

NEURAL BASES OF IMPLICIT LEARNING IN
YOUNG ADULTS WITH ASD AND THEIR PARENTS

by

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ABSTRACT

It is theorized that the implicit learning impairments seen in persons with ASD may be due to a more general underlying neural dysfunction evidenced by diminished activation in the basal ganglia, specifically the caudate nucleus, and diminished communication between areas of the brain in persons with ASD, specifically the caudate and medial temporal cortex. This study examined the relationship between implicit learning deficits in individuals with ASD and parents of persons with ASD and associated differences in brain activation. Twelve high-functioning children and adolescents with ASD and 17 age and verbal ability matched typically developing controls, 10 parents of participants with ASD, and 9 parents of typically developing participants completed an artificial grammar learning task while in an fMRI scanner. Behaviorally, participants with ASD showed significantly less grammar learning than typically developing participants. Additionally, parents of participants with ASD showed significantly less grammar learning than parents of typically developing participants. Activation analyses contrasting the neural response to grammatical versus nongrammatical stimuli revealed less activation in the areas of the anterior cingulate and caudate for participants with ASD compared to typically developing participants. Similar differences in these areas were also found in the parent groups. Results indicated that diminished activation in the caudate nucleus and cingulate cortex may underlie differences in implicit learning.

DEDICATION

This dissertation document is dedicated to all of those individuals and families whose time and data made this project possible.

LIST OF ABBREVIATIONS AND SYMBOLS

<i>df</i>	Degrees of freedom: number of values free to vary after certain restrictions have been placed on the data
<i>F</i>	Fisher's <i>F</i> ratio: A ration of two variances
<i>M</i>	Mean: the sum of a set of measurements divided by the number of measurements in the set
<i>p</i>	Probability associated with the occurrence under the null hypothesis of a value as extreme as or more extreme than the observed value
<i>r</i>	Pearson product-moment correlation
<i>t</i>	Computed value of <i>t</i> test
<	Less than
=	Equal to

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INTRODUCTION

Autism is a pervasive developmental disorder usually diagnosed in childhood and characterized by core impairments in the development of social and communication skills, abnormal language development, and a restricted repertoire of behaviors and interests (Klinger, Dawson, & Renner, 2003). The term Autism Spectrum Disorder (ASD) is used to include diagnoses of autism, Asperger's syndrome, and pervasive developmental disorder not otherwise specified (PDD-NOS), which include varying levels of impairment along a spectrum of the core deficits of socio-communicative skills, language, and restricted interests and behaviors. While there are a number of models of the underlying cognitive impairments in ASD, one idea is that the social and language processing impairments are secondary effects of primary deficits in one or more cognitive skills. Klinger, Klinger, and Pohlig (2007) hypothesized that these social and language processing impairments may be caused by a dysfunction in implicit learning, and subsequent research has provided evidence for this as a possible precursor to the social impairments characterized by ASD. Additionally, recent studies have also pointed to ASD as a neurological disorder, with anatomical, activation, and connectivity differences associated with some of the behavioral differences in individuals with ASD. It is theorized that the implicit learning impairments seen in persons with ASD may be due to a more general underlying neural dysfunction, specifically diminished activation in the basal ganglia, specifically the caudate nucleus, and diminished communication between areas of the brain in persons with ASD, specifically the basal ganglia and medial temporal cortex. This study will examine the

relationship between implicit learning deficits in individuals with ASD and parents of persons with ASD and associated differences in brain activation.

Implicit Learning

Reber (1993) defined implicit learning as the learning of knowledge without the conscious effort to learn, and without the conscious knowledge of what was learned. Implicit learning has been found to be independent of differences in intelligence (Atwell, Conners, & Merrill, 2003; Reber, Walkenfeld, & Hernstadt, 1991, but see also McGeorge, Crawford, & Kelly, 1997; Fletcher, Maybery, & Bennett, 2000) and chronological age (Hayes & Taplin, 1993; Lee, Klinger, Klinger, & Atwell, 2001, but see also Howard, Howard, Dennis, & Yankovich, 2007), and is thought to underlie the development of social intuition (Lieberman, 2000). This is in contrast to explicit learning in which persons have conscious knowledge of what was learned. Explicit learning is the use of effortful, strategic mental processes to learn information. This is dependent on intelligence (McGeorge, Crawford, & Kelly, 1997; Reber et al., 1991) and chronological age (McGeorge et al., 1997). Implicit learning may play an important role in learning the many unspoken rules that govern social interaction and language, two of the main areas of impairment in persons with ASD. The ability to automatically abstract information across experiences allows persons to understand these social rules without requiring the ability to consciously describe these rules (Lewicki & Hill, 1987). This implicit learning of the rules of social interaction is a type of automatic cognitive skill that is present in the first year of life (Meltzoff, 2005). Additionally, implicit learning is vital to language development, as young children seem to implicitly learn the rules of their language and the unspoken implications of messages before they are able to verbalize those rules (Gomez & Gerkin, 1999; Saffran et al.,

1996; 1997). This implicit understanding of social interaction and language continues across the lifespan.

Seger (1997) theorized that there are two main types of implicit learning: Implicit learning that relies primarily on motor responses (such as the serial reaction time task), and implicit learning that relies primarily on judgments (such as the prototype, weather prediction, and artificial grammar tasks). Implicit learning that relies on motor responses for learning are often discussed as procedural learning, or more generally as motor-linked implicit learning. Nissen and Bullemer (1987) first studied motor-linked implicit learning through the serial reaction time (SRT) task. During this task participants respond with button presses to locations of stimuli presented. Unknown to the participant, there is a sequence of locations where the stimuli appear, typically of adequate length to prove impossible for the participant to glean. With practice, the participant's reaction times of responses to stimuli decrease; however, reaction times increase when the stimuli fail to follow the established pattern. While participants do not seem to possess conscious knowledge of the sequence (though most feel there was some pattern to the task), this reaction time difference indicates that participants show some benefit due to sequence knowledge. This knowledge is theorized to be gained implicitly. Theories of how motor-linked implicit learning occurs vary, yet most researchers agree that specific sequences of stimuli are not stored in memory (Hoffman, Martin, & Schilling, 2003; Kelly, Burton, Riedel, & Lynch, 2003). There is some support that what is stored in the learning process is a series of stimuli-independent response locations (Willingham et al., 2000).

Judgment-linked implicit learning typically involves more conceptual, abstraction-based learning. In a typical judgment-linked implicit learning task, participants garner the implicit knowledge of a concept (as opposed to motor-linked locations) through exposure to multiple

instances of a concept, where abstraction of the general concept is presumed to occur. One common example of a judgment-linked implicit learning task is the artificial grammar learning task (Reber, 1967). The artificial grammar learning task looks at the learning of a complex Markovian grammar (see Figure 1). Participants are initially exposed to strings of letters or shapes. The strings of typically three to eight letters or shapes all follow the rules of the grammar. Participants are then told that there was a complex set of rules used to generate the previous strings. Then, they are asked during a test phase to judge whether or not new strings are “grammatical” or follow the rules. Participants are often instructed to use intuition or their gut feeling to make decisions. Although participants typically express low confidence in being able to judge strings, most research shows a consistent pattern of above chance performance on this task. Additional tasks of judgment-linked implicit learning include the prototype learning task (Posner & Keele, 1968) and the weather prediction task (Knowlton, Squire, & Gluck, 1994), where the same patterns of learning without the ability to consciously identify relationships is seen. It should be noted that this judgment linked implicit learning does not always involve visual information. Gomez and Gerken (1999) used an auditory artificial grammar task in infants to show that infants can discriminate grammatical strings from nongrammatical strings after a habituation period to the grammatical string sounds. The primary difference between judgment-linked implicit learning and motor-linked implicit learning is that judgment-linked implicit learning involves this abstraction of a concept as measured through an explicit classification or judgment, whether the abstraction is rule-based or exemplar based. Motor-linked implicit learning involves some automatic learning of locations or motor movements, typically measured by a motor response. More evidence dissociating these two types of implicit learning with regard to neurological associations will be discussed below.

Implicit Learning in ASD. Several studies have compared the categorization abilities of individuals with ASD to individuals with typical development using an implicit (prototype) learning task. Klinger and Dawson (2001) used a prototype learning task using cartoon animals in persons with ASD compared to individuals with typical development. After an exposure phase in which participants saw variations of an animal category which varied on four features (e.g., length of leg, width of neck), participants were given a forced-choice test phase to choose the correct category member between a novel exemplar of the target animal paired with either the prototype animal or a target animal that was previously seen. While children with typical development chose the prototype animal 79% of the time, individuals with ASD did not choose the prototype significantly greater than chance (54%), suggesting that they did not base category judgments on a stored representation of the prototype. However, on a rule-based category learning task in which category membership was determined by a simple rule, the performance of individuals with ASD was similar to typically developing individuals. This suggests that explicit learning may not be impaired in individuals with ASD.

Molesworth, Bowler, and Hampton (2005) showed somewhat conflicting results in a study of recognition memory and prototype learning in high functioning individuals with ASD and typical development. Though the authors used a task similar to that used by Klinger and Dawson (2001), the study had the participants decide if they remembered the animal, as opposed to having participants choose which animal was the target animal as in Klinger and Dawson's study. Persons with ASD and typical development showed similar prototype effects on this task. Klinger, Klinger, and Pohlig (2007) have suggested that mental age differences between the participant groups may be the cause of the contrasting findings in the Klinger and Dawson

(2001) and the Molesworth et al. (2005) studies, as the participants in the Molesworth et al. (2005) study were older and had less mental retardation.

Klinger et al. (2007) compared children with ASD and typical development on two implicit learning tasks. One of the tasks was the prototype learning experiment; the other was an artificial grammar learning task. On both tasks individuals with typical development performed significantly better than individuals with ASD, replicating the Klinger and Dawson (2001) finding of impaired implicit learning in persons with ASD. Additionally, the relation between implicit learning and explicit reasoning was examined in this study. A composite measure of explicit reasoning derived from the Woodcock-Johnson Concept Formation and Analysis-Synthesis scales (2001) and the KBIT Matrices scale (Kaufman & Kaufman, 1990) was correlated with implicit learning task performance. For typically developing participants explicit reasoning was weakly related to implicit learning task performance. However, for participants with ASD implicit learning task performance on both tasks was strongly related to explicit reasoning. This indicates that individuals with ASD may use explicit reasoning processes to compensate for implicit learning impairments. Thus, the reason why Klinger and Dawson (2001) and Molesworth et al. (2005) showed different results patterns may have been due to differences in the explicit reasoning abilities of their participants. Klein, Klinger, & Klinger (2007) also examined prototype formation in young adults with ASD. The effect size for the difference in prototype effect due to diagnosis was Cohen's $d = .68$, very similar to the effect size of diagnosis on prototype learning observed in the Klinger and Dawson (2001) and the Klinger, Klinger, and Pohlig (2006) studies using similar prototype tasks, $d = .68$ and $d = .75$ respectively. This study echoed the finding of differences between persons with ASD and persons with typical development in prototype learning.

Thus, we have evidence that judgment-linked implicit learning seems to function differently in persons with ASD. Younger children with ASD seem to show large impairments in implicit learning. However, older individuals (i.e., young adults) with ASD seem to show less impaired implicit learning task performance. This dissertation examines the theory of impaired implicit learning in persons with ASD by using neuroimaging methods to understand the underlying brain mechanisms used in implicit learning in persons with ASD. In this way it is possible to observe similarities or differences in these underlying brain mechanisms.

Neurological Evidence of Implicit Learning

A number of studies have used fMRI to examine brain activity in implicit learning tasks using typically developing adults and adults with neurological disorders. As mentioned earlier, previous research in implicit learning can be broadly divided into two types of tasks: tasks that involve learning procedural information (motor-linked implicit learning) and tasks that involve conceptual abstraction (judgment-linked implicit learning); I will examine the neuroimaging evidence in the same way.

Numerous studies examining both judgment-linked and motor-linked implicit learning have implicated the basal ganglia. The basal ganglia are a group of insular nuclei made up of the caudate nucleus and the putamen (collectively known as the striatum), the globus pallidum, the subthalamic nucleus, and the substantia nigra. The basal ganglia receive input directly from a variety of neural structures, including most of the cerebral cortex, amygdala, hippocampus, and thalamus. As such, the basal ganglia have been tied to a number of functions, including motor movements, cognition, and learning (Middleton & Strick, 1994; Schultz, 2006).

A number of studies have examined the neurocorrelates of sequential learning of complex motor sequences using the SRT (Rauch et al., 1997; Rauch et al., 1998). The vast majority of

these studies have found that motor-linked implicit learning is tied to increased activation in the tail of the caudate and the putamen (Ashby, Alfonso-Reese, Turken, & Waldron, 1998; Rauch et al., 1997). Additionally, Rauch et al (1997) found that the amount of implicit learning from an SRT task was highly correlated with activation of the putamen. Specifically, the magnitude of change (increase) in the activation of the putamen was significantly correlated with the increased speed in responding to sequenced locations (evidence of implicit learning). Moreover, evidence from this study as well as others suggests a right-lateralized nature to the striatum (the caudate nucleus and putamen) recruitment during motor-linked implicit learning (Rauch et al., 1995, 1997). Other studies have shown that this lateralization to be less uniform, and may be more of an individual difference (Rauch et al., 1996).

Judgment-linked implicit learning, including sequential learning of complex patterns without a large motor component, has been associated with increased activation in the head of the caudate and decreased activation of visual cortex (Ashby et al., 1998; Lieberman, 2004). This may occur because the caudate is crucial for understanding how one event or object predicts another event or object (McClure, Berns, & Montague, 2003). Studies investigating brain activity in implicit learning tasks involving incidental category learning have consistently shown that implicit learning is linked to decreased activation in visual cortex V1 and V3, possibly due to some form of habituation to familiar stimuli and stimulus features (Aizenstein, 2000; Reber et al., 2003). Thus, depending upon the task, judgment-linked implicit learning has been tied to the caudate in the basal ganglia and visual cortex V1 and V3. We know that while judgment linked-implicit learning differs from motor-linked implicit learning, the basal ganglia seem to be connected to both forms of implicit learning. Additionally, we know from evidence in other neurological disorders that different forms of implicit learning can be affected in two different

disorders of the basal ganglia. Lieberman (2004) discussed the differences in two neurological disorders of the basal ganglia, Parkinson's and Huntington's disease, where individuals with Parkinson's disease show impairments in social behavior as well as motor-linked implicit learning, whereas individuals with Huntington's disease are marked by impairments in social perception as well as judgment-linked implicit learning. This link between forms of implicit learning and basal ganglia function could be an important one for understanding impairments in social-communication skills in individuals with ASD.

Behaviorally, it is difficult to differentiate clearly between the underlying brain mechanisms of implicit and explicit learning processes because it is possible to use explicit processes when solving implicit learning tasks (Reingold & Merikle, 1988). However, brain imaging has offered possibilities for distinguishing between these two processes. Rauch et al. (1997) showed that individuals with typical development and individuals with obsessive compulsive disorder (OCD) behaviorally performed similarly on an implicit motor learning task. However, typically developing individuals showed increased basal ganglia activation while persons with OCD showed increased activation in the medial temporal cortex. Rauch suggested that individuals with OCD used a more explicit approach to the task than typically developing individuals. Similarly, Lieberman (2004) found evidence for a dissociation between caudate and medial temporal cortex activation during an artificial grammar learning task in typical adults. Specifically, the Lieberman (2004) study employed a balanced chunk strength design, which used both low chunk strength and high chunk strength stimuli. Typically, researchers are interested in the ability to automatically learn the grammar rules; however, by design, grammatical strings contain more chunks (groups of two or three elements) that are more superficially similar to other grammatical strings than nongrammatical strings. These chunks, or

groups of common letters may be easily explicitly remembered by participants. A confound for researchers using this task is that not accounting for chunk strength prevents the researcher from completely understanding whether participants are learning the grammar or are making judgments based on memory for specific chunks. Balancing chunk strength allows the researcher to observe the grammar learning process independent of chunk strength. Lieberman found that during a balanced chunk strength design, activation in the caudate and medial temporal cortex was highly negatively correlated ($r = -.88$) suggesting that participants were either using caudate-related processes (i.e., an implicit approach) or medial temporal processes (i.e., an explicit approach), but not both simultaneously.

