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COMPARISON OF NEUROLOGICAL ACTIVATION PATTERNS OF CHILDREN WITH

AND WITHOUT AUTISM SPECTRUM DISORDERS WHEN VERBALLY

RESPONDING TO A PRAGMATIC TASK

by

Daphne U. Hartzheim

A dissertation submitted in partial fulfillment
of the requirements for the degree

of

DOCTOR OF PHILOSOPHY

in

Disability Disciplines

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UTAH STATE UNIVERSITY
Logan, Utah

2015

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ABSTRACT

Comparison of Neurological Activation Patterns of Children With and Without Autism Spectrum Disorders When Verbally Responding to a Pragmatic Task

by

Daphne U. Hartzheim, Doctor of Philosophy

Utah State University, 2015

Major Professor: Ronald Gillam, Ph.D.
Department: Special Education and Rehabilitation

This study examined the neurological activation of children with autism spectrum disorders (ASD) while performing a pragmatic judgment task. In this study, children between the ages of 9 and 15 years responded to questions regarding a social situation, taken from the *Comprehensive Assessment of Spoken Language,* while concurrently having their brain activity measured. We targeted four brain regions for analysis: dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), superior temporal gyrus (STG), and the inferior parietal lobule (IPL).

Ten children with ASD and 20 typically developing (TD) children participated. Matching occurred in a bracketing manner with each child in the ASD group being matched to two control children to account for natural variability. Neuroimgaging was conducted utilizing functional Near-Infrared Spectroscopy (fNIRS). Oxygenated and deoxygenated blood concentration levels were measured through Near-Infrared light cap with 44 channels. The cap was placed over frontal lobe and the left lateral cortex. The placement was spatially registered using the Polhemus.

Analysis indicated that children in the ASD group performed significantly poorer than their controls on the pragmatic judgment task. Mixed repeated-measures analysis of variance of neurological data indicated that the children with ASD had lower concentration levels of oxygenated and total hemoglobin across the four regions. There were significantly higher concentration levels for oxygenated and total hemoglobin in the STG. Analysis of correct and incorrect responses revealed significantly more activation in the OFC when responses were correct. Additionally, there was a significant interaction of Accuracy and Group in left DLPFC. Children with ASD presented higher oxygenated hemoglobin concentration values when responding correctly, while children in the control group presented higher oxygenated hemoglobin concentration values for the incorrect items. Statistical Parametric Mapping was performed for each triad to assess the diffusion of neural activation across the frontal cortex and the left lateral cortex. Individual comparisons revealed that 7 out of 10 children with ASD demonstrated patterns consistent with more diffuse brain activation than their TD controls.

Findings from this study suggest that an fNIRS study can provide important information about the level and diffusion of neural processing of verbal children and adolescents with ASD.

(169 pages)

PUBLIC ABSTRACT

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CHAPTER I

INTRODUCTION

Difficulty with pragmatic communication skills, also referred to as social communication and social rules of interaction, is one of the core deficits of Autism Spectrum Disorders (ASD). Pragmatic language encompasses a large subset of skills that involve social cognition, which includes comprehension of emotions and taking the perspective of the conversational partner. Other skills include Theory of Mind (ToM), displaying flexibility in thought and overcoming robust routines, working memory, auditory and semantic processing, attention and spatial cognition, and conflict resolution.

Given pragmatic language abilities to be a core deficit in individuals with ASD, we often see limited eye contact, unresponsiveness to one's own name, echolalia, and stereotypic language. Individuals with more verbal abilities typically display a lack of comprehension of figurative language and irony, deficits with social conventions of language, such as topic maintenance and turn-taking. Contradictory to some theories, we do not see differing response times (RTs) in children with ASD when compared to their typical peers. A more comprehensive description follows.

While a great deal of research has been conducted behaviorally, there is still limited knowledge about the neurological processes underlying pragmatic language. Previous neuroimaging studies have utilized SPECT, PET, EEG and fMRI to investigate the relationships between neural processing and specific aspects of pragmatic language such as comprehension of metaphors, Theory of Mind (ToM), understanding of irony, comprehension of figurative language and prosodic features of the speakers. The majority of these studies were conducted with healthy adults or adolescents. A few of them, however, involved individuals with ASD.

Many of these neural imaging technologies are not conducive to collecting data in a naturalistic communication context. This is problematic because a variety of environmental factors involved in communication are crucial to the study of pragmatic language. Studies in more naturalistic settings are necessary to understand those changes in neurological activation. While the more naturalistic environment the more complex it is to understand the underlying patterns. Detailed findings from those studies are summarized below.

Greater understanding of the neurological patterns underlying the performance of a variety of pragmatic skills by children with ASD could enhance our understanding of how individuals with this disorder process and learn. An imaging technology known as Functional Near Infrared Spectroscopy (fNIRS) provides researchers with the opportunity to perform neuroimaging in-vivo with great temporal resolution. Because verbal responses are possible with such a technology, it is possible to assess neural processing as individuals are actively engaged in communicative acts such as verbally demonstrating knowledge of basic rules of politeness, understanding of relevant remarks to a question, identification of conversational topics and judgment of the listener's knowledge and expectations.

Understanding neurological processes that are underlying these skills can inform us of the differences between children with ASD and typically developing

(TD) children. This information, in turn, could provide guidance in creating more effective interventions in which targeted skills are more likely to generalize into everyday life.

The study described herein was designed to increase our understanding of the neural activation processes underlying pragmatic judgment in children with and without ASD. The use of functional Near Infrared Spectroscopy (fNIRS) is a cost-effective procedure for obtaining neural activation data from children with and without ASD as they respond in-vivo to functional tasks in which they provide verbal responses to descriptions of specific social situations. This is one study in a set of investigations designed to improve our understanding of neural activation patterns in children with ASD and the development of successful treatment approaches for social communication.

The review of the literature begins with a description of behavioral research on the pragmatic language of individuals with ASD. The second section summarizes neuroimaging studies of pragmatic language in the typically developing (TD) individuals followed by a summary of what is known about neurological differences in individuals with ASD. There is a summary of two current theories of cognitive processing in ASD. The introduction ends with an explanation of the difficulties inherent in performing neuroimaging studies with this particular population, followed by a section examining the advantages of fNIRS with children with ASD.

Pragmatic Language in Autism Spectrum Disorders

Pragmatic language is a linguistic subfield that encompasses the study of speech acts, conversational implicature and interaction. Unlike the structural language domains (phonology, semantics, syntax, and morphology), the study of pragmatic language examines the meaning of an utterance while taking into consideration not exclusively structure, but also preexisting knowledge of speaker and listener in the context of the environment (Liu, 2005). Therefore, pragmatic language skills include knowing the difference between what is said and what is implicated (conversational implicature). A spouse mentioning to her partner that guests will be arriving in 2 hours may imply that the house needs to be cleaned. The actual structure of the sentence does not indicate such a request. Furthermore, certain contexts narrow down the meaning of a sentence. If one says: "She is wearing a blue dress." Or "Her lips are blue." The interpretation of the color blue is dependent on the context and changes its meaning. The first sentence is context-invariant and its meaning remains the same, while labeling the lips as blue implies a certain outside temperature, it is context-dependent content (McNally, 2013).

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the criteria for the diagnosis of Autism Spectrum Disorder (ASD) are: "(a) Persistent deficits in social communication and social interaction across multiple contexts; (b) restricted, repetitive patterns of behavior, interests, or activities; (c) symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life); (d) symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning; and (e) these disturbances are not better explained by intellectual disabilities or global developmental delay" (APA, 2013, p. 50).

While a pragmatic language deficit is a core characteristic of ASD, the nature of children's communication deficits differs across individuals with ASD. For example, in many children with ASD, social deficits co-occur with marked difficulties with vocabulary and grammar. However, a small number of individuals diagnosed with ASD do not show developmental language delays (Le Couteur, Bailey, Rutter, & Gottesman, 1989).

Norbury (2014) defined pragmatics as, "a child's understanding of speaker intentions and the verbal and nonverbal cues that signal those intentions, as well as the child's interpretation of the environmental context, societal norms and expectations and how these coalesce with structural aspects of language (e.g., vocabulary, syntax, and phonology) to achieve successful communication" (p. 204). Even though language abilities are highly variable within the population of children with ASD (Tager-Flusberg, Paul, & Lord, 2005), deficits in the pragmatic language domain are universal across all individuals with ASD. This is manifested by engagement in a number of socially inappropriate behaviors such as repetitive and restrictive behavior, narrow topic interests, lack of motivation for social interaction, difficulty comprehending figurative language, and a tendency to focus on details, rather than processing a situation holistically (Happé, & Frith, 2006). Specifically related to word use, children with ASD often have knowledge of words, but fail to use them in normal ways within particular speaking contexts (Tager-Flusberg et al., 2005). For example, children with ASD rarely use mental state (i.e., happy, disappointed, sad, etc.) terms or describe cognitive states (i.e., plan, hope, think, etc.), and they exhibit difficulties understanding social emotional states (Dodd, Ocampo, & Kennedy, 2011). Initiating conversations and engaging in discourse has also been found to be difficult for children with ASD regardless of the severity level (Klin & Volkmar, 1997).

Pragmatic language encompasses a wide range of skills and is sometimes difficult to define, let alone teach. A number of different sub-skills such as attention, working memory, and perception play a role in pragmatic language. Some of the most common pragmatic difficulties exhibited by children with ASD include (a) the absence of early nonverbal communicative intents, such as requesting objects, calling attention to objects and events, greeting, and commenting; (b) unusual language use with delayed echolalia or neologisms; (c) decreased rate of initiation of spontaneous communication; (d) difficulties in identifying topics of conversation; (e) decreased ability to judge the listeners knowledge base; (f) challenges gaging how much information is relevant for discourse; (g) difficulties turn taking; (h) providing an inadequate or tangential response to questions; and (i) challenges with referential communication acts (Tager-Flusberg et al., 2005). It is likely that these pragmatic skills rely on underlying mechanisms related to attention, memory and perception. These complex communicative processes require the activation of many different neurological areas.

Intuitively, we may anticipate that due to the complexity of such a language task those children may take a longer time to process and respond. Increases in response time (RT) with behavioral tasks however have been inconsistent with individuals with ASD with a majority of studies suggesting similar RTs. RT has been studied with recognition of facial emotions (Fink, de Rosnay, Wierda, Koot, & Begeer, 2014), processing of emotion words (Lartseva, Dijkstra, Kan, & Buitelaar, 2014) and a go/no go task in comparison with children with ADHD and typical development (Adamo et al., 2014).

Adamo et al. (2014) analyzed RT in 128 children (46 with ADHD, 46 with ASD and 36 TD) ages 7 through 11; 9 years. Children in the ASD group however were divided into two groups, one group with co-occurring ADHD (ASD+) and one group without co-occurring ADHD (ASD-). Each participant completed a 5.5 min session with a go/no go task. Results from the study indicated that increased RT was noted for the ADHD and ASD+ group. RT for the TD and the ASD- group was similar. These findings are suggestive of increased RT being linked to ADHD, but not to a diagnosis of ASD.

Fink et al. (2014) recruited a total of 259 children (ages 7-13 years) with high-functioning ASD and typical development. Children were asked to match a static facial expression that was presented on a tablet to an emotion word at the bottom of the screen. Data was analyzed for accuracy and RT. Controlling for verbal ability and ASD symptom severity, no significant differences in RT were found between the groups. Children with higher verbal IQs however responded more accurately and quicker than those children with lower verbal IQs. Recognition of facial expression may not require time-consuming compensatory skills.

An EEG study that was investigating RT did not support these findings. Lartseva et al. (2014), included 21 individuals with ASD, of which 19 participated in the EEG study, and 20 typically developing adults between ages 18-36 years. 180 real words that had previously been investigated for their valence (positive or negative), arousal (relaxing or arousing) and concreteness (concrete or abstract) were identified. Those 180 words together with 180 pseudowords were randomly presented to the participant on a computer screen. Each adult had to detect if the word was a real word or not while wearing an EEG net. Contrary to previous studies, behavioral RT indicated the TD group was significantly faster in their RT. Results further implied individuals with ASD were not “blind” to emotional valence. Participants with ASD showed increased RT with emotional words, following a comparable pattern of the TD group that also responded slower with emotional words. Authors explain differential findings with variation of participant sample and differences in the type of task. Event-related potentials (ERP) data from the study found words with negative valence to be processed differently in adults with ASD, even though differences in accuracy were not present. Neurological RT was not investigated in this study.

More evidence points toward no differences in RT between ASD and TD groups unless ADHD is involved. However, due to inconsistencies in the literature, especially with varying tasks, further investigations in the pragmatic language domain need to be conducted. A difference in RT could be an indication of individuals with ASD processing information less efficiently. Less efficient processing could therefore be linked to decreased pragmatic language skills. Verbally responding to a pragmatic language task involves more complex skills than forced choice or go/no-go tasks, which may result in differential outcomes.

The next section describes some of the processes and brain regions that are involved in pragmatic language. A number of studies are summarized that investigated an isolated pragmatic language skill (i.e., sarcasm, metaphors, Theory of Mind) in typically developing individuals, followed by studies exploring neurological activity of individuals with ASD when engaging in one aspect of pragmatic language.

Neural Activity During Pragmatic Language Tasks

Neurological activity has been studied with a variety of neuroimaging techniques, such as SPECT, PET, fMRI, and NIRS. The literature suggests that there are four cortical regions that are related to processes that play a role in pragmatic language skills: the dorsolateral prefrontal cortex (DLPFC), the orbitofrontal cortex (OFC), the superior temporal region (STG), and the inferior parietal lobule (IPL). Some subcortical structures are also involved in pragmatic language, such as the anterior cingulate cortex (ACC) and amygdala.

Dorsolateral Prefrontal Cortex

The dorsolateral prefrontal cortex (DLPFC, Figure 1) together with ACC is associated with cognitive control. This control is referred to as solving difficult, novel, or complex tasks, overcoming habitual responses, and correcting errors (Cohen, Dunbar, & McClelland, 1990; MacDonald, Cohen, Stenger, & Carter, 2000). "DLPFC activity in the absence of ACC activity has been found for tasks that require maintenance and manipulation of information in working memory" (Baker, Frith, Frackowiak, & Dolan, 1996). Such skills are required for appropriate pragmatic language. During a conversation, speech partners have to continuously maintain and manipulate incoming information and react accordingly.

Orbitofrontal Cortex

The orbitofrontal cortex (OFC, see Figure 2) is part of the prefrontal cortex and receives neural connections from all sensory modalities. Rolls (2000, 2002) has

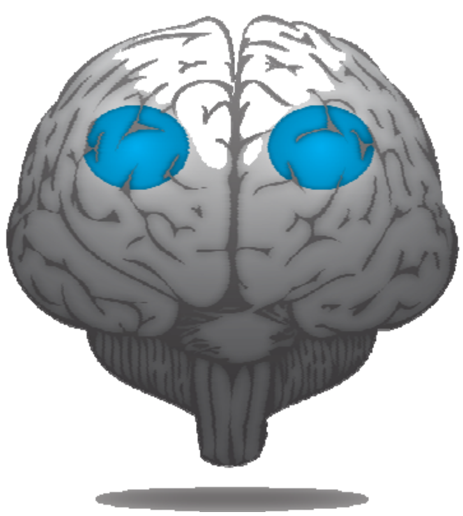


Figure 1. Dorsolateral prefrontal cortex (DLPFC) left and right.

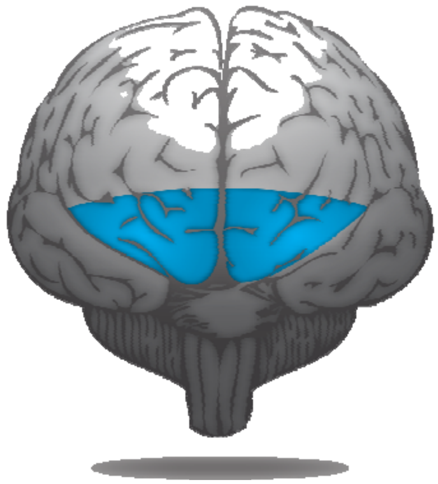


Figure 2. Orbitofrontal cortex (OFC).

described the function of the orbitofrontal cortex to be part of the reward center of the brain, because it processes primary reinforcers that involve taste and somatosensory input. While the orbitofrontal cortex is a secondary and tertiary association area for the senses, it also sends and receives projections from the amygdala, which is directly related to emotions (Kringelbach & Rolls, 2004). They have reviewed the literature and conclude “the reward and punishment values of primary (unlearned) reinforcers such as taste, touch and pain, and visual and olfactory stimuli which become secondary (learned) reinforcers by association with a primary reinforcer, are represented in the orbitofrontal cortex.” The orbitofrontal cortex appears to be important for rapid emotion-related learning (Rolls, 1999). While engaging in social communication acts, it is imperative to interpret emotions and react appropriately. Proper function of the orbitofrontal cortex is therefore crucial for pragmatic language development.

Superior Temporal Gyrus

The superior temporal gyrus (STG, Figure 3) has been identified to be involved in language, and more specifically in auditory processing tasks. Auditory processing is important for receptive language skills. A number of recent studies support the involvement of the STG in social cognition (Pelphrey, Viola, & McCarthy, 2004; Ruby & Decety, 2004; Skuse, Morris, & Lawrence, 2003). The STG is not isolated in its involvement with social cognition, but interacts with other areas, such as the amygdala and the prefrontal cortex (Adolphs, 2003; Takahashi et al., 2004). Some of the core deficits of ASD, such as repetitive behavior (i.e., perseverative responding, echolalia), language delay and faulty self-monitoring could be related to a dysfunction of the neural circuitry (Bigler et al., 2007) that involves the STG.

Inferior Parietal Lobule (IPL)

The IPL (Figure 4) is made up of two distinct structures, angular gyrus and supramarginal gyrus. While the supramarginal gyrus in the left hemisphere is

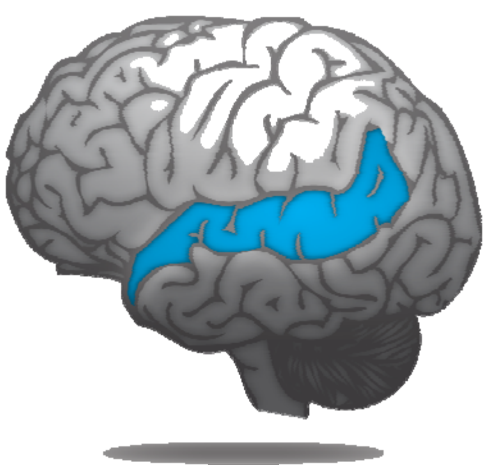


Figure 3. Superior temporal gyrus (STG).

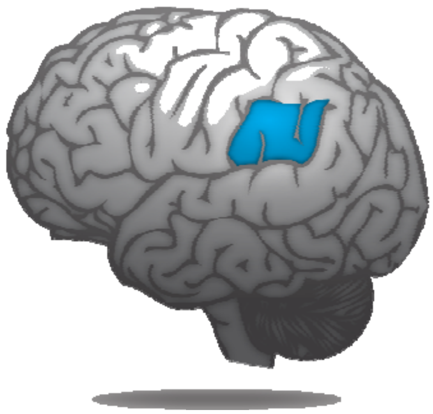


Figure 4. Inferior parietal lobule (IPL) left.

related to phonological decision making, the left angular gyrus plays more of an important role in pragmatic language skills. It has consistently been found to be involved in semantic processing, attention and spatial cognition, memory retrieval, conflict resolution, Theory of Mind, and social cognition (Seghier, 2013). The angular gyrus serves in the convergence network of multisensory input to be able to serve those multiple functions.

While cortical areas and their networks have been shown to play a role in pragmatic language, a number of studies have explicitly assessed neural activation during the performance of specific pragmatic language tasks. In an fMRI study with typically developing adults, participants were presented with a nonsarcastic condition (e.g., “When Takuya’s mother came home, his clothes were strewn all over his room. When she saw this, she said to him: Why do you always leave your room so messy?”) and a sarcastic condition (e.g., “When Takuya’s mother came home, his clothes were strewn all over his room. When she saw this, she said to him: How do you always keep your room so tidy?"). Neural substrates were measured during the presentation of these two different conditions. The adults activated left inferior frontal gyrus (LIFG), temporal poles, superior temporal sulcus (STS), medial pre-frontal cortex (MPFC), pre-supplementary motor area (preSMA), and the cerebellum bilaterally when identifying sarcastic sentences vs. non-sarcastic sentences. Activation that was predominantly associated with sarcasm occurred in the inferior frontal gyrus, which is part of the OFC. This area might therefore interact with language processing and mentalizing during sarcastic statement detection. (Uchiyama et al, 2006).

Rapp, Leube, Erb, Grodd, and Kircher (2004) investigated another aspect of pragmatic language processing using fMRI. They examined neural substrates when participants were presented with metaphors. Fifteen healthy adults laid supine in the MR-scanner and were visually presented with 60 short German sentences and 15 resting stimuli (i.e., grey background without sentences). Half of the sentences were metaphors and half were to be taken literally. Left inferior temporal gyrus and left posterior middle/inferior temporal gyrus were activated at higher levels during metaphor comprehension as compared to literal sentences, indicating that metaphoric sentence processing is left lateralized to the temporal gyrus. These findings support the involvement of the STG during pragmatic tasks.

Brunet, Sarfati, Hardy-Baylé, and Decety (2000) conducted a PET scan study with eight healthy male adults. They used drawings of Theory of Mind tasks instead of written words, investigating the cortical areas involved in attributing intentions to others. Participants were presented with a comic strip and three pictures displaying possible endings to the story. Only one of the three solution pictures was a logical answer, the other two were distractor pictures. Participants were instructed to respond as quickly as possible with the correct ending to each comic story. Results indicated specifically activation in MPFC during this visual ToM tasks. The DLPFC includes MPFC regions.

Another fMRI study involving tasks of social norm transgressions from Berthoz, Armony, Blair, and Dolan (2002) showed activation of MPFC, temporal poles, and STS, as well as areas responding to aversive emotional expressions such as anger. Twelve right-handed males without a history of neurological disorders were recruited. Four different conditions were created: (a) a description of a normal situation, (n) a description of an embarrassing situation, (c) a description of a story in which the protagonist intentionally breaks social norms, and lastly (d), sentences of unrelated words. The beginning of each story was presented visually on a monitor and read by the participant. Differing endings, depending on the condition, were then presented and the participants were asked to think about how the ending would make them feel. Interestingly, the authors detected the most activation in the orbitofrontal and temporo-parietal regions. All of those regions were more active in the condition with embarrassing stories and also when social norms were intentionally violated as compared to the description of a normal story. It is important to note though, that the most activation in the medial frontal cortex was detected during the condition in which the social norms were intentionally broken.

This is an indication that there is differential activation with intentional and unintentional norm violations. Again, this supports the involvement of OFC and STG for processing of pragmatics.

Superior temporal structures are also active during story comprehension (Ferstl & von Cramon, 2002; Fletcher et al., 1995; Gallagher et al., 2000; Vogeley et al., 2001). Fletcher et al. utilized PET technology with six adult male volunteers. Three types of stories (ToM stories, physical stories, and unlinked sentences) were presented to the participants and they were asked to answer questions about each story. Posterior cingulate cortex, as well as superior temporal gyrus were active, especially during ToM stories. Gallagher et al. recruited six healthy male adults and created a similar procedure using fMRI, of a ToM condition, non-ToM condition and unrelated picture condition. This time the stimulus was not written, but was a cartoon displaying the different conditions. Results from this study confirmed the results from the Fletcher et al. study noting activation in the medial prefrontal cortex and temporo-parietal junction during mentalizing tasks. These findings were further extended in an fMRI study conducted with eight male participants (Vogeley et al., 2001). The original stories used by Fletcher et al. were translated into German and were controlled for complexity and sentence structure. Two additional conditions were added with a self-perspective in the presence and absence of ToM. Original findings were replicated and extended to isolating regions of activation during the self-perspective conditions in the right temporo-parietal junction and medial aspects of the superior parietal lobe. It is important to note that during the

ToM tasks with self-perception, activation is recorded in the right prefrontal cortex. This supports the model that integration between these two tasks requires activation of the STG.

Ferstl and von Cramon (2002) created a different set of stimuli for their fMRI study in which a logic (objects only) and a ToM (references to people) condition were created with a sentence pair that was either coherent (e.g., Mary's exam was about to begin. Her palms were sweaty) or incoherent (e.g., Mary's exam was about to begin. Some friends had remembered her birthday). Participants were to indicate via button press whether the story was coherent or incoherent. Fronto-median cortex, part of the dorso-lateral prefrontal cortex and bilateral temporal cortex, which is part of the STS area, was involved during ToM tasks, replicating Vogeley et al. (2001) results.

Interpretation of figurative aspects of language, such as metaphors and irony, also include activation patterns in the right hemisphere (Bottini et al., 1994). This study was performed using PET scans in which six participants performed three different linguistic tasks (i.e., metaphorical comprehension, literal comprehension, and lexical-decision making task). Metaphor and literal comprehension activated OFC, as well as left middle and inferior temporal gyri, temporal poles and left parietal cortex, as part of STG. During metaphors right prefrontal cortex, right middle temporal gyrus, precuneus and posterior cingulate were activated in addition to the left hemisphere. These findings support the hypothesis of right hemispheric involvement in nonliteral language comprehension.

Studies have also been conducted with individuals with ASD to study their activation patterns with isolated pragmatic language tasks. Those studies are described in the next section.

Neural Activity: Pragmatic Language for Individuals with ASD

Tesink et al. (2009) investigated the underlying neurological structure of children with ASD as they completed a pragmatic task in which the speakers' utterance was congruent or incongruent with the feature of the speaker (i.e., adult vs. child, female vs. male). The researchers presented participants with 314 sentences (160 speaker-inference sentences, 108 world knowledge sentences, 42 reversed speech items and four neutral filler sentences). Six different stimuli lists were created that were pseudorandomized to include the same amount of different sentence types for each list. While lying in a MR scanner, participants listened to the sentences via headphones and were instructed to process each sentence attentively for comprehension. At the conclusion of the scanning session, each participant answered questions about the sentences. Both groups performed similarly on the behavioral task, but neurologically they showed some differences. Both groups showed similar activation of the left inferior frontal gyrus (LIFG) during this task. This region is related to unifying information when processing language. Individuals with ASD, however, activated the right inferior frontal gyrus (RIFG) more during those pragmatic comprehension tasks. The authors conclude that the increased activation in RIFG, which is typically involved in forming and updating a situation model, points to greater effort and difficulty forming and revising that situation model, requiring individuals with ASD to activate a broader area of cortex. This points to less neural efficiency. No significant behavioral differences were found in the control vs. the adult ASD group, which suggests that the increase in neural activation to other brain regions may have been related to compensatory strategies for solving the task at hand.

