University of Nevada, Reno

Is Autism a Disconnection Syndrome?

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Arts in Psychology

By

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May, 2013

University of Nevada, Reno
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We recommend that the thesis
prepared under our supervision by

CORINNE E. JUNG

entitled

Is Autism A Disconnection Syndrome?

be accepted in partial fulfillment of the
requirements for the degree of

MASTER OF ARTS

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May, 2013

Abstract

Reduced cortical connectivity has been implicated as the underlying cause of cognitive and behavioral deficits associated with autism spectrum disorders (ASD). This research used two stimulus-response experiments to compare connectivity across hemispheres in boys with ASD to neurotypical boys. Experiment 1 recorded reaction times to bilaterally and unilaterally presented stimuli. Only the ASD group benefited greatly in bilateral conditions and, for unilateral conditions, when the stimulus appeared in the visual field across from the response hand. These condition types only affected reaction times for the ASD group, suggesting compromised interhemispheric transfer. Experiment 2 compared accuracy and efficiency for processing simultaneously presented patterns in both visual fields. When these patterns were the same, the task was easier for the neurotypical group, while the ASD group performed comparably whether the patterns were the same or different, suggesting greater isolation in each hemisphere. Impaired interhemispheric transfer supports overall cortical underconnectivity as the cause of cognitive impairments associated with this disorder.

Acknowledgements

I would like to thank my advisor, Dr. Jeffrey J. Hutsler, for all his help and his contribution to this project. I would also like to thank Dr. Debra C. Vigil, from the Speech Pathology and Audiology Department at the University of Nevada, Reno, for facilitating participant recruitment.

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1. Introduction

Complex cognition, coordinated motor activity, and a cohesive experience of the sensory world depend on the integrity of the connections between brain regions. The connectivity hypothesis of autism implicates a failure of integration across brain regions, disrupting these higher order processes (Just et al. 2007). Interhemispheric transfer is one route of long-distance communication within the brain, and using behavioral measures to explore the efficiency with which this process occurs can help elucidate the relationship between reduced connectivity and the severity of behavioral deficits in autism.

Previous studies with ASD subjects have supported this theory by showing impairments in long-range connections that affect the dynamics of brain synchronization during complex cognitive tasks, such as coordinating motor activity and achieving a cohesive experience of the sensory world (Frith 2003; Just et al. 2004). Functional connectivity is one way to determine how correlated activation is across different brain regions of interest. ASD groups have demonstrated reduced functional connectivity between pairs of regions of interest (Just et al., 2007), which suggests a general deficit in interregional communication. Specifically, studies of sentence comprehension (Just et al., 2004), theory of mind (Castelli et al., 2002), and memory (Luna et al., 2002) have supported underconnectivity during these complex cognitive tasks that are often affected in ASD.

The corpus callosum, a structure consisting of a large bundle of axons, connects and facilitates communication between the two cerebral hemispheres, making it the focus of studies examining interhemispheric underconnectivity in syndromes such as callosotomy and agenesis of the corpus callosum (ACC) (Bloom and Hynd 2005). This structure has been postulated as the integrating link that allows each hemisphere to specialize in different functions, while still maintaining access to information in the other hemisphere (Gazzaniga 2000). The relationship between the corpus callosum and autism has been studied and, although results are mixed, neuroimaging research generally reports size reduction (Vidal et al. 2006; Just et al. 2007; Frazier and Hardan 2009). This includes reductions in both the total volume and subdivisions of the structure (Coben and Myers 2008; Hardan et al. 2009). Reduced white matter density has been found in subregions of the corpus callosum, specifically in the genu, rostrum, and splenium (Chung et al. 2004). Diffusion tensor imaging (DTI) studies have also revealed smaller corpus callosum volumes, high mean diffusivity, low anisotropy, and increased radial diffusivity in ASD groups (Alexander et al. 2007). Magnetization transfer imaging (MTI), a magnetic resonance imaging (MRI) technique sensitive to the presence of myelin, has revealed abnormal myelin development in the corpus callosum, which may contribute to altered interhemispheric connectivity in autism (Gozzi et al. 2012). Additionally, research supports a negative correlation between corpus callosum deficits and interhemispheric functional connectivity (Quigley et al. 2003).