In addition, researchers have found regarding the link between basal ganglia dysfunction disorders like Parkinson's and Huntington's disease and impaired implicit learning (Ferraro, Balota, & Connor, 1993; Knowlton, Mangels, & Squire, 1996; Knowlton, Squire, Paulsen, Swerdlow, & Swenson, 1996). Additionally, implicit learning seems to be intact in patients with medial temporal damage (Knopman & Nissen, 1987; Knowlton, Mangels, & Squire, 1996), supporting Lieberman's (2004) notion that the medial temporal cortex may underlie more explicit forms of processing, while the basal ganglia underlie more automatic forms of processing. It is also important to note that all of these studies examined implicit learning during a test phase, telling us how the brain activates when individuals are using knowledge gained during an earlier exposure phase to make these judgments. The areas underlying the actual abstraction of concepts (such as during an exposure phase), whether the same or different, are still unknown.

Several researchers (Aizenstein et al., 2001; Reber et al., 2003) have also compared implicit and explicit learning processes in a category learning paradigm. Some participants were

told to explicitly learn a new category. Others were exposed to the category without being explicitly told to learn it. Those given the explicit instructions showed increased medial temporal and prefrontal cortex activation (Reber et al., 2003). However, participants who learned the category implicitly showed neither medial temporal activation nor prefrontal activation but instead showed changes in visual cortex activation. These findings mirror those of Lieberman (2004) in finding different neural pathways for implicit and explicit learning. Taken together, there is a growing body of evidence suggesting that implicit learning tasks can be performed “implicitly” through activation of the basal ganglia or visual cortex or “explicitly” through activation of the medial temporal cortex or prefrontal cortex.

Brain Differences in ASD

The findings of differences in the anatomy of brains of individuals with ASD have been mixed. The most consistent finding is that individuals with ASD show differences in overall brain volume. Overall volume enlargement seems well recognized in ASD, from toddlers (Courchesne et al., 2001) to older children (Sparks et al., 2002) and adolescents (Piven et al., 1992, 1995; Hardan et al., 2001). However, when separated into analyses of gray matter and white matter, the finding of enlargement is not as well-defined. In a study of males between ages 8 and 18 years, Lotspeich, et al. (2004) found gray matter volume to be higher in persons with autism compared to typically developing controls, while finding no differences in the volume of white matter. However, Herbert, et al. (2004) found cerebral white matter enlargement in children with autism, especially in the frontal lobe. Additionally, 2 year old children with autism were found to have a greater volume of gray matter in frontal and temporal lobes, and in white matter in the frontal and parietal lobes (Carper, Moses, Tigue, & Courchesne, 2002). One lone exception to the general pattern of enlargement is that several studies have found a reduction in

volume of the white matter of the corpus callosum (Piven, Bailey, Ransom, & Arndt, 1995; Manes et al., 1999; Hardan, Minshew, & Keshavan, 2000). So while total brain volume is consistently found to be larger persons with ASD, the evidence is mixed with some, but not all, studies showing generally increased gray matter and white matter and reduced volume of the corpus callosum in persons with ASD.

There is also evidence for structural differences within the basal ganglia of persons with ASD. Increased caudate volumes (Sears et al., 1999) and reduced areas of lenticular nucleus (Gaffney, Kuperman, Tsai, & Minchin, 1989) have been found, while there have been no differences reported in the size of the putamen (Sears et al., 1999). Much like other morphological studies in persons with ASD, there are conflicts in reports of basal ganglia volume. A more recent study in basal ganglia size by Hardan and colleagues (2003) found no differences in caudate or putamen size when controlling for overall brain volume among 40 individuals with ASD compared to 41 typically developing individuals. This more recent evidence supports a notion that differences previously seen in basal ganglia size may have been due to overall size differences or use of psychotropic medication (known to affect the size of the basal ganglia), which they controlled for in this study.

Studies of activation differences in persons with ASD have historically fallen along two theoretical lines: social processing deficits and general cognitive deficits. Much of the research in activation studies stem from what are to believed to be impairments in individuals with ASD or original models of neural dysfunction in ASD, such as the frontal and medial lobes and the striatum (Damasio & Maurer, 1978). Neural evidence for social processing deficits include reduced or absent activation in the fusiform face area (Dalton et al., 2005) and abnormalities in the amygdala (Pelphrey et al., 2004) in persons with ASD during face processing and reduced

activation in the amygdala (Baron-Cohen et al., 1999) and medial prefrontal cortex (Happe et al., 1996) in persons with ASD during theory of mind tasks. Neural evidence for general cognitive deficits include lower activation in the dorsolateral prefrontal cortex and posterior cingulate regions for spatial working memory in persons with ASD (Luna et al., 2002), lower left frontal activation and higher activation in posterior brain areas for working memory of persons with ASD (Koshino et al., 2005), reduced lateralization of the frontal lobe and abnormal temporal activation during language processing of persons with ASD (Wang, Lee, Sigman, & Dapretto, 2006), and lower Broca's area activation and higher Wernicke's area activation in persons with ASD during sentence comprehension (Just, Cherkassky, Keller, & Minshew, 2004). What is clear from the numerous activation studies in persons with ASD is that activation differences are dependent on the task. While there are several cognitive processes that show greater activation for individuals with ASD (working memory, sentence comprehension, etc.), the majority of studies reveal a reduction in local brain activation.

Though there have been no neuroimaging studies of judgment-linked implicit learning in persons with ASD, a recent study examined a form of motor-linked implicit learning, using a modified SRT paradigm. Muller, Kleinmans, Kemmotsu, Pierce, and Courchesne (2003) used fMRI to examine brain activation of participants with ASD and control participants while they performed finger presses according to a repeating 6 digit sequence, with response times decreasing significantly throughout the task for both groups. While participants with ASD showed activation in the premotor cortex area similar to control participants, they displayed a more scattered pattern of activation in the superior parietal area, suggesting a possible difference in the direction of visuospatial attention. Additionally, the researchers found that participants

with ASD have greater activation in the prefrontal cortex, a finding consistent with a more explicit form of learning the sequence.

Functional Underconnectivity in ASD

While much of the research in neural function of persons with ASD remains focused on localized activations or structural differences from persons with typical development, more recent research has centered on more integrative methods based on interregional activation and anatomical interactions. The cortical underconnectivity theory of autism (Just et al., 2004) is a recent theory which bridges differences between persons with ASD and typical development in both anatomical and activation areas. The underconnectivity theory posits that ASD is related to dysfunction in the interbrain circuitry (specifically connective white matter), causing an asynchrony in the exchange of information from different network systems in the brain. The result of this underconnectivity is that information at the neural and cognitive levels is incorporated inefficiently. Particularly, it is the case that communication is required between frontal and posterior areas of the brain, synchronization should be lower (Just, Chervassky, Keller, Kana, & Minshew, 2007). Evidence for the underconnectivity theory of autism include reduced connectivity (activational asynchrony) for persons with ASD during tasks of sentence comprehension (Just et al., 2004; Kana, Keller, Chervassky, Minshew, & Just, 2006), executive functioning (Just et al., 2007), inhibitory control (Kana, Keller, Minshew, & Just, 2007), working memory (Koshino et al., 2005; Koshino et al., 2008), and theory of mind (Kana, Keller, Chervassky, Minshew, & Just, 2008).

In addition to functional connectivity findings, this theory has also been supported by differences in anatomical morphometry. While studies examining morphometry in the lobes find a mixed pattern of enlargement, several studies have found abnormalities, mostly a reduction in

volume, of the white matter of the corpus callosum (Piven, Bailey, Ransom, & Arndt, 1998; Manes et al., 1999; Hardan, Minshew, & Keshavan, 2000), which seems to be especially prominent in a number of morphometry studies examining anatomical differences in individuals with ASD. Chung, Dalton, Alexander, and Davidson (2004) also found specific areas of reduction in white matter density in the corpus callosum, including the genu, rostrum, and splenium taken as a measure of neural connectivity in the corpus callosum, and suggesting an impairment in the efficiency of communication on an interhemispheric and interlobal scale. Differences in the structural connectivity in persons with ASD provides further supporting evidence that behavioral impairments in ASD may be the result of some more general underconnectivity in the brain of persons with ASD. So while there may be process-dependent areas of high and low activation, or varying differences in anatomical structures, the cortical underconnectivity theory of autism attempts to explain numerous cognitive impairments through a lack of regional communication.

Parents of Individuals with ASD

Although ASD is generally considered to have a strong genetic component, the specific genes involved in the disorder are as of yet unclear (Pickles et al., 1995). Although much of the research on genotypes in ASD points to a subset of qualitatively different diagnoses, many researchers theorize that there are a number of susceptibility genotypes which increase the likelihood of developing certain symptoms (Dawson, Webb, Wijsman, & Schellenberg, 2005). One way of understanding this disorder from a genetic point of view is to study the pattern of autism-like traits in family members of persons with autism. This is known as the study of the broader autism phenotype (BAP). While there is currently no unifying theory of how BAP ties into genetics, concordance rates for autism-like traits among monozygotic twins are around 90%

(Bailey, Palferman, Heavey, & Le Couteur, 1998), much higher than for the full disorder, providing support for a milder form of autism that clearly implicates autism as a wide *spectrum* of impairments. A number of studies show wide ranging autism-like traits in parents of persons with ASD when compared to parents of either persons with typical development or persons with developmental disabilities. Parents of persons with ASD have been found to show more deviant social behavior (specifically fewer and lower quality of friendships) (Piven et al., 1997; Santangelo & Folstein, 1995), higher levels of aloofness, anxiety, and rigidity (Piven et al, 1994, 1997; Wolff, Narayan, & Moyes, 1988), and worse conversational skills (Landa et al., 1992). Additionally, parents of persons with ASD have been shown to perform worse on tasks of executive function (Hughes, Leboyer, & Bouvard, 1997) and better on the block design task mirroring findings in persons with ASD (Happe, Briskman, & Frith, 2001). Thus, across a wide variety of tasks and situations parents of persons with ASD show behavior that can place them upon the same spectrum of behavior as their children.

While it is important to show these behavioral similarities in the parent and child groups within the autism spectrum, few studies have examined the tie between behavior and brain function for these groups. In a rare study, Dawson, Webb, Wijsman, and Schellenberg (2005) examined brain function during face processing in individuals with ASD and parents of individuals with ASD. Face processing is a process long known to be different in persons with ASD (Boucher & Lewis, 1992) as well as parents of individuals with ASD (Baron-Cohen, Wheelwright, & Jolliffe, 1997). Dawson and colleagues (2005) examined event-related potential (ERP) of the posterior temporal lobe of persons with ASD and parents of persons with ASD while viewing faces. In typically developing individuals, there is a specific pattern of activation in this region in response to face stimuli. Specifically, it has been found that there is lateralized

fusiform gyrus activity in response to viewing faces, where the right fusiform area activates much greater than the left (Kanwisher, McDermott, & Chun, 1997). Dawson and colleagues (2005) found that individuals with ASD showed reduced activity in the right fusiform gyrus compared to typically developing individuals. This resulted in a pattern of bilateral activity of the fusiform area for individuals with ASD in response to faces. Parents of individuals with ASD showed a similar though weaker pattern. This study is one which seems to reveal a biological link between individuals with ASD and their parents, providing us with a way to potentially bridge the genetics of ASD with the thinking processes seen in ASD.

Current Study

The current study examined differences in brain activation in persons with ASD and parents of persons with ASD compared to persons with typical development and their parents during an artificial grammar learning task. I examined behavioral differences as well as activation and connectivity differences in individuals with ASD and parents of persons with ASD, and compared them to those of individuals with typical development. Additionally, I compared the relationship between performance and neural activation between my groups. In addition, I examined the relationship between behavioral symptomatology in persons with ASD and neural activation. Working from a theory of impaired implicit learning in individuals with ASD, as well as a theory of cortical underconnectivity in individuals with ASD, several outcomes were expected, outlined as followed.

Behavioral Hypotheses

First, based upon previous studies using the artificial grammar learning task (Klinger et al., 2007), I expected that individuals with ASD will display slightly less grammar learning compared to typically developing individuals. However, this study used older participants (ages

12-24) than Klinger et al. (2007) (ages 5-17). The older individuals with ASD in the Klinger et al. (2007) study showed similar performance to typically developing individuals on implicit learning. It was hypothesized that the older individuals may have compensated for impairments in implicit learning by explicitly reasoning through the task, as explicit reasoning is shown to be partially dependent on age (McGeorge et al., 1997). In selecting the participant age range for the current study, an older age range was chosen in part to achieve more similar behavioral performance on the implicit learning task, as well as being better suited to the demands of fMRI research, particularly motion errors. Thus, any brain activation differences could then be inferred from differences due to diagnosis, and not solely on behavioral performance differences.

Activation Hypotheses

Similar to previous studies (Lieberman et al., 2004) I expected to find high local activation in the areas of the basal ganglia, specifically the caudate, in individuals with typical development during the artificial grammar learning task, supporting the notion that the basal ganglia is important to implicit learning. Additionally, I expected to find little activation in the medial temporal cortex in persons with typical development, when compared to individuals with ASD. I expected this pattern of basal ganglia and medial temporal activation in typically developing individuals based on previous research exploring this same paradigm in typically developing individuals (Lieberman, 2004). Additionally, though there is no prior evidence to support what pattern of activation should be expected during the actual learning phase (exposure, which has been performed outside of the scanner in past studies), I expected that in the exposure phase of the artificial grammar task, typically developing individuals would display greater activation of the basal ganglia and less activation of the visual cortex areas V1 and V3. I expected this because if the basal ganglia are responsible for picking up on abstract relationships,

they would be recruited more as more was learned. Additionally, the visual cortex areas V1 and V3 were hypothesized to show reduced activity as participants moved through the exposure phase if activation in these areas was related to familiarity.

In individuals with ASD, I expected to find reduced local activation in the areas of the basal ganglia, specifically the caudate, during the artificial grammar learning task. Additionally, because of prior evidence supporting that more explicit routes to completing implicit learning tasks involve accessing the medial temporal cortex and the prefrontal cortex, I expected to find significantly greater activation in these areas for individuals with ASD compared to individuals with typical development. It was expected that the high functioning, older participants in this study might be especially prone to complete the artificial grammar learning task in an explicit fashion. Again, though there are no prior studies to support what pattern of activation should have been expected during the exposure phase, I expected that individuals with ASD would not show the changes expected in TD participants, including increases in activation of the basal ganglia or the visual cortex areas V1 and V3. This was expected because the basal ganglia are theorized to be responsible for picking up on abstract relationships in the environment (Reber et al., 2003). If this was the case in the current study, and individuals with ASD did not pick up on the abstract relationships between the letters of the strings, then it follows that a differential pattern of activation throughout the exposure phase would be expected. Additionally, the visual cortex areas V1 and V3 were expected to show no differential activity as individuals with ASD move through the exposure phase if activation in these areas is related to familiarity, given that familiarity is typically linked to implicit learning processes which are theorized to be impaired in individuals with ASD.

Connectivity Hypotheses

I also expected that individuals with ASD will show significantly reduced connectivity during the artificial grammar learning task, particularly connections between the basal ganglia and temporal lobe, and possibly between frontal and posterior lobes of the brain. This is in line with research supporting underconnectivity between regions of the brain of individuals with ASD. Because I expect that the basal ganglia, specifically the caudate, is responsible for much of the implicit learning of the grammar strings, less communication between this area and the medial temporal cortex could provide good support for an underlying mechanism of why implicit learning is impaired in individuals with ASD. While I expect essentially an opposite pattern of activation in the medial temporal cortex and the basal ganglia in individuals with ASD (when compared to individuals with typical development), I think that the strong inhibitory connection (-.88) between these two areas seen in typically developing individuals (Lieberman, 2004) will be reduced in individuals with ASD. I also expect to find functional underconnectivity between frontal and posterior regions of the brain in persons with ASD, as previous research has focused successfully on underconnectivity between these regions in individuals with ASD across a number of cognitive and social processing tasks (Kana et al., 2008; Koshino et al., 2008).

Additionally, I will also include a set of exploratory analyses examining performance, activation, and functional connectivity in parents of individuals with ASD and typical development. While exploratory, I expect that parents of participants with ASD will display a similar pattern of results to that seen in their children, with a slightly smaller implicit learning effect, reduced activation of the basal ganglia, greater activation of the prefrontal and medial temporal cortices, and reduced functional connectivity between the basal ganglia and medial temporal cortex when compared to control parents, but the differences will be smaller than those between participants with ASD and control participants. The rationale for these hypotheses stems

from the evidence of research showing similar patterns of cognitive processing impairments and advantages between individuals with ASD and their parents (Happé, Briskman, & Frith, 2001; Hughes, Leboyer, & Bouvard, 1997) and a very small body of research indicating that parents of individuals with ASD share some neural differences during tasks that tap into core deficits, such as Dawson and colleagues (2005).

