# SOCIAL COOPERATION SKILLS AND FNIRS-BASED CORTICAL ACTIVATION IN CHILDREN WITH AND WITHOUT AUTISM SPECTRUM DISORDER

by

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# ABSTRACT

Many everyday skills are learned by observing and moving with others during cooperative actions. A majority of the social cooperative action research has focused on young preschool children and little is known about the developmental changes in social cooperation in typically developing (TD) school-age children. Hence, the first aim of this thesis focused on understanding the developmental changes in social cooperation behaviors between younger and older school-age children. Another focus of this research is to better understand the atypical patterns of social cooperation in children with Autism Spectrum Disorder (ASD). Children with ASD present with significant social-perceptual impairments and comorbid deficits in visuo-motor coordination that might affect their ability to adjust their actions to others during social cooperation tasks. Difficulties with social cooperation will ultimately affect an ASD individual's ability to learn through observation and to connect with their peers/caregivers. Hence, the second aim of this thesis compared social cooperation behaviors between children with and without ASD.

Our lab's previous work has reported improved affect, verbalization, and motor skill performance following 8-weeks of socially-embedded movement interventions offered to children with ASD; however, the neural activation patterns underlying such changes were unclear. Various cortical regions may be activated during social cooperation behaviors including but not limited to the Mirror Neuron Systems consisting of the Inferior Parietal Lobe (IPL), Superior Temporal Sulcus (STS) and Inferior Frontal Gyrus (IFG), the sensori-motor cortices or the Pre /Post

Central Gyri (PCG), as well as prefrontal cortices or the Middle Frontal Gyrus (MFG). The task requirements of social cooperation such as reorienting attention to the task elements/partners, working memory, motor planning, motor anticipation and execution would result in activation within the aforementioned cortical regions. Hence, within each aim we will examine both, the behavioral patterns of social cooperation and associated cortical activation during a naturalistic social cooperation building game using functional near-infrared spectroscopy (fNIRS), a cutting-edge, safe, and child-friendly neuroimaging tool.

Study 1 (Aim 1) examined developmental differences in behavior and cortical activation between younger and older TD children using fNIRS technology during a Lincoln Log building game involving four conditions (Coincide, Lead, Follow, and Turn-take). Our first finding was that younger children had greater motor, spatial and planning errors compared to older children. Second, we noted an age-related increase in prefrontal and mirror neuron system activation but not in the sensori-motor cortices. All TD children showed more left lateralization in the sensorimotor cortices in spite of the bimanual nature of the task. An additional hemispheric difference found was greater right lateralization in the IPL region of the older children, which could be due to their better visuo-motor and visuo-spatial processing abilities. In terms of task-based differences, the superior temporal cortices had greater activation in the more social, Coincide and Turn-Take conditions compared to the other two conditions. Finally, younger children with greater cortical activation had better motor performance and fewer behavioral errors and older children with greater cortical activation showed better socialization skills.

In study 2 (Aim 2), we compared behavioral and fNIRS-based cortical activation patterns between children with and without ASD during the same aforementioned Lincoln Log building game. Our first finding was that children with ASD had greater behavioral errors, took more time to complete the task, and did not have established handedness patterns compared to the TD group. A second finding related to hemispheric lateralization was that children with ASD did not have strong lateralization as was found in the TD group which aligns with findings of atypical or non-existent lateralization in ASD. Third, in terms of task-based differences children with ASD showed no differential activation in the superior temporal cortices as was evident in the TD children, which could be due to lack of social information received and poor visuo-motor correspondence to partner's actions. In terms of group differences, we found that children with ASD had reduced activation in the STS region and greater activation in the IPL region compared to the TD group. We have related these findings to differences in social-perceptual information processing, visuo-motor coordination, as well as executive functioning in the children with ASD.

Taken together, these behavioral and activation patterns offer important neurobiomarkers of social cooperation impairments in children with ASD. This project has uncovered neural mechanisms of cooperative actions that can be used as objective biomarkers to examine effects of therapies targeting social cooperation skills of children and adolescents with ASD. In the future, we plan to develop training activities to facilitate social cooperation and will also examine objective changes in various impaired cortical regions following the intervention.

# Chapter 1

# OVERVIEW OF SOCIAL COOPERATION

## 1.1 Social Cooperation and its Importance to Development

Social cooperation is defined as a form of social interaction in which individuals work towards a common goal by matching actions in time and space with other social partners (Sebanz, Bekkering, & Knoblich, 2006). Many activities performed in daily life such as carrying large objects, playing sports, or singing a duet require individuals to work towards a common goal while engaging in social cooperation. Socially cooperative behavior allows adults to adapt to a partner's movements, understand their emotional states and goals, and establish a greater sense of affiliation or interconnectedness with them (Burling & Lu, 2018; Michael, Sebanz et. al., 2016; Lakin, Jefferis, Cheng, & Chartrand, 2003). Children who participate in social cooperation show increased logical reasoning, improved fine motor control, and better self-regulation (Ashton & Chartrand, 2009; Finkle, Brunell, Dalton, Scarbeck, & Chartrand, 2006). When children synchronized their actions with adults, they began to use more helping behaviors towards them (Tuncgenc & Cohen, 2016). For example, children were assigned to synchronous or asynchronous tap-clap conditions. After completion, those assigned to the synchronous condition were more likely to help a partner later in picking up fallen objects and showed increased enjoyment, eye contact, and mutual smiles directed to the partner (Tunçgenç & Cohen, 2016). In the long-term such cooperation can help facilitate positive attitudes towards social partners, increased socialization, higher self-esteem, and higher feelings of acceptance to a social group, aiding in successful integration into an environment and the development of relationships (Hooper, 1992). Therefore, one of the broad goals of this research is to study the developmental changes in social cooperation throughout childhood.

### 1.2 Different types of Social Cooperation tasks

Social cooperation has not been widely studied and studies completed involve relatively simple actions such as finger tapping (Rabinowitch & Knafo-Noam, 2015), lifting (Richardson, Marsh, & Baron, 2007), drumming (Kirschner & Tomasello, 2010), whole-body swaying (Sofianidis, Hatzitaki, Grouios, & Johannsen, 2012), and walking (Wiltermuth & Heath, 2009). Additionally, social cooperation can involve discrete, continuous, or more complex tasks such as turn-taking behaviors between social partners. For example, in a discrete task, two people would engage in imitation, which involves separate actions to reproduce the partner's actions such as actions performed in a Simon Says game (e.g. Meltzoff, 2007; Nadel, 2015). Imitation can also involve dyadic exchanges such as simultaneous eye blinks or communicative gestures, or triadic exchanges involving imitation of actions upon objects (Nadel, 2015; Smith and Bryson, 2007). However, imitation is a simpler form of social cooperation since it involves a finite number of actions rather than continuous moment-to-moment synchronization over time. A more complex form of social cooperation is interpersonal synchrony (IPS), where partners' synchronize their actions moment-to-moment for example when tapping fingers, lifting large objects, or walking together (Richardson et al., 2007; Rabinowitch & Knafo-Noam, 2015; Wiltermuth & Heath, 2009). Turn-taking is another form of social cooperation involving complementary yet unique actions. For example, during a building task, one partner places a block in one location as the other partner responds with their own unique block placement (Gräfenhain, Behne, Carpenter, & Tomasello, 2009). Our previous research has mainly focused on imitation and IPS behaviors in children (Kaur, Srinivasan, & Bhat, 2017; Bhat et al., 2017). In our current research, we extend the work to socially cooperative actions during a Lincoln Log building game between two social partners - a child and an adult.

During social cooperation, partner roles vary depending on task demands. During turn-taking tasks, one individual within a pair of social partners may be the leader of the pair and will need to move in an anticipatory manner based on their own individual task goals and their past understanding of the pair moving together to complete the shared task goals, whereas the follower within the pair will need to actively monitor the movement patterns of the leader and use more real-time feedback to control their movements (Candidi et al., 2017; Sacheli, Tidoni, Pavone, Aglioti, & Candidi, 2013). In contrast, during imitation/IPS tasks, partners move concurrentl*y*, making moment-to-moment changes to match their actions together. In this research, we will examine differences in performance between conditions in which partners Coincide, Lead, Follow, or Turn-Take (i.e., complementary actions). The Coincide condition involves two partners working individually on dissimilar cue cards but at the same time (sometimes partners perceived this as a competitive condition), the Follow condition requires interpersonal synchrony to match actions of a partner and build one’s own creations, and the complementary, Turn-take condition involves alternating turns to build a single creation. Lastly, we included a Lead condition which serves as a Control as it requires one partner to lead and form their own individual creation. Note: During the Lead condition, the other partner is supposed to Follow the Leader and complete the Follow condition. Each partner has equal opportunity to Lead and Follow.

### 1.3 Requirements of Social Cooperation

Different types of social cooperation place distinctive requirements on participant pairs, which differ depending on the role a partner has taken on. First, participants must understand the shared goals of the cooperative task as well as their particular role in the task. Therefore, overall goals are shared and similar; yet, each partner's goals can be individual and distinct, depending on the nature of the cooperative task. An example of social cooperation is moving a table with a partner, with the shared goal being the placement of the table in the desired end location. The individual goals in this task could differ i.e., one partner walks forward with the other walking backwards to bring the table to the desired location. Second, participants must observe the environment and the partner's preparatory actions to anticipate how to shape one's own actions in response. In the table-carrying task for example, it is necessary for the individual to scan their environment for objects that may block successful movement of the table. In addition, each individual must be attuned to their partner's actions to understand how to efficiently transport the table. If one partner is carrying the table quickly, the other partner must speed up their movements to remain in synchrony with the partner. Conversely, if one partner is smaller in size/younger, the larger/older partner might compensate by sharing more of the table's weight. Third, participants engaging in cooperative actions must anticipate and plan one's own actions. This requires the individual to think about how they will position their body in relation to the table before beginning the task. A crucial aspect of this step is for the individual to perceive sensory information they receive from their environment and their partner and integrate that into their motor plan. Examples of such self-anticipation includes how an individual orients his/her body towards the table and whether they widen their base of support by keeping their feet a certain distance apart, etc. The remaining two requirements of cooperative action are coordinating and executing an action and adjusting one's own actions in response to self or other's errors using feedback-based corrections of one's own movements. As mentioned earlier, I have developed a novel social cooperation game between two partners using Lincoln Logs involving each of the aforementioned processes. The requirements for each partner will vary depending on their roles across the four conditions of Lead, Coincide, Follow, and Turn-take.

### 1.4 Developmental differences in Social Cooperation

The requirements of social cooperation gradually develop during childhood including goal understanding, awareness of the partner and environment, anticipation and planning of actions, coordinating and executing the actions, and corrective movements based on feedback of individual's and partner's actions. As stated above, the first requirement of social cooperation is understanding the partner's goal; in order to do so, children must observe their social partner, whether it is a teacher, classmate or a parent. As early as 2 months of age infants partake in dyadic interactions with a parent and by 9 to 12 months infants begin to show triadic interactions involving objects in their surroundings as parents either look towards objects or point to them (Mundy & Newell, 2007). This ability to respond to social bids of caregivers is called joint attention. Around the same time, infants also demonstrate the ability to anticipate how they should move their arms in response to changes in their environment. For example, older infants anticipate the direction of an object's motion and successfully reach towards its destination. Between 12 and 24 months, infants progress from performing one-step sequences to two and three-step sequences that require more feedforward planning (Willats & Rosie, 1989). Around 2 years of age, children begin to sustain dual-limb, rhythmic actions requiring greater coordination such as stable in-phase and anti-phase drumming compared to younger toddlers (Brakke, Fragaszy, Simpson, Hoy, & Cummins-Sebree, 2007). Between 3 and 7 years, children further improve the consistency of their dual-limb actions. During clapping actions, 7-year-old children had significantly reduced variability compared to 3-year-olds (Fitzpatrick, Schmidt, & Lockman, 1996). Furthermore, between 4 to 6 years, children have high variability in their multi-limb actions such as walk and clap motions. However, there is a developmental shift occurring between 6 and 8 years in which children progress to performing more stable and consistent multi-limb actions, with adult-like consistency by 8 to 10 years of age (Getchell & Whitehall, 2003). It is necessary for children to understand how to coordinate their own limb movements in order for them to effectively synchronize with a partner. Improvements in motor capabilities throughout the course of development will facilitate interpersonal synchronization as children become less variable and more consistent in their motion. For example, the level of synchrony was lower in a pair of young children drumming together compared to pairs of older children or adults drumming together. In short, with development, children become more organized and less variable in their movements, which enhances their social cooperation skills (Kleinspehn- Ammerlahn, Riediger, Schmiedek, Oertzen, & Lindenberger, 2011).

The third form of cooperation, i.e., complementary actions or turn-taking within a social task and a child’s commitment to working with adults emerges around the second year of life, but solidifies in the preschool years between 3 and 5 years of age.

Grafenhein et al. found in a series of activities, capable of being performed in cooperation or alone, that 3-year-old children were more likely to re-engage a social partner who broke off from a cooperative activity if both individuals had previously made commitments to each other to complete the activity. Additionally, 3- and 4-year-olds who had indicated commitment at the beginning of social cooperation would acknowledge to their partner if they planned to leave the activity (Grafenhein et al., 2009). In terms of feedback-based adaptation, younger, preschool children are not proficient at adapting to moment-to-moment task relevant features. This could be attributed to their own motor incoordination or to their inability to carefully attend to others. During a drumming activity, typically developing (TD) children were able to synchronize their drumming more easily in time to the actions of an adult partner compared to an invariable, non-social drumming machine (Kirshner & Tomasello, 2009). This might occur because the adult partner adjusted their drumming motions to accommodate the child's inconsistencies, which the drumming machine could not do. However, as children reach the 8 to 10-year mark, they will exhibit better action synchronization, more similar to adults (Kleinspehn et al., 2011). Based on the developmental progressions discussed above, we anticipate developmental differences in social cooperation within our Lincoln Log task as children age and improve both their own motor coordination as well as their ability to coordinate with a moving partner. Therefore, the initial aim (i.e., Chapter 2) of this research will examine developmental differences in social cooperation within the Lincoln Log task.

## 1.5 Deficits in Social Cooperation in Children with ASD

One in 59 children in the U.S. are diagnosed with Autism Spectrum Disorder (ASD), making it a cause for concern and further study (Baio et al., 2018). Children with ASD have primary impairments in communication, social interaction and restrictive repetitive behaviors (American Psychiatric Association, 2014). They also have significant comorbid motor and cognitive impairments including motor incoordination, poor balance, as well as impaired imitation and motor planning (Bhat et al., 2011; Minshew, Sung, Jones, & Furman, 2004; Kaur et al., 2017; Dziuk et al., 2007), and poor executive functioning/cognitive flexibility (Freeman, Lock, Rotheram-Fuller, & Mandell, 2017; Hughes, 1997). The primary impairments in social communication such as poor social gaze/eye contact and social awareness directly affect an ASD individual's ability to perceive the non-verbal cues of his/her partner and, in turn, affect social cooperation performance. Additionally, the inability to effectively plan, anticipate, and coordinate one's own limb movements as well as poor adaptation to a partner's actions based on moment-to-moment alterations also affects their social cooperation performance. Finally, the executive functioning impairments in ASD such as poor working memory and cognitive flexibility will affect their ability to plan motor actions to achieve a shared goal. Taken together, these impairments cause children with ASD to forego the long-term positive outcomes of social cooperation mentioned earlier. These positive outcomes such as increased reasoning skills and self-regulation, improved motor control, increased feelings of affiliation and closeness to a partner, and an improved view about the world and others are lost to children with ASD. Therefore, the second crucial aim (Chapter 3) of this research is to examine social cooperation deficits in children with ASD during the Lincoln Log task by comparing their performance to a group of age-matched typically developing (TD) children without

ASD. Based on our findings, we plan to make recommendations to clinical researchers about certain behavioral strategies that could help improve the social cooperation skills of children with ASD.

### 1.6 Neural substrates for imitation, interpersonal synchrony, and social cooperation - Mirror Neuron System, Somatosensory Cortices, and Prefrontal Cortices

There are few studies on the underlying mechanisms of complementary/turn-taking behavior, but an abundance of literature exists on the neural substrates of imitation, which is a simpler form of social cooperation. Different neuroimaging techniques in TD individuals have confirmed that the putative Mirror Neuron System (MNS), consisting of the Superior Temporal Sulcus (STS), the Inferior Frontal Gyrus (IFG) and the Inferior Parietal Lobule (IPL), is important for performing imitative actions (Iacoboni et al., 2005; Jeon & Lee, 2018; Rizzolatti & Fogassi, 2014). Mirror neurons are said to be active during all components of imitation including observation only, execution only, as well as imitation (i.e., matching of observation and execution) during goal-directed actions (Iacoboni et al., 2005). The STS is active when observing biological motions or other's intentions (Newman-Norlund, van Schie, van Zuijlen, & Bekkering, 2007; Pelphrey et al., 2003). The IFG plays an important role in understanding the goals of a task and the IPL is important for planning the kinematic aspects of actions (Iacoboni et al., 2005).

As described under "task requirements", individuals need to organize their attention to task components and utilize planning and working memory abilities to engage in social cooperation. For these reasons, social cooperation tasks may also engage the middle frontal gyrus (MFG) which is known to be important for reorienting attention and spatial working memory (Japee, Holiday, Satyshur, Mukai, & Ungerleider, 2015; Leung, Gore, & Goldman-Rakic, 2002). Specific to our task/research, the Lincoln Log game will require partners to organize their attention to task elements as well as their partner and retain spatial memory of their partner's actions while placing the blocks. The Post-Central Gyrus is important for processing sensory information and the Pre-Central Gyrus is important for executing motor commands to muscle groups involved in a motor task (Gazzola & Keysers, 2009). Each partner will need to perceive sensory information from the overall environment as well as coordinate and execute their individual actions, hence, the Pre and Post Central Gyri (PCG), also known as the sensorimotor cortex, will play an important role as well. Taken together, several functional magnetic resonance imaging (fMRI) studies have reported greater activation in the aforementioned cortical regions during object-related imitation and complementary action tasks and these same regions will be a focus of study in this research (Newman-Norlund et al., 2007; Ocampo, Kritikos, & Cunnington, 2011; Shibata, Suzuki, & Gyoba, 2007; Sacheli, Candidi, & Aglioti, 2015; Gazzola & Keysers, 2009; Japee, Holiday, Satyshur, Mukai, & Ungerleider, 2015; Leung, Gore, & Goldman-Rakic, 2002).

### 1.7 Benefits of fNIRS technology over fMRI

The majority of the previous studies on imitation and cooperation utilize fMRI, the gold standard of neuroimaging. At the same time, there are several significant limitations to using fMRI during (a) motor tasks and (b) tasks involving two people. In the scanner, subjects are limited to simple finger tapping, hand grasping, and visual response tasks. The fMRI testing environment itself is unnatural and constrained, limiting the ability to test naturalistic social interactions between individuals. fMRI studies are challenging to conduct with children with developmental disabilities or infants since these groups have difficulty remaining still for long periods of time and this technology is particularly vulnerable to motion artifacts (Makowski, Lepage, & Evans, 2019). In contrast, functional Near Infrared Spectroscopy (fNIRS) technology is only constrained by a cap and provides robust data in the presence of motion artifacts, allowing for natural limb movements during a variety of activities such as walking, juggling, playing the piano or sport (i.e. table tennis) (Leff et al., 2011; Carius et al., 2016, Balardin et al., 2017). The fNIRS technology is effective for testing children as it is safe, it does not involve the use of tracer substances in the blood, does not expose them to radiation, and does not require sedation. In comparison to other neuroimaging modalities, it is relatively low-cost and has high temporal resolution compared to fMRI and positron emission tomography (PET) and better spatial resolution than magnetoencephalography (MEG) and electroencephalography (EEG) (10 Hz vs. fMRI is typically 1 Hz) (Lloyd-Fox et al, 2010; Gervain et al., 2011). In terms of spatial resolution, channels are 30 mm apart and underlying gyri can be distinguished using spatial registration approaches. One drawback is that it has lower depth resolution and only captures activation across a 20 mm depth from the skull surface (i.e., mainly the cortical surface). Since our research involves socially embedded actions of children with and without ASD, we chose to implement fNIRS technology to allow for naturalistic social interactions and natural movements. Lastly, children with ASD are known to have significant cortical abnormalities as seen by local hyper-connectivity in the prefrontal, frontal, parietal and temporal cortices and long-distance hypo-connectivity across different cortical regions (Courchesne & Pierce, 2015).

Additionally, there is substantial evidence for cortical impairments in the Mirror Neuron Systems of children with ASD, which contributes to their imitation, synchrony, and social cooperation difficulties (Iacoboni et al., 2005). For this reason, we have chosen to use fNIRS as a measure to examine underlying cortical mechanisms of social cooperation during the proposed Lincoln Log game. Our lab has previously utilized fNIRS technology for an interpersonal synchrony task in children with and without ASD and found that children with ASD tended to have lower overall cortical activation in certain regions of the brain (i.e., IFG and STS) and greater IPL activation during the more social Together condition compared to a TD control group. In this research, we extend our previous work to a novel Lincoln Log building task in which children will wear the fNIRS cap and perform various contexts of social cooperation using leader and follower roles and cooperative, complementary turn-taking. I will expand upon additional neuroimaging findings (fMRI and fNIRS) within the chapters 2 and 3 of this thesis. Lastly, Chapter 4 will summarize the key findings of this research and discuss the implications of our findings as well as directions for future research.

## 1.8 Specific Aims

**Aim 1 (**Younger TD vs. Older TD): To compare behavioral patterns and cortical activation between younger and older TD children during a social cooperation building game involving four different conditions (Lead, Coincide, Follow, and Turn- Take).

**H1.1 (Age-related correlations):** Age will correlate with cortical activation patterns during the cooperative building game.

**H1.2 (Behavioral Differences):** We expect to find differences in behavioral errors, hand use, and time to task completion between younger and older children.

**H1.3 (Condition-related differences):** Multiple cortical regions will show more activation in the more social Turn-Take condition compared to the other conditions of the cooperative building game in older and younger children.

**H1.4 (Hemispheric Differences):** There will be greater lateralization found in the older children compared to the younger children.

**H1.5 (Brain-behavior Relations):** Cortical activation will correlate with social and behavioral performance on the standardized questionnaires (Social Responsiveness Scale and Vineland Adaptive Behavioral Scale) as well as task-related, behavioral performance.

**Aim 2 (**TD children vs. children with ASD): To compare behavioral patterns and cortical activation between children with ASD and age-matched, TD children during a social cooperation building game involving four different conditions (Lead, Coincide, Follow, and Turn-Take).

**H2.1 (Behavioral Differences):** Children with ASD will have more behavioral errors, show mixed handedness, and take more time to complete actions compared to TD children.

**H2.2 (Group Differences):** Compared to the TD group, children with ASD will show lower cortical activation in certain regions (e.g. STS and IFG) as well as compensatory higher activation in other cortical regions (e.g., IPL).

**H2.3 (Condition-related Differences):** TD children will show an increase in cortical activation during the more social conditions (Coincide, Follow, and Turn-take) compared to the Lead condition. In contrast, children with ASD will not show similar increases in cortical activation across the different conditions.

# Chapter 2

# DEVELOPMENTAL TRAJECTORY OF SOCIAL COOPERATION

## 2.1 Introduction

Social cooperation requires individuals to work together towards a common goal by matching actions in time and space with social partners (Sebanz, Bekkering, & Knoblich, 2006). Examples of social cooperation include carrying large objects, playing sports, musical duets and synchronized walking. Three types of cooperation between two people exist. First, *imitation* involves discrete actions to reproduce a partner's movements (Nadel, 2015). Second, *interpersonal synchrony* involves continuous moment-to-moment synchronization to a partner's actions (Richardson, Marsh, & Baron, 2007). Third, *turn-taking* involves complementary yet different actions, i.e., one partner takes a turn to perform an action and then the other partner performs a different action appropriate for task completion (Tomasello & Hamann, 2011). Children who participate in social cooperation are known to show increased logical reasoning, fine motor control, and self-regulation (Ashton-James & Chartrand, 2009; Finkel et al., 2006). In one research study, when children synchronized their actions with a partner, they later used more helping behaviors towards their partner (Tunçgenç & Cohen, 2016). For example, children were assigned to synchronous or asynchronous tap-clap conditions. After completion, those assigned to the synchronous condition were more likely to assist a partner in picking up fallen objects and showed increased enjoyment, eye contact, and mutual smiles with their partner (Tunçgenç & Cohen, 2016). Over the long-term, such cooperation helps in facilitating positive attitudes towards social partners, increased socialization, higher self-esteem and higher feelings of acceptance to a social group which all aide in successful integration into the environment and the development of relationships (Hooper, 1992). Therefore, it is important to understand the developmental trajectory of social cooperation behaviors. While there is some work done in pre-school age children and adults (Richardson et al., 2007; Ray & Welsh, 2011; Kirschner & Tomasello, 2010), few studies have examined the developmental differences in social cooperation behaviors between younger and older school-age children. Moreover, the underlying neural mechanisms of social cooperation have not been well studied. In this study, we compared four types of social cooperation behaviors and associated cortical activation patterns using functional Near Infrared Spectroscopy (fNIRS) between younger and older typically developing (TD) children.

### 2.1.1 Task Requirements of Social Cooperation and Roles of the Partners

Social cooperation tasks require multiple complex perceptuo-motor and cognitive skills. These include understanding task-related goals; not only individual task goals but also shared goals related to the overall task. For example, during a "jug-handing" task, participants handed a jug to their partner by holding it close to their body and leaving the handle exposed to facilitate the partner's grasping motions, suggesting that they modified their own actions to accommodate the actions of their partner (Ray & Welsh, 2011). Additionally, during social cooperation, individuals must perceive task-relevant cues from the environment as well as their partner for successful cooperation. First, they must plan their individual action and anticipate their partner's action. Second, the individual must adapt to moment-to-moment changes in the partner's action while still using their own error feedback while moving. For example, when adults lifted and moved planks together they not only adjusted their actions to the environment but also to their partner (Richardson et al., 2007).

Task demands also varied based on partner roles during social cooperation. Leaders within a social cooperation task will need to move in an anticipatory manner based on their own individual task goals and their past understanding of the pair moving together to complete the shared task goal (Candidi et al., 2017; Sacheli et al., 2013). In contrast, the follower needs to actively monitor the movement patterns of the partner and use real-time feedback to adjust their own actions (Candidi et al., 2017; Sacheli et al., 2013). In this study, we developed a novel Lincoln Log building task involving conditions of Lead, Coincide, Follow and Turn-Take. In general, the building task required some level of executive functioning, visuo-spatial, and visuo-motor skills as multiple logs were put together to form a log structure. In the Lead condition, one partner (i.e., the Leader, either the tester or the child) was provided the cue card with the structure to build and was spear-heading the movements within the pair. At the same time, the other partner (i.e. child or tester) "followed", by mirroring the partner's actions and building their own structure (i.e., requiring interpersonal synchrony). No cue card was provided to the follower, and as a result they were required to base their actions upon the Leader's actions. In the Coincide condition, both child and tester were asked to build the structure on the cue card placed in front of them, with each building a different structure. Though we expected a solo building effort, children may have perceived competition and seemed to move faster to build their structure before that of the adult. In the turn-take condition, both the child and the adult were shown the same cue card and they alternated turns to complete half the number of placements, three each, in this task. We have scored participants' motor, planning, and spatial placement errors, time to task completion, type of hand use (right, left, or both/mixed) as well as underlying cortical activation patterns using functional Near Infrared Spectroscopy (fNIRS) during each of the aforementioned conditions to understand how behavioral errors and neural activation patterns varied based on partner roles and task requirements.

### 2.1.2 Developmental Changes in Cooperation

Few studies have described the developmental changes in social cooperation skills during childhood. Late in the first year of life, infants begin to follow parental looks or points made towards objects in the environment, also known as *joint attention* (JA; Mundy & Newell, 2007). JA can be a precursor to the development of many social skills such as imitation, word learning, and pretend play (Mundy & Newell, 2007). In the first two years of life, infants transition from the imitation of discrete actions that are simple and one-step to unfamiliar multi-step sequences (Jones, 2007). By two and a half years, they can perform sustained rhythmic actions that require synchronization such as drumming with a partner (Kirschner & Tomasello, 2010; Brakke, Fragaszy, Simpson, Hoy, & Cummins-Sebree, 2007). However, young children's coordination of limb and body movements dramatically changes over the next 6 to 8 years. The consistency of clapping actions of 7-year-old children was greater compared to 3-year-olds (Fitzpatrick, Schmidt, & Lockman, 1996). Furthermore, for multi-limb actions such as walk and clap, 4- to 6-year old children have greater variability compared to 6- to 8-year-old children, suggesting a developmental shift in coordination around that time. Moreover, by 8 to 10 years, children are able to perform stable and consistent multi-limb actions, similar to adults (Getchell & Whitall, 2003). Taken together, children improve basic social perception/awareness as well as their own motor coordination between infancy and school age, i.e., by 8 to 10 years of age they have stable coordination patterns similar to adults. These changes will help school-age children to better engage in socially cooperative actions.

Through development as children improve their motor coordination they are more equipped to engage in interpersonal synchrony with other partners. Preschool children are able to more effectively synchronize their moment-to-moment drumming patterns to that of an adult drumming partner compared to a drumming machine (Kirschner & Tomasello, 2011). This may be because the adult partner will adapt to the child's variability in order to make it easier for the child to synchronize, whereas the machine will not. In fact, similar to their inherent motor coordination patterns, children gradually improve their interpersonal synchrony skills during childhood. A study by Kleinspehn-Ammerlahn and colleagues found that young elementary school-aged child-child pairs had the lowest levels of IPS during synchronous drumming followed by middle school child-child pairs and lastly, young adult-adult pairs (Kleinspehn-Ammerlahn et al., 2011). By adulthood, individuals are able to perceive and successfully adjust their movements to overall task requirements to engage in individual or socially cooperative actions. Richardson et al. (2007) found that during a plank-carrying task, adults chose to move planks individually when they were small and engaged in social cooperation when the size of the planks became large enough that it was more effective to lift them cooperatively with their partner's help (Richardson et al., 2007). Generally, previous research has focused on social cooperation in preschool children and adults, but very few studies have examined how social cooperation develops from childhood through adolescence.

### 2.1.3 Cortical Regions Important for Social Cooperation

Few studies have described the neural substrates underlying complementary, socially cooperative actions, however, the Mirror Neuron System (MNS) we focused on is clearly implicated in imitation (Iacoboni, 2005) and is also found to play a role during interpersonal synchrony (Bhat et. al., 2017). The MNS includes the Inferior Frontal Gyrus (IFG), Superior Temporal Sulcus (STS), and Inferior Parietal Lobule (IPL). Within the context of imitation, the posterior STS is important for establishing a visuo-motor correspondence between two partners (Molenberghs, Brander, Mattingley, & Cunnington, 2010; Pelphrey et al., 2003), the IFG plays an important role in understanding task goals (Iacoboni, 2005), and the IPL is said to be important for planning the kinematic aspects of the imitated actions (Iacoboni, 2005). During social cooperation individuals utilize executive functioning skills to organize their attention to task components, to monitor their partner/environment, and to inhibit their motor responses when appropriate. Given this requirement of social cooperation tasks, children may also engage the middle frontal gyri (MFG) or the dorsolateral prefrontal cortices (DLPFC) which contribute to executive functioning, reorienting attention, and spatial working memory skills (Rubia, 2013; Japee, Holiday, Satyshur, Mukai, & Ungerleider, 2015; Leung, Gore, & Goldman-Rakic, 2002). Lastly, each partner must perceive sensory information from the environment as well as coordinate and execute their actions (Gazzola & Keysers, 2009); hence, the Pre and Post Central Gyri (PCG) should be activated as well. It is important to note that during social cooperation behaviors no region works alone. Each works with one another in addition to working with premotor cortices, supplementary/pre-supplementary motor cortices, cingulate insular cortices, cuneus/precuneous as well as subcortical structures such as the cerebellum, basal ganglia, and others (Gazzola and Keysers, 2009; Iacoboni, 2009). In this study, we examined cortical activation across the three components of the MNS (IFG, IPL, and STS), Pre and Post Central Gyri and prefrontal cortices (i.e., middle frontal gyrus) as children performed cooperative building across four conditions (Lead, Coincide, Follow, Turn-Take).

