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The Cerebellum and Divided Attention in Autism Spectrum Disorders

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The Cerebellum and Divided Attention in Autism Spectrum Disorders

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Dedication

This dissertation is dedicated to my family and friends.

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The Cerebellum and Divided Attention in Autism Spectrum Disorders

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Divided attention, or the ability to respond to more than one task simultaneously, is an important skill for navigating complex social, communicative, academic, and professional settings. The purpose of the current study was to understand the association between the volume of the posterior cerebellum and divided attention in individuals with autism spectrum disorders (ASDs) and control participants. It was hypothesized that the ASD group would have worse divided attention abilities and smaller posterior cerebellar volumes compared to the control group. Furthermore, reduced posterior cerebellar volume was expected to be associated with weaker divided attention abilities. Participants were young adult males with high-functioning autism spectrum disorders (n=15) and controls matched for age, handedness, and nonverbal IQ (n=19). Results showed partial support for worse divided attention performance in ASDs and for a positive association between posterior cerebellar volume and divided attention performance. There were no group differences in posterior cerebellar volume, and accounting for intracranial volume did not affect findings. Limitations of the current study and future directions are discussed.

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Chapter One: Introduction

Autism spectrum disorders (ASDs) are one of the most prevalent developmental disorders, which is alarming given that autism was only formally recognized by diagnostic manuals three decades ago (Autism and Developmental Disabilities Monitoring [ADDM], 2012; American Psychiatric Association [APA], 2000). Recent estimates report that one in every 88 children meets criteria for diagnosis (ADDM, 2012). ASDs are five times more common in males, with prevalence being one in every 54 boys and one in every 252 girls (ADDM, 2012).

The precise causes of ASDs remain unknown. However, research indicates that ASDs are disorders with a strong genetic component (i.e. characterized by high heritability rates) that may also be associated with environmental risk factors. Evidence for the role of environmental variables, including prenatal viral exposure, early childhood vaccinations, and antibiotics, is inconclusive (Fallon, 2005; Kawashima et al., 2000; Libbey, Sweeten, McMahon, & Fujinami, 2005; Miller & Reynolds, 2009). However, more research is needed to understand how environmental factors may interact with genetic factors to influence the expression of ASDs. It is possible that individuals with a genetic susceptibility for ASDs may be more sensitive to prenatal or postnatal exposure to biological or chemical environmental agents, which may serve as a trigger. There is preliminary evidence suggesting industrial mercury exposure (Palmer, Blanchard, & Wood, 2009), prenatal exposure to antidepressants (Croen, Grether, Yoshida, Odouli, & Hendrick, 2011), and a number of maternal health and neonatal birth factors may be implicated in ASDs (Gardener, Spiegelman, & Buka, 2009; 2011).

The conceptualization of autism has changed considerably over the years, reflecting the emergent understanding of the disorder. Diagnostic criteria allowing for the inclusion of a wider spectrum of autistic behavior may be one factor contributing to the increased prevalence of ASDs (Fombonne, 2005; Wing & Potter, 2002). Increased public and professional awareness of the disorder may also have contributed to an increased rate of diagnosis.

The disorder first appeared in the 1980 version of the DSM-III as "Infantile Autism" and was later renamed "Autistic Disorder" in the 1987 revision (DSM-III-R, APA). At that time, autism was not yet considered a spectrum of disorders, but was conceptualized as a single distinct disorder characterized by delayed language and cognitive development, along with deficits in social reciprocity and repetitive behaviors. However, reports of individuals with normal language and intellectual development but with impaired social relatedness and a restricted range of interests began to emerge. As a result, the conceptualization of autism began to broaden to include a spectrum of related disorders that shared common features of social impairment and restricted behaviors. In the 1994 version of the DSM, "Asperger's Disorder" was added as a subtype of ASDs (DSM-IV, American Psychiatric Association).