METHOD

Design

The study used a 2 X 2 X 2 X 2 mixed design. Age (young adults and parents) and diagnosis (typical development and ASD) were treated as classification variables, while test stimulus type (grammatical versus nongrammatical) and chunk strength (low versus high) were used as repeated measures. The design also has two main types of dependent variables, behavioral responses to the task and hemodynamic responses to stimuli.

Participants

Participants for the ASD group were recruited from the University of Alabama Autism Spectrum Disorders Research Clinic. Using the associated research database, only participants with IQ scores in the normal range (greater than 70) were recruited for participation. Participants in the typical development group were recruited from the Houston, Texas area. Participants with a history of the following were excluded from recruitment: left-handedness, history of seizures, head injuries resulting in more than 10 min of unconsciousness, neurological disorder, or any magnetized metal in body. For the young adult group participants were 16 males with ASD and 19 males with typical development, participating in the study in exchange for compensation for time and effort. All participants with ASD had been previously diagnosed using the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994), and were the only child in the home with a diagnosis of ASD. See Table 1 for ADI-R scores for participants with ASD. Participants were matched on the basis of verbal performance on the Kaufman Brief

Intelligence Test 2 (K-BIT2; Kaufman & Kaufman, 2004). See Table 1 for IQ information for both young adult groups. Finally, it is noted that a small number of participants with ASD did report psychotropic medication: sertraline (n = 2), atomoxetine (n = 1), methylphenidate (n = 1).

Parents of the young adult participants in both groups were also recruited to participate in this research. Twelve parents of persons with ASD and 9 parents of persons with typical development elected to participate. All participants received monetary compensation in exchange for their time. This group did not complete the K-BIT2 and was not matched on the basis of IQ.

After preprocessing, 8 participants were dropped due to excessive motion, leaving 12 participants with ASD (all male), 17 participants with typical development (all male), 10 parents of participants with ASD (6 female, 4 male), and 9 parents of participants with typical development (4 female, 5 male) Only one young adult with ASD had both parents included in data analyses.

Measures

Autism Diagnostic Interview-Revised (ADI-R). The ADI-R (Lord, Rutter, & Le Couteur, 1994) was used to confirm a diagnosis of ASD. It is a semi-structured 2-hour parent interview that covers social skills, communication skills, and repetitive behaviors during the preschool years and the current year. Symptoms of autism are often most obvious during the preschool years, and the ADI-R provides an opportunity to diagnose persons of any age based on their behavior during those years. A diagnosis is based on scoring an algorithm that is consistent with DSM-IV and ICD-10 diagnostic criteria.

Kaufman Brief Intelligence Test 2 (K-BIT2). The K-BIT2 (Kaufman & Kaufman, 2004) is a standardized measure of intellectual ability containing three subtests, with one measure of nonverbal intelligence (Matrices) and two measures of verbal intelligence (Verbal Knowledge

and Riddles). The K-BIT2 takes about 30 minutes to administer. The K-BIT2 has appropriate norms for ages four to 90 with IQ scores ranging from 40 to 160. Test-retest reliability for the K-BIT2 IQ Composite is excellent, with a mean of $r = .90$. K-BIT2 IQ Composite scores correlate highly, $r = .77$, with the Weschler Intelligence Scale for Children-IV (WISC-IV). The individuals with ASD and typically developing individuals were matched in verbal mental age (raw score on combined Verbal Knowledge and Riddles). The K-BIT2 was not completed for either of the parent groups.

Demographic Information. Caregivers of all participants were asked to provide information on their son's age, sex, ethnicity, previous diagnoses, SES, and contraindications for fMRI procedures.

Children's Social Behavior Questionnaire (CSBQ). The CSBQ (Luteijn, Luteijn, Jackson, Volkmar, & Minderaa, 2000) is a parent-based questionnaire that assesses the social behavior problems of individuals with ASD. This questionnaire was developed with the idea that other measures did not assess all aspects of the wider spectrum of disorders, such as PDD-NOS and higher-functioning autism. The CSBQ has 49 items, and reports scores on six subscales, representing the following social dimensions: not optimally tuned to the social situation (Not tuned), reduced contact and social interest (Contact), difficulties in understanding social information (Understanding), orientation problems in time, place or activity (Orientation), stereotyped behavior (Stereotyped) and fear of and resistance to changes (Changes). The CSBQ has good test-retest reliability ($r = .80-.90$) and has a medium correlation with the current ADI-R behavioral total domain score ($r = .52$).

Apparatus and Stimuli

All scans were performed on a Siemens 3.0 Tesla Allegra scanner at Baylor College of Medicine in Houston, Texas. Initial high resolution T1-weighted scans were acquired using an MP-RAGE sequence (Siemens). Continuous whole-brain imaging was performed as participants engaged in the artificial grammar learning task. Imaging run details were as follows: echo-planar imaging, gradient recalled echo; repetition time (TR) = 2000 ms; echo time (TE) = 40 ms; flip angle = 90°; 64 x 64 matrix, 26 4 mm axial slices acquired parallel to the anteroposterior commissural line for measurement of the BOLD effect (Kwong et al., 1992; Ogawa et al., 1990, 1990). Scanning yielded functional 3.3 mm x 3.3 mm x 4.0 mm voxels.

While in the scanner, participants were given two button boxes to hold, each with two buttons. A projector was used to present the visual stimuli and prompts to the participants while in the scanner. The participants were also fitted with headphones to receive instructions from the experimenter (in an overlooking control room) during the experiment.

Stimuli were constructed using a Markovian grammar chain, seen in Figure 1. Grammatical strings were constructed by entering the chain at the starting point and following the arrows, adding letters to the stimulus string along the way, until the grammar chain was exited (example: VXVV). All letter strings contained at least three letters, and no more than eight letters. Additionally, letter strings were constructed with a balanced chunk strength design, similar to stimuli used in the Lieberman (2004) study. Thirty-nine (23 exposure, 16 test) grammatical strings were constructed according to the rules of the grammar chain, while there were 16 nongrammatical letter strings constructed for the test phase. The 16 nongrammatical letter strings were also constructed of the same letters between three and eight letters in length, however these letter strings did not follow the rules of the grammar chain (example: TXJV).. Chunk strength was addressed by averaging the number of bigrams (sub-strings within the

stimuli of just two letters) and trigrams (sub-strings within the stimuli of just three letters) in the exposure phase (all grammatical), then creating test stimuli that used those bigrams and trigrams at either high frequencies (high chunk strength) or lower frequencies (low chunk strength). The 32 letter strings created for the test phase had an equal number of high chunk strength and low chunk strength items, such that there were 16 low chunk strength letter strings (8 grammatical and 8 nongrammatical) and 16 high chunk strength letter strings (8 grammatical and 8 nongrammatical).

Procedure

Persons with ASD and parents of persons with ASD were recruited from Alabama and flown to the Human Neuroimaging Lab at Baylor College of Medicine in Houston, Texas. These participants were scheduled for two sessions over the period of two days in Houston. Participants and parents were given informed consent forms and provided with all information regarding what they would be asked to do before the trip to Houston began, in a session approximately a week before the trip. In addition, participant families were given a small monetary sum as reimbursement for their time and effort as participants in the study. This monetary sum was given to participant families before the trip to Houston. In the first session, participants entered the lab and were again given an informed consent form with a brief overview of the experiment or their parent was given the consent form if participants were younger than age 18. Participants under the age of 18 were also asked to read a brief description and provide verbal assent. Upon completion of the consent procedures, participants were given more specific instructions. If participation was scheduled over the course of more than one day, informed consent was obtained at the beginning of each subsequent day. Participants were also given a schedule of what would happen in what order during the course of the study.

Additionally in the first session, most participants completed the K-BIT2, and the parents of participants were given history, demographic, and behavior reports to complete. Some participants and parents completed forms prior to the beginning of the trip to Houston. Additionally, participants were given some training on remaining still in response to the loud sounds that the scanner makes before the trip to Houston, as well as again in the Human Neuroimaging Lab at Baylor College of Medicine. Participants with typical development and parents of persons with typical development were recruited from the Houston area, and scheduled for one session which included the K-BIT2 and a second session for the scanner task, in addition to providing informed consent/verbal assent. In addition, participants completed one or two other scanner tasks unrelated to the current study during the second session or a third session.

Artificial grammar learning task. In the second session, participants were given visual and verbal instructions for the artificial grammar learning task. They were told that they would see pictures of rows of letters, and they were told that they should look at the letter strings while keeping their head and body as still as possible. Participants were instructed that they would see 23 letter strings and they should look at each letter string until it disappeared, as they would have to answer memory questions about them later. Participants were told after all 23 letter strings that they would have to answer some questions about what they saw. Participants had the opportunity to ask any questions, the questions were answered, and participants began the task.

The exposure phase of the task involved participants viewing 23 examples of randomly-ordered letter sequences shown one at a time for 8 seconds each. There was a blank interval of 4 - 6 seconds between letter sequence presentation (a process called “jittering”, used to assure equality in timing of brain images acquired). After the exposure phase, participants were told:

“The rows of letter you just saw all followed a complex set of rules. These rules determined which letters were used and their order. All the rows of letters you just saw followed these rules. We are now going to show you more rows of letters. We want you to tell us whether each new fits the rules or not. If you DO think a sequence follows the rules, press one of the “yes” buttons with your (Left or Right) hand. If you DO NOT think a sequence fits the rules, press one of the “no” buttons with your (Right or Left) hand. The rules are very complex so you may not be able to figure them out. Instead, you might want to go with your gut feeling, your hunch, which may feel like a guess. When you have finished looking at all the rows, the scanner will stop.”

The position of yes and no in relation to left and right button boxes was counterbalanced across participants. The test phase included 64 letter sequences shown one at a time. Participants indicated whether they believed each sequence followed the rules used to create the exposure set of letter sequences or not. During the test phase, participants completed two blocks of 32 randomly-ordered test trials composed of 16 grammatical letter strings, and 16 nongrammatical letter strings. The length of time for presentation of the test stimuli was user-defined, with a jittered inter-stimulus interval of 4 - 6 seconds. Fixation crosses were presented throughout the task for baseline measurement.

Upon completion of the study, participants were debriefed about the study, questioned for any possible strategies or hypothesis guessing, and asked about any adverse effects from being in the fMRI scanner. All participants were advised to stay seated for a few minutes subsequent to the scanning sessions to avoid any possible dizziness or injuries due to dizziness. Participants

were also given the opportunity to view images of their brains from the scanner session, and given CDs with images from their structural scan to keep.

RESULTS

Analysis of the current study began by examining differences in behavioral responses to the artificial grammar learning task played in the fMRI scanner between the two young adult groups and the two parent groups. Next, neurological activation during the artificial grammar learning task was compared between the two young adult groups and the two parent groups. Then, differences in functional connectivity between the two young adult groups and the two parent groups were examined. Finally, correlational analyses were performed examining relations between areas of activation and between activation and behavioral results for all groups.

Behavioral Analyses

Judgment responses (i.e., participant says stimulus does or does not follow the rules) were recorded for each type of stimulus presented during the test phase with a mean percent of affirmative responses (participant says that string does follow rules) calculated for grammatical and nongrammatical trials, as well as high chunk strength and low chunk strength trials. A grammar effect was calculated as the difference between the proportion of affirmative responses to grammatical test items and nongrammatical test items. A greater percentage of affirmative responses to grammatical items during test would indicate learning of the relationships between the letters (i.e., learning the rules of the grammar), and is taken as evidence of implicit learning. An initial analysis of the effect of test block (first versus second) revealed no significant effect of block on responses to the stimuli, $F(1, 45) = 1.81, p = .18$, nor any interaction between block and group, $F(3, 43) = 1.15, p = .33$. In addition, an analysis of the effect of block on reaction time

revealed a marginal effect of block, $F(1, 45) = 3.59, p = .06$. However, there was no interaction between block and group, $F(3, 43) = .77, p = .52$. All groups showed slightly reduced reaction times in block 2 ($M = 3536$ milliseconds) than in block 1 ($M = 3790$ milliseconds). Because of the nonsignificant effect of block on the behavioral performance across the groups, further analyses were collapsed across blocks. Means for affirmative responses in grammatical and nongrammatical conditions are presented in Table 2. As can be seen in Table 2, participants with ASD showed fewer affirmative (grammatical) responses to grammatical strings ($M = .51$) than participants with typical development ($M = .60$). Participants with ASD were slightly higher in grammatical responses to nongrammatical strings ($M = .47$) than participants with typical development ($M = .43$), showing that participants with ASD were less accurate and more likely to call nongrammatical stimuli grammatical. This resulted in a smaller grammar effect (grammatical minus nongrammatical) for participants with ASD ($M = .04$) than participants with typical development ($M = .17$). In addition, parents of participants with ASD showed slightly fewer grammatical responses in classifying grammatical letter strings ($M = .60$) than parents of participants with typical development ($M = .63$), but showed greater grammatical responses ($M = .56$) in classifying nongrammatical letter strings than parents of individuals with typical development ($M = .43$). This resulted in a smaller grammar effect for parents of participants with ASD ($M = .04$) than parents of participants with typical development ($M = .20$). With string type (grammatical or nongrammatical) as a within-subjects factor and diagnosis (ASD or typical development) and age (young adult or parent) as between subjects factors, a mixed-design ANOVA revealed a significant effect of string type on percent grammatical responses, $F(1, 43) = 26.24, p < .001$ using a Greenhouse-Geisser correction for sphericity. This indicates that participants were more likely to judge grammatical strings as grammatical than nongrammatical

strings (i.e., they learned the grammar). In addition, an interaction of diagnostic group by string type was found, $F(1, 43) = 9.79, p = .003$, while there was no main effect of age group, $F(1, 43) = .80, p = .38$, and no interaction between diagnosis and age group, $F(1, 43) = .03, p = .87$. Follow up comparisons revealed that participants with ASD showed a significantly smaller grammar effect ($M = .04$) than typically developing adolescent participants ($M = .17$), $t(27) = 2.33, p = .03$. Additionally, parents of participants with ASD also showed a smaller grammar effect ($M = .05$) than parents of typically developing participants ($M = .20$), $t(17) = 2.21, p = .04$.

The effect of chunk strength (low or high) on percent grammatical responses was also evaluated. A chunk effect was calculated as the difference between the proportion of correct responses to high chunk strength test and low chunk strength test items. Larger chunk effects are representative of larger benefits of superficial similarities of the strings, as opposed to the grammaticality of the strings. By examining differences in performance based on chunk strength, the learning of the grammar rules can be evaluated independent of these more superficial similarities. Means for grammatical responses in low chunk strength and high chunk strength conditions are presented in Table 3. As can be seen in Table 3, participants with ASD showed fewer grammatical responses for high chunk strings ($M = .51$) than participants with typical development ($M = .54$). Participants with ASD also showed fewer grammatical responses for low chunk strings ($M = .52$) than participants with typical development ($M = .60$). This resulted in a small chunk effect (high chunk minus low chunk conditions) for participants with ASD ($M = -.01$) and participants with typical development ($M = -.06$). In addition, parents of participants with ASD also showed fewer grammatical responses for high chunk strength strings ($M = .53$) than parents of participants with typical development ($M = .60$), and showed fewer grammatical responses ($M = .54$) than parents of individuals with typical development ($M = .60$) for low chunk

strength strings. This resulted in a small chunk effect for both parents of participants with ASD ($M = -.01$) and parents of participants with typical development ($M = 0$). With chunk strength (high versus low) as a within-subjects factor and diagnosis (ASD or typical development) and age (young adult or parent) as between subjects factors, a mixed-design ANOVA revealed no effect of chunk strength on percent grammatical responses, $F(1, 43) = .87, p = .35$ using a Greenhouse-Geisser correction for sphericity. In addition, no effect of diagnosis on percent grammatical responses by string type was found, $F(1, 43) = .193, p = .66$, nor was an effect of age group, $F(1, 43) = .77, p = .39$, nor an interaction between diagnosis and age group, $F(1, 43) = .49, p = .49$. From these results, it is clear that the chunk strength had no real effect on the behavioral performance (percent grammatical responses) in this task.