Groen et al. (2010) wanted to investigate the hypothesis that adolescents with ASD would integrate situational information less into a composite whole than typically developing individuals in the LIFG. Four classes of sentences were presented (correct sentences, sentences with a semantic anomaly, sentences with a world-knowledge anomaly, and sentences with a speaker inference anomaly). While participants were lying in an fMRI scanner, they listened to 80 pairs of sentences that only differed in the speaker's voice, 36 triplets of sentences that differed in regards to one critical word (no anomaly, semantic anomaly, and world-knowledge anomaly) and 36 speech-like noise fragments. While participants in the ASD group activated the LIFG during world knowledge, semantic knowledge and noise contrasts to a similar extent as the control group, they activated this area less during social contrasts. Again, the LIFG has been found to be involved in the unification and integration of knowledge. Incongruent trials require more activation of the LIFG. Participants with ASD however activated the LIFG less when a social component was part of the trial.

The authors speculated that the findings from the Tesink et al. (2009) study, together with this study suggest that the compensatory strategy of involving the RIFG to solve social situations has not yet developed in adolescents with ASD. Groen et al. (2010) further suggested that decreased functional connectivity could explain the hypoactivation of the LIFG in individuals with ASD. The decreased LIFG could be a result of lower order areas not being connected properly, and therefore the unification portion of the brain (LIFG) not being activated as much as for those individuals without ASD. The pattern is congruent with the model of complex information processing, in which increased complexity of a task necessitates the recruitment of additional cortical areas.

Because Theory of Mind (ToM) is believed to play an important role in the development of pragmatic skills and in pragmatic disorders, ToM tasks have been used in neuroimaging studies with individuals with ASD. An example of a ToM task is telling the individual a story in which he or she has to take the perspective of the protagonist and answer questions that show whether he or she is able to change the perspective. For example, "A burglar who has just robbed a shop is making his getaway. As he is running home, a policeman on his beat sees him drop his glove. He doesn't know the man is a burglar, he just wants to tell him he dropped his glove. But when the policeman shouts out to the burglar, "Hey, you! Stop." The burglar turns round, sees the policeman and gives himself up. He puts his hands up and admits that he did the break-in at the local shop. Question: What was the burglar thinking?" (Gallagher et al., 2000). Adolescents with ASD might answer something like, "He was bad," indicating a lack of ability to assume the perspective of the burglar.

Early neuroimaging studies using SPECT, PET, EEG and fMRI have identified regions of the brain that are associated with ToM (Baron-Cohen & Ring, 1994; Fletcher et al., 1995; Gallagher et al., 2000; Gallagher & Frith, 2003; Vogeley et al., 2001). Results from these studies consistently indicate neural activation in the anterior cingulate cortex (ACC) during ToM tasks. Baron-Cohen and Ring (1994) and Fletcher et al. identified the left medial frontal gyrus as signaling activation during ToM tasks. A later study by Vogeley et al. recorded activation in the right prefrontal cortex as opposed to the left medial frontal gyrus, which both belong to the DLPFC or OFC. This difference in findings may be explained by the use of more sophisticated neuroimaging techniques. The earlier studies were all conducted with healthy individuals using SPECT and PET and later utilizing fMRI or EEG. Gallagher and Frith specified the activation from the anterior cingulate cortex (ACC) to the anterior paracingulate cortex, which is considered part of the ACC, which corresponds with BA 9 and 32 (left and right hemisphere, respectively).

ToM is an innate and high-level cognitive task that requires the incorporation of a number of different skills, such as memory, perception, sensory integration and knowledge of mental states (Gallagher & Frith, 2003). Therefore, ToM tasks have a high cognitive load and require well-functioning connectivity between different brain regions. According to the complex information processing model, children with ASD present disrupted cortical connectivity, which could account for their difficulties with ToM tasks.

Differences in cortical connectivity manifest with less focal activation patterns during ToM tasks. Kana, Cherkassky, Minshew, and Just (2009) conducted an fMRI study with 12 adults with high-functioning autism and 12 typical controls. During the experiment, the participants were presented with geometrical animations that moved through a white background in three different ways: ToM, goal-directed, and random. In the ToM condition, the two geometrical figures were engaged with each other. Their engagement was based on thoughts and feelings. In the goal-directed condition, the figures moved with a purpose, doing what the other character did. In the random condition, the character did not interact and randomly moved across the white background. After viewing the short animation, four words appeared on the screen and the participants were asked to choose one word that best described the movement. Results from the fMRI data suggested that participants with ASD showed reduced functional connectivity within the ToM network (medial frontal regions) relative to their controls, showed reduced brain activation in the frontal areas (medial frontal gyrus, anterior paracingulate cortex, inferior orbital frontal gyrus) of the brain, but no difference in posterior ToM region. The authors also examined the functional connectivity between the areas involved in the ToM network. Underconnectivity was found in participants with ASD. The findings further suggested that even though isolated regions of ToM in the frontal regions were activated less and connectivity was decreased, individuals in the ASD group compensated by recruiting right hemisphere areas that were not active in the control group. This suggested that due to the increased cognitive load, children with

ASD are more likely to recruit surrounding cortical structures, resulting in overall increased neural activity to solve ToM tasks.

In conclusion, while there is some variation across studies and across age groups regarding neural activation patterns, neural activation in individuals with ASD appears to be lower when compared to their controls. The regions involved vary depending on the nature of the task under investigation. Typically, studies also noted while there was overall less activation in the expected areas for the task, individuals with ASD compensated by activating other cortical areas. Besides researching isolated brain regions, some studies also measured connectivity and networks between areas. Two theories of activation and connectivity have crystalized and are explained in the following section.

Theories of Neural Activation

In recent years, two theories explaining neural activity in individuals with ASD have become more prominent; frontal-posterior underconnectivity theory (Just, Keller, Malave, Kana, & Varma, 2012) and the complex information processing theory (Minshew & Goldstein, 1998). The theory of frontal-posterior underconnectivity proposes that there is lower synchronization between frontal and posterior cortical areas due to a decreased communication bandwidth between these areas in autism (Just et al., 2012). Just and his colleagues postulated that tasks which require the integration and coordination of frontal and posterior brain regions are more susceptible to disruption, especially when the complexity of the task increases. Engaging appropriately in pragmatic language situations requires the processing and integration of many different stimuli such as visual, auditory, and tactile stimuli in multiple cognitive processes such as working memory, long-term memory, attention, planning, and problem-solving. The tasks require high levels of computational capacity of the brain. These interconnected processes demand the communication and synchronization of frontal and posterior cortical regions. This underconnectivity was shown in the study conducted by Kana et al. (2009). The ToM network, which usually integrates frontal and posterior brain regions, was weaker in adults with ASD. Connectivity was also decreased for the other experimental tasks. Given such connectivity deficits, activation in specialized brain regions was reduced for the participants with ASD.

The Complex Information Processing model is based on general information processing mechanisms and incorporates information from neuropsychological and neuroimaging studies of ASD (Minshew, Webb, Williams, & Dawson, 2006). Williams, Minshew, and Goldstein (2015) summarize the model and its development. The model was initially described based on behavioral results. Minshew and Goldstein (1998) administered 35 different tests to older children and adults with and without ASD. Those tests included simple attention, complex attention, immediate memory, delayed memory, formal language, pragmatic language and abstraction. Differences occurred in complex memory and problem-solving when language was involved. There were no differences in simple and complex attention, associative memory, attribute identification, or rule learning of abstract reasoning. Based on these results, the authors proposed that the deficits that individuals with ASD exhibit are not due to a specific modality, but rather generalized difficulties with tasks that involve multiple modalities. Other studies followed that verified these results with children and adults (Minshew et al., 1998; Williams, Goldstein, & Minshew, 2006).

With advancements in neuroimaging, this model has received support. One initial fMRI study by Just, Cherkassky, Keller, and Minshew (2004) researched sentence comprehension in adolescents and younger adults with and without ASD. The findings suggested that the brain of someone with ASD is organized the same as their control, but the regions were not synchronizing and integrating the information with each other to support language functions. As task demands increase, so does the demand to integrate information increase. It appears that children with ASD show a breakdown with those increased demands. Pragmatic language tasks require a high synchronization of cortical areas. It demands processing of a number of different stimuli simultaneously, which is complex.

Challenges of Neuroimaging with ASD Population

There are a number of reasons why there are so few investigations of the neurophysiological mechanisms underlying autism spectrum disorder. The technology is expensive and difficult to master, the fMRI imaging environment is not child-friendly, and the analyses are complex. In addition, no neuroimaging studies of individuals with ASD have measured neural activity in-vivo, as participants perform social-pragmatic tasks. In addition to the expensive technology and difficult-to-master analyses, there are reports of increased overall hypersensitivity for children with ASD, making imaging studies even more challenging. For example, a study by Baker, Lane, Angley, and Young (2008) reported that out of the 22 participants with ASD 82% had some sort of sensory processing difficulty according to a parent questionnaire. They further report the occurrence of children who exhibit both hypo- and hyper-responsiveness. Sensory-over-responsivity was found in the cluster of tactile sensitivity, movement sensitivity and visual/auditory sensitivity. Poor sensory processing was associated with higher levels of behavior and emotional problems. Baranek, Boyd, Poe, David, and Watson (2007) observed hyper-responsive sensory patterns to be characteristic of developmental delays in general, including those children with ASD.

A study conducted by Blakemore et al. (2006) confirmed hypersensitivity to tactile stimuli for those diagnosed with Asperger's syndrome. Grooming and hygiene tasks posed a particular challenge in 60.9% of children with ASD (Tomchek & Dunn, 2007), indicating the head and facial area to be particularly sensitive. These hypersensitivities pose a significant challenge in relation to neuroimaging, where children are required to lay still in small tubes for long periods of time, with packing around their heads and/or bodies.

Kana, Libero, and Moore (2011) describe special techniques that were employed with individuals with developmental disabilities to ensure successful testing with fMRI's. They (1) used social stories, explaining the unusual environment and often confusing situation for children with ASD. Social stories have been shown to be effective in helping children adjust to unknown situations (Thiemann & Goldstein, 2001). They (2) recorded scanner sounds to acclimate the individuals with ASD to the sounds that are produced by the scanner. (3) A discarded old mock-MRI scanner was used to acclimate participants to the environment. (4) A tour of the MRI scanner was provided prior to the scanning, to again familiarize the individual with the equipment as well as the upcoming procedures. Great measures were taken to (5) make the MRI scanner child-friendly by decorating it with stickers, providing blankets and making the scanner look like an item of interest (e.g., trains). Lastly, (6) the participants were given the option of watching cartoons or movies during the anatomical and DTI acquisition. Even though extensive preparatory measures were taken to make MRI scanning most successful with this group of participants, motion artifacts, anxiety and refusal to enter the scanner were still a major concern and some data had to be excluded from the analysis due to the special considerations of this population.

Even though motion artifacts and the confined space are not as concerning with NIRS as they are with fMRI's, it is still important to prepare children with ASD for the upcoming procedures. Sensory desensitization training could be helpful for getting hypersensitive children with ASD to wear the NIRS caps. Sensory desensitization training has been shown to be successful getting children with ASD to wear EEG caps. A gradual process was employed to approximate the end goal of wearing the net for 10 minutes. Ten out of the 12 participants completed the training successfully and were therefore able to finish the actual EEG tasks (Roesler et al., 2013). NIRS caps have a similar set-up as an EEG net.

Rationale for fNIRS Instrumentation for Neuroimaging with Children with Autism Spectrum Disorders

A new neural imaging instrument, called Near Infrared Spectroscopy (NIRS) has the potential to contribute to our understanding of ASD. Near Infrared Spectroscopy (NIRS), a procedure that measures oxygen/hemoglobin levels in different areas of the brain, makes in-vivo brain imaging possible. This technology is especially useful for children because their brain activity can be assessed as they sit in a chair, listen to and/or look at stimuli, and respond in button-press, touchscreen, or verbal modalities. Neural processing during more naturalistic behaviors, like engaging in conversation, can be studied functionally.

A NIRS cap, which is equipped with 22 receiving (blue) and 22 sending (red) optodes, is placed on the head, and positioned over regions of interest. The optodes send and receive a low-level laser light signal through fiber optic cables. NIRS monitors the concentration of oxygenated (OHb) and deoxygenated (HHb) hemoglobin by measuring spectral changes in light every .1 sec. When a region of the brain is activated, blood flows to that area (oxygenation) and firing neurons consume oxygen from the blood (deoxygenation). The cap allows investigators to collect data from participants who complete tasks as they are seated in front of a computer screen. Many of the effects that are related to head and body movements can be filtered out before the data is analyzed (Izzetoglu, Chitrapu, Bunce, & Onaral, 2010).

Two advantages of NIRS relate to the on-line measurement of stimulus onset and oxygenation of the regions of interest (ROI), and the measurement of brain activation while participants respond verbally to tasks. Given the level and impact of the cognitive and communication deficits of individuals with ASD, it may be informative to investigate the underlying neural activity in a more natural state. At some point in the future, increased knowledge of neural activation patterns may inform the creation of effective treatments that enhance efficient neural activation patterns and greater neural connectivity, resulting in improved performance on pragmatic, syntactic and cognitive tasks. This, in turn, could help the individual with ASD be more successful in his or her interactions, which could have important academic, social, and occupational implications.

An ASD diagnosis is based, in part, on stereotyped behavior often associated with hand-flapping, finger-flicking, rocking, spinning and self-injury. The placement of the NIRS cap could potentially pose a challenge to children with ASD due to recorded hypersensitivity (Baker et al., 2008; Baranek et al., 2007; Blakemore et al., 2006; Tomcheck & Dunn, 2007) or excess movement. Therefore, any plan to conduct NIRS with children with ASD should also include plans to desensitize the child to wearing the NIRS cap for the total time of wearing the cap (i.e., 10-12 minutes in this study).

The Study

This study was designed to assess the hemodynamic response in children with and without ASD using fNIRS as they answer questions about a social situation. The neurological scanning occurred in-vivo. The specific research questions and associated hypotheses were:

1. To what extent does a child or adolescent with ASD tolerate wearing the NIRS cap while performing a pragmatic language task as compared to typically developing children?

Some children with ASD show hypersensitivities especially the facial regions. We hypothesized that some children with ASD will need to complete systematic desensitization training, customized to their specific needs, to be able to wear the NIRS cap for the duration of the pragmatic tasks. We expected most typically developing children to be able to tolerate the cap without desensitization training.

2. *To what extent do children with ASD and typically developing, age-matched children differ on behavioral responses to a verbal pragmatic language task?*

We hypothesized that children in both groups will be able to verbally respond to the scenarios presented via audio and visual stimuli. Children in the control group should respond in age-appropriate ways, while children in the ASD group should display difficulties verbalizing appropriate solutions to each social scenario, especially for the later occurring items.

3. *Are there differences between children with ASD and typically developing children in their response time (RT) during a pragmatic judgment task?*

Response time for language tasks has been shown to be comparable for individuals with ASD. We therefore anticipated that the behavioral response time data would reveal comsparable activation times.

4. *Are there differences between children with and without ASD in brain activation patterns observed in four cerebral regions of interest (DLPFC, OFC, ST, IPL) as they complete a pragmatic language task*? This question had two parts:

4a. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI's for the first 25 responses?*

4b. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI's when comparing accuracy of responses (correct vs. incorrect)?*

We hypothesized that there would be decreased hemodynamic responses for individuals with ASD. We further anticipated there to be lesser activation in the four identified regions involved in pragmatic language (DLPFC, OFC, STG and IPL). We hypothesized that we would see a difference in hemodynamic responses based on the accuracy of the response.

CHAPTER II

METHODS

Participants and Pretesting

After receiving approval from the Institutional Review Board at Utah State University regarding this study, we recruited participants through the Center for Persons with Disabilities (CPD). Flyers (see Appendix A) were distributed at the CPD and sent to clinical staff, which forwarded them to parents of children with ASD. Previous participants, who had agreed to be contacted again for further studies from our lab, were also contacted for participation in the study. Informed consent (see Appendix B) was obtained for all participants. Forty-two of children were screened for eligibility for participation in the study.

Each child completed a battery of eligibility tests that included the *Clinical Evaluation of Language Fundamentals-4* (CELF-4,; Semel, Wiig, & Secord, 2003), an the abbreviated version of the *Universal Nonverbal Intelligence Test* (UNIT; Bracken & McCallum, 1998), and the *Children's Communication Checklist-Second Edition, U.S. Edition* (CCC-2; Bishop, 2003). Nonverbal IQ was measured with the abbreviated version of the UNIT, which includes the cube design and symbolic memory subtests. Results are reported in Table 1. The abbreviated version was standardized on children between the ages of 5 and 17 years. The average reliability coefficient calculated with a split-half method and corrected by the Spearman-Brown formula lies at r = .91, indicating an excellent reliability. This test is a nonverbal measure, in

Table 1

Results From Behavioral Pretest Measures for the ASD and TD Groups

Test	Mean	*SD*	*p* value	Cohen's *d*
UNIT**	ASD: 15.90 TD: 22.50	7.031 4.161	.018*	-1.142
CELF-4**	ASD: 83.00 TD: 107.85	27.105 10.594	.018*	-1.207
CCC-2**	ASD: 39.30 TD: 92.90	12.910 8.861	.000*	-4.84
TOLD-I	ASD: 18.10 TD: 30.30	13.453 8.285	.021*	-1.092
WCJ	ASD: 9.70 TD: 12.40	4.001 2.458	.073	-0.813

*Statistically significant differences between the two groups.

which the instructions are provided only through gestures. Practice items are provided prior to the actual test, to give feedback to the child. Those children who were not able to meet basal (items 1 and 2 answered correctly) requirements on this measure were excluded from the study. All other children were required to have a score of 3 or greater to be eligible.

The CELF-4 is designed to assess the current overall language skills of individuals between the ages 5 and 21 years. The core language skills assessment of the CELF-4 includes subtests of: recalling sentences (RS), formulated sentences (FS), concepts & following directions (C & FD), word classes (WC-T), which is a composite score of receptive and expressive language; and word definitions (WD), for those children who are older than 13 years old. The subtests RS, FS, WC-T, and WD require the child to verbally respond to a given stimulus. Prior to the actual test items, practice stimuli are provided on which feedback and further explanation can be given to the participant. Children who were not able to reach the basal (three items answered correctly consecutively) requirements on these subtests were excluded from the study. The test/retest reliability for core language scores for all ages lies at the corrected correlation coefficient of $r = .92$. Internal consistency of test items for the core language score were calculated and reported for all ages to be coefficient alpha of $r = .95$, indicating an excellent internal consistency between the test items. Coefficient alpha was also reported for clinical groups. For children with ASD, the coefficient alpha values were $r = .98$ for concept and following directions, $r = .92$ for word structure, $r = .97$ for recalling sentences, and $r = .96$ for formulating sentences, indicating excellent internal consistency across all four subtest within the core language score. To be eligible for the study, children must have had a prior diagnosis of ASD and had to be able to meet the basal criteria on a pragmatic language task.

In addition, we had each child's parents complete the CCC-2 (Bishop, 2003). The CCC-2 measures children's communication skills in the areas of pragmatics, syntax, morphology, semantics, and speech. CCC-2 can be used with children ages 4 years to 16 years and 11 months who are verbal and whose primary language is English. The CCC-2 is reliable as demonstrated by Cronbach's coefficient alphas ranging from .65 to .79 for all scales averaged across all ages. In addition, test retest reliability ranged from .86 to .96, reflecting strong stability of the scores from the first to the second rating. Children were excluded from the study if the CCC-2 could not be completed because the participant was nonverbal.

Finally, each parent filled out an initial intake form with basic developmental and educational information about their child. The intake form is attached in Appendix C. The parents indicated on the intake form if an Individualized Education Plan (IEP) was in place at the time of testing. Children were excluded from the typically developing children if they had an IEP. Children were excluded from the ASD group if they no longer received special services in an educational setting.

Twelve children with diagnoses of ASD received the eligibility testing. Two children with ASD were excluded from the study. One child was excluded because he was not able to meet basal criteria on the CELF-4 during pretesting. Another child was excluded because no IEP goals were in place at the time of testing. The final group of children with ASD included 10 children between the ages of 9 and 15 years. Each child had been diagnosed with ASD according to scores on the Autism Diagnosis Observation Scale (ADOS, Rutter, DiLavore, Risi, Gotham, & Bishop, 2012). Initial diagnostic reports were obtained for the participants with ASD. Consistent with the Diagnostic and Statistical Manual of Mental Disorders: DSM-5, all children in the ASD group had a history of deficits in social communication skills, language delay, as well as restrictive and repetitive behavior.

The control group consisted of 20 typically-developing (TD) children without a diagnosis of ASD who were each age- and gender-matched to a child with ASD. Following a bracketing approach (Shadish, Cook & Campbell, 2002) we matched each child with ASD to two children who were developing typically. Ten TD participants were up to 6 months of age above the age of a participant with ASD, and

10 children were up to 6 months below the age of a child with ASD. According to Shadish, Cook and Campbell (2002), the bracketed approach to matching is an appropriate solution for increasing power in situations in which it is more feasible to find control subjects than experimental subjects. Further, bracketing is a good method for accounting for natural developmental variability between two populations of interest.

In addition to the eligibility measures, each child completed a morphological judgment task from the *Test of Language Development-Intermediate* (TOLD-I; Hammill & Newcomer, 2008) and the auditory working memory subtest of the *Woodcock-Johnson Test of Cognitive Ability* (WCJ; Woodcock & Johnson, 1989) as control measures.

We anticipated that the groups of children with ASD and TD would perform differently on the UNIT abbreviated battery, the CELF-4 core language scale, the CCC-2, TOLD-I morphological judgment task, and WCJ working memory task. We tested the hypothesis by performing independent-samples *t* tests on each measure. The test was significant for UNIT, CELF-4, CCC-2, and TOLD-I. Results were reported in Table 1.

Experimental Task

The participants answered social language questions drawn from the *Comprehensive Assessment of Spoken Language* (CASL; Carrow-Woolfolk, 1999) Record Form 2. The adapted protocol can be found in Appendix D, corresponding pictures for each item in Appendix E. Pictures were presented via a with 17" Dell computer screen. Children were seated at a desk approximately 30 cm away from the screen. The experimenter, a Speech-Language Pathologist, was seated directly to the right of each child. The experimenter provided the stimuli verbally to the children as they looked at pictures. After four practice items were completed and questions were resolved, the actual experiment began. All the children wore the NIRS cap for the actual experimental items.

After the experimenter read the question, she pushed a button, which signaled to the child that he/she could now answer the question. There was no time limit for the response. Prompts (i.e., "Is there anything else?," "Are you finished?") were only provided to the extent allowed by the standardized procedures from the CASL. Each child started with item 1 from the protocol. Questions became more difficult with the progression of the experimental task. The experiment was terminated when the child reached ceiling criteria (five consecutive items of 0). A total of 60 items were possible.

Response time during the CASL was measured using the waveform visualization function in ELAN. We marked the period of time between the tones at the end of each stimulus (i.e., "ding") until the vocal onset of the response of each participant. The start of the response was determined to be the start of their actual sentence. Filler words such as "uhm" or "uh" were ignored.

Instrumentation

We used functional near-infrared spectroscopy (fNIRS) to obtain cortical concentration values for oxygenated (HbO), deoxygenated (HbR), and total (HbT) hemoglobin (Hoshi, 2003; Obrig & Villringer, 2003). Changes in HbO, HbR and HbT are hemodynamic responses, which characterize the dynamic interplay of physiological responses that are associated with cortical activation. Hemodynamic responses are based on physiological parameters such as speed of blood flow, the local oxygen consumption, capillary recruitment and dilation or constriction of the blood vessels. Changes in concentration levels of HbO, HbR and HbT can be translated into cortical activation based on the assumption of uniform hemoglobin distribution within the scanned tissue (Firbank, Okada & Delpy, 1997). Figure 5 displays the interplay between the parameters that play into hemodynamic responses (adapted from Fantini, 2014). fNIRS particularly measures tissue concentration levels of HbO, HbR, and HbT, as well as oxygen saturation of hemoglobin (Fantini, 2002).

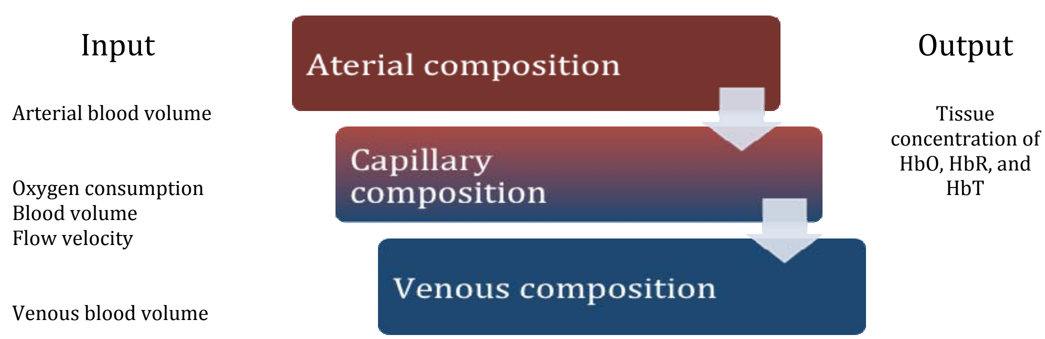


Figure 5. Parameters of hemodynamic responses.

fNIRS is a noninvasive neuroimaging technique that has the ability to map activation of the cortex up to 3 cm deep. Human tissue is relatively transparent to near-infrared light (NIR) with a spectral window of 650-1000nm. When certain areas of the brain are activated, the hemoglobin concentration changes, and with those changes the light absorption and scattering of the NIR light is altered. NIR light is emitted and detected through different colored optodes as displayed in Figure 6. Red ring (eight) around an optode signals infrared light emitters and the blue (seven) ring photo detectors. Channels are in between two adjacent optodes with a 33mm distance between the optodes.