The following version of the DSM (DSM-IV-TR, American Psychiatric Association, 2000) included autistic disorder, Asperger's disorder, and Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS), which were all considered to be on the autism spectrum. Asperger's disorder was characterized by normal development of language, cognitive skills, and adaptive behavior whereas autistic

disorder was characterized by delays in language, symbolic play, social interaction, and restricted interests and behaviors prior to three years of age. A diagnosis of PDD-NOS was appropriate when an individual exhibited a marked impairment in reciprocal social interaction but did not meet full symptom criteria for autistic disorder or Asperger's disorder.

Prior to the 2013 publication of the DSM-5 (American Psychiatric Association), there was significant concern about whether autistic disorder, Asperger's disorder, and PDD-NOS represented qualitatively distinct diagnoses. Research found that clinician diagnosis tended to be made based on severity, language level, and intelligence rather than on symptom criteria that distinguish between disorders (Rosenberg et al., 2009). Based on these findings, the fifth edition of the DSM (DSM-V) replaced separate diagnoses with a single broader diagnosis of autism spectrum disorder. Asperger's disorder, Autistic Disorder, and PDD-NOS were no longer included as diagnoses.

The current diagnostic criteria require more symptom behaviors than the DSM-IV-TR, and criteria fall under two symptom domains of social-communication and restricted, repetitive interests. Distinctions are now made based on severity of presentation, in relation to chronological age (Lord & Bishop, 2010). Clinicians specify whether the social-communication deficits and restricted interests require support, substantial support, or very substantial support. Diagnosis also requires specifying if the individual has an accompanying intellectual impairment or language impairment and whether the diagnosis is associated with a known medical, genetic, or environmental factor.

The considerable changes in diagnostic classification over time reflect the ongoing efforts to understand a disorder with a heterogeneous presentation and no clear genetic or environmental etiology. Research examining cognitive and brain differences within ASDs is needed to increase understanding and identify potential subtypes that represent true qualitative distinctions.

ASDs are associated with abnormalities of brain structure and function (Folstein & Rowen-Sheidley, 2001). Several brain regions have been found to be atypical in ASDs, including the cerebellum, the hippocampus, the anterior cingulate gyrus, and the amygdala (Acosta & Pearl, 2004; Bauman, Anderson, Perry, & Ray, 2006; Folstein & Rowen-Sheidley, 2001). In addition, overall brain size appears to be enlarged in early childhood. Though brain volume appears to be normal at birth, by two years of age, it is enlarged, compared to healthy controls (for review, see Bauman, Anderson, Perry, & Ray, 2006). However, by adolescence and adulthood, brain volume is again typical.

The most consistently reported site of abnormality in ASDs is the cerebellum, a highly connected structure involved in sensorimotor, cognitive, and affective functions (for review, see Allen, 2005; Allen, 2011). The cerebellum is connected to all major areas of the brain, with an afferent: efferent ratio of 40:1 (Allen et al., 2005; Middleton & Strick, 2001; Schmahmann, 1996). Though it only represents 10% of the brain's volume, the cerebellum contains more neurons than the remainder of the brain combined (Ito, 1984; Williams & Herrup, 1988).

The cerebellum was traditionally thought to be solely a motor coordination area. However, evidence from cerebellar patient studies and brain imaging studies now point to

a cerebellar role in a wide range of cognitive and emotional functions as well. Studies of patients with cerebellar lesions report impaired attention, working memory, verbal fluency, and visuospatial processing (Gottwald et al., 2004; Levinsohn, Cronin-Golomb, & Schmahmann, 2000; Schmahmann & Sherman, 1998; Trillenberg, Verleger, Teetzmann, Wascher, & Wessel, 2004). Imaging studies of neurotypical participants show cerebellar activation during attention, reasoning and problem solving, expressive language, and positive emotion tasks, to name a few (Allen et al., 1997; Desmond, Gabrieli, Wagner, Ginier, & Glover, 1997; Doyon et al., 2002; Stoodley & Schmahmann, 2009; Xiang et al., 2003).