Additionally, analyses of overall reaction time were conducted. Reaction times were recorded for each trial, and then trimmed, cutting reaction times less than 250 milliseconds (ms) as well as reaction times over 2 standard deviations for each participant. Mean reaction times were then calculated for each participant. A main effect of diagnosis on reaction time was not found, $F(1, 43) = .08, p = .78$, nor was there a main effect of age group, $F(1, 43) = .57, p = .45$, nor an interaction between diagnosis and age group, $F(1, 43) = .14, p = .71$.

Activation Analyses

The data were analyzed using Statistical Parametric Mapping (SPM2b; Wellcome Department of Cognitive Neurology, London, UK) (see Friston et al., 1995). Motion correction to the first activation scan was performed within subjects using a six-parameter rigid-body transformation. The average of the motion-corrected images was co-registered to each individual's structural MRI using a 12-parameter affine transformation. The images were then spatially normalized to the Montreal Neurological Institute (MNI) template (Talairach &

Tournoux, 1988) by applying a 12-parameter affine transformation, followed by a nonlinear warping using basis functions following the method of Ashburner and Friston (1999). Images were subsequently smoothed with an 8 mm isotropic Gaussian kernel and bandpass filtered in the temporal domain. Regions of interest (ROIs) were outlined using the SPM2 canonical T1 image. General linear model (GLM) procedures in SPM2 on individual and group data were performed, with group analyses conducted with a random-effects model. Image data were grouped according to task stimuli presented, and then analyzed following an ROI analysis with the following planned contrasts: grammatical versus nongrammatical, and the exposure trials (all grammatical) versus fixation. These analyses allowed me to test my hypotheses regarding basal ganglia, medial temporal, and visual cortex areas V1 and V3 (middle occipital) activation during the process of learning (exposure phase) and using the learned information (test phase). Fixation trials were included in comparisons as a measure of baseline performance, in that no decisions were being made by the participant on these trials. In addition, several exploratory contrasts were performed: exposure versus baseline, novel grammatical versus baseline, familiar grammatical versus baseline, nongrammatical versus baseline, and the effect of block on activation differences. An extent threshold of 12 voxels was used, with a $p < .005$ level, uncorrected voxel-level threshold of significance, and a cluster-level family wise error (FWE) threshold of $p < .05$, essentially employing Bonferroni corrections.

Overall Similarities. While the goal of the analyses was to highlight areas of activational differences, it is important to note that there were several areas of common activation during the task across the four groups of participants. Contrasts of grammatical versus baseline, nongrammatical versus baseline, grammatical versus nongrammatical, and high chunk strength versus low chunk strength were examined to find areas common to the four groups of

participants. Specifically, the areas of the bilateral inferior frontal gyrus, bilateral middle occipital region, bilateral middle cingulate, left fusiform gyrus, and left caudate were shown to be significantly activated across all contrasts for all groups of participants. This common activation of the middle cingulate and basal ganglia (caudate) seems particularly important as it relates to areas thought to underlie implicit learning, of which all groups showed behavioral evidence. These areas showed up as significantly activated throughout all contrasts within each group, but were also contrasted between groups. So while there may be much greater activation within one area for one group, it is not the case that there was absolutely no activation in that area for the comparison group. The following analyses all examine differences in activation between groups.

Individuals with ASD versus typically developing individuals. The only comparison of activation during the exposure phase was examining which areas showed greater activation over the course of exposure to grammatical stimuli. In the analysis of activation for the two young adult groups during the exposure phase, the analysis was performed with a height threshold of $t(27) = 3.42, p < .05$ (FWE). Participants with ASD did not show any areas of activation in the ROIs that were significantly greater than that of participants with typical development across the exposure phase. However, participants with ASD had significantly less activation than typically developing individuals in the basal ganglia, including the left caudate, left putamen, and left global pallidum (see Table 4 and Figure 4), areas that have been previously associated with implicit learning during test phases (Lieberman et al., 2004), and here are seen apparently to be involved in the actual learning process as well. Additionally, I found no significant differences in activation in the medial temporal or visual cortex ROIs. In the analysis of activation for the two young adult groups during the test phase, the analyses were performed with a height threshold of

$t(27) = 3.42, p < .05$ (FWE). In the main comparison of all grammatical trials versus all nongrammatical trials, participants with ASD had significantly less activation in the areas of the basal ganglia, including the left caudate, left putamen, and left global pallidum, as well as the right hippocampus of the medial temporal cortex (Table 6). There were no significant differences between the two groups in visual cortex activation. Again, the areas of the basal ganglia showing increased activation is consistent with the behavioral data (more implicit learning) and previous evidence of these areas in judgment linked implicit learning. Within this comparison, the participants with ASD did not show any areas of significantly greater activation compared to typically developing individuals. In addition, I followed this main analysis with several exploratory analyses.

Exploratory Analyses of Young Adults. Another region we were interested in for the exploratory analyses was the cingulate cortex. During exposure and test phases, differences were found in both the right and left middle and anterior cingulate cortex. During exposure, participants with ASD had significantly lower activation in the bilateral middle and anterior cingulate cortex compared to typically developing individuals at a threshold of $p < .05$ (FWE). During the test phase, these same areas were again found to have significantly lower activation in participants with ASD compared to individuals with typical development.

While the pattern of activation differences examined between the two groups in the comparison of grammatical versus nongrammatical trials for the main hypothesis combined trials across both blocks, analyses for each block separately (first or second) revealed that largely those same activation differences were evident in both the first and second block of test trials, with the only differences being that during the second block (for grammatical versus nongrammatical trials) less activation was seen in the right superior medial frontal, right middle

frontal, and right inferior frontal gyrus for participants with ASD. This shows that there were no meaningful effects of having seen the same stimuli twice.

I also compared differences in activation during trials with stimuli of high chunk strength versus trials with stimuli of low chunk strength (again, without regard to grammaticality) to examine whether there was a different pattern of brain activation between participants with ASD and participants with typical development. Though behavioral performance was approximately equal, it was thought that there may still be differences in brain activation patterns between the two groups. Across all high chunk strength trials versus all low chunk strength trials, participants with ASD showed no areas of significantly greater activation participants with typical development, but did show significantly lower activation in the right middle frontal region. This middle frontal region may be linked to higher, executive functioning, with perhaps greater reliance on more thoughtful processing of those strings that had high chunk strength.

Parents of individuals with ASD versus parents of typically developing individuals. The only comparison of activation during the exposure phase was examining which areas showed greater activation over the course of exposure to grammatical stimuli. In the analysis of activation for the two parent groups during the exposure phase, the analysis was performed with a height threshold of $t(17) = 2.92, p < .05$ (FWE). Parents of participants with ASD showed significantly greater activation than that of parents of participants with typical development in no areas. Parents of participants with ASD had significantly less activation than parents of typically developing individuals in the basal ganglia areas of the right and left caudate. (Table 5 and Figures 5 and 6). As mentioned previously, these are areas that have been empirically associated with implicit learning during test phases, and appear to be involved in the actual learning process

as well. I found no significant differences in activation in the medial temporal or visual cortex ROIs.

In the analysis of activation for the two parent groups during the test phase, the analyses were performed with a height threshold of $t(17) = 2.92, p < .05$ (FWE). In the main comparison of all grammatical trials versus all nongrammatical trials, parents of participants with ASD had significantly less activation in the area of the left putamen (Table 7 and Figures 7 and 8). Within this comparison, the parents of participants with ASD also showed significantly greater activation in the right middle frontal region when compared to parents of typically developing individuals. Again, the area of the putamen showing increased activation is consistent with the behavioral data (more implicit learning) and previous evidence of these areas in judgment linked implicit learning. Again, I found no significant differences in activation in the medial temporal or visual cortex ROIs.

Exploratory Analyses in Parents. As before, I followed this main analysis with several exploratory analyses. To test for any effects of memory for strings in the test phase, a comparison of first and second blocks of the test phase was examined. While the pattern of activation differences between the two groups in the comparison of all grammatical versus nongrammatical trials combined trials across both blocks, an analysis of block (first or second) revealed that those same activation differences were in both blocks of the test phase. In addition, a comparison of male and female parents of individuals with ASD revealed no activation differences.

I also compared differences in activation during trials with stimuli of high chunk strength versus trials with stimuli of low chunk strength (again, without regard to grammaticality) to examine whether there was a different pattern of brain activation between parents of participants

with ASD and parents of participants with typical development, though behavioral performance was not significantly different. Though behavioral performance was approximately equal, it was thought that there may still be differences in brain activation patterns between the two groups. Across all trials considered to be of high chunk strength versus all of those considered to be of low chunk strength, parents of participants with ASD showed significantly greater activation in the areas of the left hippocampus, left putamen, left caudate, left middle temporal region, right cerebellum, and left middle occipital region, while showing significantly less activation in the right caudate, left and right middle frontal region, left inferior parietal region, and right inferior frontal gyrus. This pattern of activation is a bit mixed in what it can tell us, as there are areas associated with implicit learning with greater activation in both groups. This could be indicative of chunk strength really having minimal bearing on performance, or perhaps the development of different strategies by the two groups for deciding on which strings followed the rules. In addition, this increased activation in left sides of the brain may indicate some verbally mediated process affecting performance.

Functional Connectivity Analysis

Functional regions of interest (ROIs) were defined to include the main clusters of activation during the grammatical versus baseline contrast and the nongrammatical versus baseline contrast. These ROIs were mapped out manually from the within groups activation map from each group, and defined in terms of their location in Talairach coordinates and diameter. These ROIs included the areas (according to the MNI dataset) which had significantly higher activation (within group) for that contrast, and were the left caudate [L Caudate], left pallidum [L Pallidum], left putamen [L Putamen], right hippocampus [R Hippocampus], bilateral middle cingulate [RMCG and LMCG], bilateral insula [R Insula and L Insula], bilateral inferior frontal

gyrus [RIFG and LIFG], bilateral medial frontal gyrus [RMFG and LMFG], left fusiform [L Fusiform], bilateral middle occipital [R Middle Occipital and L Middle Occipital], and left inferior parietal region [LIFP]. For each of these ROIs two spheres (one for each group) were defined for each cluster with a radius of 4 to 12 mm.

The activation during the contrasts (grammatical versus baseline and nongrammatical versus baseline) for each of the clusters was measured for each participant, including only those participants with activated voxels within each cluster for each specific analysis. A Pearson correlation was then used to measure the relationship between voxel activation in each of the clusters for each group. This correlation is taken as the measure of functional connectivity. Fishers r to z transformation was performed on the correlations, giving a standardized score representing the strength of the connectivity between regions of the brain. Independent samples tests were then performed on these z -scores to test for differences between groups as well as between grammatical and nongrammatical conditions.

Functional Connectivity in individuals with ASD and typically developing individuals. In a comparison of participants with ASD to participants with typical development during the exposure phase of the experiment, I found significantly lower functional connectivity in participants with ASD (Mean $z = .28$) than in participants with typical development (Mean $z = .59$), $t(27) = 5.68$, $p < .001$. Then, I examined the specific connections with significant differences in their correlations. Participants with ASD showed significantly lower functional connectivity between the left fusiform area and the left middle cingulate (Mean $z = .27$) than participants with typical development (Mean $z = .82$), $t(27) = 5.36$, $p = .003$. Participants with ASD also had significantly lower functional connectivity between the left middle cingulate and the left middle occipital region (Mean $z = .14$) compared to participants with typical

development (Mean $z = .45$), $t(27) = 2.58$, $p = .04$. In addition, participants with ASD showed marginally lower functional connectivity between the left middle cingulate and the right middle occipital region (Mean $z = .19$) than participants with typical development (Mean $z = .46$), $t(27) = 2.41$, $p = .05$. (Figure 9)

During test trials participants with ASD showed significantly higher functional connectivity overall (Mean $z = .59$, across all functional ROIs) than participants with typical development (Mean $z = .53$), $t(27) = 2.37$, $p = .02$. However, the connectivity between the left insula and left middle frontal region was the only specific area that showed a significantly (marginally) greater correlation in the group of participants with ASD (Mean $z = .88$) compared to the participants with typical development (Mean $z = .54$), $t(27) = 2.21$, $p = .05$. In addition, participants with ASD had two ROI connections that showed significantly lower functional connectivity than participants with typical development: the connectivity between the left fusiform area and the left inferior frontal gyrus (participants with ASD, Mean $z = .46$, participants with typical development, Mean $z = .67$), $t(27) = 2.39$, $p = .04$), as well as the connectivity between the left inferior parietal region and the left inferior frontal gyrus (participants with ASD, Mean $z = .46$; participants with typical development, Mean $z = .67$), $t(27) = 2.64$, $p = .04$. (Figure 10) In the comparison of functional connectivity between the two young adult groups during nongrammatical conditions of the test phase, I found no overall significant differences, nor any specific differences between areas or activation.

Functional Connectivity in parents of individuals with ASD and parents of typically developing individuals. In a comparison of parents of participants with ASD to parents of participants with typical development during the exposure phase of the experiment, I found significantly lower functional connectivity in parents of participants with ASD (Mean $z = .36$)

than in parents of participants with typical development (Mean $z = .51$), $t(16) = 3.45$, $p < .001$. I then examined the specific connections with significant differences in their connectivity scores. Parents of participants with ASD showed significantly lower functional connectivity between the left fusiform area and the left middle occipital (Mean $z = .53$) than parents of participants with typical development (Mean $z = .96$), $t(16) = 2.54$, $p = .04$. Parents of participants with ASD also had significantly lower functional connectivity between the left middle occipital and the right middle occipital region (Mean $z = .14$) compared to parents of participants with typical development (Mean $z = .84$), $t(16) = 2.61$, $p = .03$. In addition, parents of participants with ASD showed marginally lower functional connectivity between the left middle cingulate and the right middle occipital region (Mean $z = .21$) than participants with typical development (Mean $z = .46$), $t(16) = 2.24$, $p = .067$. (11)

During the test phase trials, parents of participants with ASD showed significantly lower functional connectivity overall (Mean $z = .38$) than parents of participants with typical development (Mean $z = .48$), $t(16) = 3.79$, $p < .001$. Regarding specific areas of connectivity differences, parents of participants with ASD showed lower connectivity between the left pallidus and right middle cingulate (Mean $z = .12$) compared to the parents of participants with typical development (Mean $z = .52$), $t(16) = 2.67$, $p = .04$. In addition, parents of participants with ASD showed significantly lower functional connectivity than parents of participants with typical development between the left pallidus and the right inferior frontal gyrus (parents of participants with ASD, Mean $z = .07$, parents of participants with typical development, Mean $z = .47$), $t(16) = 4.25$, $p = .01$. I also found a marginal difference in connectivity between the left insula and the left pallidus (parents of participants with ASD, Mean $z = .25$, parents of participants with typical development, Mean $z = .75$), $t(16) = 2.41$, $p = .06$. (Figure 12) In the

comparison of functional connectivity between the two parent groups during nongrammatical conditions of the test phase, I found no overall significant differences, nor any specific differences between areas or activation.

Relational Analyses

Following the behavioral, activation and connectivity analyses, and series of exploratory relational analyses were conducted to look at predictors behavioral performance, activation, and connectivity. Because of smaller sample sizes, parent groups analyses were excluded in these analyses. The following analyses include only the young adult groups. First, I looked at the relations between behavioral performance, activation, and connectivity. Specifically, I examined the relationship between behavioral task performance and peak activation within several ROI's (including those areas which appeared to be most important during activation analyses, the signal activation difference between grammatical and nongrammatical trials, as well as the overall connectivity scores. Though the power was low for these relational analyses due to small sample sizes, I did find that there was a significant positive relation between the grammar effect for participants with ASD and basal ganglia activation, $t(11) = .60, p = .04$. Increased performance (presumably due to implicit learning) was met with increased activation of the basal ganglia region (Table 8). This same relation between the grammar effect and basal ganglia activation was not shown to be significant in participants with typical development (although it was a medium effect) (Table 9). Additionally, numerous nonsignificant medium ($r > .30$) and large ($r > .50$) effects were observed. Given the low power of these tests, it is difficult to conclude that there is not a greater link between performance and brain activation. With a larger sample clearer results would likely emerge.

