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RESEARCH ARTICLE

Dysfunction in interpersonal neural synchronization as a mechanism for social impairment in autism spectrum disorder

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Abstract

Social deficits in autism spectrum disorder (ASD) have been linked to atypical activation of the mentalizing network. This work, however, has been limited by a focus on the brain activity of a single person during computerized social tasks rather than exploring brain activity during in vivo interactions. The current study assessed neural synchronization during a conversation as a mechanism for social impairment in adults with ASD (n = 24) and matched controls (n = 26). Functional near-infrared spectroscopy (fNIRS) data were collected from the prefrontal cortex (PFC) and tempoparietal junction (TPJ). Participants self-reported on their social communication and videos of the interaction were coded for utterances and conversational turns. As expected, controls showed more neural synchrony than participants with ASD in the TPJ. Also as expected, controls showed less social communication impairment than participants with ASD. However, participants with ASD did not have fewer utterances compared with control subjects. Overall, less neural synchrony in the TPJ was associated with higher social impairment and marginally fewer utterances. Our findings advance our understanding of social difficulties in ASD by linking them to decreased neural synchronization of the TPJ.

Lay Summary: The coordination of brain responses is important for efficient social interactions. The current study explored the coordination of brain responses in neurotypical adults and adults with ASD to investigate if difficulties in social interactions are related to difficulties coordinating brain responses in ASD. We found that participants with ASD had more difficulties coordinating brain responses during a conversation with an interacting partner. Additionally, we found that the level of coordination in brain responses was linked to problems with social communication.

KEYWORDS
ASD, neural synchrony, social communication impairment, social deficits, TPJ

INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits with reciprocal social interactions and social communication, as well as restricted interests and repetitive patterns of behaviors (American Psychiatric Association, 2013). Social deficits in ASD have received substantial attention given their primary role in identification and diagnosis, as well as their uniqueness to ASD (American Psychiatric Association, 2013; Frith, 2003; Kanner, 1943; Wing & Gould, 1979). This impairment in social communication and social reciprocity is thought to stem from problems with the basic components of social processing typically acquired early in life by neurotypical children (Dawson et al., 1998; Jones & Klin, 2009). Behavioral work has consistently demonstrated that ASD is associated with deficits in skills such as facial visual attention (Klin

et al., 2002; Pelphrey et al., 2002), identification of social cues (Chambon et al., 2017; Jones & Klin, 2009), perception of biological motion (Klin et al., 2009; Nackaerts et al., 2012), theory of mind (Baron-Cohen et al., 1985; Burnside et al., 2017; Ozonoff et al., 1991), and general social motivation (Burnside et al., 2017; Chevallier, Grèzes, et al., 2012; Chevallier, Kohls, et al., 2012), all basic components of stimulus processing necessary for effective social interactions. For example, Pelphrey et al. (2002) found that when looking at pictures of faces, participants with ASD spent more time looking at non-feature areas of the face and had greater difficulties recognizing emotions based on facial expressions. In a similar study, Klin et al. (2002) found that individuals with ASD fixated on the eyes of characters when watching video clips less than controls. They also found that more time fixating on objects and less time fixating on mouths was linked with decreased social functioning and greater social impairment in individuals with ASD (Klin et al., 2002). Taken together, findings from these studies offer evidence for the links between basic components of social processing and social impairment in ASD.

While there is substantial evidence that deficits in these basic components are key diagnostic features of ASD, there is still a significant amount of unexplained variability in social impairment in this group (Pelphrey et al., 2011; Sally & Hill, 2006; Wing, 1988). Neuroimaging work in individuals completing computerized social tasks has shown that the components of social processing (e.g., the ability to interpret social cues and attribute mental states) are linked to a network of regions including the temporoparietal junction (TPJ), the superior temporal sulcus (STS), the medial prefrontal cortex (mPFC), and the posterior cingulate cortex, among other regions, typically referred to as the mentalizing network (Decety & Lamm, 2007; Kleinhans et al., 2008; Krall et al., 2015; Schultz, 2005; Schultz et al., 2000). These regions exhibit atypical patterns of activation and connectivity in ASD (Kleinhans et al., 2008; Krall et al., 2015; Lombardo et al., 2010; McPartland et al., 2011). For example, one study found that while adults with ASD demonstrated activation of the STS during a gaze shifting paradigm similarly to controls, participants with ASD were unable to modulate activity in these regions based on the context of the gaze shift (i.e., following vs. violating expectations of where the actor should look (Pelphrey et al., 2005). In another study, children and adolescents with ASD showed reduced activation of various regions including the left TPJ, the mPFC, the posterior cingulate cortex (PCC), the left inferior gyrus, and the left cerebellum during a theory of mind task condition where the figures' movements can be interpreted as stemming from thoughts and feelings (White et al., 2011). However, when looking at conditions where the figures interact in a simple way or when the figures did not interact at all, the same differences in brain activation were not found (Kana et al., 2015). The findings from these studies suggest that the deficits in social interactions observed in individuals with ASD, such as the difficulties found in the theory of mind tasks like the ones described above, likely stem from disrupted functioning of the mentalizing network. However, this research has been limited by a focus on the brain activity of a single individual while completing computerized tasks, reducing our ability to understand to what extent brain activity within these regions during in vivo interactions plays a role in these social deficits.