The cerebellum is divided functionally and anatomically in different subregions. The anterior cerebellum consists of hemispheric lobules I-V while the posterior cerebellum consists of hemispheric lobules VI-X. The posterior cerebellum is the phylogenetically younger region and has functional connections to the prefrontal and posterior parietal areas of the brain, which are involved in planning, emotional regulation, and attention (Allen et al., 2005; Barlow, 2002; O'Reilly et al., 2009). Functional imaging studies show anterior cerebellar involvement during motor tasks (Allen, Buxton, Wong, & Courchesne, 1997; O'Reilly et al., 2009) and posterior cerebellar involvement in cognitive and executive functioning tasks (Allen, Buxton, Wong, & Courchesne, 1997; Allen & Courchesne, 2003; O'Reilly et al., 2009).

At a cellular level, the Purkinje neurons play a primary role in the functioning of the cerebellar cortex, integrating incoming information from the rest of the brain and regulating projections to the rest of the brain. Purkinje neurons inhibit output from deep

cerebellar nuclei and are the sole output source of the cerebellar cortex (Eccles & Szentgothai, 1967). In autistic brains, postmortem studies have consistently found Purkinje cell reduction (Bailey et al. 1998; Fehlow et al. 1993; Kemper & Bauman 1998; Lee et al. 2002; Ritvo et al. 1986; Vargas et al. 2005; Wegiel 2004; Whitney et al. 2008; Williams et al. 1980). Although it is unclear whether this cell reduction is diffuse or specific to a subregion of the cerebellum, the posterior cerebellum appears to be consistently affected. The majority of structural MRI studies have found reduced posterior cerebellar volume while several postmortem studies have found Purkinje cell reduction to be restricted to the posterior cerebellum (Bauman & Kemper, 1985; Kemper & Bauman, 1998; Whitney et al., 2008).

The trajectory of cerebellar gray and white matter development appears to be atypical in ASDs. A structural imaging study found an overproduction of white matter during early childhood, followed by an underproduction (i.e., abnormally slowed growth) from early childhood to adolescence (Courchesne et al., 2001). From early childhood to middle childhood, gray matter decreased by 1%, compared to a typical trajectory growth of 12% during this developmental period (Courchesne et al., 2001). Measures of overall cerebellar volume are somewhat consistent with this abnormal white and gray matter development. Overall cerebellar volume was reported to be increased in early and middle childhood (Herbert et al., 2003; Sparks et al., 2002), which may reflect the early overproduction of white matter. Larger overall cerebellar volume was reported in one study of adolescents and young adults (Palmen et al., 2004), while another study found reduced overall cerebellar volume in adults with ASDs (Hallahan et al., 2009).

Functional imaging studies point to atypical cerebellar functioning in ASDs. A number of studies show increased cerebellar activation in response to simple sensory and motor tasks (Allen, Muller, & Courchesne, 2004; Muller et al., 1998; Muller, Pierce, Ambrose, Allen, & Courchesne, 2001). In contrast, cerebellar activation appears to be decreased during higher-order cognition, including tasks of attention (Allen & Courchesne, 2003), facial expression (Critchley et al., 2000), auditory detection (Gomot et al., 2006), semantic processing (Harris et al., 2006), and visual-motor learning (Muller, Kleinhaus, Kemmotsu, Pierce, & Courchesne, 2003).

A functional imaging study using a visual selective attention paradigm found reduced activation in the cerebellum of individuals with ASDs, in contrast to the pattern of bilateral activation of the Crus I (i.e., cerebellar hemisphere lobule VIIa) in typically developing participants (Allen & Courchesne, 2003). This reduced activation in the posterior cerebellar hemispheres may reflect the pathology of these regions in ASDs. Volume of the Crus I was correlated with activation in this region during the visual attention task in both the ASD group and the control group. Furthermore, within the ASD group, the size of the Crus I was associated with performance accuracy. Thus, there is evidence that the Crus I is involved in attention and that the structure of the region is correlated with both activation and performance.