NIR light is emitted from the source and either absorbed or scattered by the human tissue (Figure 7). Pigmented compounds, such as hemoglobin chromophore, absorb the NIR light, while surrounding tissue has scattering properties (Ferrari & Quaresima, 2012). Flexible fiber optics carry the NIR light to the optodes, which are secured into a cap. The cap is set up to capture the brain regions of interest. This set up is conducive to any head position and posture.

Figure 6. Optode set up.

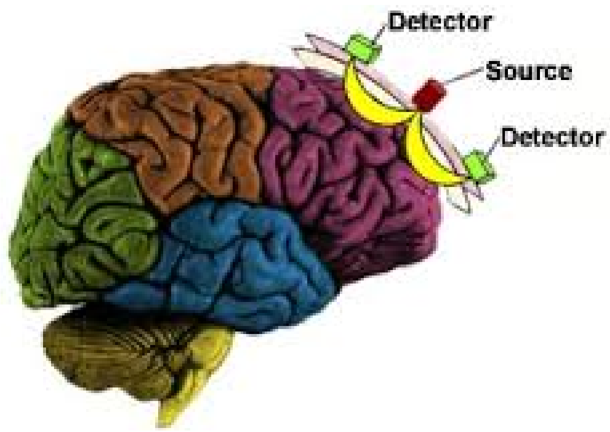


Figure 7. NIR emitters and detectors.

Continuous waveforms are created, separated into HbO, HbR and HbT. A sample of such waveforms is seen in Figure 8 (Ferrari & Quaresima, 2012). HbO specifically signals the level of oxygenated blood in a certain area. Increases in HbO indicate increased activation. HbR signals deoxygenated blood concentration levels. Decreased HbR signals increased activation. HbT is the sum of HbO and HbR. Bigger HbT values suggest higher activation in those cortical areas (Ferrari & Quaresima, 2012; Scholkmann et al., 2014).

Even though fNIRS cannot measure subcortical structures, it has several advantages over functional Magnetic Resonance Imaging (fMRI) and Positron Emissions Tomography (PET). As noted above, fNIRS employs optical properties with near-infrared light sources that reflect off of hemoglobin flowing through the blood vessels in the cortical structures, instead of having to employ radioactive or magnetic instrumentation. Due to the frequent measurements (every 1/10 of a second) the changes in hemodynamic responses has a better temporal resolution than fMRI or PET. The participant is seated comfortably at a desk, with few mobility restrictions, but no noise disturbances, making the testing situation more natural. Functional NIRS is further less susceptible to motion artifacts. Motion artifacts still occur in different shapes, frequencies and timings, but certain techniques have been developed to account for those, making fNIRS more suitable for difficult-to-scan populations, such as children with ASD. Motion artifacts can be due to head movement, but also movement of other facial muscles. In post-processing, inherent changes in amplitude and frequency of the signal are filtered after a principal component analysis (PCA), correlation-based signal improvement (CBSI), and wavelet filtering (Brigadoi et al., 2014).

Data was recorded with a continuous wave system (ETG 4000, Hitachi Medical Co., Japan; see Plichta et al. (2006) for a comprehensive description). The optodes were placed into two 3x5 probe sets that were secured with elastic bands. Each set had 22 channels that were recording the data.

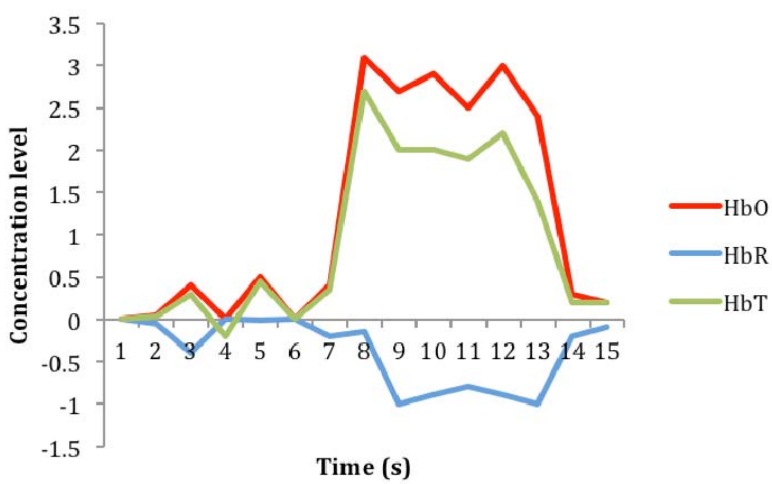


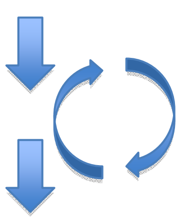
Figure 8. Activation pattern for HbO, HbR and HbT.

The experimental stimuli were presented using a Dell PC desktop running WindowsXP®, running with E-Prime Stimulus Presentation Software (Schneider, Eschman, & Zuccolotto, 2002). E-Prime is a software package specifically designed to administer experiments that are computerized. It was temporally synched with the raw data recording from the NIRS equipment. E-Prime programming included markers to identify specific time periods that were of interest for our data analysis. We set stimulus markers (F markers), indicating when a stimulus started. These markers ideally mapped onto NIRS data for real-time events. Table 2 explains the detailed markers.

In order to acquire time stamps for each participant, we recorded all sessions with digital video equipment. At the conclusion of the experimental session the video was uploaded and converted to .wav format. We then identified time stamps and real-time events with EUDICO Linguistic Annotator v. 4.7.3 for Windows (ELAN, Hellwig, Van Uytvanck, Hulsbosch, Somasundaram, & Tacchetti, 2011).

Table 2

E-Prime Marker Descriptions

Marker	Time period
F1	Starting rest onset
F2 	Stimulus presentation onset: repeated until ceiling or last item is reached
F3	Stimulus presentation offset/response onset: repeated until ceiling or last item is reached
F4	Ending rest onset

3D Magnetic Space Digitizer

ELAN was employed to identify processing time for all participants. Processing time is the time period between the end of the experimental stimulus and the onset of the response provided by the participant.

Head shape and size varies among individuals, resulting in some degree of variability in the relationships between the fixed optode locations in our caps and the cortical structure covered by each NIRS channel. The FASTRAK, Polhemus (Tsuzuki & Dan, 2014) was used to assess the location of each channel. For accurate comparison between participants, the functional regions of interest (fROI) needed to be registered. The fROI's determined from the literature cited above were the orbitofrontal cortex, dorsolateral prefrontal cortex left and right, left superior temporal areas, and left inferior parietal lobule. Because of the varying head sizes and shapes, the locations of the optodes in the caps fluctuated slightly among participants. We accounted for individual variance in the registration of channels for the corresponding fROI's using the Montreal Neurological Institute (MNI) standardized neurological coordinate system (Okamoto et al., 2004).

Measurements yielded channel locations with corresponding fROI's (Singh, Okamoto, Dan, Jucak, & Dan, 2005). We correlated each channel location with the brain regions of interest. After the regions were registered with the Polhemus, we extracted Brodmann's areas for each channel. Multiple channels measured hemodynamic responses for one region of interest (ROI). Those ROI's were averaged beta-weights from the channels that covered more than 66% of that area.

A list of the channels for each ROI is displayed in Table 3.

Table 3

Channel Locations for Each ROI for Each Participant

Participant	DLPFC left	DLPFC right	OFC	STC	IPL
A06	27, 32, 41, 42	26, 38, 39, 43, 44	24, 25, 28	3, 4, 12	20, 16, 21
A08	18, 27, 32, 36, 37	26, 34, 38, 39, 44	25, 24	2	10, 11, 15, 16, 20
A09	36, 37, 41	34, 38, 43	23	2, 3, 7, 11	19
A11	27, 32, 37, 41	38, 39, 44	24, 25	07, 3	11, 12, 16, 20, 21
A12	37, 41, 42	38, 39, 43	23, 25	12, 2, 3, 7, 11	Not captured
A13	27, 41	35, 39, 43	23, 24, 25	12, 16, 2, 3, 7, 8, 11	21
A14	27, 32, 37	34, 38, 39, 44	25	8, 12, 16, 3, 7	20, 21
A25	27, 41	31, 43, 44	24, 25, 28, 30	12, 2, 3, 4, 7, 8, 16	21
A26	36, 41, 42	35, 39, 43	23, 25,	2, 3, 7, 11	19, 20
A28	27, 32, 37, 41	26, 34, 38, 39	23	07, 11, 2, 3	15, 16, 20, 21
C15	27, 32, 37, 41, 42	35, 39, 43,	24, 25	07, 11, 3	15, 16, 21, 20
C16	36, 41	30, 34, 38, 42, 43	23, 24	12, 06, 2, 3, 7, 11	Not captured
C17	27, 32, 37, 41, 42	43	24, 25	02, 26, 3, 7	15, 16, 20, 21
C18	27, 41, 42	35, 39, 43	23, 24, 25	7, 2, 26, 3, 11	15, 16, 19, 21, 20
C19	27	35, 39	24, 25, 28	11, 02, 3, 7	19, 20
C20	27, 32, 37	38, 39, 44	23, 24, 25	3, 7	15, 16, 20, 21
C21	28, 33, 38	31, 35, 39, 44	24, 26	3, 4, 8	16, 17, 20, 21
C22	27, 41, 42	35, 39, 43	24, 25, 28	08, 02, 3, 7	15, 20, 21
C23	32, 36, 37, 41	30, 33, 34, 38, 39, 44	23	08, 3, 4, 7	15, 16, 20, 21
C24	27, 32, 37, 41, 42	35, 38, 39, 43	24, 25	2, 3, 7, 8, 12, 16	20, 21
C27	27, 41, 42	31, 35, 39, 43	24, 25, 28	7, 8, 3	15, 16, 20, 21
C29	27, 37, 41, 42	39, 43	24, 25	7, 3	15, 16, 20, 21
C30	27, 32, 37, 39, 41, 42	31, 35, 38, 43, 44	24, 25, 26	12, 3, 8, 16	20, 21
C31	27, 32, 37, 41, 42	31, 43, 44	24, 25, 30	7, 3	11, 15, 16, 20
C33	37, 41, 42	32, 43, 44	24, 25, 30	12, 3, 4, 7, 8	20, 21
C32	32, 37, 38, 41	39, 43, 44	24, 25	3, 4, 7, 8	16, 20, 21
C35	32, 37, 41, 42	31, 35, 39, 43, 44	24, 25	3, 4, 8, 12	20, 21
C37	42	40, 43, 44	24	3, 4, 8, 12	20, 21
C38	41, 42	31, 39, 43	25	2, 3, 7, 8, 12, 16	20
C39	36, 41	42, 43	23, 24, 25	2, 3, 7, 11	20, 21
C40	32, 37	38, 39, 43	25	3, 8, 12	21

Cap Desensitization

Prior to initiating the study, we gathered information from each child's parents about potential hypersensitivities. This was done regardless of a diagnosis of ASD. Irrespective of reported hypersensitivities, each of the participants received a tour of the testing room, the instrumentation, and cap set-up. They were further provided with a child-appropriate explanation of the capping procedures, as well as the measures that were gathered. At the conclusion of the experimental session, duration under the cap was determined, via video recordings from a Sony® digital video recording device.

One mother reported concern of her child's ability to wear the cap for the entirety of the session. For this child we developed an individualized desensitization procedure, which included a Brief Multiple-Stimulus Without Replacement (Brief MSWO) preference assessment (Higbee, Carr, & Harrison, 2000) and token economy system. We initially interviewed the mother about potential toys that could function as a reinforcer for the child. Five of those toys were selected and placed in front of the child prior to each session. The toys were placed on a table at equal distanced from each other in front of the child and instruction of "pick one" was given to the child. The item, which was chosen first, was recorded. After the child had chosen one item, the remaining four items were rearranged and placed in front of the child again with the same succinct instruction "pick one." The item that was picked this time was also recorded. This was repeated until all five items were gone. The entire procedure was completed three times. Each rank was recorded each time, and the ranks were added. The lowest sum was determined to be the highest preferred item and was used as the reinforcer for the session. The reinforcer was placed in front and out of reach of the child during the remainder of the session.

In addition to establishing an item that could function as a reinforcer, we introduced a token economy. A sheet with ten boxes was placed in front of the child. The data sheet that was used for the Brief-MSWO and the token economy is attached in Appendix F. A box was checked after a time period, which was determined at the beginning of each desensitization and scanning session. The time period varied depending on the progression of the desensitization. The timer was placed in front of the child to track the time. When all ten boxes were checked, the cap was taken off the child and the reinforcer was delivered. During the first desensitization session, the cap was placed on the child's head without any optodes placed. Each box represented one minute of wearing the cap.

The child was seated in a chair facing the computer screen to familiarize him with the actual scanning session. The experimenter was seated next to the child, asking questions. This setup approximated the actual experimental session as closely as possible. This arrangement was consistent throughout all sessions. During the second session, the cap was placed on the child's head for the first 10 minutes without any optodes, but the time for each check of the box increased to two minutes per checkmark for the first five boxes. For the remainder of the boxes, half of the optodes were placed into the cap and the time to earn a check mark was lowered to one minute. The third session was started with half of the optodes placed in the cap. The first five boxes were checked after two minutes elapsed. We then added the remainder of the optodes to the cap and placed it on the child's head. A checkmark was earned after each minute of wearing the cap for an entire minute. During the fourth sessions the child was able to wear the cap for a total of 10 minutes with all optodes in place. This time period was the approximate time that was previously determined to be necessary to answer at least 30 items on the experimental task. We therefore determined that the child was sufficiently prepared for participating in the actual fNIRS session.

Neural Imaging Procedure

After the desensitization to the cap with the optodes, we further practiced registering cap placement with the Polhemus (see procedures described above). We had the child switch chairs to sit closer to the Polhemus magnet. The cap without optodes was still on the child's head. Complete 3D spatial registration procedures are described hereafter. It is important to note though, that the participant has to hold completely still during the registration process. We practiced the procedure and completed all the steps that would be done during the actual session. While the registration was not accurate during the first desensitization session, we were able to get accurate results during session three.

Practice

Prior to the actual neuroimaging, the participants completed a practice procedure to familiarize them with the tasks that will occur during the recording session. During practice, the cap was not placed on the participants' heads. The participants were exposed to a shortened resting state (30 seconds) and the practice items of the CASL pragmatic judgment task. Any question that a participant had were resolved during this time. The stimuli were presented in the same manner as during the actual scanning session to hold those variables constant. It gave the children the opportunity to receive clarification about any potion of the tasks that were unclear. The caps were placed on each participant's head after successful practice.

Cap Placement

The lasers were warmed up and the optodes placed into the cap 15 minutes prior to the arrival of the participant for optimal functionality. Probe set 1 (10 series) was placed over the left tempo-parietal lobe, with the red 12 optode midline superior to the left ear and the bottom front corner directly above the canthi. Probe set 2 (20 series) was placed over the left and right frontal lobe with red 22 optode directly above the nasion. Following the placement of the probe sets, the laser were activated and the connectivity between optodes and hemoglobin was examined through Auto Gain. If all channels marked sufficient connectivity, the actual experimental tasks began. The fNIRS was armed for measurement and the actual tasks started through E-prime. Markers that were programmed into E-Prime indicated start and end time of certain periods in the procedure. E-Prime was synched to start recording simultaneously to NIRS. Placement of the cap is displayed in Figure 9.

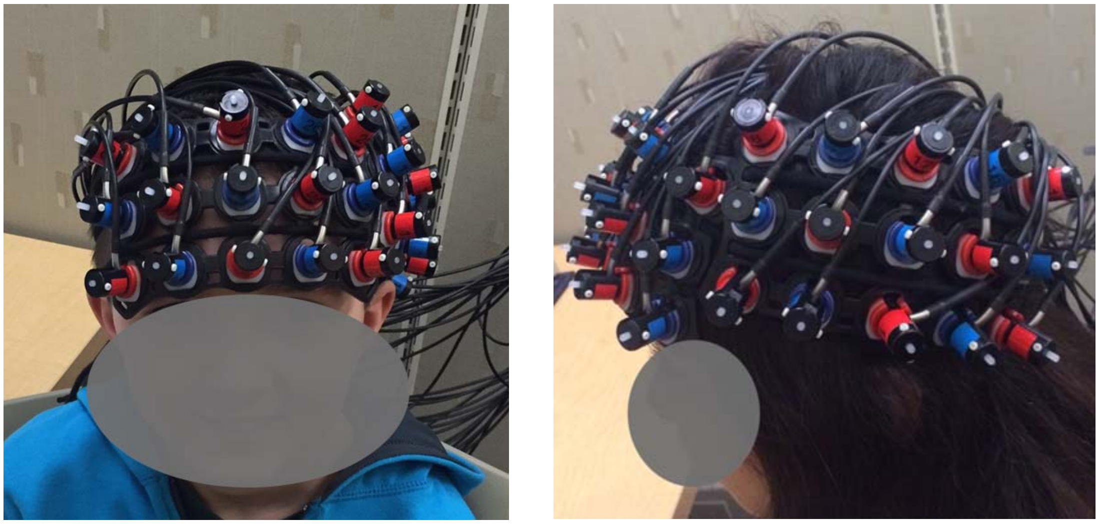


Figure 9. Placement of optode cap: Frontal lobe and left hemisphere.

Neuroimaging

Neuroimaging was conducted after cap placement was completed using Hitachi ETG-4000. The imaging period included a starting rest, stimulus presentation with verbal responses from the child and an ending rest. See Figure 10 for the progression of the tasks.

Starting Rest

Baseline measures on hemodynamic response to a visual stimulus were collected by exposing the child to a black cross (72pt. font) on a grey background on the computer monitor. Simultaneously, the child was given a squeeze ball and instructed to squeeze the ball in the left hand while focusing their eyes on the cross and clearing their thoughts. Duration for this starting rest was 60 seconds.

Figure 10. Progression of events during the experiment

Stimulus Presentation

The CASL has a total of 60 items. A minimum of 25 items was administered to each participant while they were wearing the cap regardless if they had reached ceiling criteria (five consecutive items of 0 points). Only one participant (A12) hit ceiling criteria before item 25. He still continued to wear the cap until item 25 was reached. If a child reached ceiling at item 25 or before, neuroimaging was terminated after the response to item 25. If ceiling criteria was not met at that point, we continued the neuroimaging session either until ceiling criteria was reached, or if the child reported discomfort to wearing the cap. See Table 4 for an overview of how many items were answered while under the cap.

The entire session was recorded digitally with video equipment for later analysis of behavioral data and ELAN coding of onsets and durations, which were necessary for processing the raw fNIRS data.

Jitter Rest

Between each experimental item a jitter rest was inserted with a length of 2-6 seconds. The length was randomly determined with a computerized random number generator. The purpose of the jitter rest was to decrease the effects of anticipating when a new item would be presented.

Table 4

Last Items on the CASL Under the Cap for Each ASD Participant and Their Two TD Matches

ASD participant	DOB	Last CASL item	TD match	DOB	Last CASL item
A06	1/7/2003	39	C33	5/27/2004	40
			C24	10/8/2003	48
A08	1/7/2003	60	C23	3/20/2003	48
			C20	1/4/2003	52
A09	9/27/1999	44	C18	8/6/1999	60
			C27	12/2/1999	60
A11	4/6/2002	41	C35	7/18/2002	60
			C19	10/6/2001	60
A12	4/6/1999	25	C37	5/6/1999	60
			C31	1/1/1999	60
A13	11/17/2002	30	C40	12/30/2002	50
			C38	10/19/2002	45
A14	5/5/2005	32	C16	8/22/2005	56
			C17	11/9/2005	53
A25	5/22/2002	51	C32	1/22/2002	60
			C39	11/25/2002	42
A26	9/9/2000	49	C15	6/3/2000	60
			C30	2/12/2001	60
A28	6/9/2002	44	C29	1/12/2002	60
			C22	12/12/2002	60

Ending Rest

This resting period signaled the end of the experimental task. It was designed with the same stimulus and length as the starting rest, with comparable purpose. This ending rest served as a second indicator of hemodynamic response levels for a task with no language or problem-solving elements.

Optode Placement Registration

After the conclusion of the ending rest, the laser was turned off and the actual optodes were removed from their place in the cap. The cap itself was left on the head. The midpoint of the head was determined by measuring the distance between the nasion and inion and dividing by 2 and then measuring the distance between the two preauricular points and dividing by 2. A magnet was placed exactly over the midpoint. The Polhemus was then placed at exactly 10 cm distance from the inion. The participant was instructed to hold as still as possible. If that presented to be difficult, a second trained experimenter gently held the child's head in place. First, we registered the head points of Nasion, right preauricular point, left preauricular point, inion and Cz. Second, we registered the optode locations within probe set 1 and the optode locations within probe set 2. Figure 11 displays the registered channels for a typical participant.

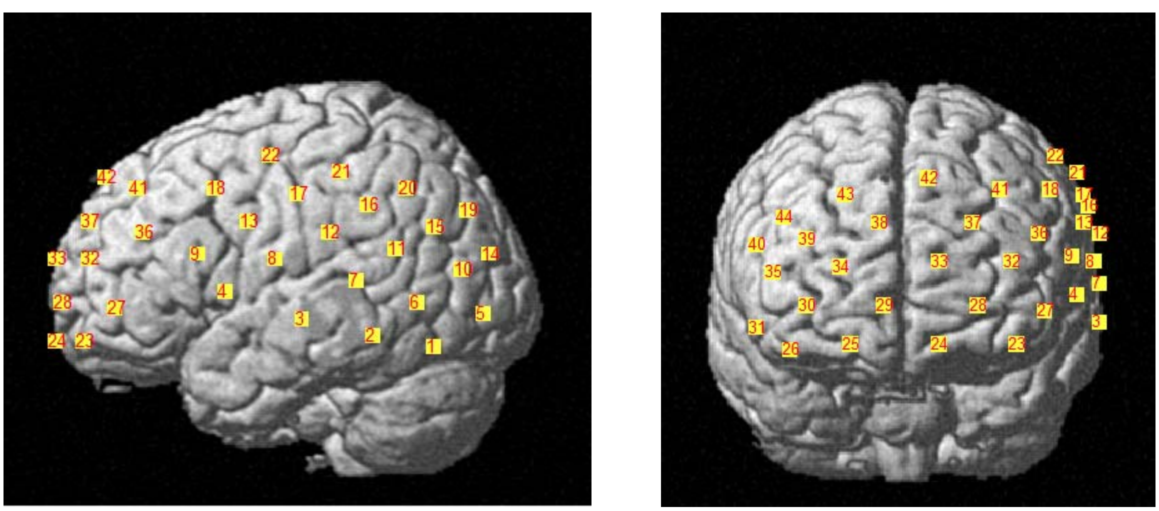


Figure 11. Registered channels.

Data Preparation

Initially, the raw fNIRS data was extracted from the ETG 4000 following each recording session. Exact onsets and durations were obtained. After corroborating the onsets and durations between E-prime and NIRS output files and establishing task specific start times as reference marks, the preprocessing for each functional scan included (a) normalization using EPI estimation; (b) spatial smoothing via a Gaussian kernel with FWHM = 6 mm; and (c) removal of linear trend and band-pass temporal filtering (0.01-0.1 Hz), which resulted in the extraction of beta-weights. Onsets and durations for each participant were attained for preprocessing to determine hemodynamic responses (oxygenated, deoxygenated and total oxygen levels) during distinctive time periods. Each set of onsets and durations was preprocessed to receive beta-weights for further statistical analysis. Beta-weights are a weighted representation of the linear slopes of hemoglobin concentration values at each channel. Movement artifacts were accounted for through discrete cosign transformation (DCT's). We extracted beta- weights for all 44 channels.

The data was analyzed for the entire epoch (stimulus, processing time, and response) for each channel for the first 25 items. That was the minimum amount of items that each participant was able to answer before the cap was removed and neuroimaging was discontinued. Since every participant was under the cap for the amount that it was comfortable to them, the amount of items under the cap varied. Some participants wore the cap until they reached ceiling requirements on the CASL (five items with a 0 score in a row). Some participants never met ceiling criteria and tolerated wearing the cap for the entire 60 items. Some participants never met ceiling criteria behaviorally, but were not able to tolerate wearing the cap for the entire 60 items. Each participant wore the cap for at least 25 test items. Table 4 lists the participant with ASD, their TD matches and which item from the CASL was last answered wearing the NIRS cap. After preprocessing, beta-weights for the first 25 items were extracted. Those beta-weights could then be used for further statistical analysis of Independent samples *t* test and mixed repeated measures Analysis of Variance (ANOVA), analyzing between-group and within-group differences. Methodology to obtain data followed the same sequence as in Research Question 4a until preprocessing. Instead of obtaining onsets and duration for the entire epoch for 25 items, onsets and durations were separated into those items answered correctly and incorrectly. The preprocessing was conducted in the same manner as described in 4a. However, we extracted beta-weights for correct and incorrect responses. Those beta-weights could then be used for further statistical analysis.

We again used Independent samples *t* test and mixed repeated measures analysis of variance (ANOVA), analyzing between-group and within-group differences. The formal research questions were as follows.

1. To what extent does children between the ages of 9-15 years with ASD tolerate wearing the NIRS cap as compared to typically developing children?

2. To what extent do children with ASD and typically developing, age-matched children differ on behavioral responses to a verbal pragmatic language task?

3. Are there differences between children with ASD and typically developing children in their behavioral reaction time (RT) during a pragmatic judgment task?

4. Are there differences between children with and without ASD in brain activation patterns observed in four regions of interest (DLPFC, OFC, STG, IPL) as they complete a pragmatic judgment task?

a. Are there differences between children with and without ASD in brain activation patterns observed in four ROI's when comparing the first 25 items?

b. Are there differences between children with and without ASD in brain activation patterns observed in four ROI's when comparing accuracy of responses (correct vs. incorrect)?

CHAPTER III

RESULTS

The purpose of the study was to assess neural activation patterns as children and adolescents with ASD and their typically developing controls perform functional pragmatic language tasks. This chapter is organized according to the four research questions that motivated the study.

Research Question 1

The first research question was: *To what extent does a child or adolescent with ASD tolerate wearing the NIRS cap while performing a pragmatic language task as compared to typically developing children?*

All children in both groups were able to wear the fNIRS caps while they responded to a minimum of 25 experimental items. Children in the ASD group had a duration under the cap that ranged from 10.48 to 26.63 minutes with a mean of 19.51 minutes and a standard deviation of 6.48 minutes. The range of duration under the cap for the TD group was 14.25 to 29.87 minutes, with a mean of 21.57 minutes and a standard deviation of 3.76 minutes. The length of time that the fNIRS cap was tolerated during the experimental procedure did not differ statistically for the two groups, $t(12.289) = -.93$, $p = .37$, $d = .39$. See Table 5 for minutes under the cap for each participant.

