Title
Increased Neural Response to Reward in Adolescents With ASD After PEERS Social Skills Intervention

Author
Baker, Elizabeth

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Increased Neural Response to Reward in Adolescents With ASD After PEERS Social Skills Intervention

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by

Elizabeth D. Baker

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Thesis Committee:
Dr. Katherine Stavropoulos, Chairperson
Dr. Jan Blacher
Dr. Wesley Sims

The Thesis of Elizabeth D. Baker is approved:

Committee Chairperson

University of California, Riverside

ABSTRACT OF THE THESIS

Increased Neural Response to Reward in Adolescents With ASD After PEERS Social Skills Intervention

by

Elizabeth D. Baker

Master of Arts, Graduate Program in Education
University of California, Riverside, March 2021
Dr. Katherine Stavropoulos, Chairperson

The reward system has been implicated as a potential neural mechanism underlying social-communication deficits in individuals with autism spectrum disorder (ASD). However, it remains unclear whether the neural reward system in ASD is sensitive to behavioral interventions. The current study measured the reward positivity (RewP) in response to social and nonsocial stimuli in seven adolescents with ASD before and after participation in the Program for the Education and Enrichment of Relational Skills (PEERS) intervention. This study also included seven neurotypical adolescents who were tested at two timepoints but did not receive intervention. RewP mean amplitude was examined across the course of an electroencephalographic (EEG) task by comparing brain activity during the first versus second half of trials to understand patterns of responsivity over time. Improvements in social skills and decreased social-communication impairments for teens with ASD were observed after PEERS. Event-related potential (ERP) results suggested increased reward sensitivity during the first half of trials in the ASD group after intervention. Adolescents with ASD who exhibited less reward-related brain activity before intervention demonstrated the greatest behavioral benefits from the intervention. These findings have implications for how brain-based investigations can be used as an objective outcome measure before and after intervention in ASD.

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Introduction

Autism Spectrum Disorder (ASD)

Autism spectrum disorder (ASD) is characterized by social communication deficits and the presence of restricted or repetitive behaviors (American Psychiatric Association, 2013). ASD is classified as a neurodevelopmental disorder where poor eye contact, language impairments, cognitive delays, and motor deficits are some of the defining features that give rise to later social impairments (Zwaigenbaum et al., 2005). Advances in symptom identification, as well as the investigation of early biomarkers of ASD, have elucidated specific behavioral, familial, and genetic risk factors for ASD, though there is still much to be understood about the enduring impacts that social deficits have across developmental stages in ASD.

Habituation and Sensitization

Relative to social skills deficits and the presence of restricted and repetitive behaviors, less attention has been paid to how individuals with ASD habituate to stimuli in their environment and how modulation of attentional resources may impact their interactions with the social world (Maes et al., 2011). The cognitive process of habituation can be conceptualized in a variety of ways but is generally considered to be a decreased response to stimuli after repeated exposure (Thompson & Spencer, 1966). Conversely, sensitization is a process by which responses are enhanced after repeated exposure (Peeke, 1984; Thompson & Spencer, 1966).

Individuals with ASD display altered rates of habituation. Specifically, individuals with ASD do not habituate to social information at the same rate as neurotypical controls, as evidenced through amygdala activation to faces over time (Kaartinen et al., 2016; Kleinhans et al., 2009; Swartz et al., 2013; Tam et al., 2017; Webb et al., 2010). In individuals with ASD, repeated presentation of social information elicits activation rates similar to that of novel stimuli for neurotypical subjects (Vivanti et al., 2018). In neurotypical individuals, habituation tends to occur at a slower rate for stimuli that are more salient, intense, or stimulating (Rankin et al., 2009; Thompson & Spencer, 1966). As such, salient information may cause sensitization to stimuli such that heightened responses can be observed over time (McSweeney & Murphy, 2009; Thompson & Spencer, 1966).

One explanation for slowed habituation rates in response to faces is that individuals with ASD find processing social information more challenging than their neurotypical peers and thus must employ more cognitive resources. Alternatively, a lack of habituation could reflect sensitization in this population. The role of habituation in autism becomes more complex when considering reinforcements and rewards.

Social Motivation and Reward

The reward system has been discussed at length in relation to the core symptoms of ASD. According to the social motivation hypothesis, individuals with ASD experience social interactions as less rewarding than their neurotypical peers, which may lead to reduced social initiation during critical periods of social development (Chevallier et al., 2012). Investigations utilizing electroencephalography (EEG) to measure reward specific event-related potentials (ERPs) suggest that children with ASD tend to find nonsocial stimuli more salient than social stimuli and that children with ASD have less reward-related brain activity than their neurotypical peers in response to faces (Stavropoulos & Carver, 2014a). Thus, it is not that the reward system in ASD populations is under-active in response to all stimulus types, but that it is selectively functioning for some categories and not others (McPartland et al., 2012). However, the literature is mixed on whether the reward system is globally hypoactive in individuals with ASD (Kohls et al., 2012, 2013). If the reward system is selectively functioning in ASD, this system might be malleable, meaning behavioral intervention strategies that focus on social reinforcement might increase brain activity in response to social stimuli in this population. This hypothesis is supported by previous literature demonstrating neural changes in participants with ASD from pre- to post-intervention (Dawson et al., 2012; Van Hecke et al., 2015; Venkataraman et al., 2016; Ventola et al., 2014; Voos et al., 2013; Yang et al., 2016; Yang et al., 2018). Additional investigations are needed to further characterize reward in order to examine how social motivation can be increased in youth with ASD, with particular emphasis on ERPs.

