Rutherford, 2009).

ASD is the fastest-growing neurodevelopmental disorder in the United States (CDC, 2016). Zablotsky et al. (2019) showed that the prevalence of ASD has more than doubled from 2009 to 2017, to as many as 1 in 40 children. While social interaction deficits are a key diagnostic feature for ASD (APA, 2013), Baron-Cohen and Wheelwright (2004) demonstrated that individuals with ASD who possess higher empathy abilities also show improved social relationships and overall social functioning, highlighting the need for more effective and efficient treatment interventions for improving empathy-related skills. One such skill involves the processing of facial of emotions (Baron-Cohen et al., 1995), which remains a challenge in ASD even when controlling for gender, verbal ability, and age. The impact of this challenge is pervasive as it impairs the initiation and maintenance of meaningful relationships (Reichow & Volkmar, 2010) and contributes to isolation, substance use, and depression (Hedley et al., 2016; Hofvander et al., 2009).

Currently, evidence-based treatment interventions that target empathy and facial emotion recognition abilities include computer-based, interactive formats for recognizing complex emotions and mental states (Golan & Baron-Cohen, 2006), utilizing a visual framework and video-feedback (Kern Koegel et al., 2016), and using a caregiver-mediated, manualized intervention for improving empathy and social cognition (Laugeson et al., 2015). While there are reports of positive effects from these approaches, the number of evidenced interventions remains scarce, particularly for adults with ASD, indicating a need to pursue additional interventions to increase efficacy.

One potential way to improve the efficacy of facial emotion recognition and empathy interventions utilizing a computer-based, interactive format is to pair these interventions with transcranial direct current stimulation (tDCS; Gill et al., 2015). Studies utilizing tDCS in neurotypical individuals have demonstrated improvements on empathy-related tasks, such as perspective taking and evaluation of self against others (Santiesteban et al., 2012), inferring others' mental states when identifying deception (Sowden et al., 2015), or when making moral judgments (Ye et al., 2015). Improvements in recognizing facial emotions have been demonstrated after tDCS was applied over the cerebellum (Ferrucci et al., 2012), the right orbital frontal cortex (Willis et al., 2015), and over the superior temporal cortex (Boggio et al., 2008). However, the singular task of recognizing a facial emotion requires less in-depth analysis of emotional perceptual stimuli than what is required for facial emotion recognition that also incorporates the processing of that emotion and the development of empathy (Adolphs, 2003; Krysko & Rutherford, 2009).

To target these multiple processes, the right temporoparietal junction (rTPJ) may be optimal for stimulation, because of the rTPJ's role as part of a large-scale neural network for social cognition (Kennedy & Adolphs, 2012). The rTPJ contributes lower-level processing of environmental sensory-perceptual stimuli, such as discriminating between self and others, as well as higher-level social-cognitive processing, such as perspective-taking, empathy, theory of mind (ToM; Decety & Lamm, 2007) emotion verbal fluency (Esse Wilson, Trumbo, et al., 2018), and social functioning (Esse Wilson, Quinn, et al., 2018). The rTPJ is also specifically associated with deficits in empathy and ToM in individuals with ASD (Lombardo et al., 2011). Anodal (increases cortical excitability) tDCS applied over the rTPJ in neurotypical individuals shows improved social functioning on tasks for perspective taking and evaluation of self against others (Santiesteban et al., 2012). These findings suggest that altering the cortical excitability of the rTPJ with tDCS may influence performance on tasks used during social cognition. Further, impaired facial emotion recognition and processing (FERP) has been shown to affect the typical processing of threat-based facial expressions (e.g., anger, fear), more so than other emotions (e.g., happiness, sadness, surprise, disgust; Ashwin et al., 2007; Krysko & Rutherford, 2009), suggesting a lack of vigilance and self-preservation may be a concern for individuals with ASD (Ohrmann et al., 2007). However, there are currently no studies examining the use of tDCS with individuals with ASD paired with treatment interventions for empathy and FERP, including recognition of threatening facial expressions.