One child in the ASD group required desensitization training in order to tolerate the fNIRS optode caps during the imaging procedure. The progression of

Table 5

Time Under the Cap in Minutes Displayed As Decimals

ASD	Time under cap	TD Match	Time under cap
A06	14:50	C33	25:58
		C24	20:01
A08	26:38	C23	N/A
		C20	29:52
A09	26:02	C18	20:36
		C27	19:59
A11	25:17	C35	20:48
		C19	21:10
A12	10:29	C37	19:50
		C31	22:41
A13	13:22	C40	16:25
		C38	16:46
A14	12:01	C16	22:32
		C17	26:01
A25	22:07	C32	22:45
		C39	14:15
A26	16:05	C15	19:43
		C30	21:46
A28	26:32	C29	22:09
		C22	26:43

cap tolerance during training is displayed in Figure 12. During the first desensitization session, this child was able to wear the cap without optodes for 10 minutes. During the next session, he tolerated wearing the cap for 5 minutes with half of the optodes in place, which was then increased to 10 minutes during the next session. The following session he was able to wear the cap for 5 minutes with all optodes in place. During the last desensitization session, he wore the cap for 10 minutes with all optodes in place. He was able to increase cap tolerance to a total of

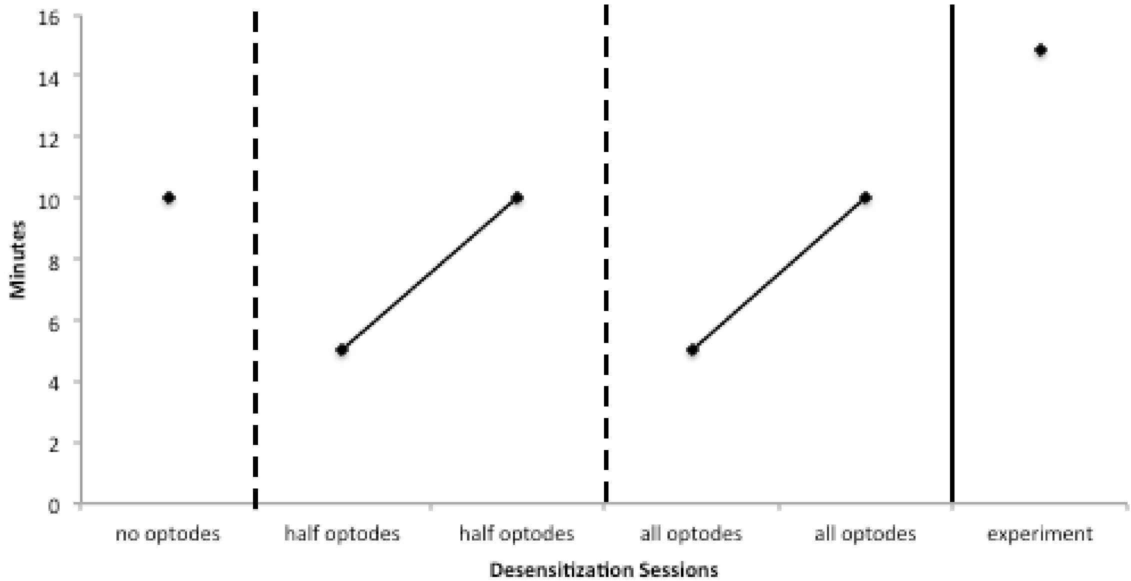


Figure 12. Desensitization progression for participant A06.

14.83 minutes during the experiment. These results suggested that both children with and without ASD in the age range of 9-15 years are able to tolerate wearing the cap for approximately 20 minutes. While children with ASD wore the cap with slightly lesser duration, they were able to successfully participate in the study. The employed desensitization procedure was also effective for at least one child for which the mother had reported hypersensitivities.

Research Question 2

The second research question was: *To what extent do children with ASD and typically developing, age-matched children differ on behavioral responses to a verbal pragmatic language task?*

An independent-samples *t* test was conducted to evaluate the hypothesis that students with ASD would score lower on a pragmatic judgment task compared to age- and gender-matched typically developing children. See Figures 13-15 for the distribution of raw CASL scores in relation to the children's ages.

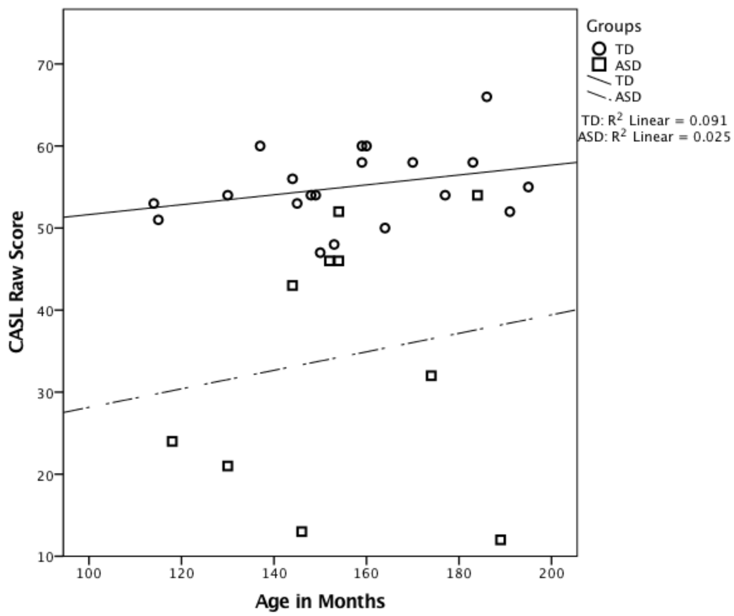


Figure 13. Scatterplot of CASL score x age with regression lines per group.

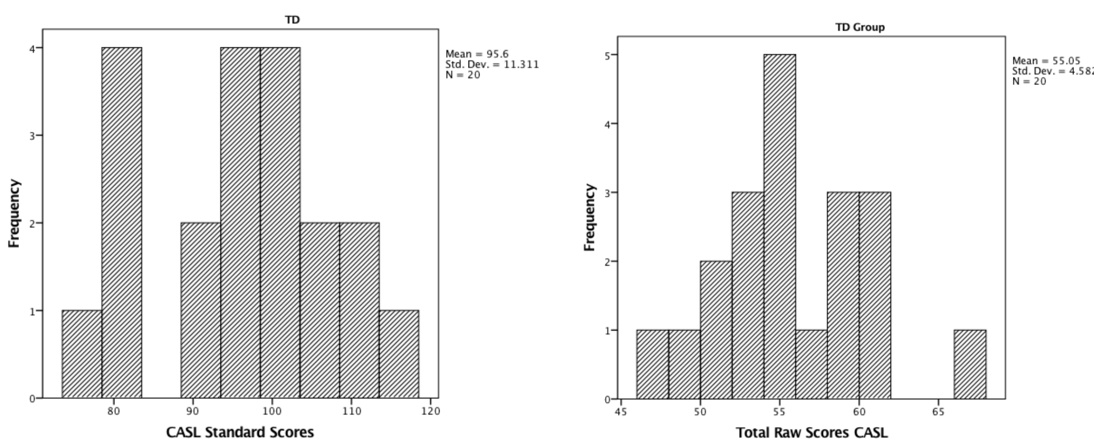


Figure 14. Histogram of CASL scores for the TD group.

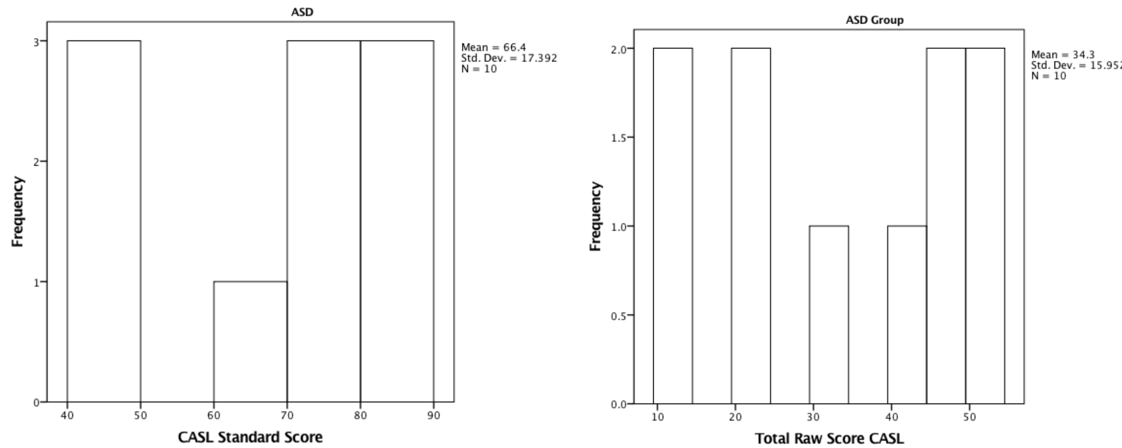


Figure 15. Histogram of CASL scores for the ASD group.

Children with ASD scored significantly lower on the pragmatic language task (M = 66.40, SD = 17.392) than children in the TD group (M = 95.60, SD = 11.311). Lavene's test for Equal Variance was significant ($p < .001$), which means that the assumption of equal variance between the two groups was not met. With equal variance not assumed, the t test was significant, $t(9.750) = -4.031$, $p = .003$, d= 1.99, supporting our hypothesis that children with ASD would present more pragmatic language difficulties than their typically developing controls. Variability between the groups differed with the ASD group presenting large variability, with standard scores on the CASL ranging from 40-81, while children in the TD group scored between 81 and 124, with only five participants scoring between 81 and 85 and the remainder scoring closer to 90 or above.

Research Question 3

The third research question was: *Are there differences between children with*

ASD and typically developing children in their response time (RT) during a pragmatic judgment task?

The average response time on the pragmatic language task was 1.46 seconds (*SD* = 1.07) for the ASD group and 1.1 seconds (*SD* = .793) for the TD group (see Figure 16). An independent samples *t* test was not statistically significant, $t(28) = 1.04$, $p = .307$, $d = -.38$, meaning that the hypothesis that the children with ASD needed more time to process and respond to the questions was not confirmed.

It is possible that children in one or both groups took more time to answer questions when they were inaccurate. To test this possibility, we conducted a mixed-effects ANOVA with Accuracy (correct vs. incorrect) as the within-subjects factor, Group (ASD vs. TD) as the between-subjects factor, and response time as the dependent variable. Figure 17 shows the accuracy by group graphs. The group main effect was not significant. There was a main effect for accuracy, $\Lambda = .536$, $F(1, 28) = 24.203$, $p = .000.$, $p\eta^2 = .464$, indicating that children and adolescents in both groups

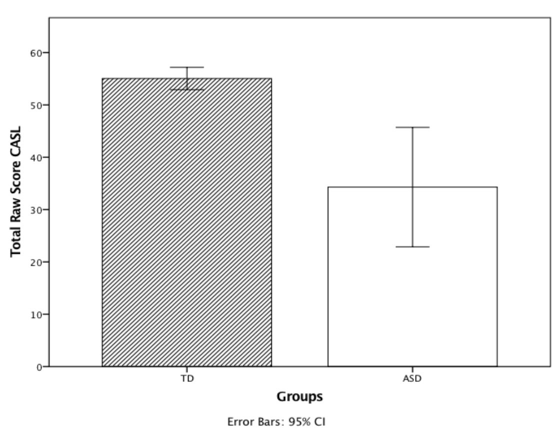


Figure 16. Total CASL pragmatic language scores for the TD and ASD groups.

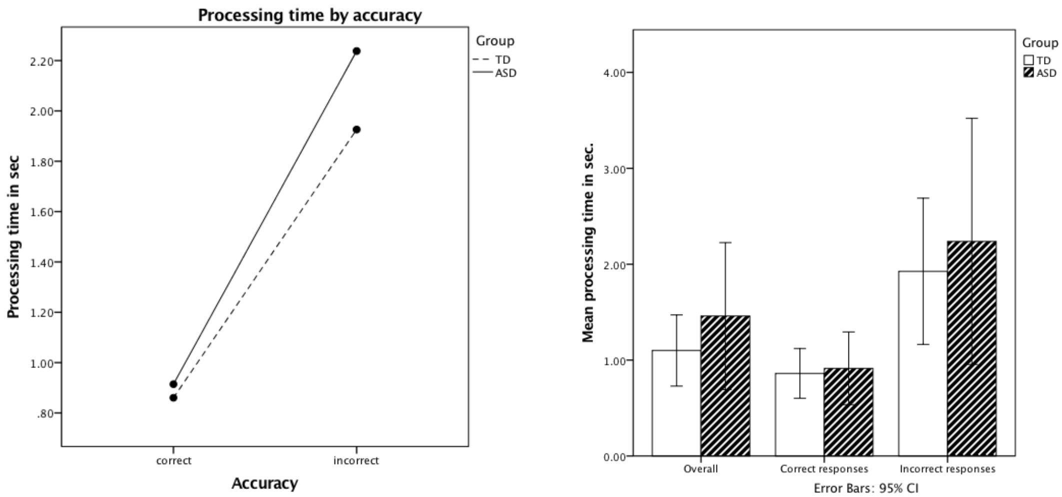


Figure 17. Response time by group x accuracy.

had longer response times for questions that were answered incorrectly (the more-difficult questions for each child). The Group x Accuracy interaction was not significant.

Research Question 4

The fourth research question was: *Are there differences between children with and without ASD in brain activation patterns observed in four cerebral regions of interest (DLPFC, OFC, ST, IPL) as they complete a pragmatic language task*? This question had two parts:

4a. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI's for the first 25 responses?*

4b. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI's when comparing accuracy of responses* *(correct vs. incorrect)?*

fNIRS concentration values are individualized relative to each participant's brain at rest. The testing protocol included a 60 sec. resting period before and after the pragmatic language task. Preliminarily, we conducted a resting state analysis to determine whether the HbO concentration values for the two groups differed at the beginning or ending rest. A mixed effects, repeated measures ANOVA with Rest time (beginning, ending) as the within-subjects variable and Group as the between-subjects variable was conducted for HbO. There was a significant difference for Rest time (beginning vs. ending) for IPL, $\Lambda = .838$, $F(1, 26) = 5.037$, $p = .034$, $p\eta^2 = .162$, and DLPFC left, $\Lambda = .775$, $F(1, 28) = 8.113$, $p = .008$., $p\eta^2 = .225$. Concentration values for the ending rest were higher than those for the beginning rest in both cases. There were no main effects for Rest time, Group or the Rest time x Group interaction for the STG and OFC regions. This suggests that the ending rest was more restful, with less activation as opposed to the starting rest in IPL and DLPFC left. Since there were no significant interactions in any region, there was no need to use rest as a covariate in our subsequent analyses. There were significant differences in Rest time (beginning vs. end) for the IPL and DLPFC regions, suggesting that there were lower concentration values (indicating lower activation) in the IPL and DLPFC regions for both groups (see Figure 18).

4a. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI's for the first 25 responses?*

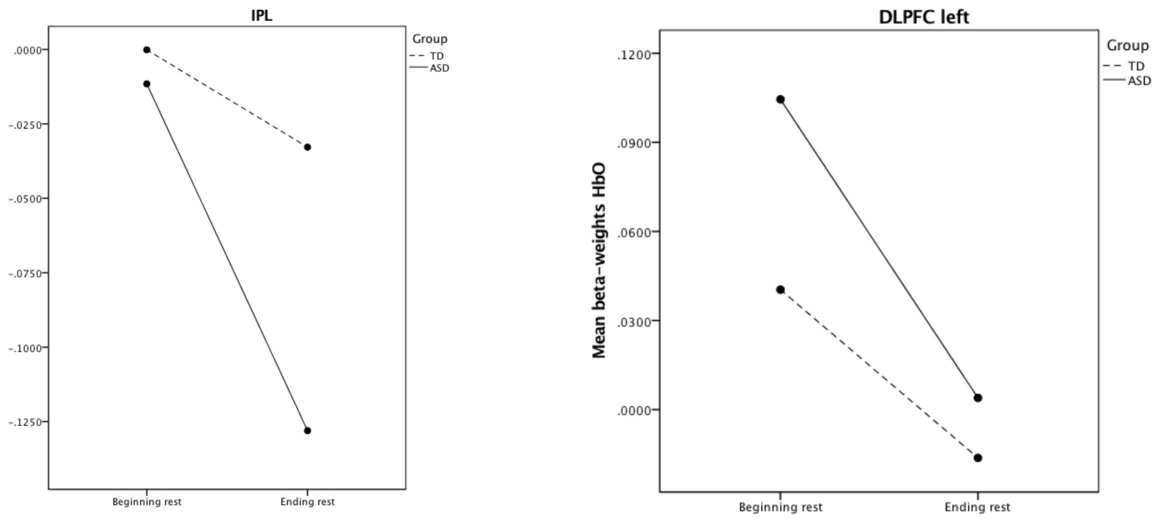


Figure 18. Beginning vs. ending rest HbO in IPL and DLPFC left.

Oxy (HbO)

A mixed, repeated-measures ANOVA was conducted using the extracted beta-weights to evaluate effects of the four ROI's, which had been previously shown to play a role in pragmatic language tasks. The within-subjects factor was ROI with four levels (DLPFC, OFC, ST, and IPL). The between-subjects factor was Group with two levels (ASD and TD). The dependent variable was HbO. For oxygenated blood concentration levels, there was a significant main effect for ROI, $\Lambda = .584$, $F(3, 24) = 5.696$, $p = .004$, $p\eta^2 = .416$. There was also a significant main effect for Group, F=(1, 26) = 10.318, $p = .003$, $p\eta^2 = .284$, with lower HbO values for the ASD group (Table 6) than the TD group (Table 6). The ROI x Group interaction was not significant.

Follow-up pairwise comparisons among the four ROIs indicated that, across the two groups, the HbO values for the STG region were significantly higher than

Table 6

Descriptive Statistics for Significant Group Effect HbO

	ASD		TD		
ROI	Mean	*SD*	Mean	*SD*	Cohen's *d*
DLPFC left	-.0829	.1326	-.0076	.0894	-.665
OFC	-.1072	.2017	.0188	.1322	-.738
STG	-.0114	.0679	.1025	.0933	-1.395
IPL	-.0660	.0816	.0136	.0757	-1.011

those of the other regions (Table 7). Our hypothesis of increased activation during a pragmatic judgment task for both groups of children in all four ROI's is partially supported for one region. Specifically, there was increased activation in the STG, but not in DLPFC left, OFC, and IPL. Across groups, our hypothesis that children with ASD activate less than children in the TD group was confirmed. Variability, demonstrated by the error bars (Figure 19), was markedly higher for the ASD group, indicating a heterogeneous ASD group.

Deoxy (HbR)

A mixed, within- and between-subjects ANOVA was conducted using the extracted beta-weights to evaluate effects of the four ROIs, which had been previously identified to be playing a role in pragmatic language tasks. The within-subjects factor was ROI with four levels (DLPFC, OFC, STG, and IPL). The between-subjects factor was Group with two levels (ASD and TD). The dependent variable was HbR. No significance was found for ROI, and there was not a significant

Table 7

Pairwise Comparison ROIs for HbO

ROI	ROI	Mean difference	Std. error	Sig.[a]	95% confidence interval for difference[a] Lower bound	Upper bound
DLPFC	OFC	-.002	.028	.957	-.060	.057
	STG	-.099*	.028	.002	-.157	-.041
	IPL	-.025	.020	.219	-.065	.016
OFC	DLPFC	.002	.028	.957	-.057	.060
	STG	-.097*	.032	.005	-.162	-.032
	IPL	-.023	.034	.502	-.093	.047
STG	DLPFC	.099*	.028	.002	.041	.157
	OFC	.097*	.032	.005	.032	.162
	IPL	.074*	.021	.001	.032	.117
IPL	DLPFC	.025	.020	.219	-.016	.065
	OFC	.023	.034	.502	-.047	.093
	STG	-.074*	.021	.001	-.117	-.032

Note. Based on estimated marginal means.
* The mean difference is significant at the .05 level.
a. Adjustment for multiple comparisons: Least Significant Difference (equivalent to no adjustments).

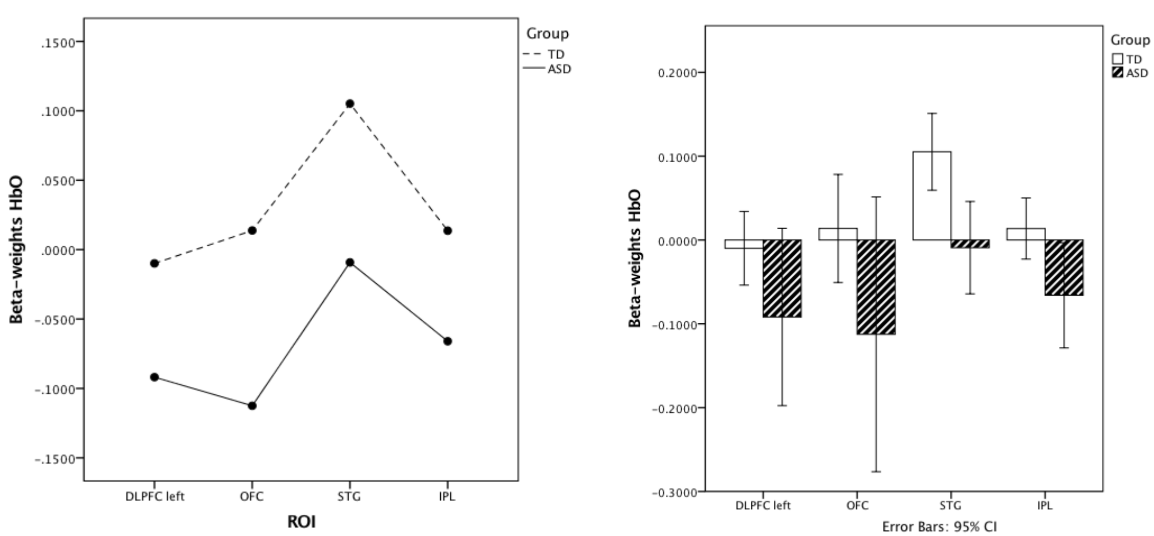


Figure 19. Means of HbO beta-weights for four ROIs for both groups.

interaction between ROI and Group. There was a significant main effect for Group, F = (1, 26) = 5.303, p = .03, pη^2 = .169, with the ASD group having lower deoxy concentration values, indicating greater activation than the TD group (see Figure 20). These findings are not consistent with our findings from HbO and HbT analysis, in which children with ASD activate less in the different ROIs. Lower HbR values mean higher activation.

Total (HbT)

A mixed, within- and between-subjects ANOVA was conducted on the extracted HbT beta-weights. The within-subjects factor was the ROI with four levels (DLPFC, OFC, ST, and IPL). The between-subjects factor was Group with two levels (ASD and TD). As for HbO and HbR, there was a significant main effect for Group, F=(1, 26) = 5.280, p = .03, pη^2 = .169, with the children with ASD earning lower HbT concentration values. Neither the main effect for ROI nor the ROI X Group

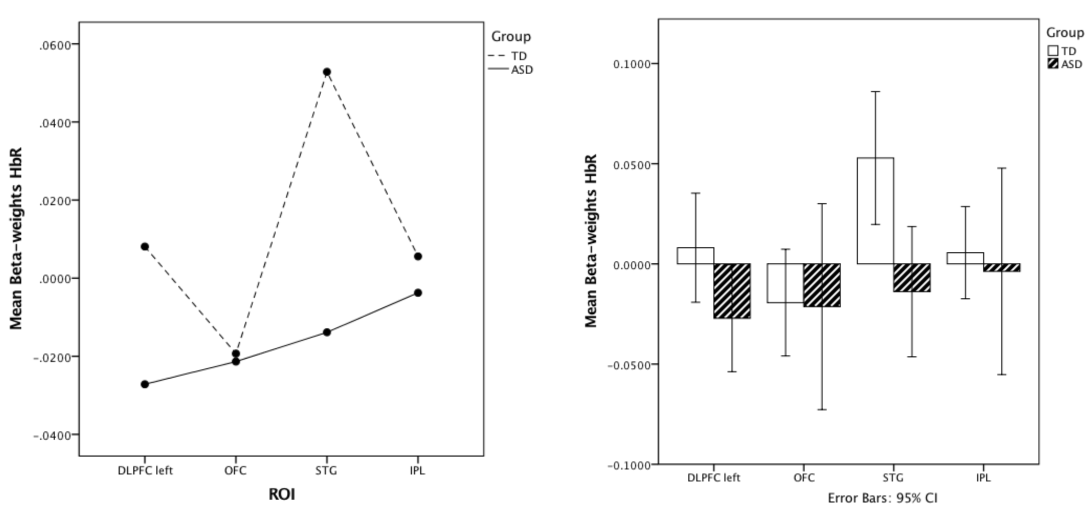


Figure 20. Means of HbR beta-weights for four ROIs for both groups.

interaction was significant. Figure 21 displays those differences. Error bars again denote high variability within the ASD group.

4b. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI's when comparing accuracy of responses (correct vs. incorrect)?*

We conducted two-way mixed ANOVA for HbO, HbR and HbT at each of the four regions of interest (DLPFC, OFC, STG, and IPL). In each case, the within-subjects factors were Accuracy with two levels (correct and incorrect), and the between-subjects factor was Group with two levels (ASD and TD).