Reward-Related Positivity (RewP)

The reward-related positivity (RewP) is a positive ERP component that peaks between 250-350 ms after being presented with stimuli that is found to be rewarding (Miltner et al., 1997; Tunison et al., 2019). Several studies have shown that the RewP is elicited by positive feedback (Baker & Holroyd, 2011; Foti et al., 2011) and suppressed by negative feedback (Bress et al., 2012) in both adults and adolescents. Previous research on winning and losing suggests that the elicited RewP is larger in amplitude when feedback is associated with actual rewards and is smaller in amplitude for feedback without rewards (Bress & Hajcak, 2013; Carlson et al., 2011; Holroyd et al., 2008).

Response to Intervention

It is known that interventions modify behavior and can improve symptoms of ASD (Howlin et al., 2009; McConachie & Diggle, 2007; Rao et al., 2008; White et al., 2007). However, less is known about the effects of intervention on biologically sensitive and objective measures of change (e.g., measures of brain activity). Combining behavioral measures of symptom improvement with biological measures can further inform the effects of intervention. For example, it is possible that specific patterns of biological change relate to improved outcomes and, furthermore, that baseline characteristics may help stratify children based on the likelihood of response to intervention. Recognizing that one size does not fit all in terms of treatment (i.e., not all children benefit equally from a given intervention), researchers may be better served by employing brain-based outcome measures to more rigorously understand change.

There are a variety of interventions which currently exist for individuals with ASD (Eikeseth et al., 2007; Grynszpan et al., 2014; Krasny et al., 2003; Virués-Ortega, 2010) and the utilization of sensitive outcome measures is increasingly important to monitor change. Measures of change should not only be sensitive but also should be related to the content of the treatment. As such, the goal of outcome research relies on the identification of meaningful outcomes measures, with an emphasis on measuring improvement of core symptoms.

Considerations of habituation or sensitization before and after such interventions are pertinent not only to the effectiveness of intervention, but also the interpretation of outcomes. Understanding how reward-related brain activity changes across the course of a task for individuals with and without ASD can increase our understanding of whether habituation or sensitization occurs at a similar rate across populations (i.e., neurotypical and ASD) and whether such activity is affected by participation in a social skills intervention. One method for measuring change in brain activity across a task is analyzing brain activity during the first and second halves of a task separately.

Current investigation

In the current study, we sought to understand processes of habituation and sensitization to social stimuli among adolescents with ASD by examining patterns of reward-related neural responses to social versus nonsocial stimuli across a task (i.e., activity in the first versus second half of a task) before and after participation in a social skills intervention.

Methods

Participants

Participants included 7 adolescents with ASD and 7 age- and gender-matched neurotypical (TD) adolescents. Detailed information about participant demographics can be found in Table 1. No significant differences in age or IQ were observed between groups ($p > .70$).

ASD

Flyers for the study were placed in local schools and community centers; interested families were contacted by phone or email. Exclusionary criteria for ASD participants (n = 7, *M* = 13.88, *SD* = 2.21, 6 male) included a history of seizures/epilepsy, history of brain injury or disease, or a diagnosis of intellectual disability. Commonly co-occurring disorders were not exclusionary, though a history of serious psychiatric illness (e.g. schizophrenia, bipolar disorders) was exclusionary, or a recent (within 6 months) psychiatric hospitalization. Participants needed to be between 11 to 18 years of age to participate and hold a current ASD diagnosis, confirmed with the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-II) (Lord et al., 2012). Additionally, participants needed to have an IQ of at least 70 to be included in the study. ASD adolescents needed to have English as a primary language to be included in the intervention, while their parents could primarily speak English or Spanish. Participants indicated their willingness to participate in the 16-week intervention, which would involve attending weekly sessions and completing study-related tasks. Parents of participants also needed to commit to attending intervention sessions.

TD

TD participants (n = 7, *M* = 13.46, *SD* = 2.29, 6 male) were recruited through a secured university database. The database consisted of a list of families who had previously given their permission to be contacted by university researchers. Exclusionary criteria included: a history of seizures/epilepsy, history of brain injury or disease, or a diagnosis of intellectual disability and/or ASD. For the TD group, immediate family history of ASD or developmental disabilities and any psychiatric diagnosis for the adolescent was exclusionary. TD participants needed to have an IQ of at least 80 to be eligible to participate. TD participants were not enrolled in the PEERS intervention and instead were seen at two timepoints, 16 weeks apart, to complete the same lab-related tasks as the ASD participants.

Table 1. Descriptive characteristics of the ASD and TD groups.

Variable	ASD	TD
Gender	6 male, 1 female	6 male, 1 female
Age in years, *M (SD), Range*	13.88 (2.21), 11.26 – 16.98	13.46 (2.29), 10.10 – 17.10
IQ, *M (SD), Range*	104.14 (17.36), 77 - 129	102.50 (17.96), 80 - 128
White *n*	2	1
Latino *n*	4	4
Mixed Race *n*	1	2
Maternal Education Level		
Less Than College	5	2
College and Above	2	3
Missing Data	0	2
Household Income		
Up to $50,000	3	1
$50,001 - $100,000	2	1
Over $100,001	2	2
Missing Data	0	3

IRB

This study was approved by the Institutional Review Board at the University of California, Riverside. Informed consent was obtained from all caregivers, and adolescents provided assent.

Measures

Assessments

For adolescents in both groups, cognitive abilities were tested using the 2-subtest Wechsler Abbreviated Scales of Intelligence (WASI-II) (Wechsler, 2011). For adolescents with ASD, diagnosis was confirmed using the Autism Diagnostic Observation Schedule, 2nd Edition (ADOS-II) (Lord et al., 2012). Willingness to participate in the intervention was assessed in ASD participants using the Mental Status Checklist, used to assess motivation to learn how to make and keep friends (Laugeson & Frankel, 2011). As these measures were used to confirm eligibility, they were completed only prior to the intervention and were not repeated.