Attentional abnormalities are one of the earliest identifiable features in ASDs. Difficulty in disengaging attention is seen within the first year of life, and attentional abnormalities appear to continue to adulthood (Elsabbagh et al., 2009). It is possible that atypical attention can affect the input and processing of social stimuli and language, as

well as contribute to an insistence on sameness and focus on parts rather than wholes. The abilities to selectively attend to a focus of interest, maintain attention, disengage attention, and shift attention are essential skills that form the basis for social, communicative, and academic learning. Thus, atypical attention functioning has implications for a wide range of developmental outcomes.

Studies that have examined attention functioning in ASDs report overly selective attention, impaired shifted attention, and impaired rapid orienting of attention in ASDs (Allen & Courchesne, 2001). There are relatively few studies of divided attention in ASDs, and there is substantial variability of task type between studies. Single modality visual divided attention appears to be intact (Bogte, Flamma, Van Der Meere, & Van Engeland, 2009) or superior (Rutherford, Richards, Moldes, & Sekuler, 2007) in ASDs. However, performance on divided attention tasks with high working memory demand appears to be impaired in both single modality auditory (Yerys et al., 2011) and cross-modality auditory and visual paradigms (Casey, Gordon, Mannheim, & Rumsey, 1993; Garcia-Villamisar & Della Sala, 2002; Sinzig, Bruning, Morsch & Lehmkuhl, 2008). Good auditory divided attention under high working memory demand was also associated with less severe social and communication symptoms of autism in children with high-functioning ASDs (Kenworthy, Black, Harrison, Della Rosa, & Wallace, 2009).

Given the small number of studies and the inconsistencies in task type between studies, whether divided attention in ASDs is impaired remains a question. However, there is evidence to suggest that divided attention tasks with high working memory demand are more difficult for individuals with ASD. There is a need for more research,

using a reliable measure of divided attention, in order to better understand divided attention abilities in ASD.

Cerebellar involvement in divided attention has also been shown through patient studies and imaging studies in the neurotypical population. One research group found that patients with focal cerebellar lesions showed impaired cross-modality auditory and divided attention performance (Gottwald, Mihajlovic, Wilde, & Mehdorn, 2003; Gottwald, Wilde, Mihajlovic, & Mehdorn, 2004). Another study found that patients with isolated cerebellar infarcts showed impaired performance on the Paced Auditory Serial Addition Test (PASAT; Gronwall & Sampson, 1974), a task of auditory divided attention with high working memory demand (Neau, Anllo, Bonnaud, Ingrand, & Gil, 2000).

Imaging studies of Multiple Sclerosis patients also provide evidence for cerebellar involvement in divided attention. Patients with Relapsing Remitting Multiple Sclerosis (RRMS) showed increased activation of the Crus I while performing the PASAT, relative to controls, despite normal task performance (Lesage et al., 2010). Lesage and colleagues (2010) suggest that the posterior cerebellum plays a key part in compensating for neural effects of RRMS (i.e., white matter degeneration, diffuse neural pathology) while performing tasks that require acquired cognitive skills. Cerebellar structure may also be related to performance on the PASAT for individuals with RRMS. A voxel-based morphometry study found that lower scores on the PASAT were correlated with decreased gray matter volume in the right cerebellum, for patients with RRMS (Morgen, et al., 2006).

Imaging studies in neurotypical participants help to clarify the cerebellar role in divided attention tasks. These studies allow for the isolation of cognitive operations, apart from the speech and motor components of the task. Studies of PASAT performance in neurotypical participants that accounted for listening and speech production (i.e., included a control condition of simply repeating the numbers) found activation in the cerebellum bilaterally (Forn et al., 2008; Lockwood, Linn, Szymanski, Coad, & Wack, 2004), in the medial cerebellar cortical lobule VII (Hayter, Langdon, & Ramnani, 2007), and in the left cerebellum (Audoin et al., 2005). A research group also compared overt performance of the PASAT to covert performance (i.e., silently completing the task) in order to control for cerebellar activation due to speech production in a different paradigm (Forn et al., 2006; Form et al., 2008). Results showed that although the overt condition activated a larger region of the cerebellum, the covert condition also activated the cerebellum bilaterally. Thus, the cerebellum appears to be involved in the cognitive components of the PASAT task, even after listening and speech production are taken into account.

