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Brain and motor synchrony in children and adolescents with ASD—a fNIRS hyperscanning study

Jana A. Kruppa,[1,2] Vanessa Reindl,[1,2] Christian Gerloff,[1,2,3]
Eileen Oberwelland Weiss,[1,2] Julia Prinz,[1] Beate Herpertz-Dahlmann,[4]
Kerstin Konrad,[1,2] and Martin Schulte-Rüther[1,2,5]

[1]Child Neuropsychology Section, Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Medical Faculty, RWTH Aachen University, 52074 Aachen, Germany, [2]JARA-Brain Institute II, Molecular Neuroscience and Neuroimaging (INM-11), RWTH Aachen & Research Centre Jülich, 52428 Jülich, Germany, [3]Department of Psychiatry, Psychosomatics, and Psychotherapy, University Hospital RWTH Aachen, 52074 Aachen, Germany, [4]Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Medical Faculty, RWTH Aachen University, 52074 Aachen, Germany and [5]Department of Child and Adolescent Psychiatry and Psychotherapy, University Medical Center Göttingen, 37075 Göttingen, Germany

Correspondence should be addressed to Vanessa Reindl, Department of Child and Adolescent Psychiatry, Psychosomatics, and Psychotherapy, University Hospital RWTH Aachen, Neuenhofer Weg 21, 52074 Aachen, Germany. E-mail: vreindl@ukaachen.de.
Jana A. Kruppa and Vanessa Reindl shared first-authorship.

Abstract

Brain-to-brain synchrony has been proposed as an important mechanism underlying social interaction. While first findings indicate that it may be modulated in children with autism spectrum disorder (ASD), no study to date has investigated the influence of different interaction partners and task characteristics. Using functional near-infrared spectroscopy hyperscanning, we assessed brain-to-brain synchrony in 41 male typically developing (TD) children (8–18 years; control sample), as well as 18 children with ASD and age-matched TD children (matched sample), while performing cooperative and competitive tasks with their parents and an adult stranger. Dyads were instructed either to respond jointly in response to a target (cooperation) or to respond faster than the other player (competition). Wavelet coherence was calculated for oxy- and deoxyhemoglobin brain signals. In the control sample, a widespread enhanced coherence was observed for parent–child competition, and a more localized coherence for parent–child cooperation in the frontopolar cortex. While behaviorally, children with ASD showed a lower motor synchrony than children in the TD group, no significant group differences were observed on the neural level. In order to identify biomarkers for typical and atypical social interactions in the long run, more research is needed to investigate the neurobiological underpinnings of reduced synchrony in ASD.

Key words: fNIRS hyperscanning; brain-to-brain-synchrony; motor synchrony; autism spectrum disorder; parent–child interaction

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Introduction

Autism spectrum disorders (ASDs) are a group of neurodevelopmental disorders, characterized by impairments in reciprocal social interaction, communication and repetitive stereotypic behavior (American Psychiatric Association, 2013). Deficits in social interaction are considered as most central to the disorder (Scott-Van Zeeland *et al.*, 2010). Several lines of research have indicated that behavior and brain functions related to diverse aspects of social interaction are altered in ASD, such as theory of mind (e.g. Kimhi, 2014), social reward processing (e.g. Scott-VanZeeland *et al.*, 2010; Kohls *et al.*, 2013; Kruppa *et al.*, 2019), joint attention (e.g. Oberwelland *et al.*, 2017) or spontaneous conversation (e.g. Jasmin *et al.*, 2019). Most studies investigating the underlying mechanisms of social interaction deficits in ASD focused on specific brain regions or networks ('social brain,' Pelphrey *et al.*, 2004, 2011) and corresponding behavioral responses. However, in order to capture the dynamic exchange during interpersonal encounters, simultaneous recordings of interacting brains may be necessary (e.g. Hari *et al.*, 2015). This is especially important in the light of evidence that individuals with ASD display less difficulties in social processing during passive observation of static social or non-social stimuli than during real-time social interactions (Bolis and Schilbach, 2018). Hence, examining interacting brains rather than a single person's brain seems a valuable tool to capture the neural mechanisms of social interaction deficits in ASD.

One important mechanism for the coordination of behavior during social interaction is synchronization. Synchrony describes a specific form of coordinated temporal relationship between events. Across mammalian species, synchrony already occurs during the earliest stages of social development. For example, the bond of parent and child is associated with processes of bio-behavioral synchrony, such as the coupling of parent's and child's physiology and behavior during social contact (Feldman, 2012, 2015). Bio-behavioral synchrony has been described as a central element of the socio-emotional development of the child (Feldman, 2012, 2015). Synchrony increases social bonding behaviors and enhances social perception and social cognition (Mogan *et al.*, 2017). In addition to behavioral (Feldman, 2015), physiological (Bornstein and Suess, 2000; Manini *et al.*, 2013) and endocrinological (Papp *et al.*, 2009) synchrony, 'neural' synchrony between parent–child dyads has been described recently (Reindl *et al.*, 2018; Miller *et al.*, 2019). Neural synchrony, also termed brain-to-brain synchrony, can be assessed using 'hyperscanning,' i.e., the simultaneous measurement of two individuals' brain activities while interacting with each other (Babiloni and Astolfi, 2014). Neural synchrony is based on joint neural oscillations reflecting bio-behavioral synchrony (Hasson *et al.*, 2012). It can be assumed that being mutually engaged in a given task or situation drives similar cognitive processes in both brains, resulting in similar neural oscillations. An increase in neural synchrony may reflect optimized interactive behavior, driven by internal predictions about the self and the other during (social) interactions (Dai *et al.*, 2018).

In a previous functional near-infrared spectroscopy (fNIRS) hyperscanning study of our research group, we demonstrated enhanced synchronization of parent's and child's brain activation (in comparison to stranger–child dyads) in the dorsolateral prefrontal and frontopolar cortex during a cooperative game (Cui *et al.*, 2012) but not during a competitive condition, in which dyads had to respond faster than the partner (Reindl *et al.*, 2018). Such effects in brain-to-brain synchrony may be

explained as emerging from mutual interaction during a task, with the interaction being characterized by a common goal and shared attention and behavioral adaptation processes (Reindl *et al.*, 2018). This approach has been applied in several other studies with healthy adults (e.g. Cui *et al.*, 2012; Cheng *et al.*, 2015; Baker *et al.*, 2016; Pan *et al.*, 2017), however, systematic investigation of parent–child dyads remains scarce. Furthermore, the few available studies have focused on infancy (e.g. Leong *et al.*, 2017) or early childhood (e.g. Reindl *et al.*, 2018; Nguyen *et al.*, 2020). Adolescence is a critical phase of life between late childhood and adulthood associated with a number of individual developmental changes which can be particularly challenging in ASD (Anderson *et al.,* 2011). In addition to physical maturation, adolescence is accompanied by profound mental and emotional changes, including the emotional separation from parents together with the development of increased autonomy and stronger identification with peers (Christie and Viner, 2005; Jager *et al.*, 2015). Functional neuroimaging research suggests a fundamental reorganization of the brain during this period (Konrad *et al.*, 2013). In particular, behavioral changes related to social cognition are paralleled by functional changes in the 'social brain,' e.g., functional activation of the medial prefrontal cortex during mental state attribution (Blakemore, 2008). Given such marked socio-cognitive and neurodevelopmental changes during adolescence, age-related changes in brain-to-brain synchrony from childhood to adolescence are a particularly important target of investigation, but have not been investigated yet.