Wechsler Abbreviated Scale of Intelligence, 2nd edition (WASI-II) (Wechsler, 2011). Participants were administered two subtests of the WASI-II: Vocabulary and Matrix Reasoning. The Vocabulary and Matrix Reasoning Composite scores are combined to create a full-scale IQ-2 (FSIQ-2) subtests composite score, which serves as a measure of IQ. Reliability for the FSIQ-2 is .94 (McCrimmon & Smith, 2013).

Autism Diagnostic Observation Schedule, 2nd edition (ADOS-II) (Lord et al., 2012). The ADOS-II is a semi-structured, standardized assessment of symptoms of ASD by eliciting spontaneous examples of social interaction and restricted or repetitive behaviors (Lord et al., 2000). This measure is considered one of the gold-standard tools used to assess autism spectrum disorders across the lifespan. The ADOS-II consists of five modules based upon the individual's language ability and age. In this study, Modules 3 and 4 were used, as all ASD participants had fluid verbal language. TD participants were not administered the ADOS-II.

Questionnaires

Caregivers in both ASD and TD groups completed the Social Responsiveness Scale, Second Edition (SRS-2) (Constantino, 2012) and the Social Skills Improvement System (SSIS) (Gresham & Elliott, 2008). Both the SRS-2 and SSIS were completed before the intervention began (Time 1) and immediately after intervention completion (Time 2). Times 1 and 2 were approximately 4 months apart, as the duration of the PEERS intervention is 16 weeks. Neurotypical adolescents (TD participants) did not complete PEERS, but had visits spaced 4 months apart. In addition, all adolescents completed the Test of Adolescent Social Skills Knowledge (TASSK) (Laugeson et al., 2009), which measures acquisition of the concepts taught in PEERS.

Social Responsiveness Scale, 2nd Edition (SRS-2) (Constantino, 2012). The SRS-2 is a standardized 65-item parent-report rating scale used to assess the severity of autism symptoms and social responsiveness in children ages 4 to 18. Previous research has found the SRS-2 to have high internal consistency and to be sensitive in detecting intervention-related changes in social functioning in children with ASD (Frazier et al., 2014).

Social Skills Improvement System (SSIS) (Gresham & Elliott, 2008). The SSIS is a standardized 79-item parent-report measure of social and behavioral functioning for children ages 3 to 18. The measure is designed to assess treatment-related changes in social skills and problem behaviors. Parents are asked to indicate how often their child displays a particular behavior by rating items on a 4-point Likert scale as “never,” “seldom,” “often,” or “almost always.” The SSIS has been found to have high internal consistency (Gresham & Elliott, 2008).

Test of Adolescent Social Skills Knowledge—Revised (TASSK-R) (Laugeson & Frankel, 2011). The TASSK-R is a 30-item self-report measure that assesses an adolescent’s knowledge of the social skills taught in the PEERS intervention. The questionnaire includes sentence stems that can be completed from two possible choices based on the PEERS didactic lessons. Only one possible choice is correct. The TASSK-R has been found to have high internal consistency and to be sensitive to intervention related change (Schohl et al., 2014).

Behavioral Intervention

***Program for the Education and Enrichment of Relational Skills (PEERS)* (Laugeson, 2013; Laugeson et al., 2009, 2015; Laugeson & Frankel, 2011).** PEERS is a 16-week, outpatient, manualized intervention designed to help adolescents make and keep friends (Laugeson et al., 2012). The PEERS intervention consists of 16 weekly, 1.5-hour group sessions for parents and teens. Parent groups are conducted in a separate room from adolescent groups. Each group is led by a trained interventionist. A separate room for parents is provided to allow parents to learn how to support their adolescents by helping their teens practice and maintain skills learned in the intervention sessions. In this investigation, portions of the PEERS intervention were translated for Spanish-speaking families, including the parent materials as well as the intervention itself. The adolescent groups were conducted in English only, and the parent groups were conducted in both English and Spanish, consecutively, by a bilingual group leader. As such, the interventionist running the parent group would first speak in English and would then translate all statements into Spanish. All procedures were supervised by a licensed psychologist.

Intervention sessions focused on teaching social skills specific to making and keeping friends and handling peer conflict and rejection. Skills were taught using didactic instruction in a group format, which included role-play demonstrations, behavioral rehearsal activities with reinforcement and corrective feedback, and weekly homework assignments related to social engagement (Ellingsen et al., 2017). To promote generalization of the skills, parents were trained to become social coaches for their teens by encouraging their teens to practice in-class activities at home, providing feedback when practicing skills at home, and identifying appropriate extracurricular activities to increase opportunities for their teens to make friends. Each session, parent handouts and homework assignment sheets were provided outlining discussed topics (Ellingsen et al., 2017; Laugeson et al., 2009, 2012).

Topics of instruction included: using appropriate conversational skills; choosing appropriate friends; using social media and texting appropriately and safely; using humor appropriately; initiating and joining conversations with peers; organizing get-togethers;

being a good sport when playing games; handling arguments; and handling rejection, teasing, and bullying (Laugeson et al., 2014).

Electrophysiological (EEG) Measures

EEG Stimuli and Task

The EEG task was completed by ASD and TD participants at Time 1/pre-intervention and Time 2/post-intervention. Before the EEG task began, participants were told that they were to play a guessing game, and that if they guessed correctly, they would see a ring of intact Oreo cookies. However, the cookies would be crossed out for incorrect answers. The EEG task included two blocks of 50 trials each, with two feedback responses (correct and incorrect) and two conditions (social and nonsocial). In both blocks, at the beginning of each trial, a fixation cross appeared on the screen for 500 milliseconds (ms). After the fixation cross, two boxes were displayed for 3000 ms; each box contained a question mark. A question mark box was placed on the left and right side of the screen. Participants were instructed to indicate their guess via a button pad whether the left or right stimulus was "correct." After participants chose the left or right box, an arrow appeared, indicating their choice, between the question marks for 2000 ms (e.g., the arrow pointed left if the participant chose the left box and right if the participant chose the right box). This was done to reinforce the idea that participants had control over the task and that their responses were being recorded.