Imaging studies in the neurotypical population and patient studies provide preliminary evidence to suggest that the cerebellum is involved in divided attention. Within ASDs, the cerebellar role in divided attention remains unknown. However, given the cerebellar structural and functional abnormalities in ASDs, performance on divided attention tasks may also be impaired for individuals with ASDs. The research on divided attention in ASDs is relatively scarce, and variability in task type between studies make findings difficult to interpret. Given the need for a reliable and valid measure of divided

attention in ASDs, the current study will use the PASAT, a commonly used neuropsychological measure of divided attention that has been shown to activate the cerebellum in several functional imaging studies.

Few studies have systematically examined cerebellar structure in relation to behavior in individuals with ASDs. Given the evidence for cerebellar pathology in ASDs, research linking neuroanatomy to behavior is an important step in understanding a neurodevelopmental disorder whose etiology is still unknown. The current study aims to understand how cerebellar structure may be associated with attentional performance. Specifically, reduced posterior cerebellar volume is expected to be related to impairments in divided attention performance.

Chapter Two: Methods

Participants

Participants were males with high-functioning ASD (i.e., autistic disorder, Asperger's disorder, and PDD-NOS) and healthy controls. Participants were diagnosed based on criteria from the DSM-IV-TR, which was the current diagnostic manual at the time data were collected. All participants were within the ages of 18-26 years, with a Performance IQ of 85 or above. The mean age for the ASD group was 21.23 years (*SD*=2.24) and for the control group was 21.52 years (*SD*=2.27) at time of the divided attention task. Recruitment was monitored so that groups were matched for age and handedness. Participants were also screened for substance abuse and neurological problems. In addition, individuals who had contraindications to the MRI procedure, such as surgical clips and pacemakers, were excluded.

Fifteen ASD participants and 19 control participants completed the divided attention measure, and 19 ASD participants and 21 control participants completed the structural MRI scans. Because the divided attention measure was added during year two of the three-year study, fewer participants were able to complete this measure. An additional ASD participant attempted the divided attention task but was unable to complete the measure.

Participant racial and ethnic group information was available for 28 of the 40 participants. Of this group, 17 respondents self-identified as White, Non-Hispanic

(60.7%), nine identified as White or Other, Hispanic (32.1%), and two identified as Asian/Pacific Islander, Non-Hispanic (7.1%).

All participants were screened for previously diagnosed mental health concerns. Control participants were excluded if they had a history of developmental, psychiatric, or neurological disorders. ASD participants were excluded if they had bipolar disorder or schizophrenia but were included if they had diagnoses of depression, ADHD, and anxiety. Table 1 lists participants' previous diagnoses and medication use.

Table 1

Previous psychiatric diagnoses and medication use in ASD group

Group/Variable	Count	Percentage	Details
PASAT Participants (*n*=15)			
ADHD	4	26.67%	
Depression	6	40%	
Obsessive Compulsive Disorder	3	20%	
Social Anxiety	1	6.67%	
Psychiatric Medication Use	1	6.67%	Lexapro/SSRI
Structural MRI Participants (*n*=19)			
ADHD	7	36.84%	
Depression	7	36.84%	
Obsessive Compulsive Disorder	3	15.79%	
Social Anxiety	1	5.26%	
Psychiatric Medication Use	1	5.26%	Lexapro/SSRI

Instrumentation

Participants were administered autistic diagnostic measures, a brief cognitive assessment, and a divided attention task. They also completed structural brain imaging scans.