Behavioral studies suggest that synchrony is reduced in individuals with ASD (Marsh *et al.*, 2013; Fritzpatrick *et al.*, 2016, 2017; Noel *et al.*, 2017; Curioni *et al.*, 2017). For instance, individuals with ASD showed less coordination of movements with their parents in a rocking chair paradigm (Marsh *et al.*, 2013), synchronized pendulum swings (Fitzpatrick *et al.*, 2016) and exhibited less interpersonal synchrony and complex movements in an interview setting (Noel *et al.*, 2017). The neural mechanism underlying reduced behavioral synchrony in individuals with ASD is poorly understood; hardly any studies have used hyperscanning during social interaction in ASD (but see Tanabe *et al.*, 2012 for fMRI hyperscanning during a joint attention task in adults with ASD). With respect to parent–child dyads in ASD, first evidence was provided by a recent fNIRS hyperscanning study. Wang *et al.* (2020) found that children with more severe ASD symptoms showed lower levels of behavioral and neural synchronization in the right superior frontal cortex with their parents during an adapted version of a cooperation game (Cui *et al.*, 2012). A competition condition was not investigated, even though this type of control condition would be necessary to ensure that it is not the temporal proximity of the dyads' responses alone that accounts for the increase in brain-to-brain synchrony during cooperation (see Cui *et al.*, 2012; Reindl *et al.*, 2018). Furthermore, the study did not include typically developing (TD) control subjects. To the best of our knowledge, no study to date has investigated in ASD whether the familiarity of the interaction partner (Pan *et al.*, 2017; Reindl *et al.*, 2018) might modulate brain-to-brain synchrony, taking into account potential age-related changes across childhood and adolescence. Since previous findings have demonstrated altered neural activity in children and adolescence with ASD during interactions with their mother as compared to a female stranger (Oberwelland *et al.*, 2017), influences of familiarity on brain-to-brain synchrony seem likely.

Hence, in the present study, we aimed at investigating brain-to-brain synchrony in ASD and TD participants during social

Table 1. Demographic data of the final participant samples

Characteristic	TD—complete (N = 41) M (s.d.)	ASD (N = 18) M (s.d.)	TD—matched (N = 18) M (s.d.)	t statistic*
Child age (years)	12.66 (2.79)	13.54 (2.96)	13.53 (2.99)	$t(34) = 0.010$, $P = 0.992$, $d = -0.00$
Parent age (years)	44.98 (5.14)	46.49 (5.57)	47.15 (4.68)	$t(34) = -0.386$, $P = 0.702$, $d = 0.13$
Stranger age (years)	23.40 (3.72)	25.00 (2.27)	23.53 (4.40)	$t(30) = 1.190$, $P = 0.243$, $d = -0.42$
IQ[a]	111.26 (12.23)	108.94 (17.47)	115.76 (14.50)	$t(32) = -1.239$, $P = 0.224$, $d = 0.43$
SRS total[b]	33.81 (20.35)	84.53 (33.29)	33.47 (19.03)	$t(25.45) = 5.490$, $P < 0.001$, $d = -1.88$
SCQ total[c]	3.43 (2.52)	17.72 (6.08)	3.50 (2.33)	$t(21.91) = 9.271$, $P < 0.001$, $d = -3.09$
FBB-HKS total[d]	9.82 (9.23)	24.94 (13.12)	7.61 (6.06)	$t(22.23) = 4.969$, $P < 0.001$, $d = -1.70$

[a]Intelligence quotient (IQ); TD—complete: 3 missing, ASD: 1 missing, TD—matched: 1 missing.
[b]SRS; TD—complete: 5 missing, ASD: 1 missing, TD—matched: 1 missing.
[c]SCQ; TD—matched: 4 missing.
[d]ADHD rating scale [FBB-HKS]; TD—complete: 3 missing, ASD: 1 missing.
*Independent-samples *t*-tests were conducted (two-sided) to compare ASD and TD-matched participants.

cooperation and competition, while accounting for the influence of the familiarity of the interaction partner as well as possible developmental effects across childhood and adolescence. In order to address these issues, we used a well-established cooperative and competitive computer game (see Reindl *et al.*, 2018) where children and adolescents with ASD played with their parents (as compared to TD children and adolescents and their parents) and with adult strangers, respectively. To assess group effects, a group of participants with ASD was compared to closely age-matched TD participants and to assess developmental effects, we investigated a larger control sample of TD children and adolescents.

Materials and methods

Participants

In total, 22 individuals with ASD (aged between 8 and 18 years) and 55 TD participants (aged between 8 and 18 years) took part in the study with one of their parents, as well as an adult stranger. Children and their parents were recruited at the Department of Child and Adolescent Psychiatry in Aachen (RWTH Aachen University) and from a database of participants from previous studies. Adult strangers were recruited via local advertisement. From the individuals with ASD, four dyads had to be excluded from the final analysis for various reasons (multiple psychotropic medication of parent and/or child, *n* = 2; multiple co-morbidities with antidepressant medication of the child, *n* = 1; data quality problems, *n* = 1). From the TD sample, nine dyads were excluded because of male sex of the parent (except for one ASD-match), in order to reduce potential sex effects (Cheng *et al.*, 2015; Baker *et al.*, 2016). Additional four dyads had to be excluded because of data quality problems and one dyad because of a current neurological diagnosis of the stranger. See Table 1 for demographic information of the final participant sample.

For the final analyses of the TD group (control sample), 41 children and their parents were included. All children, except for one, participated with their mothers. This father–son dyad was included as a match for the ASD sample (as described below). In addition, 32 adult strangers performed identical tasks with the participating children. Seven strangers participated twice and one stranger three times. The sex of the stranger was matched to the sex of the respective parent, but the mean age differed between strangers and parents (see Table 1).

For a group comparison of children with ASD and TD children (matched sample), TD participants were selected from the larger

dataset to provide a close match in age with the ASD group (±6 months). In the final matched sample analyses, 18 male individuals with ASD and their parents as well as 18 male TD participants and their parents were included. One child in the ASD and the TD group each participated with their fathers. In this matched-sample, 32 adult strangers participated. Of these, two strangers took part twice and one stranger three times.

All participants with ASD had received a diagnosis by experienced clinicians and reached cut-offs on the autism diagnostic observation schedule-generic (ADOS-G; Lord *et al.*, 2000, one patient with missing values) and/or the autism diagnostic interview-revised (ADI-R; Lord *et al.*, 1994, one patient with missing values). Thirteen of them had a comorbid diagnosis of attention-deficit/hyperactivity disorder (ADHD), in line with the literature reporting comorbidity rates with ASD ranging from approximately one-third (Simonoff *et al.*, 2008) to three-quarters (Lee and Ousley, 2006). One individual diagnosed with ASD had a comorbid hyperkinetic disorder of social behavior. If the patients typically received stimulant treatment, medication was discontinued to ensure stimulant-free testing. One patient did not comply and was thus medicated with stimulants (Methylphenidate; Ritalin LA®) at the time of testing. One mother reported having a depressive episode in remission and was medicated at the time of testing with a selective serotonin reuptake inhibitor (SSRI; Citalopram). All results were replicated after removing the two dyads, which included the medicated child, the child with missing values in ADOS/ADI-R and the medicated mother (see 'Statistical analyses'). TD participants, their parents and adult strangers had no indication of developmental delay or any neurological or psychiatric disorder, as assessed by a brief clinical interview. All participants filled in questionnaires to control for social communicative abilities (German versions of the social responsiveness scale; SRS; Bölte and Poustka, 2008 and social communication questionnaire; SCQ; Bölte and Poustka, 2006) as well as a German ADHD rating scale (FBB-HKS; Döpfner and Lehmkuhl, 2000) to screen for ADHD symptoms.