After 2000 ms, feedback about whether the participant guessed correctly appeared on screen for 1000 ms. In the social block, feedback was an image of a smiling face surrounded by Oreo cookies for correct answers or an image of a frowning face surrounded by crossed out Oreo cookies for incorrect answers. In the nonsocial block, feedback was an image of an upward arrow surrounded by Oreo cookies for correct answers or an image of a downward arrow surrounded by crossed out Oreo cookies for incorrect answers. If no choice was made, the trial ended, and the fixation cross appeared again signaling the beginning of the next trial. The two conditions (face/"social" trials and arrow/"nonsocial" trials) were tested in separate blocks, each composed of 50 trials. A computer program predetermined correct versus incorrect answers in semi-random order such that participants got 50% "correct" and 50% "incorrect," with no more than three of the same feedback in a row. That is, each trial was marked to be correct vs. incorrect regardless of the participant's response.

Participants were verbally told that the reward for correct answers was a pack of Oreo cookies. If participants did not want the Oreo cookies, they were told that they could trade in cookies for fruit snacks. Importantly, in both the social and nonsocial feedback trials, the face/arrow information was incidental: it was not necessary for the participant to determine whether their response was correct. The participants were told that correct vs. incorrect responses were signaled by whether the Oreo cookies were intact or crossed out.

Incidental stimuli in the social condition were faces obtained from the NimStim database (Tottenham et al., 2009) that were smiling for "correct" answers and frowning for "incorrect" answers. The faces were presented in semi-random order, with no face appearing more than once in a row. Incidental stimuli in the nonsocial condition were composed of scrambled face elements from the social condition formed into an arrow that pointed upwards for “correct” answers and downwards for “incorrect” answers. Whether individuals viewed the social versus nonsocial block first was counterbalanced between participants. Refer to Figure 1 for feedback stimuli and refer to Figure 2 for an example of presentation order.

Figure 1

Feedback stimuli. (A) and (B) are nonsocial stimuli presented to participants during the nonsocial condition. (A) depicts an upward facing arrow surrounded by intact Oreos to indicate a correct response, while (B) depicts a downward facing arrow surrounded by crossed-out Oreos, indicating an incorrect response. (C) and (D) are social stimuli presented to participants during the social condition. (C) depicts a smiling face surrounded by intact Oreos to indicate a correct response, while (D) depicts a frowning face surrounded by crossed-out Oreos, indicating an incorrect response.

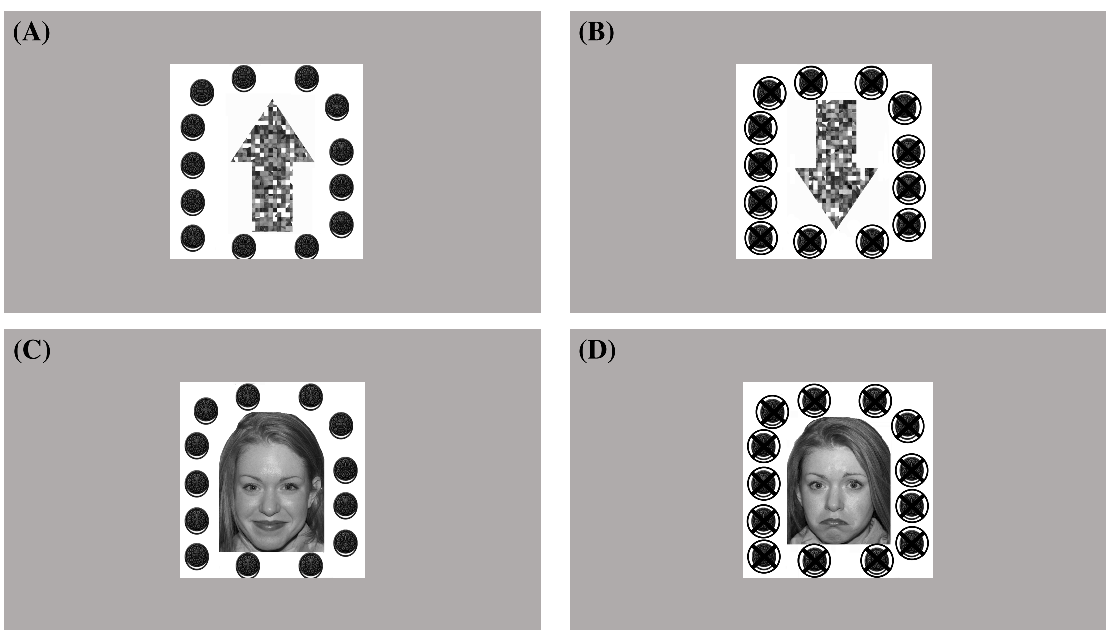
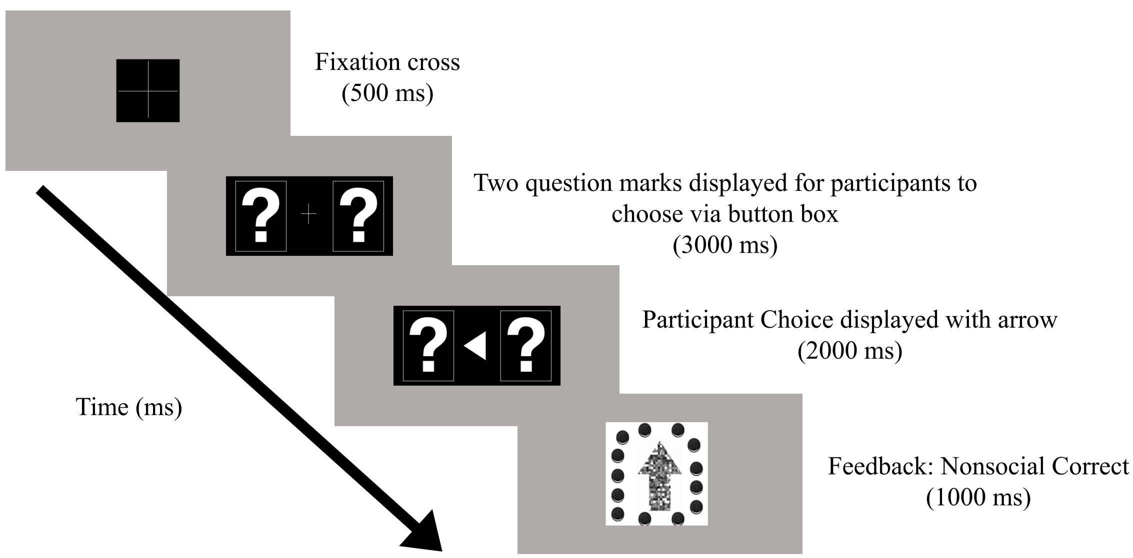