Long-range underconnectivity can be linked to the abnormal patterns of socialization, communication, and behavior, as seen in ASD (Coben and Myers 2008). Studies examining disconnection syndromes have also revealed consistent behavioral phenotypes that are presumed to arise strictly from the corpus callosum deficit (Gazzaniga 1974). Children with ACC show similar social deficits as children with ASD , such as problems maintaining conversations, developing peer relationships, and understanding social etiquette (Badaruddin et al. 2007). Theory of mind, the ability to understand that other people have thoughts and feelings of their own that may differ from oneself, is characteristically diminished in autism (Mason et al. 2007). Based on narratives of pictures depicting people in various situations, individuals with ACC also show deficiencies imagining and inferring the mental, emotional, and social functioning of others (Turk et al. 2010). Communication, a hallmark deficit in autism, is abnormal in all cases of ACC (O'Brien 1994). For those that do have speech, echolalia, which is automatic, meaningless repetition of words and phrases commonly observed in children with autism, is present in about 86% of those with ACC (Badaruddin et al. 2007). Individuals with autism have problems accurately and rapidly shifting attention (Courchesne et al. 1994), a deficit also characteristic of ACC (Reuter-Lorenz et al. 1990). The combination of these deficits consequently impact all aspects of development for these populations.

Although callosal impairment in callosotomy patients is not developmental, and they generally exhibit few personality changes after surgery, abnormal behaviors arise that are characteristic of autism. Some patients display dramatically altered emotional responses, appearing unaffected by traumatic events that elicit strong emotions for others (Hoppe and Bogen, 1977). They demonstrate diminished theory of mind in tasks that require them to make judgements about one's actions in hypothetical situations. Their responses were based on the actual outcomes of events, rather than the agents' beliefs, despite demonstrating correct comprehension of the scenarios (Miller et al. 2010). The natural ability to ascribe beliefs and intentions onto other people requires a network of brain regions, including the medial prefrontal cortex, superior temporal sulcus at the temporo-parietal junction, and temporal poles (Brunet et al. 2000). Deficits in theory of mind in both ACC and callosotomy suggest that a disconnection between hemispheres may impact this higher order cognitive process. Additionally, patients cannot identify the social faux pas in a variety of scenarios (Miller et al. 2010), suggesting changes in how they approach social situations following surgery. Problems understanding and following the rules of social etiquette are reliable indicators of social interaction deficits that are characteristic of autism.

Populations with diminished interhemispheric connectivity have demonstrated specific reaction time deficits in stimulus-response tasks. Individuals with ACC and callosotomy benefit more from presentation of bilateral stimuli compared to unilateral stimuli (Roser and Corballis 2003). This benefit, referred to as the redundancy gain, is characterized by faster reaction times to bilateral stimuli and is not experienced by neurotypical groups. Patient groups also have especially prolonged reaction times to unilateral stimuli presented to the visual field contralateral to, or opposite of, the response hand, compared to stimuli presented to the visual field ipsilateral to, or on the same side of, the response hand. The difference between these reaction times is known as the crossed-uncrossed difference (CUD) and has been shown to be about 4 ms in typical adults. It increases to 30 ms for those with agenesis of the corpus callosum (ACC) and 70 ms for adults with callosotomy (Roser and Corballis 2003), suggesting an increase in CUD with the severity of the corpus callosum deficit. The greater redundancy gain and CUD are presumably attributed to less interaction between the hemispheres. When a single stimulus is presented to the hemifield opposite of the response hand, activation must cross hemispheres to initiate movement of the response hand. This process is less efficient and can take longer for patient groups with reduced interhemispheric connectivity. If this is the case in autism, performance should resemble those of the ACC and callosotomy participants on similar tasks: redundancy gain and CUDs should be significantly greater than those of neurotypical individuals.

In cases where conflicting stimuli are presented to each visual field, neurotypical groups struggle to process both sets of information, but patient groups are not negatively impacted (Holtzman and Gazzaniga 1985). When each hemisphere functions in isolation, processing two different patterns, one lateralized to each visual field, happens independently and therefore the overall perceptual load does not increase. Performance of neurotypical individuals presumably suffers because the more two tasks interfere with each other, the more they compete for common processing (Treisman and Davies 1973). If autism is associated with diminished interhemispheric transfer, these individuals should perform comparably whether information in each visual field is the same or different.

Although support for the connectivity theory has been identified in ASD groups, the efficiency of interhemispheric transfer has not been studied behaviorally in the specific case of

ASD. In this study, we used two different behavioral measures to assess interhemispheric connectivity in ASD, as compared to in neurotypicals. Experiment 1 tested redundancy gain and CUD with a stimulus-response task. We predicted significantly enhanced redundancy gain and CUD due to delayed information transfer across hemispheres. Experiment 2 tested the effects of perceptual load on performance in both groups. We predicted performance of the ASD participants would not depend on whether perceptual load was increased or not, while performance of the neurotypical group would suffer when competing information had to be processed. These outcomes suggest that the characteristics associated with ASD may arise from a neurobiological disorder of integrative processes that affect connectivity at both the neural and cognitive levels.