#### 2.1.4 Condition-related differences in cortical activation during social cooperation

Several functional magnetic resonance imaging (fMRI) studies have compared MNS activation across the components of imitation behaviors, specifically, comparing observation, execution, and imitation tasks involving gestures or actions on objects. A study by Molenberghs and colleagues found that activation was greater in the bilateral STS during imitation compared to action observation and execution, suggesting that this region provides a visual description of the observed action and compares that to the planned actions (Molenberghs et al., 2010). In another study, Newman-Norlund, using a manipulandum grip task, found greater Blood-Oxygen-Level-Dependent (BOLD) signal in the bilateral IPL and right IFG during preparation for complementary actions compared to imitative actions (Newman-Norlund, van Schie, van Zuijlen, Bekkering, 2007). Two other studies found IFG and STS activation in adults during incongruent or unnatural actions compared to congruent actions, indicating that these regions are important for understanding a partner's intention in action (Ocampo, Kritikos, & Cunnington, 2011; Shibata, Suzuki, & Gyoba, 2007). Sacheli et al. (2015) applied continuous theta burst stimulation to the anterior intraparietal sulcus (aIPS) during performance of complementary and imitative hand grips on a manipulandum, which interfered with complementary grips but not the imitative grips, indicating that the aIPS plays a more important role in understanding the shared goals of complementary actions (Sacheli, Candidi, Era, & Aglioti, 2015).

Given the goal-oriented reaching and placing of objects involved in the Lincoln Log building task, greater left hemispheric activation is often reported during object-based gestural actions (Buxbaum, Kyle, & Menon, 2005; He, Li, & Yin, 2019). A study by Kroliczak et al. found that planning tool-based actions using the dominant right hand or non-dominant left hand led to greater left- lateralized activation within parietal (intraparietal sulcus/supramarginal gyrus, superior parietal gyrus), frontal (dorsal premotor cortex, right Middle Frontal Gyrus), and temporal regions (caudal Middle Temporal Gyrus) (Kroliczak & Frey, 2009). On the other hand, many studies report that imitation is bilateral in nature or involves greater right-hemispheric activation compared to the contralateral nature of individual actions (Biermann-Ruben et al., 2008; Aziz-Zadeh, Koski, Zaidel, Mazziotta, & Iacoboni, 2006; Caspers, Zilles, Laird, & Eickhoff, 2010). Aziz-Zadeh et al. found bilateral IFG and IPL activation in the imitation and observation conditions during a unilateral button pressing task compared to solo execution which involved more contralateral activation (Aziz-Zadeh et al., 2006). Similarly, another study found that complementary actions involve greater right IFG activation (Brass, Derrfuss, & von Cramen, 2005). Taken together, there appears to be region-specific variations in hemispheric lateralization within the Lincoln Log task.

### 2.1.5 Functional and structural changes in cortical development during childhood

Children undergo significant structural and functional changes in the cortices as they transition from childhood to adolescence and adulthood. Structural imaging studies show that grey matter volume reduces and white matter volume increases over development (Lenroot & Giedd, 2006; Giedd et al., 1999). Such grey matter loss and white matter gains are associated with enhancements in cognitive development (Casey et al., 2005). These broad maturational changes occur in the primary sensorimotor cortices within the first two years of life followed by similar changes throughout childhood and adolescence in the higher-order association areas such as the DLPFC and the inferior parietal and superior temporal gyri (Liu, Flax, Guise, Sukul & Benasich, 2008; Gogtay et al., 2004, Sowell et al., 2004, Chugani, Phelps, & Mazziotta, 1987). Functional imaging studies have supported this fine-tuning of brain structures from childhood to adulthood, evidenced by a shift from more diffuse activation to more focal recruitment of brain regions (Durston et al., 2006; Marguiles et al., 2007). A study by Lin et al. comparing resting state functional connectivity between 2-week-old, 1-year-old, and 2-year-old children found greater connectivity as early as 2 weeks in the sensorimotor cortices compared to the visual cortices, suggesting that sensorimotor cortices develop much earlier in life compared to visual cortices (Lin et al., 2008). Similarly, multiple fMRI studies report an age-related linear increase in task-based activation and inter-regional connectivity in the fronto-temporo-parietal networks between childhood and adulthood. These changes in functional activation and connectivity are associated with improvements in executive functions such as task-related attention, motor timing, response inhibition, spatial and working memory, cognitive shifting, and performance monitoring between late childhood and adolescence (Rubia, 2013).

### 2.1.6 Gaps in research and value of fNIRS

The majority of studies on changes social cooperation behaviors are focused in young preschool children or adults. There are few studies examining the developmental changes in social cooperation behaviors between childhood and adolescence. Additionally, there are limited studies on cortical activation patterns associated with social cooperation in children given the complex, real-world nature of such tasks. Finally, many brain imaging studies on social cooperation have used fMRI, the gold standard of neuroimaging, and report on patterns during observation and imitation of finger and hand movements but not during real-world cooperative games such as cooperative block building. We chose to use functional Near Infrared Spectroscopy (fNIRS) technology, which utilizes near infrared light to indirectly measure changes in the concentration of oxygenated, deoxygenated and total hemoglobin levels as oxygen changes occur in the cortical tissues of the brain during metabolic processes (Lloyd-Fox, Blasi, & Elwell, 2010). This technology is ideal in that it provides robust data in the presence of motion artifacts and allows for ecologically relevant study of naturalistic face-to-face tasks, as is often the case with socially cooperative games (Kim, Seo, Jin Jeon, Lee, & Lee, 2017). In addition to providing robust data during movement tasks, fNIRS has better spatial resolution than Magnetoencephalography (MEG) and Electroencephalography (EEG) and better temporal resolution than fMRI and Positron Emission Tomography (PET) (Lloyd-Fox et al, 2010; Gervain et al., 2011). Compared to fMRI, fNIRS is weaker in its spatial resolution, an issue we address by using spatial registration methods developed by our collaborator Daisuke Tsuzuki (Tsuzuki et al., 2012).

## 2.2 Methods

### 2.2.1 Participants

Seven TD children between the ages of 6 and 11 years (Average: 7.89 and Standard Error (SE): 0.79; 4 Males and 3 Females; younger group) and ten children between the ages of 11.4 and 17 years (Average: 14.22 and Standard Error (SE): 0.78; 5 Males and 5 Females; older) participated in this study (See Table 1 in Appendix). Individuals were recruited using online postings through various listservs, fliers, and word-of-mouth. Before testing, we completed screening interviews with potential participants to exclude individuals with any known neurological or psychiatric diagnoses, those taking psychotropic medications, and those with any other challenges/difficulties that would prevent them from successfully performing this task design. A standardized handedness survey was administered to participants and found that sixteen children were right handed while one child was weakly left handed (Coren, 1992). This left-handed participant had activation patterns consistent with our group results so these data were not excluded. All participants had normal or corrected to normal vision. Parents of children completed the Vineland Adaptive Behavioral Scale (VABS) to report their child's adaptive functioning across domains of communication (receptive, expressive, written), socialization (interpersonal relationships, play and leisure, coping skills), daily living (person, domestic, community), and motor subscales (Sparrow, Balla, & Cicchetti, 1984). All children had typical levels of subdomain function and overall adaptive functioning on the VABS measure (Table 1 in Appendix). In addition, we administered the Bruininks-Oseretsky Test of Motor Proficiency-2 (BOT-2)'s manual dexterity subtest in our participant groups (Table A.1 in Appendix). The Manual Dexterity (MD) subtest involves various reaching, grasping and bimanual actions involving small objects such as card sorting, placing pegs in a peg board and penny transfer games (Bruininks, 1978). The University of Delaware International Review board (IRB protocol id #: 12227966-1) approved the protocol of this study and all human procedural testing was carried out in accordance to their recommendations. Prior to participating in the study, all parents of participants gave their written informed consent for participation in accordance with the Declaration of Helsinki. Children who were able gave their written informed consent for participation.

### 2.2.2 Data Collection

The Hitachi ETG-4000 system was used to capture changes in oxygenated and deoxygenated hemoglobin (Hitachi Medical Systems, Tokyo, Japan) (Sampling Rate: 10 Hz). The probe set was positioned over frontal, temporal and parietal regions of the brain. The midline of the probe set was aligned with the Nasion/base of the nasal bridge and the lower border of the probe set was aligned just above the eyebrow and just above the ears and extended just past both ears. Pairs of probes, located 3 cm apart, acted as emitters and receivers for two wavelengths of light - 695 and 830 nm. Light travels from the emitter in a banana-shaped arc through the skin and skull to reach the capillary bed in the cortical tissue of the brain at the midpoint between the two probes. Using the Modified Beer-Lambert law, changes in light attenuation were then used to determine changes in the concentration of oxygenated ($HbO_2$) and deoxygenated hemoglobin

(HHb) per each channel pair. During task performance or the stimulation period, neural activation leads to an increase in metabolic rate and oxygen consumption/demand and an increase in blood flow to the capillary bed supplying the brain region; which in turn leads to an increase in oxygenated hemoglobin ($HbO_2$) and a slight decrease in deoxygenated hemoglobin (HHb, Hb molecules with no $O_2$ attached) (Lloyd-Fox et al, 2010; Scholkmann et al., 2014; Wolff et al., 2002). The light attenuation data was exported from the Hitachi system in the form of a comma separated value (.csv) file for post processing. E-prime software (version 2.0) marked the baseline and stimulation periods using a Windows PC computer to trigger the Hitachi machine via a serial port. It also cued the participant about the start and end of the stimulation period and the start and end of the trial using an auditory cue/beep. The entire session was videotaped using a camcorder synchronized with the Hitachi fNIRS system, which later enabled students to visually code aspects of behavior occurring during the session.

### 2.2.3 Experimental Design

Each child was seated at a table across from the tester and fitted with a 3x11 fNIRS probe set (Figures 2.1 and 2.2). The child and tester were given a container of Lincoln Logs consisting of four plain brown logs and four colored support logs. The container was set on the child's left side, which may have led to a left-hand bias compared to the child's natural tendency to use their dominant right hand, as our handedness survey indicated. For each condition, a cue card was placed in a holder located either in front of one or both participants during set-up. At the start of the stimulus period, depending on the condition, the participants flipped the cue card and began building the structure shown on the card. The task consisted of four conditions and followed a randomized block design, giving a total of 16 trials and 4 blocks (Figure

2.1a). In the Coincide (C) condition, non-identical cue cards were given to both participants and they were asked to independently build the structures shown (Figure 1.1d). In the Lead (L) condition, the participant was asked to build based on the cue card shown to them (Figure 2.1b). In the Follow condition (F), the participant was asked to observe and mimic the building action of their partner who was the only one shown the cue-card (Figure 2.1b). In the Turn-Taking condition, the cue card was visible to both partners and one partner was asked to begin the building process with turns alternating between partners (Figure 2.1c). During set-up, the tester placed the supplies (cue card and logs) into original position. A pre-stimulation period of 10 seconds was used to avoid baseline drift and a post-stimulation period of 15 seconds was used to allow the hemodynamic response to return to baseline before beginning the next trial. During the pre and post baseline periods, participants were asked to observe a cross-hair on the wall.

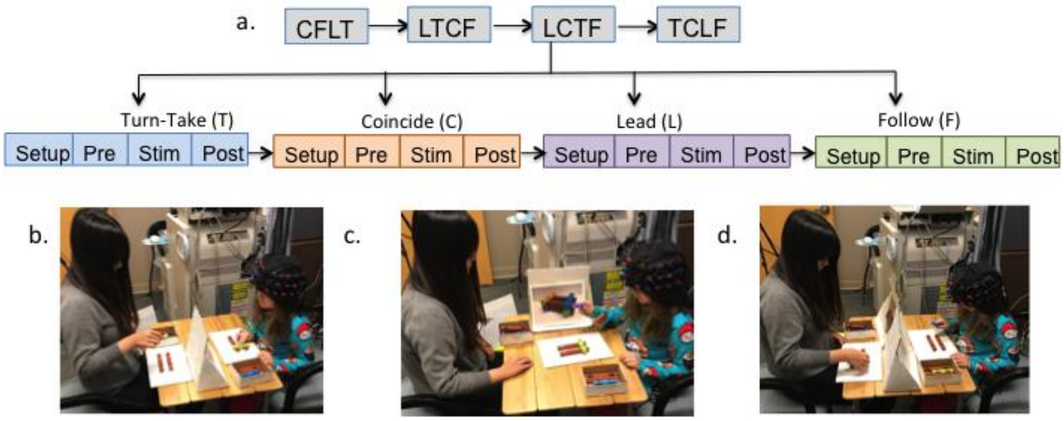


Figure 2.1 Experimental set-up. (a) Randomized block design (b) Lead/Follow (c) Turn-Take (d) Coincide conditions

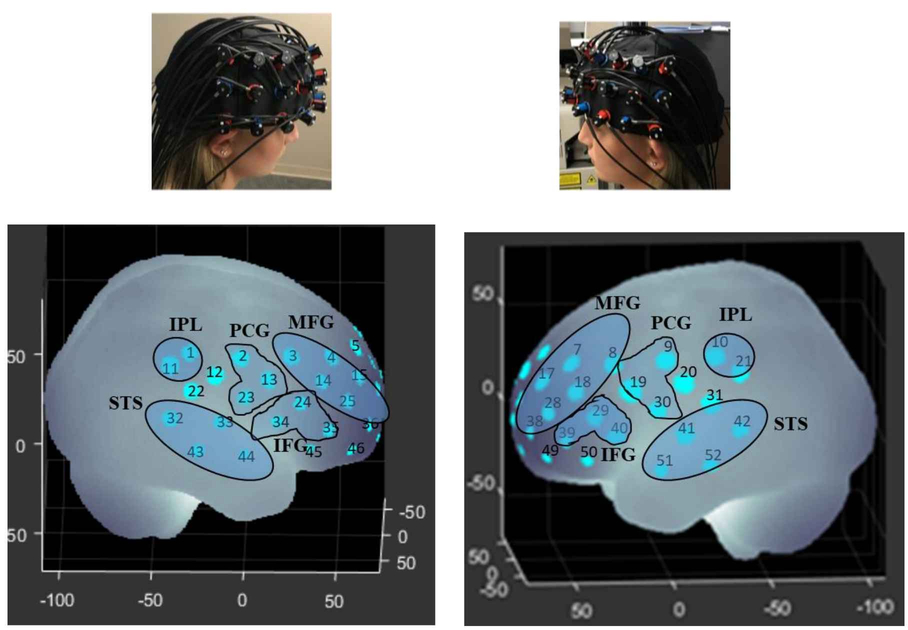


Figure 2.2 Cap placement on child and spatial registration method output

### 2.2.4 Data Processing

We used our own custom MATLAB (The Mathworks Inc., Natick, MA) codes that incorporated functions from open-source software such as HOMER-2 (Huppert et al., 2009) and Hitachi POTATo (Sutoko et al., 2016) to process the nirs output files from the ETG-4000 system. Furthermore, we re-organized our data by pooling across participants using MS Excel. First, data from each channel was band-pass filtered between 0.01 and 0.5 Hz to remove lower or higher frequencies associated with body movements and other physiological signals such as respiration, heart rate, and skin blood flow (Figure 2.3 in Appendix). Motion artifacts were removed using the wavelet method as implemented in the HOMER-2 software (Sato et al., 2006; Huppert et al., 2009, Figure 2.3a). The General Linear Model, as implemented in the HOMER-2 software, estimated the hemodynamic response function using Gaussian basis functions and a third order polynomial drift regressor (Huppert et al., 2009, Figure 2.3a). Baseline correction was completed by calculating the trend line between the pre-trial baseline and post-trial baseline and subtracting it from values in the stimulation period, as implemented within Hitachi POTATo (Sutoko et al., 2016, Figure 2.3b). For each trial, an average $HbO_2$ and HHb value was obtained for the stimulation period (Figure 2.3b). Since $HbO_2$ profiles have a greater signal to noise ratio compared to HHb and are more often reported in the fNIRS literature, we chose to report these values (Sato et al., 2005).

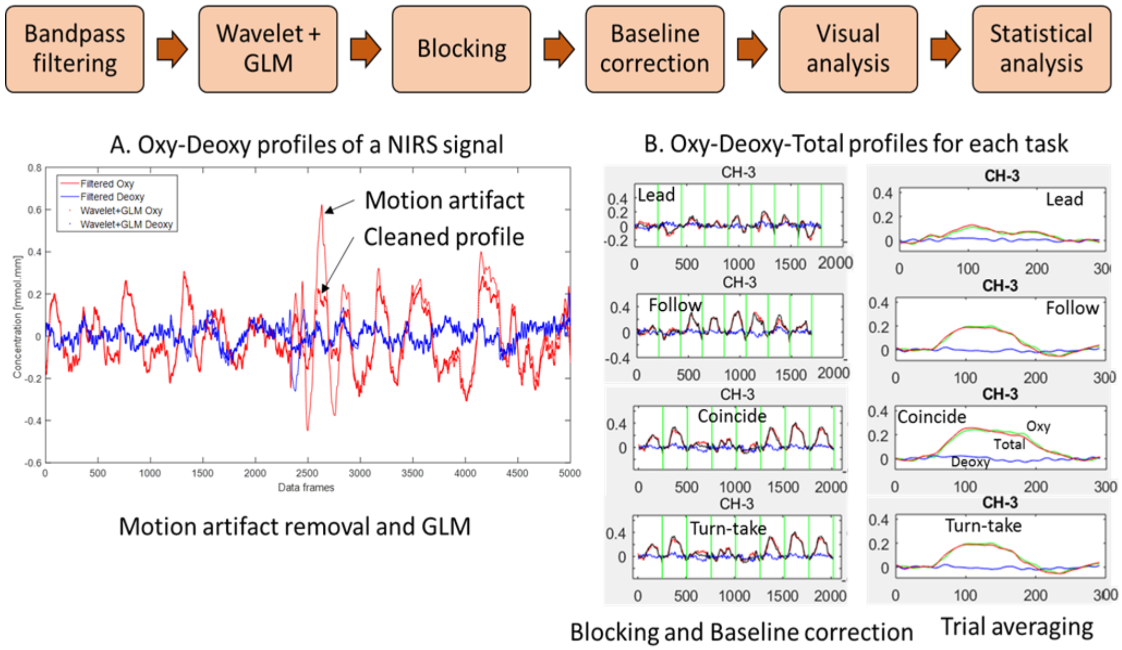


Figure 2.3 Data Processing Steps

### 2.2.5 Visual Analysis of Data

As the data was processed, Matlab graphs were created and examined at each step of the analyses listed in the previous paragraph. Within each condition, we visually analyzed the hemoglobin profiles for all 52 channels. We ensured that data followed the canonical hemoglobin response that is consistently reported in the field (Figure 2.3b). If channels were flat, indicating that the channel was not picking up activity, we excluded them from the final data set. Ultimately, we eliminated 13.2% of the overall older child data and 20.98% of the overall younger data due to persistent motion artifacts. Specifically, in the younger child group, 5.9% of Turn-Take, 4.6% of Follow, 5.4% of Coincide, and 5.1% of Lead trials were excluded. In the older child group, 3.3% of the Follow, 4.2% of the Lead, 2.7% of the Turn-Take and 3% of the Coincide conditions were also excluded.

### 2.2.6 Spatial Registration Approach

We recorded the 3D location of standard cranial landmarks (nasion, inion, right and left ear) and each fNIRS probe with respect to a reference coordinate system using a Polhemus electromagnetic motion analysis system and the ETG hardware. We utilized an anchor-based, spatial registration method developed by our collaborator (Tsuzuki et al., 2012), which transformed the 3D spatial location of each channel to the Montreal Neurological Institute (MNI)'s coordinate system for adult brains. The structural information from a database of 17 adults (Okamoto et al., 2004) was used to provide estimates of channel positions in a standardized 3D brain atlas (Tsuzuki et al., 2012). The LONI Probabilistic Brain Atlas (LPBA) was used to label estimated channel locations based on MRI scans of 40 healthy adults (Shattuck et al., 2008). We chose to focus on the putative MNS regions, namely, STS, IPL, and IFG as well as the primary sensorimotor cortices (i.e., pre and post-central gyri or PCG) and the MFG region (middle frontal gyrus). Based on the regions covered by our channels, we determined five regions of interest (ROIs) on each side (Table A.2 in Appendix, Figure 1.2): (i) The MFG region included areas of the middle frontal gyrus and left channels 7,8,17,18,28,38 and right channels 3, 4,14,15, 25,36 (ii) The PCG region included areas of the pre and post central gyri and included left channels 9,19, and 30 and right channels 2, 13, and 23 (iii) The IFG region included areas of the inferior frontal gyrus and orbitofrontal gyrus included left channels 29,39,40, and 50 and right channels 24,34,35, and 45 (iv) the STS region included channels over the superior, middle, and inferior temporal gyri and included left channels 41, 42, 51 and 52 and right channels 32, 33, 43, 44 (v) the IPL region included channels over the supramarginal and angular gyri and included left channels 10 and 21 and right channels 1 and 11. Channels 5, 6, 12, 16, 20, 22, 26, 27, 31, 37, 46, 47, 48, and 49 did not fall in one specific ROI and as a result data from these channels have been excluded to avoid spatial uncertainty within the averaged activation data. We also excluded channels whose homologous channels did not fall within the same ROI. In this way, we were able to assign 38 out of the 52 channels to one of the aforementioned ROIs in the children (See Table A.2 in Appendix).

### 2.2.7 Behavioral Coding

One trained researcher scored the behavioral performance of the children in the task. We confirmed that the children followed task instructions and such trials have been included. We established >90% intra-rater and >85% inter-rater reliability for the error codes between a primary coder and a secondary coder. Intra-class correlations (ICCs) were used to measure test-retest reliability. Once reliability was established, the primary coder coded the entire dataset. Each session was scored for three error types: (a) planning error occurred if the participant hesitated over a block and then changed placement location (ICC=92.94); (b) spatial error occurred if there was an incorrect color or location placement of the block (ICC=95.29) and (c) motor errors occurred if the child dropped a block or knocked over the cue card or block box (ICC=96.47). Additionally, we scored hand preferences (left, right, both) for each pick up and place down action performed during each of the trials. For each trial, a coder indicated which hand was used to perform these pick up and place down actions. Using this information, the proportion of right, left, and both hand use was calculated for all trials in each child. A right or left-hand preference was assigned if the child used a given hand during 55%

or more of the total actions performed. If either hand preference was less than 55% then the preference was termed “unclear”. We also calculated the proportion of children within each group with a left-hand, right-hand or unclear preference. Finally, we had coders time the stimulus period for each trial in each subject which was used to obtain an average value of time to task completion for each condition (Coincide, Lead, Follow, Turn-Take).

### 2.2.8 Statistical Analyses

Activation within a channel was based on the average $HbO_2$ value for a given stimulation period as is often reported in the fNIRS literature given its consistency and higher signal to noise ratio (Lloyd-Fox et al., 2010; Strangman, Culver, Thompson, & Boas, 2002). In addition, the data was averaged across channels within the same region of interest (ROI) based on the anchor registration output (See Figure 2.2, See Table A.2 in Appendix, Tsuzuki et al., 2012). We determined activation for five ROIs (MFG, Pre/Post Central Gyri, IFG, STS, IPL) in both hemispheres. Using IBM SPSS, we conducted a multivariate, multifactorial ANOVA with within-group factors of condition (Coincide, Lead, Follow, and Turn-Take), regions (MFG, PCG, IFG, STS, IPL), hemisphere (Left, Right) and between-group factor of group (Younger, Older). Upon obtaining a 4-way interaction, we explored task-related and group-related differences. When our data violated Mauchly’s test of sphericity, we applied Greenhouse-Geisser corrections. Post-hoc comparisons involved paired and independent t-tests. For behavioral errors, we conducted non-parametric tests such as Mann-Whitney U and Wilcoxon Signed Rank tests for between and within-group comparisons. In our multiple *post-hoc* comparisons, specified significance was set to 0.05 and was corrected using the Benjamini-Hochberg False Discovery Rate (FDR) method (Singh & Dan, 2006). We also applied Spearman's correlations to study brain-behavior relations between activation data and behavioral errors (motor, planning, spatial) and Pearson's correlations to study relations between activation data and questionnaire data, specifically, VABS socialization scores and BOT Manual Dexterity raw scores.

## 2.3 Results

### 2.3.1 Behavioral Findings

#### 2.3.1.1 Behavioral Errors between Young and Older TD Children

Wilcoxon Signed Rank tests showed that younger children had significantly greater errors in planning (6±1.6), spatial matching (3.7±0.6), and motor performance (0.6±0.3) compared to the older children (older planning 0.8±0.5, $p$=0.006, older spatial 1.8 ± 0.6, $p$=0.03, older motor 0.1 ± 0.1, $p$=0.049, Figure 2.4, Table A.3 in Appendix).

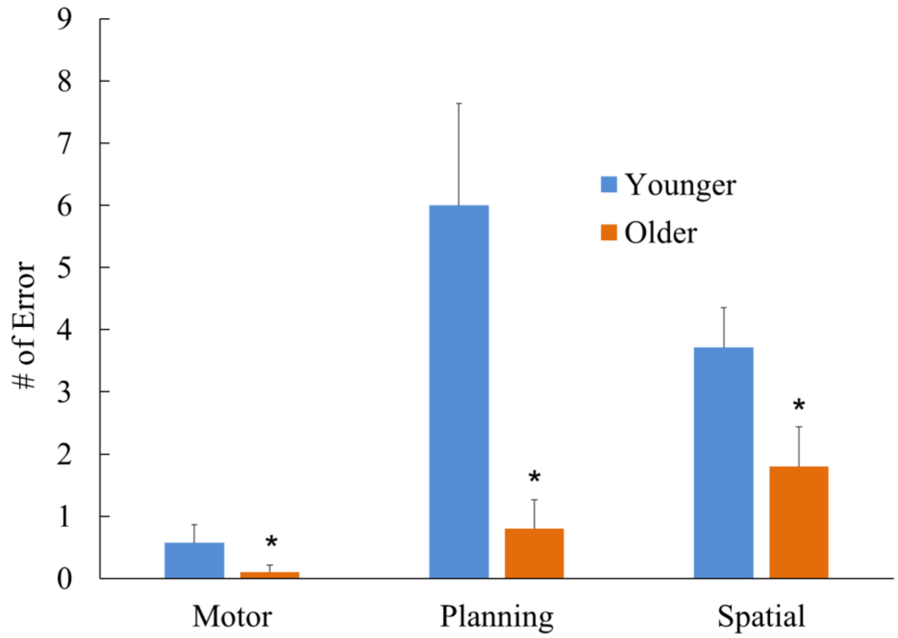


Figure 2.4 Behavioral Errors (**indicates statistical significance*)

#### 2.3.1.2 Differences in Time to Task Completion

In terms of group differences in time to task completion, older children took less time to complete all tasks compared (Average time taken=21.3 seconds) to the younger children (Average time taken=26.6 seconds). In the younger children, the average stimulation period durations were: Coincide=25.78±1.68; Lead = 27.43 ± 1.49; Follow =26.5± 1.2; Turn-Take =26.89 ± 1.88 seconds. No significant differences were found between conditions in the younger children ($p$>0.1). Older children took significantly longer to build in the Lead (24.1 ±0.68) and Follow (23.65± 0.59) conditions compared to the Coincide (19.55 ± 0.42, $ps$<0.05) and Turn-Take conditions (17.93 ± 0.49, $ps$<0.05).

#### 2.3.1.3 Differences in Hand Preference Between Younger and Older Children

Based on the Coren Handedness Survey, we found that except for one child, parents reported all children as being right-handed. However, within our task, which allowed children to use both hands freely and bimanually, we did not see similar hand use. Instead, in the younger children, only 14.29% showed a right-hand preference, 42.86% showed a left-hand preference, and 42.86% used both hands equally. In contrast, in spite of presenting the block container on the left-hand side, 60% of the older children showed a right-hand preference, 30% had a left-hand preference, and 10% used both hands. A Chi-square test conducted on handedness between younger and older children ($p < 0.0001$ ($X^2 = 149.8$)) suggested that more children in the older group showed consistent right-hand use and younger children showed mixed-handedness.

### 2.3.2 Cortical Activation Findings

#### 2.3.2.1 Correlational Analyses between Age and Cortical Activation

We found multiple significant correlations between cortical activation and age (Table A.4 in Appendix). The left and right MFG and IFG regions had significant positive correlations between age and activation across all four conditions. The left PCG had similar correlations in the Follow condition while the right PCG had similar correlations for the Lead and Follow conditions. The left STS region showed similar correlations for the Coincide, Follow, and Turn-Take while the right STS had similar correlations for the Lead condition. All significant positive correlation values ranged between 0.25 and 0.64 (Table A.4 in Appendix). Overall, in multiple instances the MFG, IFG, and STS were showing developmental changes in activation whereas such changes were not as frequent for the PCG and IPL regions. These findings further justified the use of age as a factor in our Analysis of Variance.

#### 2.3.2.2 Cortical Activation Analyses

A repeated measures ANOVA of condition (3) x hemisphere (2) x ROI (5) with between subjects factor of age revealed a main effect of region (F(3.04,209.56)=34.52, p=0.0001) and an interaction between region x age (F(3.04, 209.56)=9.73, p=0.0001), condition x hemisphere (F(2.68,185.19)=3.27, p=0.03), condition x region (F(8.46, 583.76)=3.81, p=0.0001), hemisphere x region (F(3.31,228.41)=9.43, p= 0.0001), hem x region x age (F(3.31,228.41)=4.03, p= 0.006), and 3-way interactions of condition x hemisphere x region (F(8.12, 560.38)=2.67, p=0.006) and a condition x hemisphere x region x age (F(8.12, 560.38)=1.74, p=0.084). We further explored the 3-way interactions using post-hoc t-testing (Table A.5 in Appendix).

#### 2.3.2.3 Developmental Differences in Cortical Activation

We found that older children had greater cortical activation compared to younger children in the left and right MFG (*ps*< 0.0001), left and right IFG (*ps* <0.01) as well as the right STS region (*p*=0.01). A similar trend was seen in the left STS region (*p*=0.04, Figure 2.5, Table A.5 in Appendix). In contrast, the older children had lower cortical activation in the left IPL region compared to the younger children *(p*< 0.0001). Such differences were not seen in the PCG regions or the right IPL region.

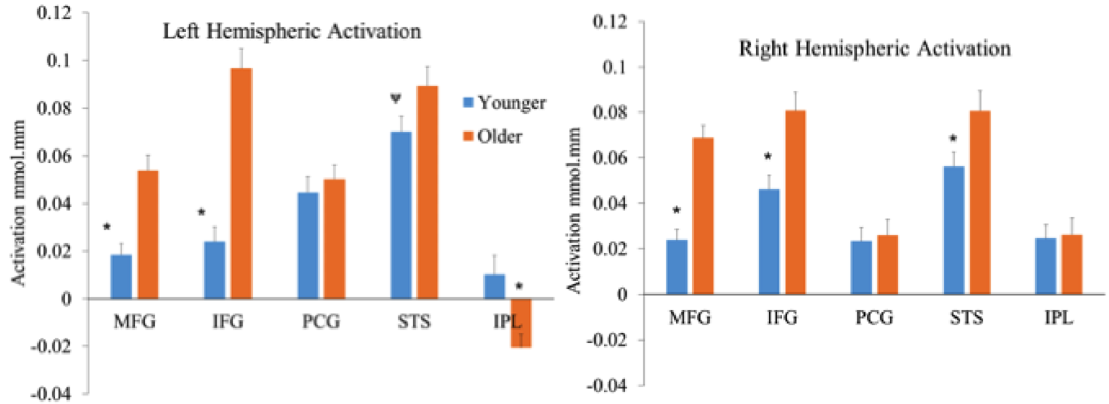


Figure 2.5 Developmental Differences in Cortical Activation Younger and Older Children (**indicates p<0.05 and Ψ indicates a statistical trend of p<0.01*)

#### 2.3.2.4 Hemispheric Differences in Cortical Activation

In younger children, we found greater left hemispheric activation compared to right in the PCG and STS regions (*ps*<0.05, Figure 2.6, Table A.5 in Appendix). In contrast, the IFG region had greater right than left hemispheric activation (*p*<0.0001). In older children, we found greater left hemispheric activation compared to right in the PCG and IFG regions (*ps*<0.01, Figure 2.6). In contrast, the MFG and IPL regions had greater right than left hemispheric activation (*ps*<0.001, Figure 2.6).