Figure 2

An example of stimulus presentation order. A fixation cross is displayed for 500 ms, followed by two question mark boxes for 3000 ms. The participant chose either the left or right question mark via button box. An arrow appears for 2000 ms, pointing in either the left or right direction to indicate the participant's choice. Feedback is then presented on the screen for 1000 ms. Note that in this example, correct nonsocial stimuli is depicted with an upward facing arrow surrounded by intact Oreos. Refer to Figure 1 for examples of possible social and nonsocial feedback stimuli.



EEG Recording

Participants wore a standard, fitted cap (Brain Products ActiCap) with 32 silver/silver-chloride (Ag/AgCl) electrodes placed according to the extended international 10-20 system. Continuous EEG was recorded using Brain Vision Recorder with a reference electrode at Cz and re-referenced offline to the average activity at left and right mastoids. Electrode resistance was kept under 50 kOhms. Continuous EEG was amplified with a directly coupled high pass filter (DC) and notch filter (60Hz). The signal was digitized at a rate of 500 samples per second. Eye movement artifacts and blinks were monitored via horizontal electrooculogram (EOG) placed at the outer canthi of each eye and vertical EOG placed above and below the left eye. Trials were time locked to the onset of the feedback stimulus. To measure reward processing, the baseline period was set to -100 to 0 ms, and the data were epoched from -100 to 800 ms. Trials with no behavioral response, or containing electrophysiological artifacts, were excluded.

For the RewP, based on previous studies, mean amplitude was calculated for each condition taken from the frontocentral electrodes, Fz, between 275 and 425 ms. The RewP was then calculated as the difference between the correct and incorrect feedback for the social and nonsocial conditions, respectively.

Artifacts were removed via a four-step process. Data were visually inspected for drift exceeding +/-200 mV in all electrodes, high frequency noise visible in all electrodes larger than 100 mV, and flatlined data. Following inspection, data were epoched and eyeblink artifacts were identified using independent component analysis (ICA). Individual components were inspected alongside epoched data, and blink components were removed. To remove additional artifacts, we utilized a moving window peak-to-peak procedure in ERPlab (Lopez-Calderon & Luck, 2014), with a 200 ms moving window, a 100 ms window step, and a 150 mV voltage threshold.

For both conditions (face, arrow) and both feedback types (correct, incorrect), mean brain activity was calculated between 275 and 425 ms after feedback onset. The RewP was defined as a difference wave where brain activity in response to “incorrect” feedback was subtracted from brain activity in response to “correct” feedback. For statistical analysis, mean amplitude of the RewP between 275 and 425 ms was utilized.

Splitting ERP Trials in Half

A unique methodology was employed to analyze the first and last half of trials within each condition separately, rather than averaging across all trials. The benefit to splitting trials this way is that habituation to the stimuli and feedback over time can be accounted for. Thus, the reaction to initially presented trials in a condition can be examined separately from the last half of presented trials to compare RewP average amplitude differences. To compare reward-related brain activity during the first half and second half of trials, the first half and last half of all accepted trials (i.e., trials that were not removed through any of the processes mentioned above) were extracted for each of the two conditions (faces and arrows). To be included in statistical analysis, subjects had to have a minimum of 6 trials in each half of each condition. Our final analyses included 7 adolescents with ASD and 7 TD adolescents.

Statistical Analyses

All analyses were conducted using SPSS Version 26 (2019). Prior to analysis, correlations between ERP amplitude by half and condition, age, and IQ were conducted. No significant relationships were observed (p's > .421). An independent samples t-test was conducted to test for differences in the number of acceptable trials between ASD and TD groups to ensure that TD participants and ASD participants provided sufficient useable EEG data. To test the differences in ERP condition (social, nonsocial), ERP half (first, last), time (time 1, time 2), and group (ASD, TD), a repeated-measures analysis of variance (ANOVA) was conducted. Likewise, a repeated-measures ANOVA was conducted to test differences between groups on behavioral questionnaires, including the SRS-2 total score, SSIS Social Skills score, and TASSK-R score. Bonferroni post hoc tests for all repeated-measures ANOVA were set to .05. Finally, Pearson correlations were conducted to examine how change on the behavioral measures from pre- to post-intervention related to ERP results. Difference scores were calculated for the SRS-2, SSIS social skills subscale, and TASSK-R by subtracting post-intervention scores from pre-intervention scores.