2. Experiment 1: Redundancy Gain

Experiment 1 required manual responses from each group to bilaterally and unilaterally presented colored squares. Faster reaction times to bilateral stimuli would suggest that transfer time is considerably impacted by whether or not information is presented directly to both hemispheres. Additionally, because crossed unilateral stimuli need to activate the opposite hemisphere to initiate the response hand, they may elicit different reaction times than uncrossed stimuli. We predicted that reaction times for bilateral and unilateral stimuli would differ significantly for the ASD group, with reaction times being longer for unilateral stimuli, while reaction times for each condition would be comparable for the neurotypical group. We also expected that the ASD group would have greater reaction times for crossed stimuli than uncrossed stimuli, while reaction times for the neurotypical group would not significantly differ for conditions.

2.1. Methods

Participants

Participants in this study were 12 boys with a diagnosis of ASD and 13 typically developing boys. All participants were between the ages of 6-17. They were assessed using the Wechsler Abbreviated Scale of Intelligence (WASI) to determine Full Scale, Verbal, and Performance IQ, the Edinburgh Inventory (Oldfield 1971) to determine a laterality quotient (LQ), and the Gilliam Autism Rating Scale 2 (GARS-2) for the ASD group only. Parents and guardians filled out information for the Edinburgh Inventory and the GARS-2. They indicated the boys' hand dominance for 10 different everyday activities to obtain an LQ for each participant. Participants with ASD had been previously diagnosed by a licensed clinical psychologist or medical doctor not associated with this research. The diagnosis of each individual in the ASD group was confirmed using the GARS-2. Parents and guardians provided current ratings of how often they observed their children exhibit certain characteristics in the following categories: stereotyped behaviors, communication, and social interaction. There were no significant differences between groups in these measures, except for in the full-scale IQ measure (Table 1). However, verbal and performance IQ are the components that determine full-scale IQ, and these were not significantly different between groups. No participant had a history of a medical disorder known to cause characteristics associated with ASD. Neurotypical participants had no current or past diagnosis of ASD or other psychiatric or neurological disorder. Parents and guardians signed written consent forms, and all participants provided verbal assent prior to testing.

Procedure

Participants sat 57 cm away from a 13.5 inch LCD laptop monitor. Stimuli were presented on the monitor, and participants made all responses on the keyboard. The order in which participants did the experiments, as well as the order in which they used their response hands, were counterbalanced.

Participants were instructed to make a manual key press in response to visual stimuli. A yellow center fixation point remained in the center of the screen that participants stared at throughout the duration of each block of trials. Stimuli were small red- or green- filled squares that subtended a visual angle of .638°. They were presented on a black background and flashed to symmetric positions on the right visual field, left visual field, or both sides, 9.552° from center fixation. Participants attempted to press the spacebar key as soon as they saw the stimuli.

The experiment consisted of two blocks of 40 trials. Participants alternated response hands in between blocks. Stimuli were either unilateral, presented to the left or right side of fixation, or bilateral, presented simultaneously to both the left and right sides of fixation. There were eight possible display types: four unilateral displays (Green Left, Green Right, Red Left, Red Right) and four bilateral displays (Green + Red, Red + Green, Green + Green, Red + Red) (Fig. 1). Each block of 40 trials consisted of 8 randomly generated presentations of each display type. Participants could practice with up to 10 trials if they needed, prior to beginning the experiment.

Participants initiated the beginning of the experiment by pressing the spacebar key with the hand they were using for that block of trials. The fixation point then appeared and remained on the monitor until the end of the block. After a randomly generated time between 500 and 5000 ms, stimuli appeared. The stimuli remained on the screen until participants responded by pressing spacebar, or until 5000 ms elapsed. RTs were recorded from stimulus onset to key press. If the participant did not make a response after 5000 ms, the session timed out and moved to the next trial in the block.

Data Analysis

Mean reaction times, in milliseconds (ms), were calculated for each participant. Trials for which the reaction times reached 5000 ms and timed out were treated as unattended trials, and were not included in the data analysis. Initially a full mixed model was run with the variables of diagnosis (ASD and neurotypical groups), condition (bilateral or unilateral), and hand (left or right). Within the bilateral condition, color (single color presented twice or two different colors presented) was a nested factor. Within the unilateral condition, cross type (stimulus crossed or uncrossed from the response hand) and color were nested factors. The variables of condition, its nested factors, and hand were repeated measures. Compound symmetry was assumed for the repeated measures. Variables that were not significant were removed, and the final model included diagnosis and condition. Age, IQ, and LQ were later included in the model as covariates.