Within this mentalizing network, the TPJ has been primarily implicated in processing the meaning of social signals, with connectivity to the mPFC (Saxe & Kanwisher, 2003; Van Overwalle, 2009; Young et al., 2010). In a study with young adults involving an MRI task where they were asked to identify the most logical ending to a series of comic strip vignettes, participants with ASD showed decreased connectivity within the theory of mind network during causal attributions (Murdaugh et al., 2014). Decreased connectivity within this network was specific to the TPJ, suggesting that the TPJ might be a particularly important region within the mentalizing network for healthy social interaction skills (Murdaugh et al., 2014). In another study, while individuals with ASD and controls showed activation of the mentalizing network, individuals with ASD showed less activity than controls in the TPJ during an episode of a popular sitcom show depicting naturalistic social interactions (Pantelis et al., 2015). Thus, while the mPFC and the TPJ both play crucial roles in social impairment in ASD, the TPJ appears to be a particularly important region for understanding social impairment in ASD.

While past neuroimaging work has demonstrated deficits in the neural processing of social interaction in ASD, especially in the TPJ, most of this work has not used an in vivo examination of the brain during real-time interactions, limiting the inferences that can be made about how neural processing might be disrupted *during* these interactions in ASD (Dumas et al., 2010; Rolison et al., 2015). Thus, approaches that allow for real-time measurement of the brain of interacting partners are needed to clarify the neural underpinnings of social reciprocity (Schilbach et al., 2013). There is substantial evidence that humans have a natural tendency to coordinate behavioral and physiological responses (Chartrand & Bargh, 1999; Marsh et al., 2009) and research suggests that this ability is disrupted in individuals with ASD (Baker et al., 2015; Fitzpatrick et al., 2016). For example, one study found that adolescents with ASD showed less synchronization with their parents in both intentional and spontaneous interpersonal coordination during a pendulum coordination paradigm (Fitzpatrick et al., 2016). Given that there is some work to suggest that the coordination of responses during social interactions may be disrupted in ASD, and that there seem to be some links between deficits in neural processing and social responding in this group, research on the examination of in vivo neural

coordination could be particularly useful for clarifying what might be the biological mechanisms for these deficits.

In the past decade, hyperscanning has allowed for the study of the coordination of neural responses (i.e., neural synchrony) during in vivo exchanges, allowing to circumvent constraints of ecological validity that affected previous studies (Cui et al., 2012; Hasson et al., 2004; Montague et al., 2002; Quiñones-Camacho et al., 2019). Research on neural synchrony has revealed increased coupling during cooperative singing (Osaka et al., 2015), face-to-face communication (Jiang et al., 2012), cooperative Jenga (Liu et al., 2016), and in classroom settings among students and between students and teacher (Bevilacqua et al., 2019; Dikker et al., 2017). Relevant to the study of in vivo social interactions, Jiang et al. (2012) found that dyads showed increased neural synchrony in the IFG, a region of the PFC, during face-to-face conversations compared with a back-to-back conversation, a face-to-face monologue, or a back-to-back monologue. Additionally, neural synchrony during the face-to-face conversation predicted communicating behavior (e.g., facial expressions and gestures) during the interaction, suggesting that measures of neural synchrony are useful for understanding social communication behaviors. While this study did not include participants with ASD, and thus, does not directly speak to differences in social communication in ASD, their findings suggest a potential neural mechanism for social communication that could be relevant for research on ASD. Specifically, it is possible that social communication impairment be linked with difficulties in the synchronization of neural responses with an interacting partner, but more work is needed to test this hypothesis.