Results

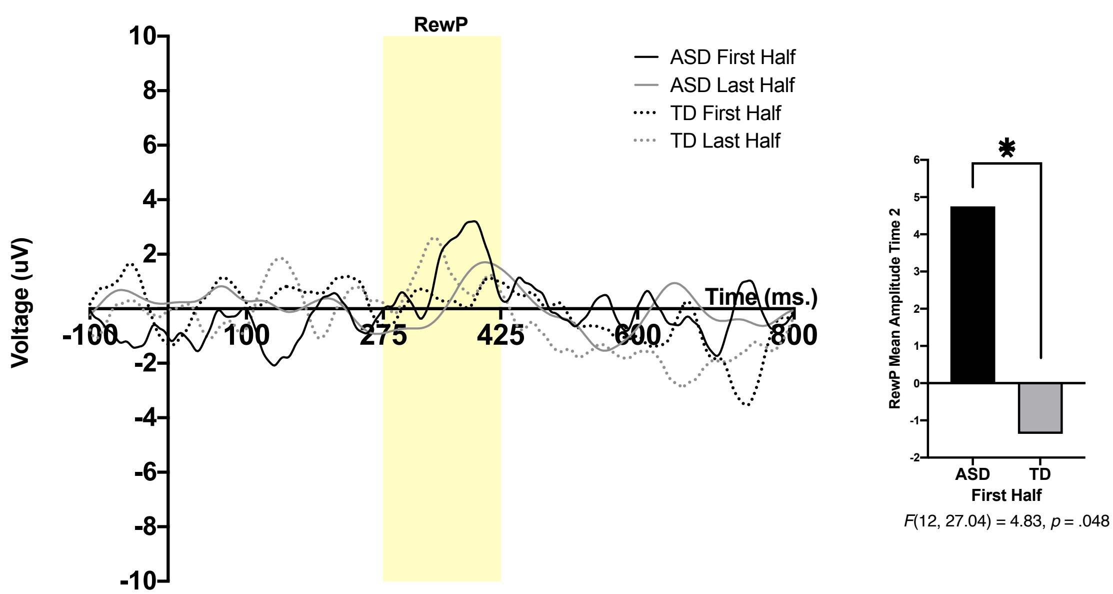
ERP results

An independent samples t-test was conducted to ensure no significant differences in the number of acceptable trials were present between groups (all *p'*s > .638).

A 2 (group) x 2 (condition) x 2 (time) x 2 (half) repeated-measures ANOVA was run. Condition (social, nonsocial), time (pre-intervention, Time 1; post-intervention, Time 2), and half (RewP amplitude during the first and second half of the task) were within-subjects variables, and group (TD, ASD) was used as a between-subjects variable. A significant 3-way interaction was found between time, half, and group; $F(12, 20.76) = 5.20$, $p = .042$. Pairwise comparisons revealed a significant effect of group such that the ASD group had significantly larger RewP amplitude compared to the TD group in the first half of trials at Time 2 (post-intervention); $F(12, 27.04) = 4.83$, $p = .048$. Thus, regardless of condition, the ASD group had larger reward-related brain activity in the first half of presented trials after completing intervention compared to the TD group. No other significant main effects or interactions were observed. See Figure 3 for grand average waveforms at Time 2.

Figure 3

Grand average waveforms during the first and second half of trials in TD and ASD participants at Time 2 (post-intervention). Significant differences were observed between the ASD and TD groups during the first half of trials at Time 2 (post-intervention). Note that for the purposes of this figure, the ERP was filtered using a 25 Hz low-pass filter.



Behavioral Results

To understand how behavioral measures changed over time for each group, 2 (Group) x 2 (Time) repeated measures ANOVAs were conducted on measures of autism symptoms (SRS-2), social skills (SSIS social skills subscale), and PEERS-specific knowledge (TASSK-R).

For the SRS-2, a main effect of group was observed, $F(1,12) = 9.51$, $p = .009$, such that the TD group had significantly lower SRS-2 scores than the ASD group. Lower SRS-2 scores indicate less severe social impairments. A marginally significant interaction between group and time was observed, $F(1, 12) = 4.56$, $p = .054$. Post-hoc follow-up tests using Bonferroni corrections revealed a significant difference between groups on the SRS-2 at Time 1 (pre-intervention), such that the TD group had lower scores than the ASD group ($p = .001$). The difference between the two groups was no longer significant at Time 2 (post-intervention). Pairwise comparisons also revealed a marginally significant effect of time for the ASD group such that SRS-2 scores decreased from pre- to post-intervention ($p = .07$), whereas no effect of time was observed for the TD group.

For the SSIS social skills subscale, a marginally significant interaction between group and time was observed, $F(1,12) = 4.20$, $p = .063$. Post-hoc follow-up tests using Bonferroni corrections revealed a significant effect of time for the ASD group, such that SSIS social skills subscale scores increased from pre- to post-intervention ($p = .035$), whereas no effect of time was observed for the TD group. Higher scores on the SSIS social skills subscale indicate better social skills. Pairwise comparisons also revealed a marginally significant difference between groups on the SSIS social skills subscale at Time 1 (pre-intervention) such that the TD group had higher scores than the ASD group ($p = .071$), whereas the difference between groups was not significant at Time 2 (post-intervention).

