VISUAL PERCEPTION IN CHILDREN WITH SPINA BIFIDA MYELOMENINGOCELE AND THE IMPACT OF POSTERIOR CORTICAL CHANGES

_____

A Master's Thesis

Presented to

The Faculty of the Department

Of Psychology

University of Houston

_____

In Partial Fulfillment

Of the Requirements for the Degree of

Master of Arts

_____

By

Emily C. Maxwell

August, 2012

VISUAL PERCEPTION IN CHILDREN WITH SPINA BIFIDA MYELOMENINGOCELE AND THE IMPACT OF POSTERIOR CORTICAL CHANGES

Emily C. Maxwell

APPROVED:

Paul Cirino, Ph.D.
Committee Chair

Jack Fletcher, Ph.D.

Jenifer Juranek, Ph.D.
University of Texas Health Science Center
Department of Pediatrics

John W. Roberts, Ph.D.
Dean, College of Liberal Arts and Social Sciences
Department of English

VISUAL PERCEPTION IN CHILDREN WITH SPINA BIFIDA MYELOMENINGOCELE AND THE IMPACT OF POSTERIOR CORTICAL CHANGES

An Abstract of a Master's Thesis

Presented to

The Faculty of the Department

Of Psychology

University of Houston

In Partial Fulfillment

Of the Requirements for the Degree of

Master of Arts

By

Emily C. Maxwell

August, 2012

Abstract

The present study investigated categorical and coordinate visual perception in 81 children with spina bifida myelomeningocele (SBM) relative to 28 controls, and related this performance to indices of cortical thickness, gray matter volume, and white matter volume for a subset of these participants. Results revealed weaknesses for children with SBM on both the categorical and coordinate visual perception tasks relative to controls, though both groups were more accurate on the categorical task than the coordinate task. Children with SBM demonstrated smaller values of cortical thickness, gray matter volume, and white matter volume relative to controls in regions of interest (inferior parietal cortex, superior parietal cortex, middle temporal gyrus, and superior temporal gyrus). There were no relations of corpus callosum volumes to visual perception performance, but relations were noted for cortical thickness, gray matter volume, and white matter volume. The findings supported the Dennis et al. (2006) model and provided insight as to the brain regions impacting visual perception performance for children with SBM.

Keywords: visual perception, spina bifida myelomeningocele, cortical thickness, gray matter volume, white matter volume

Table of Contents

List of Tables and Figures

Visual Perception in Children with Spina Bifida Myelomeningocele and the Impact of Posterior Cortical Changes

The present study investigated variability of visual perceptual functioning in children with spina bifida myelomeningocele (SBM) using the framework proposed by Dennis, Landry, Barnes, and Fletcher (2006), and related this variability to callosal and cortical variables. Below, a review of the state of knowledge regarding SBM is provided, along with rationale for the present study.

Background. Spina bifida, a neural tube defect that causes a deformation of the spinal cord, is the most common permanently disabling birth defect affecting the central nervous system (CNS) (Liptak, 2008). Spina bifida develops when the neural tube fails to close during early embryogenesis (Anderson, Northam, Hendy, & Chatterjee, 2001). Spina bifida occurs in approximately 2 per 10,000 live births in the United States (Agopian et al., 2012; Au, Ashley-Koch, & Northrup, 2010; Williams, Rasmussen, Flores, Kirby, & Edmonds, 2005). Hispanic births have the highest incidence of spina bifida, followed by non-Hispanic white births (Agopian et al., 2012; Williams et al., 2005). Myelomeningocele is the most common form of spina bifida and carries with it the most associated impairments (Anderson et al., 2001; Fletcher et al., 2005), and is the focus of the present study. These individuals are likely to have a Chiari II malformation, which may cause hydrocephalus, and the majority will require shunting (Bryan, 1994, as cited in Anderson et al., 2001). Characteristic difficulties of spina bifida include difficulties with ambulation (Williams, Broughton, & Menelaus, 1999) and incontinence (Verhoef et al., 2006). Both physical and cognitive impairments tend to be more significant for individuals with SBM that have higher spinal lesions relative to those with lower spinal lesions (Fletcher et al., 2005).

Socioeconomic opportunity also impacts functioning in SBM. For example, children with SBM and lower socioeconomic status (SES) have slower rates of cognitive and language growth (Lomax-Bream, Barnes, Copeland, Taylor, & Landry, 2007). The impact of SES is broad, however; for example, children with and without SBM that have lower SES show lower verbal scores regardless of ethnicity (Swartwout, Garnaat, Myszka, Fletcher, & Dennis, 2010). Lower socioeconomic opportunity also raises risk for issues such as maternal diabetes and environmental toxins, which are in turn associated with increased risk of the development of spina bifida (Canfield et al., 2009; Padmanabhan, 2006).

CNS abnormalities in SBM. The most characteristic abnormality is the Chiari II malformation, which occurs as a result of a smaller posterior fossa that is also distorted in appearance (Barkovich, 2005; McLone & Dias, 2003). Hydrocephalus (Del Bigio, 2004) and difficulties due to shunt malfunction and revision are also common in SBM. Volumetric changes in the cerebellum have been noted (Dennis et al., 2004; Salman, Blaser, Sharpe, & Dennis, 2006), including both increases and reductions in gray matter depending on region relative to controls (Juranek, Dennis, Cirino, El-Messidi, & Fletcher, 2010). Callosal abnormalities including agenesis or hypoplasia (thinning) are common in children with SBM as a result of hydrocephalus (Fletcher et al., 1996; Hannay, 2000); a recent study of 193 children with SBM found that only 4.1% of the children had a normal corpus callosum (Hannay, Dennis, Kramer, Blaser, & Fletcher, 2009). Most areas of the corpus callosum are affected, particularly rostral, posterior, and splenial portions (Barkovich, 2005; Hannay et al., 2009).

Children with SBM have a reduction in total cerebral white matter relative to controls, but without a difference in total cerebral gray matter (Juranek et al., 2008). In

addition to overall volumes, thinning of the posterior cortex has been noted (Dennis et al., 1981; Juranek et al., 2008; Juranek & Salman, 2010), first discovered using pneumoencephalography and computed tomography scans and more recently with surface-based analyses from MRI scans. However, contrary to normal development, an increase in frontal cortical thickness is reported children with SBM (Juranek et al., 2008; Juranek & Salman, 2010).

Cognitive and behavioral deficits in SBM. At a broad level, children with SBM have higher verbal abilities (Verbal IQ) than perceptual and motor skills (Performance IQ) (Dennis et al., 1981; Fletcher et al., 1992, 1996; Wills, 1993). Features of a nonverbal learning disability, which is broadly characterized by poor visual-perceptual-organizational, psychomotor coordination, and tactile-perception skills (Harnadek & Rourke, 1994), are also common in children with SBM (Yeates, Loss, Colvin, & Enrile, 2003). While the above pattern may be heuristically useful, it is likely an overgeneralization and may mask more subtle distinctions relevant for understanding brain behavior relationships in SBM.

A more specific model has been proposed by Dennis et al. (2006) and is discussed further in Dennis and Barnes (2010). In brief, this model suggests that the pattern of primary and secondary CNS insults noted above cause three core cognitive and behavioral deficits in: (a) movement (Colvin, Yeates, Enrile, & Coury, 2003; Dennis et al., 2004; Dennis, Fletcher, Rogers, Hetherington, & Francis, 2002; Edelstein et al. 2004; Hetherington & Dennis, 1999; Salman et al., 2005); (b) timing (Dennis & Barnes, 2010; Fletcher et al. 1996); and (c) attention orienting (Burmeister et al., 2005; Dennis et al., 2005a, 2005b). The modal pattern of cognitive functioning for individuals with SBM involves strengths in associative processing (the ability to activate or categorize information) and weaknesses in

assembled processing (the ability to assemble and integrate information). These strengths and weaknesses cut across broad cognitive functions and conversely can also manifest within a given traditional domain. For example, functions that rely on associative processing include motor adaptation, implicit memory, language stipulation, reading decoding, exact calculations, and behavior activation and are often intact in SBM. Assembled processing is utilized in online control (Brewer, Fletcher, Hiscock, & Davidson, 2001; Fletcher et al., 1996), perceptual relations, explicit memory (Scott et al., 1998; Yeates, Enrile, Loss, Blumenstein, & Delis, 1995), language construction (Barnes & Dennis, 1998; Dennis, Jacennik, & Barnes, 1994), reading comprehension (Barnes & Dennis, 1998; Barnes, Faulkner, & Dennis, 2001), math algorithms (Barnes et al., 2006), and behavior regulation, all of which may be impaired in SBM. This modal cognitive pattern increases in flatness in the context of adverse environmental factors and severity of CNS insults. The goal of the present study is to evaluate visual perceptual skill within the framework set forth by Dennis et al. (2006); specifically, categorical visual processing would be considered an associative skill, and coordinate visual processing would be considered an assembled skill.

Visual perceptual processes. Visual perception is an important process used from a very early age to learn and organize our surroundings. Additionally, it is helpful in distinguishing objects from one another and informing visually guided movements such as pointing, grabbing objects, and driving (Kosslyn, Chabris, Marsolek, & Koenig, 1992). Visual perception and visuospatial abilities are also involved in the development of basic numerical skills (Geary, 1993; Lonnemann, Krinzinger, Knops, & Willmes, 2008). For the current study, the term visual perception will be operationalized as identifying and discriminating visuospatial distances between objects.

A common way that cognitive neuroscientists conceptualize these functions is by how they are organized or represented in neural structure. In this regard, there appears to be both a ventral and a dorsal visual pathway; both of these pathways begin in the striate but terminate in the inferior temporal cortex and the posterior parietal cortex, respectively (Carlson, 2010). Functions such as visual memory, object recognition, face recognition, and form perception are maintained by the ventral visual pathway. Conversely, functions including spatial attention, visuomotor integration, mental rotation, and motion perception utilize the dorsal visual pathway (Creem & Proffitt, 2001; Klaver, Marcar, & Martin, 2011). This approach to categorizing visual perceptual functions is common and useful, though is not the only method to consider ways in which visual perceptual function associates with brain structure (or function). For example, a hemispheric approach has also been taken to conceptualize how visual perceptual functions are represented in the brain. Under either approach, it is often difficult to assign commonly used clinical tasks exclusively to one pathway (dorsal vs. ventral) or one hemisphere (right vs. left).

Within the neuropsychological literature, a large number of tasks have been used to assess visual perception. While such measures of visual perception are informative clinically, their specific relationship to hemispheric specialization (or to “dorsal” versus “ventral” specialization) in visual perception is not always clear. Alternative measures, which are designed specifically to discriminate between different visual perceptual functions in visual perception, can be helpful in this regard. This is particularly relevant in populations whose pattern of neurodevelopment may affect certain areas of visual perception relative to others. Therefore, the present study takes a more experimental approach toward the assessment of visual perception.

Categorical/coordinate visual perception task. The Categorical-Coordinate task (as used in Hellige & Michimata, 1989) was developed under the hypothesis set forth by Kosslyn (1987) that categorization is more closely associated with the left hemisphere, and metric or coordinate processing is associated with the right hemisphere. This hypothesis has been supported through several studies (Amorapanth, Widick, & Chatterjee, 2010; Baciu et al., 1999; Hellige & Michimata, 1989; Kosslyn et al., 1989; Laeng, 1994; Trojano et al., 2002), and this hemispheric specialization has even been found in children as young as five years of age (Koenig, Reiss, & Kosslyn, 1990).

Categorical visual perception requires the creation of classifications for spatial relations such as up/down or left/right, and is important for accurately localizing objects in various spatial classifications. Categorical visual perception may also be associated with the ventral visual pathway and neurons with small non-overlapping receptive fields (Haxby et al., 1991; Kosslyn et al., 1992). Functional imaging studies find the categorical task to be related to activity in the left angular gyrus (Baciu et al., 1999), the left superior parietal lobule (Trojano et al., 2002), the left inferior frontal gyrus, left supramarginal gyrus, left angular gyrus, and superior temporal gyrus (Amorapanth et al., 2010).

On the other hand, coordinate visual perception involves discriminating specific distances between objects, allowing individuals to navigate properly and accurately reach for various items. The posterior parietal lobes are particularly involved in coordinate visual perception (Kosslyn, Thompson, Gitelman, & Alpert, 1998; Laeng, 1994) including the dorsal visual pathway and neurons with large overlapping receptive fields (Haxby et al., 1991; Kosslyn et al., 1992). Functional imaging studies suggest a relation between coordinate visual perception and activity in the right superior parietal lobe (Kosslyn et al.,

1998; Trojano et al., 2002), as well as the right superior temporal gyrus, right supramarginal gyrus, right angular gyrus, and right middle temporal gyrus (Amorapanth et al., 2010; Baciu et al., 1999).

Advantages of structural indices. While the studies reviewed above focus on brain activation during visual perception tasks, future research may benefit from structural indices of brain integrity to more comprehensively address the role of specific regions of interest. Key structural indices worth investigating include gray matter and white matter volume, as well as cortical thickness which represents the average shortest distance between the pial surface and the white matter boundary. These indices are particularly important to investigate in the context on SBM. Cortical thickness is a variable of interest due to past research indicating a thinning of the posterior cortex (Dennis et al., 1981; Juranek et al., 2008; Juranek & Salman, 2010) and the association of thinning to visual perception (Dennis et al., 1981; Fletcher et al., 1996; Lehmann et al., 2011). Gray matter volume is less likely to be reduced in SBM relative to controls at an overall level (Juranek et al., 2008), but may show more specific changes. Thus replication in this population would help to support the existing literature by focusing on specific regions of interest. White matter volume, on the other hand, is particularly vulnerable in children with SBM. Specifically, white matter changes are common in hydrocephalus, with periventricular white matter experiencing the majority of damage from enlarged ventricles (Del Bigio, 2010; Del Bigio, Wilson, & Enno, 2003), which also stretches the corpus callosum and can lead to atrophy (Del Bigio, 2004). In addition, white matter changes have been associated with visual perceptual difficulties (Hoeft et al., 2007; Holzapfel, Barnea-Goraly, Eckert, Kessler, & Reiss, 2006) and nonverbal learning disabilities (Rourke, 1995). Together, these three structural indices can

provide a comprehensive structural look at a particular region of interest. Based on activation studies, relationships to the categorical-coordinate task would be expected in specific areas including the angular gyrus, superior parietal lobule, and middle temporal gyrus. However, there are no known studies to investigate these relationships in children with SBM, who have characteristic patterns of both cognitive function and brain structure.