Though there is little evidence to date for this, recent work is starting to emerge demonstrating the utility of using social neuroscience approaches for understanding social impairment in ASD (; Liu et al., 2019; Pan & Cheng, 2020). For example, a study using fNIRS to explore neural synchrony during a conversation in neurotypical adults found that higher scores on a measure of broad ASD phenotype were negatively associated with synchronous activation of the prefrontal cortex and the superior temporal sulcus, primary regions for social cognition (Suda et al., 2011), supporting the idea that social deficits are linked with difficulties in the synchronization of brain responses in the ASD spectrum. In a more recent study with children with ASD, more severe autism symptoms were associated with lower levels of parent–child neural synchrony of the PFC during a cooperation task (Wang et al., 2020). In another recent study with 8–18-year-olds, participants with ASD showed decreased behavioral synchrony compared with a control group, but the same was not true when looking at neural synchrony of the PFC (Kruppa et al., 2020). While surprising, the authors suggest that this lack of significant group differences may be due to the task design and that the use of a more naturalistic design where higher levels of social interaction are needed may be warranted to identify these group differences. Given the mixed results and how little work currently exists on brain-to-brain synchronization during in vivo interactions in ASD, more work is needed to disentangle the role of neural synchrony as a potential neural marker of social impairment in ASD. The current study sought to extend this work by exploring differences in neural synchrony as a potential marker of social impairment in adults with ASD. We used fNIRS to assess medial prefrontal cortex (mPFC) and TPJ activation in ASD and control participants during a conversation with an unfamiliar partner (always the same partner) extending previous work on neural synchrony by exploring synchrony of the TPJ as well as the PFC and by focusing on neural synchrony during a more complex form of social interaction (i.e., a conversation). fNIRS is a useful technique for the study of social difficulties in ASD given its noninvasive nature, ease of use, and high tolerance to the movement (Aslin & Mehler, 2005; Iwanaga et al., 2013; Zhang & Roeyers, 2019). Participants self-reported on their social communication impairment, and conversations were coded for conversational turns and subject utterances. We hypothesized that participants with ASD would show lower neural synchrony during a conversation with a stranger compared with controls. Additionally, we expected less neural synchrony to be associated with more social communication impairment and fewer subject utterances.

METHOD

Participants

30 adults with ASD and 31 control adults (18–43-years-old; matched for age, sex, race, and income) consented to participate in the study, which was approved by the University of Pittsburgh. Participants were recruited through postings, local message boards, and referrals from clinics serving individuals with ASD. Exclusion criteria for all participants included low proficiency in English, history of trauma or loss of consciousness, history of seizures, being born prematurely, or having had medical complications during birth. Lastly, control participants were excluded if a first-degree relative had been diagnosed with ASD. Participants in the ASD group were screened to ensure a formal ASD diagnosis based on the Autism Diagnostic Observation Schedule – Second Edition (ADOS; Lord et al., 2012) during the last 3 years. The ADOS is a semi-structured assessment of communication, social interaction, and play for individuals suspected of having ASD, and is considered the gold standard for diagnosing autism spectrum disorder. If participants could not provide formal records of ADOS scores or their ADOS testing was completed 3+ years before their visit, a licensed speech-language pathologist with formal

ADOS research training administered the ADOS-2 (Modules 3 and 4) to confirm ASD diagnosis. Participants also completed the Kauffman Brief Intelligence Test (KBIT-2; Kaufman & Kaufman, 2004) at the beginning of the study to ensure their IQ was above a cutoff of 70 before taking part in any of the tasks. Out of the other 61 participants who consented to participate, 26 controls and 25 ASD participants qualified for the study and had usable data fNIRS Conversation Task. The race of the participants was mostly white (84%), with some participants reporting their race as Black (12%) or Asian (4%).

Social responsiveness scale

The Social Responsiveness Scale (SRS-A; Constantino & Todd, 2005) is a 65-item measure of traits associated with ASD. Each item is scored on a 4-point Likert scale (*3 = almost always true*; *0 = not true*). Items assess elements of reciprocal social communication, social use of language, and behaviors that are characteristic of ASD. Within the social domain, items assess awareness of social cues (Social Awareness subscale), appropriate interpretation of social cues (Social Cognition subscale), the ability to engage in reciprocal communicative responses (Social Communication subscale), and motivation to engage in social interactions (Social Motivation). In addition to these social domain scores, the SRS yields a general social communication impairment score (SCI; the mean of all four social subscales), a Restricted Interests and Repetitive Behaviors score (RIRB), and a Total Impairment score (mean of the SCI and RIRB scores). Higher scores on any of the scales indicate a higher degree of ASD-related social impairment. For the current study, we focused on these SCI and RIRB scores. This allowed us to test our hypothesis that greater impairment in social communication, but not necessarily other ASD traits such as restricted interests and repetitive behaviors, would be associated with neural synchrony. Additionally, because scores on this measure have been found to be dimensionally distributed in the general population (Constantino & Todd, 2003), all participants completed this measure, and associations were assessed for the entire sample as well as at the group level. The Cronbach's alpha reliability was high (SCI α =0.956; RIRB α =0.911).