The study was approved by the local ethical committee of the University Hospital RWTH Aachen, Aachen, Germany (EK 344/14). All experimental procedures were conducted at the Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital RWTH Aachen in Aachen, Germany, with written informed consent of all participants (for children age <18 years, their legal guardian gave written informed consent and all children gave their verbal assent) after they had received a complete description of the study.

Procedure

The participating children and adolescents were playing a cooperative and competitive computer game, once with their parent and once with an adult stranger in counterbalanced order. Participants were sitting next to each other in front of a computer screen while playing the computer game and being recorded with fNIRS. They were instructed to rest their heads on a chin rest and not to talk during the fNIRS measurement. To reduce the participants' ability to view each other's motor activities, a towel was placed over their hands (for a video showing the set-up and procedure, see Reindl *et al.*, 2019).

Experimental task

We employed a computer-based cooperation game, originally introduced by Cui *et al.* (2012) and modified to be suitable for children by Reindl *et al.* (2018). At the beginning of each trial, two cartoon dolphins (the game characters of the two players) were shown on the screen. After 2 s, a black circle appeared above the dolphins ('Ready' signal). After a random delay of 0.6–1.5 s, the circle turned into a red-white ball ('Go' signal).

In the 'cooperation' condition, the dyads were asked to respond as simultaneously as possible to the 'Go' signal via button press, in order to let their dolphin jump to the ball (feedback screen, presented for 1.5 s) and catch the ball together (result screen, presented for 1.5 s) in order to win shared points. If the difference between the response times (RT) of the two players was above a given threshold ($T = 1/8$ (RT1 + RT2)), only the faster dolphin jumped to the ball (feedback screen), no dolphin caught the ball (result screen) and both players lost a point.

In the 'competition' condition, dyads were instructed to respond faster than the interaction partner to the 'Go' signal in order to let their dolphin jump to the ball (feedback screen, presented for 1 s), catch the ball (result screen, presented for 1 s) and win more points than their interaction partner. Only the faster dolphin jumped to the ball and earned a point, whereas the player with the slower dolphin lost a point. However, if both players reacted simultaneously with a margin of error of 50 ms, both dolphins jumped to the ball, caught the ball and each player won a point.

Each task condition consisted of two task blocks with 20 trials each and three 30 s resting blocks: one before the beginning of the first and the second task block, respectively, and one after the second task block. Before the beginning of the experiment, five practice trials of each condition were completed. The order of the two task conditions (cooperation/competition) was counterbalanced across children but kept constant for both dyads (parent-/stranger–child) of each child. Furthermore, the order of playing first with the parent or the adult stranger was counterbalanced accordingly, however, due to the matching procedure, no perfect balance could be achieved in the final sample (see Supplementary Table S1). See Figure 1 for an illustration of the cooperation (A) and competition (B) condition of the task.

Task behavior measurements

Adult's and child's response times were recorded during the tasks. As a measure of motor synchrony, the mean of the absolute differences in response times of each dyad was calculated (mean-DRT). Task performance was further quantified by the percentage of joint wins during cooperation and the percentage of child wins and joint wins during competition.

Functional near-infrared spectroscopy

fNIRS data acquisition. fNIRS data were acquired using the ETG-4000 NIRS device (Hitachi Medical Corp., Tokyo, Japan) in order to measure concentration changes in oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) in two participants simultaneously (sampling frequency = 10 Hz, number of measurement channels (CHs) = 22, source-detector distance = 3 cm). Easycaps (Easycap GmbH, Herrsching, Germany) with an attached measurement patch (3×5 optodes) were placed symmetrically over the participants' foreheads as described elsewhere (Cui *et al.*, 2012; Reindl *et al.*, 2018). For further details of the fNIRS data acquisition protocol, refer to Reindl *et al.* (2018, 2019).

Estimation of anatomical locations. To estimate the most probable spatial location of the channels, we used the virtual registration method, which is based on simulations (Singh *et al.*, 2005; Tsuzuki *et al.*, 2007). In this method, virtual probe holders are placed on synthetic heads with varying size and shape. Channels are projected on the synthetic brain and positions normalized to MNI space. For Hitachi probe holders and our current probe holder placement, virtual registration results are provided by the Jichi University (http://www.jichi.ac.jp/brainlab/virtual_registration/Result3x5_E.html). For each channel, the Brodmann areas (BA) with the highest probability were determined based on the Talairach Daemon (Lancaster *et al.*, 2000). The brain regions covered by this optode set-up include: BA 8, BA 9, BA 10 and BA 46 (Figure 2).

Since differences in head size and shape may lead to differences in optode localization, channels were clustered to six regions, in order to enhance the reliability of region specification (see also Nguyen *et al.*, 2020). The assignment of the channels to regions was determined based on their BAs. More specifically, channels located over BA 8 formed one region (BA 8, 2 channels). Channels located over the left and right dorsolateral prefrontal cortex (including BA 9 and BA 46) also formed one region each (lDLPFC and rDLPFC, both 3 channels). The remaining 14 channels, located over BA 10, were clustered to three regions in the left lateral, right lateral and medial frontopolar cortex (lFPC and rFPC both with four channels, mFPC with five channels; Figure 2). For each region, brain-to-brain synchrony values were averaged across channels (see also Baker *et al.*, 2016; Miller *et al.*, 2019). Thus, one synchrony value was obtained for each participant in each region (if at least one channel had valid data).