Screening

Social Communication Questionnaire (SCQ). The SCQ is a parent report questionnaire designed to screen for autism symptoms. The 40-item measure examines both current functioning and developmental history for individuals with a mental and chronological age of 2 years or older. A total score of 15 or greater indicates a possible autism spectrum disorder and a need for a full diagnostic evaluation (Rutter, Bailey, & Lord, 2003).

The SCQ has been standardized on a sample of 200 individuals with ASD. The measure has demonstrated good reliability and validity. Internal consistency estimates range from .71 to .93. The SCQ shows high accuracy in differentiating between individuals with ASD and those without ASD, with validity scores ranging from .88 to .90 (Chandler et al., 2007; Eaves, Wingert, Ho, & Mickelson, 2006; Rutter, Bailey, & Lord, 2003; Skuse, Mandy, & Scourfield, 2005).

Autism Diagnostic Interview – Revised (ADI-R). The ADI-R is a clinical interview that assesses early development, language acquisition, current functioning, and social development. Information provided by a parent/caregiver is used to inform the diagnosis of ASD. Inter-rater reliability estimates range from .93 to .97 for the three domains of reciprocal social interaction, communication, and restricted, repetitive, and stereotyped patterns of behavior (Lord, Rutter, & Le Couteur, 1994). Test-retest reliability estimates for these domains range from .93 to .97 (Lord, Storoschuk, Rutter, & Pickles, 1993).

Autism Diagnostic Observation Schedule (ADOS). The ADOS is a semi-structured assessment that allows the examiner to observe social and communication behaviors in standard contexts. The ADOS Module 4 is designed for adolescents and adults with fluent speech. Inter-rater agreement in diagnostic classification for ASD versus non-ASD was .90 for Module 4 (Lord, Rutter, DiLavore, & Risi, 2008). Inter-rater reliability ranged from .82 to .93 for algorithm totals for stereotyped behaviors and restricted interests, social interaction, communication, and communication-social interaction (Lord et al., 2008).

Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). The WASI is a brief measure of cognitive functioning that includes four subtests. The Verbal IQ is comprised of the Vocabulary and Similarities subtests, and the Performance IQ is comprised of the Matrix Reasoning and Block Design subtests. The Full Scale IQ is derived from all four subtests. Reliability for the WASI is adequate. Test-retest reliability estimates range from .83 to .95 for different subtests.

Divided Attention

The Paced Auditory Serial Addition Test (PASAT; Gronwall & Sampson, 1974). The PASAT is one of the most commonly used neuropsychological measures of divided attention (Tombaugh, 2006). Originally designed to measure functioning in patients with traumatic brain injury (i.e., TBI), the test is now widely used in Multiple Sclerosis and other disorders, including chronic fatigue syndrome and depression (Tombaugh, 2006). The PASAT has been used to assess attentional functioning in patients with cerebellar damage (Neau et al., 2000) and research points to cerebellar involvement during task

performance (Hayter, Langdon, & Ramnani, 2007; Morgen et al., 2005). There have been no published studies of PASAT performance in an ASD population.

The PASAT requires performing multiple cognitive operations simultaneously within a limited amount of time. For test administration, an audio recording of a series of single digit numbers is presented at the rate of three seconds during the first trial and two seconds during the second trial. Participants are to sum the two most recent numbers together and report the answer. This process requires recalling the previous number, listening for the new number, silently summing the two numbers, and then verbally reporting the answer within a limited amount of time (e.g., two or three seconds, depending on trial).

The PASAT has been normed on samples of healthy subjects, TBI patients, and MS patients. Reliability and validity are adequate. The split-half reliability estimate is .96 (Egan, 1988). The test-retest reliability estimates are between .93 and .97, though there are practice effects with repeated administrations (McCaffrey et al., 1995). Construct validity of the PASAT with other common measures of attention is also reported to be adequate (O'Donnell et al., 1994).