Visual perception performance in SBM. Children with SBM have weaknesses relative to controls on tasks of visual-motor integration, drawing, spatial learning, and visuospatial ability (Andersson et al., 2006; Dennis et al., 2002; Jansen-Osmann, Wiedenbauer, & Heil, 2008; Sandler, Macias, & Brown, 1993; Wiedenbauer & Jansen-Osmann, 2006; Wills, Holmbeck, Dillon, & McLone, 1990). However, many of these studies used clinical tasks and had small sample sizes that are worth expanding. Relevant to the present study, Dennis et al. (2002) found that relative to their own performance, children with SBM have better performance on object-based visual perception tasks, such as object and face recognition, relative to action-based visual perception tasks, such as figure-ground perception, visual navigation, and tracking to moving objects. In this regard, both the categorical and coordinate tasks can be construed as object-based assessments, in that they both involve detecting spatial relations relative to an object independent from the viewer.

Structural correlates of SBM relevant to visual perception. The previously mentioned thinning of the posterior cortex seen in children with SBM has been suggested to impact visual perception (Dennis et al., 1981; Fletcher et al., 1996), though no known study has directly related structural brain indices to behavioral visual perceptual performance in SBM. Dennis et al. (2002) investigated visual perception behavior in SBM thoroughly; however, no brain variables were examined. Previous research has also related IQ to

neurological variables of interest such as hydrocephalus, shunt treatment, and the pattern of cortical thinning (Dennis et al., 1981). Additionally, Fletcher et al. (1996) examined the corpus callosum/whole brain ratio, lateral ventricle/hemisphere ratio, and internal capsule/hemisphere ratio to several verbal, nonverbal, motor, and executive functions. Therefore the present study aims to fill this gap in the research by directly relating visual perception to structural brain indices.

Evidence for the impact of cortical thinning on visual perception has been observed in research with adults with Posterior Cortical Atrophy (PCA), which is marked by a progressive and selective decline in visual processing and is associated with tissue loss in the parietal, occipital, and temporal-occipital cortical regions (Benson, Davis, & Snyder, 1988). An analysis conducted by Lehmann et al. (2011) found that the thinning that occurs in the occipital and superior parietal regions is associated with observed space perception deficits, while thinning in the inferior temporal regions is associated with impairments in object perception. Taken together, these findings exemplify the relationships among visual perceptual and spatial difficulties and posterior cortex. They also highlight the vulnerable nature of the posterior cortex in SBM and the need to further understand visual perceptual function in this population.

Hannay (2000) proposed that visual motor integration may be negatively impacted by agenesis and hypoplasia of the corpus callosum in SBM. This is relevant in that many children with SBM have agenesis or hypoplasia of the corpus callosum (Fletcher et al., 1996; Hannay, 2000), with particular abnormalities in the splenium and posterior body (Barkovich, 2005; Hannay et al., 2009). Given that the inferior temporal lobe and posterior parietal lobe are highly involved during visual perception, and fibers from one hemisphere

to its homologous representation contralaterally pass through the splenium and posterior body (Hofer & Frahm, 2006), this hypothesis is plausible, but has not been directly evaluated with regard to visual perception in children with SBM.

Other factors relevant to visual perception in SBM. Hydrocephalus has been implicated because the lateral ventricles are in close proximity to the posterior visual pathways (Andersson et al., 2006; Fletcher et al., 1992). Therefore it is necessary to consider the impact of hydrocephalus when investigating visual perception performance in SBM. Researchers have also investigated the impact of cognitive and behavioral variables (such as those considered to be core deficits in SBM) on tasks involving visual perception. For example, motor functioning is a core deficit proposed in the Dennis et al. (2006) model, but studies have indicated that children with SBM had difficulty on visual tasks that require substantial motor control (e.g., Beery Visual-Motor Integration), but also on visual tasks that do not (e.g., Recognition-Discrimination Test and Judgment of Line Orientation Test) (Fletcher et al., 1992). To the extent that the categorical and coordinate visual perception task requires more elemental processes, it is important to understand the impact of such components, including basic motor speed as well as basic response time.

The present study. Evaluation of visual perception in SBM can be expected to extend existing literature in several ways. First, utilizing the framework proposed by Dennis et al. (2006) allows for a direct test of its impact on visual perceptual skills by dissociating assembled and associative components within a single task. Second, the framework more broadly can provide a template for examining other potential dichotomies within traditional cognitive domains. Third, understanding visual perception within SBM in this manner also allows for comparison to other neurodevelopmental populations with significant visual

perceptual difficulties (e.g., Williams Syndrome; Wang, Doherty, Rourke, & Bellugi, 1995). Fourth, the current research is designed to investigate the impact of cortical thinning on visual perception in SBM, which will also allow us to gain a better understanding as to the pattern of thinning in SBM. Previous research has demonstrated that cortical thinning occurs in the posterior brain regions (Juranek et al., 2008); however, to date no study has informed us as to the specific structures that experience cortical thinning in SBM or the lateralization of cortical thinning, all while utilizing large sample sizes. Lastly, understanding visual perception within SBM can be directly relevant for daily functioning of children with SBM. Impaired visual perception has implications for any task that uses spatial distances to guide actions such as driving, using hazardous objects (e.g., knives), reaching for objects, mathematical performance, and recreational activities. Thorough understanding of visual perception in children and its neural and cognitive concomitants can reveal mechanisms about how they interact, which might in turn inform interventions and accommodations that in turn will help to enhance the quality and safety of these children's lives.

Hypotheses. Based on the previous review, a number of hypotheses were generated regarding visual perception in SBM. Hypotheses 1 and 2 concern group differences between typically developing children and those with SBM, whereas Hypotheses 3 and 4 concern differences and relationships within children with SBM. Specifically:

1. There will be a behavioral difference between groups such that children with SBM will perform below the level of controls on visual perception tasks, consistent with previous work (Dennis et al., 2002; Sandler et al., 1993; Wills et al., 1990). However, within the group of children with SBM, performance is

expected to be better on the categorical visual perception task than the coordinate visual perception task. In other words, a group by task interaction is expected.

2. Compared to controls, children with SBM are hypothesized to show changes in cortical thickness, gray matter volume, and white matter volume in several specific posterior regions of interest including: inferior parietal cortex, the superior parietal cortex, and superior and middle temporal gyri, as evidenced by previous studies which found these areas to be involved in categorical and/or coordinate visual perception. There is a hemispheric specialization for all regions of interest, such that left cortical areas are correlated with categorical performance and right cortical areas are correlated with coordinate performance (Amorapanth et al., 2010; Baciu et al., 1999; Hellige & Michimata, 1989; Kosslyn et al., 1989; Trojano et al., 2002). Taken together, it is anticipated that children with SBM will show cortical changes in both the left and right cortical regions of interest compared to controls. Callosal differences between children with SBM and controls are well-established, so although we expect more abnormalities in the former group, these are not explicitly hypothesized.
3. Children with SBM will be divided into groups based on the qualitative severity of hypoplasia in the splenium and posterior body. Given that fibers involved in visual perception travel through the splenium and posterior body of the corpus callosum, which are particularly abnormal in SBM (Barkovich, 2005; Hannay et al., 2009), it is hypothesized that children with SBM with more severe hypoplasia will perform worse on both categorical and coordinate visual perception tasks than those with less severe hypoplasia. This hypothesis will also be evaluated

quantitatively; specifically, volumes of the posterior body and splenium will be correlated with visual perception performance in SBM, and volumes of more anterior portions of the corpus callosum will not.

4. Previous studies have suggested a relation between decreased visual perception and cortical thinning in the posterior cortex in children with SBM (Dennis et al., 1981; Fletcher et al., 1996), as well as hemispheric specialization of the categorical (left) and coordinate (right) task (Amorapanth et al., 2010; Baciu et al., 1999; Trojano et al., 2002). Therefore, we expect that performance on categorical visual perception in children with SBM will be correlated with posterior cortical changes (in cortical thickness, gray matter volume, white matter volumes) in the regions of interest in the left hemisphere, whereas coordinate visual perception will be correlated with cortical changes in the regions of interest in the right hemisphere.

For between-group Hypotheses (1 and 2), we consider important demographic and medical covariates when examining performance specific to children with SBM in order to further understand the factors and mechanisms of visual perception. For example, given that lower SES has been associated with lower rates of cognitive and language growth, as well as lower verbal performance (Lomax-Bream et al., 2007; Swartwout et al., 2010), SES will likely be correlated with visual perception performance. Age will also be considered as a covariate due to its influence on brain development. Previous literature has indicated that cortical thickness and gray matter volume decrease with age (Sowell et al., 2004), while white matter volume increases (Paus et al., 2001; Wilke, Krägeloh-Mann, & Holland, 2007). Additional factors include simple reaction time and manual dexterity, which further help

elucidate the specific differences between groups on visual perception. For Hypotheses considering only children with SBM (3 and 4), lesion level will also be considered as a covariate since upper level lesions are usually associated with more significant cognitive difficulties (Fletcher et al., 2005). On the other hand, simple reaction time and manual dexterity are more relevant to analyses that involve the visual perceptual task (Hypotheses 1, 3, and 4), rather than those that focus on structural differences (Hypothesis 2). Lastly, although the present study does not have any specific hypotheses regarding the relationship between cortical changes and callosal abnormalities, the interaction of these variables will be included in the analyses to determine whether these factors operate independently or synergistically in their impact on visual perception performance. In all, we expect that the combination of medical, environmental, imaging, and basic cognitive processing variables will substantially explain variability in visual perceptual task performance in children with SBM.

Methods

Participants. The sample was comprised of 81 children with SBM and 28 controls (mean age = 13.16, SD = 2.81), ranging in age from 7.87 to 17.99 years. This subset of participants came from a larger sample that was recruited from clinics in Houston and Toronto and consisted of those who had completed the Categorical/Coordinate visual perception task. English was the primary language of all participants. All of the participants in the SBM group were diagnosed with spina bifida myelomeningocele at birth and had shunt-treated hydrocephalus. Participants in the control group were age-matched to the SBM group. Exclusion criteria for controls included diagnosed learning disabilities, psychiatric disorders, or central nervous system disorders. Additionally, participants were excluded for

having IQ scores below 70 on the Verbal Reasoning and the Abstract/Visual Reasoning of the Stanford-Binet Test of Intelligence (Thorndike, Hagen, & Sattler, 1986) or Verbal Reasoning scores above 120. Informed consent to participate was obtained from the guardians of all participants in accordance with the ethics board. Participants were given the following measures as part of a larger battery aimed to determine variability in functional deficits of individuals with SBM. Of the participants that completed the visual perception task, 60 children with SBM and 22 controls received an MRI. The cortical thickness, gray matter volume, white matter volume, and corpus callosum volume data was available for 55 children with SBM and 19 controls. Table 1 provides additional information regarding demographics, and Table 2 details SBM characteristics.

Measures. In the Categorical/Coordinate visual perception task, children were instructed to pretend that they were an umpire in baseball game. For the categorical task, participants indicated by button press whether the "ball" (a dot) fell above or below the "bat" (a line) by using the left blue button for above and the right red button for below. In the (precise) coordinate task, participants determined via button press whether the ball was closer or further than 3mm than the bat by using the left blue button for farther and the right red button for closer. For both conditions, the children were given practice trials and then proceed to complete four blocks of 48 trials. Before each trial, a signal (a six-pointed star) appeared for 400 ms, followed by a blank screen for 500 ms. Then a fixation point appeared for 400 ms immediately after which the baseball appeared in one of 12 possible locations for 150 ms. The primary variables of interest are accuracy and reaction time. Variations of this task have been used in previous research as an assessment of visual perception (Hellige & Michimata, 1989; Koenig et al.,1990; Kosslyn et al., 1992, 1998), and the current version is

most similar to that of Koenig et al. (1990). The conditions described previously (categorical and coordinate) were two of 4 possible tasks the participants completed. The other two (structured and unstructured) were not used so as to keep the task as similar to previous studies as possible. In both of these alternative tasks, the participant was to indicate whether the ball was "in" or "out" based on a previously shown distance, but was not given a specific unit of measurement with which to make this decision as in the precise coordinate task. In the structured condition, there was a yellow color gradient displayed above and below the line.

Simple reaction time was assessed by asking participants to press a button using their preferred hand any time a downward pointing arrow appeared in the center of the screen. Time between the stimuli randomly varied over the trials. The primary variable of interest is average reaction time measured in milliseconds.

The Purdue Pegboard Test is a measure of manual dexterity (Purdue Research Foundation, 1948). During this task, participants are asked to place pegs in holes first using their preferred hand, then their other hand, and lastly both hands simultaneously. Each condition lasts 30 seconds. The reliability ranges from <.60 to .79 for single-trial administrations, but is >.80 for three-trial administration (Buddenberg & Davis, 2000), potentially as a result of practice effects. It has been shown to relate to psychomotor functions and thus will be used to assess the core deficit of movement. The primary variable of interest is the z-score obtained for both hands. Since 32% of the children with SBM were not right handed, this variable was chosen to eliminate the issue of handedness.