The objective of the present study was to conduct a randomized controlled pilot study to investigate the feasibility of combining anodal tDCS over the rTPJ paired with a computer-based interactive FERP, emotion, and empathy intervention, and to evaluate the result of the stimulation on measures of the Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004) and a FERP test with adults with ASD. We anticipate that this pilot study will provide a basis for a future randomized controlled trial. We hypothesize that participants will demonstrate (a) higher scores on the EQ, (b) a reduction of

inaccurate identifications on a FERP test for threat expressions, and (c) increased accuracy on the FERP test overall, after receiving verum tDCS compared to sham tDCS.

Methods

Participants

Study procedures were approved by the local Internal Review Board (IRB), the Human Research Protections Office of the University of New Mexico (UNM). Each participant also completed an informed consent process and provided signed consent before their participation in the study. Seven right-handed, English-speaking adults with mean age of 26.1 years (five males; two females; see Table 1 for complete demographics) with ASD met the study inclusion criteria and completed both sessions of the study. Participants were recruited by word of mouth and flyer postings at the UNM campus, the UNM Accessibility Resource Center, and through a posting to the Autism Speaks *Participate in Research* webpage.

Procedure

Participants attended two sessions spaced 7 days apart at the UNM Psychology Clinical Neuroscience Center and followed the procedure of our previous study examining tDCS with social functioning and social cognition (Esse Wilson, Trumbo, et al., 2018). Similar to that study, participants were screened for ASD with the Autism Quotient (AQ; Baron-Cohen et al., 2001), a reliable instrument that measures the degree adults with normal intelligence display social/behavioral traits associated with ASD (Hoekstra et al., 2008; Ruzich et al., 2015). The AQ has been found to demonstrate good psychometric properties and to adequately distinguish people with ASD from those without ASD (Lundqvist & Lindner, 2017; Zhang et al., 2016). Additionally, based on research demonstrating that 80% of adults with ASD with normal or above cognitive functioning score a 32 or above on the AQ (Baron-Cohen et al., 2001), we required a score of 32 or higher on the AQ for study participation. Last, participants were screened for right-handedness with the Edinburgh Handedness Inventory (Oldfield, 1971) and for cognitive function with the Shipley-2 (Shipley et al., 2009). The Shipley-2 is a standardized measure that provides standard scores with a mean of 100 and a standard deviation of 15. Thus, a standard score of 70 is two standard deviations below the mean on the Shipley-2. For this reason, we determined that a standard score of 70 or higher was required on the Shipley-2 for study participation.

Two pretreatment-intervention tests were administered in randomized order: (1) The Empathy Quotient (EQ; Baron-Cohen & Wheelwright, 2004) and (2) a FERP test.

The EQ is a 60-item measure for global empathy (Baron-Cohen & Wheelwright, 2004; Lawrence et al., 2004) consisting of statements about empathic skills which are rated on a 4-point Likert scale (*strongly agree*, *slightly agree*, *slightly disagree*, and *strongly disagree*). It has shown validity and reliability for measuring cognitive empathy, emotional reactivity, and social skills, both trait and state components of empathy, processes of empathy (Reniers et al., 2012), and an individual's beliefs about their own empathy. The EQ also encompasses differing aspects of empathy, such as empathic concern and perspective taking.

The FERP test consisted of 48 trials where participants viewed neutral and emotional photographic images taken from the NimStim set of normed, multicultural male and female facial emotion expressions (Tottenham et al., 2009). We designed the FERP test using a neutral-emotion-neutral presentation of faces (Matsumoto & Hwang, 2011) with each trial first presenting a face showing a neutral expression for 1000 ms, followed by an emotional image of the same face presented for 1000 ms showing one of the six facial emotion expressions of sadness, happiness, fear, surprise, disgust, or anger (Ekman, 2003), followed by another 1000 ms of the same face in a neutral expression. The participant was then asked to identify from a multiple-choice list which of the six emotions had been presented. The goal of the FERP test design was to access participants' higher-level, emotion-based cognitive processes, rather than measuring participants' abilities to identify "microexpressions" (facial emotions presented for < 250 ms) or participants' ability to use compensatory strategies for facial emotion recognition (Harms et al., 2010), which may have occurred if facial emotions were presented for > 1000 ms.