For the TASSK-R, a main effect of group was observed, $F(1,12) = 5.4$, $p = .038$ such that adolescents with ASD had higher scores on the TASSK-R compared to neurotypical teens. Higher scores on the TASSK-R indicate more understanding of PEERS-specific skills. A significant effect of time was observed, $F(1,12) = 45.82$, $p < .001$ such that TASSK-R scores increased from Time 1 (pre-intervention) to Time 2 (post-intervention). A significant interaction between time and group was observed, $F(1,12) = 25.7$, $p < .001$. Post-hoc follow-up tests using Bonferroni corrections revealed a significant effect of time for the ASD group such that scores on the TASSK-R increased from pre- to post-intervention ($p < .001$). No effect of time was observed for the TD group. Pairwise comparisons also revealed a significant difference between groups on the TASSK-R at Time 2 (post-intervention), such that the ASD group had higher scores on the TASSK-R compared to the TD group ($p = .001$), whereas the difference between groups was not significant at Time 1 (pre-intervention).

Table 2. Behavioral measures for time 1 and time 2 in ASD and TD groups.

Variable	ASD	TD
Time 1 *M (SD), Range*		
SRS-2	69.14 (14.18), 47 – 90	44.00 (4.55), 39 – 52
SSIS Social Skills	85.86 (25.13), 41 - 121	106.71 (11.93), 94-125
TASSK-R	14.29 (3.09), 10 - 19	14.57 (3.69), 10 – 21
Time 2 *M (SD), Range*		
SRS-2	61.43 (14.89), 45 - 88	48.00 (14.46), 39 – 80
SSIS Social Skills	93.57 (22.78), 51 - 120	105.00 (9.27), 96 - 119
TASSK-R	24.29 (4.61), 17 - 29	16.00 (2.65), 14 - 21

Brain and Behavior Correlations

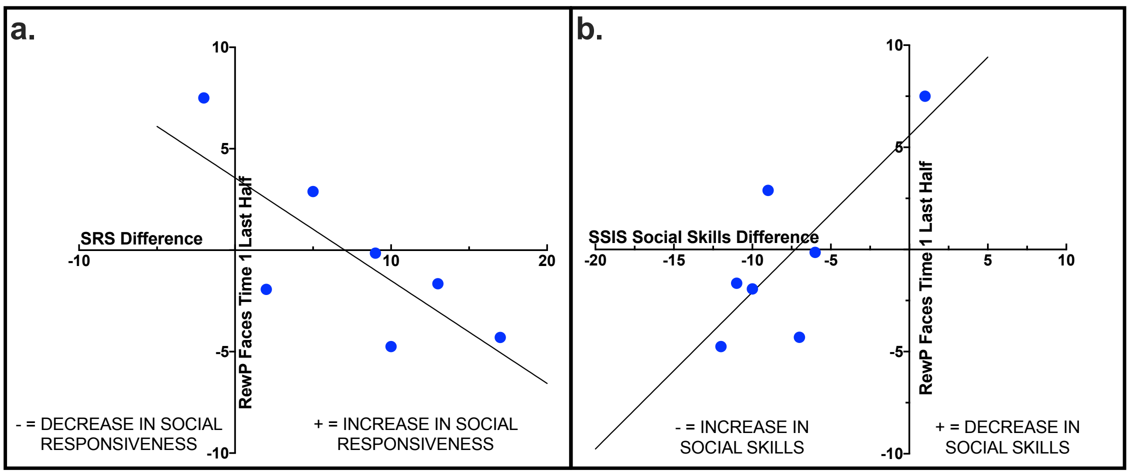
Within the ASD group, correlations were conducted to examine how change on the behavioral measures from pre- to post-intervention related to ERP results. Difference scores were calculated for the SRS-2, SSIS social skills subscale, and TASSK-R by subtracting post-intervention scores from pre-intervention scores. A significant negative correlation was observed between the SRS-2 difference score and RewP amplitude in the last half of the social condition at Time 1 ($r = -.77$, $p = .044$), such that participants with ASD who had less reward-related brain activity in response to social stimuli at Time 1 (pre-intervention) displayed larger improvements on the SRS-2 compared to individuals with more robust social reward-related brain activity at Time 1. See Figure 4a.

A positive correlation was observed between RewP amplitude in the last half of the social condition at Time 1 (pre-intervention) and SSIS social skills subscale difference score ($r = .78$, $p = .038$), such that adolescents with ASD who displayed less social reward-related brain activity during the last half of trials in the social condition at Time 1 exhibited greater improvements in social skills from pre- to post-intervention compared to those who displayed more robust reward-related brain activity prior to intervention. See Figure 4b.

Figure 4

a. Correlation between SRS-2 difference score before and after intervention in the ASD group and RewP mean amplitude in the last half of the social condition at Time 1, (*r* = -.77, *p* = .04).

b. Correlation between SSIS Social Skills difference score before and after intervention in the ASD group and RewP mean amplitude in the last half of the social condition at Time 1, (*r* = .78, *p* = .04).



Finally, a negative correlation was found between the TASSK-R difference score and RewP amplitude in the last half of the social condition at Time 2 (post-intervention) (*r* = -.79, *p* = .035), such that participants with ASD who demonstrated larger increases in their knowledge of intervention-specific knowledge displayed larger social reward-related brain activity in response during the second half of trials compared to participants who had smaller increases in intervention-specific knowledge from pre- to post-intervention.

No significant correlations were observed between behavioral measures and reward-related brain activity in the nonsocial (arrow) condition.

Discussion

This study investigated the effect of the PEERS social skills intervention on both neural correlates of reward processing and social behaviors in adolescents with ASD. Specifically, we sought to understand how reward-related brain activity changed throughout the course of a task by comparing brain activity during the first and second half of trials.