SES was determined using the Hollingshead 4-Factor Scale (Hollingshead, 1975). To determine SES, parent education and occupation status was obtained via self-report for each

parent and were then weighted to obtain one score (8-66), with higher score designating higher SES. A composite score was then calculated to determine SES based of the reports of both parents. For participants with only a single parent, the weighted score for the parent was used.

Qualitative evaluation of the corpus callosum was done by a radiologist with expertise with SBM. If a corpus callosum was identified as abnormal, the expert then indicated for the rostrum, genu, body, and splenium whether it was present, absent, or hypoplastic. If any of these areas were hypoplastic, severity (mild, moderate, or severe) was then recorded. Quantitative assessment of corpus callosum volume is described below.

Imaging acquisition. A Philips 3T scanner with SENSE (Sensitivity Encoding) technology was used to obtain high-resolution brain MR images obtained in the coronal plane. In order to cover the whole brain, a three-dimensional T1-weighted sequence was implemented, following a standard scout sequence. This particular T1 image was chosen for its contrast between gray matter and white matter, which is optimal when examining cortical thickness, The following lists the T1-weighted 3D turbo fast echo sequence acquisition parameters: TR/TE=6.5–6.7/3.04–3.14ms; flip angle=8°; square field-of-view=24cm; matrix=256×256; slice thickness =1.5mm; in-plane pixel dimensions (x,y)=0.94, 0.94; number of excitations (NEX)=2.

Imaging analyses. All analyses conducted were blind to age, gender, and diagnosis. Before completing morphometric analyses, image quality of the T1-weighted images was assessed. Freesurfer v4.0.5 software (www.surfer.nmr.mgh.harvard.edu) was utilized on a 64-bit Linux computer, to complete a fully-automated program which skull-stripped (removed any non-brain tissue) and divided each brain into 3 categories of voxels: white

matter, gray matter, and CSF (Dale, Fischl, & Sereno, 1999; Dale & Sereno, 1993). To determine these three types of voxels the program first used intensity values (i.e., the brightness of each voxel), followed by probabilistic information for where each type of nuclei should be located. Using Freesurfer's Tkmedit viewer, the accuracy of the voxel categories was visually examined. Occasionally the computer program cannot pick up subtle differences in voxel categories that the human eye can. Thus some manual edits were made by an expert (JJ) to accurately outline the segmentation boundaries. This was to ensure that difficult boundaries to determine (e.g., deep gray matter, hippocampus, and amygdala) were appropriately outlined using the expert's knowledge of brain anatomy. Again using Freesurfer, an automated cortical reconstruction technique was performed to create a geometric description of the gray matter, white matter, and CSF boundaries of the neocortical mantle (i.e., neocortex). The geometric description was comprised of a regular tessellation (a pattern of identical shapes) of the cortical surface consisting of ~150,000 equilateral triangles (known as vertices) in each hemisphere. This process allows us to obtain sub-millimeter resolution for the cortical thickness values as opposed to a 1mm resolution. Values of cortical thickness were obtained within Freesurfer on a vertex-by-vertex basis by calculating the average shortest distance between the pial surface and the white matter boundary (Fischl & Dale, 2000).

Within each hemisphere, 32 cortical parcellations (sections) of the neocortex were automatically identified and labeled using the Desikan atlas of gyral-based definitions included within Freesurfer's automatic cortical parcellation procedure (Desikan et al., 2006). Three morphometric variables (cortical thickness, neocortical volume, and surface area) were examined in each parcellation unit. Each variable was averaged across all vertices

within each parcellation for each subject, which produced three separate matrices of 32 average measurements per hemisphere per subject per morphometric variable. For the current study, the focus is on cortical thickness, gray matter volume, and white matter volume for regions of interest that were selected based on the hypotheses and metrics available. For gray and white matter volume, uncorrected values refer to the raw measures without considering the volume of the rest of the brain. Corrected values are the raw measures divided by the whole brain volume (not including the ventricles). The present study will focus on uncorrected values in an attempt to reveal more noticeable group differences; however, corrected values will also be explored in order to determine the robustness of the results. This process of reporting both uncorrected and corrected gray and white matter volumes has been done in studies involving typically developing children, as well as children with developmental disorders (Sowell et al., 2003; Sparks et al., 2002; Wilke et al., 2007).

Analysis approach. The primary types of analyses utilized were forms of ANOVA. Assumptions of ANOVA (independence of cases, normal distribution, and homogeneity of variance) were tested and necessary adjustments for violations to these assumptions were made. One individual's Purdue Pegboard score (outlier), four individuals' visual perception scores (reliability), and one individual's simple reaction time (reliability) were not included for analyses in which those variables were utilized.

Covariates considered included age, SES, manual dexterity, simple reaction time, and lesion level. A covariate was included if there was a significant correlation between the variable and the visual perception outcome measures for both groups together or for SBM only. The model first included group as the independent variable, the covariates, and the

interaction between group and each of the covariates. If an interaction term was not significant, it was excluded from the model. Then, the model was run again using just group and the covariates. Any covariates that were not significant were then excluded from the model. Lastly, lesion level was included by dividing the participants into upper versus lower lesion, resulting in three-group analyses. It should be noted that manual dexterity and simple reaction time were not covariates of interest for Hypothesis 2 and thus were not considered. Additionally, SES was not correlated to white matter volume of the corpus callosum or imaging variables (cortical thickness, gray matter volume, and white matter volume) for children with SBM. Thus, SES was excluded from analyses for Hypotheses 3 and 4.

Some of the later analyses (Hypotheses 3 and 4, and follow-up) have a smaller sample size which increases the chance of Type 1 error. However, due to the uniqueness of these analyses within SBM, they remain of importance to investigate. Further, Cohen's *d* effect sizes (the difference between the group means divided by the pooled standard deviation) for the following analyses are included in Tables 1, 3 and 4.

Results

Hypothesis 1. Repeated measures AN(C)OVA was used to determine differences between children with SBM and controls on the categorical and coordinate visual perception tasks. Group was the between-subjects factor, and task was the within-subjects factor. Table 3 displays the means and standard deviations between the groups for visual perception performance.

Accuracy. The interaction between type of task and group was not significant, indicating that group differences on visual perception accuracy did not vary according to task type, $F(1, 107) = 2.54$, $p = 0.11$. There was however a significant effect for group, $F(1,$

107) = 11.10, $p = 0.001$, such that children with SBM performed below the level of controls across tasks. There was also a significant difference between performance on the two tasks, $F(1, 107) = 103.78$, $p < 0.0001$, such that across groups, performance was poorer on the coordinate relative to the categorical task.

Once age and manual dexterity were added as covariates, there was no longer a significant group, $F(1, 100) = 0.13$, $p = 0.72$, or task, $F(1, 100) = 0.29$, $p = 0.59$ effect. When lesion level was also included, there was no change from the model with covariates. These results indicate that age, $F(1, 100) = 41.46$, $p < 0.0001$, and manual dexterity, $F(1, 100) = 9.96$, $p = 0.002$, were particularly relevant for differences between groups.

Reaction time. The interaction between type of task and group was significant, $F(1, 107) = 12.55$, $p = 0.0006$, such that controls were significantly slower on the coordinate task compared to children with SBM, but there were no group differences on the categorical task (see Figure 1). There was also a significant effect for task, $F(1, 107) = 16.68$, $p < 0.0001$, with children in both groups having slower reaction times on the coordinate task relative to the coordinate. Given the pattern of the interaction, it is not surprising that there was no significant difference between groups for visual perception reaction time, $F(1, 107) = 0.61$, $p = 0.44$.

Once age and reaction time were added as covariates, there was still a significant interaction between group and task, $F(1, 104) = 10.88$, $p = 0.001$, such that controls were significantly slower on the coordinate task compared to children with SBM, but there were no group differences on the categorical task.. However, there was no longer a significant task effect, $F(1, 104) = 0.22$, $p = 0.64$. These results indicate that age, $F(1, 104) = 6.40$, $p = 0.01$ and reaction time, $F(1, 104) = 5.30$, $p = 0.02$, were particularly relevant for differences

between tasks. When lesion level was also included, there was no change from the model with covariates, but the interaction was slightly altered, $F(2, 103) = 8.85$, $p = 0.0003$. On the categorical task, there were no significant differences between any of the groups. On the coordinate task, SBM children with upper lesions were faster than SBM children with lower lesions, who in turn were faster than controls. Significant differences occurred between the controls and SBM children with upper lesions, as well as controls and SBM children with lower lesions.

Hypothesis 2. Repeated measures AN(C)OVA was used to analyze the differences in cortical thickness and uncorrected gray matter and white matter volumes between groups. The four primary regions of interest corresponded with Desikan et al. (2006) labels: inferior parietal cortex (IPC), superior parietal cortex (SPC), middle temporal gyrus (MTG), and superior temporal gyrus (STG). Across areas (4 levels: IPC, SPC, MTG, STG), hemispheres (2 levels: left, right), metric (3 levels: cortical thickness, gray matter volume, white matter volume), and group (2 levels: SBM and control), the overall 4-way interaction was significant, $F(6, 426) = 4.28$, $p = 0.0003$. Follow up analyses within metric yielded significant 3-way interactions of area, hemisphere, and group for cortical thickness, $F(3, 213) = 6.23$, $p = 0.0004$, gray matter volume, $F(3, 213) = 4.73$, $p = 0.003$, and white matter volume, $F(3, 213) = 3.95$, $p = 0.009$. Therefore, follow up analyses focused within both metric and area, which still allowed for the evaluation of group by hemisphere effects, which were of primary interest.

Cortical thickness. Means by group and hemisphere appear in Table 4 and Figure 2. For both MTG and STG, there were significant group by hemisphere interactions (MTG, $F(1, 71) = 6.90$, $p = .01$; STG, $F(1, 71) = 18.46$, $p < 0.0001$). For MTG, children with SBM

had less cortical thickness than controls on the right hemisphere and no difference on the left hemisphere. For STG, children with SBM had less cortical thickness than controls for both hemispheres, but the difference was greater on the right hemisphere than the left hemisphere. In addition, the overall group effect was significant for both STG, $F(1, 71) = 39.42$, $p < 0.0001$, and MTG, $F(1, 71) = 9.13$, $p = 0.004$; the main effect of hemisphere was not significant for either of these regions. For IPC, there were no significant interactions of group by hemisphere, $p > 0.05$, but there were main effects for both hemisphere, $F(1, 71) = 5.24$, $p = 0.03$, and group, $F(1, 71) = 8.88$, $p = 0.004$, with cortical thickness values greater on the left hemisphere and for controls. For SPC, there was no significant interaction of group by hemisphere, $p > 0.05$, and no effect for group, $F(1, 71) = 1.89$, $p = 0.17$, but there was a main effect for hemisphere, $F(1, 71) = 4.54$, $p = 0.04$, with cortical thickness values greater on the left hemisphere relative to the right.

Adding age and lesion level as covariates did not change the results for MTG and STG. For both IPC and SPC, when age was included into the model, there was no longer a significant hemisphere effect (IPC, $F(1, 70) = 3.09$, $p = 0.08$; SPC, $F(1, 70) = 0.11$, $p = 0.74$). Furthermore, when lesion level was added to the model with age for IPC, a significant interaction between group and hemisphere appeared, $F(2, 69) = 5.85$, $p = 0.005$. For the left hemisphere, controls had significantly greater cortical thickness than SBM children with lower lesions. On the right hemisphere, controls had significantly greater cortical thickness than SBM children with lower lesions and controls had significantly greater cortical thickness than SBM children with upper lesions.

Gray matter volume. Means by group and hemisphere appear in Table 4 and Figure 3. For STG, there was a significant group by hemisphere interaction, $F(1, 71) = 17.32$, $p <$

0.0001, in which children with SBM had less gray matter volume than controls for both hemispheres, but the difference was greater on the right hemisphere than the left hemisphere. Additionally, the overall group, $F(1, 71) = 39.98$, $p < 0.0001$, and hemisphere, $F(1, 71) = 17.42$, $p < 0.0001$, effects were significant, with higher values for controls and for the left hemisphere. For both IPC and MTG, there were no significant interactions of group by hemisphere, $p > 0.05$, but the main effects for both group (IPC, $F(1, 72) = 43.30$, $p < 0.0001$; MTG, $F(1, 71) = 16.40$, $p = 0.0001$) and hemisphere (IPC, $F(1, 72) = 68.57$, $p < 0.0001$; MTG, $F(1, 71) = 7.75$, $p = 0.007$) were significant; gray matter values were greater on the right hemisphere relative to the left, and for controls relative to SBM. For SPC, there were no effects for group, $F(1, 72) = 0.00$, $p = 0.98$, hemisphere, $F(1, 72) = 0.03$, $p = 0.864$, or their interaction, $p > 0.05$.

Adding age and lesion level as covariates did not change the results for IPC and SPC. For both MTG and STG, when age and SES were included into the model, there was no longer a significant hemisphere effect (MTG, $F(1, 68) = 0.97$, $p = 0.33$; STG, $F(1, 68) = 1.22$, $p = 0.27$). When lesion level was also included, there was no change from the model with covariates.

White matter volume. Means by group and hemisphere appear in Table 4 and Figure 4. For STG, there was a significant group by hemisphere interaction, $F(1, 71) = 14.94$, $p = 0.0002$, in which children with SBM had lower white matter volumes than controls for both hemispheres, but the difference was greater on the right hemisphere than the left hemisphere. Additionally, the overall group, $F(1, 71) = 35.02$, $p < 0.0001$, and hemisphere effects, $F(1, 71) = 18.50$, $p < 0.0001$, were significant, with higher volumes for controls, and for the left hemisphere. For both IPC and MTG, there were no significant interactions of

group by hemisphere, $p > 0.05$, but the main effects for both group (IPC, $F(1, 72) = 37.37$, $p < 0.0001$; MTG, $F(1, 71) = 17.92$, $p < 0.0001$) and hemisphere (IPC, $F(1, 72) = 67.88$, $p < 0.0001$; MTG, $F(1, 71) = 7.08$, $p = 0.01$) were significant, with white matter values greater for the right hemisphere and for controls. For SPC, there were no effects for group, $F(1, 72) = 2.12$, $p = 0.15$, hemisphere, $F(1, 72) = 0.02$, $p = 0.88$, or their interaction, $p > 0.05$.