fNIRS data preprocessing. Preprocessing was conducted using the SPM for fNIRS toolbox (https://www.nitrc.org/projects/spm_fnirs/; SPM12: http://www.fil.ion.ucl.ac.uk/spm/software/spm12/) and the Homer2 toolbox (https://www.nitrc.org/projects/homer2). First, raw attenuation data were converted to optical density (Homer2 function: 'hmrIntensity2OD') and motion artifacts were reduced by applying the MARA algorithm (Scholkmann *et al.*, 2010) (Homer2 functions: 'hmrMotionArtifactByChannel' and 'hmrMotionCorrectSpline'; parameters: tMask = 1, std_thresh = 13, amp_thresh = 0.4, tMotion = 1 and $P = 0.99$, respectively). Next, optical density data were converted to changes in HbO and HbR according to the modified Beer–Lambert law (Homer2 function: 'hmrOD2Conc'), while the differential pathlength factor was calculated in dependence on wavelength and the participants' individual age (Scholkmann and Wolf, 2013). Afterwards, data were detrended using a high-pass filter based on a discrete cosine transform set (spm for fnirs function: 'spm_fnirs_dct,' cut-off: 128).
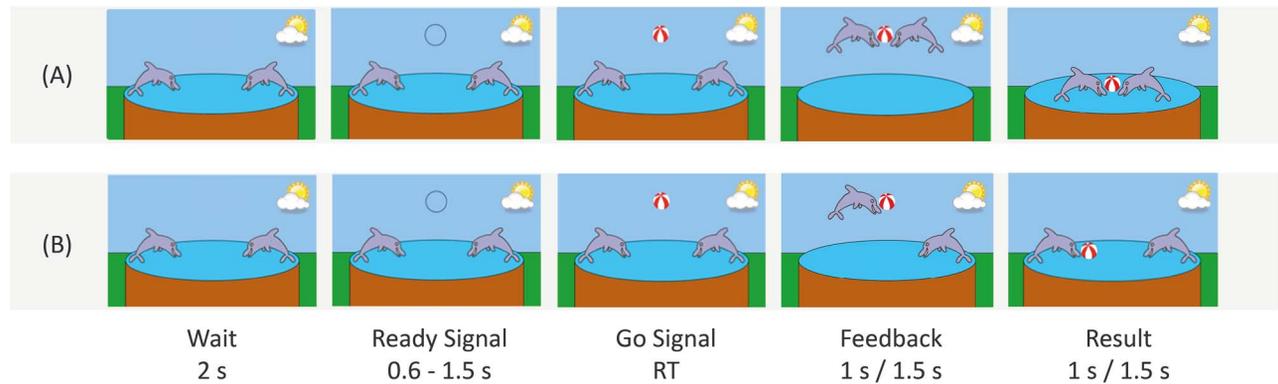
Fig. 1. Illustration of the task design. (A) Cooperative game, (B) competitive game. RT is the response time of (A) the slower participant and (B) the faster participant.
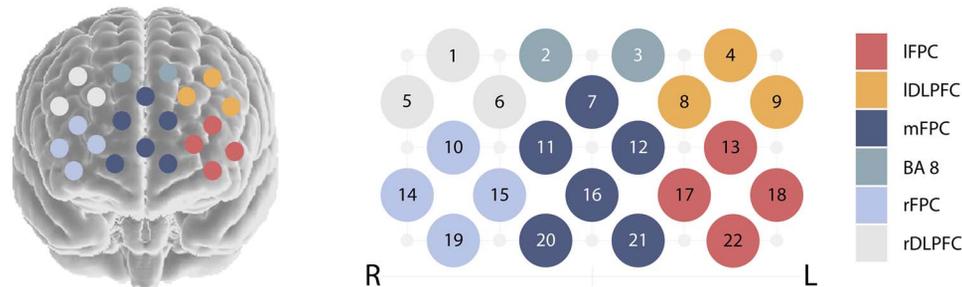

Fig. 2. Optode localization and region specification.

Noisy channels were identified based on a combination of objective criteria, including the coefficient of variation, the correlation between HbO and HbR and a 'flat' line detection, as well as visual inspection. The procedure is described in more detail in the Supplementary Text S1. Noisy channels were excluded from all further analyses (approximately 5%). If at least 12 channels (≥50%) were classified as 'noisy,' the fNIRS measurements of this dyad in the respective condition were excluded. As a result, data were excluded of two dyads in one condition each (1× CoopP, 1× CoopStr) and of one dyad in two conditions (1× CoopP, 1× CompStr).

fNIRS synchrony analysis. As a measure of brain-to-brain synchrony, the wavelet coherence was calculated based on routines from the AStoolbox (Aguiar-Conraria and Soares, 2014) and JLab toolbox (Lilly, 2019) (adapted from Reindl *et al.*, 2018; for more details see Supplementary Text S2). The wavelet coherence was calculated both for the HbO and HbR signals for corresponding channels between adult (parent/stranger) and child. In noisy settings, the mean of the wavelet coherence will be higher than zero. Thus, to increase the robustness of the brain-to-brain synchrony estimator, we only considered 'salient' wavelet coherence values that were above a cut-off of 0.65 for HbO and 0.67 for HbR. This cut-off was calculated based on the coherence of surrogate time series, which were constructed by fitting an AR(1) model to the fNIRS signals of the adult and child and building new time series by bootstrapping (for the construction of surrogates, see Aguiar-Conraria and Soares, 2014). As outcome measures, the number of wavelet coherence values higher than the cut-off value in a task-related frequency band between 0.08 and 0.5 Hz (period length: 12.80–2.02 s), relative to the total number of wavelet coherence values in this frequency band, is

reported (Reindl *et al.*, 2018). It should be noted that the task-related frequency band includes the trial duration (~7 s for cooperation, ~6 s for competition). Thus, for each dyad and condition (CoopP, CompP, CoopStr and CompStr), one coherence value was obtained in each channel.

Validation procedure. To investigate brain-to-brain synchrony, which is specific to the dyad's interaction, we implemented a validation strategy correcting for signal similarities of independent subjects performing the same task (see also Reindl *et al.*, 2018). To this end, wavelet coherence was calculated for all random adult–child pairs who did not play together but were recorded under the same experimental condition (for further details, see Supplementary Text S3). For each child, sets of random pairs were constructed by varying the adult partner within the same diagnostic group (TD or ASD), while holding the condition and channel fixed. Using the same blockwise permutation scheme, we additionally calculated sets of random pairs for each adult by holding the adult fixed and varying the corresponding child's signals. Next, a dyad-, condition- and channel-specific mean random pair coherence value was derived by averaging across the coherence values of both child-fixed and adult-fixed random pair sets in each condition and channel. Finally, all coherence values of the actual dyads were corrected by subtracting the corresponding mean random pair coherence value. This procedure allows us to investigate the dyad's coherence that goes beyond group, condition, or channel-related brain activity patterns. Importantly, it enables us to control for potential differences in within-brain connectivity (e.g., King *et al.*, 2018) or brain activation patterns between children in the ASD and TD group, which may lead to increased or decreased brain-to-brain synchrony not related to dyadic influences during the interaction. All statistical

analyses were performed with this corrected coherence value.

Statistical analyses

Both behavioral and neural data were analyzed in a two-step procedure. First, differences between conditions (CoopP, CompP, CoopStr and CompStr) as well as influences of child's age were analyzed in the control sample. Second, group differences between the ASD group and TD group were examined in the matched sample. The analysis for the behavioral and neural data is described in more detail below.

Statistical analyses were performed in R (version 3.6.2; R Core Team, 2019). First, outliers, defined as ±3 s.d. from the mean, were winsorized by replacing them with the lower and/or upper boundary values. Winsorizing was conducted across conditions, over all behavioral scores or all coherence values in a specific region for the behavioral and neural data, respectively. To analyze condition, age and group effects, we calculated linear mixed models (LMMs) using the R package 'lme4' (Bates *et al.*, 2015). All initial LMMs included the maximal random effects structure justified by the design. Models were then simplified by removing non-significant random slopes backwards using likelihood ratio tests. For statistical inference, the final models were fitted using REML and P-values were derived by the 'ANOVA' function of the 'lmerTest' package (Kuznetsova *et al.*, 2017) using the Satterthwaite approximation for the degrees of freedom. 'Pseudo-R^2' for the models was calculated using the R package 'r2glmm' (Jaeger, 2017) and the approach by Nakagawa and Schielzeth (2013). Continuous predictors were grand-mean centered. Analyses were checked for potential confounds by (i) including condition order as a predictor and (ii) excluding medicated subjects (including the child with missing values in ADOS/ADI-R), which did not change any of the main findings.

Behavioral analyses. First, to examine differences in motor synchrony in the control sample, LMMs were applied with the mean-DRT (mean absolute differences in response times) as the dependent variable (DV). The full model included the fixed effects of task (0 = competition, 1 = cooperation), partner (0 = stranger, 1 = parent) and the task × partner interaction, as well as a random intercept for subject and by-subject random slopes for task and partner. Differences between parent–child and stranger–child dyads in cooperative and competitive task performance were further investigated by a series of LMMs with task performance as DV (child wins during competition/joint wins during cooperation/joint wins during competition) and partner as fixed effect. Subsequently, the main and interactive effects of child's age were entered in the LMMs predicting motor synchrony and task behavior. Group differences between children with ASD and TD-controls were analyzed in the matched sample by adding the main and interaction effects of group (0 = TD, 1 = ASD) to the LMMs described above. Relationships between behavioral variables and ASD/ADHD symptom severity were assessed in the ASD group by including the SCQ, SRS and FBB-HKS questionnaire scores as fixed effects in the LMMs.