2.2. Results

The variable of color and the nested variable of color type for bilateral conditions were not significant as main effects or with their combinations with other variables. They were both removed from the model. The variable of hand and its combinations with other variables were not significant and was also removed. After assessed for fit, the final model was a 2x2 mixed model with the variables of diagnosis and condition.

There were significant main effects of both diagnosis ($F(1, 21.925) = 8.021$, $p = .009$) and condition ($F(1, 1945.048) = 22.005$, $p < .001$) and a significant interaction between diagnosis and condition ($F(1, 1945.048) = 6.853$, $p = .009$). The ASD group had faster reaction times for bilateral stimuli than unilateral stimuli compared to the neurotypical group, whose reaction times did not differ as greatly across conditions (Fig. 1). The crossed versus uncrossed condition was a nested term within the unilateral trials, and it had a significant main effect ($F(1, 1944.913) = 6.208$, $p = .013$). The interaction between diagnosis and the crossed versus uncrossed condition approached significance ($F(1, 1944.913) = 2.975$, $p = .085$) (Fig. 2), with the ASD group having more prolonged reaction times for crossed stimuli than uncrossed stimuli, compared to the neurotypical group.

When age was added as a covariate, it changed the significance of the interaction between diagnosis and condition (p = .41). Adding both age and IQ as covariates also changed the significance of this interaction (p = .41). Results failed to converge when laterality quotient was added as another covariate. The separate test including only the ASD group with the GARS score as a covariate did not produce significantly different results than when the model was run without diagnosis.

2.3. Discussion

This simple stimulus-response task provided a means for assessing the efficiency of interhemispheric information transfer. Reaction times depended on diagnosis and whether the stimuli were presented bilaterally or unilaterally. Color did not impact performance in either group, regardless of how it was presented in bilateral and unilateral conditions. As predicted, there was a significant interaction between diagnosis and condition. The ASD group had faster reaction times for bilateral stimuli than unilateral stimuli, while the neurotypical group did not exhibit significant reaction time differences for these conditions.

These results suggest that there was a greater redundancy gain for the ASD group than for the neurotypical group. When stimuli were presented in both visual fields, both hemispheres were directly activated without the need for interhemispheric transfer. The notable benefit the ASD group showed in performance for bilateral conditions resembles that of populations affected by impaired interhemispheric transfer, such as individuals with ACC.

Although results did not reach significance, reaction times for crossed and uncrossed unilateral conditions differed greatly for the ASD group but not the neurotypical group. The ASD group took longer to respond to crossed conditions, which matches our prediction that activating the response hand takes longer when the opposite hemisphere needs to wait for information. As expected, the neurotypical group showed a smaller difference in reaction times between the crossed and uncrossed trials. The results from adding covariates show that age and IQ affected the interaction between diagnosis and condition. The influence of these covariates can be attributed to the wide age and IQ range of participants included in this study, and they do not weaken the case for impaired information transfer in autism, as supported by the significance of this interaction.

3. Experiment 2: Perceptual Load

Experiment 2 compared the effects of two levels of perceptual load on processing performance in the ASD and neurotypical groups. This task was based on a study comparing a callosotomy patient with two neurotypical participants (Holtzman and Gazzaniga 1985). Participants had to remember patterns presented to both visual fields. Pattern presentations could either be the same on both the left and right side (redundant) or different (mixed). When different patterns of stimuli are presented to each visual field, they may have to compete for common processing mechanisms. This should impair performance when interhemispheric connectivity is intact, as conflicting information from each hemisphere must be processed. However, if hemispheres function more independently, whether the patterns are the same or different should not have as much of an impact on processing. We predicted that mixed conditions, in which patterns are different, would be detrimental to performance for the neurotypical group, but not the ASD group. We also predicted that the neurotypical group would excel in redundant conditions, whereas performance for the ASD group would not differ greatly across conditions.

3.1. Methods

Participants

All of the participants were the same as in Experiment 1, and had provided scores for the WASI, GARS 2, and Edinburgh Inventory. One participant from the ASD group in Experiment 1 did not demonstrate an understanding of Experiment 2 and his behavior suggested he was reluctant to continue. This experiment therefore had 11 boys in the ASD group, and 13 boys in the neurotypical group

Procedure

Participants sat 57 cm away from the same 13.5 inch LCD laptop from Experiment 1. For all trials, participants fixated on a black central fixation point, presented on a white background. In both the right and left visual fields, there was a 3x3 grid of squares that remained on screen throughout the duration of the experiment. Trials began with both grids displaying target sequences: red filled squares that blinked successively in four different cells. The red squares were displayed in each cell for a duration of 150 ms, with 500 ms separating each display. Upon completion of the target sequences, a fixed 1.5 sec ISI elapsed, and then a unilateral probe sequence in only the left or right grid followed. This probe sequence either followed the same pattern as the target sequence in that visual field, or the second or third square blinked in a different cell (Fig. 3). The program then prompted the participant to indicate with a key press if the probe sequence matched the target sequence.