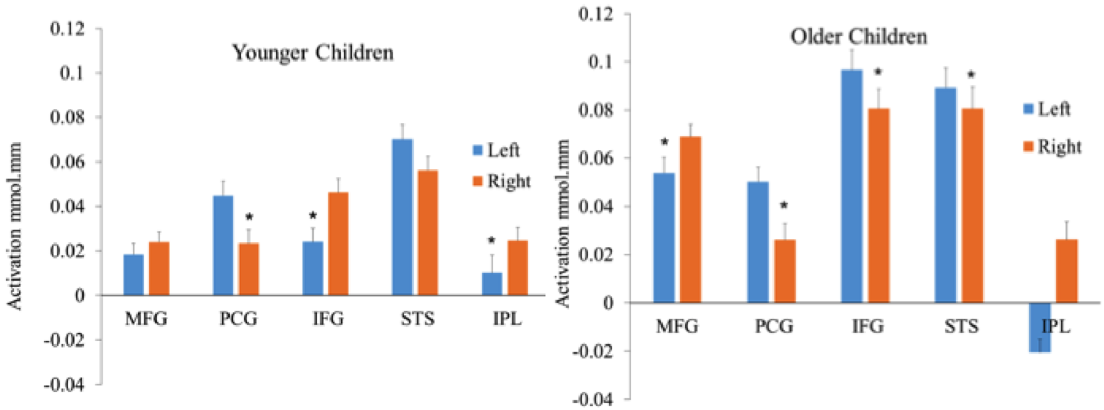


Figure 2.6 Hemispheric Differences in Cortical Activation in Younger and Older Children (**indicates $p<0.05$*)

#### 2.3.2.5 Conditional Differences in Cortical Activation All Children

In the left hemisphere, in the IPL region the Coincide and Follow conditions had average positive activation whereas the Lead and Turn-Take conditions had average negative activation. In terms of differences, we found that the Coincide condition had greater cortical activation than the Lead and Turn-Take conditions and the Follow condition had greater activation than the Lead condition (*ps*<0.01, Figure 2.7, Table A.5 in Appendix). In the right hemisphere, in the STS region we found that the Coincide and Turn-Take conditions had greater activation than the Lead and Follow conditions (*ps*<0.01).

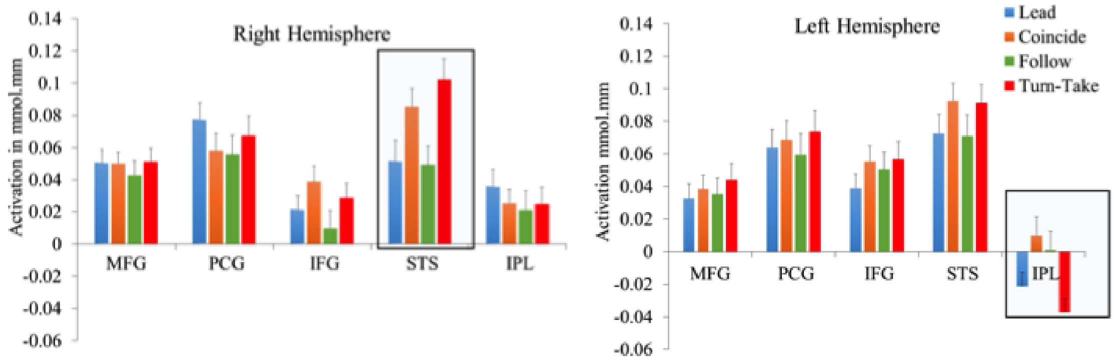


Figure 2.7 Conditional Differences in All Children (*black box indicates statistical significance differences*)

### 2.3.2.6 Cortical Activation-Motor Performance Correlations

In the younger children, multiple brain regions/conditions positively correlated with the BOT manual dexterity scores (i.e., 20 significant positive correlations ranging from 0.3 to 0.83 and only one negative correlation of -.373, Table A.6 in Appendix) indicating that these regions were more active in individuals who were performing better on the manual dexterity task. However, this relationship was not seen in the older children, except for two correlations. Overall, these findings indicate that motor performance and brain activation during the building task was rapidly changing in the younger children between 6 and 11 years of age and not much in the older children except for the right STS region.

### 2.3.2.7 Cortical Activation - Social Performance Correlations

In the older children, activation in multiple brain regions positively correlated with the VABS socialization measure (16 positive correlations ranging from 0.3 to 0.54, Table A.6 in Appendix). However, not as many correlations were seen in the younger children (10 positive correlations ranging from 0.3 to 0.59 across multiple conditions and regions and one negative correlation of -0.44). This indicates that social performance on the VABS and brain activation during the building task was changing rapidly in the older children and somewhat in the younger children.

#### 2.3.2.8 Cortical Activation – Task-based Behavioral Error Correlations

During the building task, cortical activation in the younger children was negatively correlated with the planning and spatial errors but not motor errors (16 negative correlations ranging from -0.31 to -0.61 and 2 positive correlations between 0.36-0.4, Table A.7 in Appendix). But this was not seen in the older group. This suggested that the older children were performing at ceiling levels with little variation in their behavioral errors, whereas the younger children were showing that lower cortical activation was associated with greater planning and spatial errors.

## 2.4 Discussion

This study compared social cooperative behaviors and associated cortical activation between younger and older school-age children. In terms of behavioral outcomes, we found that younger children had significantly greater motor, planning, and spatial errors compared to the older children. Additionally, the younger children also took significantly longer to complete the building task across all conditions compared to the older children. Finally, despite being right-handed when allowed to move freely, the majority of the older children had a right- hand preference whereas younger children did not show clear right- or left-hand preferences. In terms of cortical activation, age positively correlated with activation in multiple cortical regions including the MFG, STS, and IFG regions but not the PCG and IPL regions. In terms of developmental differences, the older children had greater activation in the MFG, IFG, and STS regions in both hemispheres compared to the younger children. In contrast, the older children had lower left IPL activation compared to the younger children. In terms of hemispheric differences, we found changing lateralization patterns across age which will be discussed later.

In terms of conditional differences, on pooling data across both groups the right STS region was more activated during the Coincide and Turn-Take conditions compared to the Lead and Follow conditions. For brain-behavior correlations between activation and manual dexterity scores, only younger children showed positive correlations between cortical activation in multiple regions/conditions and dexterity performance suggesting that motor performance and cortical activity was rapidly changing and associated in the younger children. Interestingly, for the brain-behavior correlations between activation and socialization scores, older children showed many more positive correlations suggesting that that the older children with better social performance also showed greater cortical activation during the building task. In terms of task-related behavioral performance, only planning and spatial errors (and not motor errors) negatively correlated with cortical activation in the younger children for multiple brain regions (bilateral MFG, IFG, PCG, and STS) indicating that lower cortical activation was associated with greater planning/spatial error.

### 2.4.1 Motor planning/executive functioning, visuo-spatial skills and visuo-motor coordination improved with development

In the Lincoln Log building task, older children had fewer errors and took less time to complete all conditions, as well as had differences in time to complete conditions between conditions, compared to younger children who took more time to build during the Lead and Follow conditions compared to the Coincide and Turn-Take. Finally, when correlating activation with the BOT manual dexterity subtask, we found that cortical activation and motor performance was rapidly changing in the younger group with lower cortical activation being associated with greater spatial errors.

The differences in motor and spatial errors between younger and older children may be due to improvements in visuo-motor and visuo-spatial skills over time. Similar to a computerized visuo-motor task where young adults and older children were found to have decreased reaction time and improved response accuracy compared to younger children (i.e. Liu et al. 2006), our older group took less time to complete the task and had reduced errors compared to the younger group. The Lincoln Log task involved matching a 3-D constructed model to a 2-D visual displayed on a cue card. Children were required to perform a series of coordinated arm movements of picking, placing, and if needed rotating logs. For all conditions, children would have to utilize their internal model of reaching/building in a feedforward manner while integrating sensory feedback from the environment to correct their actions (Ghez, Hening, & Gordon, 1991). However, during cooperative actions children will not only need to consider their own goals but also the joint goals with their partner. Additionally, they are required to use more feedback-dependent control to monitor and adjust to their partner's actions. In short, they need to integrate their feedforward and feedback control of arm movements to successfully complete the required actions. Kagerer and Clark (2015) found that visuo-motor skills improved across development as evidenced by faster movement time and decreased spatial errors in older versus younger children. However, their study also showed that when visual information was taken away, 7 to 8-year-old children had less accuracy in drawing a line to a target compared to 5-year-old and 11-year-old children (Hayes, 1978). They hypothesized that younger 5-year-old children used more feedforward control whereas 7 to 8 year-old children were learning to combine feedforward and feedback control during arm movements. In contrast, children 11 years and above have more refined control of arm movements and appropriately utilize feedback using proprioceptive inputs. This may explain be why we see fewer correlations between activation and visuo-motor performance (BOT or spatial errors), in the older children in our study.

Feedforward control involves internal motor representations that initiate a motor plan before sensory input is received to adjust the motion for errors (Ghez, Hening, & Gordon, 1991). In our task, younger children may have heavily relied on the initial internal model that does not account for sensory information from the environment about the partner and objects involved in the task, contributing to their motor and spatial errors. In contrast, feedback control involves integrating sensory information into new motor commands that create adjustments in the occurring movement (Desmurget & Grafton, 2000). Older children perhaps had fewer motor and spatial errors because they not only performed arm movements based on feedforward control; but they were also continuously adapting their actions to sensory feedback from the environment (task-related and partner-related information). This is also confirmed by the differential time to completion in the older children i.e., they took longer to complete the Lead and Follow conditions compared to Coincide and Turn-Take conditions. During the Lead and Follow conditions they were asked to monitor their partner's actions and make sure they were waiting for their partner to complete each step before performing the next step. The tester also noticed that the older "leaders" were waiting or moving slowly or in exaggerated ways to help their tester with the necessary cues to successfully follow them. Vesper et al. also found that coordination processes change when visual information is available such that partners increase their time to completion as they use sensorimotor communication through spatial deviations from the most efficient path to advise the partner how to move (Vesper, Schmitz, Safra, Sebanz & Knoblich, 2016). In addition, Satta et al. showed that during cooperative actions of 8 to 9-year-old children began to utilize more online monitoring of their partner to facilitate successful cooperative performance (Satta, Ferrari-Toniolo, Visco-Comandini, Comaniti, & Battaglia- Mayer, 2017). Therefore, our findings of reduced time to completion, fewer motor and spatial errors, and condition-specific differences in time to completion in the older children align with the current literature on visuo-spatial, visuo-motor, and social cooperation skill development.

Additionally, we found that the older children had fewer planning errors compared to the younger children perhaps due to their better executive functioning skills. In addition, planning errors correlated with activation across multiple regions/conditions in the younger children, but not the older children. Executive functioning encompasses various processes that underlie goal-directed behaviors such as attention shifting, working memory, mental rotation, and response inhibition, which were all relevant to our Lincoln Log building task (Stuss & Benson, 1986). Attention shifting is simply shifting back and forth between multiple task components (Allport, Styles, & Hsieh, 1994). In the Lincoln Log task, children were required to attend to the various task elements and shift their attention from the cue card, to the 3D model to the partner and their actions and so on. Working memory is a collection of cognitive processes that retain information for carrying out mental tasks in addition to monitoring and coding moment-to-moment incoming information, which can replace older information no longer relevant to the task (Cowan, 1998). In the Lincoln Log task, these cognitive processes are required in order to realize which steps are complete and which need to be performed next as well as who should perform them (self or partner) depending on the condition. Inhibition is the ability to inhibit dominant automatic responses (Logan & Cowan, 1984). Within our task, children had to inhibit their own actions when they were taking turns with or following or leading the partner. Study by Huizinga et al. found that these three components of executive functioning reached adult levels by 11 to 15 years of age with accuracy increasing, and error rates and reaction time decreasing, over age in all domains during standard executive functioning tasks such as the Wisconsin Card Sorting and Tower of London Tasks (Huizinga, Dolan, & van der Molen, 2006). Thus, the younger children in our study might have been undergoing developmental changes in executive functioning and related cortical regions and this association was perhaps captured in the building task. Lastly, spatial memory and mental rotation are the abilities needed to rotate 2D or 3D objects in our minds and develop in middle childhood (Sun et al., 2018). These skills would also be important within the Lincoln Log task as children observe the cue card and determine the exact placement of logs to recreate the 2D visual model shown to them. These skills improve during middle childhood with 11 to 12-year-olds showing better performance during hand rotation tasks compared to 7 to 8-year-olds (Sun et al., 2018). Overall, the older children in our study may have advanced executive functioning, visuo-spatial, visuo-motor skills which led to better behavioral performance (i.e., planning, spatial, and motor performance and time to completion) within the Lincoln Log building task compared to the younger children.

### 2.4.2 Greater Cortical Activation with Development

In terms of developmental differences, as age increased, there was an increase in activation in MFG, IFG, and STS regions across multiple conditions. This was reconfirmed when studying developmental differences in cortical activation. We found that older children had greater overall cortical activation in the MFG, IFG and STS regions compared to younger children but this was not seen consistently for the PCG region. Additionally, the left IPL region showed lower activation in the older children compared to the younger children. These findings are consistent with the literature showing that structural changes in connectivity in the primary sensorimotor areas occur in the first two years of life, followed by the higher-order association areas such as the dorsolateral prefrontal cortices and the inferior parietal and superior temporal gyri (Lin et al., 2008; Gogtay et al., 2004; Sowell et al., 2004). Multiple studies have described the developmental changes in functional activation between childhood, adolescence and adulthood during a variety of executive functions including task-related attention, motor timing, response inhibition, spatial and working memory, cognitive shifting, and performance monitoring between late childhood and adolescence (Rubia, 2013). Changes in activation were associated with improvements in executive functioning generally between the ages of 10 and 17 years. It is important to note that the literature reports different age ranges for the developmental trajectories of these skills. For example, studies in task-related attention compared children from 8-13 years and adults and found that adults had greater activation in regions associated with selective attention, perceptive attention allocation and sustained attention (Smith, Halari, Giampietro, Brammer, & Rubia, 2011; Rubia, Hyde, Halari, Giampietro, & Smith, 2010; Konrad et al., 2005). In contrast, studies in motor timing were completed in older children and adolescents between 12 and 19 years and found improvements in motor timing and motor performance occurred in late adolescence, while behavioral variables related to temporal discrimination and synchronized motor tapping were shown to improve around age 8 to 10 years (Rubia et al., 2000; Drake, Jones, & Baruch, 2000). In our study, we observed children between 6 and 17 years of age, hence, our older group may have undergone the developmental changes associated with improvements in the executive functioning skills. This was also evident in their behavioral performance with reduced planning and spatial errors during the building task.

### 2.4.3 Left-Lateralization seen in the Sensori-motor Cortices

In this study, one child was reported to be left-handed and all remaining children were right-handed. However, within the task children were allowed to use hands freely. The block placement was biased to the left-hand as the blocks were placed close to it. In spite of this, the majority of the older children used their right hand (60%) to build the structures. In contrast, the younger children showed mixed/unclear hand preferences (i.e., 43% left, 14% right, and 43% both). In terms of cortical activation, the PCG region was more left-lateralized for both older and younger children which indicates that the left hemisphere was clearly their more dominant hemisphere. These findings fit with fMRI-based activation findings reported in the literature of left-hemispheric dominance observed in right-hand individuals, regardless of hand use (Gut et al., 2007). Gut and colleagues found that dominant hand index finger tapping elicited greater left hemispheric activation in the primary sensorimotor cortices and non-dominant index finger tapping elicited greater right hemispheric activation. In fact, complex unimanual finger motions (sequential finger tap vs. single finger tap) elicited more bilateral activation in the primary sensorimotor cortices. However, complex right-hand tapping was largely contralateral in control whereas complex left-hand tapping was bilaterally controlled. They concluded that right-hand movements are contralaterally controlled, whereas left hand movements are bilaterally controlled. Our findings align with those in the literature indicating that older children have a general pattern of left-lateralization/left-hemisphere dominance perhaps due to greater right-hand use in daily activities. In the task, perhaps they used the right hand with larger grip forces or used it as a primary manipulator compared to the left hand, which was used more gently or played a supporting function.

### 2.4.4 Right-Lateralization seen in Inferior Parietal Cortices and other hemispheric differences with development

In contrast, to the PCG region, the IPL region showed greater right-lateralized activation in all children. We believe this may be associated with the visuo-spatial nature of the task and the role played by the right IPL region during visuo-spatial and visuo-motor tasks as well as socially cooperative actions. The IPL region is important for visuospatial working memory as it retains memory traces of the spatial locations of important task elements (Pisella, 2015). Additionally, patients with damage to the right inferior parietal lobule experience constructional apraxia that affects their ability to map important visual information, leading to poor spatial awareness, and affects their ability to copy geometric shapes or reproduce three- dimensional structures (Pisella, 2004). Our task clearly involved visuo-spatial matching and visuo-motor coordination and this may explain the greater right IPL activation seen across all tasks. In addition, our task involved socially embedded actions. Multiple studies have reported greater right hemispheric activation during imitative actions compared to individual actions (Aziz-Zadeh et al., 2006; Caspers et al., 2010). Hence, both the visuo-spatial matching and the social cooperative nature of the building task in this study may have led to greater IPL activation. Lastly, it is important to note that we also found small shifts in lateralization in the IFG and STS regions across development. However, these shifts were smaller (shown in Figure 2.6) compared to the developmental increases in bilateral IFG and STS activation (shown in Figure 2.5). As reported in the introduction section, children undergo developmental changes in cortical structure, functional activation and connectivity between elementary and middle school years including inferior frontal and superior temporal gyri which may contribute to the differences in hemispheric activation with development (Rubia, 2013; Uddin, Supekar, & Menon, 2010).

### 2.4.5 Superior Temporal Cortices play an important role during cooperation/competition

In terms of task/context-related differences, we found that both groups showed greater STS activation in the Coincide and Complementary/Turn-take conditions compared to the Lead and Follow conditions. The Coincide condition led to more competition than cooperation, with children competitively attempting to move faster than the adult tester to complete their model sooner. The Complementary/Turn-Take led to more cooperation as each partner had to let go of a turn to give a turn to their partner so that each partner performed half the number of actions. A good portion of time was spent in anticipation as they waited, observed their partner, and organized their next move. In contrast, the Lead and Follow condition led to more imitative actions on the part of the follower and the leader mainly checked on the partner to ensure that the partner completed the previous action before moving onto the next step shown on the cue card. In short, all conditions were social in nature and involved activation of the STS region. However, STS activation was greater when the actions were more complementary/competitive than imitative in nature. These findings fit with fMRI studies describing the importance of the STS region during socially embedded movements such as action observation, imitation, and cooperation. Pelphrey and colleagues (2003) showed that the right STS region was more active when observing biological motions of humans or robots walking compared to non- biological motions such as mechanical and clock movements. Molenberghs et al. (2010) took this a step further and showed that during action imitation, solo execution, as well as passive observation bilateral STS regions are activated; however, STS activation is greater in the imitation condition compared to passive observation and execution alone (Molenberghs, 2010). They posited that during imitation, the STS does not merely passively register observed biological motion, but instead actively represents visuomotor correspondences between one's own actions and the actions of others. In the recent years, multiple fNIRS studies have reported on the role of STS in social contexts. Bolling et al. found that there was greater STS activation when observing biological motion after playing a computerized ball toss game in an inclusive social context compared to playing in a socially exclusive context (Bolling, Pelphrey, & Kaiser, 2013). It should be noted that subjects in this study only observed motion displayed on monitors and did not engage in a game or movements of their own. In another computerized cooperative game requiring key presses, greater right STS region synchronization between players was reported for both competitive and cooperative conditions compared to other ROIs (Liu, Saito, Lin, & Saito, 2016). Our study took these past findings one step further to engage children in various real-world social cooperation tasks and we too found that the right STS region had the greatest activation during tasks requiring complementary actions (vs. imitative actions).

### 2.4.6 Inferior Parietal Cortices are more suppressed with development and during certain social cooperation conditions

We found suppressed activation in the IPL during the Lead and Complementary/Turn-Take compared to the Coincide and Follow conditions. We also found a developmental shift to greater suppression in the IPL regions in the older children compared to the younger children. We believe that this form of suppression in the left IPL region is associated with the level of cognitive demands placed by each task and improved executive functioning with development. The Lead condition required the subject to anticipate and plan the log placements on their own and spearhead the performance of the pair; hence, cognitive demands placed were higher. The Complementary/Turn-Take condition required partners to alternate their building actions and perform what is required of them based on what their partner just did. Hence, this task involved a variety of cognitive processes such as response inhibition, working memory, as well as mental rotations to complete the task. The left IPL is part of the Default Mode Network (DMN), which tends to be suppressed during tasks that involve higher cognitive demands such as the various aspects of executive functioning (Anticevic, Repovs, Schulman, & Barch, 2010). A variety of research groups have found that depressed DMN activity is associated with better performance in working memory encoding and task-based visual searches (Anticivic, Repovs, Schulman, &

Barch, 2010; White et al., 2012; Shulman, Astafiev, McAvoy, d'Avossa, & Corbetta, 2012; Daselaar, Prince, & Cabeza, 2004). Such DMN activity could play an important role during social interactions and help in mentalizing to understand not only the mental state of a partner, but also their goals and intention (Mars et al., 2012). In our study, we believe the Lead and Turn-take conditions involved more aspects of executive functioning such as social/visual monitoring and working memory which may have led to greater IPL suppression. Finally, with development there was improved executive functioning, which may have contributed to the pattern of IPL suppression in the older children.

### 2.4.7 Developmental Implications

In our study, school-age children showed rapid changes in executive functioning, visuo-spatial and visuo-motor skills, as well as social cooperation. Construction and building-related games such as those using Lincoln Logs, Legos, etc. may facilitate activation in brain regions important for cognitive, social, and sensori-motor performance. Additionally, our study showed meaningful correlations during the building task and standardized motor and social performance suggesting that the building task activated multiple social and sensori-motor regions. As is reported in the past, constructional games could also engage children in positive relationships/friendships with peers, increased social interactions and self-esteem, and enhance their feelings of acceptance within social groups. While this study did not study direct intervention effects of visuo-motor and social cooperation activities we believe we offered indirect evidence for how constructional games may facilitate brain activation in cognitive, sensori-motor, and social brain regions.

### 2.4.8 Study Limitations

This pilot study involved a relatively small sample; however, provided us with multiple significant findings. We were unable to compare/correlate activation between partners in each pair. In the future, we plan to conduct a hyperscanning study to examine brain coherence between individuals engaging in socially cooperative activities. We may have biased hand preferences by our task constraints, for example, placing the container on the left versus the right hand. During naturalistic tasks, it is difficult to control the time to task completion and that limits our ability to standardize the duration of the stimulation period. Currently, the fNIRS field struggles with this question, as there is no better way to handle this issue since cutting down the time will lead to the loss of hemodynamic profiles in some participants. Ideally, we should have included a standardized executive functioning task; which we plan to do in the future. Finally, although we followed the International 10-20 system in our placement of the probe sets, variation in participant head sizes and probe placement could have added to inconsistency and variability in our final spatial registration output.

### 2.4.9 Conclusions

In conclusion, during a novel Lincoln Log building task, the younger children had more errors in time taken as well as the spatial and planning abilities compared to the older children, revealing developmental differences in executive functioning, visuo-spatial, visuo- motor coordination, as well as social cooperation skills. fNIRS technology was successful in detecting developmental variations in cortical activation patterns consistent with the current fMRI literature. Older children showed greater activation in the prefrontal cortices, inferior frontal gyri, pre/post-central gyri, and superior temporal cortices. In addition, there were hemispheric differences in that all children showed greater left-lateralization in sensori-motor cortices and more right-lateralization in the inferior parietal cortices. Additionally, the left IPL region also showed activity suppression with development. In terms of task-related contextual differences STS activation was greater in the competitive (Coincide) and the cooperative (Turn-take) conditions compared to the Lead and Follow conditions for both groups. This highlighted the importance of the STS region not only in passive observation of a partner's actions but also when actions are performed in the context of a social partner, competitively or cooperatively. For brain-behavior correlations, we found that younger children with greater cortical activation had fewer spatial and planning errors as well as better manual dexterity. In contrast, older children with greater cortical activation had better socialization skills. In summary, this pilot study revealed a strong developmental trajectory for social cooperation behaviors in school-age children between 6 and 17 years of age. Future studies must extend this work to larger samples, other cooperative tasks, and to special populations such as children with ASD which will also be the focus of our next chapter.

# Chapter 3

# SOCIAL COOPERATION DIFFERENCES IN CHILDREN WITH AND WITHOUT AUTISM SPECTRUM DISORDER

## 3.1 Introduction

Autism Spectrum Disorder (ASD) is a common pediatric neurodevelopmental disorder affecting 1 in 59 children (Baio et al., 2018). Children with ASD have primary impairments in communication, social interaction as well as restricted and repetitive behaviors (American Psychiatric Association, 2014). In addition, they have significant comorbid motor impairments including poor motor coordination, balance, impaired imitation, dyspraxia and difficulty performing movement sequences (Bhat, Landa, & Galloway, 2011; Minshew, Sung, Jones, & Furman, 2004; Kaur, Srinivasan, & Bhat, 2017; Dziuk et al., 2007). In terms of cognitive impairments, children with ASD have detriments in executive functioning including poor attention shifting, working memory, and response inhibition (Freeman, Lock, Rotheram-Fuller, & Mandell, 2017; Hughes, 1996). Aligned together, these primary and comorbid impairments contribute to difficulties with social cooperation experienced by children with ASD. Because many everyday skills are learned through observing other's actions and by working with others during cooperative actions, difficulty with social cooperation ultimately affects a child with ASD's ability to learn and build social connections with others. The expansive goal of this research is to more effectively understand social cooperation deficits of children with ASD as well as associated brain activation patterns. Within this study, we utilized functional Near Infrared Spectroscopy (fNIRS), a safe and noninvasive neuroimaging tool to examine differences in cortical activation during a novel Lincoln Log building game between children with and without ASD.

### 3.1.1 Behavioral studies on imitation, interpersonal synchrony, and social cooperation in individuals with ASD

Social cooperation encompasses three types of behaviors - imitation, interpersonal synchrony and complementary actions/turn-taking. While limited literature on complementary and turn-taking behaviors in children with ASD exists, there is a vast amount of literature on imitation performance. Children with ASD have impairments in copying object-related gestures, communicative gestures, as well as meaningless gestures (Roger, Hepburn, Stackhouse & Wehner, 2003; Smith & Bryson, 2007). A study comparing children with ASD, Fragile X Syndrome, Developmental Disability, and typically developing (TD) children found that during object-based imitation and meaningful facial imitation, children with ASD performed poorly compared to other groups (Roger, Hepburn, Stackhouse, & Wehner, 2003). Smith and Bryson et al. found that the production of symbolic gestures involving object-based pantomime actions were impaired in children with ASD when compared to TD controls (Smith & Bryson, 2007). Imitation is a simpler form of social cooperation as it involves a finite number of actions rather than continuous, moment-to-moment synchronization over time. Interpersonal synchrony (IPS) is a form of social cooperation requiring synchronized actions between partners such as finger tapping, lifting large objects or walking together (Richardson, Marsh, & Baron, 2007; Rabinowitch & Knafo-Noam, 2015; Wiltermuth & Heath, 2009). When partners took turns leading, following, and jointly improvising motions using a pair of handles, adults with ASD had reduced co-occurring actions with a partner during the “follow” condition due to their difficulties modulating movement velocity to match their partner (Brezis et al., 2017). Few studies have compared social cooperation in children with and without ASD (Marsh et al., 2013; Fitzpatrick et al. 2017, Kaur et al., 2017; Curioni, Mineo-Paluello, Sacheli, Candidi, & Aglioti, 2017). Marsh et al. (2013) studied spontaneous synchronization in children with and without ASD as they rocked in a chair while their parent read to them while seated in their own, separate chair. TD children exhibited more in-phase rocking behavior with their parents than children with ASD. As a result, this research group postulated that deficits in social monitoring and motoric coordination might reduce a child with ASD's ability to coordinate interpersonally in a social context (Marsh et al., 2013). Additionally, in a grasp task, individuals with ASD were unable to follow a partner's action of grasping a plastic bottle compared to a non-social grasp condition (Curioni et al., 2017). During spontaneous and intentional social synchronization, adolescents with ASD attempted to swing a pendulum in synchrony with their parents but exhibited poor synchronization in both conditions. Interestingly, the adolescents with ASD tended to lead the parent in terms of synchronization (Fitzpatrick et al, 2017). Conceivably, the adolescents with ASD did not attend to their parents, which forced the parents to adjust their own movements to remain in synchrony. This lab's previous work has shown that children with ASD have poor interpersonal synchrony during various rhythmic actions of clapping, marching, and drumming while performing simple, dual-limb and complex, multi-limb actions compared to children without ASD (Kaur et al., 2017). Finally, few studies have reported on complementary/turn-taking impairments in children with ASD. Colombi et al. observed children with ASD and developmental delays (DD) during imitation, joint attention, intentionality and complementary tasks and found that children with ASD responded less to social cooperation bids compared to children with DD (Colombi et al, 2009). Likewise, social cooperation skills in children with ASD correlated with their imitation and joint attention performance. The various deficits in social cooperation in children with ASD have been attributed to their poor social awareness as well as poor coordination and praxis impairments. Given the limited number of studies on social cooperation skills of children with ASD, in this study we will examine differences in socially cooperative behaviors between children with and without ASD during a novel Lincoln Log building task.

### 3.1.2 Neural Deficits in Children with ASD

Deficits in imitation, synchrony, and social cooperation may be linked to the cortical abnormalities associated with ASD. Children with ASD are known to have significant cortical abnormalities as seen by local hyper-connectivity in the prefrontal, frontal, parietal and temporal cortices and long-distance hypo-connectivity across different cortical regions (Courchesne & Pierce, 2005). The aforementioned cortical regions encompass the putative Mirror Neuron Systems (MNS), considered necessary for imitation, intentional understanding, and other social processes. Specifically, three regions of the MNS system are postulated to be active during imitation performance as well as observation and execution of goal-directed actions: the Superior Temporal Sulcus (STS), the Inferior Frontal Gyrus (IFG) and the Inferior Parietal Lobule (IPL). No region works independently but rather in unison with each other as well as with premotor cortices, supplementary⁄pre-supplementary motor cortices, cingulate⁄insular cortices, cuneus⁄precuneous as well as subcortical structures such as the cerebellum, basal ganglia, and others (Gazzola and Keysers, 2009; Iacoboni, 2009). There is substantial evidence supporting atypicalities in MNS activation in children and adults with ASD. The STS and IFG regions are said to be less active (Freitag et al., 2008; Jack

& Morris, 2014; Perkins, Bittar, McGillivray, Cox, & Stokes, 2015; Mori et al, 2015). In contrast, the IPL region is said to be hyperactive **(**Martineau, Andersson, Barthelemy, Cottier, & Destrieux, 2010). Meta-analyses of functional magnetic resonance imaging (fMRI) studies involving imitation and language performance tasks report similar findings of hypo-activation in more frontal and temporal regions such as the IFG and STS and hyperactivation in regions such as the IPL in individuals with ASD and as well as greater compensatory right hemispheric activation when there is poorer task performance (Yang & Hoffman, 2015; Herringshaw, Ammons, DeRamus, & Kana, 2016). There are only two studies reporting fNIRS activation during imitation tasks (Kajiume, Aoyama-Setoyama, Saito-Hori, Ishikawa, & Kobayashi, 2013; Mori et al., 2015). Kajiume et al. found atypical lower activation in the posterior IFG and ventral premotor cortex in children with ASD compared to controls during observation and imitation of a person opening and closing a bottle (Kajiume et al., 2013). Mori et al. found that children with ASD had lower activation in the IFG compared to TD controls during observation and imitation of facial expressions (Mori et al., 2015).