Conversation task

Participants completed a conversation task with an experimenter while both members of the dyad wore fNIRS caps. The experimenter, a carefully trained female research assistant, served as the experimenter for all participants. The experimenter was introduced to the participants as a member of the laboratory, who was going to be doing tasks with them. The use of a single unknown experimenter allowed us to control for the level of intimacy within a dyad, as she was a stranger to all participants. Additionally, having a single experimenter for all participants reduced experimenter-driven variability in the interaction based on cross-person differences in intonation, physical appearance, and general behavioral patterns. The task started with a 15-s baseline, after which the prompt was displayed on the screen and the participant and experimenter were free to converse. The task consisted of four prompts. Each prompt served as a starting point for the dyad to converse. The prompts were: (a) "*where would you go on vacation?*"; (b) "*plan your perfect weekend day*"; (c) "*if you could have any job in the world, what would it be*?"; and (d) "*what is your favorite childhood memory*?". Before the task began, the dyad was told that a prompt would appear on the screen and that they would have 2 minutes to talk about the topic. After this, the dyad was left alone in the room. All dyads received the same four prompts in the same order.

The experimenter was trained to give the same initial response to the prompt for all participants and to attempt to keep the conversation going for the full period. However, the experimenter was trained to engage in naturalistic conversation as she normally would outside the laboratory. For example, in response to prompt 1, the experimenter said, "*I would go anywhere in the Caribbean because I love the beach and sunshine. I love the ocean and just relaxing watching the waves*." After this, the experimenter responded to the subject's comments and questions as she normally would. Therefore, while the general idea of the responses was the same, the experimenter content and count of utterances varied across dyads. The participant could choose if they wanted to answer the prompt first or if they preferred that the experimenter begin.

Conversational turns and utterance coding

Participants' verbal exchanges with the experimenter were offline coded. Trained coders were blind to the participants' group status and research questions of the study. A conversational turn was defined as *a discrete pair of utterances with at least one utterance by each member of the dyad*. We constrained the response to the initial utterance to within 5 s from the initial utterance to count the exchange as a conversational turn. For example, if the experimenter spoke and the subject responded, but then the experimenter spoke again and the subject did not respond, this was coded as a single conversational turn. An utterance was defined as *a continuous piece of speech beginning and ending with a clear pause*. These definitions are consistent with previous studies of verbal exchanges in both neurotypical participants and participants with ASD (Adams et al., 2002; Adams & Bishop, 1989b; Bishop & Adams, 1989; Bishop et al., 1998; Gilkerson et al., 2018; Romeo et al., 2018). If

the speaker paused after an utterance and then spoke again with a new idea (e.g., made a comment, paused, then asked a question about something else), this was counted as a separate utterance even if it happened within the same conversational turn. Due to the possibility of having multiple utterances within one conversational turn, these two scores represent separate, yet related, measures of social communication. The same procedures were used to code the experimenter's utterances. Coders completed coding for an initial set of six videos with the master coder, after which they coded independently. A total of 44 videos were codeable. Missing video data was due to the video not recording or missing audio. Participants missing video data did not significantly differ in any of our variables of interest, all ps > 0.36. Conversational turns and utterances were each summed to create three different scores: total conversational turns, total utterances by the experimenter, and total utterances by the subject. Coder consistency was good, ICCs = 0.74–0.88.

fNIRS data acquisition and preprocessing

A NIRScout system was used to collect fNIRS data using a continuous-wave (NIRx Medical Technologies LLC, Glen Head, NY). The light was emitted at 760 and 850 nm from 8 LED light sources and measured from 4 photodiode light detectors. Optical signals were collected at 15.625 Hz. The source-detector distance was 2.9–3.1 cm and the sensors were placed on a neoprene head cap. The 10–20 international coordinate system was used to position the fNIRS head cap for all participants. Sources were placed over AF3/AF4 and Fp1/Fp2 for the prefrontal cortex (PFC) and over CFC7/CFC8 and CCP7/CCP8 for the TPJ (see Supplemental Material S1 for a 3D view of the optode placement). Probes were registered to the Colin27 Brain Atlas (Holmes et al., 1998). Hair was manually parted under the optodes when necessary to improve signal detection. Preprocessing and activation analyses were conducted in the NIRS Brain AnalyzIR toolbox (Santosa et al., 2018). First, the fNIRS raw intensity signals were converted to changes in optical density. These optical density signals were then corrected for motion artifacts using the temporal derivative distribution repair (TDDR) method (Fishburn et al., 2019). The TDDR method has been shown to be superior to other motion correction methods such as MARA, CBSI, tPCA, k-Wavelete, and Spline-SG in activation-detection performance (Fishburn et al., 2019). The corrected optical density signals were then resampled to 4 Hz to reduce computation time for the synchrony calculations. Signal drifts in the data were then detrended by regressing out a discrete cosine transform regressor matrix with a maximum frequency of 1/128 Hz. After this, signals were converted to oxygenated hemoglobin concentration using the modified Beer–Lambert law.