Next, I looked at the relations between measures of intellectual functioning and behavioral performance, activation, and connectivity. A test of the relationship between intelligence measures and behavioral task performance, and the hemodynamic responses for the participants was also conducted, including verbal intelligence, nonverbal intelligence, and overall intelligence as measured by the K-BIT2. As seen in Table 10, no significant relationships between intelligence measures and behavioral task performance or hemodynamic responses were found for individuals with ASD. Again, the lack of power due to a small sample size makes evidence of a lack of relations inconclusive. However, I did find a significant relation between verbal intelligence (K-BIT2 Verbal raw score) and the grammar effect (grammatical responses – nongrammatical responses), $r(16) = .57, p = .02$ in the individuals with typical development (Table 11).

Next, I looked at the relations between measures of ASD symptomology and behavioral performance, activation, and connectivity. As seen in Table 12, signal difference and connectivity scores were not significantly correlated with any ASD symptomatology measures. I did find two areas of peak activation that did show a significant relationship with these measures: the middle occipital region. For participants with ASD, repetitive behavior scores on the ADI-R were significantly positively correlated with middle occipital region peak activation, $r(10) = .61, p = .05$. That is, participants with greater repetitive behavior symptoms also showed more middle occipital region peak activation. In addition, the anterior cingulate was negatively correlated with verbal communication scores on the ADI-R, $r(10) = -.67, p = .02$. This shows that participants with greater verbal communication symptoms also showed less anterior cingulate region peak activation. The previously mentioned negative correlation between basal ganglia activity and medial temporal activity (Lieberman et al., 2004) was not found here. Again, given

the low power of these tests, it is difficult to conclude whether relations exist between symptomatology and brain activation for many of the nonsignificant correlations. Results of these analyses would likely be clearer with a larger sample size.

DISCUSSION

The current study found differences in implicit learning in persons with ASD compared to typically developing individuals, as well as underlying neural activation differences and neural connectivity differences. Relational analyses also compared behavior to neural activation. Similar differences in implicit learning, activation, and functional connectivity between parents of young adults with ASD and parents of young adults with typical development were found. In the following discussion, I will examine the specific behavioral, activation, connectivity, and relational differences between the two groups, as well as implications for this study, and limitations and future directions of this research.

Behavioral Results

Young Adults. In the artificial grammar learning task, I found evidence of less implicit learning in participants with ASD when compared to typically developing control participants. While previous studies had found a smaller implicit learning effect in participants with ASD (Klinger & Dawson, 2001; Klinger, Klinger, & Pohlig, 2007), those studies used participants of a younger age. It was expected that by including older, high functioning participants with ASD, the implicit learning difference would be small (but in the proposed direction). Yet the current study found significantly less implicit learning in individuals with ASD. In addition, Klein et al. (2007) found a smaller, marginal implicit learning effect (while a moderate effect size) using a judgment-linked task involving memory instructions. However, in contrast to the Klinger et al. (2007) study, the current study found no relationship between implicit learning (the grammar

effect) and explicit reasoning (measured here by the K-BIT2 nonverbal raw score). On the basis of the Klinger et al. (2007) study, it was theorized that if the use of explicit reasoning was responsible for compensating for implicit learning deficits, then selecting older participants would result in greater explicit reasoning ability, and thereby result in comparable implicit learning effects to individuals with typical development. While the explicit reasoning (as measured by the K-BIT2 nonverbal score) was approximately the same between our two young adult groups, one possible explanation for significantly reduced amount of implicit learning in participants with ASD compared to typically developing individuals in this study may lie in the complexity of the grammar rules. It is possible that at younger ages (or, lower explicit reasoning ability) the implicit learning tasks used by Klinger et al. (2007) might be just difficult enough in the abstractions needed to successfully judge category members. That is, though individuals with ASD do implicitly learn, they still may be inefficient at it, and use it less often. In the case of a moderately difficult implicit learning task, those that can use explicit reasoning to compensate for implicit learning differences do so. However, in the current study participants were placed in a very unfamiliar environment that may have been very cognitively taxing. Participant focus on not moving too much and coping with their environment may have left participants with fewer explicit resources at their disposal. In this way, participants with ASD may have been unable to compensate for differences in implicit learning with explicit processing resources, thereby showing a smaller grammar effect. In addition, our measures that would typically be related to explicit compensation, nonverbal intelligence (KBIT2 Nonverbal IQ) and medial temporal activation, showed no significant relationship with grammar learning. So, it could be that in some cases, individuals with ASD may compensate explicitly when resources are available, and

just did not do so here, or they do not explicitly compensate at all; in this case we have no evidence for explicit compensation.

Parent Group. This study also found less implicit learning in parents of participants with ASD than parents of participants with typical development, in a similar pattern to that of the young adults. This was particularly surprising. While it was hypothesized that there may be somewhat smaller implicit learning effects, it was not expected that the difference would be on the same magnitude as the difference between the young adult groups. It is clear that there are similarities in cognitive task performance, as parents of persons with ASD have been shown to perform worse on tasks of executive function (Hughes, Leboyer, & Bouvard, 1997) and better on the block design task mirroring findings in persons with ASD (Happé, Briskman, & Frith, 2001). This may indicate more evidence for the existence of a broader autism phenotype, resulting from underlying genotypes leading to specific autistic characteristics. However, as there were no measures of autism symptomatology collected for the parent group, I have no objective measure of shared behavioral characteristics.

Chunk Effect. In addition, it is interesting to note that this study found no effect of chunk strength on the implicit learning effect. While this is not predicted based on research by Lieberman et al. (2004), which found greater endorsement of items as grammatical in high chunk strength conditions than low chunk strength conditions (though this was mainly carried by very low endorsement of low chunk strength nongrammatical items), it is not uncommon. Forkstam, Elwér, Ingvar, and Petersson (2008) found a nearly opposite pattern of results from those of Lieberman et al. (2004), using similar tasks and instructions in persons with typical development, and suggested that this may be due to small differences in instruction or design, as well as the amount of explicit processing evoked by the task. It is important to note that while the artificial

grammar learning task is a well-known example of an judgment linked implicit learning task, the instructions used in this study theoretically evoke more explicit processing during the test phase than a preference-based set of instructions, as in studies by Reber (1967) and Lieberman et al. (2004) (the reveal to the participant that there are ‘rules’ can possibly lead to the participant explicitly trying to figure these rules out, even when told that this was very improbable).

Activation Results

Young Adults. This study also found significant activation differences between participants with ASD and as compared to typically developing control participants. During the exposure phase, several areas were found to have significantly less activation in participants with ASD compared to participants with typical development, consistent with previous research by Just et al. (2004) and Kana et al. (2006) finding lower overall activation in persons with ASD. Most notably, I found differences in the basal ganglia, including the caudate, putamen, and pallidum, yet no differences in the amount of activation between individuals with ASD and typically developing individuals in the medial temporal region or the occipital region.. All of these areas were implicated by Lieberman et al. (2004), which found activational correlates in the midline structures (mainly basal ganglia), as well as medial temporal region and occipital region (V1 and V3) during the test phase of the artificial grammar task in typically developing individuals. However, the current study shows these same areas being active during the actual learning phase. While it is certainly the case that there may be different areas of activation during acquisition (exposure) than during classification (test), it does seem sensible that there would be overlap in the systems/processes involved. It is especially logical when one considers that the participants were instructed prior to the exposure phase to pay close attention to the letter strings, as we would test their memory regarding them at a later point, as opposed to simply asking them

to passively view the letter strings. In fact, previous evidence supports the notion of different brain structures underlying the different effects of mere exposure (simply instructed to view, then testing for preference) and a judgment linked implicit learning recognition task (Elliot and Dolan, 1998; Zajonc, 2001). While Lieberman et al. (2004) found the midline structures, occipital regions, and medial temporal regions involved in the judgment linked implicit learning, parietal structures and frontal regions are thought to underlie the preference type of tasks (Elliot and Dolan, 1998). However, one alternate explanation for this difference in activation in the middle cingulate could simply be sort of a default processing that is going on during exposure. It is the case that there was nothing for the participant to actually perform, besides observing the stimuli. It may be that participants defaulted to thinking about other things, in which it is very likely that participants were engaged in self-referential thought processing (thinking about themselves in some way). It is also the case that there are limitations that are inherent to an exposure-then-test paradigm. The results of this contrast of how participants' brains responses to sequence trials changed over time may be partially due to learning as well as partially due to how their brains responded when doing anything over an extended period of time. There are many things that might have changed over the course of exposure for all subjects (boredom level, thinking about when the game would be over, what they would do afterward, etc.) with only one of these being how much they knew about the sequences. Though what caused these changes for sure is unknown, the fact that they are consistent with previous studies helps us to infer that learning of the grammar may underlie them.

During the test phase, I found the area of the putamen to have significantly lower activation in participants with ASD compared to typically developing participants for the main contrast, grammatical versus nongrammatical trials. This largely supports my hypothesis of

lower activation in the midline structures, including the basal ganglia. However, there was no difference in the medial temporal or middle occipital region activation between the groups. One consideration for this lack of difference would be that my hypotheses were based in large part on a study examining typically developing individuals only. While the occipital region may be an important part of the implicit and explicit learning processes, this part may not be the most important part, or at least not the part explaining poorer performance on the behavioral task in persons with ASD. However, both groups did show activation in the occipital region, just not activation that differed between the groups, which may point to its underlying role in part of the implicit and explicit learning process. For the young adults with ASD, significantly lower level of activation in the caudate and cingulate cortex may point to those areas as particularly important to differentiating grammatical from nongrammatical letter strings, and thereby important for implicit learning. In addition, previous research has already indicated the important differences in the basal ganglia (Sears et al., 1999; Geller, 2005) and cingulate cortex (Chui et al., 2008), and the current study provides more evidence to that notion. Sears et al. (1999) showed differences in the sizes of the caudate in individuals with ASD, and the current study shows decreased activation in the same area during learning. Additionally, Geller (2005) found the abnormal sizes of the caudate were related to repetitive behaviors in individuals with ASD, such that greater sizes of the caudate were associated with increased repetitive behaviors. While the current study does not address structural differences of the brain associated with ASD, it is interesting that differences in the activation of the caudate were found, and that the main area of symptomatology of individuals with ASD associated with activation was repetitive behaviors (positively correlated with the middle occipital region). In addition, Klein et al. (2007) found that the only symptomatology measure of the ADI-R that was associated with implicit learning

(measured with a prototype learning task) was repetitive behaviors. Obviously, things that stand out as important differences about individuals with ASD are the structure and function of the caudate, as well as how repetitive behaviors and notions are related to more automatic forms of learning. Additionally, the current study showed marginally less activation in the middle cingulate for individuals with ASD, an area not typically associated with forms of implicit learning. However, this is an areas previously associated with hypoactivation during representation of the self in persons with ASD (Chui et. al, 2008) as well as pain interference (Vogt et al., 2003). It is difficult to speculate on the specific role that the middle cingulate would have in this particular task, especially coupled with the increased activation in this area for parents of participants with ASD (who performed worse on the task).

An important consideration here is that while we found some differences in activation during exposure, and less differences during the test phase, it is the case that any changes taking place during exposure most likely have an effect on behavior in the task, as well as activation during the test phase. Those participants who used brain areas that are linked with implicit learning, (i.e., basal ganglia) during the learning phase should by definition, show more implicit learning. And two groups who perform a task differently would most likely employ a different set of brain areas to achieve the goal of the task. While it would have been interesting to see similar behavior, with underlying brain activation differences, it is still interesting in spite of the fact that there were behavioral differences. Both the behavioral and activation difference during the exposure phase are both evidence to the fact that individuals with ASD perform these implicit learning tasks differently than individuals with typical development.

Parent Group. In the parent group, I found significant differences again in the caudate, and marginally in the middle cingulate. On one hand, the parents of participants with ASD

showed a well documented pattern of overall lower amounts of activation in individuals with ASD when compared to typically developing individuals. This again speaks to the idea and evidence for a broader autism phenotype, in which parents may not only show behaviorally shared symptomology, but also show ASD-like cognitive characteristics and neural profiles as well. On the other hand, it is interesting that the middle cingulate in parents of participants with ASD showed greater activation than parents of typically developing participants. This is an area previously associated with hypoactivation during representation of the self in persons with ASD (Chui et. al, 2008), but may be responsible for other, more automatic functions as well.

In the main contrast of grammatical versus nongrammatical test trials in the parent group, I found very similar areas of significantly lower activation in the parents of participants with ASD, including the putamen and overall significantly lower activation. While activation in this area in typically developing individuals supports the notion that the areas of the basal ganglia may be particularly important structures underlying implicit learning, the fact that there was greater activation in these areas than in individuals with ASD who performed worse on the task reveals a difference in the neural functions underlying the differences in the automatic learning process. It is also the case that areas such as the medial temporal region and middle occipital regions remain important as well, but are typically thought of as the more explicit structures for thought processes. However, the artificial grammar learning task, while mainly an implicit learning task, is influenced by explicit reasoning as well, with participants likely trying to recall specific instances or applying ad-hoc rules. This part of the task cannot be overlooked, and this evidence supports the notion that the structures underlying implicit and explicit processes point to the fact that both are need to perform well on the task. It seems that while the more explicit part of the learning process in this task cannot be overlooked, the implicit and explicit processes

involved may have different underlying brain mechanisms. Additionally, these mechanisms are likely all important, as lower activation in the individuals and parents of individuals with ASD was accompanied by lower performance in the behavior task.

Functional Connectivity Results

In a comparison of functional connectivity in participants with ASD and parents of participants with ASD compared to typically developing control participants, I found significantly lower connectivity during the exposure phase between different areas and the middle cingulate. Recent evidence has suggested this area as being intricately linked with self processing, and being an area with significantly different activation in persons with ASD (Chiu et. al, 2008). One possible explanation for this difference in connectivity could simply be sort of a default processing that is going on during exposure. It is the case that there was nothing for the participant to actually perform, besides observing the stimuli. It may be that participants defaulted to thinking about other things, in which it is very likely that participants were engaged in self-referential thought processing (thinking about themselves in some way). This would be consistent with the idea that persons with ASD are different on a neurofunctional level in self processing, and provide some support that this is also the case for parents of persons with ASD.

During test phases, it was clear that connectivity with the inferior frontal gyrus was of importance, as I found differences in connectivity (significantly less in the ASD and parents of ASD groups) for areas connecting here. This is an interesting area for connections to be important in an artificial grammar learning task, as the inferior frontal gyrus is intricately implicated in language processing (Foundas, Leonard, Gilmore, Fennell, & Heilman, 1996). In particular, the structure or syntax of the grammar chains may be of importance to building appropriate models or rule abstraction on an unconscious level. If thought about on a purely

grammatical basis, the building of words and sentences follows a number of rules that are extremely explicit, though many of them seem illogical. In some ways, this area may be an additional mechanism underlying the more explicit parts of the learning process, much as the medial temporal region and middle occipital region. In fact research by Badre and Wagner (2007) points to the inferior frontal gyrus as centrally important for explicit memory processes, as opposed to more automatic remembering. However, as this area was not correlated with any measure of performance, it may be more of a stage mechanism of the overall process of learning, insomuch that the explicit memory is checked before relying on more automatic forms of memory. Or perhaps when judgments are more difficult, this process is used more frequently.

ASD is a very heterogeneous disorder (Bill & Geschwind, 2009). One of the goals of this study was to attempt to use behavioral and brain activation patterns to explain some of this heterogeneity. I used the relational analyses to do this. However, the analyses did not explain very much heterogeneity within my group of participants with ASD. In addition, I found few of the ASD symptomatology measures related to activation in the middle occipital region and the medial temporal region. Activation in these areas is typically found to be decreased in relation to implicit learning in somewhat of an explicit fashion (taken as a measure of dehabituation to rule-consistent stimuli) (Aizenstein, 2000; Reber et al., 2003). So this is a surprising finding that, as autistic symptoms increased, level of activation decreased in the middle occipital region, especially when the participants seemed to perform worse with increasing symptoms (autistic mannerisms). One hypothesis would be that the habituation process, which is theoretically in part automatic, is somehow procedurally different in persons with ASD. Additionally, I found that basal ganglia activation was positively correlated with the amount of implicit learning shown by participants with ASD (as well as weakly for participants with typical development). While the

power for these relational analyses was weak, this particular relation is interesting. I hypothesized that the basal ganglia would be an important area related to implicit learning, and this finding is in line with that idea. Further analysis of this area and its relation to implicit learning could be noteworthy. I did not include measures of ASD symptomatology for parents of participants with ASD, and have no ability to draw similarities in this case.