Additionally, during executive functioning tasks, individuals with ASD have reduced activation in the prefrontal regions of the brain (Uritani et al., 2019; Silk, Rinehart, Bradshaw, Egan, O'Boyle, & Cunnington, 2006; Christakou et al., 2013). Silk et al. found decreased frontal lobe activation in adolescents with ASD during a block placement task involving working memory and mental rotation as well as aspects of visuo-motor and visual-spatial integration (Silk et al, 2006). Similarly, using fNIRS, Uratani et al. found decreased activation in the prefrontal cortices of male children with ASD during a Stroop task requiring response inhibition (Uratani et al., 2019). Finally, several groups have found impaired connectivity between pre- and post-central gyri regions of the brain and the cerebellum in individuals with ASD (Wang et al, 2019; Mostofsky et al., 2009). During visuo-motor gripping or tapping tasks, individuals with ASD had reduced functional connectivity across pre-frontal regions and the cerebellum, which was associated with greater grip force variability in the task (Wang et al, 2019). Mostofsky et al. found similar atypical patterns of connectivity between the motor cortices and the cerebellum in individuals with ASD during a sequential visuo-motor finger-tapping task (Mostofsky et al., 2009). Our lab has conducted a reaching synchrony task and reported reduced STS and IFG activation and greater IPL activation in school-age children with ASD compared to those without ASD specifically during movement conditions (Hoffman et al., 2017).

### 3.1.3 Gaps in research and value of fNIRS

Only two behavioral studies have reported on social cooperation in children with ASD. The majority of the cortical activation studies focus on adults, not children with ASD, and do not involve naturalistic social cooperation tasks. A majority of the neuroimaging studies on social cooperation have been completed using fMRI, the gold standard of imaging, and report on patterns during observation and imitation of finger and hand movements. We chose to use fNIRS technology as it provides robust data in the presence of motion artifacts and allows for ecologically relevant study of naturalistic face-to-face tasks, as is often the case with socially cooperative games (Kim, Seo, Jin Jeon, Lee, & Lee, 2017). In addition to providing robust data during movement tasks, fNIRS has better spatial resolution than Magnetoenchephalography (MEG) and Electroencephalography (EEG) and better temporal resolution compared to fMRI and Positron Emission Tomography (PET) (Lloyd-Fox et al, 2010; Gervain et al., 2011.

Compared to fMRI, fNIRS is weaker in its spatial resolution, an issue we address by using spatial registration methods developed by our collaborator, Dr. Tsuzuki (Tsuzuki et al., 2012).

### 3.1.4 Aims and Hypotheses

Social cooperation skills play a crucial role in social and motor development and, as such, are valuable to understanding how social cooperation is altered in school-age children diagnosed with ASD and what cortical impairments contribute to these deficits. To date, no study has compared cooperation behaviors between children with and without ASD during a naturalistic building game and associated cortical activation. Therefore, this study investigated differences in social cooperative behaviors and associated cortical activation patterns between children with and without ASD as they performed Coincide, Lead, Follow, and Complementary/Turn-Taking actions during a novel Lincoln Log building task. In terms of behavioral performance, we hypothesized that children with ASD would have greater motor, spatial, and planning errors compared to TD children. For group differences, we hypothesized that children with ASD would have lower cortical activation compared to the children without ASD in all regions, except for the IPL region, which would show greater activation in children with ASD. In terms of hemispheric differences, we anticipated TD children would have more left-lateralization in the pre-/post-central gyri (or sensorimotor cortices) whereas such lateralization would be lacking in children with ASD. For conditional differences, we expected TD children to show more activation in the MNS regions (IFG, STS, and IPL) during the more social conditions (Coincide and Turn-take compared to Lead and Follow). We did not expect the children with ASD to show such differential activation across conditions. Finally, in terms of brain-behavior correlations, we expected to see correlations between cortical activation and motor or social performance measures as well as task-related behavioral errors in one or both groups.

## 3.2 Methods

### 3.2.1 Participants

Fifteen children with ASD between the ages of 6 and 17 (Average: 11.5 and Standard Error (SE): 0.8; 12 Male and 3 Female) were age-matched to fifteen TD children between the ages of 6 and 17 years (Average: 12.2 and Standard Error (SE): 0.9; 8M, 7F). Based on parent reports, there were no age, handedness, or ethnicity differences found between groups (*ps*>0.1). There were significant differences in Sex based on chi-square tests ($\chi 2$ Sex differences= 45.563, $p<0.001$, See Table 2.1 in Appendix). Children were recruited using online postings through various listservs, fliers, and word-of-mouth recruitment at local schools, community centers, and clinical services. Before testing, we completed screening interviews with potential participants to exclude children with known neurological or psychiatric diagnoses, those taking psychotropic medications, and those with any other difficulties that would prevent them from successfully performing the task. The Coren handedness survey was administered to all participants and fourteen TD children were strongly right-handed while one child was weakly left-handed. In the ASD group, there were thirteen right-handed children and two left-handed children (Coren, 1992). These left-handed participants had activation patterns consistent with our group results so their data have been retained. All participants had normal or corrected to normal vision. Parents of children completed the Vineland Adaptive Behavioral Scales (VABS, Volkmar et al., 1987) as well as the Social Responsiveness Scale-2 (SRS-2) for their child. The SRS is a continuous measure of social ability (ranging from impaired to above average) in which higher scores are associated with more severe social impairments (Constantino & Gruber, 2005). The Vineland Adaptive Behavioral Scale is a parent-questionnaire measuring adaptive functioning across domains of communication (receptive, expressive, written), socialization (interpersonal relationships, play and leisure, coping skills), daily living (person, domestic, community), and motor behaviors (Sparrow, Balla, & Cicchetti, 1984). The VABS measure also provides an overall adaptive behavior composite (ABC) score as a measure of overall adaptive functioning. On the VABS measure, the TD group had typical levels of subdomain function and overall adaptive functioning while the ASD group fell below typical levels for subdomain and overall adaptive functioning and as a result significant developmental differences were found between the TD and ASD groups (See Table 2.1 in Appendix). In addition, we administered the manual dexterity subtest from the Bruininks-Oseretsky Test of Motor Proficiency-2 (BOT-2) and found significant differences in manual dexterity raw scores between the TD and the ASD group ($p<0.01$, Table A.8 in Appendix; Bruininks, 1987). The Manual Dexterity (MD) subtest involves various visuo-motor skills of reaching, grasping and bimanual actions involving small objects such as card sorting, placing pegs in a peg board and penny transfer games (Bruininks, 1978). The University of Delaware International Review board (IRB protocol id #: 12227966-1) approved the protocol of this study and all human procedural testing was carried out in accordance to their recommendations. Prior to participating in the study, all parents of participants gave their written informed consent for participation in accordance with the Declaration of Helsinki. Children who were able signed child-appropriate versions of assent forms.

### 3.2.2 Experimental Design

Each child was seated at a table across from the tester and fitted with a 3x11 fNIRS probe set (Figures 3.1 and 3.2). The child and tester were given a container of Lincoln logs consisting of four plain brown logs and four multi-colored supporting logs. The container was set on the child's left side, which may have led to a left-hand bias compared to the natural tendency of using their dominant right hand, as our handedness survey indicated. For each condition, a cue card was placed in a holder located either in front of one or both participants during the set-up period. At the start of the stimulus period, depending on the condition, the participants flipped the cue card and began building the structure shown on the card. The task consisted of four conditions and followed a randomized block design, giving a total of 16 trials and 4 blocks (Figure 3.1a). In the Coincide (C) condition, non-identical cue cards were given to both participants and they were asked to independently build the structures shown to them (Figure 3.1d). In the Lead (L) condition, the participant was asked to build based on the cue card shown to them (Figure 3.1b). In the Follow condition (F), the participant was asked to observe and mimic the building action of their partner who was the only one shown the cue-card (Figure 3.1b). In the Complementary/Turn-Taking condition, the cue card was visible to both partners and one partner was asked to start off the building process in which turns were alternated between partners (Figure 3.1c). We included a set-up period at the beginning of each trial in which the tester placed the supplies such as cue card and the logs into position. A pre-stimulation period of 10 seconds was used in order to avoid baseline drift and a post-stimulation period of 15 seconds was used to allow the hemodynamic response to return to baseline before beginning the next trial. During the pre and post baseline periods, participants were asked to observe a cross-hair on the wall. All conditions were cued through an external computer using the E-Prime software and sessions were videotaped for subsequent behavioral coding.

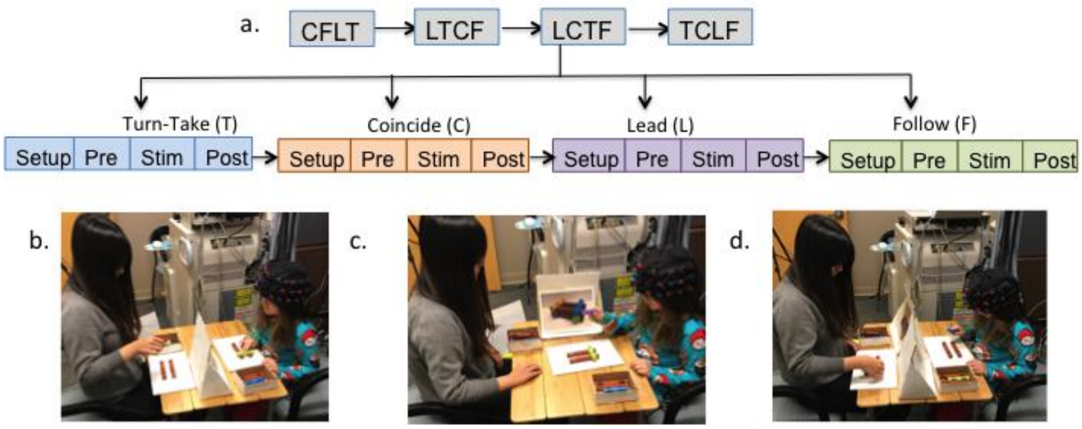


Figure 3.1 (a) Randomized Block Design and (b) Lead/Follow (c) Turn-Take and (d) Coincide conditions.

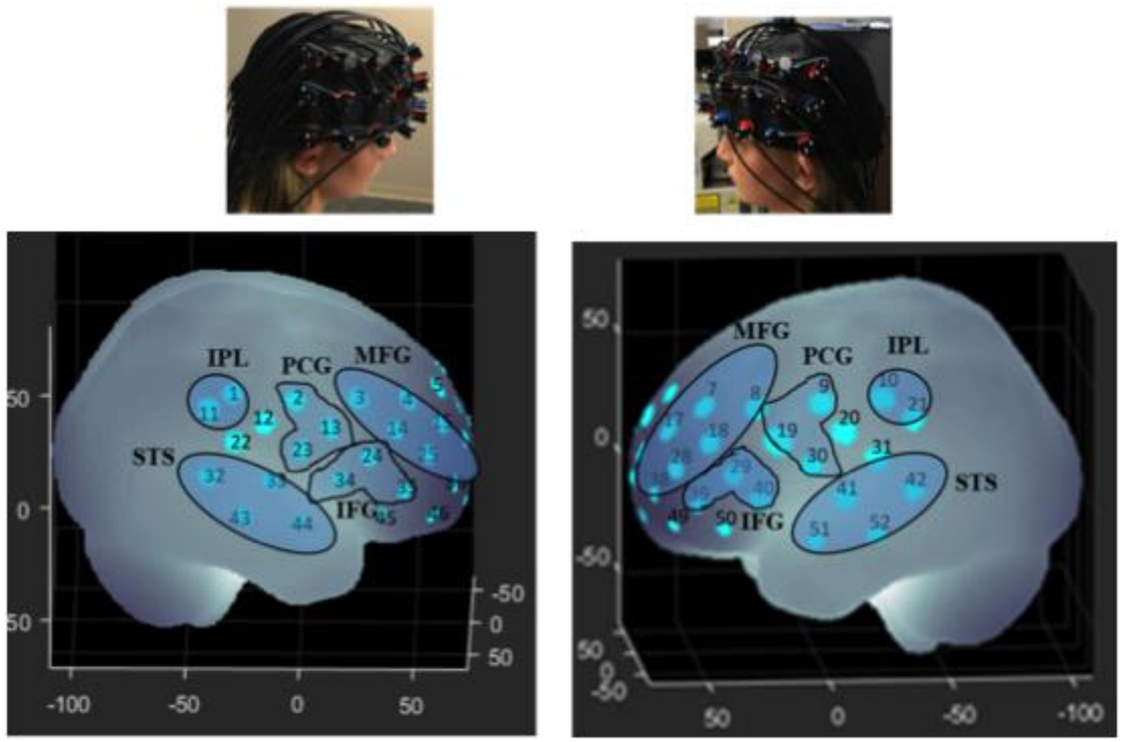


Figure 3.2 Cap Placement on Child and Spatial Registration Output

### 3.2.3 Data Collection

The Hitachi ETG-4000 system was used to capture changes in oxygenated and deoxygenated hemoglobin (Hitachi Medical Systems, Tokyo, Japan; Sampling Rate: 10 Hz). The probe set was positioned over frontal, temporal and parietal regions of the brain. The midline of the probe set was aligned with the nasion/nasal bridge and the lower border of the probe set was aligned just above the eyebrow, just above the ears, and extended just past both ears. Pairs of probes, located 3 cm apart, acted as emitters and receivers for two wavelengths of light - 695 and 830 nm. light travels from the emitter in a banana-shaped arc through the skull to reach the capillary bed of the cortical tissue of the brain at the midpoint between the two probes. Using the Modified Beer-Lambert law, changes in light attenuation were used to determine changes in the concentration of oxygenated ($HbO_2$) and deoxygenated hemoglobin (HHb) per each channel pair. During task performance, or the stimulation period, neural activation leads to an increase in metabolic rate and oxygen consumption/greater demand and an increase in blood flow to the capillary bed supplying the brain region; which in turn leads to an increase in oxygenated hemoglobin ($HbO_2$) and a slight decrease in deoxygenated hemoglobin (HHb, Hb molecules with no $O_2$ attached) (Lloyd-Fox et al, 2010; Scholkmann et al., 2013; Wolff et al., 2002). The light attenuation data was exported from the Hitachi system in the form of a comma separated value (.csv) file for post processing. E-prime software (version 2.0) marked the baseline and stimulation periods using a Windows PC computer to trigger the Hitachi machine via a serial port and conveyed the start and end of each stimulation period and trial using an auditory cue/beep. The entire session was videotaped using a camcorder that was synchronized with the Hitachi fNIRS system.

### 3.2.4 Data Processing

We used our own custom Matlab (The Mathworks Inc., Natick, MA) codes that incorporate functions from open-source software such as Homer2 (Huppert, Diamond, Francheschini, & Boas, 2009) and Hitachi POTATo (Sutoko et al., 2016) to process the nirs output files from the ETG-4000 system. Additionally, we also re-organized our data by pooling across participants using MS Excel. First, data from each channel was band-pass filtered between 0.01 and 0.5 Hz to remove lower or higher frequencies associated with body movements and other physiological signals such as respiration, heart rate, and skin blood flow (Figure 3.3). Motion artifacts were removed using the wavelet method as implemented in the Homer2 software (Sato et al., 2005; Huppert et al., 2009, Figure 3.3a). The General Linear Model, as implemented in the Homer-2 software, estimated the hemodynamic response function using Gaussian basis functions and a third order polynomial drift regressor (Huppert et al., 2009, Figure 3.3a). Baseline correction was completed by calculating the trend line between the pre-trial baseline and post-trial baseline and subtracting it from values in the stimulation period, as implemented within Hitachi POTATo (Sutoko et al., 2016, Figure 3.3b). For each trial, an average $HbO_2$ and HHb value was obtained for the stimulation period. Since $HbO_2$ profiles have a greater signal to noise ratio compared to HHb and are more often reported in the fNIRS literature, we chose to use and report these values (Sato et al., 2005, Figure 3.3b).

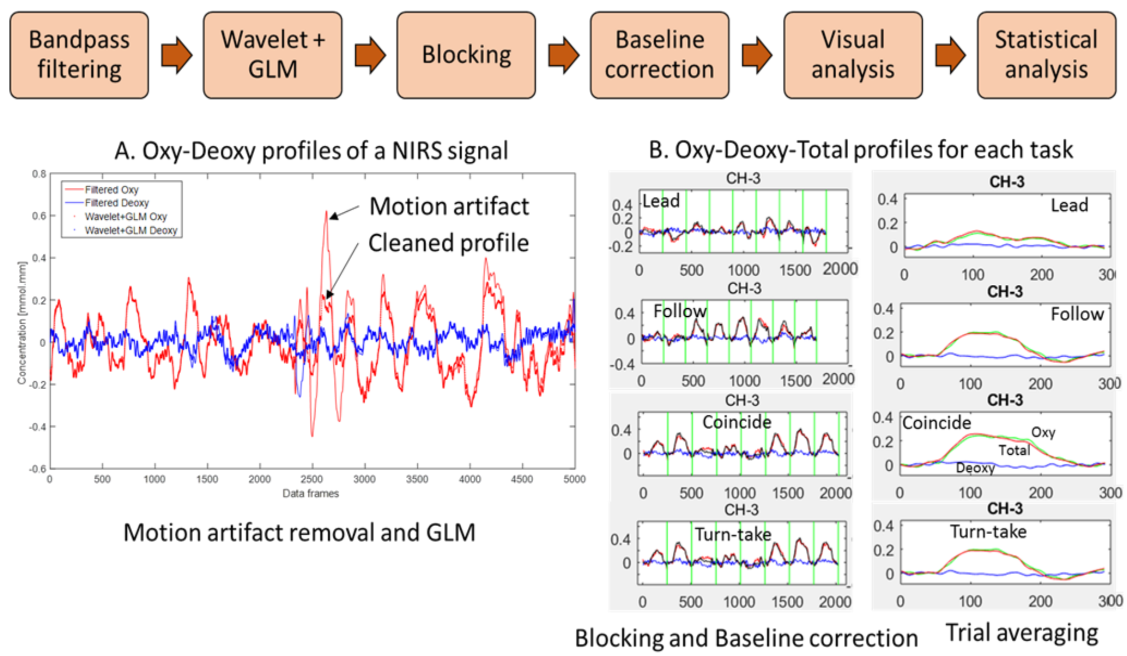


Figure 3.3 Matlab data processing steps including (a) Motion artifact removal from oxygenated and deoxygenated hemoglobin profiles and (b) blocking, baseline correction and trial averaging steps for an oxygenated and deoxygenated hemoglobin profile

### 3.2.5 Visual Analysis of Data

As the data was processed, Matlab graphs were examined for each section of the analyses listed in the previous paragraph. Within each condition, we visually analyzed the hemoglobin profiles for all 52 channels. We ensured that maintained data followed the canonical hemodynamic response that is consistently reported in the field. If channels were flat, indicating that the channel was not picking up activity, we excluded them from the final data set. Ultimately, we eliminated 6.9% of the TD child data and 20.9% of the data of the children with ASD due to persistent motion artifacts. Specifically, in the TD group, 1.9% of Turn-Take, 1.5% of Follow, 1.7% of Coincide and 1.8% of Lead trials were excluded. In the ASD group, 4.3% of the Follow, 7.2% of the Lead, 3.8% of the Turn-Take and 5.6% of the Coincide condition were also excluded.

### 3.2.6 Spatial Registration Approach

We recorded the 3D location of standard cranial landmarks (nasion, inion, right and left ear) and each fNIRS probe with respect to a reference coordinate system using a Polhemus electromagnetic motion analysis system and the ETG hardware. We utilized an anchor-based, spatial registration method developed by our collaborator Tsuzuki et al. (2012) which transformed the 3D spatial location of each channel to the Montreal Neurological Institute (MNI)'s coordinate system for adult brains. The structural information from a database of 17 adults (Okamoto et al., 2004) was used to provide estimates of channel positions in a standardized 3D brain atlas (Tsuzuki et al., 2012). The LONI Probabilistic Brain Atlas (LPBA) was used to label estimated channel locations based on MRI scans of 40 healthy adults (Shattuck et al., 2008). We chose to focus on the putative MNS regions, namely, STS, IPL, and IFG as well as the primary sensorimotor cortices (i.e., pre and post-central gyri or PCG) and the MFG region (middle frontal gyrus). Based on the regions covered by our channels, we determined five regions of interest (ROIs) on each side (see Table A.9 in Appendix, Figure 3.2): (i) The MFG region included areas of the middle frontal gyrus and left channels 7,8,17,18,28,38 and right channels 3, 4,14,15, 25,36 (ii) The PCG region included areas of the pre and post central gyri and included left channels 9,19, and 30 and right channels 2, 13, and 23 (iii) The IFG region included areas of the inferior frontal gyrus and orbitofrontal gyrus included left channels 29,39,40, and 50 and right channels 24,34,35, and 45 (iv) the STS region included channels over the superior, middle, and inferior temporal gyri and included left channels 41, 42, 51 and 52 and right channels 32, 33, 43, 44 (v) the IPL region included channels over the supramarginal and angular gyri and included left channels 10 and 21 and right channels 1 and 11. Channels 5, 6,12, 16, 20, 22, 26, 27, 31, 37, 46, 47,48, and 49 did not fall in one specific ROI and as a result data from these channels have been excluded to avoid spatial uncertainty within the averaged activation data. We also excluded channels whose homologous channels did not fall within the same ROI. In this way, we were able to assign 38 out of the 52 channels to one of the aforementioned ROIs in the children (Table 3.2 in Appendix).

### 3.2.7 Behavioral Coding

A trained student researcher scored the behavioral performance of the children during task completion. We confirmed that the children followed task instructions and such trials have been included. We established >90% intra-rater and >85% inter-rater reliability for the error codes between a primary coder and a secondary coder. Intra-class correlations (ICCs) were used to measure test-retest reliability. Once reliability was established, the primary coder coded all of the dataset. Each session was scored for three error types: (a) planning error occurred if the participant hesitated over a block and then changed placement location (ICC=92.94);(b) spatial error occurred if there was incorrect color or location placement of the block (ICC=95.29) and (c) motor errors occurred if the child dropped a block or knocked over the cue card or block box (ICC=96.47). Furthermore, we scored hand preferences (left, right, or both) for each pick up and place down action performed during each of the trials. For each trial, a coder indicated which hand was used to perform these pick up and place down actions. With this information, the proportion of right, left, and both hand use was calculated for all trials in each child. A right- or left-hand preference was assigned if the child utilized a given hand during 55% or more of the total actions performed. If either hand preference was less than 55%, the preference was termed "unclear". We also calculated the proportion of children within each group with a left-hand, right-hand or mixed-hand preference. Finally, we had coders time the stimulus period for each trial in each subject. From this, we obtained the average time to task completion for each condition (Coincide, Lead, Follow, Turn-Take).

### 3.2.8 Statistical Analyses

Activation within a channel was based on average $HbO_2$ values for a given stimulation period as is often reported in the fNIRS literature given its consistency and higher signal to noise ratio (Lloyd-Fox et al., 2010; Strangman, Culver, Thompson, & Boas, 2002). In addition, data was averaged across channels within the same region of interest (ROI) based on the output of our spatial registration program (see Figure 3.2 and Table A.9 in Appendix). We determined activation for five ROIs (MFG, Pre and Post Central Gyri, IFG, STS, IPL) in both hemispheres. Using IBM SPSS, we conducted a multivariate, multifactorial ANOVA using within-group factors of condition (Coincide, Lead, Follow, and Turn-Take), regions (MFG, PCG, IFG, STS, IPL), hemisphere (Left, Right), between-group factor of group (ASD, TD) and covariates of age, sex, and Vineland ABC scores to control for factors that differed between groups. Upon obtaining a 4-way interaction, we explored task-related and group-related differences. When our data violated Mauchly's test of sphericity, we applied Greenhouse-Geisser corrections. Post-hoc testing involved paired and independent t-tests. For behavioral errors, we conducted non-parametric tests such as Mann-Whitney U and Wilcoxon Signed Rank tests for between and within group comparisons. In our multiple post-hoc comparisons, specified significance was set at 0.05 and it was corrected using the Benjamini-Hochberg False Discovery Rate (FDR) method (Singh & Dan, 2006). We will also apply Spearman's correlations to study brain-behavior relations between activation data and behavioral errors (motor, planning, spatial) and Pearson's correlations to study relations between activation data and questionnaire data, specifically, VABS socialization scores and BOT Manual Dexterity raw scores.

## 3.3 Results

### 3.3.1 Behavioral Differences

#### 3.3.1.1 Differences in errors between children with and without ASD

Wilcoxon Signed Rank tests showed children with ASD had significantly greater errors in planning (Mean±SE 6.5±0.39), spatial matching (5±1), and motor performance (0.8±0.2) compared to the TD children (TD planning 2.3±0.7, $p$=0.01, TD spatial 2.4±0.5, $p$=0.03, and TD motor 0.3±0.2, $p$=0.03; Table A.10 in Appendix and Figure 3.4).

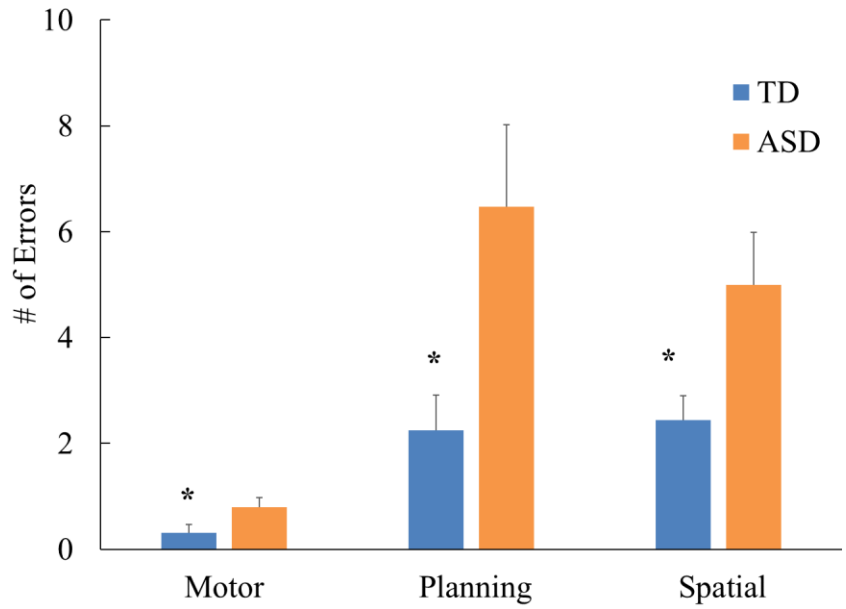


Figure 3.4 Behavioral Errors in TD and ASD Children (* *indicates p<.05*)

#### 3.3.1.2 Differences in Time to Task Completion Between Children with and Without ASD

With respect to group differences in task completion times, the ASD (Average time taken=29.78) group took longer to complete all tasks compared to the TD group (Average time taken=23.34). Children with ASD took the most time to build in the Coincide (30.86 ± 2.13) and Lead (30.81 ± 1.80) conditions compared to the Follow (27.67 ± 1.51) and Turn-Take (24.79 ± 1.24, $ps$<0.05) conditions. The TD children took the most time to build in the Lead (25.73 ± 0.78) and Follow (24.67 ± 0.64) conditions compared to the Turn-Take (21.28± 0.93) and Coincide (21.67 ± 0.86) conditions.

#### 3.3.1.3 Differences in Hand Preference Between Children with and without ASD

Based on the Coren Handedness Survey, we found that parents reported all children as being right-handed except for one child in the TD group and two children in the ASD group. However, our task allowed children to use both hands freely and we did not see similar hand use between groups. Instead, in the TD children 53.3% showed a right-hand preference, 26.7% showed a left-hand preference and 20% used both hands equally or showed mixed-handedness. In contrast, in children with ASD only 13.3% showed a right-hand preference, 53.3% showed left hand-preference, and 33.3% showed mixed-handedness. A chi-square test comparing handedness between TD children and children with ASD ($X^2$=66.2, *p-value*<0.0001) indicating that TD children had greater right-hand use (53.3% of TD children) whereas children with ASD had left or mixed handedness (86.6%).

### 3.3.2 Cortical Activation Differences

#### 3.3.2.1 Cortical Activation Analyses

A repeated measures ANOVA of condition x hemisphere x ROI with between subjects factors of group and age revealed a main effect of condition [$F_{(2.93,345.59)}$=4.25, *p*=0.006], 2-way interactions of condition x age [$F_{(2.93, 345.59)}$ =2.67, p=0.049], condition x ABC [$F_{(2.93, 345.59)}$ =3.04, *p*=0.030], condition x group [$F_{(2.93, 345.59)}$ =4.35, *p*=0.005], region x age [$F_{(3.31, 390.91)}$ =12.33, *p*=0.0001], region x group [$F_{(3.31, 390.91)}$=3.52, *p*=0.012], condition x region [$F_{(9.13, 1076.83)}$ =1.94, p=0.042], 3-way interactions of condition x hemisphere x ABC [$F_{(2.79,328.83)}$=3.90, *p*=0.011], condition x hemisphere x group [$F_{(2.79, 328.83)}$=4.42, *p*=0.006], condition x region x sex [$F_{(9.13, 1076.83)}$ =2.76, p=0.003], condition x region x group [$F_{(9.13, 1076.83)}$=2.38, *p*=0.011], hemisphere x region x age [$F_{(3.66,431.69)}$ =4.62, p=0.002], hemisphere x region x group [$F_{(3.66, 431,69)}$ =4.42, *p*=0.002], condition x hemisphere x region [$F_{(9.02,1064.74)}$=2.63, *p*=0.005] and 4-way interactions of condition x hemisphere x region x group [$F_{(9.02, 1064.74)}$ =6.10, *p*=0.0001] and condition x hemisphere x region x ABC scores [$F_{(9.02, 1064.74)}$=4.80, *p*=0.0001]. We further examined the 4-way interaction using post-hoc t-tests. Table A.11 in the Appendix shows the results of our post-hoc comparisons.

#### 3.3.2.2 Group Differences in Cortical Activation

In the STS region, the children with ASD had lower activation compared to the TD children. In contrast, in the IPL region, children with ASD showed the opposite pattern of greater activation compared to the TD children. Specifically, compared to the TD children, children with ASD had lower activation in the left STS regions for the Coincide and Turn-Take conditions (*ps*<0.01, Figure A.11 in Appendix) and in the right STS region for the Turn-Take condition only (*p*<0.01, Figure 3.5). Only in the left IPL, children with ASD had greater activation than TD children in the Lead and Turn-Take conditions (*ps*<0.001, Figure 3.5, Table A.11 in Appendix).