Quantification of neural synchrony

Previous work has demonstrated that serial correlations in time series data can artificially inflate functional connectivity estimates resulting from Pearson correlations or wavelet transform coherence (Santosa et al., 2017). This increased false discovery rate can be controlled by using a robust correlation approach with temporally whitened signals (Santosa et al., 2017). Specifically, we used an autoregressively pre-whitened iteratively reweighted least-squares (AR-IRLS) General Linear Model to control type-I errors in the fNIRS statistical model by removing serial correlations that can inflate correlation estimates (Barker et al., 2013). A conservative model order of 32 was chosen to ensure the signals were properly whitened. To address the heavy-tailed noise often found in fNIRS data, we used robust correlation coefficients that were calculated between participants using a robust regression approach (Shevlyakov & Smirnov, 2011), where the geometric mean is taken of the robust regression coefficients obtained from regressing channel X onto channel Y and vice-versa, for example, $r = \sqrt{\hat{\beta}_{X\rightarrow Y}\hat{\beta}_{Y\rightarrow X}}$. Past work shows that these models statistically address both increased false-discovery rates introduced by serially-correlated noise due to physiology in fNIRS and outliers related to motion artifacts (Huppert, 2016). This approach has been shown to have better sensitivity-specificity characteristics compared with other approaches (Santosa et al., 2017). By using TDDR and AR-IRLS GLM with robust regression weights we effectively account for both systemic and motion-related artifacts in our data, reducing our likelihood of Type 1 errors and increasing the sensitivity-specificity of our model. Synchronization was quantified using the Fisher r-to-z transform of the absolute value of the robust correlation coefficient for the entire task. This was done to assess synchrony in all possible channel-pairs. Because we had no hypotheses regarding non-reciprocal connections (e.g., channel A of the participant connected with channel B of the experimenter, but not vice-versa), reciprocal connections were enforced to reduce the number of unique connections being calculated. This was done by taking the mean of the z-value, for example, $Z_{AB} = \frac{1}{2}(Z_{A_{Parent}B_{Child}} + Z_{A_{Child}B_{Parent}})$.

Statistical analysis of neural synchrony

To determine the appropriate null distribution for the synchrony values, synchrony was calculated between all possible subject pairs for the entire duration of the task. Thus, for each channel-pair, there were synchrony values for 52 concurrent (observed) dyads and 5304 non-concurrent (null) dyads ($N_{null} = \frac{N_{subject}^2 - N_{subject}}{2} - N_{dyad}$). The p-value associated with each value from an observed dyad was computed through a permutation test by determining the proportion of values from null-pairings that

were equal to or greater than the observed value, for example, $\hat{p} = \frac{\sum(Z_{null} \geq Z_{observed}) + 1}{N + 2}$. The constant terms were selected to ensure that the resulting p-values would be within a 0 to 1 range. Adjusted z-values were then derived from these estimated p-values using the inverse cumulative density function for the standard normal distribution. One ASD dyad had an adjusted Z-value over 4 SD from the mean and was removed from further analyses, resulting in 24 ASD participants included in analyses. The resulting values were then submitted to a mixed-effects model with group (ASD vs. Control) modeled as a fixed effect and dyad ID modeled as a random effect. The presence of synchrony was assessed for each group by applying the t-contrast corresponding to a 1-sample *t* test. Differences between groups were assessed with the "Control—ASD" t-contrast. The resulting *p*-values were then corrected for multiple comparisons by calculating the Benjamini-Hochberg FDR-corrected *p*-value (Benjamini & Hochberg, 1995) across all unique channel pairs. The peak of the adjusted z-values were computed across significant ($q < 0.05$) channel-pairs for each dyad and extracted for further analyses.

RESULTS

Preliminary analyses

First, we confirmed that our groups did not differ on IQ or any sociodemographic variables of interest. The control (M = 113.35, SD = 12.55) and ASD (M = 110.13, SD = 16.31) groups did not differ on IQ, ($t_{[48]}$ = 0.786, p = 0.436), age ($t_{[48]}$ = 0.575, p = 0.568) (Control: M = 26.27, SD = 7.70; ASD: M = 25.13, SD = 6.22) or income ($t_{[45]}$ = 1.558, p = 0.126) (Control: M = 3.44, SD = 2.06; ASD: M = 2.55, SD = 1.84; a score of 2 represents an income between $20-39 k, a 3 an income of $40-59 k). Lastly, the two groups did not differ based on gender ($\chi^2_{[1,50]}$ = 0.063, p = 0.802) or race ($\chi^2_{[2,50]}$ = 0.015, p = 0.992).