Limitations and Future Research

Overall, I found that some of the areas that have been thought to be involved in judgment linked implicit learning show significantly lower activations in individuals with ASD, as well as parents of individuals with ASD when compared to typically developing control individuals, specifically the caudate, anterior cingulate cortex, medial temporal region, and middle occipital region. A major interesting part of this study was the similarities found between individuals with ASD and parents of individuals with ASD (in terms of their differences to typically developing individuals and parents of typically developing individuals). This study is limited by not having appropriate measures of ASD symptomatology for the parents of individuals with ASD, and therefore lacks the ability to draw more specific conclusions about or provide more conclusive evidence for the idea of a broader autism phenotype evident in family members of persons with ASD. However, the fact that both young adults with autism and their parents showed differences in implicit learning and functional connectivity makes it evident that there may be a relationship between ASD and implicit learning and underconnectivity. However, they are likely not hallmarks of the disorder, as parents should show much greater levels of impairment if that was the case. Future studies might examine this relationship more (though I found very few significant relationships between ASD symptomatology and behavior or neural activation patterns) through the use of those measure, as well as including other family members. In

addition, different approaches to measuring implicit learning would also provide useful, such as one that did not rely on an exposure-test paradigm, of which the limitations have already been discussed. Also, implicit learning tasks with different levels of the quantity of abstraction required may produce different behavior results between the diagnostics groups, and might be useful in explaining why some studies find differences in implicit learning in individuals with ASD and others do not.

General Conclusions and Implications

It is the case that some basic conclusions can be drawn from this study. First, there were similarities in behavioral performance on a cognitive task in individuals with ASD and their parents. Second, individuals with ASD as well as parents of individuals with ASD showed less implicit learning compared to typically developing control participants. Third, there were specific structures that appear to be important to performing well at this judgment linked implicit learning task. Finally, individuals with ASD and parents of individuals with ASD shared a pattern of neurological activation differences from typically developing individuals.

While it is the case that a simple implicit learning task is not encountered on a daily basis, the relation of the implications of this task back to the deficits often associated with individuals with ASD are important. Specifically, things in the environment that may be more abstract or implicitly learned may not be picked-up on as well by individuals (or parents of individuals) with ASD. This decreased implicit learning is theorized to play a role in the decreased social understanding and development of individuals with ASD. If the complex relationships between people, including things like facial expressions, eye contact, nonverbal gestures, sarcasm, etc., are not processed in the same way that typically developing individuals process and direct those actions, then there would presumably be things in which the individual with ASD would not

understand about human social interaction. In addition to social understanding, everyday learning may also be affected by decreased implicit learning. Many learning strategies center upon being able to draw associations or analogies between situations (i.e., problem solving), and thus, an individual with ASD may not learn some things as well as typically developing individuals because of the decrease in automatic associations drawn on their own. A common instance of non-associative thinking in typically developing individuals comes from the problem solving body of research. Research by Gick and Holyoak (1983) showed that complex problems that could be solved by drawing associations and analogies with previously encountered problems often were tough for people to solve. In fact, people were typically the most successful at solving the problems when explicitly told to use the solution to a previous problem to aid them in solving the current one. While this is a small, specific instance of non-associative thinking and not drawing information automatically that is useful, it provides an analogy for what may be happening in individuals with ASD. In teaching individuals with ASD, it may be extremely important to point out the important aspects of situations to pay attention to for guiding future learning and application. In fact, coupled with the results of Klein et al. (2007), guiding attention to important parts of complex and abstract situations may be indeed what would increase implicit learning in individuals with ASD.

Also, the current study may provide further evidence for the heritability of ASD, with parents of individuals with ASD showing a very similar behavioral and neurological profile to that of individuals with ASD, within the context of this study. This could also be taken as evidence of the broader autism phenotype (BAP), where the parents of individuals with ASD included in this study were not diagnosed with ASD (and no measures of symptomatology were administered for parents), but it is the case that there were some similarities in behavior on a

cognitive task and brain activation patterns, using comparative control groups. An alternate theory for the shared impairment in implicit learning and shared overall lower activation compared to controls, as well as lower activation in the basal ganglia may be that the implicit learning differences may play a huge role in the daily life of a person with ASD. The tendency to see the environment in very rule-based ways may have an effect on the way that a parent or sibling interacts with that person with ASD or makes plans for a person with ASD. This explicit mode of thinking may become more useful and more practiced, thereby inhibiting or making less useful the implicit learning that most typically developing individuals employ automatically. It is also clear that general functional underconnectivity appears both in individuals with ASD and parents of individuals with ASD. Future studies focusing more on parent and child profiles may provide more useful information on overall cognitive differences associated with the disorder, as well as the heritability of the disorder.

Finally, we have further evidence to evaluate the two major theories of differences in ASD tested in this study: the implicit learning deficit hypothesis as well as the functional underconnectivity hypothesis. This study clearly showed more evidence for differences in implicit learning associated with the diagnosis, through individuals diagnosed with the disorder and perhaps the BAP. However, I did not find great evidence supporting the direct link between the actual symptoms associated with the disorder and implicit learning differences, though these tests were low in power and may simply have been undetected due to this low power.

Neurological evidence did support the implicit learning deficit hypothesis, in that areas of activation that are commonly associated with implicit learning were found to be less activated in individuals with ASD and parents of individuals with ASD, both who performed poorer than typically developing individuals on the behavioral task. We also found support for functional

underconnectivity in persons with ASD (and parents of persons with ASD), finding less connectivity overall and in important regions associated with implicit learning, though these underconnectivity effects were not statistically related to the learning difficulties seen in the ASD group. Lastly, this underconnectivity may also be viewed as further neurological evidence for the behavioral differences seen in implicit learning in individuals with ASD and their parents. Overall, this study suggests the importance that the basal ganglia may play in implicit learning, particularly in ASD. Additionally, it suggests the importance of understanding the learning styles of persons with ASD as a link between their symptoms and the neural underpinnings of the disorder.

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APPENDIX

Table 1

Young Adult Participant Characteristics

	TD	ASD
N	19	16
Age (Years-Months)	17.4	16.5
<u>K-BIT</u>		
IQ	108	100
Verbal IQ	108	97
Nonverbal IQ	106	101
<u>ADI-R Domain Scores</u>		
Social	N/A	18.6
Verbal Communication	N/A	12.6
Restrictive/Repetitive Behavior	N/A	6.3

Note: All tests of difference were nonsignificant.

Table 2

Behavioral Performance by String Type during Test Phase

Group	Accuracy		Grammar Effect (Grammatical minus Nongrammatical)
	Grammatical	Nongrammatical	
Young Adults with ASD	.51 (.22)	.47 (.20)	0.04
Young Adults with Typical Development	.60 (.11)	.43 (.09)	0.17
Parents of Individuals with ASD	.60 (.13)	.56 (.18)	0.04
Parents of Individuals with Typical Development	.63 (.14)	.43 (.14)	0.20

Note: Values represent mean accuracy (out of 1.00) for test trials based on string type. Values in italics are standard deviations.

Table 3

Behavioral Performance by Chunk Strength during Test Phase

Group	Accuracy		Chunk Effect (High Chunk minus Low Chunk)
	High Chunk Strength	Low Chunk Strength	
Young Adults with ASD	.51 (.10)	.52 (.10)	-0.01
Young Adults with Typical Development	.54 (.12)	.60 (.10)	-0.06
Parents of Individuals with ASD	.53 (.09)	.54 (.07)	-0.01
Parents of Individuals with Typical Development	.60 (.10)	.60 (.11)	0.00

Note: Values represent mean accuracy (out of 1.00) for test trials based on chunk strength. Values in italics are standard deviations.

Table 4

Greater Basal Ganglia Activation in Typically Developing Participants than Participants with ASD during Exposure

Brain Region	Coordinates			Volume %
	X	Y	Z	
Left Caudate	-10	14	16	62.14
Left Putamen	-16	-2	8	6.99
Left Pallidum	-20	-4	0	48.54

Note: X,Y,Z Coordinates are listed for areas of significantly greater activation in parents of typically developing participants than parents of participants with ASD, FWE $p < .05$.

Table 5

Greater Activation in Parents of Typically Developing Participants than Parents of Participants with ASD during Exposure

Brain Region	Coordinates			Volume %
	X	Y	Z	
Left Caudate	-24	-2	26	62.14
Right Caudate	20	12	28	54.95

Note: X,Y,Z Coordinates are listed for areas of significantly greater activation in parents of typically developing participants than parents of participants with ASD, FWE $p < .05$.

Table 6

Greater Basal Ganglia Activation in Typically Developing Participants than Participants with ASD during Grammatical versus Nongrammatical Trials

Brain Region	Coordinates			Volume %
	X	Y	Z	
Left Caudate	-10	14	16	43.69
Left Putamen	-16	-2	8	6.99
Left Pallidum	-20	-4	0	48.54
Right Hippocampus	26	-32	2	35.92

Note: X,Y,Z Coordinates are listed for areas of significantly greater activation in typically developing participants than participants with ASD, FWE $p < .05$.

Table 7

Greater Activation in Parents of Typically Developing Participants than Parents of Participants with ASD during Grammatical versus Nongrammatical Trials

Brain Region	Coordinates			Volume %
	X	Y	Z	
Left Putamen	-16	-2	8	11.07

Note: X,Y,Z Coordinates are listed for areas of significantly greater activation in parents of typically developing participants than parents of participants with ASD, FWE $p < .05$.

Table 8

Relational Analyses for Behavioral Performance and Hemodynamic Responses in Participants with ASD

		Chunk Effect	Overall Connectivity	Medial Temporal Activation	Middle Occipital Activation	Anterior Cingulate Activation	Basal Ganglia Activation
Grammar Effect	Pearson Correlation	.03	.44	-.06	.42	.40	.60
	Sig. (2-tailed)	.92	.16	.85	.18	.20	.04
	N	12	12	12	12	12	12
Chunk Effect	Pearson Correlation		-.10	.18	.19	.00	.25
	Sig. (2-tailed)		.75	.58	.55	.99	.44
	N		12	12	12	12	12
Overall Connectivity	Pearson Correlation			.21	-.25	.55	.36
	Sig. (2-tailed)			.52	.43	.07	.25
	N			12	12	12	12
Medial Temporal Activation	Pearson Correlation				.36	.37	.57
	Sig. (2-tailed)				.26	.23	.05
	N				12	12	12
Middle Occipital Activation	Pearson Correlation					.27	.57
	Sig. (2-tailed)					.40	.05
	N					12	12
Anterior Cingulate Activation	Pearson Correlation						.67
	Sig. (2-tailed)						.02
	N						12

Table 9

Relational Analyses for Behavioral Performance and Hemodynamic Responses in Participants with Typical Development

		Chunk Effect	Overall Connectivity	Medial Temporal Activation	Middle Occipital Activation	Anterior Cingulate Activation	Basal Ganglia Activation
Grammar Effect	Pearson Correlation	.16	-.26	.18	.16	.42	.37
	Sig. (2-tailed)	.54	.31	.56	.54	.10	.14
	N	17	17	13	17	17	17
Chunk Effect	Pearson Correlation		.02	-.31	-.01	-.37	-.07
	Sig. (2-tailed)		.95	.30	.96	.15	.80
	N		17	13	17	17	17
Overall Connectivity	Pearson Correlation			.07	.51	.14	.25
	Sig. (2-tailed)			.82	.03	.60	.33
	N			13	17	17	17
Medial Temporal Activation	Pearson Correlation				.37	.12	-.05
	Sig. (2-tailed)				.21	.69	.88
	N				13	13	13
Middle Occipital Activation	Pearson Correlation					.24	.60
	Sig. (2-tailed)					.34	.01
	N					17	17
Anterior Cingulate Activation	Pearson Correlation						.70
	Sig. (2-tailed)						.00
	N						17

Table 10

Relational Analyses for Intelligence Scores and Hemodynamic Responses in Participants with ASD

		Grammar Effect	Chunk Effect	Overall Connectivity	Medial Temporal Activation	Middle Occipital Activation	Anterior Cingulate Activation	Basal Ganglia Activation
K-BIT2 Verbal Raw	Pearson Correlation	.01	.07	.25	.20	-.35	.32	.34
	Sig. (2-tailed)	.98	.84	.46	.56	.28	.33	.31
	N	11	11	11	11	11	11	11
K-BIT2 Nonverbal Raw	Pearson Correlation	.36	.43	.48	.27	-.18	.40	.32
	Sig. (2-tailed)	.27	.19	.14	.43	.59	.23	.34
	N	11	11	11	11	11	11	11
K-BIT2 Composite	Pearson Correlation	.20	.28	.42	.27	-.32	.41	.37
	Sig. (2-tailed)	.55	.40	.20	.42	.33	.21	.26
	N	11	11	11	11	11	11	11

Table 11

Relational Analyses for Intelligence Scores and Hemodynamic Responses in Participants with Typical Development

		Correlations						
		Grammar Effect	Chunk Effect	Overall Connectivity	Medial Temporal Activation	Middle Occipital Activation	Anterior Cingulate Activation	Basal Ganglia Activation
K-BIT2 Verbal Raw	Pearson Correlation	.57	.13	-.12	.38	-.03	.20	.06
	Sig. (2-tailed)	.02	.61	.64	.20	.90	.44	.81
	N	17	17	17	13	17	17	17
K-BIT2 Nonverbal Raw	Pearson Correlation	.18	.05	.08	.48	.35	.08	.23
	Sig. (2-tailed)	.49	.84	.77	.10	.17	.77	.38
	N	17	17	17	13	17	17	17
K-BIT2 Composite	Pearson Correlation	.21	-.52	-.09	.10	.22	.21	.30
	Sig. (2-tailed)	.42	.03	.75	.75	.40	.41	.24
	N	17	17	17	13	17	17	17

Table 12

Relational Analyses for Symptomatology Scores and Hemodynamic Responses in Participants with ASD

		Grammar Effect	Chunk Effect	Overall Connectivity	Medial Temporal Activation	Middle Occipital Activation	Anterior Cingulate Activation	Basal Ganglia Activation
CSBQ Social Insight Problems	Pearson Correlation	-.42	.32	-.27	.25	-.21	-.08	.01
	Sig. (2-tailed)	.22	.36	.45	.49	.57	.82	.97
	N	10	10	10	10	10	10	10
CSBQ Anxious Rigid	Pearson Correlation	-.01	.34	.32	.04	-.35	.35	.27
	Sig. (2-tailed)	.97	.34	.37	.91	.33	.32	.44
	N	10	10	10	10	10	10	10
ADI-R Social Interaction	Pearson Correlation	-.09	-.12	-.19	.04	.25	-.38	.07
	Sig. (2-tailed)	.79	.72	.58	.91	.47	.25	.83
	N	11	11	11	11	11	11	11
ADI-R Verbal Communication	Pearson Correlation	-.25	.25	-.29	-.13	.07	-.67	-.20
	Sig. (2-tailed)	.46	.45	.39	.71	.84	.02	.55
	N	11	11	11	11	11	11	11
ADI-R Repetative Behaviors	Pearson Correlation	.16	.05	.00	.15	.61	.13	.40
	Sig. (2-tailed)	.64	.89	.99	.65	.05	.70	.23
	N	11	11	11	11	11	11	11

Figure 1

Markovian Grammar Chain Used for Stimulus Creation

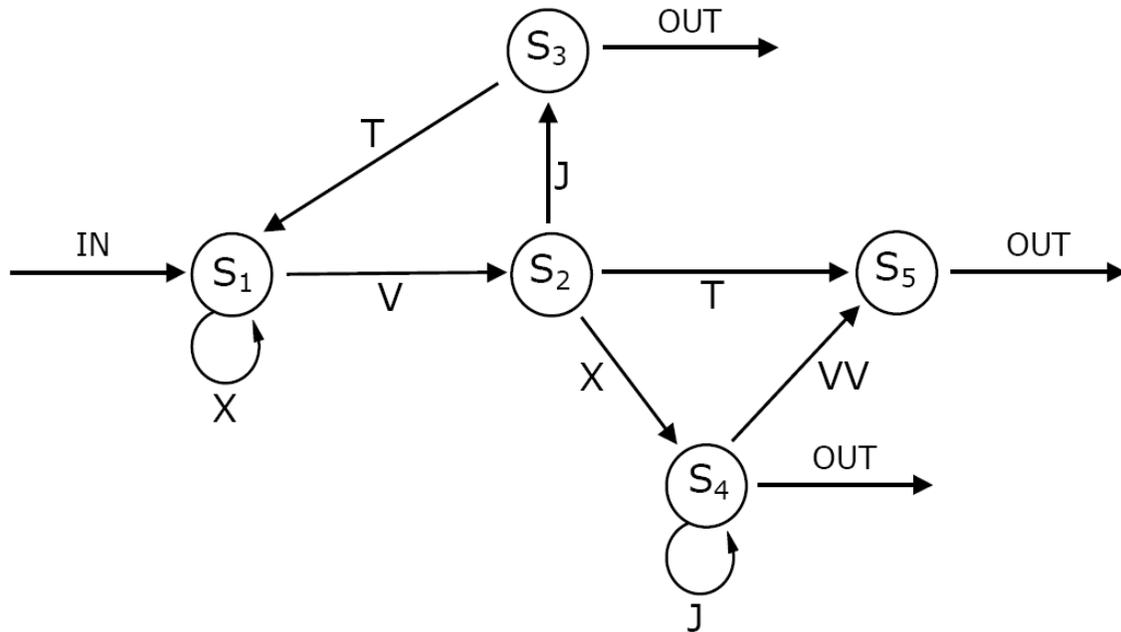


Figure Caption. This image represents the guide for how grammar stimuli were created for the exposure and test trials of the experiment.