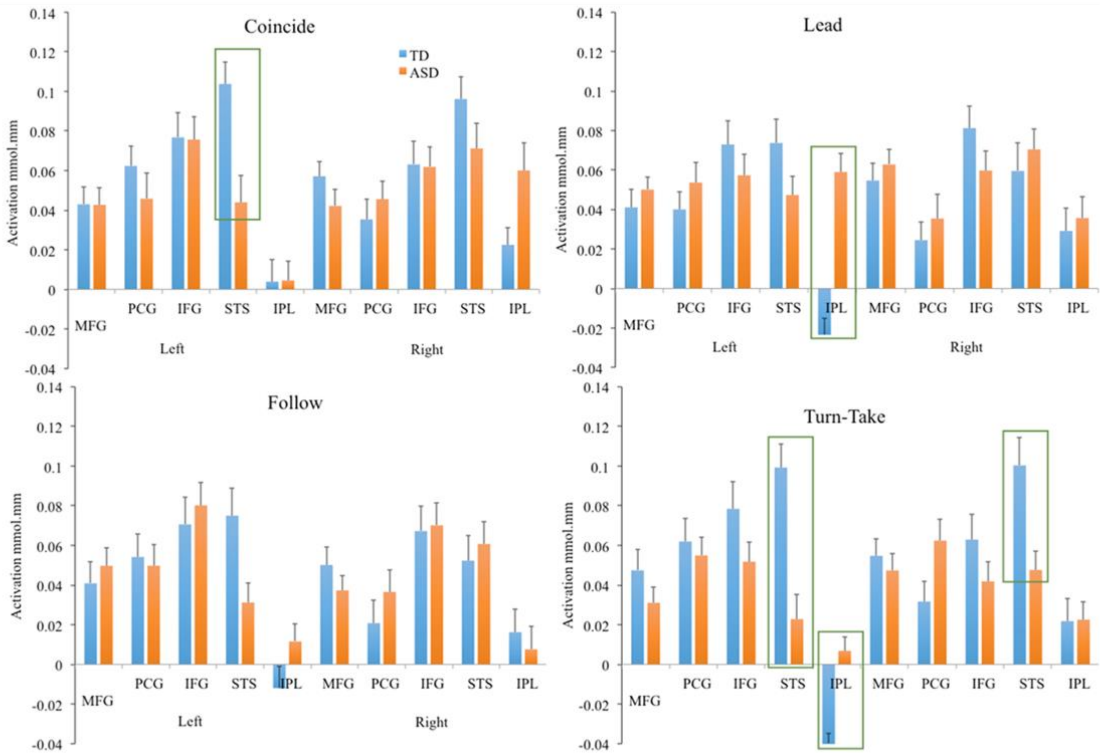


Figure 3.5 Group Differences in Cortical Activation across all regions of interest (*green boxes indicate statistical difference p< 0.05*)

#### 3.3.2.3 Hemispheric Differences in Cortical Activation

In the PCG region, the TD group had significantly greater cortical activation in the left compared to the right hemisphere in the Coincide and Follow conditions (*ps*<0.05, Figure 3.6, Table A.11 in Appendix). The PCG region also had a similar trend for greater left than right hemispheric activation in the Turn-Take condition ($p$<0.05). Conversely, children with ASD showed no such hemispheric differences in the PCG region. In the STS region, the TD group had no significant hemispheric differences. In contrast, in the STS region, children with ASD had significantly greater cortical activation in the right hemisphere compared to left hemisphere for the Follow condition ($p$<0.01). The Coincide and Turn-Take condition followed similar trends ($ps$<0.05).

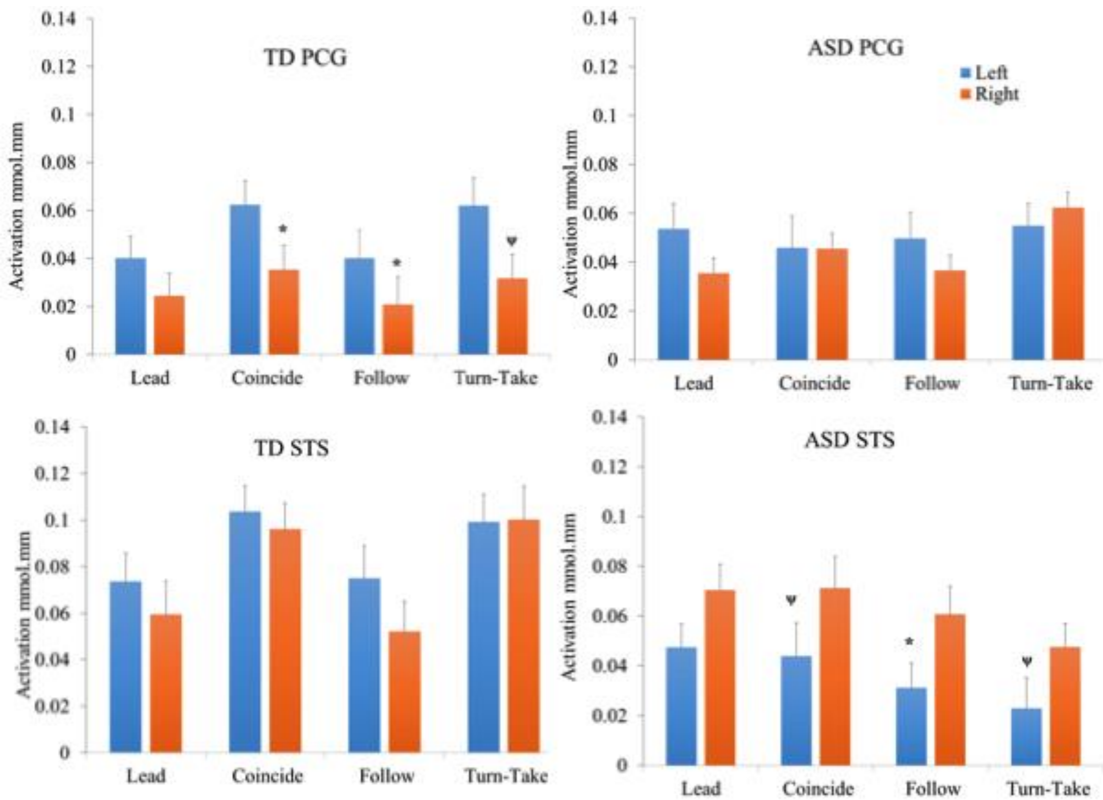


*Figure* 3.6 Hemispheric Differences between TD and ASD Children in the PCG and STS regions (* *indicates p < 0.05*)

#### 3.3.2.4 Conditional Differences in Cortical Activation

The TD group had significant differences across conditions in the right STS region, while the children with ASD showed no significant differences across conditions. Specifically, the TD group showed greater right STS activation in the

Coincide and Turn-take conditions compared to the Lead and Follow conditions (*ps*<0.01, Figure 3.7, Table A.11 in Appendix).

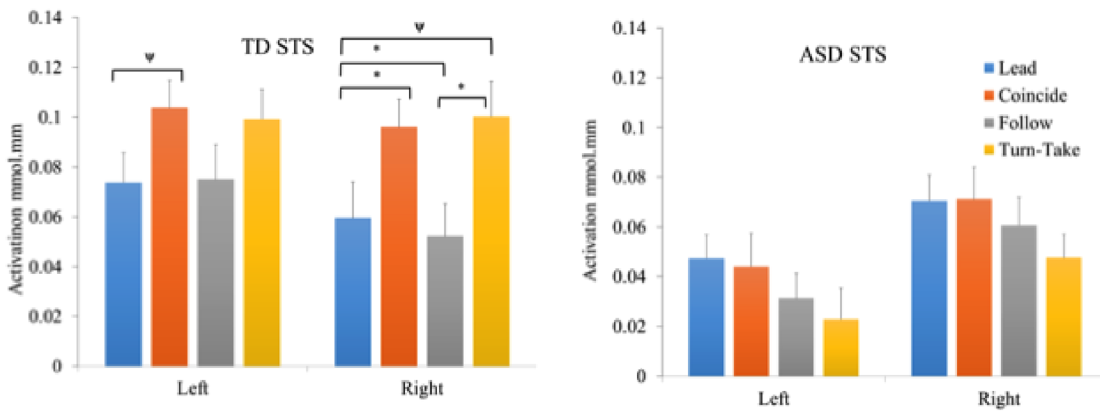


Figure 3.7 Conditional Differences in TD and ASD Children in the STS region of the brain (**indicates p<0.05 and Ψ indicates a statistical trend of p<0.01*).

### 3.3.2.5 Cortical Activation-Behavioral Error Correlations

During the building task, cortical activation in the TD children was negatively correlated with the planning errors but not with the motor or spatial errors (3 significant negative correlations ranging from -0.28 to -0.49 for the Coincide, Lead, and Follow conditions, Table A.12 in Appendix). In short, in the TD children, as activation increased in the left IFG region, planning errors decreased. In contrast, cortical activation in children with ASD positively correlated with motor, planning and spatial errors (5 significant correlations ranging from *r*=0.27-0.3 for the Lead, Follow, and Turn-Take conditions, Table A.12 in Appendix). In the children with ASD, as activation increased in the PCG or IPL regions, planning errors increased as well.

#### 3.3.2.6 Cortical Activation-Manual Dexterity Correlations

In the TD children, cortical activation in the right MFG region positively correlated ($r$=0.395) with BOT scores for the Lead condition (Table A.13 in Appendix). Similarly, positive correlations were seen between right STS activation and BOT scores for the Lead condition ($r$=0.304). In children with ASD, we found positive correlations ($r$=0.31-0.37) between left IPL activation and the BOT scores in the Lead and Coincide conditions. Similar positive correlations were also seen in the left STS and right IPL activation and BOT scores in the Coincide condition ($r$=0.324-0.327).

#### 3.3.2.7 Cortical Activation-VABS Socialization Scores

In the TD children, during the Follow and Turn-Take Conditions, the left STS, left MFG, right MFG, right IFG and right STS regions had moderate positive correlations with the VABS socialization scores (5 correlations ranging from 0.32 to 0.41, Table A.14 in Appendix). This indicates that TD children with higher socialization scores also had increased activation in the aforementioned cortical regions during the building game. This pattern was not seen in the ASD group perhaps due to floor effects in terms of their social performance on the VABS.

#### 3.3.2.8 Cortical Activation-SRS Scores

However, using the Social Responsiveness Scale (SRS), a social performance measure for children with ASD, we found significant negative correlations between right IFG activation and SRS scores for the Lead (-0.49) and Turn-Take (-0.33) conditions indicating that those with higher IFG activation had lower SRS scores or better social performance. Interestingly, left IPL activation in the Follow condition showed a reverse pattern of moderate positive correlation (0.37) with SRS scores indicating that those with low IPL activation had lower SRS scores and better social performance (Table A.15 in Appendix).

## 3.4 Discussion

Previous fMRI studies of social cooperation have been limited to simple hand movements and unnatural environments. Using fNIRS, two studies have reported differences in cortical activation during IPS versus solo actions (Bhat et al., 2017; Egetemeir et al., 2011). While IPS is a form of socially cooperative behavior that has been studied, no study to date has compared behavioral differences and underlying cortical activation between children with and without ASD during social cooperation behaviors. Therefore, our study compared both behavioral performance and cortical activation between children with and without ASD during a naturalistic and novel Lincoln Log building task. Overall, we found that children with ASD had greater motor, spatial and planning errors during task performance compared to the TD children. Additionally, the ASD group took longer to complete the building task across all conditions compared to the TD children. Finally, we found that, in spite of being right-handed, when allowed to move freely, more TD children had a right hand-preference whereas more children with ASD had a left- or mixed-hand preferences.

In terms of hemispheric differences in cortical activation, the TD children had more left-lateralized activation in the PCG region whereas the children with ASD lacked such left-lateralization. In terms of group differences, the children with ASD had lower activation in the STS region and greater activation in the IPL regions compared to the TD children in 3 out of the 4 conditions (Coincide, Lead, and Complementary/Turn-take). In addition, conditional differences were only seen in the right STS region for the

TD group. They showed greater activation in the more social conditions of Coincide and Turn-take compared to less social conditions of Lead and Follow. To be clear, no conditional differences were noted in the ASD group. In terms of activation-behavioral error correlations, in the TD children, as activation increased in the left IFG region, their planning errors decreased. In contrast, in the children with ASD as PCG and IPL activation increased so did their motor and spatial errors. In terms of activation-BOT correlations, we found that TD children with greater right MFG and right STS activation had better manual dexterity. Similar correlations were seen in the children with ASD for the left STS and left/right IPL regions. In terms of activation-VABS correlations, TD children with greater bilateral MFG and STS regions had better socialization skills. This pattern was not seen in the ASD group perhaps due to floor effects in their VABS social performance. Finally, in terms of SRS correlations we found that children with ASD having greater right IFG and lower left IPL activation had lower SRS scores or better social performance.

### 3.4.1 Behavioral Differences in Social Cooperation in Children with and without ASD

We found that children with ASD had greater motor, spatial and planning errors compared to their age-matched TD peers. In addition, ASD children took more time to complete all conditions of the task compared to TD children. In terms of activation-behavioral error correlations, in the TD children, as activation increased in the left IFG region their planning errors decreased. In contrast, in the children with ASD as PCG and IPL activation increased so did their motor and spatial errors. Children with ASD have poor social awareness, poor visuo-motor coordination and poor executive functioning skills; all of which might affect their participation and success in complementary actions such as the building game performed in this study (Leekam, Lopez, 2002; Robinson, Goddard, Dritschel, Wisley, & Howlin, 2009; Sachse et al., 2013). Poor social monitoring is a fundamental diagnostic impairment and widely reported in children with ASD. Children with ASD have difficulty with social orienting as well as responding to and initiating interactions with social partners. Children with ASD did not follow an adult partner's gaze or gestural bids to observe objects in the environment; however, they were able to shift attention towards objects after receiving non-social cues (Leekam & Ramsden, 2003; Leekam, Lopez, & Moor 2000). Difficulties in social monitoring in children with ASD may be due to their preference for non-social stimuli and impairments in processing social stimuli. Event-related potentials (ERPs) in toddlers with ASD did not differ when viewing a picture of their mother or an unfamiliar woman whereas the children differentially responded to viewing a favorite toy compared to a new toy, perhaps showing a preference for non-social stimuli (Dawson et al., 2002). Similar findings have been reported in toddlers with ASD who were shown 2D clips of a complex scene involving objects and people. They seemed to pay less attention to interactions between interacting adults and paid more attention to the surrounding background (Shic, Bradshaw, Klin, Scassellati, & Chawarska, 2011). Lastly, children with ASD also have alterations in visuo-spatial perception with more local versus global processing and enhanced parallel perception during visual search tasks. For example, participants with ASD were quicker to discern a small series of letters embedded within a larger number compared to TD controls (Mottron, Burack, Iarocci, Belleville, & Enns, 2003). Together, these social and visual perceptual impairments could impair the visuo-motor performance of children with ASD. In our study, greater focus on specific components of objects such as corners of logs or specific parts of the cue card or table or a lack of understanding of the tester's gestural cues may contribute to the greater motor and spatial errors during the building task.

Children with ASD have impairments in visuo-motor coordination based on their performance on standardized motor measures such as the BOT (Kaur et al., 2017 et al), Movement Assessment Battery for Children (MABC) (McPhillips, Finlay, Bejerot, & Hanley, 2014; Ament et al., 2015; Green et al., 2008), The Physical and Neurological Exam for Subtle Signs (Jansiewicz et al., 2006), and the Test of Gross Motor Development (Staples & Reid, 2010). Specifically, children with ASD have difficulties performing visuo-motor skills such as manual dexterity tasks, ball manipulation skills, balancing, and different forms of locomotion such as toe/heel walking, etc. In general, studies described difficulties in integrating spatial and visual information from their environment in order to perform various complex motor coordination tasks. Additionally, studies have described the kinematics of visuo-motor skills in children with ASD during circle drawing (Fleury, Kushki, Tanel, Anagnostou, & Chau, 2012), ball throwing (Whyatt & Craig, 2013), and reaching tasks (Mari, Castiello, Marks, Maraffa, & Prior, 2003). During a self-paced discontinuous circle drawing task, Fleury et al (2012) found greater variability in the arm movements of children with ASD compared to TD controls. In addition, children with ASD struggled to catch a ball thrown to them at different speeds (Whyatt & Craig, 2013). Finally, Mari et al. (2003) found that children with ASD took longer to complete reach-grasp actions (Mari et al, 2003). Taken together, the social, visual perceptual, and visuo-motor impairments of children with ASD may have affected their performance in the Lincoln Log building task leading to greater spatial and motor errors.

In our study, we found that children with ASD had increased planning errors and took longer to complete the building of structure compared to the TD children, which may be attributed to their impairments in executive functioning. A large meta-analysis including 235 studies involving over 6000 children and adults with ASD reported small to moderate effects for executive dysfunction across all subdomains including concept formation, working memory, ideational fluency, response inhibition, planning, and working memory. Another meta-analyses including 98 studies and involving ~2900 high-functioning children and adolescents with ASD also reported moderate effects in executive dysfunction in all subdomains except response inhibition which had smaller effect sizes. Sachse et al. (2013) specifically evaluated executive functioning in high-performing adults with ASD and found that while other executive functioning skills were minimally impaired in adults with ASD, spatial working memory and visuo-motor information processing impairments were compromised (Sachse et al., 2013). Consequently, we saw greater planning errors in the school-age children with ASD between 6 and 17 years given the nature of the Lincoln Log building task.

Additionally, we noted group differences in regions that had significant activation-behavior relationships. With the TD children, as activation increased in the left IFG region, their planning errors decreased. Similarly, greater right MFG and STS activation was associated with better manual dexterity and bilateral MFG and STS activation was associated with better socialization skills. In contrast, with the children with ASD, as PCG and IPL activation increased so did their motor and spatial errors. Additionally, greater left STS and left/right IPL activation was associated with better manual dexterity and greater right IFG and lower left IPL activation was associated with better social performance. Perhaps the group differences in regions correlating with the behavioral errors and standardized motor/social performance suggest alterations or compensations that occur in children with ASD when processing social, cognitive, and motor behaviors compared to what is seen in typically developing children.

### 3.4.2 Differences in Hand Preferences and Hemispheric Lateralization between children with and without ASD

In this study, 53.3% of the TD sample showed a right-hand preference, 26.7% showed a left-hand preference, and only 20% used both hands.during the building game. In contrast, only 13.3% of children with ASD showed a right-hand preference, 53.3% of the children with ASD showed a left-hand preference, and another 33.4% children with ASD used both hands. In terms of cortical activation, the PCG region was more left lateralized in the TD group whereas the ASD group showed bilaterally symmetrical PCG activation. These findings fit with what is known in the ASD literature in terms of their handedness as well as cerebral lateralization. During object manipulation tasks, TD children tended to use their right hand more whereas children with ASD did not show strong hand preferences in spite of parent’s reports of right-handedness in all children. (Forrester, Pegler, Thomas, & Mareschal, 2014). A meta-analysis by Markou et al. (2017) analyzing 21 studies on handedness involving 723 individuals with ASD revealed greater non-right handedness in 45.4% of individuals with ASD. Of those, 18.3% were left-handed individuals and 36.1% showed mixed-handedness.  Another meta-analysis by Rysstad & Pedersen et al. analyzed 12 studies on handedness involving 497 individuals with ASD. They also reported greater non-right handedness in 60% of individuals with ASD of which 16% were left-handed and 44% showed mixed-handedness. Overall, our findings concur with current literature showing that individuals with ASD have greater non-right handedness including mixed-handedness as well as left-handedness. Within our study during the building game, the TD children showed greater left hemispheric activation in the PCG, or sensori-motor cortices as is often reported (Gut et al., 2017). However, within the ASD group we saw bilaterally symmetrical activation across all conditions. This aligns with multiple studies reporting a lack of left cerebral lateralization in individuals with ASD. During a finger-tapping paradigm, fMRI-based connectivity analysis comparing right-handed individuals with and without ASD, individuals with ASD showed greater right lateralization in mean motor circuit connectivity (involving sensorimotor cortices, thalamus, putamen, supplementary motor area and cerebellum) whereas the healthy adults showed greater left-lateralized motor circuit connectivity (Floris et al., 2016). Furthermore, poorer performance on the PANESS motor coordination measure seen in individuals with ASD was associated with their connectivity scores (Jansiewicz et al., 2006). Similarly, using diffusion tensor imaging, Thompson et al. (2017) reported that manual dexterity performance in individuals with ASD was more associated with right hemispheric white matter organization whereas similar associations in typical adults were seen in the left hemisphere only. In the same study, the TD controls had higher dexterity scores for the right hand versus the left hand whereas the individuals with ASD showed similar performance across both hands. A lack of left-lateralization or greater right-lateralization in functional activation and connectivity in children with ASD has also been reported during language processing tasks (Redcay & Courchesne, 2008; Eyler, Pierce, & Courchesne, 2012; Nielsen et al., 2014; Lindel & Hudry, 2017). Taken together, our findings of non-right handedness and a lack of left-lateralized activation in our ASD group fit with the current ASD literature.

### 3.4.3 Lack of Differential STS Activation and Atypical MNS activation in ASD

While children with ASD showed no differential activation in the STS region across the various conditions of the building game, the TD children had greater activation in the Coincide and Turn-take conditions compared to the Lead and Follow conditions. In addition, TD children with higher activation in bilateral MFG and STS regions during the Follow and Turn-Take conditions of the building game also had better socialization skills using the VABS measure. While this pattern was not seen in the ASD group, based on performance on the SRS measure, children with ASD with higher activation in the right IFG and lower activation in the left IPL activation had better social performance. Several fMRI studies and meta-analyses have reported on MNS abnormalities found in individuals with ASD during a variety of tasks, however these papers present differing results (Phillip et al., 2012; DiMartino et al., 2009). Meta-analysis completed by Phillip (2012) covered 95 studies and 1083 participants with ASD and DiMartino (2009) covered 39 studies and 479 participants with ASD (Phillip et al., 2012; DiMartino et al., 2009). The studies included in these meta-analyses involved a variety of tasks related to visual processing, auditory and language processing tasks, and basic social processing (face, emotion, or biological motion processing). Both meta-analyses reported that individuals with ASD showed increased activation in the STS and IFG regions and decreased activation in the IPL region. In contrast, two different meta-analyses completed by Yang and Hoffman (2015) of 13 studies on individuals with ASD and Herringshaw et al. (2016) of 22 studies on 329 individuals with ASD involved a series of tasks that included action observation, action imitation, and language processing. They reported contradictory findings to prior meta-analyses in that individuals with ASD had reduced STS and IFG activation and increased IPL activation (Yang & Hoffman, 2015; Herringshaw, Ammons, DeRamus,

& Kana, 2016). Our research task involved increased aspects of imitation, synchrony and social cooperation and our results of decreased STS activation and increased IPL activation in the children with ASD across multiple social cooperation conditions align more with those of Yang & Hoffman (2015) and Herringshaw et al. (2016). Additionally, EEG and fMRI studies on action observation and goal discrimination have confirmed that in individual with ASD the STS and IFG regions were inactive or did not show differential activation during activities involving biological motion or facial emotion processing (Martineau, Cochen, Magne, & Barthelemy, 2008; Oberman et al., 2005; Dapretto et al., 2007). This aligns with our findings that children with ASD did not show differences in STS activation across conditions; whereas the TD children did. Additionally, past studies conducted in our lab and others using MEG and fNIRS during observation, execution and imitation tasks also report reduced activation in the STS and IFG regions and greater IPL activation in children and adults with ASD (Hoffman et al., 2017; Honaga et al., 2010).

### 3.4.4 Different Cortical Networks Used in Children with ASD during Social Cooperation Tasks

Our social cooperation task involved multiple components including monitoring of the tester's actions, visuo-spatial information processing about the task itself (from the cue card and partner), visuo-motor skills to perform the building actions, and executive functioning skills such as mental rotation, working memory, attentional shifting and inhibition to successfully complete the building structures shown. Hence the building task required the children to engage in complex interaction and integration across multiple brain regions, of which we captured activation in the MFG, PCG, IFG, STS, and IPL ROIs from both hemispheres. We found hypo-activation in the STS region and hyper-activation in the IPL region in children with ASD compared to a group of TD peers. In addition, we also found group differences in correlations between brain activation and behavior error/social/motor performance. For example, TD children with greater IFG activation had fewer planning errors whereas children with ASD with greater IPL activation had more planning errors. Interestingly, children with ASD with better social performance based on SRS scores also had greater right IFG and lower left IPL activation. In terms of motor performance, TD children with better motor performance on the BOT had greater MFG and STS activation whereas children with ASD with better motor performance on the BOT showed greater IPL and STS activation. Together these findings suggest that children with ASD process perceptual information and plan their movements differently compared those without ASD which in turn may involve different brain networks.

In terms of visual perception, children with ASD are known to be aware of low-level insignificant details in the environment than their TD peers are able to filter out, which makes it harder for them to perform tasks efficiently (O'Connor & Kirk, 2008). For example, during local-global perception tasks requiring individuals with ASD to pick small letters within a larger number, they were quicker to pick up on the smaller letters than TD controls (Mottron, Burack, Iarocci, Belleville, & Enns, 2003). Additionally, children with ASD are not aware of their social partners which may have limited the amount of social cues they received about the task. When observing social scenes, children with ASD focused on the details in their surroundings rather than the conversations between social partners (Shic et al., 2011). This may explain the lower STS activation in children with ASD as they are not actively engaging in the process of visuo-motor correspondence, an important role played by this region during social cooperation tasks. Lack of appropriate task-relevant or social information may affect their ability to understand task goals (individual and shared) which may contribute to lower IFG activation. As a result, children with ASD may have found the task more cognitively challenging and engaged in greater solo planning of actions; which in turn led to a pattern of hyperactivation in the IPL region. These findings also fit with the altered connectivity patterns reported in children with ASD. Studies in children and adults with ASD report excessive short-range connectivity within the frontal, parietal, and temporal cortices along with reduced long-range connectivity between cortices, e.g., reduced fronto-temporal or fronto-parietal connectivity (Just, Keller, Malave, Kana, & Varma, 2012; Courchesne & Pierce, 2005; Courchesne et al, 2007). Additionally, disordered or poor long-range connectivity has been reported in cortico-subcortical networks such as cortical-cerebellar (Mostofsky et al., 2009), cortico-striatal (Turner, Frost, Linsenbardt, McIlroy, & Müller, 2006), cortico-thalamic (Nair, Trieber, Shukla, Shih, & Müller, 2013) connections as well as inter-hemispheric, callosal connectivity (Frazier, Keshavan, Minshew, & Hardan, 2012). Hence, the regions of interest covered in this study most likely had some level of atypical structural and functional connectivity which may explain the fact that children with ASD engage different brain networks when processing sensory-perceptual information and planning their actions compared to TD children.

### 3.4.5 Limitations

This pilot study involved a relatively small sample size; yet several significant and meaningful findings were revealed. In spite of matching multiple factors across groups, we included a wide age range of children as well as a wide range of level of functioning in our children with ASD, which increased the variability of our study sample. Our findings are limited by the fact that our control group was typically developing. Ideally, we should have also included a developmentally-matched control group of children with low-levels of functioning without a diagnosis of ASD. There were slightly more females than males in this study. In addition, we did not use standardized tests to examine executive functioning, which could have been correlated with task performance. We were unable to relate activation between partners using a hyperscanning approach. In the future, we plan to do so in order to understand moment-to-moment relationships between individuals as they engage in cooperative behaviors. In addition, we may have biased hand preferences in our task design due to placement of the container of blocks on the participant's left side versus the more commonly used right hand. During naturalistic tasks, it is difficult to control the time to task completion and standardize the duration of the stimulation period. Finally, while we followed consistent probe placement, variation in participant head sizes and probe placement could have led to inconsistency in our final spatial registration output.

### 3.4.6 Clinical Implications and Conclusions

Our study identified multiple fNIRS-based neurobiomarkers during a social cooperation-based Lincoln Log building game across prefrontal, frontal, temporal and parietal regions of the brain. Children with ASD had greater behavioral errors (motor, spatial, and planning), took greater time to complete tasks, and showed left or mixed hand preferences. They also showed a lack of cortical lateralization compared to the TD children. In addition, children with ASD showed reduced STS activation and increased IPL activation as well as a lack of differential activation in the STS region compared to TD children. We also found group differences in brain-behavior correlations which could be attributed to the abnormal cortical connectivity in children with ASD indicating a different way of processing and producing social, motor, and cognitive behaviors compared to their TD peers. While we are currently focusing on comparing activation during social cooperation behaviors between individuals with and without ASD, we will shift to examining task-based connectivity patterns between regions given findings of poor connectivity across brain regions in individuals with ASD. The long-term goal of this research is to use the aforementioned fNIRS neurobiomarkers to assess changes in cortical activation following a bout of socially-embedded motor interventions focused on imitation, synchronization, and cooperation using musical, dance, and yoga interventions developed in our lab. Overall, fNIRS appears to be a valid and powerful child-friendly tool to examine cortical activation during cooperative constructional play such as Lincoln Logs, Legos, Jenga, etc. in both children with and without ASD.

## Chapter 4

## OVERALL DICUSSION, CLINICAL & RESEARCH IMPLICATIONS, AND FUTURE DIRECTIONS

Autism Spectrum Disorder (ASD) is a common pediatric neurodevelopmental disorder affecting 1 in 59 children (Baio et al., 2018). Children with ASD present with significant social impairments and comorbid deficits in sensory motor control that may inhibit their ability to adjust their actions to others during joint activities (Bhat et al., 2011; Kaur et al., 2017). Countless everyday skills are learned through observing and working with others during social cooperation tasks. Difficulties with social cooperation will ultimately affect child with ASD's ability to learn through observing others. Typically developing children who engage in social cooperation also show increased social connections to their partners suggesting that cooperative actions work as a "social glue" (Vicaria & Dickens, 2016). Similarly, the social cooperation difficulties of children with ASD will affect their ability to form social connections with their peers and caregivers (Marsh, Johnston, Richardson, & Schmidt, 2009). The broad goal of this thesis research is to better understand the developmental trajectory of social cooperation as well as difficulties in social cooperation in children with ASD as well as associated cortical activation patterns using functional near-infrared spectroscopy (fNIRS), a novel neuroimaging tool that is suited to the challenges of special needs children such as those with ASD. The long-term goal of this research is to develop behavioral and neural markers that can be used to develop more effective treatment contexts and intervention approaches to enhance social cooperation skills of children with ASD.

Aim 1 of this thesis examined the developmental trajectory of social cooperation by comparing behavioral patterns and cortical activation between younger and older typically developing school-age children between 6 and 17 years of age during the Lincoln Log building task. We hypothesized that age would correlate with neural activation as younger children would have more behavioral errors than older children, older children would have greater activation, differences in hand use, and hemispheric lateralization compared to younger children. In general, we hypothesized that TD children would have more activation in the social conditions of Coincide and Turn-take compared to the Lead and Follow conditions. Finally, we expected to see brain-behavior correlations in both groups. Once we understood the typical developmental trajectory of social cooperation and underlying cortical activation in the typically developing children, we expanded our analysis to children with ASD.

In Aim 1/chapter 2 we described the developmental trajectory of social cooperation in typically developing children between 6 and 17 years. We compared behavioral and activation patterns between younger (6 to 11 years) and older (11 to 17 years) children. First, we found that several findings that aligned with the literature in the field. Our first finding of greater motor, spatial and planning errors in younger children was related poor visuo-spatial and visuo-motor skills as well as poor executive functioning skills in this group compared to the older children (Kagerer & Clark, 2015; Huizinga et al., 2006). Second, we noted an age-related increase in prefrontal and mirror neuron system activation but not the sensori-motor cortices. These findings correspond with literature indicating that connectivity in the primary sensorimotor areas matures within the first two years of life and higher-order association areas such as the dorsolateral prefrontal cortices and the inferior parietal and superior temporal gyri are rapidly evolving in their functional connectivity patterns throughout early childhood and into late adolescence (Gogtay et al., 2004; Sowell et al., 2004). All TD children showed more left lateralization in the sensorimotor cortices, which can be attributed to the cerebral lateralization that seems to have occurred by 6 years of age in relation to actions performed in the building task. An additional hemispheric difference found was greater right lateralization in the IPL region of the older children, which could be due to the visuo-motor and visuo-spatial requirements of our task as lesion studies have found this region is important for visuo-spatial mapping skills (Pisella, 2015; Pisella, 2004). In terms of task-based differences, we found significant differences between elements of the task in the IPL and STS regions. In the right STS region, both groups had greater activation in the Coincide and Turn-Take conditions compared to the Lead and Follow conditions. Several groups have found that the STS region actively represents visuo-motor correspondence between one's own action and the actions of others during social cooperation tasks involving imitation and synchronization (Molenberghs et al., 2010; Bolling et al., 2013; Pelphrey et al., 2003; Bhat et al., 2017). While younger children with greater cortical activation had better motor performance and fewer behavioral errors, older children with greater cortical activation showed better socialization skills. Finally, the older children had greater suppression of activation in the left IPL region compared to the younger children. The IPL region is part of the Default Mode Network which is activated during tasks requiring greater executive functioning, which is known to be less mature in the younger children (Anticivic et al., 2010; White et al., 2012; Schulman, Astafiev, McAvoy, d'Avossa, & Corbetta, 2012; Daselaar et al., 2004).