This experiment consisted of three factors, yielding eight possible stimulus conditions. The first factor was target type: mixed or redundant. The second factor was the visual field that the probe sequence appeared on. This could be to the left or right of fixation, preventing participants from attending to one visual field over the other. The third factor was whether the probe sequence matched the target sequence or not. Each block consisted of an equal number of redundant and mixed conditions, an equal number of trials in which the probe sequence was on the left or right visual field, and an equal number of trials in which the probe sequence matched or did not match its corresponding target sequence. Presentation of trial types was randomized within blocks. All participants completed one block of 40 trials with each hand for a total of 80 trials.

Data Analysis

Mean RTs were obtained for each participant's performance with each hand and for each condition. All reaction times equal to, or exceeding, 15000 ms were assumed to be unattended trials and were excluded from data analysis. Only RTs from correct trials were included. A 2x2x2x2 mixed model was used with diagnosis (ASD and neurotypical groups), condition (mixed or redundant), match type (match or no match), and hand (left or right) as independent variables with reaction time as the dependent variable. The model was run again with age, IQ, and laterality quotient as covariates. The GARS score was added as a covariate in a separate analysis that only included data for the ASD group and compared to the model excluding diagnosis.

Accuracy was determined using the average number of trials each participant provided correct responses for in each condition. Two independent t-tests were used to compare each group's accuracy in the mixed condition and in the redundant condition. A binomial test was run to assess whether accuracy was above chance.

3.2. Results

Analysis for reaction times revealed a significant main effect of diagnosis ($F(1, 17.735) = 16.523$, $p = .001$). The ASD group had longer reaction times than the neurotypical group overall. The interaction between diagnosis and condition type was significant for reaction time ($F(1, 1140.763) = 5.347$, $p = .021$). The neurotypical group had longer reaction times for mixed conditions than redundant conditions compared to the ASD group, whose reaction times were similar for both conditions (Fig. 4). The four way interaction between diagnosis, condition type, match type, and hand was also significant ($F(1, 1137.474) = 4.64$, $p = .031$). When age, IQ, and LQ were added as covariates, the significance of the main effects and interactions did not change. The separate test including the ASD group only with the GARS score as a covariate did not produce significantly different results than the model run without diagnosis. How ASD participants scored on the GARS did not have a significant influence on reaction times in each condition.

Accuracy performance for the ASD group ($M = 24.91$, SD = 4.23) and the neurotypical group ($M = 18.38$, SD = 4.05) in the mixed condition was significantly different between groups

($t(22) = 3.85$, $p = .001$). As a group, the ASD participants had higher accuracy with mixed condition trials than neurotypical participants. However, in the redundant condition, the ASD group ($M = 26.09$, SD = 5.54) did not perform significantly different than the neurotypical group ($M = 29.08$, SD = 7.43, $t(22) = -1.098$, $p = .284$) (Fig. 5). For the binomial tests on accuracy, the ASD group performed significantly above chance in each condition ($p < .001$ in both tests). The neurotypical group performed significantly above chance for the redundant conditions ($p < .001$) but did not perform significantly better than chance in the mixed conditions ($p = .963$).

3.3. Discussion

Presentation of different, rather than identical, patterns of stimuli to the left and right visual field imposed an increased perceptual load for the visual processing system, as more information had to be encoded. This was detrimental to processing for the neurotypicals, who performed better when patterns were redundant. Considering accurate trials only, the ASD group had prolonged reaction times overall, regardless of trial type. However, the interaction of diagnosis with condition type shows that neurotypical participants had considerably longer reaction times for mixed conditions compared to redundant conditions. Thus, even when they successfully determined whether a probe matched the corresponding target sequence, they required more time. When each hemisphere functions like an independent processor, as in callosotomy, processing occurs with little interference or regard for information in the opposite hemisphere. Mixed conditions did not require additional processing time for ASD participants, which may be due to the fact that they can process contradictory information from both visual fields more independently and efficiently. The significant four way interaction between diagnosis, condition type, match type, and hand can be attributed to the main effect of diagnosis and the two way interaction between diagnosis and condition, as there were no other significant effects of match or hand. The effects of hand may be due to the high proportion of right handed participants. The results from adding covariates show that diagnosis and condition type are the primary factors that affect reaction time, which is not significantly influenced by age, IQ, and laterality quotient.