Oxy (HbO)

There was a significant main effect for Accuracy in the OFC, Λ = .833, $F(1, 28) = 5.606$, $p = .025$, $p\eta^2 = .167$ with greater HbO values (correct: $M = -.0034$, $SD = .1133$; incorrect: $M = -.0445$, $SD = .0941$) for correct as compared to incorrect items

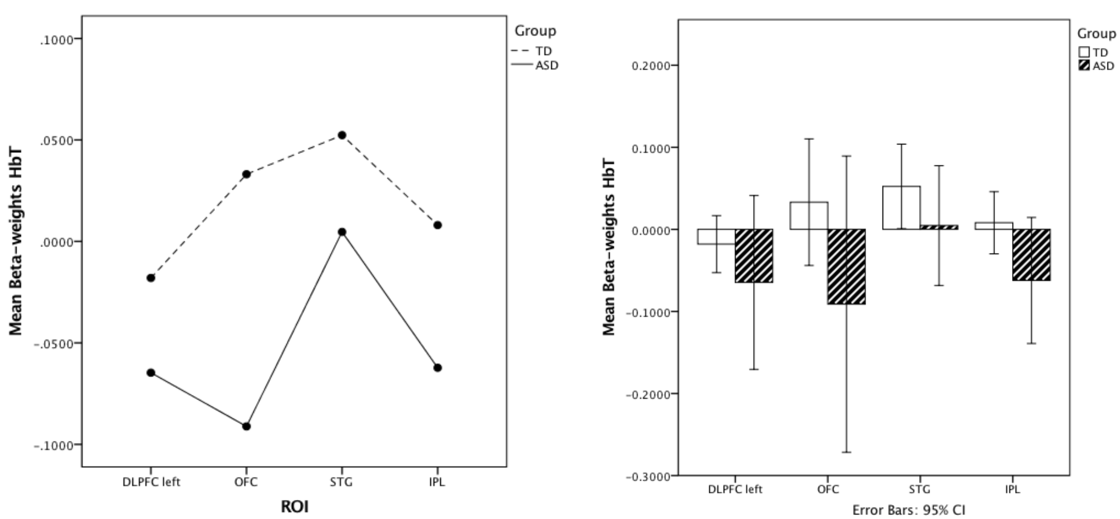


Figure 21. Means of HbT beta-weights for four ROIs for both groups.

as displayed in Figure 22. There was no main effect for Group, as well as no interaction between Group and Accuracy. For the other three ROI's (DLPFC, STG, and IPL), there were no significant main effects or interactions. These findings suggest that children, regardless of what group they are in, activate OFC more when answering questions correctly. This does not support our hypothesis that there is an increase in activation during those items that were answered incorrectly, which presumably, were more difficult for the participants.

Deoxy (HbR)

There were no significant main effects for Group or Accuracy and no significant Group x Accuracy interactions in OFC or IPL. There was a significant main effect for Group in the STG, $F(1, 28) = 4.628$, $p = .04$, $p\eta^2 = .142$, with the TD group presenting higher HbR values for both accurate and inaccurate responses. Neither

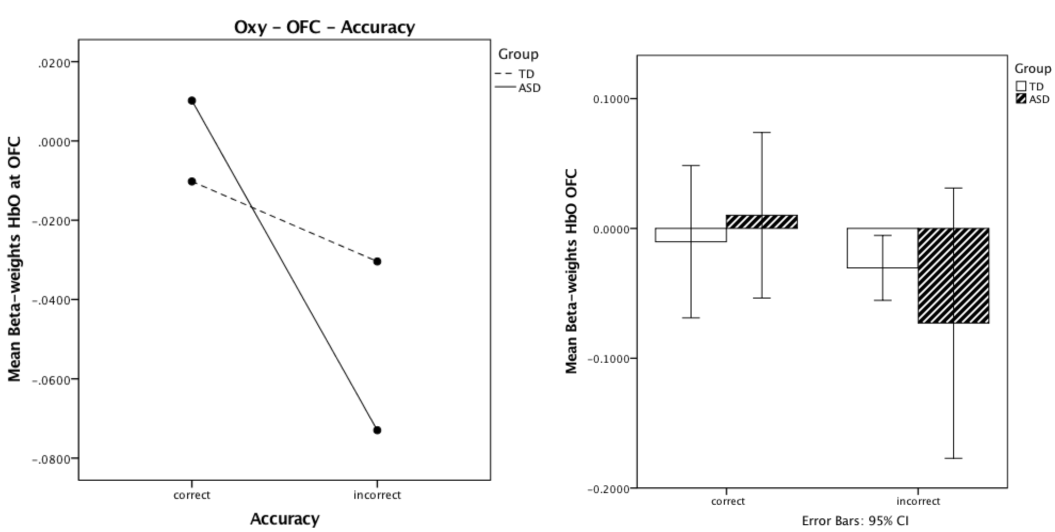


Figure 22. HbO main effect for accuracy in OFC.

the main effect for Group nor the Group x Accuracy interaction were significant. This partially supports our hypothesis that children with TD activate more in the STG (see Figure 23). There was also a significant Group X Accuracy interaction in the DLPFC left, $\Lambda = .851$, $F(1, 28) = 4.916$, $p = .035$, $p\eta^2 = .149$. The ASD group had lower HbR beta-weight values (suggestive of greater neural activation) than the TD group for the correct items (ASD $M = -.0106$, $SD = .0227$; TD $M = -.0001$, $SD = .0325$, $p < .05$) as displayed in Figure 24. The opposite finding occurred for Incorrect items, with the TD group earning lower HbR beta-weight values (suggestive of greater neural activation) than the ASD group (TD $M = -.012$, $SD = .03245$; ASD $M = .0024$, $SD = .0309$, $p < .05$). Pairwise comparison between indicate no statistically significant findings between TD vs. ASD Groups, as well as correct versus incorrect items (Tables 8 and 9).

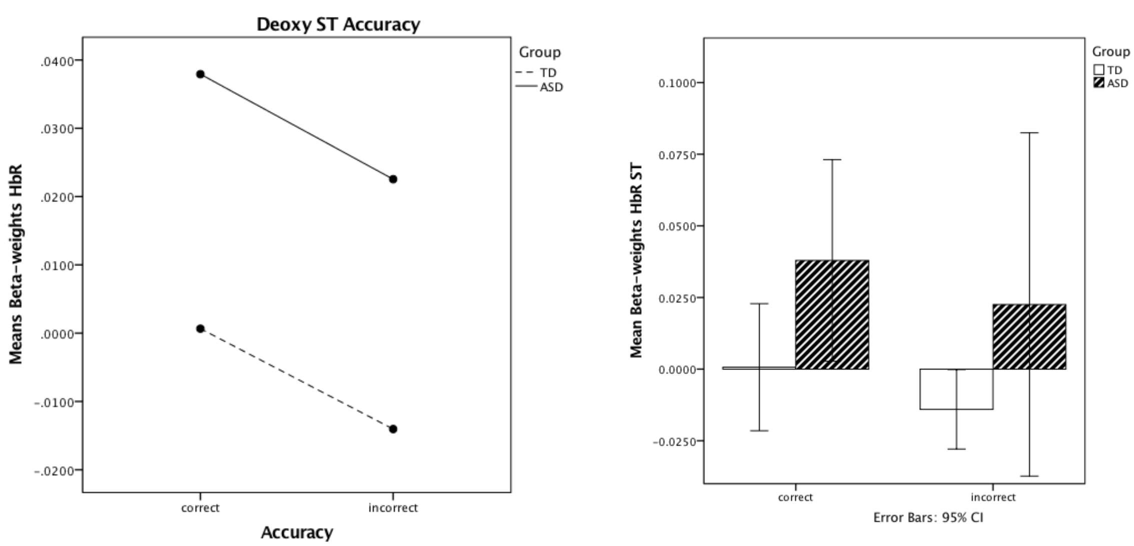


Figure 23. Mean HbR beta-weights in STG.

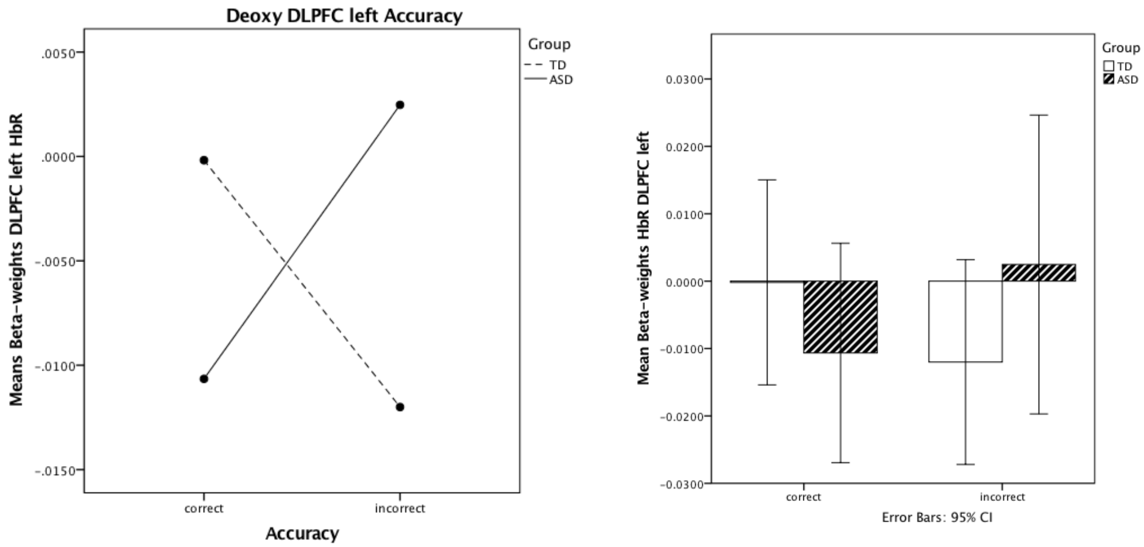


Figure 24. Mean HbR beta-weights in DLPFC left.

Table 8

Follow-Up Pairwise Comparison for Group

						95% CI for difference[a]	
Accuracy	Group	Group	Mean difference	Std. error	Sig.[a]	Lower bound	Upper bound
Correct	TD	ASD	.010	.012	.371	-.013	.034
	ASD	TD	-.010	.012	.371	-.034	.013
Incorrect	TD	ASD	-.014	.012	.253	-.040	.011
	ASD	TD	.014	.012	.253	-.011	.040

Note. Based on estimated marginal means
[a] Adjustment for multiple comparisons: Least significant difference (equivalent to no adjustments).

Total

There was a significant main effect for Accuracy in the OFC, $\Lambda = .822$, $F(1, 28) = 6.053$, $p = .02$, $p\eta^2 = .178$ with children in both groups having higher HbT values on Correct as opposed to Incorrect items (see Figure 25). There was no significant main

Table 9

Follow-Up Pairwise Comparison for Accuracy

						95% CI for difference[a]	
Group	Accuracy	Accuracy	Mean difference	Std. error	Sig.[a]	Lower bound	Upper bound
TD	Correct	Incorr	.012	.006	.079	-.001	.025
	Incorr	Correct	-.012	.006	.079	-.025	.001
ASD	Correct	Incorr	-.013	.009	.164	-.032	.006
	Incorr	Correct	.013	.009	.164	-.006	.032

Note. Based on estimated marginal means
[a] Adjustment for multiple comparisons: Least significant difference (equivalent to no adjustments).

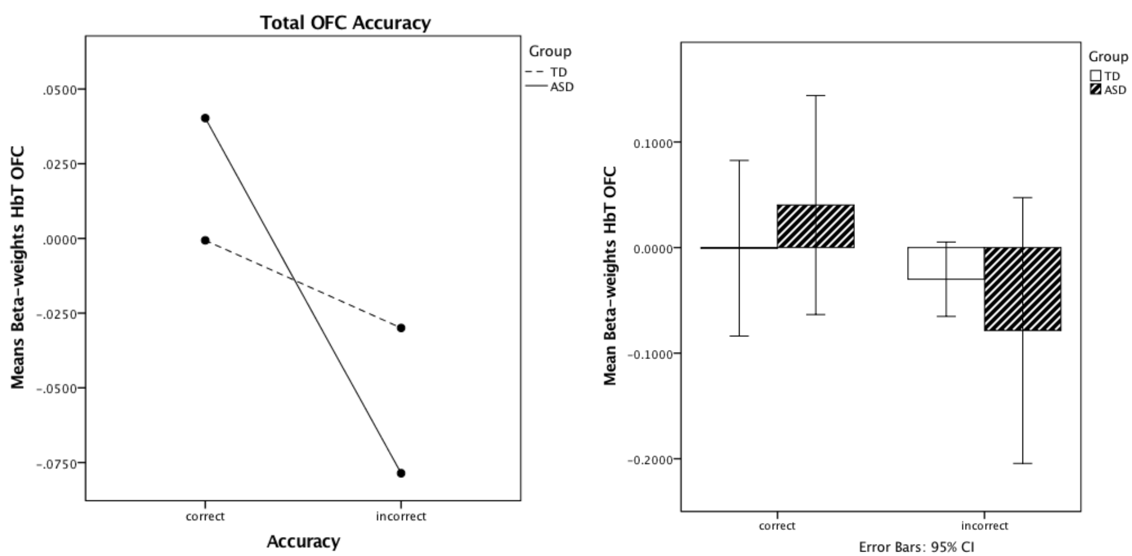


Figure 25. Mean HbT beta-weights in OFC for accuracy.

effect for Group, and no Group x Accuracy interaction. For the other ROI's, DLPFC, ST, and IPL, no significant main effects or interactions were obtained. These findings suggest that children, regardless of what group they are in, activate OFC more when answering questions correctly. This does not support our hypothesis that there is an increase in activation during those items that are answered incorrectly.

Our analysis of the beta-weights did not enable us to examine potential patterns of diffuse activation or specialization. Individual comparison with NIRS-SPM contrasts of each triad was conducted to explore the extent of variation in significant brain activity within and across all 48 channels that were covered by the NIRS caps. NIRS Statistical Parametric Mapping (NIRS-SPM) was performed for each participant individually. SPM is a method that has been used with fMRI and EEG studies. NIRS-SPM is a toolbox that analyses the raw NIRS data based on general linear modeling (GLM), to measure the output signal as a linear combination of the variable and error margins. NIRS-SPM employs a precoloring method to estimate temporal correlations of the raw data, yielding activation maps for individual participants and groups combined (Ye, Tak, Jang, Jung, & Jang 2009). Activation maps show statistically significant areas of activation displayed as t-values. We contrasted hemodynamic changes during the stimulus-response epoch in relation to the 60 sec. ending rest period.

We observed contrasts individually, taking each participant with ASD and comparing them to the averaged contrasts of his or her matches. Contrasts were performed for oxygenated blood concentration levels (HbO) only. Table 10 displays an overview of which contrasts generated significant results, with 1 indicating significance and 0 meaning nonsignificant SPM contrasts.

Table 10

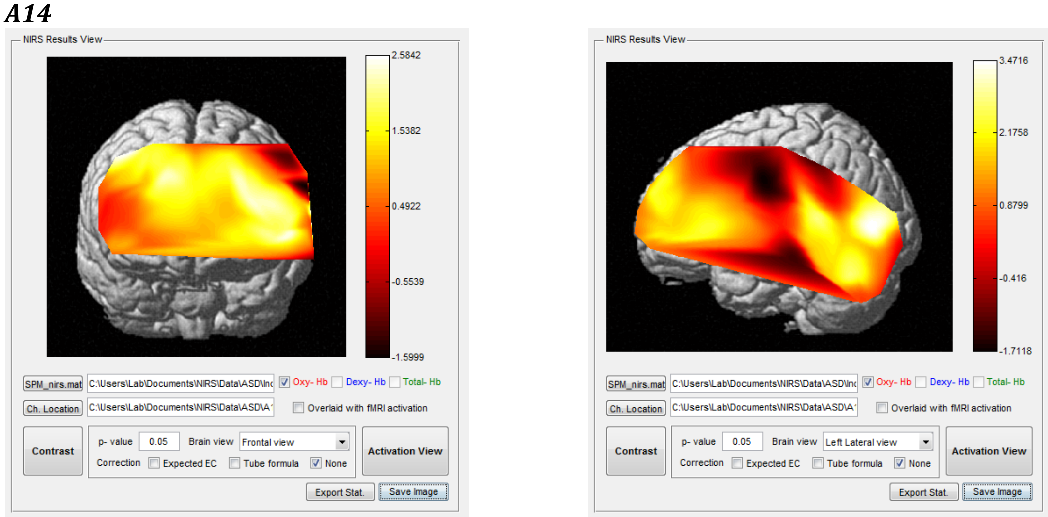
Significant SPM Contrasts for HbO

Heading	HbO front	HbO left lateral	HbO Accuracy front	HbO accuracy left lateral
A06	1	1	0	0
A08	0	1	1	1
A09	0	0	1	1
A11	0	0	0	1
A12	1	0	1	1
A13	0	1	1	1
A14	1	1	1	1
A25	1	1	1	1
A26	1	1	0	0
A28	1	1	1	1
Group ASD	0	0	0	0
C15	1	1	1	1
C16	1	0	1	0
C17	0	1	1	1
C18	1	1	1	1
C19	1	1	0	0
C20	0	1	0	1
C22	0	1	1	1
C23	1	1	1	0
C24	0	1	1	1
C27	0	0	0	0
C29	0	1	0	1
C30	1	1	0	1
C31	0	1	1	1
C32	1	1	1	1
C33	1	1	1	1
C35	0	1	0	0
C37	1	1	1	1
C38	1	0	0	0
C39	1	1	1	1
C40	0	0	1	1
Group TD	0	0	0	0

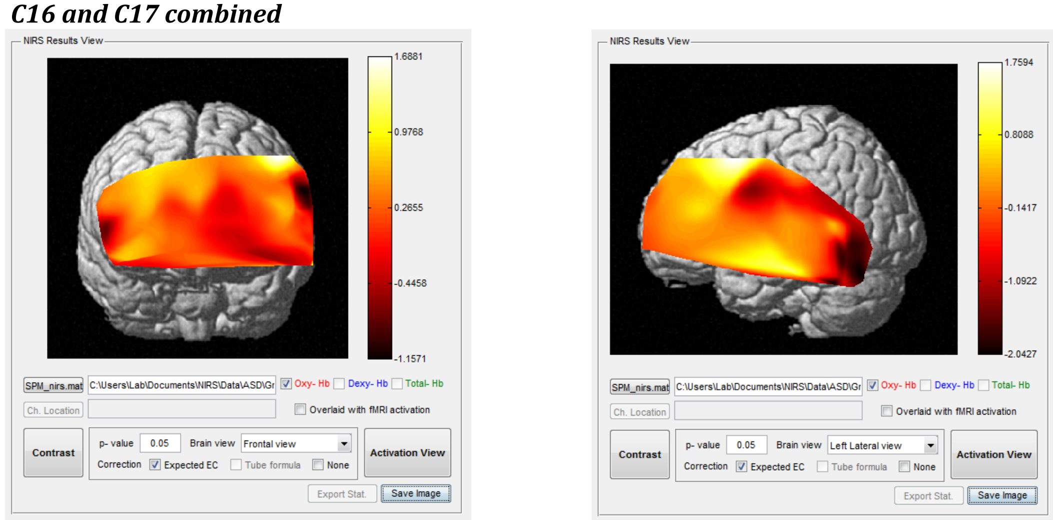
Note. HbO front = activation of the frontal lobe during the entire stimulus-response epoch for oxygenated blood concentration levels; HbO Left Lateral = activation of the left lateral brain region during the entire stimulus-response epoch for oxygenated blood concentration levels; HbO Accuracy front = contrast of activation of the frontal lobe when items are separated into correct/incorrect; HbO Accuracy Left Lateral = contrast of activation of left lateral brain region when items are separated into correct/incorrect.

A comparison of the ASD-TD triad for participant A14 is provided in Figure 26. Significantly more hemodynamic responses for the child with ASD (A14), indicated broader activation than the two typically developing peers. Matches, C16 and C17, presented no significant activation when contrasted between the ending

A14



C16 and C17 combined



Note. Contrast displayed for C16 and C17 combined, indicate no significant activation between stimulus-response epoch and ending rest period.

Figure 26. Comparison of hemodynamic responses for one triad (A14 with matches C16 and C17).

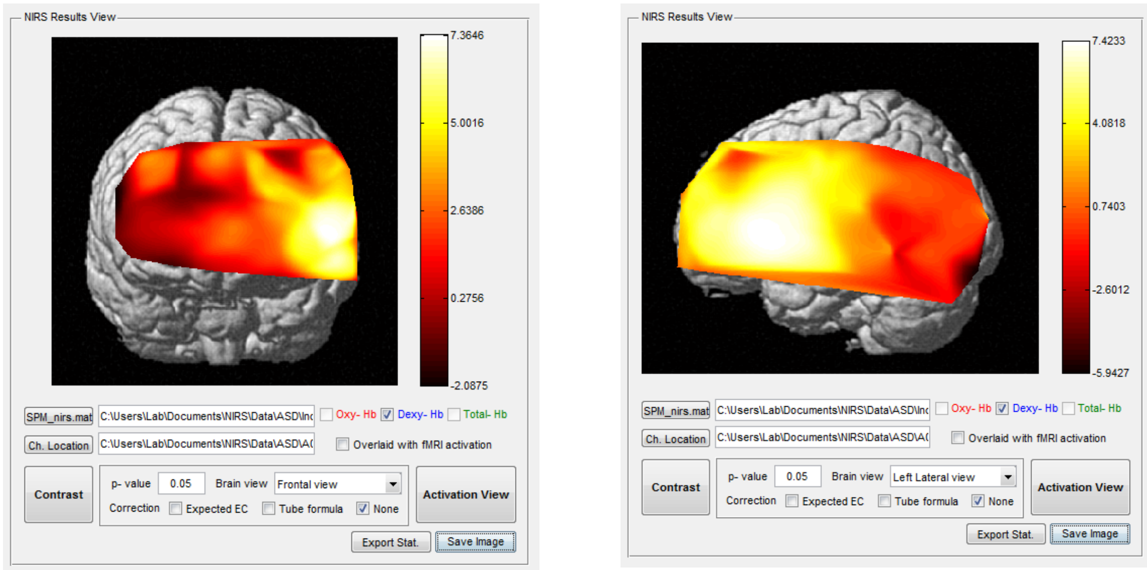
rest and the stimulus epoch for frontal lobe and left hemisphere. Increased activation could potentially be due to lack of regional specialization and a need for broader recruitment to compensate for the deficit.

Comparing at another triad involving participant A06, we see a similar pattern of wider areas of activation for the child with ASD as compared to his TD matches. Hemodynamic HbO response was substantially broader for the child with ASD in both frontal lobe and left hemisphere. The contrasts are somewhat different from the first example in that significant areas of activation occur for the TD matches as well as for the child with ASD. The spread of the activation area however is much broader for the child with ASD. Again, this could suggest recruitment of surrounding brain regions were necessary to compensate for the demands of the task (see Figure 27 for SPM contrasts).

In line with these two comparisons, 7/10 triads presented similar patterns in which a child with ASD presented broader regions of activation than the TD matches. Lack of such pattern in 3/10 triads reflects the amount of individual variation in the ASD population. Interestingly, 2 of the 3 children who did not present a diffuse pattern of activation had very low IQ scores (60 and 51). It is possible that children with lower levels of intellectual functioning have less diffuse activation because they are activating less overall. A larger ASD sample size is needed to test this hypothesis.

This study investigated behavioral and neurological differences between children with and without ASD when solving a pragmatic judgment task using fNIRS.

A06



C24 and C33 combined

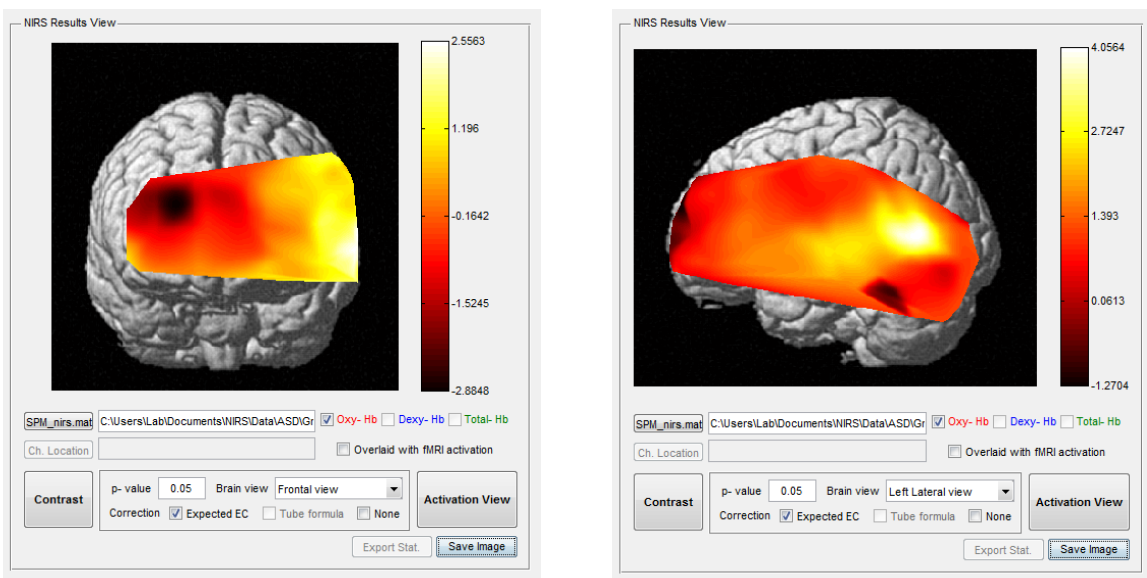


Figure 27. Comparison of hemodynamic responses for one triad (A06 with matches C24 and C33).

Initially, we asked if there is a difference across the groups (ASD vs. TD) on their ability to tolerate wearing the NIRS cap.

While all children were able to wear the cap sufficiently for the experiment, children with ASD on average wore the cap for a shorter amount of time. One child with ASD also needed desensitization training before participating in the actual study. No child in the TD group needed such preparation. There were two research questions that concerned the behavioral data collected from the pragmatic language task. Question 2 asked if there is a difference between the two groups in the accuracy of the responses to the CASL pragmatic judgment task. We analyzed the responses and conducted independent-samples *t* tests. Results showed a significant difference between the two groups aligning with our hypothesis that children with ASD score worse on a pragmatic language task. Third, we asked if there is a difference in response time between the two groups. While children with ASD respond slightly slower then TD children there was no significant difference in RT. Lastly, we analyzed the neurological data that was collected using fNIRS. After preprocessing the data in a number of different ways, we were able to extract beta-weights for the first 25 items of the CASL, as well as correct and incorrect items from the CASL for four ROI's (DLPFC left, OFC, STG, and IPL). There were main effects for Group and ROI when analyzing the same 25 items across both groups of children HbO data. Children with ASD activated less then children in the TD group. As children performed a functional pragmatic task, there was evidence of more neural activation in the STG region as compared to the other three regions (DLPFC, OFC, and IPL) When correct and incorrect items were separated, HbO and HbT beta-weights were higher for correct as opposed to incorrect items in the OFC, but not in the other ROIs. There was also a group by accuracy interaction effect for HbR beta-weights in the DLPFC left. Children with ASD had higher activation levels for incorrect items, while children in the TD group had higher activation levels when the answer was incorrect.