Neural analyses. For the neural synchrony analysis, we first examined whether the dyad's brain-to-brain synchrony was higher than brain-to-brain synchrony of dyad-specific random pairs in the same condition and region. To this end, corrected coherence values (as described in 'Validation procedure') were subjected to a series of one-sample t-tests, comparing them to zero (one-tailed). P-values were corrected for multiple

comparison using FDR correction (48 tests per group) (Benjamini and Hochberg, 1995).

Second, differences between conditions were examined in the control group using LMMs with coherence in the respective region as DV. The full model included the main and interactive effects of task and partner as fixed effects, a random intercept for region and subject, as well as by-subject random slopes for task, partner and task × partner. While these analyses were performed across regions, in a supplementary analysis, we calculated LMMs models for each region and signal type (HbO/HbR) separately to investigate region-specific effects. For these analyses, P-values were adjusted for multiple comparisons (12 tests). Subsequently, to examine potential covariates, the main and interactive effects of child's age as well as of mean-DRT were entered in separate LMMs. In the matched group analysis, differences between the ASD and TD group were examined by adding the main and interactive effects of group to the LMMs described above.

Results

Behavioral results

Control sample. In the control sample, LMMs revealed a significant effect of task ($F(1, 40.275) = 19.998$, $P < 0.001$) and partner ($F(1, 39.986) = 8.770$, $P = 0.005$) on mean-DRT, however, no significant interaction (see Supplementary Table S2 for descriptive results and Supplementary Table S3 for LMM results). The full model explained $R^2 = 12\%$ of the variance. Dyads were more synchronous in their response times during competition than during cooperation. Moreover, stranger–child dyads were more synchronous than parent–child dyads. The child's age did not significantly influence mean-DRT (no main effect or interactive effects with child's age, Ps > 0.10).

Further examining task performance, results indicate no significant differences between parent–child and stranger–child dyads in the number of joint wins during cooperation and the number of joint wins during competition (Supplementary Table S3). However, during competition, children won more often against the parent than against the stranger (partner effect: $F(1, 40.034) = 9.581$, $P = 0.004$, $R^2 = 0.08$), and older children won more often (age effect: $F(1, 39.256) = 4.456$, $P = 0.041$, $R^2 = 0.14$).

Matched sample. In the matched sample, LMMs yielded a main effect of task ($F(1, 34) = 23.411$, $P < 0.001$), partner ($F(1, 68) = 5.793$, $P = 0.019$) and group ($F(1, 34) = 5.433$, $P = 0.026$) on mean-DRT ($R^2 = 0.20$; see Supplementary Table S2 for descriptive results and Supplementary Table S4 for LMM results). In line with the results in the control sample, dyads were more synchronous during competition compared to cooperation and more synchronous with the stranger compared to the parent. Moreover, children in the ASD group were less synchronous, i.e., had a higher difference in response times than children in the TD group across conditions and interaction partners.

While no significant group effect was observed for the number of child wins during competition (Supplementary Table S4), the number of joint wins during competition and cooperation differed between children in the TD and ASD group (competition: $F(1, 68) = 7.830$, $P = 0.007$, $R^2 = 0.15$; cooperation: $F(1, 34) = 8.756$, $P = 0.006$, $R^2 = 0.14$). Consistent with the findings on mean-DRT, children in the TD group had a higher number of joint wins than children in the ASD group, irrespective of interaction partner (Supplementary Table S2). Within the ASD group, both mean-DRT and dyad's number of joint wins (cooperation/competition) were neither significantly predicted by ASD symptom severity

Table 2. Results of one-sample *t*-tests examining coherence increase in actual dyads compared to random pairs

	TD—complete		TD—matched	
	M (s.d.)	*t* statistic	*M* (s.d.)	*t* statistic
CompP—HbO				
rDLPFC	0.032 (0.055)	$t(37) = 3.624$, $P_{adj} = 0.005$, $d = 0.59$		
lDLPFC	0.025 (0.059)	$t(39) = 2.729$, $P_{adj} = 0.025$, $d = 0.43$		
rFPC	0.034 (0.051)	$t(40) = 4.272$, $P_{adj} = 0.001$, $d = 0.67$	0.044 (0.062)	$t(17) = 3.043$, $P_{adj} = 0.044$, $d = 0.72$
lFPC	0.015 (0.037)	$t(40) = 2.561$, $P_{adj} = 0.031$, $d = 0.40$	0.031 (0.042)	$t(17) = 3.121$, $P_{adj} = 0.044$, $d = 0.74$
mFPC	0.024 (0.037)	$t(40) = 4.178$, $P_{adj} = 0.001$, $d = 0.65$		
CompP—HbR				
BA8	0.014 (0.028)	$t(33) = 2.979$, $P_{adj} = 0.018$, $d = 0.51$		
rDLPFC	0.014 (0.030)	$t(37) = 2.841$, $P_{adj} = 0.022$, $d = 0.46$		
rFPC	0.020 (0.037)	$t(40) = 3.490$, $P_{adj} = 0.006$, $d = 0.55$	0.021 (0.026)	$t(17) = 3.400$, $P_{adj} = 0.041$, $d = 0.80$
lFPC	0.017 (0.033)	$t(40) = 3.232$, $P_{adj} = 0.010$, $d = 0.50$		
mFPC	0.020 (0.029)	$t(40) = 4.402$, $P_{adj} = 0.001$, $d = 0.69$	0.023 (0.028)	$t(17) = 3.476$, $P_{adj} = 0.041$, $d = 0.82$
CoopP—HbO				
rFPC	0.017 (0.046)	$t(40) = 2.355$, $P_{adj} = 0.043$, $d = 0.37$		
CoopP—HbR				
rFPC	0.013 (0.032)	$t(40) = 2.571$, $P_{adj} = 0.031$, $d = 0.40$		
lFPC	0.011 (0.029)	$t(40) = 2.465$, $P_{adj} = 0.036$, $d = 0.38$		

Notes: One-sample *t*-tests were conducted (one-sided) for each region, examining whether the sample mean is greater than zero. P_{adj} = P-values were adjusted for multiple comparisons (48 tests) using FDR correction; CompP, parent–child competition; CoopP, parent–child cooperation

(SCQ or SRS total score) nor by ADHD symptom severity (FBB-HKS total score).

To summarize, dyads were more synchronous during competition as compared to cooperation. Importantly, children in the ASD group showed a lower motor synchrony than children in the TD group both during competition and during cooperation.

Neural results

Control sample. To examine whether brain-to-brain synchrony was higher in the actual dyads as compared to the random pairs, we subjected the corrected coherence values in each region and condition to a series of one-sample *t*-tests. Results showed an increased, widespread coherence for the actual dyads in the CompP condition in five regions for HbO (rDLPFC, lDLPFC, rFPC, lFPC and mFPC) and in five regions for HbR (BA8, rDLPFC, rFPC, lFPC and mFPC) (Table 2). Moreover, increased coherence was observed for CoopP in the rFPC for HbO as well as in the rFPC and lFPC for HbR, respectively. No significantly increased coherence was observed for CoopStr and CompStr after FDR-correction of the P-values.