In mixed conditions, the ASD group had significantly better accuracy than the neurotypical group, who performed no better than chance. Performance decline in mixed conditions can likely be attributed to the increased processing load caused by contrasting information presented to each visual field. These trials did not impair performance for the ASD group, whose accuracy was well above chance in both conditions. This shows that they were not responding at random and that their accuracy indicates competence at distinctly processing information from both visual fields.

The challenging nature of this task makes the ASD group's performance on mixed conditions even more remarkable, resembling that of callosotomy patients (Holtzman and Gazzaniga 1985). However, although they performed better than neurotypicals in mixed conditions, they did not necessarily perform better in redundant conditions. This implicates an interhemispheric integration deficit, rather than a general advantage for processing spatial patterns.

4. General Discussion

Through behavioral measures, Experiments 1 and 2 support the theory of impaired interhemispheric transfer in ASD. Performance was comparable to that reported in ACC and callosotomy populations. The redundancy gain and CUD were greater, suggesting that, when information in one hemisphere needs to be accessed by the other, transfer time is longer. Additionally, performance, as expressed by accuracy and reaction time, was not impaired with increased perceptual load, as it was for neurotypicals. Deficits in interhemispheric transfer may be indicative of general long-range underconnectivity in ASD, which may account for several of the behavioral abnormalities associated with this disorder.

Interhemispheric transfer impairments can be detrimental to performance in tasks that require time efficiency, while enhancing performance when isolation of information is helpful. Results from Experiment 1 show that individuals with ASD have reduced reaction times in tasks that require information transfer from one hemisphere to the other. This pattern of impairment is comparable to findings from individuals with ACC (Roser and Corballis, 2003), strengthening the case for a compromise in this structure in autism as well. This task required interhemispheric transfer, specifically in crossed unilateral trials, where information had to be transferred across hemispheres to initiate movement of the response hand. Thus, in a task where transfer of information across hemispheres was required, ASD participants had a disadvantage.

When contrasting patterns are presented to each visual field, they interfere with each other. The better accuracy and faster reaction times from the ASD group in mixed conditions suggest that contradicting patterns lateralized to each visual field were not interfering with the task. However, the neurotypical group was hindered by presentation of mixed patterns and performed much better in redundant conditions, when patterns did not compete with each other. Additionally, we can conclude that these findings did not come from the ASD group having overall better skills at attending to spatial patterns. If this were the case, they should have performed better than the control group in the redundant conditions.

Interhemispheric underconnectivity in ASD has several implications for structuring intervention materials more effectively. One method is to exploit lateralization for the dominant hemisphere in certain types of tasks. Learning speed may increase if training sends input to one hemisphere, while sending qualitatively different input to the other as distraction. A practical example of this method is using earphones to play words to the right ear and music to the left. This forces the left hemisphere to process language in a way that minimizes its dependency on interhemispheric communication. However, promoting integration may be the most beneficial form of intervention during the developmental years. Although the use of art therapy is not yet fully understood, it has been considered one method for coordinating activity across brain regions (Silver 2001). Bilateral art is a specific form of art therapy that requires patients to use both hands to draw in order to simultaneously activate both sides of the brain (Cartwright 1999). Tracing the art drawn by one hand with the opposite hand is predicted to engage responses from both hemispheres to help with integration and balancing (McNamee 2003). Exercises that require simultaneous stimulation of both hemispheres may reinforce integration in other tasks.

The present study has several practical limitations. Although at least one experimenter monitored central fixation for every participant throughout each block of trials, we did not use an eye tracker because the study required mobility. We also determined that active monitoring would be a more beneficial and realistic method for keeping participants on task and fixated appropriately to avoid having to eliminate blocks from data analysis. Additionally, the WASI, the IQ measure we used for matching purposes, required verbal responses for a complete assessment. Hearing and speaking is impaired in several individuals with ASD, even if language comprehension is otherwise intact, making this a potentially invalid measure of IQ. However, only one participant could not complete the verbal portion of this test, and his data was not included in Experiment 2.

This study supports the proposed theory that autism is a disorder that arises from underconnectivity between brain regions, affecting both the neural and cognitive levels. The designs of these experiments specifically assessed integration across the midline and showed that the ASD group did not experience the same performance benefits or detriments from interhemispheric transfer efficiency as the neurotypical group. A corpus callosum deficit can impair interhemispheric connectivity in frontal, parietal, and occipital regions, depending on which subregions are affected. Its role in several important cognitive functions is consistently evident in studies that examine other populations that are affected by an abnormality of this structure. Disorders such as ACC, Specific Language Impairment (SLI), dyslexia, attention deficit hyperactivity disorder (ADHD), and Tourette's syndrome are fundamentally different, but each of their defining characteristics can be attributed to underconnectivity and are fundamentally similar to many symptoms of autism. The deficits seen across these disorders emphasize the importance of coordination among the multiple brain regions, as well as the repercussions when this communication is compromised.