CHAPTER IV

DISCUSSION

This study assessed the neural activation patterns of children with and without ASD while they answered questions about social situations. Neuroimaging was conducted in-vivo, enabling functional imaging as children listened to questions, thought about their answers, and responded verbally. We used fNIRS to record oxygenated (HbO), deoxygenated (HbR), and total (HbT) hemoglobin concentration values at 100 msec intervals. Based on previous neuroimaging research, we had identified four ROIs that were likely to play a role in the responses to pragmatic language tasks. Those regions were Dorsolateral Prefrontal Cortex (DLPFC) left, Orbitofrontal Cortex (OFC), Superior-Temporal Gyrus (STG) and Inferior Parietal Lobule (IPL). We hypothesized that children with ASD would activate those areas less then children in the TD group. This hypothesis was based on the theory of frontal-posterior underconnectivity and Complex Information Processing theory. The frontal-posterior underconnectivity model suggests that individuals with ASD lack synchronization of brain regions between frontal and posterior areas (Just et al., 2012). Underconnectivity between different brain regions can cause the regions to not be integrated as well into activation patterns associated with efficient processing of information. Decreased integration could result in lesser localized activation within an isolated area. A lack of connectivity, together with lesser localized activation, may have a negative impact on a variety of complex cognitive and communicative functions, including reduced pragmatic language abilities.

According to complex information processing theory, the more complex a task is, the more regions of the brain have to coordinate their activation and synchronize their neural responses (Williams, Goldstein, & Minshew, 2006). Pragmatic language requires a high degree of integration and coordination of brain areas. A lack of coordination and integration is likely to result in decreased activation of cortical regions that are known to be active during pragmatic language tasks in children with ASD.

Previous research on the neuroscience of pragmatics, which had been conducted with a variety of neuroimaging techniques such as SPECT, PET, EEG and fMRI, has shown that DLPFC, OFC, STG, IPL, ACC and amydgala are especially involved with certain portions of pragmatic language. Unfortunately, the constraints inherent in the previously mentioned imaging procedures interfere with the ability to record neural data while participants are engaged in verbal tasks. Neural images from these systems are obtained as participants press a button and/or think about an answer to a question. Further, there are no neuroimaging studies on young children with ASD; imaging research with individuals with ASD has been limited to the study of adolescents or adults with ASD. Three important reasons for the lack of imaging research with younger individuals with ASD are the expense of imaging, the necessity for participants to lie in a confined space for an extended period of time and the need for participants to be very still during the entire imaging process. fNIRS counters all these disadvantages because it is relatively inexpensive, it can be conducted in a regular room, and data processing and filtering algorithms can better account for motion artifacts in fNIRS then with other neuroimaging instrumentation (Brigadoi et al., 2014). Children can sit at a table and can interact directly with another person while being imaged.

In our study, children with ASD and their TD controls wore optode caps that captured hemodynamic responses from the frontal lobe and left hemisphere as they responded to questions about a social situation. We were interested in how well the children tolerated the cap, the accuracy with which they responded to the questions, their response time, and the extent of their neurological activation during the pragmatic language task. The discussion of the results is organized according to the research questions. We start by reviewing the desensitization procedure and results, the behavioral findings of the pragmatic task, children response times, and their neurological activation patterns. After summarizing the results, we consider limitations of the study, implications of our results and future research directions.

Research Question 1

The first research question was: *To what extent does a child or adolescent with ASD tolerate wearing the NIRS cap while performing a pragmatic language task as compared to typically developing children?*

During a neuroimaging session with fNIRS, the optode cap must sit tightly on the head of the participant. This is necessary to emit and receive the proper signal from the NIR optodes. Hypersensitivities to touch would make it difficult for children to tolerate wearing the cap for long periods, which would interfere with the ability to collect useful data. Therefore, we had to ensure that all participants would tolerate the optode cap for the duration of the task.

Early in the description of autism, Dr. Asperger described hypersensitivities of senses, especially touch, smell and taste (Asperger, 1944; Blakemore et al., 2006). A number of techniques have been developed to decrease hypersensitivities for different senses, and to eliminate phobias and anxiety. Desensitization training refers to a procedure in which the problematic situation is analyzed into its different components. This task analysis includes environmental conditions, personnel, and a step-by-step outline of the task. The situation is then recreated with one component added at a time. Mastery at each step has to be established before moving to the next step. Desensitization has been shown to be successful for children with ASD for managing dental visits (Klein & Nowak, 1998; Luscre & Center, 1996), auditory stimuli (Koegel, Openden, & Koegel, 2004), and different types of phobias (Luiselli, 1978; Rapp, Vollmer & Hovanetz, 2006; Shabani & Fisher, 2006).

All parents were interviewed prior to the experiment regarding potential hypersensitivities. Only one mother of a child with ASD reported her child to be sensitive to touch, especially to the head. None of the mothers of children in the TD group reported that their children had hypersensitivities to touch.

Development of the desensitization procedure required a detailed task analysis. We combined desensitization with a Brief Multiple-Stimulus Without Replacement Preference Assessment (Brief-MSWO) prior to each session. The child identified a highly preferred item, which was then used as a reinforcer. A token economy system with timed intervals was used throughout. Each time-interval wearing the cap earned the child a token. At the beginning of the training the child tried to remove the cap from his head. The experimenter prevented this and reminded the child about the token system used for reinforcement. While the child was wearing the cap, he was engaged in a conversation with the experimenter. After mastery of one step, more optodes were added to the cap. At each new level the child initially voiced discomfort. The frequency of those utterances decreased with the progression of training. Finally, the child was able to wear the cap during the experiment and completed all the requirements.

The individualized desensitization was successful for this child. This meant that the child did not remove the cap from his head during the experiment. While he touched the optodes occasionally, he did not remove the cap, allowing for proper scanning to occur. During the actual experiment he wore the cap for a total of 14:50 min, which was even longer then he was trained for. The chosen highly preferred item was used as a reinforcer for earning 10 tokens.

Throughout the sessions, the experimenter asked the children if they were comfortable about every 10 trials. When a child indicated discomfort, a short rest period was initiated and the cap was removed following the resting state. Children from both groups wore the cap between 10 and 29 minutes, with an average of 20 minutes. Findings suggested that children with and without ASD between the 9 and 15 years can participate in fNIRS experiments that last between 10 and 20 minutes.

These time frames need to be taken into consideration when planning new studies.

These findings also suggest that a child with hypersensitivities can be trained to tolerate wearing the optode cap for the duration of a short experimental task. However, it may be unusual to have a sample of children with ASD in which only one individual displays hypersensitivities. This might be due to the fact that we recruited higher-functioning children with ASD.

Research Question 2

The second research question was: *To what extent do children with ASD and typically developing, age-matched children differ on behavioral responses to a verbal pragmatic language task?*

Pragmatic language problems are a core characteristic of children with ASD. These problems manifest early on their development, with some children being less responsive to their own names (Lord, 1995) or their mother's voice (Klin, 1991). Later in development, children with ASD are less likely to initiate communication speech acts with peers (Stone & Caro-Martinez, 1990). Children that are higher-functioning have similarities in abnormal language use. Difficulties include following rules of politeness (Baltaxe, 1977), making irrelevant remarks (Rumsey, Rapoport, & Sceery, 1985), identifying topics of conversation (Tager-Flusberg et al., 2005), and judging how much information different listeners need (Lord et al., 1989). Turn-taking in a conversation is also a challenge for individuals on the autism spectrum (Ghaziuddin & Gerstein, 1996).

Items on the CASL pragmatic judgment task test a variety of communication skills. Children are asked to answer questions about a variety of social situations that increase in difficulty and complexity. Table 11 lists examples of CASL questions of each of the above-mentioned categories. Answers that were typical of a child in the TD group and a child in the ASD group also included.

As seen in the previous table, the CASL pragmatic judgment task assessed various aspects of pragmatic language. Answers to the questions provide insight into children's knowledge of social rules. We attempted to make the experimental situation as naturalistic as possible, with the experimenter seated next to the child and talking to him or her directly.

Based on the responses of the children, it could be noted that some children with ASD are able to formulate phonologically, semantically, and grammatically correct sentences. The content of their language and their use of language conventions were often not appropriate given the speaking contexts that were presented. One example of a lack of understanding of emotion is question #33 in Table 11, in which the appropriate response would be to recognize someone's sadness due to the loss of a family member. A child with ASD responded to the question by saying, "Hm, tell them the big news!" This answer suggests that she misunderstood the question. She seemed to think it was Amber's role to tell Eric about his grandmother's death. However, her use of the phrase *the big news* suggests that did not know the appropriate way to convey a message that was likely to be hurtful to the listener.

Table 11

Examples of CASL Questions and Sample Answers

CASL question	TD answer	ASD answer
Basic rules of politeness		Correct: Can I play with you please?
11. Mary walks over to her friends who are playing doll. Mary want to play with them. What does Mary say?	Can I play with you? (20/20 = 100%)	Incorrect: Okay. I don't know (7/10 = 70%)
33. Amber learns that Erik's grandmother has just died. She sees Erik in the hall at school. What can she say to him?	I'm really sorry for your loss. (20/20 = 100%)	Correct: Erik, I heard your grandmother died. I'm really sorry. Incorrect: Hm… tell them the big news. (6/7 = 86%)
Making irrelevant remarks		
17. Ryan goes to a restaurant to get a hamburger. When it is Ryan's turn, the man taking orders says, "What would you like?" What does Ryan say when he orders?	I would like a hamburger. (20/20 = 100%)	Correct: I would like a hamburger, please. Incorrect: Chocolate chip pancakes. (8/10 = 80%)
16. Tyrone is looking for his math book. His sister walks into the room. What do you think Tyrone asks his sister?	Have you seen my math book? (19/20 = 95%)	Correct: Where is my math book? Incorrect: Won't you find my iPad or my video game collection? (6/10 = 60%)
Problems identifying topics of conversation		
39. Linda needs a white cotton T-shirt. Her mom wants to save some time and gas so she tells Linda to call several stores in the area. Tell me three things Linda should ask when she calls the stores.	Do you have a white cotton T-shirt? How much does it cost? How long are you open? (7/20 = 35%)	Correct: Hello, do you have a white teacher t uh a cotton white t-shirt and it has to be this particular size and this particular type of shirt. Incorrect: Walmart, K-mart, Walgreens (2/7 = 28%)

(*table continues*)

CASL question	TD answer	ASD answer
Difficulty judging the listeners knowledge and expectations		
49. Jane left for school early to help a teacher. Mother got upset, because Jane left her room in a mess. She told Jane that she couldn't go to the Friday football game. Jane got angry and went to her room and slammed the door. Tell me two things Jane could have said to her mother instead of getting angry.	I'll clean it right away or I'll clean it and do some extra chores. (14/20 = 70%)	Correct: Um she could say that she'll clean it up tomorrow or on Friday or now at the time, and she could also s* ask if she could make up for it in some other way. Why don't I get to go and why do my friends get to go? (1/6 = 17%)
50. When David's little sister wants something, he can't understand her speech. What can he say to find out what she wants without telling her he can't understand her and without hurting her feelings?	Pointing and asking "this?" (16/20) = 80%)	Correct: What is it you want? Incorrect: I don't know what you're saying. Can you repeat it in how normal people would? No offense. (2/5 = 40%)

Note. Percentage below the sample answers indicate how many children in the group answered the question correctly.

The last question in Table 11 requires the person to take age and feelings into consideration in asking a clarification question without hurting someone else's feelings. This pragmatic problem is solved successfully by the child in the TD group, who suggests that the person should point to an object and ask simply "this?" The participant with ASD on the other hand, does not take into consideration the skill level of the child or her feelings. She says, "I don't know what you're saying. Can you repeat it in how normal people would? No offense." This utterance would be likely to hurt the listener's feelings. All the participants with ASD, regardless of language ability and IQ, evidenced examples of pragmatic language that conveys a lack of empathy. An item analysis for each CASL question indicates that 19 of the 60 questions yielded group discrepancies in accuracy of 30% or higher (see Table 12).

Table 12

Item Analysis CASL

CASL item	TD	ASD	CASL Item	TD	ASD
1	20/20 = 100%	10/10 = 100 %	31	13/20 = 65%	3/8 = 38%
2	20/20 = 100%	10/10 = 100%	32	18/20 = 90%	7/8 = 86%
3	20/20 = 100%	9/10 = 90%	33	20/20 = 100%	6/7 = 86%
4	20/20 = 100%	9/10 = 90%	34	20/20 = 100%	5/7 = 71%
5	19/20 = 95%	9/10 = 90%	35	17/20 = 85%	5/7 = 71%
6	20/20 = 100%	10/10 = 100%	36	16/20 = 80%	4/7 = 57%
7	18/20 = 90%	8/10 = 80%	**37**	17/20 = 85%	3/7 = 43%
8	20/20 = 100%	9/10 = 90%	38	19/20 = 95%	6/7 = 86%
9	20/20 = 100%	9/10 = 90%	39	7/20 = 35%	2/7 = 29%
10	20/20 = 100%	9/10 = 90%	40	10/20 = 50%	1/6 = 17%
11	20/20 = 100%	7/10 = 70%	41	18/20 = 90%	5/6 = 83%
12	19/20 = 95%	10/10 = 100%	**42**	15/20 = 75%	1/6 = 17%
13	20/20 = 100%	9/10 = 90%	43	11/20 = 55%	4/6 = 67%
14	20/20 = 100%	8/10 = 80%	**44**	14/20 = 70%	2/6 = 33%
15	20/20 = 100%	9/10 = 90%	45	17/20 = 85%	4/6 = 67%
16	18/20 = 90%	6/10 = 60%	46	14/20 = 30%	2/6 = 33%
17	20/20 = 100%	8/10 = 80%	**47**	16/20 = 80%	3/6 = 50%
18	20/20 = 100%	8/10 = 80%	48	4/20 = 20%	1/6 = 17%
19	20/20 = 100%	8/10 = 80%	**49**	14/20 = 70%	1/6 = 17%
20	20/20 = 100%	9/10 = 90%	**50**	16/20 = 80%	2/5 = 40%
21	16/20 = 80%	7/10 = 70%	**51**	12/20 = 60%	1/5 = 20%
22	18/20 = 90%	5/10 = 50%	**52**	14/20 = 70%	2/5 = 40%
23	20/20 = 100%	4/10 = 40%	53	7/20 = 35%	3/5 = 60%
24	17/20 = 85%	7/10 = 70%	**54**	16/20 = 80%	3/6 = 50%
25	18/20 = 90%	3/10 = 30%	**55**	15/20 = 75%	2/5 = 40%
26	19/20 = 95%	7/9 = 78%	56	9/20 = 45%	2/5 = 40%
27	20/20 = 100%	6/9 = 67%	**57**	7/19 = 37%	0/4 = 0%
28	19/20 = 95%	5/9 = 55%	58	9/19 = 47%	¼ = 25%
29	19/20 = 95%	4/9 = 44%	59	3/19 = 32%	¼ = 25%
30	19/20 = 95%	5/9 = 55%	**60**	6/18 = 33%	0/4 = 0%

Bolded numbers indicate items with a discrepancy of 30 percentage points or higher between the groups.

Behavioral responses on the experimental task were consistent with findings from previous studies. The ASD group scored significantly lower than the children in the TD group. Most of the children (19/20) in the TD group scored within the normal range (standard scores of 76-116) for their age on the CASL, with moderate degrees of variability (M = 95.60, SD = 11.311). Children in the ASD group, on average, earned scores on the CASL Pragmatic Judgment task that were more than two standard deviations below the mean (M = 66.40, SD = 17.392) with a range of 40 to 88. Children in the ASD group scored with great variability and a larger range, indicating a heterogeneous phenotype of ASD. Even though the children that were eligible for the study had the prerequisite of being verbal, their pragmatic language ability was certainly impaired and varied. The findings support our hypothesis that children with ASD in our study had significantly more difficulties responding appropriately to a social situation presented orally with pictorial support. Our behavioral results were consistent with the large body of literature showing that individuals with ASD have more difficulty with pragmatic language skills (see review from Tager-Flusberg et al., 2005).

Research Question 3

The third research question was: *Are there differences between children with ASD and typically developing children in their response time (RT) during a pragmatic judgment task?*

Research on response time (RT) has been conducted with individuals with

ASD in a number of different areas including facial emotion recognition (Fink et al., 2014; Smith, Montagne, Perrett, Gill, & Gallagher, 2010), verbal bias with facial recognition (Grossman, Klin, Carter & Volkmar, 2000), and attention tasks (Adamo et al., 2014). All these studies compared the RTs for children with ASD to that of typically developing participants or children with ADHD. All the studies reported that the RT of children with ASD was similar to that of their controls. These findings were consistent regardless of sample size. In contrast, a study examining RT and EEG when processing emotion words (Lartseva et al., 2014) found that children with ASD had longer RTs compared to the TD group. Several explanations can be given for the discrepancy. The Lartseva et al. study focused on the lexical component of the words as opposed to facial recognition or attention. The verbal component could have been a factor in the differing outcomes of RTs.

In our experiment, children were not restricted to a time window for answering the questions. Response times were calculated for all items combined as well as for correct and incorrect items separately. Children in the ASD group needed on average 1.4 seconds to respond, while children in the TD group needed about .3 seconds less (1.1 seconds). This difference was not statistically significant. Our findings are consistent with those from the majority of prior studies that reported no significant difference in RT between TD and ASD groups on behavioral tasks.

We also examined the RTs for items that were answered correctly or incorrectly. Research on orthographic and semantic processing (Polse & Reilly, 2015) of first to fourth graders found different processing speeds according to childrens' level of reading proficiency. Children who were learning to read (first graders) had longer processing times and tended to be less accurate than proficient readers (fourth graders), who had shorter RTs and more accurate responses. The authors concluded that processing becomes more efficient and faster as a function of acquiring orthographic components and adding semantic representations. Research on second language acquisition has also examined speed x accuracy interactions (Abu-Leil, Share, & Ibrahim, 2014; Taguchi, 2007). The findings were consistent, in that processing speed decreased while accuracy increased as a function of increased language proficiency.

The pragmatic judgment task on the CASL is organized by difficulty level, with more difficult items occurring in succession. Thus, we would expect RT to increase as children responded to later occurring items. Assuming that items that were answered incorrectly were more difficult for the child, we anticipated those items to be answered with a higher response latency. The hypothesis was confirmed. The difference in RT between correct and incorrect items was significant. Children in both groups needed more time to respond to items that were answered incorrectly.

At times, participants in both groups had to be prompted to respond. Whenever such a prompt was necessary the answer turned out to be incorrect. One mother of a child with ASD reported that whenever the child did not know the answer, he would not respond, as opposed to saying "I don't know." With added instruction that it was okay to respond with "I don't know," RT was decreased slightly, with frequent "I don't know!" responses.

Further analysis into neurological activation patterns during the response latency after the stimulus could provide insight into neurological underpinnings of RT. Such analysis should be taken into consideration for future studies. De Marchena and Eigsti (2010) found, for example, that while behaviors occur they may be asynchronous with the conversation. It is possible that neurological activation patterns are asynchronous as well. The neurological activation may occur, but it may happen at a later time for individuals with ASD.

Research Question 4

The fourth research question was: *Are there differences between children with and without ASD in brain activation patterns observed in four cerebral regions of interest (DLPFC, OFC, ST, IPL) as they complete a pragmatic language task*? This question had two parts.

4a. *Are there differences between children with and without ASD in brain activation patterns for the first 25 responses?*

Language includes the domains of phonology, morphology, syntax, semantics and pragmatics. Deficits in pragmatic language are prevalent in the ASD population. A number of pragmatic skills and their underlying neurological activation patterns have been studied, such as intonation and prosody of utterances (Eigsti, Schuh, Mencl, Schultz, & Paul, 2012; Hesling et al., 2010; Wang, Lee, Sigman, & Dapretto, 2006), perspective-taking (Mizuno et al., 2005), Theory of Mind (ToM; Brunet et al., 2000; Fletcher et al., 1995; Gallagher et al., 2000; Saxe & Baron-Cohen, 2006; Vogeley et al., 2001), emotion and facial expressions (Han, Yoo, Kim, McMahon, & Renshaw, 2014; Redcay et al., 2013), sarcasm (Uchiyama et al., 2006), metaphors and figurative language (Bottini et al., 1994; Rapp et al., 2004), and social judgment (Berthoz et al., 2002; Carter, Williams, Minshew, & Lehman, 2012). Language use, or pragmatic language, includes a wide range of skills.

Findings from studies of neurotypical individuals suggest that activation in DLPFC, OFC, STG, IPL, anterior cingulate cortex (ACC), medial prefrontal cortex (MPFC), and the amygdala play a role in normal pragmatic language processing (Adolphs, 2003; Baker et al., 1996; Cohen et al., 1990; Kringelbach & Rolls, 2004; Pelphrey et al., 2004a; Rolls, 2002; Ruby & Decety, 2004; Seghier, 2013; Skuse et al., 2003; Takahashi et al., 2004). We were not able to image MPFC, ACC and the amygdala in this study because they are subcortical structures that can be detected with fMRI but not fNIRS.

It is very difficult to assess pragmatic language because a variety of environmental aspects (auditory, visual, olfactory, and tactile stimuli), and at least one communication partner must be involved in any dynamic interaction. Behaviorally, a variety of pragmatic skills have been well documented in the TD population as well as in individuals with ASD (see for a review Tager-Flusberg et al, 2005). There is limited understanding of the neurological processes that are involved in pragmatic language. Neurological results from the studies that have been conducted with neurotypical individuals vary greatly due to the different skills that have been assessed. Unfortunately, the data collection contexts for those experiments rarely resemble actual social situations and never include imaging during verbalization. We were interested in creating a neuroimaging context that was more naturalistic. For this purpose we utilized fNIRS, in which children sat comfortably in a chair and responded verbally to questions about social situations that required them to indicate what participants in those situations should say. We chose the pragmatic judgment task of the CASL because the questions targeted knowledge of social rules. In addition, the children were able to speak directly to a conversational partner.

The 30 children in this investigation answered a set of pragmatic language questions while wearing optode caps, which enabled us to record their hemodynamic responses in the frontal lobe and left hemisphere. All children who met eligibility criteria answered at least 25 questions. Using the beta-weights for the first 25 items as the dependent variable meant that the hemodynamic response was compared for the same items across groups. Because children in the TD group answered more items correctly before reaching the ceiling of five incorrect items in a row, and because later questions increased in their difficulty, beta-weights based on all the items that each participant completed would not have yielded interpretable comparisons between the two groups.

HbO and HbT beta weights suggested that children with ASD activated less than children in the TD group, across all ROIs. In a somewhat surprising finding, there were lower HbR values for children in the ASD group, which would suggest that those children activated more than children in the TD group. Children with ASD cannot activate less and more at the same time. Research on the consistency between HbO and HbR suggests that HbR measures are more consistent with BOLD analysis of fMRI and therefore are more representative of actual activation patterns. HbR values tend to be smaller in magnitude and also less reliable. Thus, the validity of HbR continues to be debated (Baird et al., 2002; Bartocci et al., 2000; Bortfeld, Fava, & Boas, 2009; Chen et al., 2002; Hoshi & Tamura, 1993; Jasdzewski et al., 2003; Kato, Kamei, Takashima, & Ozaki, 1993; Strangman, Culver, Thompson, & Boas, 2002; Strangman, Franceschini, & Boas, 2003). We did find smaller effect sizes for HbR values with $p\eta^2 = .169$, which is consistent with findings from other studies. HbO however yielded a $p\eta^2$ of .284 for the group main effect, which is large in magnitude.

There are two possible explanations for the group differences in HbO and HbT measures favoring the TD group. Recall that HbO refers to oxygenated blood concentration levels and HbT refers to the sum of HbO and HbR (deoxygenated blood concentration level). The group differences for HbO and HbT suggest that children with ASD activated regions of the brain less than their TD matches. This finding could have occurred because the children with ASD have brains that are less specialized than typically developing children and therefore recruit more broad and variable regions when solving a task. This explanation is consistent with the variations that were evident when the triads were compared individually to each other with NIRS-SPM contrasting. Each child with ASD was matched with two TD children. One TD child was within 6 months below the age of the child with ASD, the other within 6 months above in age. With use of this bracketing approach, we accounted for natural variability in pragmatic language skill level. The three children formed the triad for individual NIRS-SPM contrasting.

Theories of underconnectivity in children with ASD suggest that cortical regions may be poorly synchronized and integrated resulting in inefficient processing. This lack of integration across different regions could cause decreased neural activation in the areas we had identified as relevant. However, activation across the entire brain may not be less. Since fNIRS limits our ability to scan only selected regions of interest, we cannot confirm or deny this hypothesis.

One region of interest, the superior temporal gyrus (STG), was activated to a greater extent than DLPFC, OFC and IPL. Our findings indicate that for a social language task such as the pragmatic judgment subtest on the CASL, the STG is predominantly activated for all participants. While children with ASD still activated all areas less than their TD matches, they were consistent in their elevated STG activation compared to the other ROIs. This finding is consistent with previous studies showing that the STG is involved in tasks such as processing auditorily presented linguistic stimuli and comprehending language, but also particularly in social cognition (Pelphrey et al., 2004a; Ruby & Decety, 2004). Pelphrey et al. suggested that the STG is involved in the analysis and interpretation of the other people's intentions. In their study, eye movement indicated the intention of the conversational partner. Changes in eye gaze then signaled a shift in the intention.

Interpreting the change in intentions activated STG in typical participants but there was decreased activation for those with ASD. Nonetheless, participants with ASD still activated the area, only with less intensity. Our findings confirm particular involvement of the STG during a pragmatic judgment task. Social cognition skills are required to answer questions related to social situations.

Recall that the DLPFC, OFC and IPL were not particularly active during the CASL pragmatic judgment task. The DLPFC has been shown to be particularly active during tasks that involve problem-solving, holding information in working memory and/or error correction (Baker et al., 1996; Cohen et al., 1990). These skills were not required during the CASL pragmatic judgment task. Overall involvement of the OFC, the reward center of the brain (Kringelbach & Rolls, 2004), was not significant when all items were analyzed as a whole. Tasks on the pragmatic judgment task of the CASL were not specifically designed to test ToM knowledge. However, some of the items on the CASL involve aspects that require certain ToM skills (i.e., “Mandy is driving in a new town. She can’t find Maple Street where her friend lives. What can she say in asking for directions?” requires the person responding to evaluate Mandy’s knowledge and how much information she requires.). It has been suggested that OFC is involved in ToM abilities (Seghier, 2013). Limited involvement of OFC can be linked the task not exclusively targeting ToM skills.