In the next step, we directly compared the different conditions using LMMs with the corrected coherence value as the DV, and task, partner and the task × partner interaction as fixed effects (Table 3). For HbR, results showed a highly significant effect of task, with higher coherence for competition as compared to cooperation across regions, as well as a marginally significant effect of partner, with higher coherence for parent–child compared to stranger–child dyads. For HbO, a marginally significant effect of partner and marginally significant interaction between task × partner were observed across regions. Coherence was highest in the CompP condition for HbO and HbR, as indicated by Figure 3. Separate LMMs analyses for each region and signal type did not yield any significant effects after P-value adjustment (except for one marginally significant task effect for HbR in the rFPC, see Supplementary Text S4).

While no significant influences were found for child's age on HbO coherence, results showed a significant three-way interaction between task × partner × age for HbR (Table 3).

Breaking down this interaction, we found a significant two-way interaction between task × age only for parent-child (F(1, 417.25) = 10.357, P = 0.001, R^2 = 0.04) but not for stranger–child dyads (F(1, 427.98) = 0.010, P = 0.92, R^2 = 0.01). Age had a positive slope for CompP and a negative slope for CoopP, indicating that coherence in the CompP condition increased with higher age, while coherence in the CoopP condition decreased. However, it should be noted that age effects were not significant in separate models for CompP (P = 0.16) and CoopP (P = 0.09).

In an exploratory analysis, we further examined whether task differences in coherence can be explained by differences in motor synchrony. To this end, the main and interactive effects of mean-DRT were added to the LMMs. Neither in the model for HbO nor in the model for HbR the mean-DRT emerged as a significant predictor (no main or interactive effects with mean-DRT, Ps > 0.05; see Supplementary Table S5). Thus, increased coherence for competition compared to cooperation in HbR is unlikely to be explained by increased motor synchrony.

To summarize, we observed a strong and widespread brain-to-brain synchrony for parent–child competition in comparison to random pairs consistently in the control sample. Moreover, significant increases were observed for parent–child cooperation in more localized regions, located over the rFPC (and lFPC only for HbR). These results were consistent for both HbO and HbR. Furthermore, findings for HbR indicate that parent–child brain-to-brain synchrony during cooperation and competition is differentially influenced by the child's age from childhood to adolescence. To account for these age effects, ASD participants were compared to age-matched TD participants in the subsequent analyses.

Matched sample. In the ASD sample, no significant increases in coherence were observed for actual dyads in comparison to random pairs (one-sample *t*-tests, FDR correction). In the control sample, higher coherence of the actual dyads compared to random pairs was observed for CompP in the rFPC and lFPC for HbO and in the rFPC and mFPC for HbR (Table 2). Furthermore, no significant group differences between the ASD and TD group were

Table 3. Fixed effects estimates (top) and variance-covariance estimates (bottom) for the LMM predicting coherence in the control sample

	HbO		HbR	
	Est (SE)	F(P)	Est (SE)	F(P)
Fixed effect				
Intercept	0.003 (0.005)		0.007 (0.004)	
Task	0.004 (0.007)	1.276 (0.266)	−0.005 (0.002)	13.680 (<0.001)
Partner	0.023 (0.009)	3.586 (0.066)	0.008 (0.004)	3.474 (0.070)
Age	<0.001 (0.002)	1.526 (0.224)	<−0.001 (0.001)	0.001 (0.978)
Task × partner	−0.019 (0.010)	3.275 (0.078)	−0.003 (0.003)	0.630 (0.427)
Task × age	0.003 (0.002)	0.095 (0.760)	<0.001 (0.001)	4.989 (0.026)
Partner × age	0.002 (0.003)	0.100 (0.753)	0.001 (0.001)	0.008 (0.928)
Task × partner × age	−0.005 (0.004)	1.795 (0.188)	−0.003 (0.001)	5.685 (0.017)
Random part				
Intercept ID	<0.001 (0.027)		<0.001 (0.018)	
Task by ID	0.001 (0.038)			
Partner by ID	0.003 (0.053)		<0.001 (0.018)	
Task × partner by ID	0.004 (0.060)			
Intercept region	<0.001 (0.005)		<0.001 (0.003)	
Residual	0.001 (0.034)		<0.001 (0.026)	
R^2	0.04		0.02	

Notes: For the fixed effects, estimates are presented with the SE in parenthesis. For the random part, variances are presented with the s.d. in parenthesis. Partner is coded 0 = Stranger, 1 = Parent. Task is coded 0 = Competition, 1 = Cooperation. Age is the child's age in years (centered); ID is the child's subject number. Significance was calculated using the ANOVA function and Satterthwaite approximation for degrees of freedom.
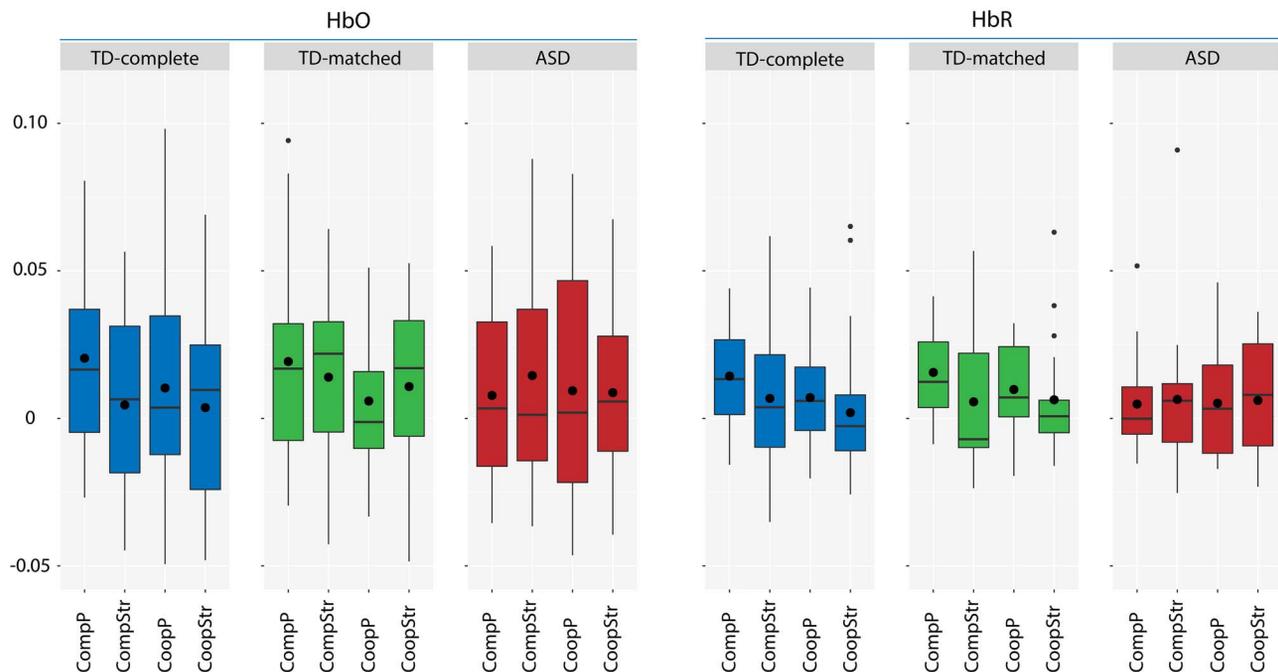
Fig. 3. Differences between parent–child cooperation (CoopP), parent–child competition (CompP), stranger–child cooperation (CoopStr) and stranger–child competition (CompStr) in coherence, measured in HbO and HbR, for the TD-complete, TD-matched and ASD group. Boxplots are depicted. The lower and upper hinges correspond to the 25 and 75% percentiles. The lower and upper whiskers extend from the hinge to the lowest/largest values with a maximum of 1.5 times the inter-quartile range. The median value is represented by the horizontal bar and the mean by the black circle.

found in the LMMs, both across regions (Supplementary Table S6) and for each region separately. In an exploratory analysis based on the findings of Wang *et al.* (2020), we examined group differences in LMMs separately for the parent conditions (CoopP, CompP). In line with the findings of the one-sample *t*-tests, we found a marginally significant effect of group for CompP across regions for HbR ($F(1, 34.66) = 3.860$, $P = 0.058$, $R^2 = 0.03$), indicating that there was a trend for higher scoherence in the TD compared to the ASD group (Figure 3).