Between-group differences in self-reported social communication

As expected, the ASD group (M = 74.083; SD = 20.555) reported significantly more social communication impairment, ($t_{[48]}$ = 6.765, $p < 0.001$) than the control group (M = 35.769; SD = 19.490) as measured by the SRS-A. This was true for all aspects of social communication (Table 1): social Awareness ($t_{[48]}$ = 4.675, $p < 0.001$), social cognition ($t_{[48]}$ = 7.155, $p < 0.001$), social communication ($t_{[48]}$ = 6.020, $p < 0.001$), and social motivation ($t_{[48]}$ = 5.092, $p < 0.001$). The ASD group also reported more restricted interests and repetitive behaviors ($t_{[48]}$ = 6.269, $p < 0.001$) (ASD group: M = 18.708; SD = 7.135; Control group: M = 7.039; SD = 6.017).

Between-group differences in observed social communication

The Control group did not engage in more conversational turns $t_{(38)}$ = 0.256, p = 0.799, more experimenter utterances $t_{(38)}$ = 0.280, p = 0.781, or more subject utterances $t_{(38)}$ = 0.518, p = 0.608. This was likely due to the experimenter drawing out conversation from the subjects.

Between-group differences in neural synchrony

Neural Synchrony (i.e., neural synchrony between the experimenter and the participant) for each group relative to the null distribution derived from permutation testing can be found in Figure 1a and the group comparison can be seen in Figure 1b. The Control group showed significant neural synchrony with the experimenter during the

TABLE 1 Descriptive statistics for ASD and control groups

	ASD (n = 24)		Control (n = 26)		t test
	Mean	**SD**	**Mean**	**SD**	***p* value**
Social communication impairment	74.083	20.555	35.769	19.490	**< 0.001**
Social awareness	10.625	2.901	7.385	1.941	**< 0.001**
Social cognition	16.292	5.505	5.769	4.893	**< 0.001**
Social communication	31.333	10.128	14.500	9.643	**< 0.001**
Social motivation	15.833	5.411	8.296	5.283	**< 0.001**
Restricted interests and repetitive behaviors	18.708	7.135	8.115	5.302	**< 0.001**
Conversational turns	25.688	6.426	25.391	7.884	0.799
Experimenter utterances	36.125	8.785	37.261	12.388	0.781
Subject utterances	36.438	12.951	34.044	8.921	0.608
Neural synchrony	0.012	0.008	0.020	0.010	**0.004**

Note: Bold = t test significance $p < 0.05$. All six SRS subscales represent self-reported impairment (i.e., higher scores represent greater impairment).

conversation task compared with the null distribution (Peak channel: M = 0.020, SD = 0.010, Min = 0.001, Max = 0.035). For the ASD group, there was no significant neural synchrony between participants and the experimenter (Peak channel: M = 0.012, SD = 0.008, Min = 0.001, Max = 0.027). Between-group comparisons revealed significant differences between groups. The control group showed more neural synchrony of the right and left TPJ with the experimenter compared with the group with ASD (see Supplemental Material S2 for results with the deoxyhemoglobin signal).

Correlations between self-reported social communication and neural synchrony

As expected, more social communication impairments ($r_{[50]}$ = −0.283, p = 0.047; Figure 2) but not more restricted interests and repetitive behaviors ($r_{[50]}$ = −0.210, p = 0.144) were associated with less neural synchrony (Table 2) for the whole sample. Correlations did not reach significance for each of the groups separately. This was primarily driven by the social communication ($r_{[50]}$ = −0.279, p = 0.050) and social cognition ($r_{[50]}$ = −0.285, p = 0.045) subscales.

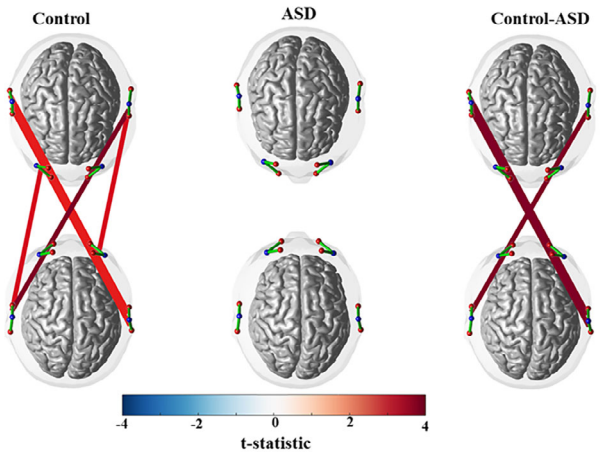

FIGURE 1 (a) Mean inter-subject synchronization for the conversational task relative to the null distribution derived from permutation testing. (b) Comparisons of inter-subject synchronization between the two groups

Correlations between observed social communication and neural synchrony

No significant correlations emerged with conversational turns ($r_{[40]}$ = 0.017, p = 0.917) or experimenter utterances ($r_{[40]}$ = −0.043, p = 0.794) combining across the two groups or looking at the two groups separately. However, higher subject utterances were marginally associated with stronger neural synchrony ($r_{[40]}$ = 0.288, p = 0.071).