Comparing ASD to populations affected by underconnectivity reveals important similarities and distinctions that can be used to determine the physiological basis of a disorder that is not as well understood. This study was one of the first to use behavioral measures to test these relationships, and its results suggest that autism shares an underlying deficit with disorders of the corpus callosum. Further exploring the contributions of interhemispheric underconnectivity to the sensory, cognitive, and behavioral problems specifically associated with ASD will move research and the autism community forward towards a better understanding of this disorder and how to improve current intervention efforts.

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Appendix A: Tables

Table 1 – Subject measures

	ASD		**NT**		**t-value**	**p-value**
	Mean	*SD*	*Mean*	*SD*		
Age	11.08	4.379	11.08	3.968	0.004	0.997
Verbal IQ	95.73	16.347	106.23	14.446	-1.671	0.109
Performance IQ	98.5	21.719	113.38	17.614	-1.889	0.072
Full-scale IQ	96.27	17.39	110.85	16.268	-2.119	0.046
LQ	65.17	57.725	80.31	19.006	-0.896	0.38
GARS-2	80.5	24.123	-	-	-	-

Appendix B: Figures

Figure 1. Average reaction times (ms) for bilateral and unilateral conditions in the ASD and neurotypical groups. Both groups had faster reaction times for bilateral trials, but only the ASD group gained a significant advantage for these trial types. Error bars represent standard error of the mean.

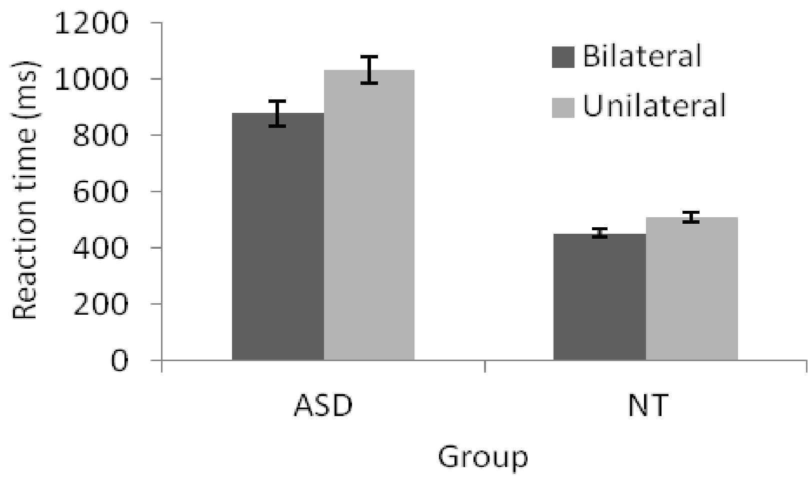


Figure 2. Average reaction times (ms) for crossed and uncrossed unilateral conditions in the ASD and neurotypical groups. The ASD group had prolonged reaction times for crossed trials while the neurotypical group performed similarly in both conditions. Error bars represent standard error of the mean.

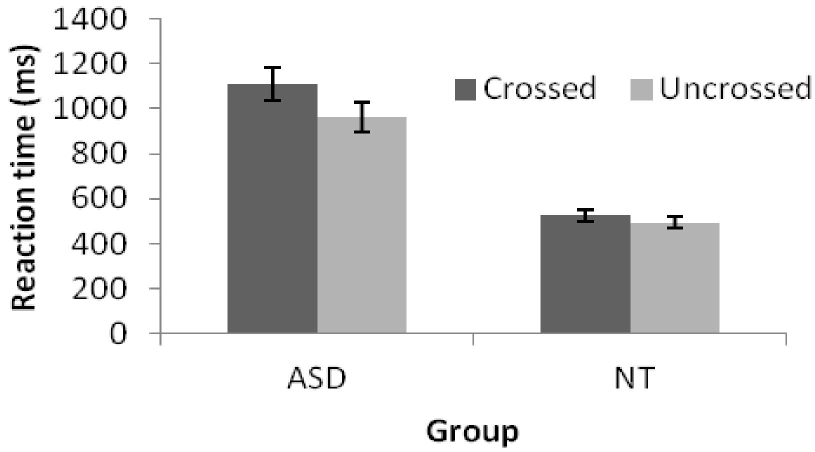


Figure 3. Experiment 2 stimuli. (a) Possible mixed target stimuli. Arrows represent the path the red squares blink along. (b) Possible match probe stimuli in the left visual field. (c) The sequence of frames for each trial. representing a redundant no match trial. The target and probe frame were displayed a total of 2.6 seconds, separated by an ISI of 1.5 seconds.