To conclude, while we partly replicated our findings of the complete control/TD group in the smaller matched control/TD group, which showed an increased brain-to-brain synchrony during parent–child competition, no significantly increased brain-to-brain synchrony was found in the ASD group. Group comparisons between the ASD and matched control group did not yield significant differences.

Discussion

Using fNIRS hyperscanning, we investigated brain-to-brain synchrony in parent–child dyads with and without ASD and the influence of the familiarity of the interaction partner, taking into account potential age-related changes across childhood and adolescence. We administered a social cooperation (joint button press with interaction partner) and competition (faster button press than interaction partner) game in a larger sample of control participants and compared groups in a smaller matched sample of children and adolescents with and without ASD. On the behavioral level, we observed overall smaller differences in response times (i.e., increased synchrony) during competition than during cooperation across all dyads and increased synchrony for stranger–child dyads in comparison to parent–child dyads. For dyads in the ASD group, a lower motor synchrony was evident in comparison to the TD group. On the neural level, we

found enhanced widespread brain-to-brain synchrony during competition with parents in the control sample, paralleled by increased brain-to-brain synchrony during parent–child cooperation in specific regions (i.e., frontopolar cortex; FPC). Parent–child synchrony in HbR signals was modulated by the child's age, indicating that across childhood and adolescence synchrony may increase for competition and decrease for cooperation. In contrast to the control group, no significantly increased brain-to-brain synchrony was found for children and adolescents with ASD. Direct group comparisons in the matched sample yielded merely marginally significant effects.

Motor synchrony

In line with Reindl *et al.* (2018), dyads in the control sample showed a higher synchronization of their response times during competition than during cooperation for both parent–child and stranger–child dyads. Moreover, we found higher synchronization in stranger–child dyads than in parent–child dyads across task conditions (i.e. during both cooperation and competition). Particularly for competition, response times between strangers and children were more similar than between parents and children, which most likely induced the overall higher synchronization in stranger–child dyads. It seems plausible that strangers were more competitive than parents, or that parents may have been less motivated to win themselves and have let their children win occasionally to avoid frustration (Reindl *et al.*, 2018).

In the matched sample, children in the ASD group showed a lower overall motor synchrony than children in the TD group during both competition and cooperation, independent of the familiarity of the interaction partner. The lower motor synchrony in the ASD group is in line with previous findings, demonstrating that lower levels of action synchronization in children

with ASD are associated with higher ASD severity symptoms during cooperation with their parents (Wang et al., 2020). In the present study, however, we did not find any associations with symptom severity scores, as assessed by parent-rated questionnaires (SRS, SCQ). Previous studies have consistently reported lower motor synchrony in ASD for a range of motor-related synchrony tasks (e.g. Marsh et al., 2013; Fitzpatrick et al., 2016, 2017; Curioni et al., 2017; Noel et al., 2017). Motor impairments, which are frequently observed in children with ASD (Bhat et al., 2011; Kaur et al., 2018), may contribute to difficulties in the ability to synchronize movements with others. Furthermore, since most of these studies involve synchronizing one's movements while directly observing the other person, lower synchrony in ASD could be explained by lower sensitivity and decreased attention to the movements of the other person (e.g. Fitzpatrick et al., 2016). In the present study, however, participants had no direct sight of the partner's moving hand and no instruction to explicitly synchronize movements. Thus, differences in synchrony might not only result from motor impairments and deficits in attention to motor cues. Alternatively, differences in higher order cognitive processes, such as the ability to predict the behavior of the other person, could also play an important role.

To sum up, the present finding of a lower motor synchrony in ASD as compared with their TD peers parallels other studies administering social motor synchrony tasks. Since previous studies further showed that social motor synchrony was related to social competences and ASD symptom severity in children with ASD (Fritzpatrick et al., 2017), it may potentially be a useful marker for early identification of children at risk for ASD.

Neural synchrony

In the control sample, a widespread enhanced brain-to-brain synchrony during competition with the parent was observed, paralleled by localized increases in brain-to-brain synchrony for cooperation with parents in the FPC. Furthermore, these parent-specific effects were differentially modulated by age, with a tendency for increased overall synchrony with age during competition and decreased synchrony during cooperation.

Previous studies typically found higher brain-to-brain synchrony during cooperation with the more familiar interaction partner (Cui et al., 2012; Pan et al., 2017; Reindl et al., 2018; Miller et al., 2019; Wang et al., 2020), but not all of these studies have investigated cooperative and competitive contexts within the same experimental task. Furthermore, these studies investigated either younger ages with a smaller age range (Reindl et al., 2018; Miller et al., 2019; Wang et al., 2020), or adults (Cui et al., 2012; Pan et al., 2017). Competitive conditions within a social context (such as in the present study), however, also may induce social comparison processes between the interaction partners (Balconi and Vanutelli, 2018) and thus involve enhanced socio-cognitive processing. Accordingly, other studies have also reported enhanced brain-to-brain synchrony during competitive tasks that involve taking the actions of the interaction partner into account, such as in a simplified poker game in a fNIRS hyperscanning study (Piva et al., 2017). However, in the present study, the best strategy to compete would be to focus on one's own action (i.e., faster button press) in order to perform better than the interaction partner, which would not necessarily involve enhanced socio-cognitive processing.

An alternative explanation might be synchronized emotional responses, induced by the competitive character of the task, where participants are affectively involved during similar periods of the game. Emotional valence and arousal have been shown to promote a synchronization of brain activities, for instance in participants listening to the same affective story (Nummenmaa et al., 2014) or watching the same movie clip (Nummenmaa et al., 2012). Time-locked increases and decreases in emotional arousal (e.g., in response to the 'ready' signal, 'go' signal or feedback) may not only lead to an enhanced neural synchrony but also to an enhanced synchrony in other biological systems, such as the autonomic nervous system (ANS). For example, interpersonal synchronization of the heart rate has been observed during cooperative and competitive games in electrocardiography studies (Järvelä et al., 2014), in particular in a competitive context (Chanel et al., 2012). Although the heart rate (∼1 Hz) is outside the task-related frequency band (0.08–0.5 Hz), cardiovascular influences generally show a strong effect on the fNIRS signal (for instance, respiration at ∼0.3 Hz or arterial blood pressure waves, so called 'Mayer waves,' at ∼0.1 Hz; Yücel et al., 2016). Furthermore, the enhanced coherence during competition being widespread rather than localized may indicate that it is not solely caused by neural synchrony. Thus, widespread coherence might reflect a mixture of ANS influences as well as socio-cognitive, and emotional processing. Accordingly, bio-behavioral synchrony is considered a multimodal phenomenon (Semin, 2007; Hari et al., 2015), which may be established in different behavioral but also biological systems, including ANS activities or hormonal levels, and which may also be influenced by ASD symptoms (Baker et al., 2015).