Aim 2 of this thesis compared differences in social cooperation behaviors between school-age children with and without ASD. We hypothesized that children with ASD would have more behavioral errors (motor, spatial, and planning errors), would take longer to complete the task, may lack hemispheric lateralization, and would show lower STS and IFG activation and greater IPL activation compared to the TD children. Lastly, we expected to see brain-behavioral correlations in both groups, TD and ASD.

Several major findings that surfaced in our study comparing social cooperation behaviors and related activation between children with and without ASD, align with what is currently known about children with ASD. Our first finding was that children with ASD had greater overall behavioral errors, took more time to complete the task, and did not have established handedness patterns compared to the TD group. It has been established in current literature that children with ASD have poor social awareness, poor visuo-motor/visuo-spatial skills and poor executive functioning skills which might lead to the greater errors we see in this group and impair their performance in cooperative activities (Leekam et al., 2000; Robinson et al., 2009; Sachse et al., 2013). A second finding related to hemispheric lateralization was that children with ASD did not have strong lateralization as was found in the TD group which aligns with findings of atypical or non-existent lateralization in ASD (Redcay & Courchesne, 2008; Eyler, Pierce, & Courchesne, 2012; Nielsen et al., 2014; Lindel & Hudry, 2017). Third, children with ASD showed no differentiation across conditions in the STS region as was evident in the TD children, which we believe could be due to lack of social information received as a result of their reduced social awareness (Dawson et al., 2002). In terms of group differences, we found that children with ASD had greater activation in the IPL region and decreased activation in the STS region compared to TD controls. We relate this to a variety of meta-analyses and individual studies that found hypo-activation in the STS and IFG region and hyper-activation in the IPL region of individuals with ASD during observation, execution, and imitation tasks (Yang & Hoffman, 2015; Herringshaw et al., 2016; Martineau et al., 2008; Dapretto et al., 2007). Finally, we reviewed the Enhanced Perception Theory along with the Underconnectivity Theory of Autism. The Theory of Enhanced Perception expands upon the idea that individuals with ASD process sensory information differently than TD individuals in that they focus on smaller local details over the larger global/"big" picture as well as have difficulty shifting attention between global and local contexts (O'Connor & Kirk, 2008; Mottron et al., 2003; Rinehart, Bradshaw, Moss, Brereton, & Tonge, 2001). This may affect their ability to understand both individual and shared task goals related to the cooperative building task. Children with ASD are known to have local hyper-connectivity within cortical regions and hypo-connectivity in the long-range networks that run between regions (Courchesne & Pierce, 2005). The preference for local details over the global/big picture has been associated with the local hyper-connectivity findings. Additionally, children with ASD are known to have difficulties in executive functioning and visuo-motor performance, which has also been linked to reduced long-range connectivity between motor and sensory regions (including visual cortices) as well as poor connectivity within the Default Mode Network (Mostofsky et al., 2009).

### 4.1 Limitations

While multiple, significant findings in both aims were obtained from our study, it was not devoid of limitations. Our first limitation related to the relatively small sample sizes of 15-17 children per group. In the future, it would be valuable to reproduce our study with a larger sample size. Secondly, we could have expanded our behavioral analysis to include eye tracking and motion analysis to obtain quantitative measures of perceptual information received by the children as well as the coordination and synchronization patterns between the child and the tester. Third, we could have refined some elements of our task design. During the task we placed the block container to the children's left side which could have led to a left-hand bias rather than their preference for using their dominant right hand, as was reported by parents using a handedness survey. Fourth, it would be useful to find a way to standardize the stimulus duration, though the fNIRS field has yet to come to a consensus on how to handle this problem as limiting the stimulus duration will lead to a loss of hemodynamic profiles in some individuals. Fifth, we could enhance the difficulty of the building task by adding more Lincoln Logs or even transferring to a different game such as use of Jenga Blocks or K'nex that also require visuo-motor and visuo-spatial skills. Finally, we could expand our study design to simultaneously scan or hyperscan two children or an adult and a child. Our current research focused on neural activation in one child at a time. Simultaneous scanning during building could assist in understanding how neural activity synchronizes during cooperative actions. In terms of administered subtests, it would have been useful to include standardized measures of executive functioning performance as well as more related visuo-motor measures. Finally, a major limitation of this work is the difference in level of functioning between children with and without ASD and the lack of a developmentally delayed control group without an ASD diagnosis. Future studies must consider using additional control groups, for example, children with intellectual delays to control for level of functioning.

## 4.2 Future Recommendations for Researchers and Clinicians

Our results provide a better understanding of developmental differences in social cooperation in typically developing children. In addition, we have identified valuable behavioral and neural biomarkers of social cooperation in children with ASD. In the future, we plan to use biomarkers such as lack of lateralization, STS hypoactivation and IPS hyperactivation to examine the treatment effects of social cooperation interventions. Neural activation in the Lincoln Log task could be monitored at the beginning and end of intervention to examine the neural effects of such interventions. Additionally, the building task was challenging the children with ASD in terms of social cooperation, executive functioning, and visuo-motor performance and hence, their therapeutic activities must include constructional games with other social partners (parent, caregivers, peers, etc.). While we did not show direct effects of such training in our study, we provided some indirect evidence based on the correlations we found between activation during the building task and behavioral/standardized test performance. In terms of social improvements, such play could engage children in friendships with peers, increased social interactions, and greater self-esteem, and enhance their feelings of social acceptance within their various group settings (school, daycare). It is important that clinicians remember to deconstruct the task into simpler steps as children with ASD struggle to incorporate the many social and motor requirements of cooperative action. For example, clinicians could limit the amount of information provided to children with ASD by showing only pictures for each step instead of the final structure. The amount of social feedback could be reduced by only providing manual prompts for placement. Additionally, clinicians should avoid additional mental rotations and provide references in an egocentric frame of reference (reference in relation to their own body and similar to their view of the 3D structure built in front of them). In conclusion, we feel confident that we accomplished the goals we set out to achieve: (a) described the developmental trajectory of social cooperation in school-age children and (b) identified behavioral and neural biomarkers of social cooperation difficulties in children with ASD within the context of a building game.

## REFERENCES


American Psychiatric Association. (2013) *Diagnostic and statistical manual of mental disorders,* 5th ed. (DSM-5) Arlington, VA: American Psychiatric Publishing.

Anticevic A., Repovs, G., Schulman, G.L., & Barch, D.M. (2010). When less is more: TPJ and default network deactivation during encoding predicts working memory performance. *Neuroimage, 49*(3), 2638–2648. doi: 10.1016/j.neuroimage.2009.11.008

Ament, K., Mejia, A., Buhlman, R., Erklin, S., Caffo, B., Mostofsky, S., & Wodka, E.(2015). Evidence for specificity of motor impairments in catching and balance in children with autism. *Journal of Autism and Developmental Disorders, 45*(3), 742-751. doi: 10.1007/s10803-014-2229-0.

Anderson, P. (2002). Assessment and development of executive function (EF) during childhood. *Child Neuropsychology., 8*(2), 71-82. doi: 10.1076/chin.8.2.71.8724

Ashton-James, C.E., & Chartrand, T.L. (2009). Social cues for creativity: The impact of behavioral mimicry on convergent and divergent thinking. *Journal of Experimental Social Psychology, 45*,1036-1040.

Aziz-Zadeh, L., Koski, L., Zaidel, E., Mazziotta, J., & Iacoboni, M. (2006). Lateralization of the human mirror neuron system. *Journal of Neuroscience, 26*(11), 2964–2970. doi: 10.1523/JNEUROSCI.2921-05.2006.

Baio, J., Wiggins, L., Christensen, D.L., Maenner, M. J., Daniels, J., Warren, Z.,….Dowling, N.F. (2018). Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014. *MMWR Surveillance Summaries, 67*(6), 1–23. http://doi.org/10.15585/mmwr.ss6706a1

Balardin, J. B., Zimoe Morais, G. A., Furucho, R. A., Trambaiolli, L., Vanzella, P., Biazoli, C., & Sato, J. R. (2017). Imaging Brain Function with Functional Near-Infrared Spectroscopy in Unconstrained Environments. *Frontiers in Human Neuroscience, 11*. doi:10.3389/fnhum.2017.00258

Bhat, A. N., Hoffman, M. D., Trost, S. L., Culotta, M. L., Eilbott, J., Tsuzuki, D., & Pelphrey, K. A. (2017). Cortical Activation during Action Observation, Action Execution, and Interpersonal Synchrony in Adults: A functional Near-Infrared Spectroscopy (fNIRS) Study. *Frontiers in Human Neuroscience, 11*. doi:10.3389/fnhum.2017.0043.

Bhat, A.N., Landa, R.J, & Galloway, J. C. (2011). Perspectives on motor problems in infants, children, and adults with autism spectrum disorders. *Physical Therapy*, *91*(7), 1116–1129. doi: 10.2522/ptj.20100294.

Biermann-Ruben, K., Kessler, K., Jonas, M., Siebner, H.R., Bäumer, T., Münchau, A., Schnitlzer, A (2008). Right hemisphere contributions to imitation tasks. *European Journal of Neuroscience, 27*(7), 1843-55. doi: 10.1111/j.1460-9568.2008.06146.x.

Blair, R.J., Frith, U., Smith, N., Abell, F., & Cipolotti,, L. (2002). Fractionation of visual memory: agency detection and its impairment in autism. *Neuropsychologia, 40*(1), 108–118.

Boddaert, N., Chabane, N., Gervais, H., Good, C.D., Bourgeois, M., Plumet, M.H.,

Barthelemy, C., Mouren, M.C., Artiges, E., Samson, Y., Brunelle, F., Frackowiak, R.S.,& Zilbovicius, M. (2004). Superior temporal sulcus anatomical abnormalities in childhood autism: a voxel- based morphometry MRI study. *Neuroimage*, *23*(1), 364-369. doi:10.1016/j.neuroimage.2004.06.016.

Bolling, D.Z., Pelphrey, K.A., & Kaiser, M.D. (2014). Social inclusion enhances biological motion processing: A functional Near Infrared Spectroscopy Study. *Brain Topography, 26*(2). doi: 10.1007/s10548-012-0253-y.

Brakke, K., Fragaszy, D.M., Simpson, K., Hoy, E., Cummins-Sebree, S. (2007). The Production of bimanual percussion in 12- to 24-month-old children. *Infant Behavior & Development, 30*(1), 2-15. doi:10.1016/j.infbeh.2005.08.001.

Brass, M., Derrfuss, J., & von Cramon, D.Y. (2005). The inhibition of imitative and overlearned responses: a functional double dissociation. *Neuropsychologia, 43*(1), 89–98. doi:10.1016/j.neuropsychologia.2004.06.018.

Brezis, R. S., Noy, L., Alony, T., Gotlieb, R., Cohen, R., Golland, Y., & Levit-Binnun, N. (2017). Patterns of Joint Improvisation in Adults with Autism Spectrum Disorder. *Frontiers in Psychology, 8*, 1790. doi:10.3389/fpsyg.2017.01790.

Bruininks, R. (1978). Bruininks-Oseretsky test of motor proficiency: Examiner's Manual. American Guidance Service, Circle Pines, MN.

Burling, J.M., Lu, H. (2018). Categorizing coordination from the perception of joint actions. *Atten Percep Psychophys*, *80*, 7-13. Doi:10.3758/s13414-017-1450-2.

Buxbaum, L.J., Kyle, K.M., & Menon, R. (2005). On beyond mirror neurons: Internal representations subserving imitation and recognition of skilled object-related actions in humans. *Cognitive Brain Research*, *25*, 226-239. doi:10.1016/j.cogbrainres.2005.05.014.

Candidi, M., Sacheli, L. M., Era, V., Canzano, L., Tieri, G., & Aglioti, S. M. (2017). Come together: Human–avatar on-line interactions boost joint-action performance in apraxic patients. *Social Cognitive and Affective Neuroscience, 12*(11), 1793-1802. doi:10.1093/scan/nsx114.

Carius, D., Andrä, C., Claub, M., Ragert, P., Bunk, M., & Mehnert, J. (2016). Hemodynamic Response Alteration As a Function of Task Complexity and Expertise—An fNIRS Study in Jugglers. *Frontiers in Human Neuroscience*, *10*. doi:10.3389/fnhum.2016.00126.

Casey, B. J., Galvan, A., and Hare, T. A. (2005). Changes in cerebral functional organization during cognitive development. *Current Opinion Neurobiology*., *15*(2), 239–244. doi:10.1016/j.conb.2005.03.012.

Caspers, S., Zilles, K., Laird, A.R., & Eickhoff, S.B. (2010). ALE meta-analysis of action observation and imitation in the human brain. *Neuroimage*, *50*(3), 1148–1167. doi: 10.1016/j.neuroimage.2009.12.112

Chaminade, T., Meltzoff, A.N., Decety, J. (2002). Does the end justify the means? A PET exploration of the mechanisms involved in human imitation. *Neuroimage*, *15*(2), 318– 328. doi:10.1006/nimg.2001.0981.

Christakou, A,, Murphy, C.M., Chantiluke, K., Cubillo, A.I., Smith, A.B., Giampietro, V., Daly, E., Ecker, C., Robertson, D., Murphy, D.G., & Rubia, K. (2013). Disorder-specific functional abnormalities during sustained attention in youth with Attention Deficit Hyperactivity Disorder (ADHD) and with Autism. *Molecular Psychiatry*, *18*(2), 236–44. doi: 10.1038/mp.2011.185.

Chugani, H. T., Phelps, M. E., & Mazziotta, J. C. (1987). Positron emission tomography study of human brain functional development. *Annals of Neurology*, *22*(4), 487–497.

Colby, K. M., & Parkison, C. (1977). Handedness in autistic children. *Journal of Autism and Childhood Schizophrenia*, *7*(1), 3–9.

Colombi, C., Liebal, K., Tomasello, M., Young, G., Warneken, F., & Rogers, S. J. (2009). Examining correlates of cooperation in autism: Imitation, joint attention, and understanding intentions. *Autism,13*(2), 143-163. doi:10.1177/1362361308098514.

Constantino, J.N., & Gruber, C.P. (2005). Social Responsiveness Scale (SRS). Los Angeles: Western Psychological Services.

Coren S. (1992). Handedness Questionnaire. The Left-Hander Syndrome: The Causes and Consequences of Left-Handedness. New York: NY Free Press.

Courchesne, E. & Pierce, K. (2005). Why the frontal cortex in autism might be talking only to itself: Local over-connectivity but long-distance disconnection. *Current Opinion in Neurobiology, 15,*225-230.

Courchesne, E., Pierce, K., Schumann, C., Redcay, E., Buckwalter, J., Kennedy, D., and Morgan, J. (2007). Mapping early brain development in autism. *Neuron.* 56(2), 399-413. PMID: 17964254.http://dx.doi.org/10.1016/j.neuron.2007.10.016

Daselaar, S.M., Prince, S.E., Cabeza, R. (2004). When less means more: deactivations during encoding that predict subsequent memory. *Neuroimage*, *23*(3), 921–927.

Dawson, G., Carver, L., Meltzoff, A.N, Panagiotides, H., McPartland, J., & Webb, S.J. (2013). Neural correlates of face and object recognition in young children with autism spectrum disorder, developmental delay, and typical development. *Child Development*, *73*(3), 700-717.

Decety, J., Chaminade, T., Grèzes, J., Meltzoff, A.N. (2002): A PET exploration of the neural mechanisms involved in reciprocal imitation. *Neuroimage*, *15*(1), 265–272. doi:10.1006/nimg.2001.0938

Desmurget, M., Grafton, S. (2000). Forward modeling allows feedback control for fast reaching movements. *Trends in Cognitive Science, 4*(11), 423-431, doi:10.1016/S1364-6613(00)01537-0.

Durston, S., Davidson, M.C., Tottenham, N., Galvan, A., Spicer, J.A., Fossella, J.A., & Casey, B.J. (2006). A shift from diffuse to focal cortical activity with development. *Developmental Science, 9*(1), 1-8.

Drake, C., Jones, M.R., Baruch, C. (2000). The development of rhythmic attending in auditory sequences: attunement, referent period, focal attending. *Cognition*, *77*(3), 251–288.

Dziuk, M.A., Gidley Larson, J.C., Apostu, A., Mahone, E.M., Denckla, M.B., & Mostofsky, S.H. (2007). Dyspraxia in autism: Association with motor, social and communicative deficits. *Developmental Medicine and Child Neurology, 49*(10), 734-739. doi: 10.1111/j.1469-8749.2007.00734.x

Eyler, L.T., Pierce, K., Courchesne, E. (2012). A failure of left temporal cortex to specialize for language is an early emerging and fundamental property of autism. *Brain, 135.* 949-2012.

Finkel, E.J., Campbell, W.K., Brunell, A.B., Dalton, A.N., Scarbeck, S.J., & Chartrand, T.L. (2006). High-maintenance interaction: Inefficient social coordination impairs self-regulation. *Journal of Personality and Social Psychology, 91*(3), 456-475. doi:10.1037/0022-3514.91.3.456.

Fitzpatrick, P., Romero, V., Amaral, J.L., Duncan, A., Barnard, H., Richardson, M.J., & Schmidt, R.C. (2017). Social Motor Synchronization: Insights for Understanding Social Behavior in Autism. *Journal of Autism and Developmental Disorders, 47*(7), 2092-2107. doi: 10.1007/s10803-017-3124.

Fitzpatrick, P., Schmidt, R.C., & Lockman, J. J. (1996). Dynamical Patterns in the Development of Clapping. *Child Development, 67*(6), 2691-2708. doi: 10.1111/j.1467-8624.1996.tb01883.x

Floris, D.L., Barber, A.D., Nebel, M.B., Martinelli, M.M, Lai, M.C., Crocetti, D., Baron

Cohen, S., Suckling, J., Pekar, J.J., & Mostofsky, S.H. (2016). Atypical lateralization of motor circuit functional connectivity in children with autism is associated with motor deficits. *Molecular Autism,7*, 35. https://doi.org/10.1186/s13229-016-0096-6.

Forrester, G. S., Pegler, R., Thomas, M. S., & Mareschal, D. (2014). Handedness as a marker of cerebral lateralization in children with and without autism. *Behavioural Brain Research*, *268*, 14 –21. doi: 10.1016/j.bbr.2014.03.040.

Frazier, T., Keshavan, M., Minshew, N., and Hardan, A. (2012). A two-year longitudinal MRI study of the corpus callosum in autism. *Journal of Autism and Developmental Disorders*, 42(11), 2312-22. PMID: 22350341. PMCID: PMC4384817. http://dx.doi.org/10.1007/s10803-012-1478-z.

Freeman, L.M., Lock, J., Rotheram-Fuller, E., & Mandell, D. (2017). Brief report: Examining Executive and Social Functioning in Elementary Aged Children with Autism. *Journal of Autism and Developmental Disorders, 47*(6), 1890-1895. doi: 10.1007/s10803-017-3079-3

Freitag, C. M., Konrad, C., Häberlen, M., Kleser, C., von Gontard, A., Reith, W., Troje, N.F., & Krick, C. (2008). Perception of biological motion in autism spectrum disorders. *Neuropsychologia, 46*(5), 1480-1494. doi: 10.1016/j.neuropsychologia.2007.12.025.

Gazzola, V., & Keysers C. (2009). The observation and execution of actions share motor and somatosensory voxels in all tested subjects: single-subject analyses of unsmoothed fMRI Data. *Cerebral Cortex, 19*(6), 1239–1255. doi:10.1093/cercor/bhn181

Gervain, J., Mehler, J., Werker, J.F., Nelson, C.A., Csibra, G., Lloyd-Fox, S., Shukla, M., & Aslin, R.N. (2011). Near-infrared spectroscopy: A report from the McDonnell infant methodology consortium. *Developmental Cognitive Neuroscience, 1*(1), 22-46.

Getchell, N., & Whitehall, J. (2013). How do children coordinate simultaneous upper and lower extremity tasks? The development of dual motor task coordination. *Journal of Experimental Child Psychology, 85*(2), 120-14.

Glazebrook, C.M., Gonzalez, D., Hansen, S., & Elliott, D. (2009). The role of vision for online control of manual aiming movements in persons with autism spectrum disorders. *Autism, 13*(4), 411-433. doi: 10.1177/1362361309105659.

Goldenberg G., Hermsdorfer J., Glindemann R., Rorden C., & Karnath H. (2007). Pantomime of tool use depends on integrity of left inferior frontal cortex. *Cerebral Cortex, 17*(12), 2769–2776. doi:10.1093/cercor/bhm004.

Gräfenhain, M., Behne, T., Carpenter, M., & Tomasello, M. (2009). Young children’sunderstanding of joint commitments. *Developmental Psychology, 45*(5), 1430-1443. doi:10.1037/a0016122.

Ghez, C., Hening, W., Gordon, J. (1991). Organization of voluntary movement. *Current Opinion in Neurobiology,1*(4), 664–671. doi:10.1016/S0959-4388(05)80046-7, pmid:1822314.

Giedd, J.N., Blumenthal, J., Jeffries, N.O., Castellanos, F.X., Liu, H., Zijdenbos, A., Paus,T., Evans, A.C., Rapoport, J.L. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Natural Neuroscience, 2*(10), 861-863. doi:10.1038/13158

Gogtay, N., Giedd, J.N., Lusk, L., Hayashi, K.M., Greenstein, D.A., Vaituzis, C., Nugent III, T.F., Herman, D.H., Clasen, L.S., Toga, A.W., Rapoport, J.L., Thompson, P.M. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *PNAS,101* (21), 8174-8179. doi:10.1073/pnas.0402680101.

Gut, M., Urbanik, A., Forsberg, L., Binder, M., Rymarczyk, K., Sobiecka, B., Kozub, J., Grabowska, A. (2007). Brain correlates of right-handedness. *Acta Neurobiologiae Experimentalis Journal, 67*(1), 43-51.

He, Z.H., Li, B.H., & Yin, W.G. (2019). Executive Function and Mental Rotation During Middle Childhood: The Effect of Age. *The Journal of Genetic Psychology, 180*(2), 96-102. doi: 10.1080/00221325.2019.1582474.

Herringshaw, A.J., Ammons, C.J., DeRamus, T.P., & Kana, R.K. (2016). HemisphericDifferences in Language Processing in Autism Spectrum Disorders: A Meta-Analysis of Neuroimaging Studies. *Autism Research, 9*(1), 1046-1057. doi: 10.1002/aur.1599.

Hoffman, M., Trost, S., Culotta, M., Su, W.C, & Bhat, A.(2017). Differences in fNIRSBased Cortical Activation During Interpersonal Synchrony Tasks Between Children With and Without Autism. Poster presented at: 2017 International Meeting for Autism Research. 2017, May 13-15: San Francisco, California.

Honaga, E., Ishii, R., Kurimoto, R., Canuet, L., Ikezawa, K., Takahashi, H., Nakahachi, T., Iwase, M., Mizuta, I., Yoshimine, T., & Takeda, M. (2010). Post-movement beta rebound abnormality as an indicator of mirror neuron dysfunction in autistic spectrum disorder: An MEG Study. *Neuroscience Letters*, 478, 141-145.

Hooper, S. (1992). Cooperative learning and computer-based instruction. *Educational Technology Research and Development, 44*(3), 21-38. doi: 10.1037/0022-0663.90.4.746

Hughes, C. (1996). Brief report: planning problems in autism at the level of motor control. *Journal of Autism and Developmental Disorders, 26* (1), 99-107.

Huizinga, M., Dolan, C.V., van der Molen, M.W. (2006). Age-related change in executive function: Developmental trends and a latent variable analysis. *Neuropsychologia, 44,* 2017-2036.

Huppert, T. J., Diamond, S. G., Franceschini, M. A., & Boas, D. A. (2009). HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain. *Applied Optics, 48*(10). doi: 10.1364/AO.48.00D280.

Iacoboni, M. (2005). Neural mechanisms of imitation. *Current Opinion in Neurobiology*, *15*(6), 632–637. doi: 10.1016/j.conb.2005.10.010

Iacoboni, M. (2009). Neurobiology of imitation. *Current Opinion in Neurobiology,19*(6), 661-665. doi: 10.1016/j.conb.2009.09.008

Jack, A., & Morris, J. P. (2014). Neocerebellar contributions to social perception in adolescents with autism spectrum disorder. *Developmental Cognitive Neuroscience, 10,* 77-92.

Japee, S., Holiday, K., Satyshur, M. D., Mukai, I., & Ungerleider, L. G. (2015). A role of right middle frontal gyrus in reorienting of attention: A case study. *Frontiers in Systems Neuroscience, 9*(23). doi:10.3389/fnsys.2015.00023

Jeon, H., & Lee, S.H. (2018). From Neurons to Social Beings: Short Review of the Mirror Neuron System Research and Its Socio-Psychological and Psychiatric Implications.*Clinical Psychopharmacology and Neuroscience, 16*(1), 18-31. doi: 10.9758/cpn.2018.16.1.18

Jones, S.S (2007). Imitation in Infancy: The Development of Mimicry. *Psychological Science, 18*(7), 593-599. doi:10.1111/j.1467-9280.2007.01945.x

Just, M., Keller, T., Malave, V., Kana, R., and Varma, S. (2012). Autism as a neural systems disorder: A theory of frontal-posterior underconnectivity. *Neuroscience and Biobehavioral Reviews*, 36(4), 1292-1313. PMID: 22353426. PMCID: PMC3341852. http://dx.doi.org/10.1016/j.neubiorev.2012.02.007.

Kagerer, F.A., & Clark, J.E. (2015). Development of kinesthetic-motor and auditory-motor representations in school-aged children. *Experimental Brain Research, 223*(7), 2181-2194. doi: 10.1007/s00221-015-4288-7.

Kajiume, A., Aoyama-Setoyama, S., Saito-Hori, Y., Ishikawa, N., & Kobayashi, M.(2013). Reduced brain activation during imitation and observation of others in children with pervasive developmental disorder: a pilot study. *Behavioral and Brain Functions, 9*(21).

Kaur, M., Srinivasan, S.M., & Bhat, A.N. (2017). Comparing motor performance, praxis, coordination, and interpersonal synchrony between children with and without Autism Spectrum Disorder (ASD). *Research in Developmental Disabilities, 72*, 79-95. doi: 10.1016\j.ridd.2017.10.025.

Kim, H. Y., Seo, K., Jeon, H. J., Lee, U., and Lee, H. (2017). Application of functionalnear-infrared spectroscopy to the study of brain function in humans and animal models. *Molecular Cell, 40*, 523–532. doi: 10.14348/molcells. 2017.0153.

Kirschner, S., & Tomasello, M. (2010). Joint music making promotes prosocial behavior in 4-year old children. *Evolution and Human Behavior, 31*(5), 354–364. doi: 10.1016/j.evolhumbehav.2010.04.004.

Kleinspehn-Ammerlahn, A., Riediger, M., Schmiedek, F., von Oertzen, T., Li, S.C., & Lindenberger, U. (2011). Dyadic drumming across the lifespan reveals a zone of proximal development in children. *Developmental Psychology, 47*(3), 632-644. doi: 10.1037/a0021818.

Konrad K., Neufang S., Thiel C.M., Specht, K., Hanisch C., Fan J., Herpertz-Dahlmann, B., & Fink, G.R. (2005).Development of attentional networks: an fMRI study with children and adults. *NeuroImage, 28*(2), 429–439.

Kroliczak, G., & Frey S.H. (2009). A common network in the left cerebral hemisphere represents planning of tool use pantomimes and familiar intransitive gestures at the hand-independent level. *Cerebral Cortex., 19*(10), 2396–2410. doi: 10.1093/cercor/bhn261.

Lakin,J.L.,Jefferis, V. E.,Cheng, C.M., & Chartrand,T. L. (2003). The Chameleon Effect as Social Glue: Evidence for the evolutionary significance of nonconscious mimicry. *Journal of Nonverbal Behavior, 27*(3), 145–162. doi:https://doi.org/10.1023/A: 1025389814290

Lindell, K.A., & Hudry, K. (2013). Aytpicalities in Cortical Structure, Handedness, and Functional Lateralization for Language in Autism Spectrum Disorders. *Neuropsychol. Rev., 23*, 257-270. doi: 10.1007/s11065-013-9234-5.

Langseth-Rysstad, A., & Vorland Pedersen, A. (2016). Brief Report: Non-right Handedness Within the Autism Spectrum Disorder. *Journal of. Autism and Developmental Disorder,* 46(3), 1110-1117. doi: 10.1007/s10803-015-2631-2.

Leekam, S.R., Lopez, B., & Moore, C. (2000). Attention and Joint Attention in Preschool Children with Autism. *Developmental Psychology, 38*(2), 261-273. doi: 10.1037/0012-1649.36.2.261.

Leff, D. R., Orihuela-Espina, F., Elwell, C. E., Athanasiou, T., Delpy, D. T., Darzi, A. W., Yang, G.Z. (2011). Assessment of the cerebral cortex during motor task behaviours in adults: a systematic review of functional near infrared spectroscopy (fNIRS) studies. *Neuroimage, 54*(4), 2922–2936. doi: 10.1016/j.neuroimage.2010.10.058

Leung, H.C., Gore, J. C., & Goldman-Rakic, P. S. (2002). Sustained mnemonic response in the human middle frontal gyrus during on-line storage of spatial memoranda. *Journal of Cognitive Neuroscience, 14*(4), 659-671. doi:10.1162/08989290260045882

Lenroot, R. K., and Giedd, J. N. (2006). Brain development in children and adolescents: insights from anatomical magnetic resonance imaging. *Neuroscience and* Biobehavoral Reviews, *30*(6), 718–729. doi:10.1016/j.neubiorev.2006.06.001.

Liu, T., Saito, G., Lin, C., & Saito, H. (2016). Inter-brain network underlying Turn based cooperation and competition: A hyperscanning study using near-infrared spectroscopy. *Nature, 7*(1), 8648. doi: 10.1038/s41598-017-09226-w.

Liu, W. C., Flax, J. F., Guise, K. G., Sukul, V., and Benasich, A. A. (2008). Functional connectivity of the sensorimotor area in naturally sleeping infants. *Brain Research, 1223*, 42–49. doi: 10.1016/j.brainres.2008.05.054

Lloyd-Fox, S., Blasi, A., & Elwell, C.E. (2010). Illuminating the developing brain: The past, present and future of functional near infrared spectroscopy. *Neuroscience and Behavioral Reviews, 34*,269-284.

Makowski, C., Lepage, M., & Evans, A. C. (2019). Head motion: the dirty little secret of neuroimaging in psychiatry. *Journal of Psychiatry & Neuroscience*, 44(1), 62–68. doi:10.1503/jpn.180022

Margulies, D. S., Kelly, A. M., Uddin, L.Q., Biswal, B. B., Castellanos, F. X., and Milham, M. P. (2007). Mapping the functional connectivity of anterior cingulate cortex. *Neuroimage*, *37*(2), 579–588. doi:10.1016/j.neuroimage.2007.05.019

Mars, R. B., Neubert, F. X., Noonan, M. P., Sallet, J., Toni, I., & Rushworth, M. F. (2012). On the relationship between the "default mode network" and the "social brain". *Frontiers in human neuroscience*, *6*, 189. doi:10.3389/fnhum.2012.00189

Markou, P., Ahtam, B., Papadatou-Pastou, M. (2017). Elevated Levels of AtypicalHandedness in Autism: Meta-Analysis. *Neuropsychology Review, 27*(3), 258-283. doi: 10.1007/s11065-017-9354-4.