Data Acquisition of Magnetic Resonance Images

Images were acquired on a 3 Tesla GE scanner. Three-dimensional high-resolution images of the cerebellum were acquired (echo time [TE] = Min Full; Prep Time = 450; flip angle = 15; BW = 7.81; Freq = 268; Phase = 268; Locs/Slab = 152; NEX = 1; Freq Dir = S/I; Scan plane = Coronal; field of view [FOV] = 16 cm; slice thickness = 0.6) for use in tracing of the whole cerebellum and cerebellar sub-regions. A

whole-brain high-resolution scan (TE = Min; Prep Time = 500; flip angle = 11; BW = 50; Freq = 256; Phase = 192; Locs/Slab = 176; NEX = 1; Freq Dir = S/I; Scan plane = Sagittal; FOV = 25.6 cm; slice thickness = 1.0) was also acquired for use in measuring intracranial volume.

Procedure

Approval by Human Participants Committee

Approval by the Institutional Review Board at the University of Texas at Austin and the Educational Psychology Departmental Review Committee was obtained for the project. The study abided by the American Psychological Association's ethical standards of research. Data for this study were collected as part of a larger, ongoing NIH-funded study of brain structure and function in high-functioning young adult males with ASD.

Power Analyses

Power analyses were conducted using GPOWER software to determine the number of participants needed to detect a significant effect. For a one-tailed matched pairs *t*-test, 27 pairs or 54 subjects are needed to obtain a moderate effect size (d = .50) at the level of power of .80 and an alpha of .05. Post-hoc power analyses were also conducted based on the data obtained. For the three-second divided attention *t*-test, the power level was .70, with 15 matched pairs and a moderate effect size (d = .59). For the two-second divided attention analysis, the power level was .45 with a medium effect size (d = .41). For the posterior cerebellar comparison, the power level was .18 with a small effect size (d= .20).

For a Pearson correlation, 46 subjects are needed to obtain a moderate effect size (r =.35) at the level of power of .80 and an alpha of .05. Thirty-four participants were included in the correlation analyses. Post-hoc analysis reported a power level of .41, based on a small to moderate effect size (r = .242) for the correlation between the three-second task and posterior cerebellum. For the association between performance on the two-second task and posterior cerebellar volume, the power was .59, based on a moderate effect size (r = .310).

Participant Recruitment and Screening

Participants were recruited through local autism organizations and through university and community advertisements. Potential participants and their parents completed a telephone screening administered by Educational Psychology graduate students. The screening documented medical conditions, psychiatric illnesses, and current medications in addition to potential contraindications to MRI. Parents of potential participants with ASD were also administered the Social Communication Questionnaire (SCQ) by phone as a screener for autism spectrum symptoms. Participants who received a score of 15 or higher on the SCQ were considered likely to meet criteria for ASDs and were enrolled in the study, while those with scores below the cutoff were disqualified.

Following the SCQ screener, a diagnosis of an ASD was confirmed through additional testing. Participants were administered the ADI-R and the ADOS by a licensed psychologist certified in the use of these instruments for research purposes. Those participants confirmed as having an ASD were included in the study. However,

participants were not given a specific diagnosis of Asperger's disorder, autistic disorder, or PDD-NOS.

To screen for adequate intellectual functioning (PIQ ≥ 85, FSIQ ≥ 80), the Wechsler Abbreviated Scale of Intelligence (WASI) was administered by Educational Psychology graduate students. Participants with a Performance IQ below 85 and a Full Scale IQ below 80 were disqualified due to concerns with cooperation with MRI scanning and with neuropsychological assessments. For the matched pairs analyses, each ASD participant was matched to a control participant with a Performance IQ within 5 points. The matching procedure was based on previous studies (for discussion, see Allen & Courchesne, 2003; Allen, Muller, & Courchesne, 2004). It is customary in ASD research to control for differences in cognitive functioning, despite the implications of removing important effects. Given an atypical profile of abilities in ASD, specifically impaired verbal abilities and spared nonverbal abilities, Performance IQ was chosen as the matching variable.