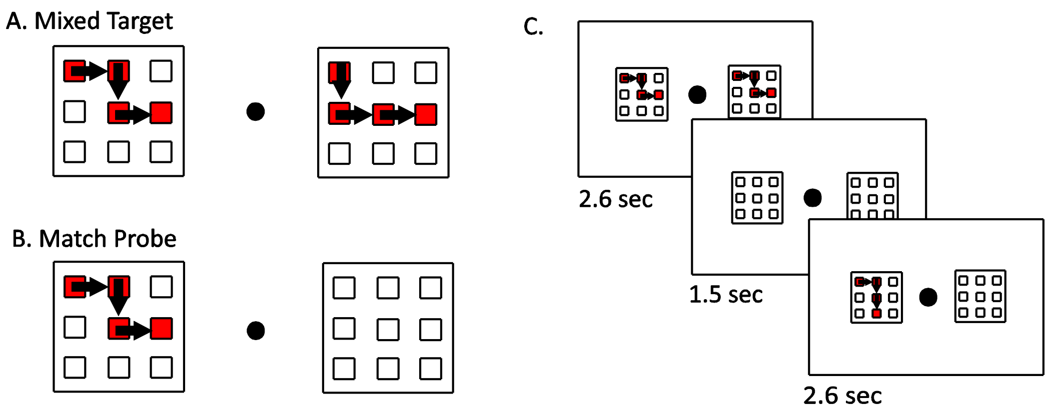


Figure 4. Average reaction times (ms) for mixed and redundant conditions in the ASD and neurotypical groups. Reaction times were similar in both conditions for the ASD group, but the neurotypical group had significantly prolonged reaction times for the mixed trials. Only reaction times for correct trials were included. Error bars represent standard error of the mean.

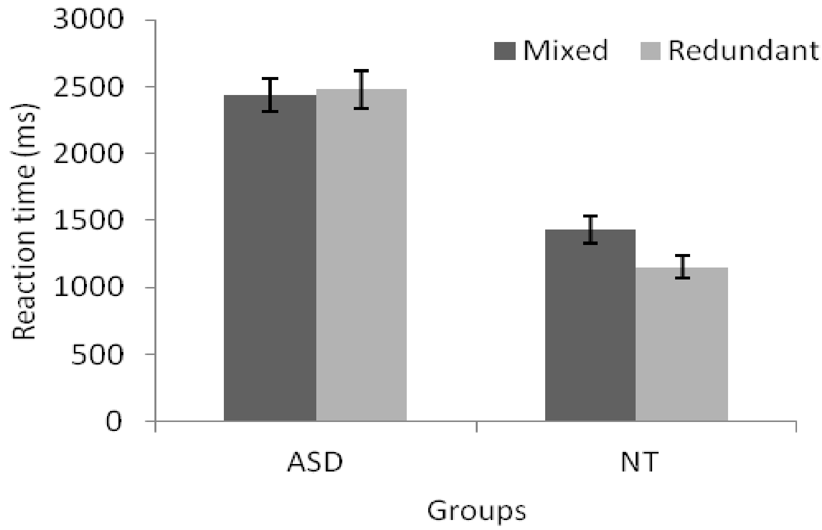
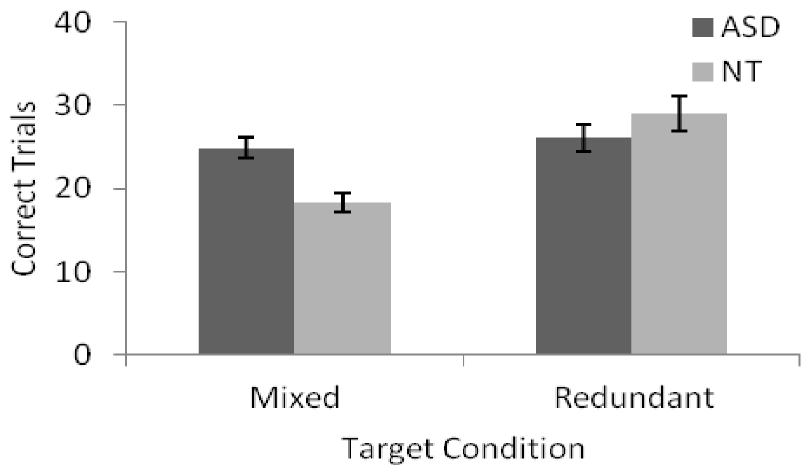


Figure 5. Average accuracy for the ASD group compared to the neurotypical group in the mixed and redundant conditions. The ASD group performed significantly better than the neurotypical group in the mixed condition, but slightly worse in the redundant condition, although the difference was not significant. Error bars represent standard error of the mean.



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