Marsh, K. L., Johnston, L., Richardson, M. J., & Schmidt, R. C. (2009). Toward aradically embodied, embedded social psychology. *European Journal of Social Psychology*, *39*(7), 1217-1225. doi:10.1002/ejsp.666.

Marsh, K. L., Isenhower, R. W., Richardson, M. J., Helt, M., Verbalis, A. D., Schmidt, R. C., & Fein, D. (2013). Autism and social disconnection in interpersonal rocking. *Frontiers in Integrative Neuroscience, 18*(7), 4. doi:10.3389/fnint.2013.00004

McCarthy, G., Blamire, A.M., Puce, A., Nobre, A.C., Bloch, G., Hyder, F., GoldmanRakic, P., Shulman, R.G. (1994). Magnetic resonance imaging of human prefrontal cortex activation during a spatial working memory task. *Neurobiology, 91*(18), 8690-8694. doi: 10.1073/pnas.91.18.8690.

Meltzo, A. N. (2007). “Infants’ causal learning: intervention, observation, imitation,” in Causal Learning: Psychology, Philosophy, and Computation, eds A. Gopnik and L. Schulz (Oxford: Oxford University Press), 47.

Miller, M., Chukoskie, L., Zinni, M., Townsend, J., & Traunder, D. (2014). Dyspraxia, Motor Function, and Visual-Motor Integration in Autism. *Behavioral Brain Research, 269,* 95-102. doi: 10.1016/j.bbr.2014.04.011

Minshew, N.J., Sung, K.B., Jones, B.L., & Furman, J.M. (2004). Underdevelopment of the postural control system in autism. *Neurology, 63* (11), 2056- 2061. doi:10.1212/01.WNL.0000145771.98657.62

Molenberghs, P., Brander C., Mattingley J. B., & Cunnington, R. (2010). The role of the superior temporal sulcus and the mirror neuron system in imitation. *Human Brain Mapping, 31*(9), 1316–1326. doi: 10.1002/hbm.20938.

Mori, K., Toda, Y., Ito, H., Mori, T., Mori, K., Goji, A., Hashimoto, H., Tani, H., Miyazaki, M., Harada, M., & Kagami, S. (2015). Neuroimaging in autism spectrum disorders: H-MRS and NIRS study. *The Journal of Medical Investigation, 6*2(1), 29-36. doi: 10.2152/jmi.62.29.

Mostofsky, S.H., Powell, S.K., Simmonds, D.J., Goldberg, M.C., Caffo, B., & Pekar, J.J. (2009). Decreased connectivity and cerebellar activity in autism during motor task performance. *Brain, 132*(9), 2413-2425. doi: 10.1093/brain/awp088.

Mottron, L., Burack, J.A., Iarocci, G., Belleville, S., & Enns, J.T. (2003). Locally oriented perception with intact global processing among adolescents with high-functioning autism: evidence from multiple paradigmns. *Journal of Child Psychology and Psychiatry, 44*(6). 904-913.

Mundy, P., & Newell, L. (2007). Attention, Joint Attention, and Social cognition. *Current Directions in Psychological Science*, *16*(5), 269–274. doi:10.1111/j.1467-8721.2007.00518.x

Newman-Norlund, R. D., van Schie, H. T., van Zuijlen, A. M., & Bekkering, H. (2007). The mirror neuron system is more activated during complementary compared with imitative action. *Nat. Neurosci.*, *10,* 817–818. doi: 10.1038/nn1911

Nadel J. (2015). Perception-action coupling and imitation in autism spectrum disorder. *Developmental Medicine and Child Neurology, 57*, 55–58. Doi: 10.1111/dmcn.12689

Nair, A., Treiber, J., Shukla, D., Shih, P., and Müller, R. (2013). Impaired thalamocortical connectivity in autism spectrum disorder: a study of functional and anatomical connectivity. *Brain*, 136(6), 1942-55. PMID: 23739917. PMCID: PMC3673456. http://dx.doi.org/10.1093/brain/awt079.

Newman-Norlund, R. D., van Schie, H. T., van Zuijlen, A. M., & Bekkering, H. (2007). The mirror neuron system is more activated during complementary compared with imitative action. *Natural Neuroscience*, *10,* 817–818. doi: 10.1038/nn1911

Nielsen, J.A., Zielinski, B.A., Fletcher, P.T., Alexander, A.L., Lange, N., Bigler, E.D., Lainhart, J.E., & Anderson, J.S. (2014). Abnormal lateralization of functional connectivity between language and default mode regions in autism. *Molecular Autism*, *5*(8).

Ocampo, B., Kritikos, A., & Cunnington, R. (2011). How frontoparietal brain regions mediate imitative and complementary actions: an fMRI study. *PLoS ONE*, *6*(10). doi:10.1371/journal.pone.0026945

O’Connor, K., & Kirk, I. (2008). Brief Report: Atypical Social Cognition and Social Behaviors in Autism Spectrum Disorder: A Different Way of Processing Rather than an Impairment. *Journal of Autism Developmental Disorder*, *38,* 1989-1997. doi: 10.1007/s10803-008-0559-5.

Okamoto M., Dan H., Sakamoto K., Takeo K., Shimizu K., Kohno S., Isobe, S, Suzuki, T., Kohyama, K., and Dan, I. (2004). Three-dimensional probabilistic anatomical cranio-cerebral correlation via the international 10-20 system oriented for transcranial functional brain mapping. *Neuroimage, 21*(1), 99–111.

Pelphrey, K. A., Mitchell, T. V., Mckeown, M. J., Goldstein, J., Allison, T., & McCarthy G. (2003). Brain activity evoked by the perception of human walking: controlling for meaningful coherent motion. *The Journal of Neuroscience, 23*(17), 6819-6825. doi:10.1523/jneurosci.23-17-06819.2003

Pelphrey, K.A., Shultz, S., Hudac, C.M., & Vander Wyk, B.C. (2012). Constraining Heterogeneity: The Social Brain and its Development in Autism Spectrum Disorder. *Journal of Child Psycholology and Psychiatry, 52*(6), 631-644.

Perkins,T.J., Bittar, R.G., McGillivray, J.A., Cox, I.I., & Stokes, M.A. (2015). Increased premotor cortex activation in high functioning autism during action observation. *Journal of Clinical Neuroscience, 22*(4), 664–669.

Pisella, L. (2015). Visual perception is dependent on visuomotor spatial working memory and thus on the posterior parietal cortex. *Annals of Physical Rehabilitation Medicine*, *60*(3),141-147.

Pisella, L., Mattingley, J.B. (2004). The Contribution of spatial remapping impairments to unilateral visual neglect. *Neuroscience Biobehavior Review*, *28*(2), 181-200.

Rabinowitch, T.C., & Knafo-Noam, A. (2015). Synchronous Rhythmic Interaction Enhanced Children's Perceived Similarity and Closeness Towards Each Other. *PLoS One, 10*(4). doi:10.1371/journal.pone.0120878

Ray, M., & Welsh, T.N (2011). Response Selection during a Joint Action Task. *Journal of Motor Behavior, 43*(4), 329-332. doi: 10.1080/00222895.2011.592871

Richardson, M.J., Marsh, K.L., & Baron, R.M. (2007). Judging and actualizing interpersonal affordances. *Journal of Experimental Psychology: Human Perception & Performance, 33*(4), 845-859. doi:10.1037/0096-1523.33.4.845.

Redcay, E., & Courchesne, E. (2008). Deviant Functional Magnetic Resonance Imaging Patterns of Brain Activity to Speech in 2-3 Year Old Children with Autism Spectrum Disorder. *Biological Psychiatry, 64, 589-598.* doi: 10.1016/j.biopsych.2008.05.020.

Rinehart, N., Bradshaw, J., Moss, S., Brereton, A., & Tonge, B. (2001). A deficit in shifting attention present in high-functioning autism but not Asperger's disorder. *Autism*, 5(1), 67–80.

Rinehart, N.J., Bellgrove, M.A., Tonge, B.J., Brereton, A.V., Howells-Rankin, D., & Bradshaw, J.L. (2006). An Examination of Movement Kinematics in Young People with High-Functioning Autism and Asperger's Disorder: Further Evidence for a Motor Planning Deficit. *Journal of Autism and Developmental Disorders, 36*(6), 757-767. doi:10.1007/s10803-006-0118-x.

Rizzolatti, G., & Fogassi, L. (2014). The mirror mechanism: recent findings and perspectives. *Philosophy Transactions of the Royal Society B Biological Sciences*., 369(1644). doi: 10.1098/rstb.2013.0420.

Robinson, S., Goddard, L., Dritschel, B., Wisley, M., & Howlin, P. (2009). Executive functions in children with Autism Spectrum Disorders. *Brain and Cognition, 71*(3), 362-368.

Rogers, S.J., Hepburn, S.L., Stackhouse, T., Wehner, E. (2003). Imitation performance in toddlers with autism and those with other developmental disorders. *The Journal of Child Psychology and Psychiatry, 44*(5), 763-781.

Rubia, K. (2013). Functional brain imaging across development. *European Child and Adolescent Psychiatry, 22*(12),719-731. doi: 10.1007/s00787-012-0291-8

Rubia, K., Hyde, Z., Halari, R., Giampietro, V., Smith, A. (2010). Effects of age and sex on developmental neural networks of visual–spatial attention allocation. *Neuroimage. 51*(2), 817–827.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S.C., Simmons, A., Andrew, C., & Bullmore, E.T. (2000) Functional frontalisation with age: mapping neurodevelopmental trajectories with fMRI. *Neuroscience and Biobehavior Review, 24*(1), 13–19.

Sacheli, L. M., Tidoni, E., Pavone, E. F., Aglioti, S. M., & Candidi, M. (2013). Kinematic fingerprints of leader and follower role-taking during cooperative joint actions. *Experimental Brain Research, 226*(4), 473-486. doi:10.1007/s00221-013-3459-7.

Sacheli, L. M., Candidi, M., Era, V., & Aglioti, S. M. (2015). Causative role of left aIPS in coding shared goals during human–avatar complementary joint actions. *Nature Communications,6*(1). doi:10.1038/ncomms8544.

Sachse, M., Schlitt, S., Hainz, D., Ciaramidaro, A., Schirman, S., Walter, H., Poustka, F., Bolte, S., & Freitag, C. M. (2013). Executive and Visuo-motor Function in Adolescents and Adults with Autism Spectrum Disorder. *Journal of Autism Developmental Disorder, 43*, 1222-1235. doi :10.1007/s10803-012-1668-8.

Sato, H., Fuchino, Y., Kiguchi, M., Katura, T., Maki, A., Yoro, T., & Koizumi, H. (2005).Intersubject variability of near-infrared spectroscopy signals during sensorimotor cortex activation. *Journal of Biomedical Optics, 10*(4), 44001. doi: 10.1117/1.1960907.

Satta, E., Ferrari-Toniolo, S., Visco-Comandini,F., Caminiti, R., & BattagliaMayer, A. (2017). Development of motor coordination during joint action in mid-childhood. *Neropsychologia, 105*, 111-122.

Scholkmann, F., Kleiser, S., Metz, A.J., Zimmermann, R., Pavia, J.M., Wolf, U., and Wolf, M. (2013). A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology. *NeuroImage, 85,* 6-27.

Sebanz, N., Bekkering, H., & Knoblich, G. (2006). Joint action: bodies and Minds moving together. *Trends in Cognitive Sciences, 10*(2), 70-76. doi: 10.1016/j.tics.2005.12.009

Shattuck D. W., Mirza M., Adisetiyo V., Hojatkashani C., Salamon G., Narr K. L., Poldrack, R.A., Bilder, R.M., & Toga, A.W. (2008). Construction of a 3D probabilistic atlas of human cortical structures. *Neuroimage, 39*(3), 1064–1080. doi: 10.1016/j.neuroimage.2007.09.031.

Shibata, H., Suzuki M., & Gyoba J. (2007). Cortical activity during the recognition of cooperative actions. *Neuroreport*, *18*(7), 697–701. doi: 10.1097/WNR.0b013e3280d94375

Shic, F., Bradshaw, J., Klin, A., Scassellati, B., & Katarzyna, C. (2011). Limited activity monitoring in toddlers with autism spectrum disorder. *Brain Research, 1380,* 246-254.

Shulman G.L., Astafiev, S.V., McAvoy, M.P, d'Avossa, G., & Corbetta, M.(2007). Right TPJ deactivation during visual search: functional significance and support for a filter hypothesis. *Cerebral Cortex*, *17*(11), 2625–2633. doi:10.1093/cercor/bhl170.

Silk, T.J., Rinehart, N., Bradshaw, J.L, Tonge, B., Egan, G, O'Boyle, M.W., & Cunnington, R. (2006). Visuospatial processing and the function of prefrontal-parietal networks in autism spectrum disorders: a functional MRI study. *American Journal of Psychiatry, 163*(8), 1440-1443. doi:10.1176/ajp.2006.163.8.1440.

Sowell, E.R., Peterson, B.S.,Thompson, P.M.,Welcome, S.E., Henkenius, A.L., Toga, A.W. (2003). Mapping cortical change across the human life span. *Natural Neuroscience, 6* (3), 309–315. doi:10.1038/nn1008.

Smith, I., and Bryson, S. (2007). Gesture Imitation in autism: symbolic gestures and pantomimed object use. *Cognitive Neuropsychology*, 24, 679–700. doi: 10.1080/02643290701669703.

Smith, A.B., Halari, R., Giampietro, V., Brammer, M., & Rubia, K. (2011). Developmental effects of reward on sustained attention networks. *Neuroimage, 56*(3),1693–1704. doi: 10.1016/j.neuroimage.2011.01.072.

Sofianidis, G., Hatzitaki, V., Grouios, G., & Johannsen, L., Wing., A. (2012). Somatosensory driven interpersonal synchrony during rhythmic sway. *Human. Movement Science, 31*(3), 553–566. doi: 10.1016/j.humov.2011.07.007.

Sparrow, S.S., Balla, D.A., & Cicchetti DV (1984). Vineland adaptive behavior scales. Circle Pines, MN: American Guidance Service.

Strangman, G., Culver, J.P., Thompson, J.H., & Boas, D.B., 2002. A quantitative comparison of simultaneous BOLD fMRI and NIRS recordings during functional brain activation. *Neuroimage, 17*(2), 719–731.

Stuss, D. T., & Benson, D. F. (1986). *The frontal lobes.* New York: Raven.

Sutoko, S., Sato, H., Maki, A., Kiguchi, M., Hirabayashi, Y., Atsumori, H, Obata, A., Funane, T., & Katura, T. (2016). Tutorial on platform for optical topography analysis tools. *Neurophotonics,3*(1), 010801. doi: 10.1117/1.NPh.3.1.010801.

Tomasello, M., Hamann, K. (2011). Collaboration in young children. *The Quarterly Journal of Experimental Psychology*, *65*(1), 1-12. doi: 10.1080/17470218.2011.608853.

Tunçgenç, B., & Cohen, E. (2016). Interpersonal movement synchrony facilitates pro social behavior in children's play. *Developmental Science, 21*(1).

Turner, K., Frost, L., Linsenbardt, D., McIlroy, J., and Müller, R. (2006). Atypically diffuse functional connectivity between caudate nuclei and cerebral cortex in autism. *Behavior & Brain Function*, 2, 34. PMID: 17042953. PMCID: PMC1635430. http://dx.doi.org/10.1186/1744-9081-2-34.

Tsuzuki D., Cai D.S., Dan, H., Kyutoku, Y., Fujita, A., Watanabe, E., & Dan, I. (2012). Stable and convenient spatial registration of stand-alone NIRS data through anchor-based probabilistic registration. *Neuroscience Research, 72*(2), 163–171. doi: 10.1016/j.neures.2011.10.008

Uddin, L.Q., Supekar, K., & Menon, V. (2010). Typical and atypical development of functionalhuman brain networks: insights from resting-state fMRI. *Frontiers in Neuroscience, 4*(21), 1-12. doi:10.3389/fnsys.2010.0021.

Uratani, M., Ota, T., Lida, J., Okazaki, K., Yamamuro, K., Nakanishi, Y., Kishimoto, N., & Kishimoto, T. (2019). Reduced prefrontal hemodynamic response in pediatric autism spectrum disorder measured with near-infrared spectroscopy. *Child and Adolescent Psychiatry and Mental Health, 13*(29). doi: 10.1186/s13034-019-0289-9.

Vesper, C., Schmitz, L., Safra, L., Sebanz, N., & Knoblich, G. (2016). The role of shared visual information for joint action coordination. *Cognition, 153,* 118-123.

Vicaria, I., & Dickens, L. (2016). Meta-analyses of intra and inter-personal coordination. *Journal of Non-Verbal Behavior*, *40*(4), 335–361. doi: 10.1007/s10919-016-0238-8.

Volkmar F. R., Sparrow S. S., Goudreau D., Cicchetti D. V., Paul R., Cohen D. J. (1987). Social deficits in autism: an operational approach using the vineland adaptive behavior scales. *Journal of the American Academy of Child and Adolescent Psychiatry, 26*, 156–161. 10.1097/00004583-198703000-00005.

Wang, Z., Wang, Y., Sweeney, J.A., Gong, Q., Lui, S., & Mosconi, M.W. (2019). Resting State Brain Network Dysfunctions Associated With Visuomotor Impairments in Autism Spectrum Disorder. *Frontiers in Integrative Neuroscience, 13*(17). doi: 10.3389/fnint.2019.00017

White, T.P., Jansen, M., Doege, K., Mullinger, K., Bert-Park, S., Liddle, E.,Gowland, P.A., Francis, S.T., Bowtell, R., & Liddle, P.F. (2012). Theta power during encoding predicts subsequent-memory performance and default mode network deactivation. *Human Brain Mapping, 34*(11), 2929-2943. doi: 10.1002/hbm.22114.

Whyatt, C., & Craig, C. (2013). Sensory-motor problems in Autism. *Frontiers in Integrative Neuroscience, 7*(51), doi: 10.3389/fnint.2013.00051.

Wiltermuth, S. S., & Heath, C. (2009). Synchrony and Cooperation. *Psychological Science, 20*(1), 1–5. doi: 10.1111/j.1467-9280.2008.02253.x

Willats, P., & Rosie, K. (1989). Planning by 12-Month-Old Infants. *Society for Research in Child Development,* 18-24.

Wiltermuth, S. S., & Heath, C. (2009). Synchrony and cooperation. Psychological Science, 20(1), 1–5. doi:10.1111/j.1467-9280.2008.02253.

Wolff, P.H., Gunnoe, C.E., Cohen, C. (1983) Associated movements as a measure of Developmental age. *Developmental and Medical Child Neurology*, *25*(4), 417–429.

Wolf, M., Wolf, U., Tornov, V., Michalos, A., Paunescu, L.A., Choi, J.H., & Gratton, E. (2002). Different Time Evolution of Oxyhemoglobin and Deoxyhemoglobin Concentration Changes in the Visual and Motor Cortices During Functional Stimulation: A Near-Infrared Spectroscopy Study. *NeuroImage, 16*, 704-712. doi: 10.1006/nimg.2002.1128.

Yang, J., Hofmann, J. (2015). Action observation and imitation in autism spectrum disorders: an ALE meta-analysis of fMRI studies. *Brain Imaging and Behavior, 10*(4), 960-969. doi: 10.1007/s11682-015-9456-7.

Zilbovicius, M., Boddaert, N., Belin, P., Poline, J.B., & Remy, P. (2000) Temporal lobe dysfunction in childhood autism: A PET study. Positron emission tomogram. *American Journal of Psychiatry, 157*, 1988-1993. doi:10.1176/appi.ajp.157.12.1988.

# Appendix A

## TABLES USED IN THESIS

Table A.1 Demographics of Younger and Older Children

| Characteristics | Older (n=10) | Younger (n=7) |
|---|---|---|
| Age | 14.22 ± 0.78* | 7.89± 0.79 |
| Sex | 5M, 5F | 4M, 3F |
| Ethnicity | 9C, 1 A* | 5C, 1Af, 1A |
| Handedness | 9R, 1L | 7R, 0L |
| VABS-II (SS)<br>Communication (SS)<br>Socialization (SS)<br>Daily Living (SS) | 65.98±8.8<br>62.07±7.77<br>78.89±5.24<br>75.27±7.0 | 71.11±8.1<br>73.89±4.8<br>75.51±8.44<br>67.44±10.37 |
| BOT II MD | 20.03±1.27* | 28.8±1.07 |

Table A.2 Spatial Registration Output of Children with ASD and TD Children

| Right Ch. #s | MNI coordinates | | | Superior Frontal Gyrus | Middle Frontal Gyrus | Inferior Frontal Gyrus | Orbito Frontal Gyrus | Pre-Central Gyrus | Post-Central Gyrus | Angular Gyrus | Supra marginal Gyrus | Temporal Gyri | | | Ch. Assignt. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | X | Y | Z | | | | | | | | | Superior | Middle | Inferior | |
| 1 | 67 | -29 | 45 | | | | | | | .01 | .99 | | | | IPL |
| 2 | 62.67 | -1.67 | 41.67 | | | | | .42 | .52 | | .06 | | | | PCG |
| 3 | 51 | 25.67 | 41.67 | | .95 | .05 | | | | | | | | | MFG |
| 4 | 33.67 | 46.67 | 40.67 | | 1 | | | | | | | | | | MFG |
| 5 | 12.33 | 57.33 | 41.67 | .58 | .42 | | | | | | | | | | Exclude |
| 11 | 68 | -40.33 | 35.33 | | | | | | | .38 | .62 | | | | IPL |
| 12 | 69 | -12.33 | 31.67 | | | | | | .55 | | .45 | | | | Exclude |
| 13 | 60 | 16.67 | 28.67 | | .03 | .31 | | .66 | | | | | | | PCG |
| 14 | 46.67 | 44.67 | 28.67 | | .8 | .2 | | | | | | | | | MFG |
| 15 | 25.33 | 61.67 | 29.33 | | 1 | | | | | | | | | | MFG |
| 16 | .33 | 63.33 | 28.67 | .6 | | | | | | | | | | | Exclude |
| 22 | 71 | -26.33 | 21.33 | | | | | | .01 | .06 | .45 | .48 | | | Exclude |
| 23 | 67 | 4.67 | 19.67 | | | .01 | | .55 | .44 | | | | | | PCG |
| 24 | 56.33 | 36.67 | 17.67 | | .01 | .99 | | | | | | | | | IFG |
| 25 | 39.33 | 59.67 | 17.67 | | .91 | .09 | | | | | | | | | MFG |
| 26 | 14.67 | 71 | 19.33 | .25 | .75 | | | | | | | | | | Exclude |
| 32 | 72 | -39.33 | 6.67 | | | | | | | | | .34 | .67 | | STS |
| 33 | 71 | -10.33 | 4.67 | | | | | | .13 | | | .84 | .03 | | STS |
| 34 | 60.67 | 25.67 | 6.67 | | | .83 | | .17 | | | | | | | IFG |
| 35 | 49.33 | 52.67 | 4.33 | | .06 | .94 | | | | | | | | | IFG |
| 36 | 28 | 69.67 | 5 | | .99 | .01 | | | | | | | | | MFG |
| 43 | 73 | -22.67 | -8.67 | | | | | | | | | .03 | .98 | | STS |
| 44 | 64.33 | 5.67 | -10.33 | | | | | | | | | .54 | .46 | | STS |
| 45 | 54.67 | 42.67 | -7.33 | | | .66 | .34 | | | | | | | | IFG |
| 46 | 39.33 | 63.67 | -7.67 | | .27 | .46 | .27 | | | | | | | | IFG |
| 47 | 14.67 | 72.67 | -7.33 | .23 | .67 | | .11 | | | | | | | | Exclude |

| Left Ch. #s | MNI coordinates | | | Superior Frontal Gyrus | Middle Frontal Gyrus | Inferior Frontal Gyrus | Orbito Frontal Gyrus | Pre-Central Gyrus | Post-Central Gyrus | Angular Gyrus | Supra marginal Gyrus | Temporal Gyri | | | Channel Assignt. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | X | Y | Z | | | | | | | | | Superior | Middle | Inferior | |
| 6 | -12.67 | 55.67 | 42.67 | .71 | .29 | | | | | | | | | | Exclude |
| 7 | -34.33 | 41.33 | 42.33 | .04 | .96 | | | | | | | | | | MFG |
| 8 | -50.67 | 18.67 | 43.33 | | .91 | | | .09 | | | | | | | MFG |
| 9 | -60 | -7.67 | 44.33 | | | | | .40 | .6 | | | | | | PCG |
| 10 | -64 | -34.33 | 46.33 | | | | | | | | 1 | | | | IPL |
| 17 | -27.33 | 57.33 | 29.67 | .008 | .99 | | | | | | | | | | MFG |
| 18 | -48 | 37.33 | 30.33 | | .99 | .004 | | | | | | | | | MFG |
| 19 | -60.33 | 9.67 | 31.33 | | .08 | .09 | | .82 | .007 | | | | | | PCG |
| 20 | -67 | -19.67 | 33.33 | | | | | | .27 | | .74 | | | | Exclude |
| 21 | -65 | -46.33 | 36.67 | | | | | | | .33 | .67 | | | | IPL |
| 27 | -16.67 | 70 | 18.67 | .40 | .6 | | | | | | | | | | Exclude |
| 28 | -41.67 | 54.67 | 18.67 | | .99 | .01 | | | | | | | | | MFG |
| 29 | -57 | 27.67 | 18.67 | | .06 | .94 | | | | | | | | | IFG |
| 30 | -66 | -3 | 21 | | | | | .35 | .65 | | .006 | | | | PCG |
| 31 | -69 | -33.33 | 22.67 | | | | | | .003 | | .5 | .49 | | | Exclude |
| 37 | -2.67 | 70.667 | 5.67 | .70 | .01 | | | | | | | | | | Exclude |
| 38 | -29.33 | 67 | 4.67 | | .99 | .007 | | | | | | | | | MFG |
| 39 | -51 | 45.33 | 4.33 | | .02 | .98 | | | | | | | | | IFG |
| 40 | -59.67 | 15.33 | 7.33 | | | .67 | | .33 | | | | .003 | | | IFG |
| 41 | -69 | -17.33 | 6.67 | | | | | | .15 | | | .7 | .15 | | STS |
| 42 | -69 | -45.67 | 9.33 | | | | | | | | .003 | .48 | .52 | | STS |
| 48 | -15.33 | 71.33 | -7.67 | .56 | .34 | | .104 | | | | | | | | Exclude |
| 49 | -40.67 | 59.33 | -8.33 | | .16 | .49 | .32 | | | | | | | | IFG |
| 50 | -54 | 34.33 | -6.667 | | | .55 | .42 | | | | | .04 | | | IFG |
| 51 | -65 | -1.33 | -9.33 | | | | | | | | | .53 | .47 | | STS |
| 52 | -71 | -29.67 | -7.33 | | | | | | | | | | .99 | 0.01 | STS |

Table A.3 Behavioral Errors in Younger and Older Children

| Video Coding Variables | Younger Child | Older Child |
|---|---|---|
| Motor Error | 0 .6±0.3* | 0.1±0.1 |
| Planning Error | 6±1.6* | 0.8±0.5 |
| Spatial Error | 3.7±0.6* | 1.8±0.6 |

Table A.4 Correlations between Cortical Activation and Age in TD children

| Hemisphere | Region | Coincide | Lead | Follow | Turn-Take |
|---|---|---|---|---|---|
| Left | MFG | 0.37** | 0.48*** | 0.48*** | 0.42*** |
| | PCG | 0.17 | 0.18 | 0.34** | 0.23 |
| | IFG | 0.52*** | 0.55*** | 0.64**** | 0.50*** |
| | STS | 0.36** | 0.19 | 0.37** | 0.38** |
| | IPL | -0.2 | -0.25 | -0.13 | -0.07 |
| Right | MFG | 0.51*** | 0.55*** | 0.44*** | 0.49*** |
| | PCG | 0.1 | 0.36** | 0.43** | 0.1 |
| | IFG | 0.39** | 0.30* | 0.44*** | 0.25* |
| | STS | 0.29* | 0.61*** | 0.22 | 0.23* |
| | IPL | 0.02 | -0.08 | 0.046 | 0.22 |

Table A.5 Group Activation Mean and SE (a) and results post-hoc comparison (b)

a.

| Group Activation Data | Coincide | | Lead | | Follow | | Turn-Take | |
|---|---|---|---|---|---|---|---|---|
| | **Mean** | **SE** | **Mean** | **SE** | **Mean** | **SE** | **Mean** | **SE** |
| **TD Younger Child** | | | | | | | | |
| *Left Hemisphere* | | | | | | | | |
| MFG | 0.027 | 0.011 | 0.004 | 0.009 | 0.013 | 0.012 | 0.029 | 0.013 |
| PCG | 0.056 | 0.015 | 0.043 | 0.014 | 0.039 | 0.019 | 0.041 | 0.016 |
| IFG | 0.036 | 0.016 | 0.03 | 0.014 | 0.001 | 0.012 | 0.029 | 0.017 |
| STS | 0.082 | 0.015 | 0.085 | 0.016 | 0.048 | 0.017 | 0.064 | 0.01 |
| IPL | 0.027 | 0.021 | 0.007 | 0.016 | 0.03 | 0.023 | -0.024 | 0.016 |
| *Right Hemisphere* | | | | | | | | |
| MFG | 0.027 | 0.009 | 0.026 | 0.01 | 0.016 | 0.013 | 0.026 | 0.011 |
| PCG | 0.053 | 0.016 | 0.019 | 0.014 | -0.008 | 0.014 | 30 | 0.014 |
| IFG | 0.04 | 0.012 | 0.07 | 0.015 | 0.019 | 0.013 | 0.056 | 0.017 |
| STS | 0.06 | 0.016 | 0.032 | 0.013 | 0.043 | 0.015 | 0.09 | 0.015 |
| IPL | 0.023 | 0.014 | 0.044 | 0.013 | 0.019 | 0.018 | 0.013 | 0.012 |
| **TD Older Child** | | | | | | | | |
| *Left Hemisphere* | | | | | | | | |
| MFG | 0.046 | 0.012 | 0.05 | 0.013 | 0.051 | 0.014 | 0.054 | 0.014 |
| PCG | 0.054 | 0.012 | 0.037 | 0.011 | 0.058 | 0.013 | 0.068 | 0.015 |
| IFG | 0.09 | 0.015 | 0.087 | 0.015 | 0.1 | 0.018 | 0.105 | 0.017 |
| STS | 0.099 | 0.015 | 0.064 | 0.016 | 0.087 | 0.019 | 0.11 | 0.015 |
| IPL | -0.002 | 0.013 | -0.041 | 0.008 | -0.019 | 0.01 | -0.045 | 0.009 |
| *Right Hemisphere* | | | | | | | | |
| MFG | 0.065 | 0.009 | 0.068 | 0.011 | 0.062 | 0.011 | 0.069 | 0.011 |
| PCG | 0.029 | 0.012 | 0.023 | 0.011 | 0.022 | 0.016 | 0.023 | 0.012 |
| IFG | 0.07 | 0.016 | 0.083 | 0.014 | 0.081 | 0.017 | 0.076 | 0.017 |
| STS | 0.103 | 0.015 | 0.065 | 0.02 | 0.056 | 0.017 | 0.111 | 0.019 |
| IPL | 0.027 | 0.011 | 0.03 | 0.016 | 0.023 | 0.016 | 0.033 | 0.016 |

b.