4b. *Are there differences between children with and without ASD in brain activation patterns observed in four ROI’s when comparing accuracy of responses (correct vs. incorrect)?*

We wanted to analyze group differences on items that were similar in difficulty. We did this by separating the children's responses into sets of correct and incorrect items. Incorrect answers were presumed to be higher in difficulty than questions that were answered correctly. Contrary to the analysis of the first 25 items, this analysis included different items for each participant. The analysis with the first 25 items yielded comparable results for hemodynamic responses of the same questions. The analysis of accurate vs. inaccurate items represented the level of difficulty for each participant individually.

While the STG has been shown to have a greater involvement in social cognition, the DLPFC plays a role in problem solving and error correction (Cohen et al., 1990). If the child engaged in some type of error correction or revisions of responses, more activation in the DLPFC might be expected. Significant results in OFC activation are discussed later.

Another fNIRS study conducted in our laboratory with children with specific language impairment (SLI; Gillam, Wan, Gillam, & Hancock, 2015) revealed that children with SLI tended to decrease their neural activation when they responded to more complex sentence structures. In that study, children with and without SLI between ages 9 and 11 years were asked to select the picture of the object that was doing an action via button press. Each trial consisted of the child listening to one of four sentence types, two canonical sentence types (subject-relative clauses and subject-verb object clauses) and two noncanonical sentence types (object-relative clauses and passive clauses) sentences. Children with SLI tended to select the easiest possible answer (the first noun mentioned in the sentence) when the task became very difficult for them, and this strategy was associated with decreased neural activation. However, their TD, age-matched controls activated more during the processing of objective relative clause and passive sentences, because they needed to work harder to hold the first noun in memory while they were listening to the verb phrase and the second noun. Then, they had to indicate that they understood that the second noun was the agent of the sentence. It is likely that the difficulty level caused an overload for the children with SLI, but not for the TD controls.

If children with SLI activated less as they processed complex sentences, it is possible that children with ASD may present similar patterns when a pragmatic task reaches a difficulty level beyond their skill level. A finding of lower neurological activation could be an indication of neural efficiency when participants are responding correctly (see review from Neubauer & Fink, 2009). According to the neural efficiency hypothesis, individuals with higher intelligence show lower brain activation when engaging in cognitive tasks because they find them to be easier. Individuals with lower intelligence however display higher levels of brain activation when engaging in the same task (Grabner, Neubauer, & Stern, 2006; Neubauer & Fink, 2009).

When we analyzed the data according to accuracy, we discovered a number of significant findings for oxygenated, deoxygenated and total blood concentration levels. There was a significant main effect for accuracy for HbO and HbT in activation of OFC for both groups. There was greater activation in OFC for questions answered correctly than questions answered incorrectly. These findings are suggestive of more difficult questions generating less neural activation. Given these results combined with results from the study with children with SLI (Gillam et al., 2015) we can conclude that difficult items with higher cognitive and linguistic demands yield lesser neurological activation. We considered HbO and HbT to be a reliable measure of activation based on explanation provided above.

The finding of increases in HbO and HbT values suggests that children activated OFC more when they answered the question correctly. For HbO and HbT, the OFC was significantly less active when children were responding to items that were answered incorrectly. Even though children with ASD activated the OFC less during incorrect responses, their activation was still higher than children in the TD group.

Decision-making processes are a key function of the OFC (Kringelbach, 2004). Patients with OFC lesions demonstrate considerable difficulty with making decisions, affect, inappropriate social behavior and irresponsibility (Blair & Cipolotti, 2000; Hornak et al., 2003; Rolls, Hornak, Wade, & McGrath, 1994). Decision-making is also critical for responding to questions about social situations. Consideration needs to be given to social cues, aspects of politeness, appropriateness, and relevance. Thus, findings of increased activation in OFC with accurate responses are suggestive of a properly working neurological network to produce the correct response. Contrary, incorrect responses yielded decreased neural activity for both groups in OFC, denoting less effective decision-making. Reduced activation could be the result of a suboptimal functioning neurological network involved in decision-making.

Decision-making and predicted rewards are linked to each other. The brain must compare the potential reward for a certain behavior during the decision-making process. Therefore, it is possible that the OFC is directly related to the reward system of the brain, as well as the processing of emotional processes. The increased activation during correct responses could be an indication that it is reinforcing for a child to be able to answer questions correctly, activating the reward system.

Additionally, correct responses may yield OFC activation due to a history of reinforcement. Such reinforcement history could have resulted from many years of language intervention and participation in social language groups. All children had participated in Speech and Language therapy at some point. The majority (6/10) of the children, as indicated on the parent intake form, received intensive applied behavior analysis early intervention. Format of typical pragmatic language instruction is the explicit description and discussion of social conventions. Rehearsal of appropriate social rules in such a setting likely results in reinforcement from the interventionist. Thus, such behavior yields a history of reinforcement. Items on the CASL are likely to have been explicitly discussed in an intervention session, especially with our age group. Contrary, incorrect responses may not activate the OFC due to a lack of history of reinforcement with such tasks. Thus, decision-making with judgment of social appropriateness could be connected to reinforcement history. Further investigation needs to be conducted to refine the speculation of reinforcement history being linked to decision-making abilities with subsequent OFC involvement.

Recall that there was a significant Group x Accuracy interaction for HbR blood concentration levels for correct and incorrect responses. Children with ASD showed significantly more HbR in DLPFC left when answering a question incorrectly, suggesting that they are activating this area less. TD children, however, displayed decreased HbR levels during incorrect responses, suggesting more activation in this area while trying to answer the question. When the answer was correct they activated less, which could again be indicative of neural efficiency (Grabner et al., 2006; Neubauer & Fink, 2009b).

The DLPFC has been found to be involved in error correction and working memory (Cohen et al., 1990; MacDonald et al., 2000). In support of those findings, activation during the incorrect tasks for the TD group are indicative of DLPFC left involvement during difficult problem solving, and error correction procedures. For example, MacDonald et al. found that during a color switching stroop task, 12 participants showed activation in the DLPFC. While laying in an fMRI scanner, participants were instructed to name the color but not read the word. In a Stroop task, naming the color instead of reading the word requires greater cognitive control. Reading the word on the other hand is more automatic for a proficient reader. Participants in this study had to inhibit their automatic response and correct their error. When responding to a social situation questions such as those on the CASL, participants are required to continuously evaluate the listeners' expectation and social appropriateness, which requires inhibitory processes to correct initial impulses that may potentially be socially inappropriate. The CASL the questions, which are testing knowledge of polite interactions, require the person to inhibit automatic responses of impolite answers (i.e., for this situation: When David's little sister wants something, he can't understand her speech. What can he say to find out what she wants without telling her he can't understand her and without hurting her feelings?, answering: "I don't know what you're saying. Can you repeat it in how normal people would? No offense."). Activation of the DLPFC is necessary for inhibition and error correction. Given the results, it appears that children with ASD lack such error correction procedures to some extent. Their activation of DLPFC left during difficult questions decreased, suggesting that they may not have the necessary neurological network activity for such complex tasks, which could be due to underconnectivity. Lower activation could be a result of lack of synchronization between different brain regions to solve complex problems and make socially appropriate decisions. Referring to the example above, the child's ability to formulate a grammatically correct sentence was observed. However, he could not account for the complexity of the situation to inhibit an impolite response. Social situations require the synchronization of many different stimuli, especially those relating to the conversational partner.

Considering that these findings are based on HbR measures only, without support from interactions shown in HbO, we need to interpret these results with caution until further evidence either confirms or opposes these conclusions. HbR values have less validity compared to HbO activity. There was no support for this finding from HbO measures. While these are interesting results, their validity needs to be tested in future studies.

Our analyses of the HbO, HbR and HbT beta-weights did not enable us to examine the diffusion of activation across frontal and left lateral cortex. Such patterns could inform our understanding of cortical specialization. We performed individual comparisons of activation patterns for each child with ASD and his or her TD controls using the NIRS Statistical Parametric Mapping (NIRS-SPM) toolbox. NIRS-SPM yielded activation maps for individual participants with ASD and the combined averages of each child's TD controls by contrasting HbO concentration values from the stimulus-response epoch with values from the final rest period (Ye et al., 2009). Activation maps depicted statistically significant areas of activation displayed as t-values. For 7 of the 10 triads, the NIRS-SPM analyses revealed oxygenated hemodynamic patterns in which the child with ASD activated broader regions than the TD matches. Our NIRS SPM analysis supports the hypothesis of more diffuse activation (suggestive of less specialization) for children with ASD compared to TD children.

Overall we see patterns of decreased activation for participants with ASD within the four ROIs of DLPFC, OFC, STG, and IPL together with less specialization (more diffuse activation) across frontal and left temporal cortex as compared to the

TD controls. Increased activation for both groups in STG when solving a pragmatic judgment task suggested that this region played a pivotal role in responding the questions about social situations.

Differences in activation of the DLPFC left depended on the accuracy of the response, Children with ASD activated more when they were answering correctly and less their answer was incorrect. Children in the TD group presented the opposite pattern. They tended to activate DLPFC less for correct responses and more for incorrect responses. These results are consistent with intact inhibitory control and problem-solving abilities in the TD group but not the ASD group.

Limitations

A number of limitations affect the degree of confidence that we have in our results and conclusions. Even though fNIRS is more conducive for imaging a population such as children with ASD related to lower cost, susceptibility to movement artifacts and ability to collect data during actual conversations, it does have its limitations. fNIRS records neural activation only in cortical structures up to 3 cm deep. Subcortical areas cannot be accounted for. This is an important limitation because of previous findings have demonstrated the importance of the anterior cingulate cortex and amygdala for pragmatic language. Given the restrictions of fNIRS, we cannot make claims about the role that these subcortical areas may play in the verbal pragmatic task that we administered. fNIRS is also limited in it's spatial accuracy, which is not comparable to the accuracy of voxel size images from fMRI. Such spatial discrepancy is due to scattering of NIR light through the tissue. This limitation in combination with head size and shape differences in our participants inhibits our ability to be certain of the precise locations of the gyri in our regions of interest. We tried to compensate for this limitation by registering the different channel locations using the Polhemus. The Polhemus enables us to localize different regions of the brain in relation to the placement of the cap.

We calculated beta-weights as our dependent variables. While HbO beta-weights have been deemed to be a reliable representation of activation, HbR values are smaller and less reliable. HbR results should not be interpreted in isolation without supporting hemodynamic response measures, such as HbO. This became relevant when our findings yielded mixed results between HbO and HbR. Recall that HbO and HbT both measured lower activity in all ROIs for children with ASD, while HbR results indicated higher activity. Interpretation of results was focused on HbO and HbT beta-weights. HbR further generated an interaction between Accuracy x Group. The reliability of those findings needs to tested through replication.

This study focused on the amount and diffusion of activation across four cortical regions. We did not conduct a time-series analysis of each channel, nor was our data analyzed for the extent of connectivity between different brain regions. Additional time-series and connectivity analyses could potentially give us more insight into the pattern of interaction between different regions. This is particularly important when we are considering the theory of frontal-posterior underconnectivity or more globally the model of complex information processing.

Both of those models base their explanation of deficits in ASD on insufficient synchronization of brain areas. Further analysis of connectivity could add to the existing literature and help refine the model.

An analysis known as Wavelet Transform Coherence (WTC) has the potential to calculate the degree of coherence between signals across two channels over time. This type of analysis can be utilized even with a single participant (Cui, Bryant, & Reiss, 2012). We are currently exploring the use of this analysis to reveal patterns of connectivity between different brain areas. This would enable us to directly address hypotheses of underconnectivity in children with ASD by the frontal-posterior underconnectivity theory and the model of complex information processing. Both theories suggest that deficits in the ASD population are caused by inefficient synchronization and integration of different brain regions. The frontal-posterior underconnectivity theory identifies a specific disrupted connection between frontal and posterior brain regions, the model of complex information processing postulates that with increased complexity of tasks the coordination and synchronization of any brain region becomes more difficult. Conducting connectivity analyses with WTC could test these hypotheses by identifying specific synchronization patterns across tasks.

Studies of low incidence populations often have restricted small sample sizes. Our study was no exception. A larger sample of children with ASD would have potentially yielded more clear activation patterns. Relatively high degrees of individual variation resulted in non-significant group contrasts. This may have contributed to Type II errors in which we claimed that there were no significant differences between the groups when such differences really exist. Only studies with larger samples of children and adolescents will be able to address this problem. Variation was apparent in different phenotypes of ASD, with participants displaying different degrees of challenging behavior and language skills. Some children exhibited few stereotypies, while others engaged in extensive repetitive behavior. Core language scores also indicated a wide skill range within the ASD group. Groups of children with ASD that showed more similar language skills as well as comparable stereotypic behavior could have resulted in clearer contrasts, as well as more differential neurological activation patterns.

Finally, the children in this study had relatively small amounts of hypersensitivity to our optode caps. Only one child required desensitization training. Development of more robust desensitization procedures would require a larger amount of individuals showing hypersensitivities. Differing patterns of behavior in children with ASD may necessitate different desensitization procedures than the ones used here.

Implications and Conclusions

This was the first imaging study to compare the concentration levels of oxygenated and deoxygenated hemoglobin in children with ASD and their typically-developing, age-matched controls as they engaged in a functional pragmatic language task. Findings from this study suggest that there are significant differences in concentration values between children with ASD and their TD controls as they respond to a task requiring them to indicate verbally how participants described in a social scenario should respond. Specifically, children in the ASD group tended to have lower concentration values, suggesting that they activate less then the TD controls, especially on items that they answered correctly. Further, it appears that their activation was more diffuse across frontal cortex and left lateral cortex.

Data collected from this study lends itself to future connectivity analyses, which could directly test the theory of frontal-posterior underconnectivity and the complex information processing model. We collected hemodynamic responses in 22 channels over the frontal lobe and 22 channels over the left lateral hemisphere. If the neural processing of children with ASD is less integrated and less specialized, as predicted by the frontal-posterior underconnectivity theory and the model of complex information processing, we should find less coherence between fNIRS channels in comparison to their TD controls. This pattern should be especially strong for tasks, like our pragmatic judgment task, that require synchronization of frontal and posterior regions. If the model of complex information processing were a reasonable explanation for deficits of individuals with ASD, we should find lower coherence between channels above DLPFC, STG, and IPL cortex, and that coherence should increase as a function of task complexity. We plan to conduct such analyses in the near future.

Our findings can give rise to future research exploring the impact of different pragmatic language intervention approaches on the neural activation. Future studies could include an intervention of the skill under investigation, with a neuroimaging scanning session prior to the intervention and right after to see if changes in activation patterns are observable. This way we also have the potential of comparing different treatment approaches and their effects on brain development.

As hypothesized by the authors of the Complex Information Processing model, it may be more beneficial to focus early intervention efforts with children with ASD on skills that require the synchronization between different brain regions (see Just et al., 2012; Williams et al., 2015). The rationale for this hypothesis stems from the behavioral measures showing that children with ASD were able to solve simple tasks in variety of different domains of language and cognition but not complex tasks. This finding has been interpreted as demonstrating that the more complex a task is, the more it requires synchronization and integration of multiple brain regions. Given current conceptions of neuroplasticity, practicing skills that demand the integration of different regions of the brain could potentially result in better pragmatic language, as well as greater generalization of learned skills to new speaking contexts. These effects, however, have to be further investigated to either support or oppose such theories.

Challenges in neuroimaging children with ASD have limited the scope of neural studies of this population. Our research suggests that fNIRS can be useful for informing our understanding of neural activation patterns in difficult to test children. Future research should focus on refining procedures to enable inclusion of younger children with ASD who may exhibit more stereotypies and challenging behavior. With the inclusion of more and younger children, studies should also focus on including children with less verbal skills to increase understanding of underlying neurological processes. Future studies should also narrow the age ranges, as well as language abilities and stereotypic behavior. Benefits include greater understanding of the relationships between neurological activation patterns and pragmatic language, the development of effective desensitization procedures and potential effects of different types of interventions.

Regardless of our growing understanding of ASD, we need to continue to investigate the underpinnings of the disorder to increase the development of more effective treatment methods. We imaged children as they completed a pragmatic judgment task. While it approximated a more naturalistic setting than studies that are conducted with fMRI and PET, it still did not involve real-life interaction with another human being. We believe the fNIRS technology provides researchers with the potential to conduct studies of neural activation during functional communication. We look forward to advancing this line of research in the future.

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APPENDICES

Appendix A

Study Flyer

Q & A

Who will conduct the research sessions?

Trained research assistants, who have previously been trained in the procedures of the research project, will conduct the research

What kind of special help will children receive?

Your child will be instructed until the tasks are clear. He or she will be able to practice before we start the actual research session.

Is there a charge for this program?

You will be compensated for your participation in the study with $15 for each session and your child will receive a toy after completing each session.

Will transportation be provided?
You are responsible for bringing your child and picking him or her up from the program site.

How will I be kept informed about the project?
We are available to talk with you by phone about questions or concerns that you may have throughout the project.

Do I have to attend sessions with my child?

No. Parents do not need to attend the sessions with their children.

Can I find out the results of the research project?

Yes. The research findings will be published and available for your review when the study is finished. Children's names will not be used in any published articles.

How long is the study?

Your child will participate for 2 sessions, which are each approximately 1 hr long.

How can I get more information?

Call Daphne Hartzheim (435) 938-1629 or email her at daphne.hartzheim@gmail.com

Or

Call Ronald Gillam, Ph.D. (435) 797-1704 or e-mail him at ron.gillam@usu.edu

Investigation into the Neural activity of children with and without Autism

LEAP Brain Imaging Lab in the Emma Eccles Jones Early Childhood Education Research Center

Utah State University

What does the brain of a child with ASD do compared to a typically developing child?

We need your help.

A group of researchers at Utah State University is looking for parents and children who are willing to participate in research that evaluates the neural activity of children while they are engaging in a variety of different tasks (e.g. pragmatic judgment, grammatical judgment and working memory)

Project Schedule

To determine whether your child is eligible for this study, he or she will complete one preliminary testing session. This initial screening will include a test of nonverbal reasoning, and speech and language tests. You will receive a short report of your child's results.

Who do we need for the study?

We need right-handed children between the ages 9-15 years old with and without a diagnosis of Autism. The child's primary language needs to be English.

Pretesting

All children will complete a battery of language, and IQ tests before the program begins.

Research session

Children will attend for about 1 hour at two different times. The sessions will take place in the LEAP Brain Imaging Lab at the Emma Eccles Jones Early Childhood Education and Research Center.

For each session the child will wear a flexible cap on the head with optodes that measure the blood flow in the brain during different computerized activities.

Response Form

If you would like to find out if your child is eligible for this project, please call Daphne Hartzheim or Dr. Ron Gillam or complete this tear-off form and return it to her by mail. Contact information is listed at the bottom of this page.

Name of child ______________ Date of birth ______________

Name of parent ______________

Address ______________

____

____

Phone ______________

We will call you to talk about your child's participation in this important study.

If you have questions or concerns, please contact:

Daphne Hartzheim
Or
Ron Gillam, Ph.d.

Address: Utah State University
Communication Disorders and Deaf Education
2610 Old Main
Logan, Utah 84322
Phone: Daphne Hartzheim (435) 938-1629
Dr. Ron Gillam (435) 797-1704
Email: ron.gillam@usu.edu
daphne.hartzheim@gmail.com

Appendix B

Informed Consent

Department of Communicative Disorders
And Deaf Education
2610 Old Main Hill
Logan UT 84322-1000
Telephone: (435) 797-1704

USU IRB Approval: Oct. 22, 2014
Approval Terminates: 10/21/2015
Protocol #6090
IRB Password Protected per IRB Administrator

INFORMED CONSENT

An Investigation into the neural activity of the brain of children during pragmatic and grammatical judgment and a working memory task as measured by Near-Infrared Spectroscopy (NIRS)

Introduction/ Purpose Dr. Ron Gillam in the Department of Communication Disorders and Deaf Education at Utah State University is conducting a research study to find out more about how children with Autism Spectrum Disorder (ASD) use their brains as they judge whether sentences are grammatical or not, decide what people should say in different social situations, and remember sequences of words and numbers You have been asked to take part because your child has been diagnosed with ASD. There will be approximately 50 children who will be asked to take part in this study, 20 children with ASD and 30 typically developing children.

Procedures If you agree for your child to be in the study he or she will first be given a language measure called CELF-5 (Clinical Evaluation of Language Fundamentals-5). This test will tell us how well your child understands and uses language. Your child will also be given a test that does not require them to speak. This test is a measure of how well your child solves problems. It is called the UNIT (Universal Nonverbal Intelligence Test). These tests should take about 1 ½ hours to finish. Only children who score 75 or higher on the language measure and 75 or higher on the UNIT will be asked to take part in the study. Children who score lower than 75 on these tests may find the things we will ask them to do in the second part of the study to be too difficult and could become frustrated or upset. For this reason, they will not participate in the second part of the study.

If your child is a good fit for the study, he or she will be asked to play some games on the computer. Some of the games are language games. In the language game, your child will be asked to say when a sentence is right (correct) or wrong (incorrect). For example, if your child sees the sentence, "He walk home" the expected answer is "wrong" because the sentence should say, "He walks home." There will be a key that your child presses to say "right" and one for "wrong." In another game, your child will be asked to solve social problems. For example, your child may be asked, "What would you say if someone spilled their lunch all over the floor?" Your child will also be asked to play a memory game. The object of the memory game is to remember words and numbers in the right order. For example, if your child is told, "Remember these things; book, 5, 2, pen." He or she will be asked repeat the words and numbers in the right order. All of the games will be shown on a computer. Your child will be given short rests between games. The rest times will also be on the computer. The screen will have a cross for your child to look at and before the next game starts. The games, including rest periods will take about 20 minutes to complete.

While your child is playing the games and taking rests, he or she will be wearing a cap that has small buttons on it. The cap is like a "swimming cap" and is connected to some wires that go to a computer. The small buttons on the cap are called optodes. Some of the optodes emit a small laser light that shines onto the scalp. Other optodes measure the amount of light that is reflected off the scalp. The nature of the light that is reflected is used to measure the oxygen that is being used by the brain. The computer

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will tell us how your child's brain uses the oxygen while he or she is playing the different games. We hope to use the information to help us learn about your child's brain activity in the front part of the brain and on the left side. The light is not warm or cold. Your child will not be able to feel the light but she or he will feel the buttons (optodes) pressing gently on the scalp. This may be a strange feeling for some children. If your child is sensitive to the optodes and asks not to play, he or she will not have to. Your child will not be asked to do anything that makes him or her uncomfortable or afraid.

If you think your child will be able to wear the cap after having some time to get used to it, we can work with him or her to see if that is possible. If your child is having difficulty wearing the cap because it too close to the head, we will slowly take steps to help him or her be comfortable with the cap. We would start out with letting the child touch the cap without the sensors inside. We would let the child put on the cap, when he/she is ready. We will reward your child for wearing the cap without the optodes. We will slowly increase the number of optodes that are placed into the cap. At each step in getting your child used to the cap, he/she will be rewarded with a preferred activity or item. If you feel your child needs to stop participating in the study at any time, he/she may do so.

If your child participates in the study, you will be asked to answer some questions about his or her speech and language development and education. You will also be asked about any medical problems that are important for us to know about. For example, if your child has a seizure disorder, we need to know what to do if there is a problem. Completing this form takes about 5 minutes.

Risks Participation in this research study are not greater than those experienced in everyday life. The amount of light used during the study is smaller than the amount of light your child experiences when walking outside on a sunny day. The amount of laser light that is shined in the scalp is well below the American National Standards Institute (ANSI) and the United States Food and Drug Administration (FDA) approved levels.

Benefits Your child's participation in this study may help us learn more about the brain activity of children with ASD as compared to their age-matched peers. The information learned from this study may have a broad impact on the knowledge base of the scientific community.

Explanation & offer to answer questions: ____________________ has explained this research study to you and answered your questions. If you have other questions or research-related concerns, you may reach Dr. Ronald Gillam at 435-797-1704.

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Payment/Compensation To thank you and your child for participation in this study, you will receive $15 in cash. When all study tasks are completed, your child will also receive a toy that he/she gets to choose from a number of different toys.

Voluntary nature of participation and right to withdraw without consequence Participation in research is entirely voluntary. If you decide to not permit your child to participate or if your child decides not to participate, there will be no consequences at all. You or your child can decide not to continue at any time during this study.

Confidentiality Research records will be kept confidential, consistent with federal and state regulations. Only Dr. Ronald Gillam and his research staff will have access to the data that will be kept in a locked file cabinet or on a password protected computer in a locked room to maintain confidentiality. To protect your privacy, personal, identifiable information will be removed from study documents and replaced with a study identifier. Identifying information will be stored separately from data and will be kept. All the research staff have been trained in confidentiality rules consistent with Federal Guideline. Your child's identifying information will be kept for 10 years so that we may analyze all the data we collect. After that time, it will be destroyed so that no one could connect your child to the data

IRB Approval Statement The Institutional Review Board for the protection of human participants at Utah State University has approved this research study. If you have any questions or concerns about your rights or a research-related injury and would like to contact someone other than the research team, you may contact the IRB Administrator at (435) 797-0567 or email irb@usu.edu to obtain information or to offer input.

Copy of consent You have been given two copies of this Informed Consent. Please sign both copies and keep one copy for your files.

Investigator Statement "I certify that the research study has been explained to the individual, by me or my research staff, and that the individual understands the nature and purpose, the possible risks and benefits associated with taking part in this research study. Any questions that have been raised have been answered."

The Research Group for this study includes Drs. Ron Gillam and Breanna Studenka

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Signature of Researcher(s)

______________________________	______________________________
Dr. Ron Gillam	*Daphne Hartzheim*
Principal Investigator	Student Researcher
435-797-1704	*435-938-1629*
ron.gillam@usu.edu	*daphne.hartzheim@gmail.com*

Signature of Participant: By signing below, I agree to allow my child to participate in this study.

______________________________	______________________________
Participant's signature	Date

Child/Youth Assent: I understand that my parent(s) or guardian(s) are aware of this research study and that they have given permission for me to participate. I understand that it is up to me to participate even if they say yes. If I do not want to be in this study, I do not have to and no one will be upset if I don't want to participate or if I change my mind later and want to stop. I can ask any questions that I have about this study now or later. By signing below, I agree to participate.