After pretreatment-intervention tests were completed, we followed the same procedures for administration of tDCS as developed in Esse Wilson, Trumbo, et al. (2018). Verum tDCS was applied over the rTPJ at 2.0 mA for 30 min, and sham tDCS was delivered with a current that increased from 0 to 2.0 mA during 20 s, then decreased to 0 mA after 30 s. The stimulation was delivered through two square 11 cm^2 saline-soaked sponge electrodes (neuroConn DC-STIMULATOR MR, neuroCare

Table 1

Participants Demographics, History, and Characteristics

Demographics	
n	7
Gender (M/F)	5/2
Age, mean years (*SD*, range)	26.1 (18–58)
History	
Category name	# of participants reporting (% of total)
Depression	4 (57)
Anxiety	4 (57)
Attention deficit	1 (14)
Hospitalization for psychiatric disorder	0 (0)
Current medication use:	
Depression	2 (29)
Anxiety	0 (0)
Illicit drug user	0 (0)
Caffeine	
Regular user	2 (29)
Used during study	2 (29)
Cigarette or other nicotine	
Regular user	0 (0)
Used during study	0 (0)
Alcohol	
Regular user	2 (29)
Used during study	0 (0)
Characteristics	
AQ score mean (*SD*)	36.14 (3.89)
Shipley-2 standard score mean (*SD*)	97 (16.95)

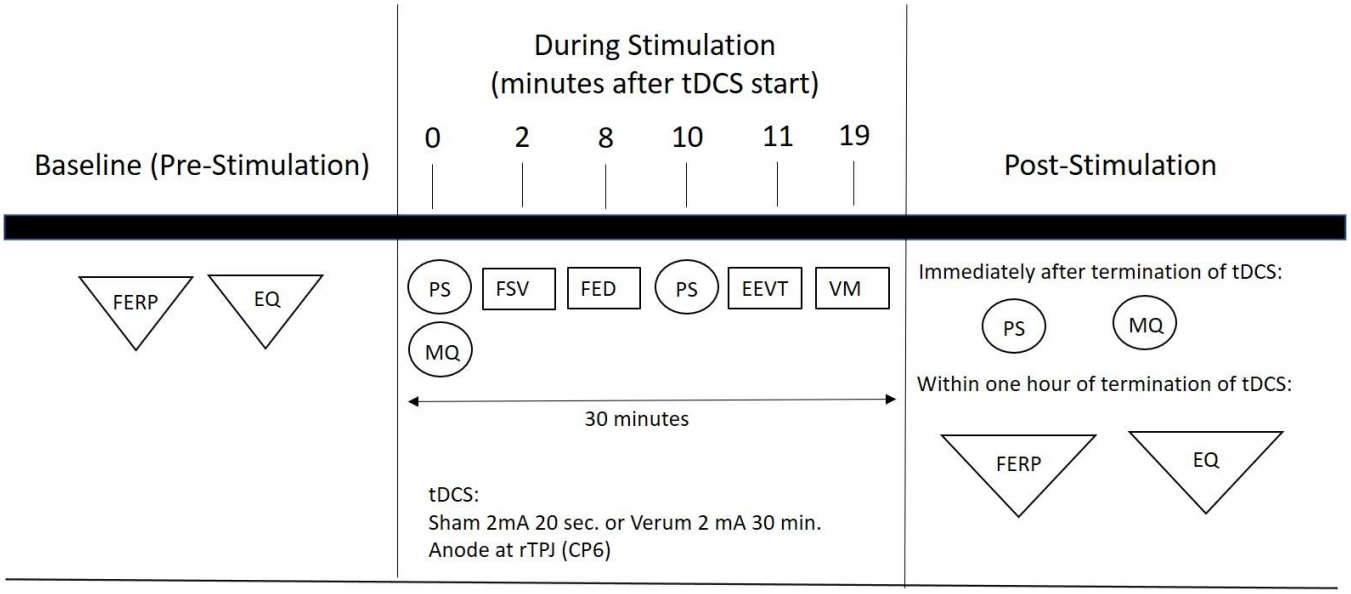
M/F = male/female; *SD* = standard deviation; tDCS = transcranial direct current stimulation; AQ = Autism Quotient

Group, Munich, Germany) with anode over CP6 (10–10 EEG system) and cathode over the ipsilateral deltoid. Participants randomly received either verum or sham tDCS during each of the two experimental sessions. If a participant was randomly assigned to receive sham tDCS in the first session, then they received verum tDCS in the second session, and vice versa. Both the assessing researcher and the participant were blinded as to which condition the participant was in until after the completion of the second visit. Blinding was accomplished through the use of a unique code for each participant that was programmed into the neuroConn stimulator by a coauthor who did not participate in assessment.