Adding age and lesion level as covariates did not change the results for IPC and SPC. For both MTG and STG, when age (and SES for STG) were included into the model, there was no longer a significant hemisphere effect (MTG, $F(1, 70) = 2.71$, $p = 0.10$; STG, $F(1, 68) = 1.44$, $p = 0.23$). When lesion level was also included, there was no change from the model with covariates.

Summary. Overall, the IPC had a significant group and hemisphere effect across metrics. For group effects, controls had higher values than children with SBM for all metrics. For hemisphere effects, the right hemisphere values were greater for gray and white matter volume, whereas the left hemisphere values were greater for cortical thickness. The SPC only had a significant effect for hemisphere with cortical thickness, which was no longer significant when covariates were included. For the MTG, there was a significant interaction between group and hemisphere for cortical thickness. There was also a significant effect for hemisphere in gray and white matter volumes and a significant effect for group across metrics, such that the right hemisphere had greater values than the left hemisphere and controls had greater values than children with SBM. For the STG, the interaction between group and hemisphere and the effect for group were significant across metrics, such that controls had higher values than children with SBM. Additionally, the effect for hemisphere was significant for gray matter and white matter volumes, with higher

values on the left hemisphere than the right hemisphere. When corrected gray and white matter volumes were used, findings were largely consistent with those that were uncorrected; however, there was no longer an effect for group for gray matter MTG or white matter MTG, and group effect for white matter SPC was now significant.

Hypothesis 3. Repeated measures ANOVA and correlations were obtained to determine the relationship between corpus callosum abnormalities and visual perception performance within children with SBM. Table 5 illustrates the varying numbers of children with SBM who had normal, hypoplastic (three severity levels), or dysgenic corpus callosum splenium or body. The pattern did not lend itself to group comparisons on these qualitative measures, so the following analyses only pertain to the correlations between white matter volume of the corpus callosum and visual perception performance. It should be noted that controls had higher values of white matter volume in all corpus callosum segments compared to children with SBM (all $p < .05$). There were no significant correlations between any of these segments and visual perceptual performance (See Table 6). When the covariates (age and manual dexterity) were added to the model, the correlation between categorical visual perception accuracy and central corpus callosum volume was significant, $r = -0.34$, $p = 0.04$.

Hypothesis 4. Correlations between the metric by area by hemisphere values and the four visual perception variables were obtained for children with SBM. Then covariates (age, manual dexterity, and simple reaction time) were included, and Table 7 displays these partial correlations. Correlations of > 0.30 were considered most relevant, and are likely significant given the current sample size (Maxwell & Delaney, 2004).

Accuracy. For categorical visual perception accuracy, there was a positive correlation with right STG gray matter volume, $r = 0.34$, $p = 0.03$, and white matter volume, $r = 0.31$, $p = 0.04$, as well as a negative correlation with the left STG white matter volume, $r = -0.30$, $p = 0.05$. There were no significant correlations of coordinate visual perceptual accuracy in any region of interest for cortical thickness, gray matter volume, or white matter volume.

When adding age and manual dexterity as covariates, only the left STG white matter volume relation remained in terms of size and direction, but the pattern was more complete in that there were three additional significant relations, including cortical thickness in the left IPC, $r = 0.34$, $p = 0.04$, gray matter volume in the left STG, $r = -0.44$, $p = 0.01$, and white matter volume in the right MTG, $r = -0.38$, $p = 0.02$. However, for coordinate visual perception accuracy, there were only two correlations that were close to significance when covariates were added. These included correlations with left MTG cortical thickness, $r = 0.32$, $p = 0.057$, and the left IPC white matter volume, $r = 0.30$, $p = 0.066$.

When corrected gray and white matter volumes were utilized, some changes were noted for categorical and coordinate accuracy. For categorical without covariates, there was no longer a significant correlation with white matter in the right STG, although the correlation was in the same direction. Additionally, there were new correlations with gray matter volume in the right MTG, $r = -0.30$, $p = 0.05$, and left STG, $r = -0.34$, $p = 0.02$, as well as white matter volume with the right MTG, $r = -0.38$, $p = 0.01$. When covariates were added, all correlations with categorical accuracy remained significant and were in the same direction as the uncorrected values. For coordinate without covariates, all correlations remained not significant. When covariates were added, there was a new correlation with

gray matter volume in the right MTG, r = -0.34, p = 0.04, and white matter volume in the right MTG, r = -0.33, p = 0.04, which were both in the same direction as the not significant correlations with the uncorrected values.

Reaction time. For categorical visual perception reaction time, there was a positive correlation with cortical thickness in the left IPC, r = 0.42, p = 0.01, and the right MTG, r = 0.3, p = 0.05. However, for coordinate visual perception reaction time, there were no significant correlations without the inclusion of covariates. When age and simple reaction time were added as covariates, categorical relations remained in terms of size and direction. For coordinate, one significant correlation was now present; specifically, with cortical thickness in the right MTG, r = 0.32, p = 0.04. When corrected gray and white matter volumes were utilized, there were no observed changes.

Prediction of visual perception performance in SBM. In order to determine the relation between the corpus callosum white matter and other structural indices on visual perception performance, four different models were created for each visual perception variable. Predictors and covariates were chosen based on the findings from the previous hypotheses. First, the interactions between segments of the corpus callosum and other structural indices were investigated to determine if the factors operate independently or synergistically; however, none of these were significant. Thus, the following reports the final models with and without covariates.

For categorical accuracy, the model including gray and white matter volume for the right and left STG, white matter volume for the right MTG, and white matter volume for the middle anterior, central, and middle posterior segments of the corpus callosum was significant, R^2 = 0.35, $F(8, 34) = 2.25$, p =0.05, with no variables being uniquely predictive.

When age and manual dexterity were included, the model was also significant, $R^2 = 0.66$, $F(10, 28) = 5.33$, $p = 0.0002$, with age and manual dexterity being uniquely predictive. For coordinate accuracy, the variables in the model were cortical thickness for the left MTG, white matter volume for the left IPC, and the anterior segment of the corpus callosum; however, the model was not significant, $R^2 = 0.10$, $F(3, 39) = 1.37$, $p = 0.2668$. When age and manual dexterity were included, the model became significant, $R^2 = 0.48$, $F(5, 33) = 6.07$, $p = 0.0004$, with age and manual dexterity being uniquely predictive.

For categorical reaction time, the variables in the model included cortical thickness for the left IPC and right MTG and the anterior and middle anterior segments of the corpus callosum. The model was significant, $R^2 = 0.34$, $F(4, 38) = 4.90$, $p = 0.003$, with the corpus callosum segments being uniquely predictive. When age and simple reaction time were added, the model was also significant, $R^2 = 0.53$, $F(6, 36) = 6.84$, $p < 0.0001$, with age, simple reaction time, cortical thickness of the right MTG, and the segments of the corpus callosum being uniquely predictive. For coordinate reaction time, the model consisting of cortical thickness for the right MTG and the middle anterior and posterior segments of the corpus callosum was not significant, $R^2 = 0.10$, $F(3, 39) = 1.43$, $p = 0.25$. When age and simple reaction time were included, the model remained not significant, $R^2 = 0.15$, $F(5, 37) = 1.34$, $p = 0.27$; however, cortical thickness of the right MTG was uniquely predictive.

Discussion

The goal of the present study was to directly test the Dennis et al. (2006) model within a single domain and understand the impact of cortical changes on visual perception in children with SBM. This study was the first to date that directly evaluated visual perception in relation to imaging variables in children with SBM.

Visual perception differences between groups. Hypothesis 1 was partially supported by the current findings. For accuracy, children with SBM did perform worse than controls, and their performance on coordinate visual perception was in fact poorer than their categorical visual perception performance. However, the controls also performed worse on the coordinate task than the categorical task, resulting in no significant interaction between task and group. These results are consistent with previous work in which children with SBM had poorer performance in assembled processing (Dennis et al., 2006; Dennis & Barnes, 2010; Dennis et al., 2002). Additionally, past studies have found better performance on the categorical task than the coordinate task in typically developing children (Koenig et al., 1990) and adult controls (Hellige & Michimata, 1989; Kosslyn et al., 1998; Michimata, Saneyoshi, Okubo, & Laeng, 2011). However, it should be noted that on the coordinate task, the accuracy of the SBM children was relatively close to 50%, which is of concern given that the task was forced choice. This could merely be the result of poorer performance on the part of the children with SBM, as evidenced by previous research which has found difficulties in assembled processing in SBM (Dennis & Barnes, 2010; Dennis et al., 2006). Additionally, the children with SBM may have had difficulty remembering which button to press since the buttons (spatially located on the left and right) were not intuitive for completing the task (left button is for “farther” and right button is for “closer”). Future research would benefit from investigating as to whether the coordinate accuracy of the children with SBM was due to chance or simply task difficulty. Furthermore, when age and manual dexterity were added as covariates, there was no longer a significant difference between the groups or between the tasks. This finding supports the Dennis et al. (2006)

model which indicates that core deficits (such as movement) moderate the impact of CNS abnormalities on cognitive performance.

For reaction time, there was no difference between children with SBM and controls, but children of both groups responded more slowly on the coordinate visual perception task than the categorical task. There also was a significant interaction, albeit in the opposite direction than anticipated. Controls were faster on the categorical task and slower on the coordinate task when compared to children with SBM. Since both controls and children with SBM had poorer accuracy on the coordinate task than the categorical task, it could be argued that the coordinate task was more difficult. In that case, the controls may have been appropriately slowing down on the coordinate task to be more accurate, while children with SBM were not. Previous research has suggested that reaction times increase with task difficulty in typically developing populations, as evidenced in undergraduate students with varying levels of motivation (Capa, Audiffren, & Ragot, 2008) and young and older adults (McDowd & Craik, 1988). For the coordinate task, accuracy and reaction time were not significantly correlated for controls, $r = 0.32$, $p = 0.1$; however, they were correlated for children with SBM, $r = 0.26$, $p = 0.02$, indicating that for SBM, slower reaction times were associated with increased accuracy. This provides support for the notion that children with SBM's significantly poorer accuracy than controls may be due to their significantly faster reaction time than controls.

An explanation as to why the controls could be taking additional time is that they may be trying to remember the correct button to select for the task. Since the buttons (spatially located on the left and right) were not intuitive to completing the task (left button is for "farther" and right button is for "closer"), controls may have been taking a more

careful approach to remember the instructions. Again this is supported by previous research demonstrating slower reaction times during more difficult tasks (Capa et al., 2008; McDowd & Craik, 1988). Further research should be conducted using other cognitive tasks that require reaction speed to determine whether children with SBM in general do not adjust their speed for more difficult tasks. If this is the case, then interventions could be implemented to help children with SBM slow down during more difficult tasks to improve performance.

Moreover, when lesion level was added to the model, the significant interaction was changed such that on the categorical task, controls were faster than SBM children with lower lesions, who in turn were faster than SBM children with upper lesions. On the coordinate task, SBM children with *upper* lesions were faster than SBM children with lower lesions, who in turn were faster than controls. In the previous interaction, children with SBM were faster on the coordinate task than controls. This could provide more support for the notion that controls appropriately slow down on a more difficult task. Alternatively, it could be that the task was challenging for those with upper level lesions and thus did not put in more effort, which would explain the close to chance accuracy. Either way, this provides support for previous literature that has found upper level lesions are associated with more difficulties than lower level lesions (Fletcher et al., 2005).

Imaging differences between groups. Hypothesis 2 was supported for all regions of interest and all imaging variables (cortical thickness, gray matter volume, and white matter volume), with the exception of the SPC for gray matter and white matter volume. In the case of cortical thickness for the IPC and SPC and gray and white matter volume for the IPC and MTG, children with SBM followed same hemispheric pattern as controls, such that if

controls had greater values in one hemisphere than the other, children with SBM would also have greater values in that hemisphere but with significantly smaller values than the controls. These findings support previous studies which found or suggested posterior cortical changes in children with SBM (Dennis et al., 1989, Fletcher et al., 2006; Juranek et al., 2008; Juranek & Salman, 2010).

However, for cortical thickness of the MTG and STG, in addition to the gray and white matter of the STG, children with SBM had lower values than controls, but did not follow the same hemispheric pattern as the controls. While the controls had greater values in the right hemisphere in these areas relative to the left hemisphere, the children with SBM had greater values in the left hemisphere in these areas relative to the right hemisphere. This finding tells us that these areas are particularly impacted areas in SBM. In a study conducted by Juranek et al. (2008), there were no differences regarding hemispheres when using broad uncorrected regions of interest (Frontal, Parietal, Temporal, Occipital, Cingulate), so the differences between hemispheres in children with SBM for the MTG and STG were unexpected. Thus while previous research indicated smaller values in these areas (except for the frontal) compared to controls (Juranek et al., 2008; Juranek & Salman, 2010), the current study provides an extension of information as to the pattern of cortical changes that occur in SBM with regards to differences between hemispheres, specifically in the MTG and STG. Further research with other regions of interest should be conducted in order to determine if there are other areas that exhibit this hemispheric differentiation in SBM.

The relation between the corpus callosum and visual perception in SBM.