DISCUSSION

The current study investigated deficits in neural synchrony with an unfamiliar partner during a naturalistic social interaction as a potential neural mechanism for social impairment in adults with ASD. We found that while on average, there was brain-to-brain neural synchronization between control participants and the experimenter, the same was not true for participants with ASD. Consistent with previous neuroimaging work that has demonstrated disrupted neural functioning during social tasks in participants with ASD (Kleinhans et al., 2008; Krall et al., 2015; Lombardo et al., 2010; McPartland et al., 2011; White et al., 2011), we found that participants with ASD did not show significant levels of neural synchronization with the experimenter during a conversation. We also found that lower levels of neural synchrony in the whole sample were associated with greater self-reported social communication impairment. However, these results need to be replicated as the correlations with each group separately were not significant. Taken

TABLE 2 Correlations for the whole sample

	1	2	3	4	5	6	7	8	9	10
1. Social communication impairment	-									
2. Social awareness	**0.736**	-								
3. Social cognition	**0.928**	**0.640**	-							
4. Social communication	**0.979**	**0.702**	**0.870**	-						
5. Social motivation	**0.909**	**0.553**	**0.785**	**0.862**	-					
6. Restricted interests and repetitive behaviors	**0.860**	**0.623**	**0.848**	**0.855**	**0.707**	-				
7. Conversational turns	−0.221	−0.059	−0.081	−0.244	**−0.329**	−0.078	-			
8. Experimenter utterances	−0.098	0.003	0.007	−0.144	−0.136	−0.064	**0.793**	-		
9. Subject utterances	−0.159	−0.158	−0.078	−0.163	−0.191	0.017	**0.699**	**0.660**	-	
10. Neural synchrony	**−0.283**	−0.120	**−0.285**	**−0.279**	−0.267	−0.210	0.017	−0.043	0.288+	-

Note: Bold = $p < 0.05$; + = $p < 0.08$. All six SRS subscales represent self-reported impairment (i.e., higher scores represent greater impairment).

together, our results suggest that the coordination of brain responses, a theorized mechanism for facilitating social interactions through shared mental states (Redcay & Schilbach, 2019; Wheatley et al., 2012), is disrupted in ASD. This is a substantial contribution to the field as most neuroimaging studies using social stimuli with participants with ASD have not used complex real-life interaction tasks to measure brain activity as we did.

Our finding that participants with ASD demonstrated lower levels of neural synchrony with the experimenter is consistent with previous behavioral and neurophysiological work (Fitzpatrick et al., 2016; Suda et al., 2011; Tanabe et al., 2012). Our findings suggest that the social difficulties often reported in participants with ASD during real-time interactions are linked to differences in the synchronization of the TPJ with an interacting partner. Given that ASD is considered a neurodevelopmental disorder, it is possible that decreased synchronization of the mentalizing network with a partner during interactions early in life complicates the coordination of behavioral responses, reducing opportunities to practice social skills, further solidifying social difficulties in this group. Studies on synchrony in young children with ASD support this, showing that impaired synchronization of biobehavioral responses is already present in early childhood (Baker et al., 2015; Hasegawa et al., 2016). Our findings also support the small but emerging line of work on neural synchronization in participants with ASD (Suda et al., 2011; Wang et al., 2020), by showing decreased neural synchronization of the TPJ in ASD vs. controls.

Our study is one of the first to show that social impairment in ASD is linked with difficulties in brain-to-brain synchronization during real-time interactions. Specifically, we found decreased synchrony of the TPJ with the experimenter compared with controls. This effect in the TPJ was expected, as several studies have demonstrated the primary role of the TPJ in social cognition (Kana et al., 2009). While we were aware that the TPJ plays an important role in social cognition from studies investigating the basic components of social interaction skills (Murdaugh et al., 2014; Young et al., 2010), our study design allowed us to extend these findings by assessing the TPJ during real-time interactions in a more ecologically valid paradigm that required social cognition skills. This finding is an important contribution to the field of ASD as it offers further evidence of neural mechanisms that may be disrupted in ASD, contributing to the social impairment often observed behaviorally. While more research is needed to identify biomarkers of social deficits in ASD and related disorders, it will be imperative for the researcher to use tasks and approaches that allow for an exploration of complex social dynamics such as the ones included in this study.