______________________________	______________________________
Name/Signature	Date

The Research Group for this study includes Drs. Ron Gillam and Breanna Studenka

Appendix C

Intake Form

LANGUAGE, EDUCATION, AND AUDITORY PROCESSING (LEAP) LAB

BACKGROUND INFORMATION

CHILD

Child's name ____
(Last) (First) (M.I.)

Address ____
(Number & Street) (Apt.)

____
(City) (State) (Zip)

Telephone ______________________ Date of Birth ________________________

Place of Birth ______________________________ Sex: M F
(State) (Country)

CHILD'S IMMEDIATE FAMILY

1. Name ____
(Last) (First)
Relationship to child ________________ Occupation __________________________

Educational Level:

High School 2-year college 4-year college Graduate School Professional Degree: RN, MSW, SLP CCC, M.D., Ph.D.

2. Name ____
(Last) (First)
Relationship to child ________________ Occupation __________________________

Educational Level:

High School 2-year college 4-year college Graduate School Professional Degree: RN, MSW, SLP CCC, M.D., Ph.D.

3. Name ____
(Last) (First)
Relationship to child ________________ Occupation __________________________

Educational Level:

High School 2-year college 4-year college Graduate School Professional Degree (M.D. Ph.D.)

4. Name ____
(Last) (First)

Relationship to child _______________ Occupation __________________________

Educational Level:

High School 2-year college 4-year college Graduate School Professional Degree: RN, MSW, SLP CCC, M.D., Ph.D.

BROTHERS & SISTERS

	Name (Last, First)	Date of Birth	Does the child have special needs?	Educational Level
1.	___________________	__________	________________	_______________
2.	___________________	__________	________________	_______________
3.	___________________	__________	________________	_______________
4.	___________________	__________	________________	_______________
5.	___________________	__________	________________	_______________
6.	___________________	__________	________________	_______________

INCOME

Approximate gross annual household income:

a) 0 - $7,000
b) $8,000 - $12,000
c) $13,000 - $15,000
d) $16,000 - $19,000
e) $20,000 - $22,000
f) $23,000 - $25,000
g) $26,000 - $29,000
h) $30,000 - $36,000
i) $37,000 - $50,000
j) $51,000 - $75,000
k) 76,000+

We are interested in whether or not the families in our program are receiving any financial assistance from government programs. At the present time are you receiving money or other help from:

a) Supplemental Security Income? YES NO
b) Veterans Benefits? YES NO
c) Public Assistance or Welfare? YES NO
d) Unemployment Compensation? YES NO
e) WIC? YES NO

SECOND LANGUAGE EXPOSURE

Are any languages other than English spoken to your child? Yes No

If yes, beginning at what age: ________ How frequent? ___________

Which language(s)? ____

Number of individuals living in the home who speak a language other than English _______

Which languages are spoken in the family home? ______________________________________

Is your child being formally taught any languages other than English in school, privately, etc.? Yes

If yes, beginning at what age: ________ How frequent? ___________

Which language(s)? ____

How well does your child speak the second language? (circle one)

Some words Simple phrases Full conversations

How much of the time does your child **speaks/talks** a second language?
(Check all that apply)

	0 minutes	**30 minute**	**1 hour**	**2 hours**	**3 hours**	**More than 3 h**
At home						
With friends						

If yes, please comment
____

____

Does your child receive speech or language therapy?

Speech: Yes _____ No _____ Language: Yes _____ No _____

If yes to either, where does your child receive therapy?

School _____ Clinic _____ Both _____

Name(s) of Speech/Language Pathologists working with your child:

____

____

At what age did your child start receiving therapy? _______________________

Does your child receive any other special services (e.g., programming for learning disabilities?)
Yes _____ No _____

If yes, please describe
____

____

Does your child have any hearing problems? Yes _____ No _____

Has your child ever had problems hearing? Yes _____ No _____

Has your child had problems with ear infections and/or episodes of middle-ear fluid?

Never _______ Occasionally _______ Frequently _______

Approximately how many ear infections and/or episodes of fluid has your child had in the last year?
____

Please indicate the month and year of his/her most recent ear infection or bout of fluid: ________

Has your child ever had tubes placed in his/her ears? Yes _____ No _____

If yes, please list month and year they were placed:

Right Ear	Left Ear
__________________________	__________________________
__________________________	__________________________

During after school activities						
Only in school						

Federal policy requires that we collect data on demographic characteristics of all people participating in our studies. Please complete this section with respect to race and ethnicity by **answering the yes/no question *and* checking all that apply to the participant**. All information will be kept confidential.

Is child Hispanic or Latino? ____ Yes ____ No

Check all that apply:
____ American Indian or Alaskan Native
____ Asian
____ Native Hawaiian or other Pacific Islander
____ Black or African American
____ White
____ Other: ___________________________

SCHOOL INFORMATION

At what age did your child first start school? ___________
Name of first school ____

__________________________ _________________________
(City) (State)

School your child currently attends ____

Current grade in school ___________________ Teacher ________________________

Is your child currently on an active Individualized Education Plan (IEP)?

Yes _____ No_____

If yes, please explain the goals and special education services you child receives

____

____

____

DEVELOPMENTAL (SPEECH AND HEARING) HISTORY

Do you have any concerns about your child's speech or language development?

Yes _____ No_____

If yes, please comment
____

____

Does your child receive speech or language therapy?

Speech: Yes _____ No _____ Language: Yes _____ No _____

If yes to either, where does your child receive therapy?

School _____ Clinic _____ Both _____

Name(s) of Speech/Language Pathologists working with your child:

____

____

At what age did your child start receiving therapy? _____________________

Does your child receive any other special services (e.g., programming for learning disabilities?)
Yes _____ No _____

If yes, please describe
____

____

Does your child have any hearing problems? Yes _____ No _____

Has your child ever had problems hearing? Yes _____ No _____

Has your child had problems with ear infections and/or episodes of middle-ear fluid?

Never _______ Occasionally _______ Frequently _______

Approximately how many ear infections and/or episodes of fluid has your child had in the last year?
____

Please indicate the month and year of his/her most recent ear infection or bout of fluid: ________

Has your child ever had tubes placed in his/her ears? Yes _____ No _____

If yes, please list month and year they were placed:

Right Ear	Left Ear
________________________	___________________
________________________	___________________

Does your child have tubes in place now? Yes _____   No _____

Right Ear? _______   Left Ear? _______   Both? _______

Does you child have a diagnosis of Autism Spectrum Disorder (i.e. ASD, Rhett syndrome, PDD-NOS)?

Yes _____   No _____

If yes, please answer the following questions:

How old was your child when diagnosed with ASD? _________________________

Where was your child diagnosed? ____

What therapy services has your child received that are related to the ASD diagnosis? State type of service and duration.

____

____

____

____

HEALTH HISTORY

Does your child have any vision problems? Yes _____   No _____

If yes, please describe ____

____

Does your child currently have any serious health problems? Yes _____   No _____

If yes, please describe ____

____

Has your child previously had any serious illness or health problems? Yes _____   No _____

If yes, please describe ____

____

Does your child take any medications on a regular basis? Yes _____   No _____

If yes, please describe ____

SPEECH AND LANGUAGE FAMILY HISTORY

Has anyone in your family had speech/language problems? Yes _____ No _____

Has anyone in your family had reading problems? Yes _____ No _____

If yes for either question, indicate relation to child participant in this study (i.e., father, mother, sister, brother, uncle, and grandparent)

Speech/language problems: ____

____

Reading problems: ____

____

What type of problem was it?

___ Articulation (difficulty with speech sounds)
___ Stuttering
___ Language (limited vocabulary, trouble putting words into sentences)
___ Late talker (few words, no sentences at age 2-3 years)
___ Other: ____

Has anyone in your family received speech/language services? Yes _____ No _____

If yes, indicate who and length of service ________________________________

Any additional comments or questions? ____________________________________

____

____

____

Name of person(s) filling out background information:

____
[Name(s)]

Relationship to child _____________________ Date _____________________

Appendix D

Adapted CASL Protocol

Adapted CASL Protocol

Protocol CASL – Pragmatic Judgment

Date:______________________ Participant ID:___________________________
Birthday:_______________

Practice

	Appropriate Responses	**Response**	**Score**
1	I am going to tell you some little stories about some children. Then I will ask you a question. You will tell me what you or the children in the stories should say or do. Listen carefully. The girl in the picture has a sister. Do you have a sister?		
2	Suppose the telephone ring. You pick it up. What do you say?		
3	I will describe some people and the things that happen to them. You are to tell me the best thing to say or do in the situation. When you are introduced to someone, as you shake hands, what can you say?		
4	Karen studied very hard last night for the big test she's taking today. Karen's mom says "good-bye" to the as she leaves for school. What else can her mom say to her?		

Experimental tasks

	Appropriate Responses	Response	
1	This child's name is Billy. Tell me your name.		
2	Billy is three. Now tell me how old you are.		
3	Mom is leaving for work. What do you say to her as she goes out the door?		
4	Josh is thinking about his two new dogs. He's going to name this one Rusty. What name would you give to his other dog?		
5	Mom is opening a box of cookies. You are very hungry. What do you say?		
6	After you've eaten a cookie, Mom says, "Would you like another one?" What do you say?		
7	What do you ask when you want to go out and play?		
8	Debby gives Tom half of her candy bar. What does Tom say to Debby?		
9	What does Debby say back to Tom?		
10	John's baby sister starts crying because she can't get down from her high chair by herself. If the baby could talk, what would she say to John?		
11	Mary walks over to her friends who are playing dolls. Mary wants to play with them. What does Mary say?		
12	Cassie spills her mild at the table. What does she say to her mother?		
13 Age 8	What do you say to your teacher, Mr. Brown, as you come into the classroom in the morning?		
14	Jason needs help carrying his books and football equipment to school. Tell me how he could ask his brother to help him.		
15	One day Dad comes home with a big box. John is curious. What do you think John asks Dad?		
16	Tyrone is looking for his math book. His		

	sister walks into the room. What do you think Tyrone asks his sister?		
17	Ryan goes to a restaurant to get a hamburger. When it is Ryan's turn, the man taking orders says, "What would you like?" What does Ryan say when he orders?		
18 Age 10	There is a new boy at school. Jenny wants to find out if he is in the third grade also. What does Jenny say to the new boy?		
19	How does Jenny ask her teacher, Mrs. Jones, if the new boy is in the third grade?		
20	Molly is having dinner at her friend Jan's home. Jan's father offer Molly dessert. Molly doesn't want any. How should Molly tell him?		
21	Your friend is on the soccer team and his team just lost a close game. What should you say?		
22	Several boys are talking about sports. Mike wants to tell about last night's game. What can Mike say to get a chance to talk?		
23	Rosa want to compliment her teacher, Mrs. White, on her pretty dress. How should she say this?		
24	Carol is in a large store with her mother. She suddenly realizes that she has lost her mother. What should Carol do and what should she say?		
25	It is a hot summer day. MayLee's friend is wearing a heavy jacket. What does MayLee ask her friend?		
26	Grandmother has come to visit. After you say "hello," what else could you say?		
27	Mandy is driving in a new town. She can't find Maple Street where her friend lives. What can she say in asking for directions?		
28	Paul answers the phone, and a man asks to speak to Paul's sister. Paul just yells to his sister, who's upstairs. What should		

	Paul have said to the man?		
29	The students are eating lunch in the cafeteria. Ted starts talking about the worm he dissected in science class. Two of the students get up and leave the table without finishing their lunch. Why?		
30	In the movie theater, everyone hears a 4-year-old say, “I want to go to the bathroom.” What’s wrong with what he does?		
31	What would an older boy do if he had to go to the bathroom?		
32	Marcus is working on a school project, but he isn’t sure of the date that his teacher wants it. What does he ask his teacher?		
33	Amber learns that Erik’s grandmother has just died. She sees Erik in the hall at school. What can she say to him?		
34	A friend invites Bonnie to a small party. Bonnie wants to go but she has already made plans for the night of the party. What can Bonnie say to turn down her friend without hurting her friend’s feelings?		
35	Danielle has never used a pay phone and needs to call her mother. Tom want to help her so he says, “Go to the pay phone in the hallway by the principal’s office. Pick up the receiver and punch in the numbers for your home telephone number. Wait for your mother to answer.” What does Tom forget to tell Danielle?		
36	Kate has two friends named Bill and Jim. Bill and Jim have never met. Kate wants to introduce these two friends to each other. Tell me what Kate will say.		
37	On Friday afternoon Maria overhears a boy at school say that there will be no school the following Monday. Maria goes home and tells her mother that she does not have school on Monday. Why could		

	Maria have been wrong?		
38	Denise listens very carefully to the teacher's explanation of the science lesson, but she still doesn't understand. Denise goes home and tells her mom that she hates science. What could Denise have done while still in class?		
39	Linda needs a white cotton T-shirt. Her mom want to save some time and gas so she tells Linda to call several stores in the area. Tell me three things Linda should ask when she calls the stores.		
40	You are going to have a party. Call and invite a friend. What four details about the party should you tell your friend when you invite him or her?		
41	Brian is driving in a new town. He is looking for the street where his aunt lives, but he can't find it. What two things could he do?		
42	Kate invites Bill to go to a movie with her family. After bill asks his mother if he can go, what more can he say so she will let him?		
43	Lisa just introduced her friend Paul to her father, Mr. Adams. What should Paul say?		
44	Suppose you are at a friend's house and you break an expensive lamp. I am your friend's mother (father). When I come home, what three things would you say to me?		
45	The coach asks Jasmine how much her father earns. Jasmine does not think it is appropriate to tell her coach. What can Jasmine say that would not offend the coach?		
46	Jan is introducing her friend Michael to her father, Mr. Black. What should Jan say?		
47	John has taken his friends to a restaurant to celebrate winning a track trophy. When he gets the check, he sees that he has been charged five dollars too much.		

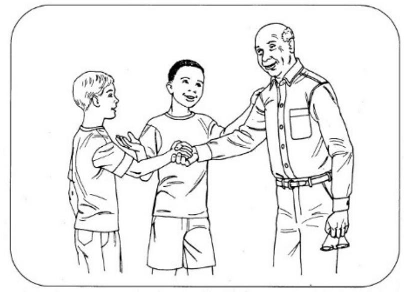
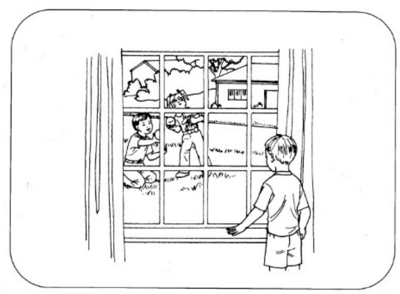
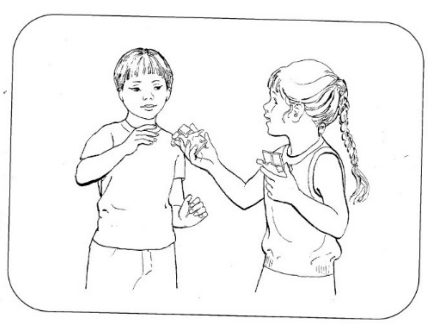
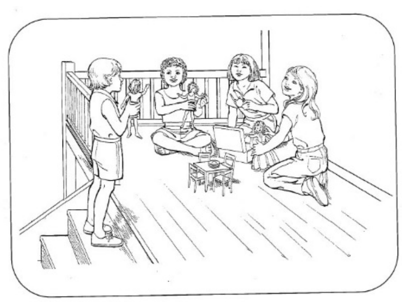
	What should he say about this?		
48	Chad's teacher, Mrs. Smith, is talking to some parents outside the classroom. The principal sends Chad to tell her that she has an emergency call. What can Chad say when he walks up to them and delivers the message?		
49	Jane left for school early to help a teacher. Mother got upset because Jane left her room in a mess. She told Jane that she couldn't go to the Friday football game. Jane got angry and went to her room and slammed the door. Tell me two things that Jane could have said to her mother instead of getting angry.		
50	When David's little sister wants something, he can't understand her speech. What can he say to find out what she wants without telling her he can't understand her and without hurting her feelings?		
51	Lamar has been asked by his coach to get information on a place for the team to stay during the state tournament. Lamar calls a motel in that city. Tell me the three most important things he should ask		
52	Jack has been stopped by a police officer for failing to stop at the stop sign. Jack got angry and yelled at the officer. The officer took Jack to jail. Tell me two things Jack could have said to prevent this action by the police officer.		
53	The teacher asks her first-grade children to tell about summer vacation. When it is Luis's turn, he stands up and says, "Last night I saw a funny movie." The teacher tells Luis to wait until later to tell about the movie. Why?		
54	Bob learns that Sara's uncle has just died. He sees Sara in the hall at school. After saying "I'm sorry," what can he say?		
55	Todd is watching his friend Jessica try on		

	frames for new glasses. She says, "I like these. What do you think?" Todd doesn't like them. How can he tell her indirectly without hurting her feelings?		
56	The new teacher says to the first grade class, "I will greatly appreciate it if you remain in the seated position while I absent myself." What could she have said?		
57	Mr. Smith is telling his friend a long story about something that happened to him when he was young. The friend starts looking at his watch and acting nervous and fidgety. What should Mr. Smith do and what should he say?		
58	The new teacher says to the first grade class, "I will greatly appreciate it if you remain in the seated position while I absent myself." The children do not obey. Why?		
59	When Kay asks the librarian for a special book on cats, the librarian says, "I'm sorry, what did you say?" How can Kay respond to the librarian? Tell me two ways.		
60	Listen for the two important things Tim had to remember. Tim, a member of the baseball team, reads this notice on the bulletin board at school: The school bus will take the baseball team to the game. The bus will take all fifteen team members. The rest of the seats will be for seniors. It will leave from the school's front door. There will be a pep rally on the bus. It will leave at three o'clock. What are the two important things Tim has to remember?		

Appendix E

CASL Pictures

CASL pictures

Example 1 	Example 3 
Item 1 	Item 3 
Item 5 	Item 7 
Item 9 	Item 11 

Appendix F

Preference Assessment and Token Economy Data Sheets

Preference Assessment and Token Economy data sheets

Preference Assessment

Date:			Participant:		
	Item 1	Item 2	Item 3	Item 4	Item 5
Rank Trial 1					
Rank Trial 2					
Rank Trial 3					
Total					

Token Economy:

Date:					Participant:					
Time interval for task										

CURRICULUM VITAE

DAPHNE HARTZHEIM

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EDUCATION

Doctor of Philosophy in Disabilities Disciplines (Speech-Language Pathology), Utah State University, Logan Utah

- 2011-2015
- Current GPA: 3.80
- Advisor: Ron Gillam, Ph.D.

Master of Science in Speech Language Pathology, Utah State University, Logan Utah, May 2005

- 2003-2005
- GPA: 3.76
- Advisor: Beth Foley, Ph.D

Bachelor of Arts in Communicative Disorders and Deaf Education, Utah State University, Logan Utah, Dec 2003

- 2000-2003
- GPA: 3.61

Brigham Young University, Jerusalem, Israel (Study Abroad)

- May 1999-July 1999

CERTIFICATIONS

- Certificate of Clinical Competence from American Speech-Language and Hearing Association (# 12085317) active since 2006
- Utah Professional Licensure: Speech Language Pathologist (# 652345-4102) active since 2011
- Board Certified Behavior Analyst (# 235734)

AWARDS

- Student Researcher of the Year of Communicative Disorders and Deaf Education (2015)
- Student Researcher Travel Award ASHA (SRTA, 2014)
- Research-Mentor Program Travel Award ASHA (RMPTA, 2014)
- Outstanding Graduate Student at Utah State University (2004)

PUBLICATIONS UNDER REVIEW OR IN PREPARATION

- Gillam, S. L., Hartzheim, D., Studenka, B., Simonsmeier, V., & Gillam, R. (2015). Narrative Intervention for Children with Autism Spectrum Disorder (ASD). *Journal of Speech, Language, and Hearing Research*.
- Pyle, N., Crowther, A., Lignugaris/Kraft, B., Gillam, S., Reutzel, D. R., Olszewski, A., Segura, H., **Hartzheim, D.**, Laing, W., & Pyle, D. (in review). Effects of expository text structure interventions on comprehension: A meta-analysis. *Journal of Educational Psychology.*

- Durán, L. K., **Hartzheim, D.**, Kohlmeier, T. L., Lund, E., Simonsmeier, V. (under review). *A review of language interventions with Dual Language Learners.*

PRESENTATIONS

- **Hartzheim, D.U.**, Gillam, S.L., & Gillam, R. (2014, November), *Narrative Intervention with children with Autism Spectrum Disorder.* 1-Hour Oral Session at ASHA. Presentation selected for Outstanding research submitted with student as the first author from ASHA (Received Student Research Travel Award – SRTA)
- **Hartzheim, D.U.,** Gillam, S.L., & Gillam, R. (2014, June). *Narrative Intervention program with children with autism*. Poster presented at Symposium on Research in Child Language Disorders in Madison, WI.
- **Hartzheim, D. U.**, Gillam, S. L., & Gillam, R. (2014, April). *Narrative intervention program with children with autism.* Presentation given at the Utah State University Graduate Research Symposium in Logan, UT.
- **Hartzheim, D. U.**, Gillam, S. L., & Gillam, R. (2014, April). *Narrative intervention program with children with autism.* Poster presented at the Utah State University Inclusive Excellence Research Symposium in Logan, UT.
- Kelley, K. N., Higbee, T. S., **Hartzheim, D. U.**, & Gunnell, J. (2013, May). *The effects of simultaneous script training and fading procedures on the mand variability of children with autism.* Presentation given at the annual Applied Behavior Analysis International Convention held in Minneapolis, MN.
- Akers, J. S., **Hartzheim, D. U.**, Brodhead, M. T., Higbee, T. S., Pollard, J. S., & Kelley, K. N. (2013, April). *Teaching social skills to children with autism and improving employee implementation of discrete trial via E-learning.* Presentation given at the Utah Valley University conference on autism in Provo, UT.
- Brodhead, M. T., Pollard, J. S., Akers, J. S., **Hartzheim, D. U.**, & Higbee, T. S. (2012, February). *Ethical considerations for applied behavior analysts.* Workshop given at the annual meeting of the California Association for Behavior Analysis in Anaheim, CA.
- **Hartzheim, D. U.**, Higbee, T. S., & Gillam, R. (2012, November). *Applied Behavior Analysis in the Treatment of Autism Spectrum Disorder in a Preschool Setting.* Poster presented at the annual American Speech-Language and Hearing Association Convention held in Atlanta, GA.
- Brodhead, M. T., Higbee, T. S., Pollard, J. S., & **Hartzheim D. U.** (2011, October). *The use of activity schedules to promote social and on-task behaviors in children with autism during a game of hide and seek.* Poster presented at the annual Nevada Association for Behavior Analysis Conference in Reno, NV.

WORKSHOPS and SEMINARS

- **Hartzheim, D. U.** (2014, September). *Functional Communication Training in Russian Special Education Schools for Children with ASD and other developmental disabilities.* Week long seminar with individual supervision given in Nizhny Novgorod, Russia. Funded by the Naked Heart Foundation.
- Brodhead, M. T., Pollard, J. S., Akers, J. S., **Hartzheim, D. U.** & Higbee, T. S. (2012, February). *Ethical Considerations for applied behavior analysts.* Workshop given at the annual meeting of the California Association for Behavior Analysis in Anaheim, CA.

REVIEW ACTIVITIES

- Reviewer of presentation proposals for ASHA Convention 2015
- Reviewer of presentation proposals for ASHA Convention 2014
- Reviewer of presentation proposals for ASHA Convention 2013

TEACHING EXPERIENCE

Utah State University

COMD 5070: Speech Science
- Position: Guest lecturer on Neurological System and Neuro-Imaging
- Duration: Fall 2014

COMD 2600: Introduction to Communicative Disorders and Deaf Education
- Position: Co-Instructor
- Duration: Fall 2013

SPED 4000: Education of Exceptional Individuals
- Position: Guest lecturer
- Duration: Fall 2013, Spring 2014, Fall 2014

SPED 5010: Applied Behavior Analysis 1: Principles, Assessment, and Analysis
- Position: Teaching Assistant
- Duration: Fall 2011, Fall 2012

USU 1010: Connections Freshman Orientation
- Position: Instructor
- Duration: Fall 2013, Fall 2014

Germany

Pediatric Speech and Language Development
- Position: Instructor
- Duration: Fall 2009, Spring 2010, Fall 2010, Spring 2011

Diagnostic and treatment of Speech and Language Disorders
- Position: Instructor
- Duration: Fall 2009, Spring 2010, Fall 2010, Spring 2011

Augmentative and Alternative Communication
- Position: Instructor
- Duration: Spring 2010, Spring 2011

Diagnostic and treatment of Dysarthria

- Position Instructor
- Duration: Fall 2009, Fall 2010

Cognitive therapy and Dementia

- Position Instructor
- Duration: Spring 2011

WORK EXPERIENCE

Assistant Professor and clinical supervisor at private Speech Therapy School – Prof. König und Leiser Schulen, October 2009-2011, Germany

- Taught following subjects to future speech therapists: pediatric speech and language development, diagnostic and treatment of speech and language disorders, dysarthria diagnosis and treatment, geriatric issues, Augmentative and Alternative Communication
- Supervision of student treatment sessions of children with speech and language impairment, patients with dysarthria and patients with cognitive impairments
- Planned and executed screening projects with local pre-schools
- Conducted evaluation and treatment of patients with speech and language impairments in single treatment and group treatment sessions (TBI, aphasia, dysarthria, articulation disorders, apraxia of speech, cognitive impairments)

Private Speech Therapist for English-speaking preschool children in Germany
Sept. 2006-Sept.2009

- Evaluation and treatment of speech and language disorders
- Trained family and educators on language facilitation techniques to help children succeed

Speech Therapist at a private practice – Logopaedische Praxis Jeanette Kapere
March 2007-Aug 2009, Germany

- Evaluation and treatment of pediatrics and adults with aphasia, dysphagia, apraxia of speech, developmental speech and language disorders in inpatient, outpatient and home health settings
- Supervised and trained of new employees
- Developed increased efficacy for treatment methods and documentation

SLP for Infinity Rehab, Portland, Oregon, USA
July 2005-June 2006 Portland, Oregon

- Evaluations and treatment of adults with aphasia, dysphagia, dyarthria, apraxia of speech, laryngectomies, aphonia, Parkinson's disease, TBI, CVA, dementia
- Created treatment plans, settings goals, family and staff education
- Training and supervising medical staff and care givers of treatment methods and techniques
- Use of AAC