Figure 2

Stimulus Presentation Diagram

Study Presentation Diagram

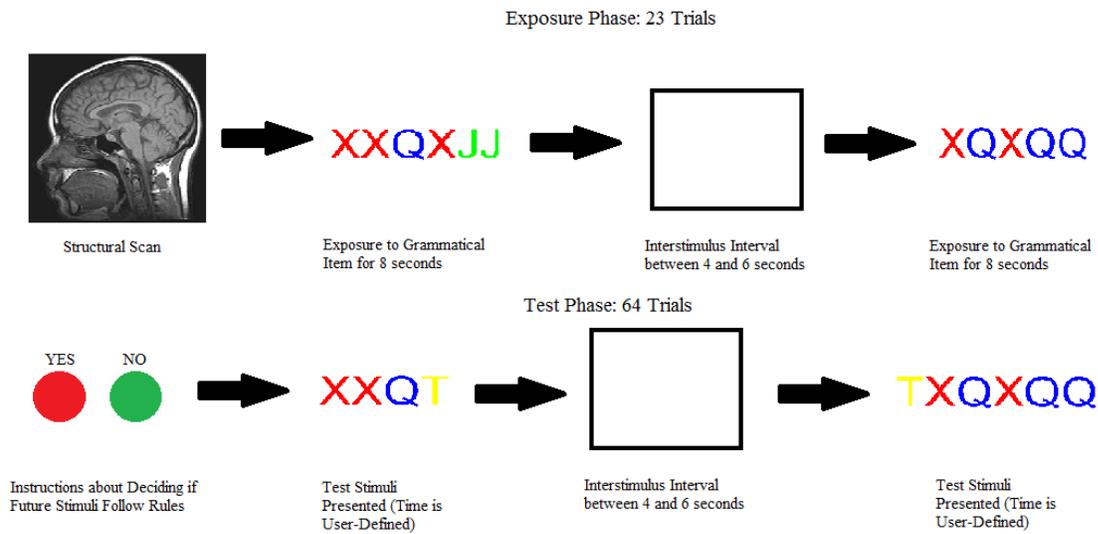


Figure Caption. This image represents the sequence of events for participants in the current research study. Participants received a structural scan, followed by 23 trials of grammatical stimuli during the exposure phase. During the test phase, participants were shown grammatical and nongrammatical stimuli and were asked to decide if the stimuli followed the same rules as the initial stimuli.

Figure 3

Grammar Effect Group Differences

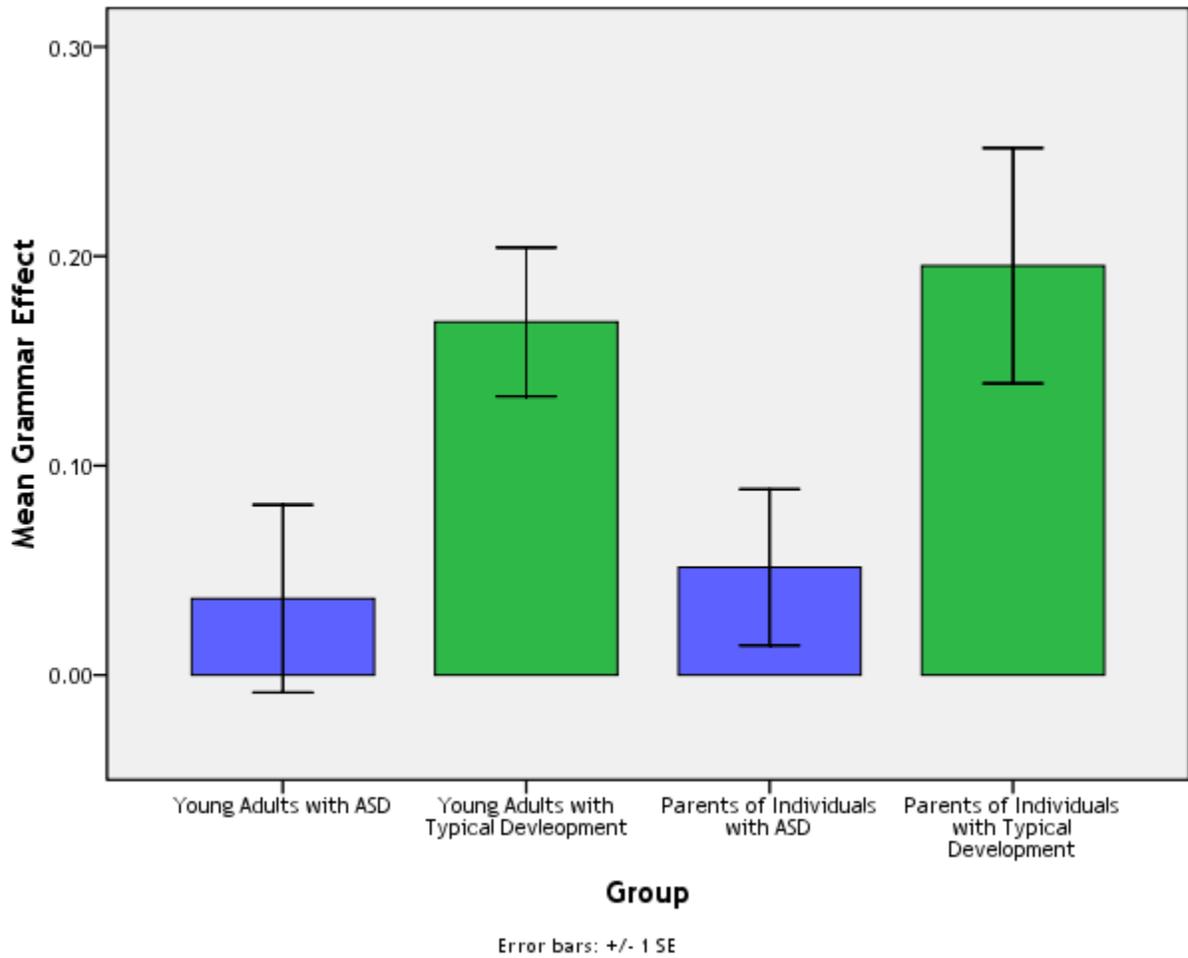


Figure Caption. Participants with ASD and parents of participants with ASD showed significantly lower amounts of grammar learning compared to typically developing control participants.

Figure 4

Section of Activation Differences between Typically Developing Participants and Participants with ASD during Exposure

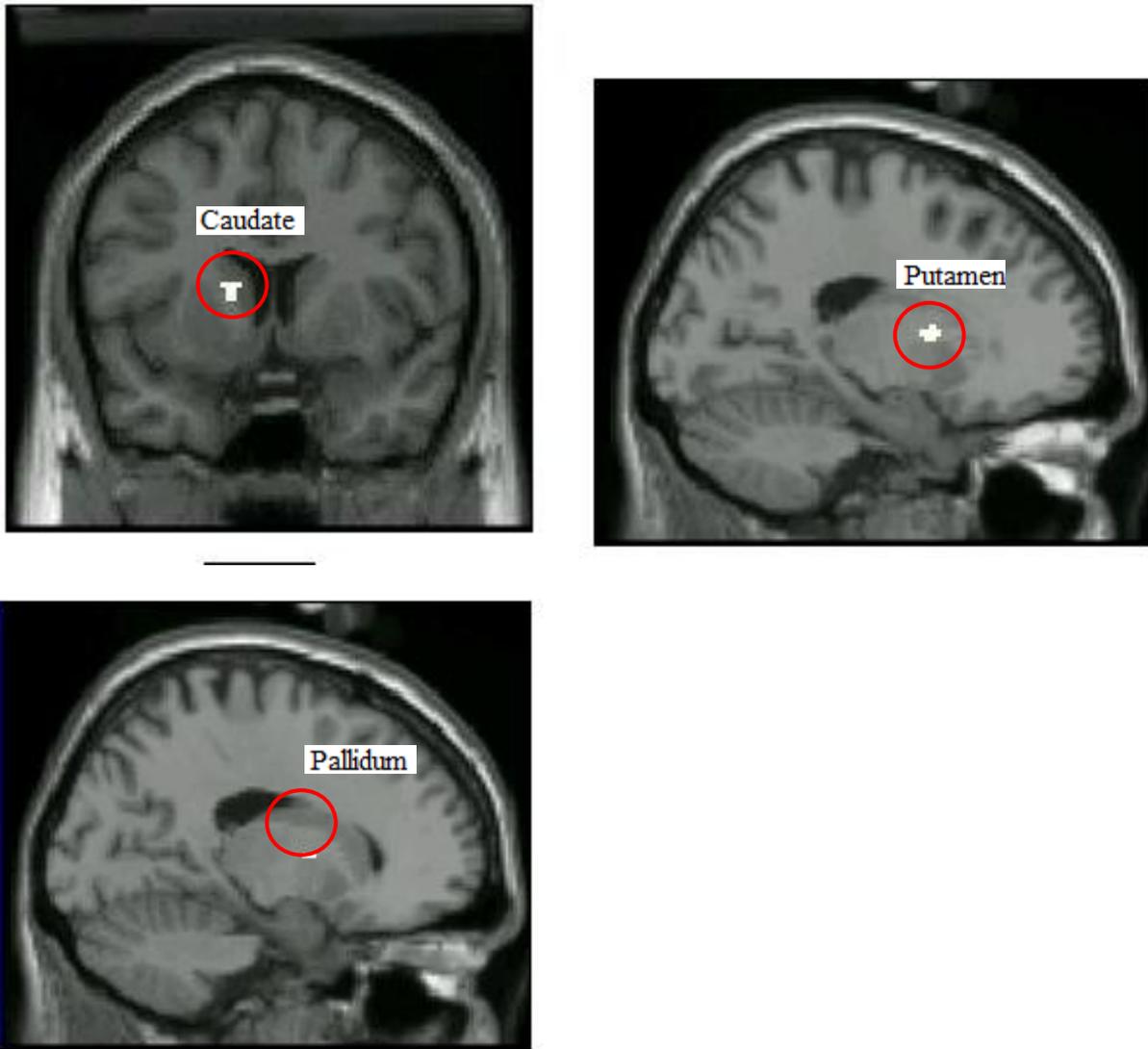


Figure Caption. Participants with typical development showed greater activation in the caudate, putamen, and pallidum during exposure trials.

Figure 5

Rendering of Activation Differences between Typically Developing Participants and Participants with ASD during Exposure

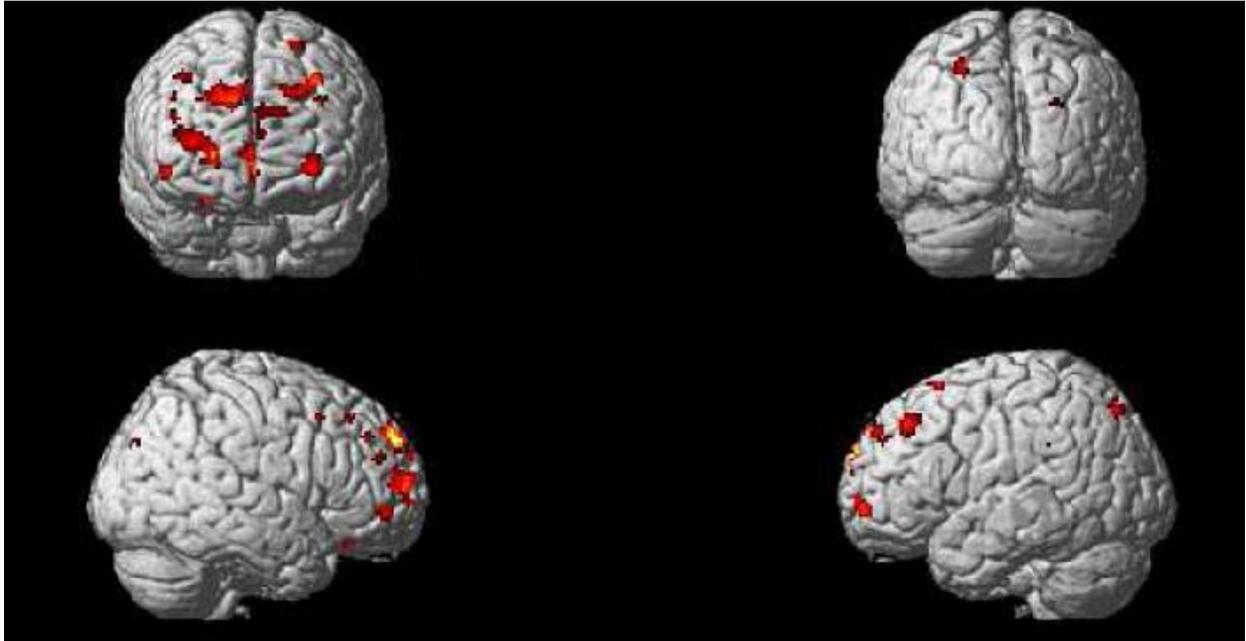


Figure Caption. Participants with typical development showed greater activation in overall brain activity, including prefrontal cortex areas during exposure trials.

Figure 6

Section of Activation Differences between Parents of Typically Developing Participants and Parents of Participants with ASD during Exposure

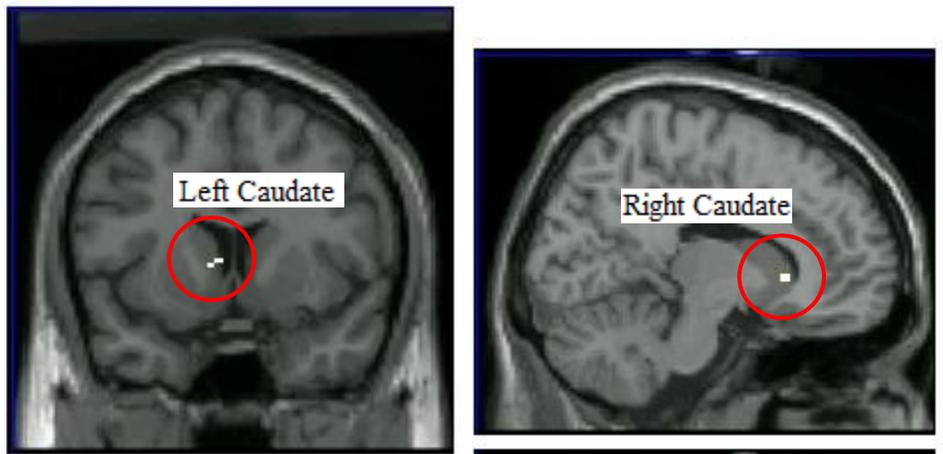


Figure Caption. Parents of participants with typical development showed greater activation in the left and right caudate during exposure trials.