Our finding that neural synchrony was associated with social communication impairment is a particularly interesting finding. Social communication impairment has been demonstrated behaviorally in the past in individuals with ASD (Bishop et al., 2016; Jones & Schwartz, 2009; Ying Sng et al., 2018). While our findings are with the whole sample as we were underpowered to test these associations at the group level, our results provide important insight into the biological drivers of these observed difficulties in social communication. It is important to note that while the participants with ASD differed from controls in self-reported social communication impairment, they did not differ in the number of conversational turns or utterances. It is possible that this lack of group differences in observed communication is driven by the fact that all participants interacted with the same experimenter who was trained to give at least initial responses that were consistent across participants. Additionally, given that all participants with ASD in our sample were verbal and had IQs of 70+, it is also possible that this lack of group differences is due to this group engaging in some form of compensatory mechanism to complete the task despite their social communication impairments. Future work should explore neural synchrony and observed social communication impairment during fully unscripted verbal exchanges to clarify these findings. Additionally, while our work focused on verbal measures of social communication such as conversational turns and utterances, there are other non-verbal forms of social behavior that might influence neural synchrony. For example, joint attention would likely influence the level of attunement within a dyad. While we did not test this directly, our measure of conversational turns could be taken as a proxy of joint attention, as joint attention would be necessary for continuous reciprocal responding. However, what specific social behaviors are most strongly associated with neural synchrony during a conversation is still an empirical question and should be carefully probed in future studies. For example, while links with verbal communication (i.e., utterance counts) may not be reflected in decreased neural synchrony, it is possible that this deficit could be driven by impairments in aspects of nonverbal communication such as joint attention and facial expressions. Additionally, given that our study focused on adults, who are likely to have had social impairments throughout their lifespan, we are unable to determine whether neural synchrony is truly a mechanism for poor social communication, or if it results as the outcome of poor social communication skills from early in life. However, longitudinal approaches starting early in life would be needed to answer this question. Taken together, our findings provide initial evidence of the utility of using hyperscanning approaches during in vivo interactions to assess the neural underpinnings of social communication impairment in ASD.

While this study has several strengths, some limitations should be noted. First, while we chose to use the same experimenter as the partner for all participants, this could have influenced the variability in subject responses

resulting in more similar conversational exchanges across participants than would have happened otherwise. Given that this is, to our knowledge, the first study on ASD to explore links between the brain activity of interacting partners and observed communicative exchanges during a real-time conversation, it was important that we controlled for variability in experimenter driven factors as this more clearly allowed us to assess differences at the subject level (rather than the dyad level). Additionally, given the nature of the study, the role the experimenter played in the study, and that she was charged with interacting with all participants, experimenter knowledge of the group each participant belonged to was possible and could have minimally influenced some of the results. However, the fact that experimenter utterances did not differ across groups and that both groups still showed comparable variability in the level of neural synchrony, it is unlikely that the experimenter's knowledge of the group the participants belonged to substantially influenced our results. Future work should aim to explore similar associations with partners beyond an experimenter to assess whether measures such as utterance counts are useful indicators of social deficits during in vivo interactions. In addition, while our sample size was comparable to other studies with clinical populations, our modest sample prevented us from being powered to find associations at the group level. However, given that we were still able to find the expected patterns, we are confident that our results demonstrate effects that methodological constraints had precluded from being tested before. While the use of fNIRS allowed us to measure brain activity during a face-to-face interaction, we were limited by the brain regions we could assess. First, given the ROI approach of fNIRS, our optodes only covered areas that we had hypothesized would show increased synchronization, thus, we cannot rule out that the synchronization pattern found here is exclusive to these regions. Additionally, given the small number of photodiodes used in the study, we were unable to get enough coverage of our regions of interest to further parcel out the role of specific regions within the PFC and TPJ. Future studies should use a larger number of optodes to get a more comprehensive understanding of the role of the PFC and TPJ in neural synchronization. It is possible that this synchronization is brain-wide and not specific to these regions. It is also possible that what we measure is a systemic response. Future studies should explore neural synchrony during in vivo interactions using measurements over the entire head or short-channels to address some of these limitations. Additionally, since fNIRS can only measure regions within the cortex, we were unable to fully probe the mentalizing network. It is possible that the regions of the mPFC particularly relevant for mentalizing are too deep to be measured by fNIRS or that this synchronization is happening at a more intricate network level. However, given that research with MRI consistently finds the TPJ to be a primary region in social cognition, it is possible that measurements of this region are enough to capture neural synchrony deficits in ASD. Lastly, future work should use different analytical techniques to further disentangle the role of neural synchrony on social deficits in ASD. For example, machine learning approaches could be used to examine whether and how accurately neural synchrony can be used to identify individuals with ASD.

The current study is among the first to show decreased neural synchrony in participants with ASD with a communication partner and the first to link this with social communication impairment. These findings advance our understanding of social difficulties in ASD by suggesting a potential biological mechanism for these difficulties. Our findings offer many avenues for future work to further explore the neural underpinnings of social interaction impairment.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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