Verum and sham tDCS were paired with computer-based, interactive FERP, emotion, and empathy interventions that included video modeling depicting the use of conversation rules across a variety of social situations, facial emotion recognition training, and complex emotion and empathy training utilizing empathy words, photos, and embedded narrated short videos. Additionally, administration of two questionnaires during both verum and sham tDCS was completed: (1) a mood questionnaire (MQ) administered twice to detect any mood changes

(given within first minutes of stimulation and immediately after termination of stimulation), and (2) a physical sensations (PS) questionnaire to detect levels of itching, heat, and tingling (taken at three separate time points—first minutes of stimulation, approximately 10 minutes after start of stimulation, and immediately after termination of stimulation). After receipt of tDCS and interventions, administration of the EQ and FERP test were completed. A timeline summarizing study's prestimulation, stimulation, and poststimulation activities is depicted in Figure 1.

Figure 1. *Timeline Summarizing Study's Prestimulation, Stimulation, and Poststimulation Activities*.



Note. Items in triangles are measures where FERP = Facial Emotion and Recognition and Processing test, and EQ = Empathy Quotient; items in circles are questionnaire assessments, PS = physical sensation questionnaire and MQ = mood questionnaire; and items in rectangles refer to treatment tasks where FSV refers to faces and shapes viewing, FED to facial emotion detection, EEVT to emotion and empathy video treatment, and VM to video modeling.

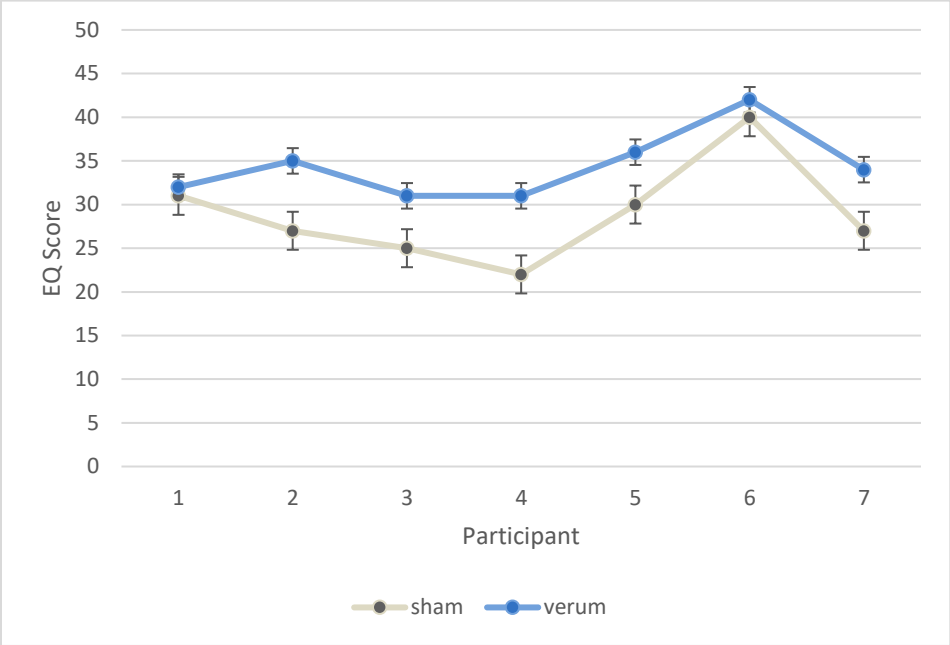
Statistical Analysis

Due to the high level of heterogeneity in the ASD population (Jeste & Geschwind, 2014), we used a within-subjects, repeated-measures design, which allowed participants to act as their own controls over the two randomly assigned (one verum, one sham), double-blinded sessions. A Wilcoxon signed-rank test was utilized to examine if group differences existed (verum tDCS, sham tDCS). This test is considered nonparametric, so minimal assumptions needed to be made about the data, such as it being normally distributed, and it is well-suited for repeated measures with paired data (Whitley & Ball, 2002). Analyses were two-tailed with an alpha level set at 0.05.