Overall, Hypothesis 3 was not supported. For visual perception reaction time, there were no relationships found with white matter volume of the corpus callosum. For accuracy, there

was only one negative correlation with categorical accuracy and the central portion of the corpus callosum when covariates were included. This is in contrast with previous research. Fletcher et al. (1996) found a pattern of correlations between a corpus callosum/whole brain ratio and performance and nonverbal measures in children with shunted hydrocephalus. Moreover, previous research involving children born preterm has found significant correlations between white matter volume of the corpus callosum (corrected for total brain volume) with IQ, as well as several other neuropsychological measures (Narberhaus et al., 2008; Peterson et al., 2000); however, it should be noted that these previous studies involving children with shunted hydrocephalus and children born preterm utilized broader measures than the present study. Additionally, in a study of healthy adult women, there was a positive correlation between the surface area of the splenium and only one of three visuospatial abilities, in addition to positive correlations between the isthmus and two of the three visuospatial abilities (Hines, Chiu, McAdams, Bentler, & Lipcamon, 1992). Thus, the neurodevelopmental population, age group, corpus callosum metric, and behavioral measure of interest are all potential factors for why there were no significant correlations between the corpus callosum and visual perception in the present study. Therefore it remains inconclusive as to whether white matter volume in different segments of the corpus callosum impacts visual perception in children with SBM to varying degrees. Future research should be conducted with adults, surface area of the corpus callosum, or other cognitive variables to better determine the relationship between the corpus callosum and behavior in SBM.

The relation between imaging variables and visual perception in SBM.

Hypothesis 4 was only marginally supported. Findings varied according to the type of visual perceptual task and dependent variable.

Categorical accuracy. One consistent pattern was a positive relation with the gray and white matter of the right STG and a negative correlation with the gray and white matter of the left STG. While this finding does provide support for the Dennis et al. (2006) model that changes in the CNS are associated with variability in the cognitive phenotype, it does not support previous research showing a specialization for categorical visual perception in the left hemisphere (Amorapanth et al., 2010; Baciu et al., 1999; Hellige & Michimata, 1989; Kosslyn et al., 1989; Trojano et al., 2002). Since the correlations involved the right STG, it is possible that for accuracy a dorsal/ventral visual stream approach is more appropriate, in which the ventral pathway would be more involved in categorical visual perception accuracy (Goodale, 2008; Ikkai, Jerde, & Curtis, 2001; Kravitz, Saleem, Baker, & Mishkin, 2011). However, this finding is of particular interest since gray and white matter of the right STG happens to be one of the areas that exhibited an exceptionally smaller value for children with SBM compared to controls. This could indicate yet another unexpected pattern found in children with SBM. Further research is needed to gain an understanding as to why this area with particular less gray and white matter volume is more important for categorical visual perception accuracy than its higher gray and white matter volume counterpart and whether other brain areas follow this same pattern when utilizing other cognitive measures.

Coordinate accuracy. In contrast to categorical accuracy, there were no clear patterns for coordinate accuracy, and the performance of the children with SBM was near chance. Perhaps the regions of interest of the current study did not include the area(s) of most importance for coordinate visual perception accuracy. Additionally, the regions of interest used from the Desikan et al. (2006) atlas could have been broader than needed to

find a precise area(s) related to coordinate visual perception. Replication of the current study using an atlas such as Destrieux, Fischl, Dale, and Halgren (2010) with more precise brain regions would be advantageous. Specifically, the angular gyrus (which has its own designation in the Destrieux et al. (2010) atlas) would be of particular interest for future research investigating visual perception in children with SBM, as it has been found to be involved in visual perception (Amorapanth et al., 2010; Baciu et al., 1999).

The correlations between cortical thickness and categorical and coordinate accuracy did not support previous research that compared cortical thickness with visual perception in adults with PCA (Lehmann et al., 2011). The present study found an opposite pattern such that categorical perception was associated with the IPC and coordinate perception was associated with the MTG. However, the present study used a different population, age group, and approach, all of which could be explanations for the discrepancy. Westlye, Grydeland, Walhovd, and Fjell (2011) studied the relation between attentional functions and cortical thickness in healthy adults and found an association between executive control and the anterior cingulate cortex, as well as a relation between the frontoparietal regions and alerting. The present study adds to this small literature in demonstrating relations between cortical thickness and behavior.

Reaction time. For visual perception reaction time, there were three significant correlations, all of which involved cortical thickness and were in the unexpected direction. This informs us that greater cortical thickness is associated with slower reaction times in children with SBM. This is a logical finding from a developmental perspective, which indicates that cortical thickness and gray matter decrease with age so as to increase efficiency (Sowell et al., 2004). Additionally, while none of the correlations between white

matter volume and reaction time were significant, the majority were in the expected direction (faster reaction times associated with more white matter volume). During development, synaptic connections are pruned and myelination of the white matter increases so as to provide more efficient connections (Paus et al., 2001; Wilke et al., 2007). The negative (although not significant) correlations with white matter volume indicate that perhaps white matter is more important for faster reaction times, which is supported in several studies looking at white matter microstructure (Konrad, Vucurevic, Musso, Stoeter, & Winterer, 2009; Tuch et al., 2005). Thus, future studies should be conducted looking at fractional anisotropy and mean diffusivity of white matter tracts in relation to visual perception reaction time in children with SBM. If diffusion tensor imaging studies were to be implemented, relations between fractional anisotropy of the white matter underlying the STG and categorical visual perception would be expected. Similarly, if future research should be conducted using fMRI techniques, it would be anticipated that areas of the right STG would be activated during the categorical visual perception task.

Impact of the corpus callosum and imaging variables on visual perception. The regression models predicting categorical visual perception accuracy presented an exceptionally clear pattern. The gray and white matter of the left and right STG and the white matter of the right MTG when added with the middle anterior, central, and middle posterior segments of the corpus callosum accounted for 35% of the variance in categorical accuracy. When age and manual dexterity were added to this same model, 66% of the variance was accounted for. Similarly, when predicting categorical reaction time, the cortical thickness of the left IPC and the right MTG with the anterior and middle anterior segments of the corpus callosum accounted for 34% of the variance. When age and simple

reaction time were added as covariates, the variance accounted for increased to 53%. For coordinate accuracy, while only 10% of the variance was accounted for by cortical thickness of the left MTG and white matter volume of the left IPC, when age and manual dexterity were included, 48% of the variance was accounted for. Together, these findings provide strong evidence for the Dennis et al. (2006) model by demonstrating the impact of core deficits and CNS insults on visual perception performance.

Limitations and future directions. The current study had some limitations that may have impacted the findings. For the first two hypotheses which investigated group differences between children with SBM and controls, the sample size of the controls was substantially smaller than that of the children with SBM. Future research would benefit from having more similar sample sizes between groups; however, the present study utilized a large sample of children with SBM, providing strong support regarding within group findings. Another potential limitation is the use of structural indices as opposed to diffusion tensor imaging or function magnetic resonance imaging. However, the present study investigated several different structural indices, used several regions of interest based on previous literature, and explored the correlations with visual perception performance. Therefore, the current study demonstrates the necessity of using various approaches to explore the impact of neural changes on behavior.

Furthermore, the near chance performance for the children with SBM on the coordinate task raised some concern. Future research would benefit from modifying the task in such a way to determine whether the coordinate accuracy was a result of forgetting the appropriate button response. This could be achieved by having the child give a verbal response out loud as (s)he is completing the task while an administrator records them.

Alternatively, a question such as, “Is the ball further than 3mm from the bat?” could be placed as a reminder at the top of the screen for every trial. Then the child could respond via button press for “yes” with a green button or “no” with a red button. While this would not remove the issue of forced choice, it would ease instruction recall and would eliminate the spatial element of remembering whether the left or right button was to be pressed for the “further” or “closer” response. This would allow for an extension of the present study and would further our understanding of visual perception performance in children with SBM.

In addition to the ideas for future research previously mentioned, our knowledge would also benefit from extending the investigation of visual perception performance in relation to brain areas in SBM to the adult population and other neurodevelopmental populations with visual perception deficits, such as Williams Syndrome (Wang et al., 1995). Additionally, extending the approach of the present study to other cognitive domains that are a weakness in children with SBM would be beneficial for furthering our understanding of the Dennis et al. (2006) model. Furthermore, activation and diffusion tensor imaging studies would add corroborating evidence for the present study as to the brain regions and white matter microstructure involved in visual perception in SBM. Finally, intervention studies are needed to decipher what strategies are most beneficial to helping improve visual perception in children with SBM.

Conclusion. The present study on visual perception performance and the neural differences in children with SBM tested and supported the Dennis et al. (2006) framework within a single cognitive domain. The findings enhanced our understanding as to the hemispheric differences in cortical changes that occur in children with SBM and provided insight as to the brain regions associated with visual perception in children with SBM.

Lastly, the current research may help to inform interventions concerning the need for children with SBM to reduce speed during more challenging tasks.

References

Agopian, A., Canfield, M. A., Olney, R. S., Lupo, P. J., Ramadhani, T., Mitchell, L. E., . . . Moore, C. A. (2012). Spina bifida subtypes and sub-phenotypes by maternal race/ethnicity in the national birth defects prevention study. *American Journal of Medical Genetics*, *158A*(1),109-115.

Amorapanth, P. X., Widick, P., & Chatterjee, A. (2010). The neural basis for spatial relations. *Journal of Cognitive Neuroscience, 22*(8), 1739-1753.

Anderson, V., Northam, E., Hendy, J., & Wrennall, J. (2001). Hydrocephalus and spina bifida. In C. Code & G. Humphreys (Eds.), *Developmental neuropsychology: A clinical approach* (pp. 185-219). Hove: Psychology Press.

Andersson, S., Persson, E. K., Aring, E., Lindquist, B., Dutton, G. N., & Hellström, A. (2006). Vision in children with hydrocephalus. *Developmental Medicine & Child Neurology, 48*(10), 836-841.

Au, K.S., Ashley-Koch, A., & Northrup, H. (2010). Epidemiologic and genetic aspects of spina bifida and other neural tube defects. *Developmental Disabilities Research Reviews*, *16*(1), 6-15.

Baciu, M., Koenig, O., Vernier, M. P., Bedoin, N., Rubin, C., & Segebarth, C. (1999). Categorical and coordinate spatial relations: FMRI evidence for hemispheric specialization. *Neuroreport, 10*(6), 1373-1378.

Barkovich, A. J. (2005). *Pediatric neuroimaging*. Philadelphia: Lippincott Williams & Wilkins.

Barnes, M. A., & Dennis, M. (1998). Discourse after early-onset hydrocephalus: Core deficits in children of average intelligence. *Brain and Language, 61*(3), 309-334.

Barnes, M. A., Faulkner, H. J., & Dennis, M. (2001). Poor reading comprehension despite fast word decoding in children with hydrocephalus. *Brain and Language, 76*(1), 35-44.

Barnes, M. A., Wilkinson, M., Khemani, E., Boudesquie, A., Dennis, M., & Fletcher, J. M. (2006). Arithmetic processing in children with spina bifida. *Journal of Learning Disabilities, 39*(2), 174-187.

Benson, D.F., Davis, R.J., & Snyder, B.D. (1988). Posterior cortical atrophy. *Archives of Neurology*, *45*(7), 789-793.

Brewer, V. R., Fletcher, J. M., Hiscock, M., & Davidson, K. C. (2001). Attention processes in children with shunted hydrocephalus versus attention deficit-hyperactivity disorder. *Neuropsychology, 15*(2), 185-198.

Bryan, D. (1994). Neural tube defects. In M.J. Robinson & D.M. Robertson (Eds.),*Practical paediatrics* (pp. 476-482). Melbourne: Churchill Livingstone.

Buddenberg, L.A. & Davis, C. (2000). Test-retest reliability of the Purdue Pegboard Test. *The American Journal of Occupational Therapy*, *54*(5), 555-558.

Burmeister, R., Hannay, H. J., Copeland, K., Fletcher, J. M., Boudousquie, A., & Dennis, M. (2005). Attention problems and executive functions in children with spina bifida and hydrocephalus. *Child Neuropsychology, 11*(3), 265-283.

Canfield, M. A., Ramadhani, T. A., Shaw, G. M., Carmichael, S. L., Waller, D. K., Mosley, B. S., . . . Olney, R. S. (2009). Anencephaly and spina bifida among Hispanics: Maternal, sociodemographic, and acculturation factors in the national birth defects prevention study. *Birth Defects Research Part A: Clinical and Molecular Teratology, 85*(7), 637-646.

Capa, R.L., Audiffren, M., & Ragot, S. (2008). The interactive effect of achievement motivation and task difficulty on mental effort. *International Journal of Psychophysiology*, *70*(2), 144-150.

Carlson, N. R. (2010). Vision. In S. Frail & A. Pickard (Eds.), *Physiology of behavior* (pp. 169-211). Boston: Allyn & Bacon.

Colvin, A. N., Yeates, K. O., Enrile, B. G., & Coury, D. L. (2003). Motor adaptation in children with myelomeningocele: Comparison to children with ADHD and healthy siblings. *Journal of the International Neuropsychological Society, 9*(4), 642-652.

Creem, S. H., & Proffitt, D. R. (2001). Defining the cortical visual systems. *Acta Psychologica, 107*(1-3), 43-68.

Dale, A. M., Fischl, B., & Sereno, M. I. (1999). Cortical surface-based analysis* 1:: I. segmentation and surface reconstruction. *NeuroImage, 9*(2), 179-194.

Dale, A. M., & Sereno, M. I. (1993). Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: A linear approach. *Journal of Cognitive Neuroscience, 5*(2), 162-176.

Del Bigio, M. R. (2004). Cellular damage and prevention in childhood hydrocephalus. *Brain Pathology, 14*(3), 317-324.

Del Bigio,M.R. (2010). Neuropathology and structural changes in hydrocephalus. *Developmental Disabilities Research Reviews*, *16*(1), 16-22.

Del Bigio, MR., Wilson, M.J., & Enno, T. (2003). Chronic hydrocephalus in rats and humans: White matter loss and behavior changes. *Annals of Neurology*, *53*(3), 337-346.

Dennis, M., & Barnes, M. A. (2010). The cognitive phenotype of spina bifida meningomyelocele. *Developmental Disabilities Research Reviews, 16*(1), 31-39.