Figure 7

Rendering of Activation Differences between Parents of Typically Developing Participants and Parents of Participants with ASD during Test Trials

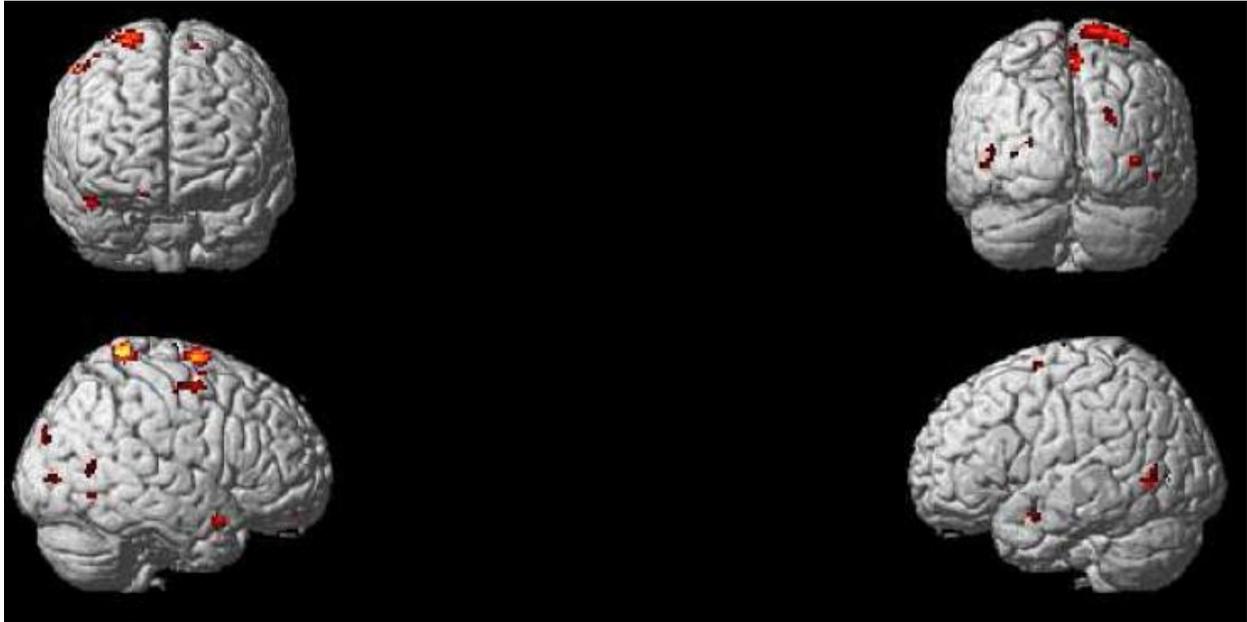


Figure Caption. Parents of participants with typical development showed greater activation in overall brain activity, including frontal and parietal areas during test trials.

Figure 8

Section of Activation Differences between Parents of Typically Developing Participants and Parents of Participants with ASD during Test Trials

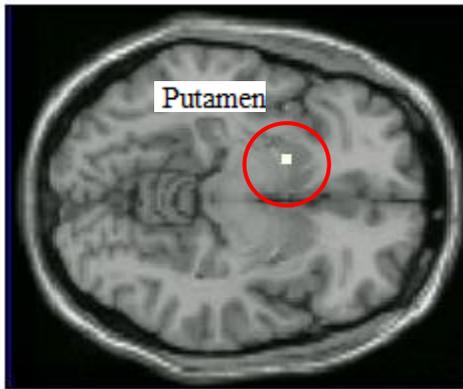


Figure Caption. Parents of participants with typical development showed greater activation in the putamen during test trials.

Figure 9

Functional Connectivity Differences between Typically Developing Participants and Participants with ASD during Exposure

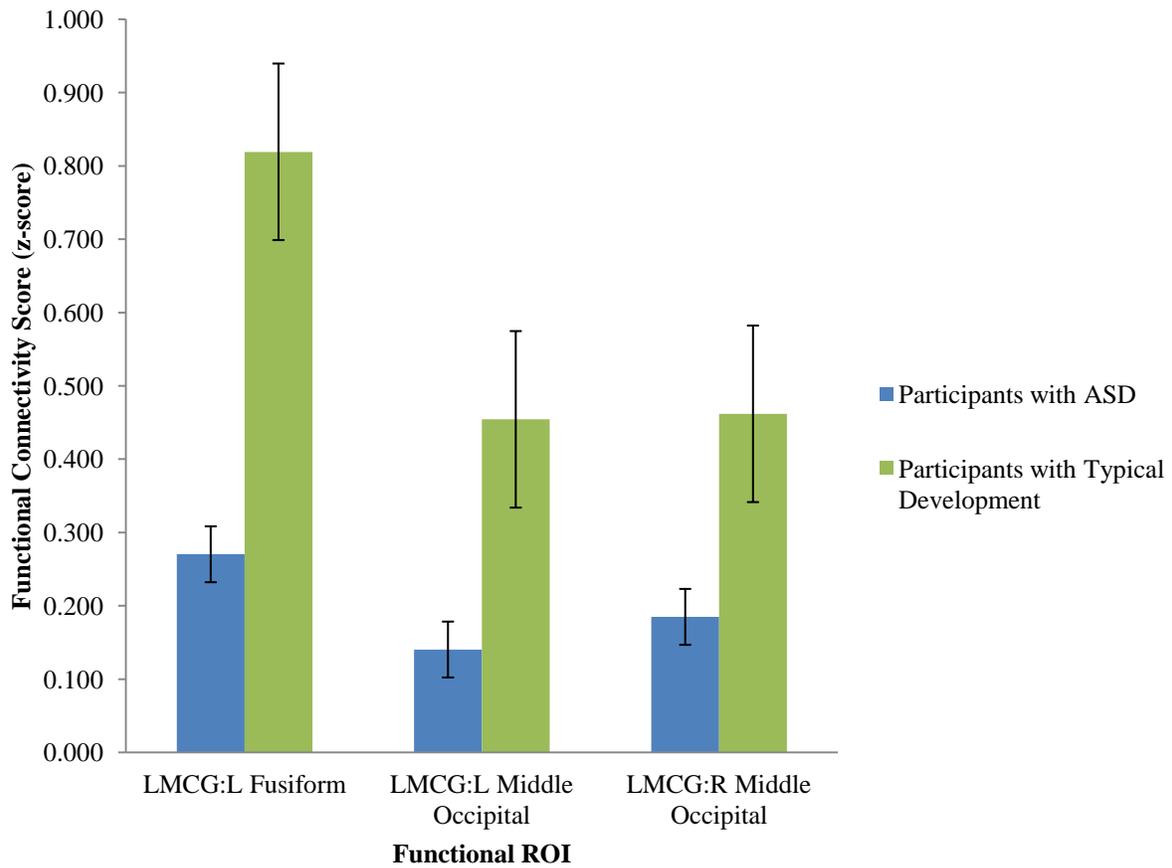


Figure Caption. Participants with typical development showed greater functional connectivity between the areas of the left fusiform area, left middle cingulate, left middle occipital region, and the right middle occipital region during exposure trials.

Figure 10

Functional Connectivity Differences between Typically Developing Participants and

Participants with ASD during Test Trials

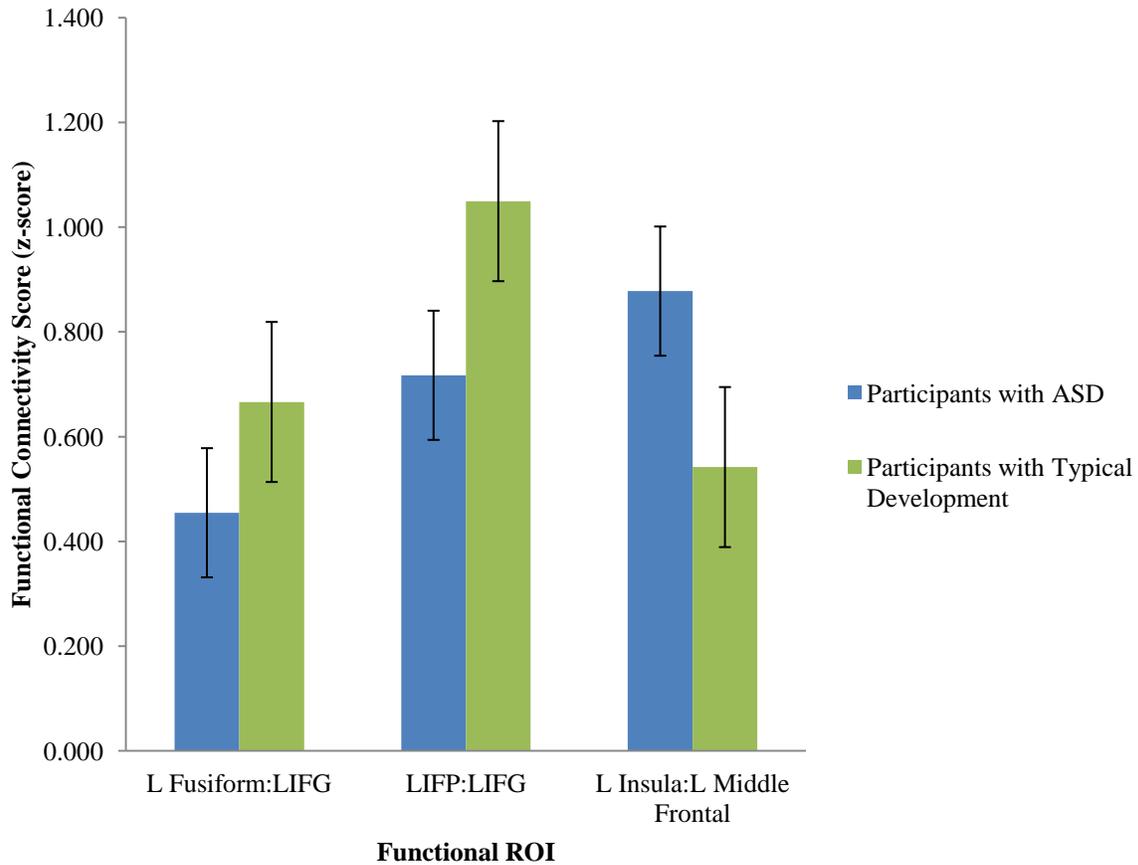


Figure Caption. Participants with typical development showed greater functional connectivity between the areas of the left insula and left medial frontal region during test trials. Participants with ASD showed greater functional connectivity between the areas of the left fusiform area, left inferior frontal gyrus, and left inferior frontal parietal during test trials.

Figure 11

Functional Connectivity Differences between Parents of Typically Developing Participants and Parents of Participants with ASD during Exposure

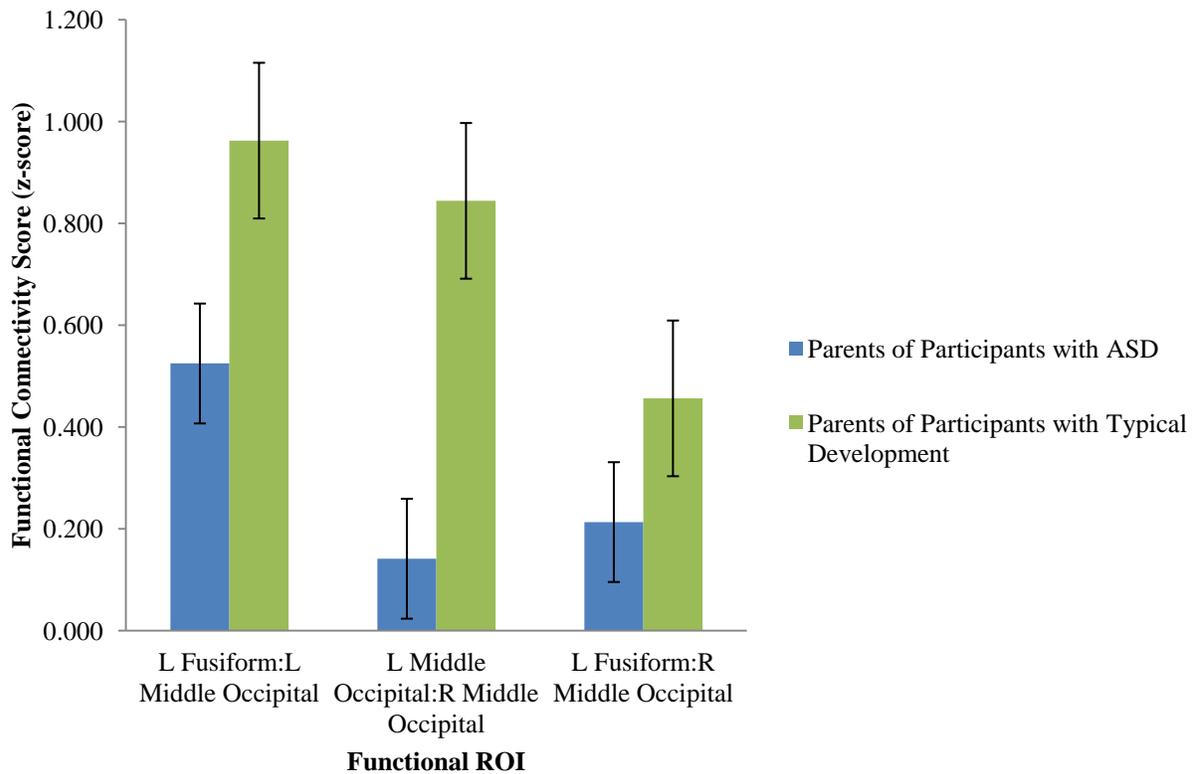


Figure Caption. Parents of participants with typical development showed greater functional connectivity between the areas of the left fusiform area, left middle occipital region, and the right middle occipital region during exposure trials.

Figure 12

Functional Connectivity Differences between Parents of Typically Developing Participants and Parents of Participants with ASD during Test Trials

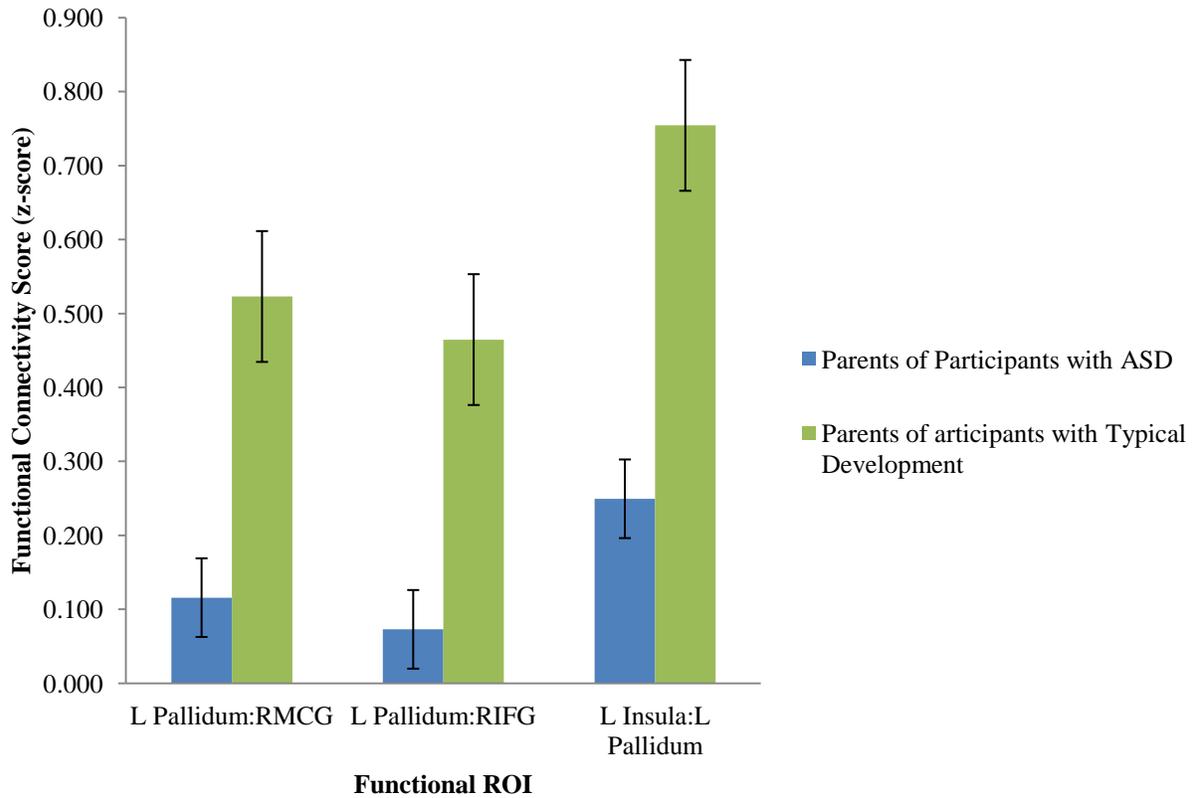


Figure Caption. Parents of participants with typical development showed greater functional connectivity between the areas of the left pallidum, right middle cingulate, right inferior frontal gyrus, and left insula during test trials.