Results

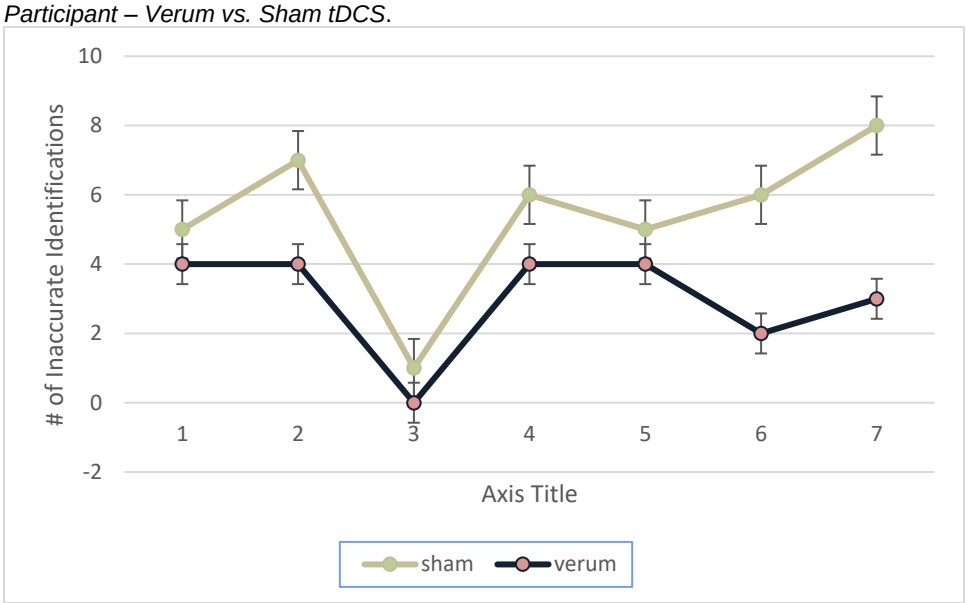
Of the seven participants who participated in the study, all met screening criteria and completed both visits for the study. No significant changes in mood from the MQ or pain from the PS questionnaires were reported from either the verum or sham tDCS sessions. Additionally, examination of mean participant rating scores from the PS questionnaire assessing tingling, burning, and itching sensations showed no significant differences when comparing verum to sham sessions (p = .39). Participants received a significantly higher score on the EQ, Z = −2.366, p < .02, r = .68, and had significantly less inaccurate identifications of threatening facial emotion expressions, Z = −1.90, p < .02, r = .55, after receiving verum tDCS compared to sham tDCS. Differences approached significance for overall accuracy in identifying the basic six emotions when comparing verum to sham tDCS, Z = −1.61, p < .06. Findings for the EQ and inaccurate identifications of threatening facial emotion expressions are depicted in Figures 1 and 2.

Figure 1. *EQ Scores by Participant – Verum vs. Sham tDCS.*



Note. Participants scored significantly higher on the Empathy Quotient after receipt of verum tDCS compared to sham tDCS ($p < .02$). Verum and sham scores are shown for each participant. EQ = Empathy Quotient; tDCS = transcranial direct current stimulation.

Figure 2. *Number of Inaccurate Identifications of Threatening Facial Expressions by Participant – Verum vs. Sham tDCS*.



Note. Participants made significantly less inaccurate identifications of threatening facial emotion expressions in the verum tDCS condition compared with the sham tDCS condition ($p < .02$). Verum and sham scores are shown for each participant. tDCS = transcranial direct current stimulation.

Discussion

The present randomized controlled pilot study compared the effects of tDCS applied over the rTPJ in verum (2.0 mA for 30 min) and sham conditions (2.0 mA for 20 s then decreased to 0 mA after 30 s) in adults with ASD who are not intellectually disabled as they completed computer-based, interactive emotion, and empathy interventions. The measures used to compare these two conditions included the EQ (measuring global empathy) and a FERP test (measuring overall recognition accuracy from briefly presented facial emotion expression images, as well as accuracy on recognition of threat expressions). It was hypothesized that participants would demonstrate (a) higher scores on the EQ, (b) less inaccurate identifications on the FERP test for threat expressions, and (e) increased accuracy on the FERP test as a whole, after receiving verum tDCS compared to sham tDCS. Our hypothesis was correct for (a) and (b) with participants scoring significantly higher on the EQ, and also reducing the number of inaccurate identifications for threat expressions on the FERP test after verum tDCS when compared to sham tDCS. Our hypothesis for (c) was found incorrect, although differences approached significance. These findings provide support for a preliminary model for the use of computer-based interactive FERP, emotion, and empathy interventions paired with tDCS applied over the rTJP for reducing inaccurate identifications of facial expressions depicting threat (fear, anger) and for increasing empathy skills.