Prior to the start of intervention, patterns of reward-related brain activity did not differ between participants with ASD and their neurotypical peers. However, after intervention, participants with ASD were more sensitive, or responsive, to all reward types (both social and nonsocial) during the first half of the ERP paradigm. Increased brain activity related to reward processing indicates increased reward responsivity in adolescents with ASD, irrespective of stimulus type, after participating in a social skills intervention. Larger reward responsivity is similar to what Kohls and colleagues (2012) have described as a “liking” response involving the consumption of rewards that are salient. Initial sensitivity to rewards (i.e., during the first half of trials) may be heightened after exposure to frequent reinforcement strategies that were utilized throughout the intervention to encourage participant engagement.

Although a lack of significant differences in brain activity between groups at Time 1 (pre-intervention) is in contrast with some previous intervention literature utilizing neuroscience methods (e.g., Van Hecke et al., 2015), changes in brain activity from pre- to post-intervention in individuals with ASD has been reported previously (Venkataraman et al., 2016; Voos et al., 2013; Yang et al., 2016; Yang et al., 2018). Notably, previous research measuring brain activity before and after intervention in individuals with ASD either did not utilize a neurotypical control group (e.g., Venkataraman et al., 2016; Voos et al., 2013; Yang et al., 2016; Yang et al., 2018), or had a neurotypical group but did not test children with ASD and the TD group at both pre- and post-intervention (Dawson et al., 2012; Van Hecke et al., 2015). Collecting data from both teens with ASD and their neurotypical peers, as well as utilizing neuroscience paradigms that are hypothesized to capture changes directly relevant to the intervention itself, are both important strategies when measuring neural correlates of change after an intervention (for a review, see Stavropoulos, 2017). In the current study, we hypothesized that increased reward-related brain activity would be observed across the course of the ERP task after teens with ASD underwent an intervention that utilized social positive reinforcement principles to increase success in making and keeping friends. To our knowledge, this is the first investigation of brain activity of both neurotypical teens and those with ASD before and after participation in an intervention (or, in the case of the TD group, before and after a delay in which no intervention took place).

Contrary to our hypotheses, brain activity did not differ in response to condition (social or nonsocial) for either group. This contrasts with previous findings using this paradigm with young children with and without ASD (Stavropoulos & Carver, 2014a, 2014b). However, this is the first time this ERP paradigm has been utilized with adolescents to study changes from pre- to post-intervention. Thus, differences between the current study and previous research might reflect developmental changes. It is plausible that adolescents with and without ASD are less overtly motivated by food rewards as they would be by other reward types (e.g., monetary), and thus may have found the paradigm less engaging/rewarding than younger children. Future studies should consider utilizing this paradigm in a cross-sectional design with different age groups to better understand the effects of age on reward responsivity.

As expected, at Time 1 (pre-intervention), the ASD group had more severe social-communication impairments associated with ASD (measured by the SRS-2) and social skills (measured by the SSIS social skills subscale) than the TD group. Adolescents with ASD improved on both measures after intervention (Time 2), which mirrors previously reported findings of the effectiveness of the PEERS social skills intervention (Laugeson et al., 2012, 2015). No differences were observed from Time 1 to Time 2 in the TD group. This was expected, as the neurotypical teens did not participate in the intervention. Importantly, only one ASD participant remained in the range for clinical concern on both the overall SRS-2 score and SSIS social skills subscale score following intervention. This is important, as it suggests that change from Time 1 to Time 2 was not only statistically significant but also clinically meaningful. Further, no significant differences were observed between groups on the SRS-2 or SSIS social skills subscale at Time 2 (post-intervention), suggesting that both social-responsiveness symptoms and social skills in our sample of adolescents with ASD began to resemble social behaviors observed in our neurotypical participants.

One of the most interesting findings of our investigation was that ASD participants who demonstrated less robust social reward-related brain activity in the second half of trials prior to the intervention (Time 1) evidenced the biggest gains from Time 1 to Time 2 in both social responsivity and social skills. This suggests that perhaps the adolescents who benefitted the most from PEERS were those who had the most "room to improve" in terms of social reward response. This also provides initial evidence that neural characteristics of reward responsiveness prior to intervention may serve as an indicator of treatment response. That is, it might be possible to utilize neural correlates of social reward responsivity to predict which individuals with ASD might benefit the most from participating in PEERS. To further investigate this potential predictor of intervention efficacy, future research with a larger sample size and a randomized control group should be conducted.

Limitations

This study is part of a larger investigation of a social skills intervention, and this report serves as an initial analysis. Thus, the current study has a small number of participants. Additionally, randomization of treatment was not performed (i.e., a waitlist control group was not utilized), and ASD participants were aware of their enrollment in the social skills intervention (i.e., parent rating forms were not completed "blind," as parents were actively participating in the PEERS intervention with their teen). Thus, we cannot rule out the possibility that improvements in parent ratings in the ASD group were due to the expectation of improvements. Finally, findings from this study cannot be generalized to all individuals with ASD, as one of the criteria for participation was that the adolescent was motivated to participate in PEERS and wanted help making and keeping friends. Thus, this sample consisted of adolescents who were highly motivated to learn social skills.

Conclusion

The results of our study have important implications for intervention outcomes in adolescents with ASD. First, these findings add to the existing literature on the efficacy of PEERS for adolescents with ASD. Second, we found evidence for increased reward sensitivity in adolescents with ASD (compared to their neurotypical peers) after participation in the intervention. This suggests that participating in PEERS increases reward system sensitivity in teens with ASD. Finally, we found that teens who benefitted the most from the intervention (i.e., had the largest gains in social skills and largest decrease in social-communicative impairments) were those with less reward-related brain activity in response to faces prior to the intervention. This relationship between symptom improvement and brain activity prior to the intervention suggests that PEERS might be most effective for teens with ASD who have “room to grow” in their social reward responsivity, whereas teens with ASD who already have higher levels of social reward responsivity might benefit less. Finally, neuroscience measures may be reliable predictors of teens’ responsiveness to treatment because they are independent of potentially biased parent ratings.

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