Dennis, M., Edelstein, K., Copeland, K., Frederick, J., Francis, D. J., Hetherington, R., . . . Brandt, M. E. (2005). Covert orienting to exogenous and endogenous cues in children with spina bifida. *Neuropsychologia, 43*(6), 976-987.

Dennis, M., Edelstein, K., Copeland, K., Frederick, J. A., Francis, D. J., Hetherington, R., . . . Brandt, M. E. (2005). Space-based inhibition of return in children with spina bifida. *Neuropsychology, 19*(4), 456-465.

Dennis, M., Edelstein, K., Hetherington, R., Copeland, K., Frederick, J., Blaser, S. E., . . . Fletcher, J. M. (2004). Neurobiology of perceptual and motor timing in children with spina bifida in relation to cerebellar volume. *Brain, 127*(6), 1292-1301.

Dennis, M., Fitz, C. R., Netley, C. T., Sugar, J., Harwood-Nash, D. C. F., Hendrick, E. B., . . . Humphreys, R. P. (1981). The intelligence of hydrocephalic children. *Archives of Neurology, 38*(10), 607-615.

Dennis, M., Fletcher, J. M., Rogers, T., Hetherington, R., & Francis, D. J. (2002). Object-based and action-based visual perception in children with spina bifida and hydrocephalus. *Journal of the International Neuropsychological Society, 8*(1), 95-106.

Dennis, M., Jacennik, B., & Barnes, M. A. (1994). The content of narrative discourse in children and adolescents after early-onset hydrocephalus and in normally developing age peers. *Brain and Language; Brain and Language, 46*(1), 129-165.

Dennis, M., Landry, S. H., Barnes, M., & Fletcher, J. M. (2006). A model of neurocognitive function in spina bifida over the life span. *Journal of the International Neuropsychological Society, 12*(02), 285-296.

Desikan, R. S., Ségonne, F., Fischl, B., Quinn, B. T., Dickerson, B. C., Blacker, D., . . . Hyman, B. T. (2006). An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage, 31*(3), 968-980.

Destrieux, C., Fischl, B., Dale, A., & Halgren, E. (2010). Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. *NeuroImage, 53*(1), 1-15.

Edelstein, K., Dennis, M., Copeland, K., Frederick, J., Francis, D., Hetherington, R., . . . Fletcher, J. M. (2004). Motor learning in children with spina bifida: Dissociation between performance level and acquisition rate. *Journal of the International Neuropsychological Society, 10*(6), 877-887.

Fischl, B., & Dale, A. M. (2000). Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proceedings of the National Academy of Sciences, 97*(20), 11050-11055.

Fletcher, J. M., Bohan, T. P., Brandt, M. E., Kramer, L. A., Brookshire, B. L., Thorstad, K., . . . Baumgartner, J. E. (1996). Morphometric evaluation of the hydrocephalic brain: Relationships with cognitive development. *Child's Nervous System, 12*(4), 192-199.

Fletcher, J. M., Copeland, K., Frederick, J. A., Blaser, S. E., Kramer, L. A., Northrup, H., . . . Villarreal, G. (2005). Spinal lesion level in spina bifida: A source of neural and cognitive heterogeneity. *Journal of Neurosurgery: Pediatrics, 102*(3), 268-279.

Fletcher, J. M., Francis, D. J., Thompson, N. M., Brookshire, B. L., Bohan, T. P., Landry, S. H., . . . Miner, M. E. (1992). Verbal and nonverbal skill discrepancies in hydrocephalic children. *Journal of Clinical and Experimental Neuropsychology, 14*(4), 593-609.

Geary, D. C. (1993). Mathematical disabilities: Cognitive, neuropsychological, and genetic components. *Psychological Bulletin, 114*(2), 345-362.

Goodale, M.A. (2008). Action without perception in human vision. *Cognitive Neuropsychology, 25*(7-8), 891-919.

Hannay, H. J. (2000). Functioning of the corpus callosum in children with early hydrocephalus. *Journal of the International Neuropsychological Society, 6*(03), 351-361.

Hannay, H. J., Dennis, M., Kramer, L., Blaser, S., & Fletcher, J. M. (2009). Partial agenesis of the corpus callosum in spina bifida meningomyelocele and potential compensatory mechanisms. *Journal of Clinical and Experimental Neuropsychology, 31*(2), 180-194.

Harnadek, M.C. & Rourke, B.P. (1994). Principal identifying features of the syndrome of nonverbal learning disabilities in children. *Journal of Learning Disabilities, 27*(3), 144-154.

Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., Mishkin, M., Carson, R. E., . . . Rapoport, S. I. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proceedings of the National Academy of Sciences, 88*(5), 1621-1625.

Hellige, J. B., & Michimata, C. (1989). Categorization versus distance: Hemispheric differences for processing spatial information. *Memory & Cognition, 17*(6), 770-776.

Hetherington, R., & Dennis, M. (1999). Motor function profile in children with early onset hydrocephalus. *Developmental Neuropsychology, 15*(1), 25-51.

Hines, M., Chiu, L., McAdams, L.A., Bentler, P.M., & Lipcamon, J. (1992).Cognition and the corpus callosum: Verbal fluency, visuospatial ability, and language lateralization related to midsagittal surface areas of callosal subregions. *Behavioral Neuroscience*, *106*(1), 3-14.

Hoeft, F., Barnea-Goraly, N., Haas, B.W., Golarai, G., Ng, D., Mills, D., . . . Reiss, A.L. (2007). More is not always better: Increased fractional anisotropy of superior longitudinal fasciculus associated with poor visuospatial abilities in Williams syndrome. *The Journal of Neuroscience*, *27*(44), 11960-11965.

Hofer, S., & Frahm, J. (2006). Topography of the human corpus callosum revisited--comprehensive fiber tractography using diffusion tensor magnetic resonance imaging. *NeuroImage, 32*(3), 989-994.

Hollingshead, A. (1975). *Four factor index of social status*. New Haven, CT: Yale University, Department of Sociology.

Holzapfel, M., Barnea-Goraly, N., Eckert, M.A., Kessler, S.R., & Reiss, A.L. (2006). Selective alterations of white matter associated with visuospatial and sensorimotor dysfunction in Turner syndrome. *The Journal of Neuroscience*, *26*(26), 7007-7013.

Ikkai, A., Jerde, T.A., & Curtis, C.E. (2001). Perception and action selection dissociate human ventral and dorsal cortex. *Journal of Cognitive Neuroscience*, *23*(6) 1494-1506.

Jansen-Osmann, P., Wiedenbauer, G., & Heil, M. (2008). Spatial cognition and motor development: a study of children with spina bifida. *Perceptual and Motor Skills, 106*(2), 436-446.

Juranek, J., Dennis, M., Cirino, P. T., El-Messidi, L., & Fletcher, J. M. (2010). The cerebellum in children with spina bifida and Chiari II malformation: Quantitative volumetrics by region. *The Cerebellum, 9*(2), 240-248.

Juranek, J., Fletcher, J. M., Hasan, K. M., Breier, J. I., Cirino, P. T., Pazo-Alvarez, P., . . . Papanicolaou, A. C. (2008). Neocortical reorganization in spina bifida. *NeuroImage, 40*(4), 1516-1522.

Juranek, J. & Salman, M.S. (2010). Anomalous development of brain structure and function in spina bifida myelomeningocele. *Developmental Disabilities Research Reviews, 16*(1), 23-30.

Klaver, P., Marcar, V., & Martin, E. (2011). Neurodevelopment of the visual system in typically developing children. *Progress in Brain Research, 189,* 113-136. doi:10.1016/B978-0-444-53884-0.00021-X

Koenig, O., Reiss, L. P., & Kosslyn, S. M. (1990). The development of spatial relation representations: Evidence from studies of cerebral lateralization. *Journal of Experimental Child Psychology, 50*(1), 119-130.

Konrad, A., Vucurevic, G., Musso, F., Stoeter, P., & Winterer, G. (2009). Correlation of brain white matter diffusion anisotropy and mean diffusivity with reaction time in an oddball task. *Neuropsychobiology, 60*(2), 55-66.

Kosslyn, S.M. (1987). Seeing and imagining in the cerebral hemispheres: A computational approach. *Psychological Review, 94*(2), 148-175.

Kosslyn, S. M., Chabris, C. F., Marsolek, C. J., & Koenig, O. (1992). Categorical versus coordinate spatial relations: Computational analyses and computer simulations. *Journal of Experimental Psychology: Human Perception and Performance, 18*(2), 562-577.

Kosslyn, S. M., Koenig, O., Barrett, A., Cave, C. B., Tang, J., & Gabrieli, J. D. E. (1989). Evidence for two types of spatial representations: Hemispheric specialization for categorical and coordinate relations. *Journal of Experimental Psychology: Human Perception and Performance, 15*(4), 723-735.

Kosslyn, S. M., Thompson, W. L., Gitelman, D. R., & Alpert, N. M. (1998). Neural systems that encode categorical versus coordinate spatial relations: PET investigations. *Psychobiology, 26*(4), 333-347.

Kravitz, D.J., Saleem, K.S., Baker, C.I., & Mishkin, M. (2011). A new neural framework for visuospatial processing. *Nature Reviews Neuroscience, 12*(4), 217-230.

Laeng, B. (1994). Lateralization of categorical and coordinate spatial functions: A study of unilateral stroke patients. *Journal of Cognitive Neuroscience, 6*(3), 189-203.

Lehmann, M., Barnes, J., Ridgway, G. R., Wattam-Bell, J., Warrington, E. K., Fox, N. C., & Crutch, S. J. (2011). Basic visual function and cortical thickness patterns in posterior cortical atrophy. *Cerebral Cortex, 21*(9), 2122-2132.

Liptak, G.S. (2008, June). *Spotlight on spina bifida*. Retrieved from http://www.spinabifidaassociation.org

Lomax-Bream, L. E., Barnes, M., Copeland, K., Taylor, H. B., & Landry, S. H. (2007). The impact of spina bifida on development across the first 3 years. *Developmental Neuropsychology, 31*(1), 1-20.

Lonnemann, J., Krinzinger, H., Knops, A., & Willmes, K. (2008). Spatial representations of numbers in children and their connection with calculation abilities. *Cortex, 44*(4), 420-428.

Maxwell, S.E. & Delaney, H.D. (2004). *Designing experiments and analyzing data: A model comparison perspective*. Mahwah: Lawrence Erlbaum Associates.

McDowd, J.M. & Craik, F.I. (1988). Effects of aging and task difficulty on divided attention performance. *Journal of Experimental Psychology: Human Perception and Performance, 14*(2), 267-280.

McLone, D. G., & Dias, M. S. (2003). The Chiari II malformation: Cause and impact. *Child's Nervous System, 19*(7), 540-550.

Michimata, C., Saneyoshi, A., Okubo, M., & Laeng, B. (2011). Effects of the global and local attention on the processing of categorical and coordinate spatial relations. *Brain and Cognition*, *77*(2), 292-297.

Narberhaus, A., Segarra, D., Caldú, X., Giménez, M., Pueyo, R., Botet, F., & Junqué, C. (2008). Corpus callosum and prefrontal functions in adolescents with history of very preterm birth. *Neuropsychologia, 46*(1), 111-116.

Padmanabhan, R. (2006). Etiology, pathogenesis and prevention of neural tube defects. *Congenital Anomalies, 46*(2), 55-67.

Paus , T., Collins, D.L., Evans, A.C., Leonard, G., Pike, B., & Zijdenbos, A. (2001). Maturation of white matter in the human brain: A review of magnetic resonance studies. *Brain Research Bulletin, 54*(3), 255-266.

Peterson, B.S., Vohr, B., Staib, L.H., Cannistraci, C.J., Dolberg, A., Schneider, K.C., . . . Ment, L.R. (2000). Regional brain volume abnormalities and long-term cognitive

outcome in preterm infants. *The Journal of the American Medical Association, 284*(15), 1939-1947.

Purdue Research Foundation. (1948). *Purdue Pegboard Test*. Lafayette, IN: Lafayette Instrument Co.

Rourke, B.P. (1995). *Syndrome of nonverbal learning disabilities: Neurodevelopmental manifestations*. New York: Guilford Press.

Salman, M. S., Blaser, S. E., Sharpe, J. A., & Dennis, M. (2006). Cerebellar vermis morphology in children with spina bifida and Chiari type II malformation. *Child's Nervous System, 22*(4), 385-393.

Salman, M., Sharpe, J., Eizenman, M., Lillakas, L., To, T., Westall, C., . . . Dennis, M. (2005). Saccades in children with spina bifida and Chiari type II malformation. *Neurology, 64*(12), 2098-2101.

Sandler, A. D., Macias, M., & Brown, T. T. (1993). The drawings of children with spina bifida: Developmental correlations and interpretations. *European Journal of Pediatric Surgery, 3*, 25-27.

Scott, M. A., Fletcher, J. M., Brookshire, B. L., Davidson, K. C., Landry, S. H., Bohan, T. C., . . . Francis, D. J. (1998). Memory functions in children with early hydrocephalus. *Neuropsychology, 12*(4), 578-589.

Sowell, E.R., Thompson, P.M., Leonard, C.M., Welcome, S.E., Kan, E., & Toga, A.W. (2004). Longitudinal mapping of cortical thickness and brain growth in normal children. *The Journal of Neuroscience, 24*(38), 8223-8231.

Sowell, E.R., Thompson, P.M., Welcome, S.E., Henkenius, A.L., Toga, A.W., & Peterson, B.S. (2003). Cortical abnormalities in children and adolescents with attention-deficit hyperactivity disorder. *The Lancet*, *362*(9397), 1699-1707.

Sparks, B.F., Friedman, S.D., Shaw, D.W., Aylward, E.H., Echelard, D., Artru, A.A., . . . Dager, S.R. (2002). Brain structural abnormalities in young children with autism spectrum disorder. *Neurology*, *59*(2), 184-192.