The results of our study suggest that the efficacy of treatment interventions can be improved when using tDCS to modulate neural processing while simultaneously completing interventions that target the building of skills for FERP and emotion and empathy processing. Our findings corroborate studies demonstrating that some individuals with ASD show improvement on measures of facial emotion recognition after they develop skills specific to this task, despite a continued underlying presence of atypical neural processing (Harms et al., 2010; Krysko & Rutherford, 2009). In our study, we capitalized on the relationship of FERP to empathy (Clark et al., 2008) during the receipt of treatment intervention, while also utilizing tDCS over the rTPJ to additionally target underlying neural processing.

Because facial expressions convey emotion, previous studies utilizing tDCS have targeted brain regions known for facial emotion recognition, such as the right orbitofrontal cortex (Willis et al., 2015), the superior temporal cortex (Boggio et al., 2008), or the posterior superior temporal sulcus (Harms et al., 2010). While anger and fear facial expressions may also implicate these brain regions, the rTPJ is specifically implicated in handling the higher-level social-cognitive information necessary for processing complex emotions (Decety & Lamm, 2007). This led our study to choose the rTPJ as a stimulation site for tDCS for processing emotions, including the complex social-cognitive construct of threat. This is an extension of previous research utilizing tDCS over the rTPJ to improve emotion processing during emotion verbal fluency tasks with adults with ASD (Esse Wilson, Trumbo, et al., 2018). Future directions may utilize tDCS over the rTPJ with individuals with ASD to examine emotion processing of facial and body expressions, as well as emotion-based words and phrases, that convey threat. Additionally, future research may incorporate tDCS applied over other brain regions, such as the orbitofrontal cortex, the superior temporal cortex, or the posterior superior temporal sulcus, in conjunction with treatment interventions for social functioning and social cognition. While the present study includes empathy and FERP measures, future studies might also investigate utilizing measures specific to ToM. Additionally, future work may also apply to other groups with deficits in socioemotional processes, such as individuals with fetal alcohol spectrum disorder.

This effort was completed as a randomized controlled pilot study on the feasibility and potential efficacy of combining tDCS paired with FERP, emotion, and empathy interventions. Participants in our study self-identified as having ASD, with a score of 32 or higher required on the AQ for participation. Future pilot studies might also confirm diagnosis with a standardized clinical assessment tool. Last, use and safety of tDCS with children suggests that this approach may be extended to adolescents with ASD (Ciechanski & Kirton, 2017; Palm et al., 2016).

Conclusions

Our study supports the feasibility and efficacy of utilizing anodal tDCS over the rTPJ during a computer-based interactive FERP, emotion, and empathy intervention with adults with ASD without an intellectual disability. All participants completed the study tasks of both sessions, as well as pre- and postassessments. Additionally, PS questionnaires were given to participants during receipt of tDCS to assess levels of tingling, burning, and itching sensations, with no adverse events reported. Verum or sham tDCS was randomly assigned in a within-subjects, repeated-measures, double-blinded design

over two visits separated by 1 week. Outcomes were assessed using the EQ and a FERP test. Paired data were analyzed to examine if group differences existed when comparing verum to sham tDCS. It was predicted that differences would be found when comparing EQ and FERP scores for verum and sham tDCS. Participants received a significantly higher score on the EQ and had significantly less inaccurate identifications of threatening facial emotion expressions after receiving verum tDCS compared to sham tDCS. These findings are consistent with a role for the rTPJ in empathy and FERP in adults with ASD and provide optimism for the use of tDCS paired with FERP, emotion, and empathy interventions.

Author Declaration

Sandia National Laboratories is a multimission laboratory managed and operated by National Technology and Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International, Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525. Opinions expressed are those of the authors and not necessarily those of the U.S. Government. Sandia Laboratory approval number SAND2021-6043 J.

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