In line with Reindl et al. (2018) and other studies, we observed localized increases in brain-to-brain synchrony during cooperation with parents in the FPC. This localized synchronization during cooperation may reflect more socio-cognitive processes, such as continuous attending to each other's actions and adapting responses in relation to the anticipated response time of the interaction partner. It may thus reflect mutual interaction, which is characterized by a common goal and shared attention and adaptation processes (Reindl et al., 2018).

Across regions, brain-to-brain synchrony during competition and cooperation with parents was modulated by increasing age (i.e., higher synchrony for competition and lower synchrony for cooperation with parents). Such age effects may also explain differences to our previous study in 5–9-year-old children, in which localized increases in brain-to-brain synchrony were found for parent–child cooperation but no effects for parent–child competition (Reindl et al., 2018). Together, this pattern of results might be associated with developmental processes related to adolescence. Adolescence is characterized by changes in the relationship with parents and peers, including a normative development of increasing separation and experience of autonomy from parents towards more relying on age mates (Jager et al., 2015). Considering the described developmental changes from childhood to adolescence, competitive, as compared to cooperative aspects during the interaction with parents seem likely to play a role in the investigated age-range of the present study (for a review about the development of parent–adolescent relationships and conflict interactions, see Branje, 2018). It might be speculated that these developmental processes in adolescence are associated with more emotional arousal and related bio-behavioral, and specifically neural, synchrony during competition and/or with less socio-cognitive processing and associated neural synchrony during cooperation. The notion of a link between emotional arousal and increased synchrony in adolescents is supported by previous findings relating adolescence to enhanced risk-taking (Smith et al., 2013), increased intensity and frequency of emotions, particularly in social contexts (Guyer et al., 2016), as

well as increased emotional responses and arousal (Lanteigne, 2011) along with adjustments in the capacity of emotion regulation (Ahmed *et al.*, 2015). Furthermore, other studies suggest a direct link between adolescents' emotional responses and their parent's emotional arousal and capacities of emotion regulation (Turpyn *et al.*, 2018). It might be speculated that synchronized emotional arousal (in our study particularly during competition conditions) in turn induces brain-to-brain synchrony and may contribute to this link. Nevertheless, the present findings should be interpreted with caution since they were only observed for HbR and not for HbO. Future studies should investigate the changes in emotional arousal, regulation and social cognitive processing during adolescence and potential interrelations with changes in brain-to-brain synchrony using a wider range of paradigms targeting specific aspects of these functions. This would be important to disentangle the contribution of mutual arousal and the ANS to processes of bio-behavioral synchrony and their influence on brain-to-brain synchrony.

In the matched sample, no group differences between TD and ASD dyads could be observed after rigorous control of random effects. Note, we used a very strict analysis strategy to rule out any possible influence of group-wise overall activation, or dyad differences on the measure for brain-to-brain synchrony (e.g. group- and channel-wise random pairs). Although we could observe reduced behavioral synchrony (also in comparison to TD), we could not replicate reductions of brain-to-brain synchrony in relation to ASD symptomatology as demonstrated by Wang *et al.* (2020) during parent–child cooperation using the same experimental task. However, this study differed in several respects: participants were much younger (5–11 years) and this study did not include a control group. Furthermore, synchrony was assessed for the same cooperation task as in our study, but in comparison to a control condition where the child responded as fast as possible and the parent merely observed. Therefore, it cannot be ruled out that the observed effects, including correlations with symptom severity, could be more related to motor synchrony rather than coordinated socio-cognitive processes during cooperation driving synchrony.

In an exploratory analysis, a marginally significant group effect for competition with parents was observed, suggesting enhanced brain-to-brain synchrony during competition with the parent in the TD but not ASD group. Furthermore, we did not find significantly increased synchrony in our sample of children and adolescents with ASD in comparison to random pairs, but effects were evident in a matched TD sample. This pattern of results is in line with the notion that synchronization during competition may be elicited via emotional arousal, and that this effect could be reduced in ASD, as has been shown in a study investigating electrodermal activity as a measure of synchrony in the ANS (Baker *et al.*, 2015). However, further studies directly targeting joint emotional arousal and neural synchrony in parent-ASD dyads are needed to investigate this potential link.

To conclude, brain-to-brain synchrony in tasks with 'minimal' motor-synchrony related interaction may either not or only slightly be different in patients with ASD at older ages. Future studies should use more naturalistic designs (for example eye contact and joint attention tasks; Oberwelland *et al.*, 2017; see also Tanabe *et al.*, 2012 for a fMRI hyperscanning study in adults with ASD) or joint problem solving tasks (Nguyen *et al.*, 2020). More naturalistic tasks could potentially reveal higher effects sizes for synchrony which is driven by social-cognitive processing and could be better suited to reveal differences in children and adolescents with ASD also on the neural level.

Limitations

The present study has some limitations with respect to the sample and fNIRS methodology that should be considered. All of our participants with ASD were male and high-functioning, so the inference drawn to the autism population in general is limited. Future studies may include participants with lower functioning ASD as well as female individuals with ASD, considering that gender differences have been reported in previous hyperscanning studies (Cheng *et al.*, 2015; Baker *et al.*, 2016). Given the high comorbidity of ASD with ADHD, future studies may also include an ADHD patient group. Methodologically, the precise localization of the fNIRS channels has to be considered with caution. Future studies may use a 3D digitizer to localize fNIRS channels onto the subject's own structural MRI scan or an age-appropriate template (Tsuzuki and Dan, 2014). Furthermore, the present findings indicate the need for multimodal hyperscanning studies, such as fNIRS-EEG or fNIRS-ANS studies, or short-distance measurements in order to differentiate between neural and non-neural sources in hemodynamic-based brain measurements. Moreover, while our optode set-up covered mainly prefrontal brain areas, no conclusion can be drawn about other brain regions. In particular, 'social brain' regions in the temporal cortex and at the temporoparietal junction are implicated in socio-cognitive processes (Frith and Frith, 2003) and play a role in brain-to-brain synchrony during social interaction (Piva *et al.* 2017).

Conclusions and future directions

Taken together, the present findings indicate that brain-to-brain synchrony may be influenced by both the child's age and the familiarity of the interaction partner in late childhood and adolescence. This highlights the importance of an age-matched control sample and contrasting conditions, in order to elucidate the brain mechanisms underlying social interactions in children and adolescents with ASD. Adolescence is a critical developmental period with marked changes in the relationship with parents and peers, as well as changes in emotional arousal, probably influencing brain-to-brain synchrony across childhood and adolescence. Although cross-sectional developmental differences between children and adolescents in brain-to-brain synchrony, as indicated by our results, are an important finding, further systematic longitudinal studies are warranted. Our results further reveal, in line with other studies, that children and adolescents with ASD show reduced motor synchrony with interaction partners, although this was not reflected on the neural level. While in the current study a highly standardized task was employed, group differences may be observed in more naturalistic designs with higher levels of social interaction. To conclude, more research is needed to investigate the neurobiological underpinnings of a reduced social (motor) synchrony in ASD, with the long-term goal to identify biomarkers for typical and atypical social interactions in order to identify at-risk subjects and evaluate treatments.

Supplementary data

Supplementary data are available at SCAN online.

Acknowledgements

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