Swartwout, M. D., Garnaat, S. L., Myszka, K. A., Fletcher, J. M., & Dennis, M. (2010). Associations of ethnicity and SES with IQ and achievement in spina bifida meningomyelocele. *Journal of Pediatric Psychology*, *35*(9), 927-936.

Thorndike, R.L., Hagen, E.P., & Sattler, J.M. (1986). *The Stanford-Binet intelligence scale* (4th ed.) Itasca, IL: Riverside.

Trojano, L., Grossi, D., Linden, D. E. J., Formisano, E., Goebel, R., Cirillo, S., . . . Di Salle, F. (2002). Coordinate and categorical judgements in spatial imagery. an fMRI study. *Neuropsychologia*, *40*(10), 1666-1674.

Tuch, D.S., Salat, D.H., Wisco, J.J., Zaleta, A.K., Hevelone, N.D., & Rosas, H.D. (2005). Choice reaction time performance correlates with diffusion anisotropy in white matter pathways supporting visuospatial attention. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(34), 12212-12217.

Verhoef, M., Barf, H.A., Post, M.W., van Asbeck, F.W., Gooskens, R.H., & Prevo, A.J. (2006). Functional independence among young adults with spina bifida, in relation to hydrocephalus and level of lesion. *Developmental Medicine & Child Neurology*, *48*(2), 114-119.

Wang, P. P., Doherty, S., Rourke, S. B., & Bellugi, U. (1995). Unique profile of visuo-perceptual skills in a genetic syndrome. *Brain and Cognition, 29*(1), 54-65.

Westlye, L.T., Grydeland, H., Walhovd, K.B., & Fjell, A.M. (2011). Associations between regional cortical thickness and attentional networks as measures by the attention network test. *Cerebral Cortex*, *21*(2), 345-356.

Wiedenbauer, G., & Jansen-Osmann, P. (2006). Spatial knowledge of children with spina bifida in a virtual large-scale space. *Brain and Cognition, 62*(2), 120-127.

Wilke, M., Krägeloh-Mann, I., & Holland, S.K. (2007). Global and local development of gray and white matter volume in normal children and adolescents. *Experimental Brain Research, 178*(3), 296-307.

Williams, E.N., Broughton, N.S., & Menelaus, M.B. (1999). Age-related walking in children with spina bifida. *Developmental Medicine & Child Neurology*, *41*, 446-449.

Williams, L. J., Rasmussen, S. A., Flores, A., Kirby, R. S., & Edmonds, L. D. (2005). Decline in the prevalence of spina bifida and anencephaly by race/ethnicity: 1995–2002. *Pediatrics, 116*(3), 580-586.

Wills, K. E., Holmbeck, G. N., Dillon, K., & McLone, D. G. (1990). Intelligence and achievement in children with myelomeningocele. *Journal of Pediatric Psychology, 15*(2), 161-176.

Wills, K. W. (1993). Neuropsychological functioning in children with spina bifida and/or hydrocephalus. *Journal of Clinical Child Psychology*, *22*(2), 247-265.

Yeates, K. O., Enrile, B. G., Loss, N., Blumenstein, E., & Delis, D. C. (1995). Verbal learning and memory in children with myelomeningocele. *Journal of Pediatric Psychology, 20*(6), 801-815.

Yeates, K. O., Loss, N., Colvin, A. N., & Enrile, B. G. (2003). Do children with myelomeningocele and hydrocephalus display nonverbal learning disabilities? An empirical approach to classification. *Journal of the International Neuropsychological Society, 9*(4), 653-662.

Table 1. Demographic Information

Variable	SBM (N = 81)	Controls (N = 28)	Cohen's *d*
Age (M (SD))	13.09 (2.78)	13.35 (2.95)	-0.09
Gender (% male)	60	53.57	
Ethnicity (%)			
Caucasian	47	39	
Hispanic	31	32	
African American	10	4	
Asian	7	18	
Other	5	7	
Handedness (% right) *	68	93	
Socioeconomic Status	38.19 (13.18)°	41.54 (12.36)	-0.26
Stanford Binet Composite Score ***	88.17 (13.41)	106.04 (11.69)	-1.42

Note: N = number of participants; SD = standard deviation; Socioeconomic Status was measured using the Hollingshead Four Factor Index; *p <0.05; **p <0.01; ***p <0.0001; °N = 79

Table 2. SBM Characteristics

Variable	SBM
Lesion Level (%) (N = 81)	
Upper	16
Lower	84
Chiari II Malformation (%) (N = 80)	96
Hydrocephalus Type (%) (N = 81)	
Hydrocephalus	98
Arrested	2
Number of Shunt Revisions (%) (N = 72)	
0	15
1	31
2-4	40
5-9	11
10+	3
Seizure (%) (N = 70)	
Current	6
Past	8
None	86
Ambulation (%) (N = 73)	
Normal	2
Independent	19
Partial	41
Unable	38

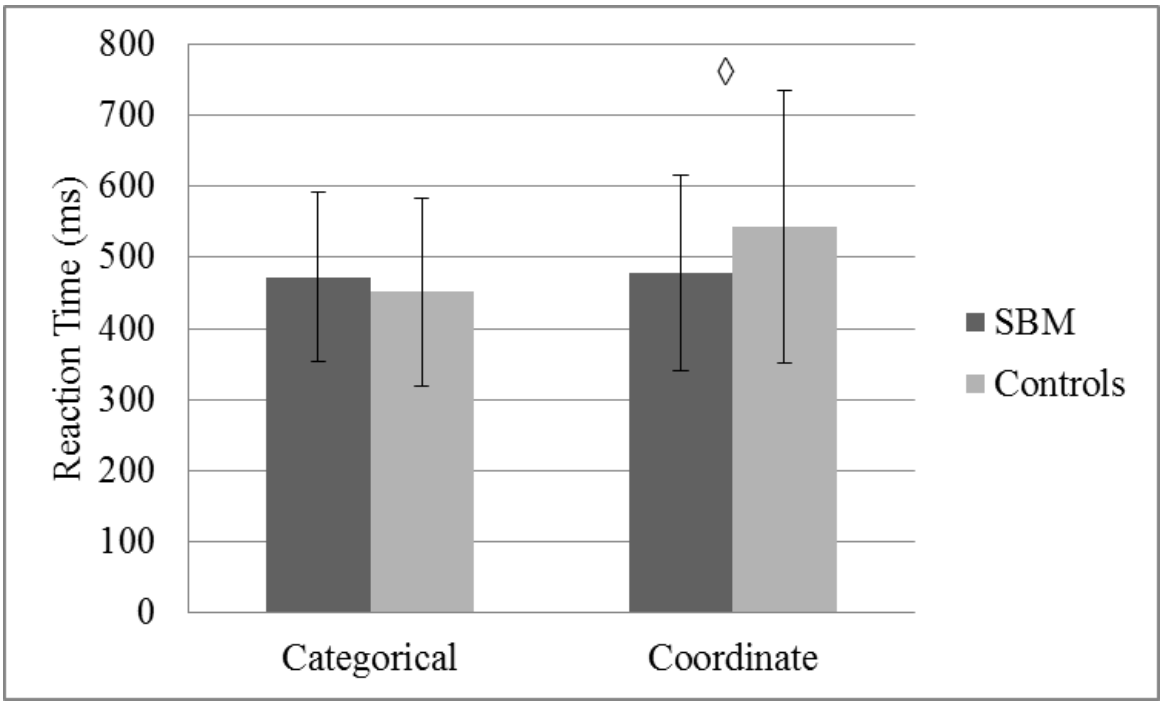
Note: N = number of participants

Table 3. Descriptive Statistics for Behavioral Data

	SBM (N = 81)	Controls (N = 28)	Cohen's *d*
Variable	Mean (SD)	Mean (SD)	
PP Both Hands (Z Score)	-3.15 (1.19)°	-0.76 (0.74)	-2.41
Simple Reaction Time (ms)	359.3 (67.25)°°	317.89 (74.77)	0.58
Categorical VP Accuracy (%)	73 (0.21)	82 (0.23)	-0.41
Coordinate VP Accuracy (%)	48 (0.16)	64 (0.16)	-1.00
Categorical VP Reaction Time (ms)	472.06 (119.23)	451.17 (131.44)	0.17
Coordinate VP Reaction Time (ms)	478.57 (137.45)	542.86 (191.08)	-0.39

Note: N = number of participants; SD = standard deviation; PP = Purdue Pegboard; VP = Visual Perception; °N = 76; °°N = 80

Figure 1. Significant Interaction between Group and Task for Reaction Time



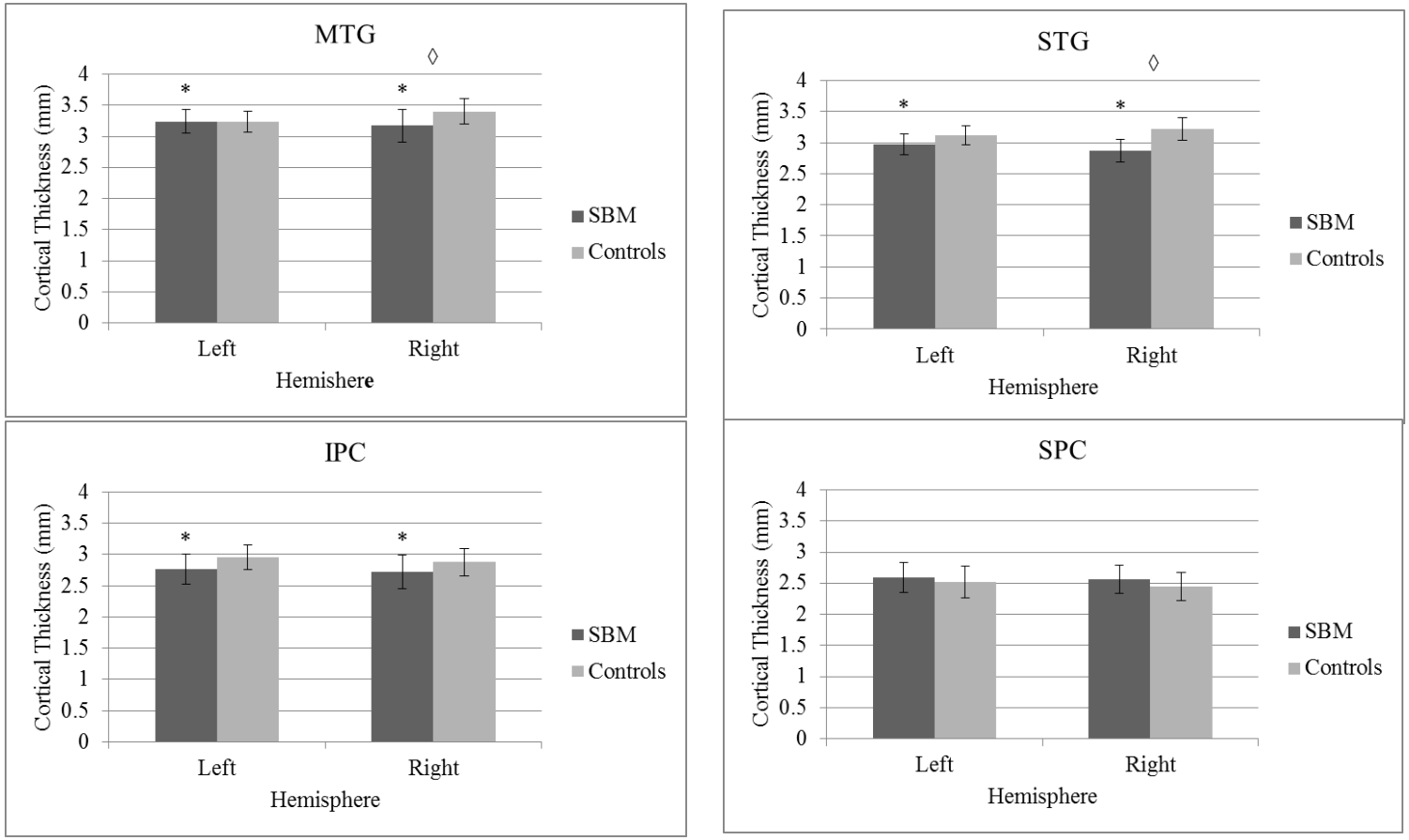
Note: Reaction time is significantly slower for controls on the coordinate task (◊). There was no difference in categorical reaction time between groups.