| **Comparison** | **Significant p-values** | **Direction of effect** |
|---|---|---|
| **Group Differences** | | |
| **Left IFG** | | |
| Lead | 0.008 | Older>Younger |
| Coincide | 0.017 | Older>Younger |
| Follow | <.001 | Older>Younger |
| Turn-Take | 0.002 | Older>Younger |
| **Right MFG** | | |
| Lead | 0.008 | Older>Younger |
| Coincide | 0.005 | Older>Younger |
| Follow | 0.01 | Older>Younger |
| Turn-Take | 0.008 | Older>Younger |
| **Left MFG** | | |
| Lead | 0.003 | Older>Younger |
| **Hemispheric Differences** | | |
| *hemisphere x region x age (pooled by group & condition)* | | |
| PCG | <.001 | Left>Right |
| IPL | <.0001 | Right>Left |
| **Task-Related Differences** | | |
| *Condition x hemisphere x region (pooled by age)* | | |
| **Lead Left IPL** | | |
| Coincide vs Lead | 0.0096 | Coincide>Lead |
| Lead vs Follow | .054 (trend) | Follow>Lead |
| Follow vs Turn-Take | <.001 | Follow> Turn-Take |
| Coincide vs Turn-Take | <.001 | Coincide>Turn-Take |
| **Lead Right STS** | | |
| Coincide vs Lead | 0.004 | Coincide>Lead |
| Follow vs Turn-Take | <.001 | Turn-Take>Follow |
| Lead vs Turn-Take | <.001 | Turn-Take>Lead |
| Coincide vs Follow | 0.0016 | Coincide>Follow |

Table A.6 Correlations between Activation and VABS and Activation and BOT in Younger and Older Children (**indicates p<.05, ** indicates p< 0.01, ***indicates p< 0.001, Red font indicates moderate correlations above 0.5*)

| | | BOT Older | BOT Younger | VAB Older | VABS Younger |
|---|---|---|---|---|---|
| **Lead** | Left MFG | 0.075 | .645** | 0.325 | 0.18 |
| | Left PCG | -0.112 | 0.302 | 0.175 | 0.251 |
| | Left IFG | 0.229 | .524** | 0.09 | 0.374 |
| | Left STS | 0.127 | 0.261 | .353* | 0.299 |
| | Left IPL | -0.192 | 0.301 | -0.11 | 0.151 |
| | Right MFG | 0.18 | .601** | 0.33 | 0.012 |
| | Right PCG | -0.013 | .609** | 0.254 | -0.018 |
| | Right IFG | 0.258 | 0.39 | 0.317 | 0.318 |
| | Right STS | .369* | .591** | .380* | 0.189 |
| | Right IPL | -0.016 | 0.345 | -0.11 | -.44* |
| **Coincide** | Left MFG | 0.148 | 0.068 | 0.102 | .478* |
| | Left PCG | -0.22 | .560** | 0.169 | 0.174 |
| | Left IFG | 0.186 | 0.29 | 0.153 | 0.423 |
| | Left STS | -0.173 | .571** | 0.067 | .435* |
| | Left IPL | -0.149 | 0.09 | 0.031 | -0.13 |
| | Right MFG | 0.174 | .444* | 0.166 | 0.278 |
| | Right PCG | 0.152 | 0.042 | 0.224 | 0.123 |
| | Right IFG | 0.194 | .521** | .424* | 0.16 |
| | Right STS | 0.073 | .581** | 0.236 | 0.028 |
| | Right IPL | 0.057 | -0.04 | -0.15 | 0.15 |
| Follow | Left MFG | 0.034 | 0.321 | .450** | 0.392 |
| | Left PCG | -0.067 | .586** | 0.314 | 0.082 |
| | Left IFG | 0.169 | .412* | 0.313 | .515* |
| | Left STS | -0.041 | 0.291 | .458** | 0.278 |
| | Left IPL | -0.12 | 0.16 | 0.241 | -0.225 |
| | Right MFG | 0.247 | 0.27 | .541** | 0.326 |
| | Right PCG | 0.214 | .834*** | 0.299 | 0.258 |
| | Right IFG | 0.107 | 0.233 | 0.332 | .586** |
| | Right STS | .323* | 0.267 | .396* | 0.138 |
| | Right IPL | -0.132 | -0.081 | 0.036 | -0.21 |
| **Joint** | Left MFG | 0.119 | 0.248 | 0.277 | 0.252 |
| | Left PCG | -0.223 | .399* | 0.147 | 0.037 |
| | Left IFG | 0.092 | 0.292 | 0.0588 | 0.085 |
| | Left STS | -0.262 | 0.179 | .446** | 0.252 |
| | Left IPL | 0.02 | -0.133 | 0.116 | -0.025 |
| | Right MFG | 0.194 | 0.138 | 0.31 | 0.227 |
| | Right PCG | -0.12 | 0.137 | 0.112 | 0.313 |
| | Right IFG | 0.105 | -0.373 | 0.192 | 0.094 |
| | Right STS | -0.112 | 0.333 | .429* | -0.258 |
| | Right IPL | 0.117 | -0.105 | 0.159 | -0.058 |

Table A.7 Correlations between Activation and Behavior in Younger and Older Children (**indicates p<0.05, **indicates p< 0.01, ***indicates p<0.001)*

| | | TD Older | | | TD Younger | | |
|---|---|---|---|---|---|---|---|
| | | Motor | Planning | Spatial | Motor | Planning | Spatial |
| Lead | Left MFG | - | - | - | - | −0.402* | −0.524** |
| | Left PSA | - | - | - | - | -0.063 | -0.127 |
| | Left IFG | - | - | - | - | −0.472* | -0.257 |
| | Left STS | - | - | - | - | −0.511** | -0.27 |
| | Left IPL | - | - | - | - | -0.089 | -0.243 |
| | Right MFG | - | - | - | - | -0.049 | 0.035 |
| | Right PSA | - | - | - | - | 0.118 | 0.06 |
| | Right IFG | - | - | - | - | 0.079 | -0.085 |
| | Right STS | - | - | - | - | -0.19 | -0.39 |
| | Right IPL | - | - | - | - | 0.094 | 0.289 |
| Coincide | Left MFG | - | -0.165 | - | -0.265 | -0.289 | -0.345 |
| | Left PSA | - | -0.079 | - | -0.15 | -0.329 | -0.287 |
| | Left IFG | - | -0.238 | - | 0.007 | -0.08 | -0.099 |
| | Left STS | - | 0.05 | - | -0.136 | -0.157 | -0.169 |
| | Left IPL | - | 0.01 | - | 0.093 | -0.178 | -0.105 |
| | Right MFG | - | -0.148 | - | 0.05 | -0.222 | -0.297 |
| | Right PSA | - | -0.09 | - | -0.122 | 0.172 | -0.017 |
| | Right IFG | - | -0.025 | - | 0.021 | 0.032 | 0.128 |
| | Right STS | - | 0.163 | - | -0.064 | −0.42* | -0.343 |
| | Right IPL | - | 0.071 | - | -0.172 | -0.288 | -0.245 |
| Follow | Left MFG | -0.187 | - | 0.147 | - | -0.312 | -0.328 |
| | Left PSA | -0.135 | - | -0.12 | - | -0.263 | -0.235 |
| | Left IFG | -0.217 | - | -0.022 | - | -0.204 | −0.453* |
| | Left STS | -0.097 | - | 0.098 | - | 0.132 | -0.232 |
| | Left IPL | -0.25 | - | 0.169 | - | -0.022 | 0.023 |
| | Right MFG | -0.0075 | - | -0.218 | - | -0.307 | −0.369 |
| | Right PSA | -0.24 | - | -0.104 | - | -0.107 | −0.573** |
| | Right IFG | -0.187 | - | -0.065 | - | -0.233 | −0.613** |
| | Right STS | -0.0075 | - | -0.305 | - | -0.1112 | -0.144 |
| | Right IPL | 0.113 | - | -0.142 | - | 0.065 | 0.005 |
| Turn-Take | Left MFG | - | 0.083 | 0.068 | -0.298 | -0.13 | 0.209 |
| | Left PSA | - | 0.098 | 0.249 | -0.25 | -0.193 | 0.241 |
| | Left IFG | - | 0.097 | 0.095 | -0.203 | 0.067 | 0.097 |
| | Left STS | - | -0.053 | 0.005 | 0.083 | -0.218 | 0.002 |
| | Left IPL | - | 0.247 | -0.035 | -0.012 | -0.137 | 0.132 |
| | Right MFG | - | 0.217 | 0.053 | -0.203 | 0.101 | 0.086 |
| | Right PSA | - | 0.172 | -0.052 | -0.012 | 0.045 | -0.046 |
| | Right IFG | - | 0.038 | -0.104 | -0.06 | 0.356 | -0.127 |
| | Right STS | - | 0.068 | -0.103 | -0.084 | 0.405* | 0.128 |
| | Right IPL | - | 0.127 | -0.186 | -0.251 | 0.214 | -0.056 |

Table A.8 Demographics of Children with and without ASD (*indicates significant difference between groups, SS=Standard Score; SE=Standard Error, M=Male, F=Female, C=Caucasian, A=Asian, Af=African-American, R=Right, L=Left, BOT II=Bruininks-Oseretsky Test of Motor Proficiency-2, VABS-II=Vineland Adaptive Behavioral Scale-2nd edition)*

| Characteristics | TD (n=15) | ASD (n=15) |
|---|---|---|
| | Mean ± SE | Mean ± SE |
| Age | 12.2 ± 0.9* | 11.5± 0.8 |
| Sex | 8M, 7F | 12M, 3F |
| Ethnicity | 12C, 2 A, 1 Af | 11C, 2A, 2Af |
| Handedness | 14R, 1L | 13R, 2L |
| VABS-II (SS) | 67.7±6.0* | 4.2±1.3 |
| Communication (SS) | 65.8±5.7* | 4.6±1.3 |
| Socialization (SS) | 77.4±4.1* | 4.8±1.8 |
| Daily Living (SS) | 74.8±5.8* | 8.7±3.4 |
| BOT MD raw | 26.3±1.5* | 21.4±1.9 |
| SRS Total T-score | NA | 79±2.1 |

Table A.9 Spatial Registration Output of Children with ASD and TD Children

| Left Ch. #s | MNI coordinates | | | Superior Frontal Gyrus | Middle Frontal Gyrus | Inferior Frontal Gyrus | Orbito Frontal Gyrus | Pre-Central Gyrus | Post-Central Gyrus | Angular Gyrus | Supra marginal Gyrus | Temporal Gyri | | | Channel Assignt. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | X | Y | Z | | | | | | | | | Superior | Middle | Inferior | |
| 6 | -12.67 | 55.67 | 42.67 | .71 | .29 | | | | | | | | | | Exclude |
| 7 | -34.33 | 41.33 | 42.33 | .04 | .96 | | | | | | | | | | MFG |
| 8 | -50.67 | 18.67 | 43.33 | | .91 | | | .09 | | | | | | | MFG |
| 9 | -60 | -7.67 | 44.33 | | | | | .40 | .6 | | | | | | PCG |
| 10 | -64 | -34.33 | 46.33 | | | | | | | | 1 | | | | IPL |
| 17 | -27.33 | 57.33 | 29.67 | .008 | .99 | | | | | | | | | | MFG |
| 18 | -48 | 37.33 | 30.33 | | .99 | .004 | | | | | | | | | MFG |
| 19 | -60.33 | 9.67 | 31.33 | | .08 | .09 | | .82 | .007 | | | | | | PCG |
| 20 | -67 | -19.67 | 33.33 | | | | | | .27 | | .74 | | | | Exclude |
| 21 | -65 | -46.33 | 36.67 | | | | | | | .33 | .67 | | | | IPL |
| 27 | -16.67 | 70 | 18.67 | .40 | .6 | | | | | | | | | | Exclude |
| 28 | -41.67 | 54.67 | 18.67 | | .99 | .01 | | | | | | | | | MFG |
| 29 | -57 | 27.67 | 18.67 | | .06 | .94 | | | | | | | | | IFG |
| 30 | -66 | -3 | 21 | | | | | .35 | .65 | | .006 | | | | PCG |
| 31 | -69 | -33.33 | 22.67 | | | | | | .003 | | .5 | .49 | | | Exclude |
| 37 | -2.67 | 70.667 | 5.67 | .70 | .01 | | | | | | | | | | Exclude |
| 38 | -29.33 | 67 | 4.67 | | .99 | .007 | | | | | | | | | MFG |
| 39 | -51 | 45.33 | 4.33 | | .02 | .98 | | | | | | | | | IFG |
| 40 | -59.67 | 15.33 | 7.33 | | | .67 | | .33 | | | | .003 | | | IFG |
| 41 | -69 | -17.33 | 6.67 | | | | | | .15 | | | .7 | .15 | | STS |
| 42 | -69 | -45.67 | 9.33 | | | | | | | | .003 | .48 | .52 | | STS |
| 48 | -15.33 | 71.33 | -7.67 | .56 | .34 | | .104 | | | | | | | | Exclude |
| 49 | -40.67 | 59.33 | -8.33 | | .16 | .49 | .32 | | | | | | | | IFG |
| 50 | -54 | 34.33 | -6.667 | | | .55 | .42 | | | | | .04 | | | IFG |
| 51 | -65 | -1.33 | -9.33 | | | | | | | | | .53 | .47 | | STS |
| 52 | -71 | -29.67 | -7.33 | | | | | | | | | | .99 | 0.01 | STS |

| Right Ch. #s | MNI coordinates | | | Superior Frontal Gyrus | Middle Frontal Gyrus | Inferior Frontal Gyrus | Orbito Frontal Gyrus | Pre-Central Gyrus | Post-Central Gyrus | Angular Gyrus | Supra marginal Gyrus | Temporal Gyri | | | Ch. Assignt. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | X | Y | Z | | | | | | | | | Superior | Middle | Inferior | |
| 1 | 67 | -29 | 45 | | | | | | | .01 | .99 | | | | IPL |
| 2 | 62.67 | -1.67 | 41.67 | | | | | .42 | .52 | | .06 | | | | PCG |
| 3 | 51 | 25.67 | 41.67 | | .95 | .05 | | | | | | | | | MFG |
| 4 | 33.67 | 46.67 | 40.67 | | 1 | | | | | | | | | | MFG |
| 5 | 12.33 | 57.33 | 41.67 | .58 | .42 | | | | | | | | | | Exclude |
| 11 | 68 | -40.33 | 35.33 | | | | | | | .38 | .62 | | | | IPL |
| 12 | 69 | -12.33 | 31.67 | | | | | | .55 | | .45 | | | | Exclude |
| 13 | 60 | 16.67 | 28.67 | | .03 | .31 | | .66 | | | | | | | PCG |
| 14 | 46.67 | 44.67 | 28.67 | | .8 | .2 | | | | | | | | | MFG |
| 15 | 25.33 | 61.67 | 29.33 | | 1 | | | | | | | | | | MFG |
| 16 | .33 | 63.33 | 28.67 | .6 | | | | | | | | | | | Exclude |
| 22 | 71 | -26.33 | 21.33 | | | | | | .01 | .06 | .45 | .48 | | | Exclude |
| 23 | 67 | 4.67 | 19.67 | | | .01 | | .55 | .44 | | | | | | PCG |
| 24 | 56.33 | 36.67 | 17.67 | | .01 | .99 | | | | | | | | | IFG |
| 25 | 39.33 | 59.67 | 17.67 | | .91 | .09 | | | | | | | | | MFG |
| 26 | 14.67 | 71 | 19.33 | .25 | .75 | | | | | | | | | | Exclude |
| 32 | 72 | -39.33 | 6.67 | | | | | | | | | .34 | .67 | | STS |
| 33 | 71 | -10.33 | 4.67 | | | | | | .13 | | | .84 | .03 | | STS |
| 34 | 60.67 | 25.67 | 6.67 | | | .83 | | .17 | | | | | | | IFG |
| 35 | 49.33 | 52.67 | 4.33 | | .06 | .94 | | | | | | | | | IFG |
| 36 | 28 | 69.67 | 5 | | .99 | .01 | | | | | | | | | MFG |
| 43 | 73 | -22.67 | -8.67 | | | | | | | | | .03 | .98 | | STS |
| 44 | 64.33 | 5.67 | -10.33 | | | | | | | | | .54 | .46 | | STS |
| 45 | 54.67 | 42.67 | -7.33 | | | .66 | .34 | | | | | | | | IFG |
| 46 | 39.33 | 63.67 | -7.67 | | .27 | .46 | .27 | | | | | | | | IFG |
| 47 | 14.67 | 72.67 | -7.33 | .23 | .67 | | .11 | | | | | | | | Exclude |

Table A.10 Behavioral Errors in children with ASD and TD Children (*indicates *statistical significance*)

| Video Coding Variables | TD (Mean ± SE) | ASD (Mean ± SE) |
|---|---|---|
| Motor Error | 0.3±0.2* | 0.8±0.2 |
| Planning Error | 2.3±0.7* | 6.5±0.39 |
| Spatial Error | 2.4±.5* | 5±1 |

Table A.11 Group Activation Mean and SE (a) and results post-hoc comparison (b)

a.

| Group Activation Data | Coincide | | Lead | | Follow | | Turn-Take | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE |
| **TD Children** | | | | | | | | |
| *Left Hemisphere* | | | | | | | | |
| Middle Frontal Gyrus | 0.043 | 0.009 | 0.041 | 0.009 | 0.041 | 0.011 | 0.047 | 0.01 |
| Pre/Post Central Gyrus | 0.062 | 0.01 | 0.04 | 0.009 | 0.054 | 0.012 | 0.062 | 0.012 |
| Inferior Frontal Gyrus | 0.077 | 0.012 | 0.073 | 0.012 | 0.071 | 0.014 | 0.078 | 0.014 |
| Superior Temporal Sulcus | 0.104 | 0.011 | 0.074 | 0.012 | 0.075 | 0.014 | 0.099 | 0.012 |
| Inferior Parietal Lobule | 0.004 | 0.011 | -0.023 | 0.009 | -0.012 | 0.011 | -0.043 | 0.008 |
| *Right Hemisphere* | | | | | | | | |
| Middle Frontal Gyrus | 0.057 | 0.007 | 0.055 | 0.009 | 0.05 | 0.009 | 0.055 | 0.009 |
| Pre/Post Central Gyrus | 0.035 | 0.01 | 0.025 | 0.009 | 0.021 | 0.011 | 0.032 | 0.01 |
| Inferior Frontal Gyrus | 0.063 | 0.012 | 0.081 | 0.011 | 0.067 | 0.012 | 0.063 | 0.013 |
| Superior Temporal Sulcus | 0.096 | 0.011 | 0.06 | 0.014 | 0.052 | 0.013 | 0.1 | 0.014 |
| Inferior Parietal Lobule | 0.022 | 0.009 | 0.029 | 0.012 | 0.016 | 0.012 | 0.091 | 0.011 |
| **ASD Children** | | | | | | | | |
| *Left Hemisphere* | | | | | | | | |
| Middle Frontal Gyrus | 0.043 | 0.009 | 0.05 | 0.006 | 0.05 | 0.009 | 0.031 | 0.008 |
| Pre/Post Central Gyrus | 0.046 | 0.013 | 0.054 | 0.01 | 0.05 | 0.012 | 0.055 | 0.009 |
| Inferior Frontal Gyrus | 0.076 | 0.011 | 0.057 | 0.012 | 0.08 | 0.012 | 0.052 | 0.01 |
| Superior Temporal Sulcus | 0.044 | 0.013 | 0.047 | 0.01 | 0.031 | 0.01 | 0.023 | 0.0125 |
| Inferior Parietal Lobule | 0.005 | 0.01 | 0.059 | 0.009 | 0.012 | 0.009 | 0.007 | 0.007 |
| *Right Hemisphere* | | | | | | | | |
| Middle Frontal Gyrus | 0.042 | 0.009 | 0.063 | 0.008 | 0.037 | 0.007 | 0.047 | 0.008 |
| Pre/Post Central Gyrus | 0.046 | 0.009 | 0.035 | 0.012 | 0.037 | 0.012 | 0.062 | 0.012 |
| Inferior Frontal Gyrus | 0.062 | 0.01 | 0.06 | 0.008 | 0.07 | 0.012 | 0.042 | 0.01 |
| Superior Temporal Sulcus | 0.071 | 0.013 | 0.07 | 0.01 | 0.061 | 0.011 | 0.048 | 0.01 |
| Inferior Parietal Lobule | 0.06 | 0.014 | 0.036 | 0.012 | 0.008 | 0.012 | 0.023 | 0.009 |

b.

| Comparison | Sig. p-values | Direction of effect |
|---|---|---|
| **Group Differences** | | |
| **Left STS** | | |
| Turn-Take | <0.001 | TD>ASD |
| Coincide | 0.001 | TD>ASD |
| **Left IPL** | | |
| Lead | <0.001 | ASD>TD |
| Turn-Take | <0.001 | ASD>TD |
| **Right STS** | | |
| Turn-Take | 0.003 | TD>ASD |
| **Hemispheric Differences** | | |
| ***Condition x hemisphere x region x group*** | | |
| **TD Children** | | |
| Coincide PCG | 0.011 | Left>Right |
| Lead PCG | 0.006 | Left>Right |
| Lead IPL | <0.001 | Right>Left |
| Turn-Take IPL | <0.001 | Right>Left |
| **ASD Children** | | |
| Coincide IPL | <0.001 | Right>Left |
| Follow STS | 0.007 | Right>Left |
| **Task-Related Differences** | | |
| ***Condition x hemisphere x region x group*** | | |
| **TD** | | |
| Right STS CvsL | 0.004 | Coincide>Lead |
| Right STS CvsF | 0.0002 | Coincide>Follow |
| Right STS FvsT-T | 0.003 | Follow>Turn-Take |
| Left IPL CvsT-T | 0.002 | Coincide>Turn-Take |
| Left IPL FvsT-T | 0.008 | Follow>Turn-Take |
| **ASD** | | |
| Left IPL LvsC,F,T-T | <0.001 | Lead>Coincide, Follow, Turn-Take |
| Right IPL CvsF | <0.001 | Coincide>Follow |
| Right IPL LvsF | <0.001 | Lead>Follow |
| Right MFG LvsF | 0.003 | Lead>Follow |

Table A.12 Correlations between Activation and Behavioral Error in TD Children and Children with ASD (*indicates $p<0.05$, ** indicates $p< 0.01$, *** indicates $p<0.001$)

| | | **TD** | | | **ASD** | | |
|---|---|---|---|---|---|---|---|
| | | **Motor** | **Planning** | **Spatial** | **Motor** | **Planning** | **Spatial** |
| **Lead** | **Left MFG** | - | -0.112 | 0.083 | 0.149 | 0.098 | 0.146 |
| | **Left PCG** | - | -0.09 | 0.1 | 0.012 | 0.02 | 0.295* |
| | **Left IFG** | - | −0.49** | -0.051 | 0.03 | -0.054 | -0.144 |
| | **Left STS** | - | -0.258 | 0.091 | -0.12 | -0.094 | -0.142 |
| | **Left IPL** | - | -0.005 | -0.107 | 0.169 | 0.194 | 0.280* |
| | **Right MFG** | - | -0.212 | -0.115 | 0.191 | 0.141 | 0.062 |
| | **Right PCG** | - | 0.084 | -0.091 | 0.278* | -0.013 | -0.082 |
| | **Right IFG** | - | -0.128 | 0.131 | 0.114 | -0.062 | -0.095 |
| | **Right STS** | - | 0.079 | 0.004 | -0.06 | -0.234 | -0.059 |
| | **Right IPL** | - | -0.103 | 0.048 | 0.148 | -0.075 | -0.012 |
| **Coincide** | **Left MFG** | -0.253 | -0.213 | -0.158 | -0.005 | -0.041 | -0.047 |
| | **Left PCG** | -0.128 | -0.168 | -0.226 | -0.23 | 0.038 | -0.192 |
| | **Left IFG** | -0.114 | −0.278* | -0.215 | -0.028 | 0.09 | 0.007 |
| | **Left STS** | -0.142 | 0.017 | 0.073 | -0.131 | -0.103 | -0.124 |
| | **Left IPL** | 0.095 | -0.084 | -0.113 | -0.14 | -0.038 | -0.172 |
| | **Right MFG** | -0.133 | -0.136 | -0.203 | -0.158 | -0.055 | -0.03 |
| | **Right PCG** | -0.026 | -0.07 | -0.226 | -0.219 | -0.13 | 0.211 |
| | **Right IFG** | -0.086 | -0.056 | -0.062 | -0.033 | -0.056 | -0.003 |
| | **Right STS** | -0.114 | 0.002 | -0.09 | -0.126 | -0.081 | -0.127 |
| | **Right IPL** | -0.107 | -0.072 | -0.028 | -0.102 | 0.096 | -0.176 |
| **Follow** | **Left MFG** | -0.131 | -0.206 | -0.03 | 0.033 | 0.044 | -0.032 |
| | **Left PCG** | -0.087 | -0.2 | 0.21 | -0.195 | 0.019 | -0.174 |
| | **Left IFG** | -0.139 | −0.336* | -0.204 | -0.183 | 0.016 | 0.029 |
| | **Left STS** | -0.067 | -0.091 | -0.09 | -0.061 | 0.115 | -0.065 |
| | **Left IPL** | -0.186 | -0.227 | -0.083 | 0.016 | 0.005 | -0.033 |
| | **Right MFG** | 0.012 | -0.201 | -0.209 | -0.024 | 0.191 | 0.092 |
| | **Right PCG** | -0.198 | 0.085 | -0.129 | .278* | 0.049 | 0.113 |
| | **Right IFG** | -0.146 | -0.103 | -0.203 | -0.029 | 0.1 | 0.116 |
| | **Right STS** | -0.012 | -0.053 | -0.234 | -0.069 | -0.246 | -0.028 |
| | **Right IPL** | 0.123 | 0.102 | -0.11 | 0.002 | 0.007 | -0.126 |
| **Joint** | **Left MFG** | -0.21 | 0.093 | 0.191 | -0.081 | 0.075 | -0.041 |
| | **Left PCG** | -0.154 | 0.031 | 0.199 | -0.193 | 0.15 | 0.1 |
| | **Left IFG** | -0.154 | -0.001 | 0.185 | -0.067 | 0.076 | -0.12 |
| | **Left STS** | -0.004 | 0.098 | 0.07 | -0.1 | -0.22 | -0.021 |
| | **Left IPL** | -0.02 | 0.221 | -0.091 | 0.221 | 0.033 | -0.149 |
| | **Right MFG** | -0.186 | 0.164 | 0.167 | 0.002 | 0.256 | 0.108 |
| | **Right PCG** | 0.012 | 0.179 | 0.156 | -0.007 | 0.268* | 0.109 |
| | **Right IFG** | -0.059 | 0.076 | -0.028 | 0.156 | -0.036 | 0.087 |
| | **Right STS** | -0.036 | 0.243 | -0.038 | -0.03 | -0.052 | 0.024 |
| | **Right IPL** | -0.115 | 0.048 | -0.093 | -0.081 | -0.031 | -0.048 |

Table A.13 Correlations between activation and the BOT MD in TD and children with ASD (**indicates p< 0.05, **indicates p< 0.01, ***indicates p< 0.001*)

| | | TD BOT MD | | ASD BOT MD |
|---|---|---|---|---|
| Lead | Left MFG | 0.267 | Left MFG | -0.005 |
| | Left PCG | 0.002 | Left PCG | -0.194 |
| | Left IFG | 0.292 | Left IFG | 0.191 |
| | Left STS | -0.035 | Left STS | 0.259 |
| | Left IPL | -0.249 | Left IPL | 0.314* |
| | Right MFG | 0.395** | Right MFG | -0.042 |
| | Right PCG | 0.188 | Right PCG | -0.08 |
| | Right IFG | 0.211 | Right IFG | -0.109 |
| | Right STS | 0.304* | Right STS | -0.07 |
| | Right IPL | 0.042 | Right IPL | 0.244 |
| Coincide | Left MFG | 0.183 | Left MFG | -0.102 |
| | Left PCG | -0.117 | Left PCG | 0.0555 |
| | Left IFG | 0.254 | Left IFG | 0.004 |
| | Left STS | -0.001 | Left STS | 0.367* |
| | Left IPL | -0.196 | Left IPL | 0.311* |
| | Right MFG | 0.272 | Right MFG | -0.027 |
| | Right PCG | 0.129 | Right PCG | 0.148 |
| | Right IFG | 0.237 | Right IFG | -0.238 |
| | Right STS | 0.158 | Right STS | 0.082 |
| | Right IPL | 0.115 | Right IPL | 0.324* |

Table A.14 Correlations between Activation and the VABS Socialization Percentile in TD Children and Children with ASD (**indicates p< 0.05, **indicates p< 0.01, *** indicates p<0.001*)

| | | TD VABS Social | ASD VABS Social |
|---|---|---|---|
| Follow | Left MFG | 0.353* | -0.155 |
| | Left PCG | 0.134 | -0.075 |
| | Left IFG | 0.192 | −0.287* |
| | Left STS | 0.405** | -0.253 |
| | Left IPL | 0.219 | −0.296* |
| | Right MFG | 0.348* | -0.176 |
| | Right PCG | 0.16 | 0.0462 |
| | Right IFG | 0.315* | -0.138 |
| | Right STS | 0.313* | -0.254 |
| | Right IPL | 0.02 | −0.141 |
| Turn-Take | Left MFG | 0.176 | -0.072 |
| | Left PCG | -0.058 | -0.158 |
| | Left IFG | 0.029 | -0.072 |
| | Left STS | 0.294 | -0.137 |
| | Left IPL | 0.238 | 0.044 |
| | Right MFG | 0.168 | -0.189 |
| | Right PCG | 0.126 | 0.024 |
| | Right IFG | 0.185 | 0.168 |
| | Right STS | 0.23 | 0.0076 |
| | Right IPL | 0.116 | -0.053 |

Table A.15 Correlations between Activation and SRS T-Scores in Children with ASD (*indicates p<0.05, **indicates p<0.01, ***indicates p<0.001)

| | | SRS T-Score |
|---|---|---|
| **Lead** | **Left MFG** | −0.274* |
| | **Left PCG** | 0.122 |
| | **Left IFG** | -0.107 |
| | **Left STS** | −0.288* |
| | **Left IPL** | 0.254 |
| | **Right MFG** | -0.016 |
| | **Right PCG** | −0.299* |
| | **Right IFG** | −0.491*** |
| | **Right STS** | −0.41** |
| | **Right IPL** | -0.005 |
| **Coincide** | **Left MFG** | -0.124 |
| | **Left PCG** | -0.073 |
| | **Left IFG** | 0.137 |
| | **Left STS** | -0.122 |
| | **Left IPL** | 0.164 |
| | **Right MFG** | -0.116 |
| | **Right PCG** | -0.171 |
| | **Right IFG** | -0.085 |
| | **Right STS** | -0.12 |
| | **Right IPL** | 0.199 |
| **Follow** | **Left MFG** | -0.153 |
| | **Left PCG** | -0.16 |
| | **Left IFG** | 0.128 |
| | **Left STS** | -0.108 |
| | **Left IPL** | 0.37* |
| | **Right MFG** | 0.077 |
| | **Right PCG** | -0.171 |
| | **Right IFG** | 0.051 |
| | **Right STS** | 0.176 |
| | **Right IPL** | 0.192 |
| **Turn-Take** | **Left MFG** | 0.053 |
| | **Left PCG** | 0.163 |
| | **Left IFG** | -0.008 |
| | **Left STS** | -0.084 |
| | **Left IPL** | 0.042 |
| | **Right MFG** | 0.159 |
| | **Right PCG** | -0.047 |
| | **Right IFG** | −0.327* |
| | **Right STS** | -0.093 |
| | **Right IPL** | 0.029 |

## Appendix B

## IRB APPROVAL LETTER

UNIVERSITY OF DELAWARE

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| | |
|---|---|
| DATE: | December 21, 2017 |
| TO: | Anjana Bhat, PT, PhD |
| FROM: | University of Delaware IRB |
| STUDY TITLE: | [930721-7] An fNIRS-based study of interpersonal synchrony in children aka "UD Autism Lab fNIRS study" |
| SUBMISSION TYPE: | Amendment/Modification |
| ACTION: | APPROVED |
| APPROVAL DATE: | December 21, 2017 |
| EXPIRATION DATE: | July 6, 2018 |
| REVIEW TYPE: | Expedited Review |
| REVIEW CATEGORY: | Expedited review category # *45 CFR 46.110 (b) (2)* |

Thank you for your submission of Amendment/Modification materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.