Table 4. Descriptive Statistics for Cortical Thickness and Uncorrected Gray and White Matter Volumes

	SBM (N = 54)	Controls (N = 19)	Cohen's *d*
Variable	Mean (SD)	Mean (SD)	
CT IPC LH	2.76 (0.24)	2.96 (0.20)	-0.91
CT IPC RH	2.72 (0.27)	2.88 (0.22)	-0.65
CT SPC LH	2.60 (0.23)	2.52 (0.25)	0.33
CT SPC RH	2.57 (0.22)	2.45 (0.23)	0.53
CT MTG LH	3.24 (0.19)	3.23 (0.17)	0.06
CT MTG RH	3.17 (0.26)	3.40 (0.20)	-0.99
CT STG LH	2.97 (0.17)	3.12 (0.15)	-0.94
CT STG RH	2.87 (0.18)	3.22 (0.18)	-1.94
GMV IPC LH	12085.05 (2654.94)°	16773.89 (2614.01)	-1.78
GMV IPC RH	15799.73 (2757.68)°	19309.74 (3024.38)	-1.21
GMV SPC LH	16207.55 (3400.10)°	16165.37 (2825.25)	0.01
GMV SPC RH	16037.38 (3612.18)°	16354.05 (2664.94)	-0.10
GMV MTG LH	12051.91 (2874.75)	13897.00 (2343.05)	-0.70
GMV MTG RH	12866.15 (2174.38)	15361.32 (2581.93)	-1.05
GMV STG LH	12433.02 (2840.69)	14478.95 (2217.13)	-0.80
GMV STG RH	9359.78 (2398.44)	14474.58 (2239.15)	-2.20
WMV IPC LH	11064.87 (2597.85)°	14967.16 (2084.22)	-1.66
WMV IPC RH	14603.64 (2514.39)°	17532.79 (2686.06)	-1.13
WMV SPC LH	15892.02 (3399.87)°	14473.63 (1856.43)	0.52
WMV SPC RH	15646.45 (3602.98)°	14827.11 (2137.01)	0.28
WMV MTG LH	12336.65 (2926.07)	14241.32 (2214.80)	-0.73
WMV MTG RH	13094.56 (2259.87)	15718.74 (2473.33)	-1.11
WMV STG LH	12598.76 (2868.65)	14408.00 (2052.81)	-0.73
WMV STG RH	9467.33 (2446.03)	14240.58 (2129.80)	-2.08

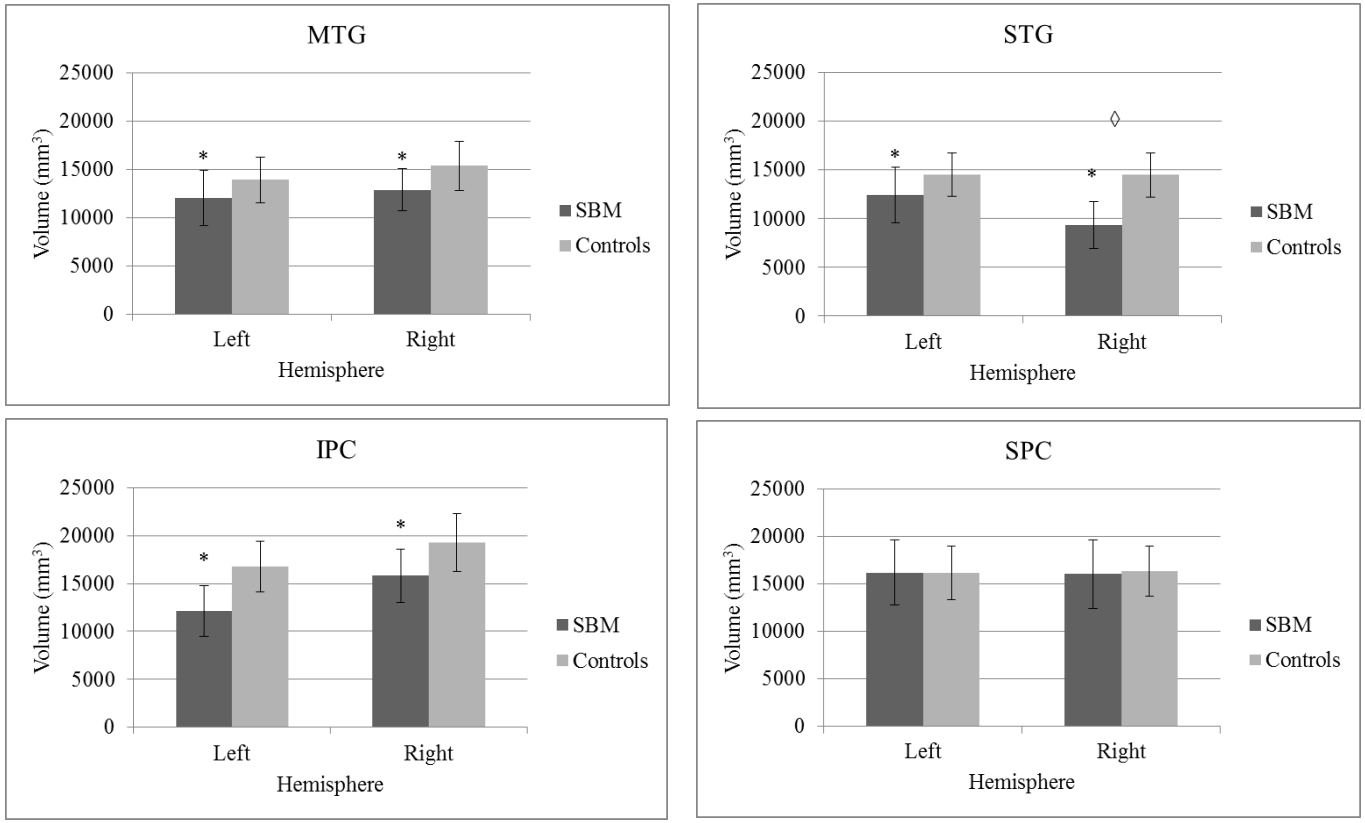
Note: CT = Cortical Thickness; GMV = Gray Matter Volume; WMV = White Matter Volume; IPC = Inferior Parietal Cortex; SPC = Superior Parietal Cortex; MTG = Middle Temporal Gyrus; STG = Superior Temporal Gyrus; LH = Left Hemisphere; RH = Right Hemisphere; °N = 55

Figure 2. Cortical Thickness for Children with SBM and Controls



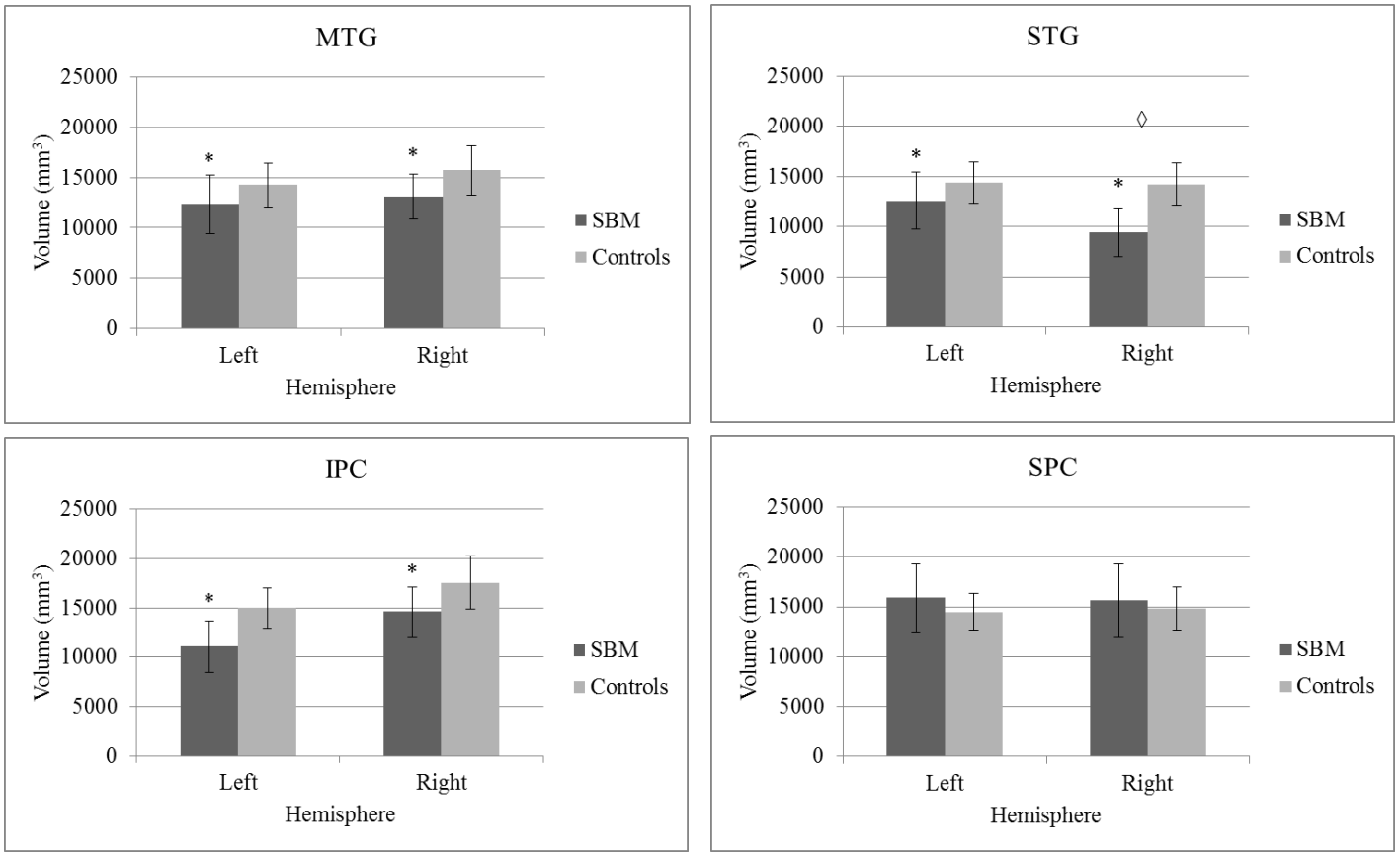
Note: IPC = Inferior Parietal Cortex; SPC = Superior Parietal Cortex; MTG = Middle Temporal Gyrus; STG = Superior Temporal Gyrus; Significant interaction effects between group and hemisphere were found for the MTG and STG (◊). Significantly less cortical thickness was found in children with SBM for the IPC, MTG, and STG (*).

Figure 3. Uncorrected Gray Matter Volume for Children with SBM and Controls



Note: IPC = Inferior Parietal Cortex; SPC = Superior Parietal Cortex; MTG = Middle Temporal Gyrus; STG = Superior Temporal Gyrus; Significant interaction effect between group and hemisphere were found for the STG (◊). Significantly less gray matter volume was found in children with SBM for the IPC, MTG, and STG (*).

Figure 4. Uncorrected White Matter Volume for Children with SBM and Controls



Note: IPC = Inferior Parietal Cortex; SPC = Superior Parietal Cortex; MTG = Middle Temporal Gyrus; STG = Superior Temporal Gyrus; Significant interaction effect between group and hemisphere were found for the STG (◊). Significantly less white matter volume was found in children with SBM for the IPC, MTG, and STG (*).

Table 5. Number of Children with SBM in the Combinations of the Corpus Callosum Body and Splenium Severity Levels

	Body of the CC				
Splenium of the CC	Present	Hypoplastic: Mild	Hypoplastic: Moderate	Hypoplastic: Severe	Absent
Present	2	0	5	4	0
Hypoplastic: Mild	0	1	1	3	1
Hypoplastic: Moderate	0	0	3	8	0
Hypoplastic: Severe	1	0	4	11	0
Absent	0	0	1	18	8

Note: CC = Corpus Callosum; Present = Intact Segment of the CC; Hypoplastic = Thinned Segment of the CC; Absent = Dysgenic Segment of the CC

Table 6. Correlations between Corpus Callosum White Matter Volume with Visual Perception Performance for Children with SBM

	Visual Perception Performance			
Region of Interest	CAT VP ACC	COOR VP ACC	CAT VP RT	COOR VP RT
WMV Ant CC	0.08	0.19	-0.22	0.02
WMV Mid Ant CC	-0.20	-0.07	0.16	0.16
WMV Cen CC	-0.26	-0.05	0.07	0.08
WMV Mid Post CC	-0.22	-0.05	-0.12	-0.09
WMV Post CC	0.13	0.13	-0.07	0.15

Note: N = 55; CAT = Categorical; COOR = Coordinate; VP = Visual Perception; ACC = Accuracy; RT = Reaction Time; CC = Corpus Callosum; WMV = White Matter Volume; LH = Left Hemisphere; RH = Right Hemisphere; *p <0.05; **p <0.01; ***p <0.0001

Table 7. Correlations between Cortical Thickness and Uncorrected Gray and White Matter Volumes with Visual Perception Performance for Children with SBM when controlling for Age, Manual Dexterity (for Accuracy), and Simple Reaction Time (for Reaction Time)

	Visual Perception Performance			
Region of Interest	CAT VP ACC	COOR VP ACC	CAT VP RT	COOR VP RT
CT IPC LH	0.34*	0.06	0.31*	0.20
CT IPC RH	0.29	0.13	0.24	0.20
CT SPC LH	0.26	-0.24	0.06	-0.0004
CT SPC RH	0.08	-0.22	0.08	0.04
CT MTG LH	0.19	0.32*	0.18	0.26
CT MTG RH	0.28	0.09	0.46**	0.32*
CT STG LH	-0.29	0.14	0.01	0.01
CT STG RH	-0.04	0.09	0.07	0.14
GMV IPC LH °	0.26	0.28	-0.15	0.11
GMV IPC RH °	0.03	0.17	-0.06	-0.10
GMV SPC LH °	0.23	0.18	0.05	-0.05
GMV SPC RH °	0.18	0.13	0.12	0.13
GMV MTG LH	-0.04	0.11	0.14	0.06
GMV MTG RH	-0.24	-0.28	-0.13	-0.24
GMV STG LH	-0.44**	-0.01	-0.25	-0.23
GMV STG RH	0.10	0.16	-0.001	0.12
WMV IPC LH °	0.16	0.30	-0.21	0.07
WMV IPC RH °	-0.16	0.19	-0.14	-0.17
WMV SPC LH °	0.04	0.20	-0.04	-0.09
WMV SPC RH °	0.05	0.11	0.05	0.10
WMV MTG LH	-0.12	0.07	0.12	0.03
WMV MTG RH	-0.38*	-0.29	-0.16	-0.28
WMV STG LH	-0.46**	-0.02	-0.25	-0.21
WMV STG RH	0.07	0.11	0.01	0.13

Note: N = 39 for CAT; N = 43 for COOR; CAT = Categorical; COOR = Coordinate; VP = Visual Perception; ACC = Accuracy; RT = Reaction Time; CT = Cortical Thickness; GMV = Gray Matter Volume; WMV = White Matter Volume; IPC = Inferior Parietal Cortex; SPC = Superior Parietal Cortex; MTG = Middle Temporal Gyrus; STG = Superior Temporal Gyrus; LH = Left Hemisphere; RH = Right Hemisphere; *p <0.05; **p <0.01; ***p <0.0001, °N = 40 for CAT; N = 44 for COOR