Data Collection

For the purposes of the larger study, participants completed three separate appointments for structural imaging, functional imaging, and neuropsychological testing. ASD participants completed one additional appointment for diagnostic purposes. The Paced Auditory Serial Addition Test (PASAT) was included as part of the neuropsychological testing battery. However, the measure was added to the study during year two of the three-year study. Those participants who had already completed all three required appointments were asked to attend an additional appointment to complete the

PASAT. Most participants completed the divided attention measure within 12 months of the structural MRI scan, and all completed the measure within 19 months of the scan. All neuropsychological testing appointments were conducted in the Department of Educational Psychology at the University of Texas at Austin by trained doctoral students.

The magnetic resonance imaging appointments took place at the Imaging Research Center (IRC) at the University of Texas at Austin. Prior to scanning, participants were screened for medical conditions, metallic implants, and other contraindications to MRI. Each scanning appointment took approximately 45 minutes. The MRI scanner was operated by IRC-approved personnel.

Structural Imaging Data Analysis

Intracranial Volume

Measures of intracranial volume were obtained to control for potential differences in overall brain size. An MRI technician trained in image processing obtained intracranial volume data using the Freesurfer Program. The procedure is based on Buckner and colleagues' method (2004), which uses an atlas-based spatial normalization procedure. The Buckner et al. (2004) template is an averaged image created from 24 healthy young and old adults, using Talairach and Tournoux's (1988) atlas as a guide.

To obtain intracranial volume, each individual's brain scan was registered to the atlas template using a single affine transformation. The skull and extracranial matter were removed using thresholding and manual tracing. Then, a semi-automatic

quantification tool within Freesurfer was used to obtain the intracranial volume measurements.

Cerebellar Volume Measurement

Image analysis was performed using Analyze software (9.0; Build ADS-0442, Mayo Foundation, Rochester, Minnesota) running in a Unix environment on an iMac computer. Analyze 9.0 has visualization, registration, tracing, and classification features that allow for accurate quantification of structural data. The software allows tracing in the coronal, sagittal, and axial planes, and cross-sections of the traces can be viewed in orthogonal planes to ensure accuracy. Tracing was conducted by research assistants who had achieved at least 0.95 reliability on a practice scan for each step of the parcellation process.

The cerebellum was traced manually on the high-resolution T1-weighted images in the Analyze Region of Interest (ROI) module and saved using the Object Map function. The traced region excludes non-brain tissue (i.e., dura mater, blood vessels, etc.) and cerebrospinal fluid (CSF). Identification of cerebellar boundaries was aided by cerebellar atlases (Schmahmann, Doyon, Toga, Evans, & Petrides, 2000). The boundary between the cerebellar peduncle and cerebellar interior white matter was traced according to the procedures described by Pierson and colleagues (2002). The cerebellar peduncles were separated from the cerebellar interior white matter by marking a straight line from the most antero-lateral portion of the fourth ventricle to the edge of the brainstem-cerebellum junction. The polygon tool was used to draw straight lines of this boundary in the axial plane.

The primary fissure was identified as the boundary between the anterior cerebellum (lobules I-V) and posterior cerebellum (lobules VI-X). The boundary was manually traced in each slice of the sagittal plane and verified through coronal and axial views. Next, the posterior cerebellum was traced on every seventh slice in the sagittal view and then automatically propagated to the remaining slices. The posterior cerebellum was then saved as an object within the object map function. Following this step, a semi-automatic tool was used to differentiate between white and gray matter in the posterior cerebellum within the coronal view. Each trace was then checked for errors prior to quantification. Volumetric measurements were calculated (in mm^3) automatically using the Sample Regions feature in the ROI module. Volumes of the gray and white matter of the posterior cerebellum and the total posterior cerebellum were obtained.

Research Questions and Hypotheses

The aim of the study was (1) to examine differences in divided attention performance between ASD participants and control participants, (2) to examine differences in posterior cerebellar volume between ASD participants and control participants, and (3) to examine the relationship between posterior cerebellum volume and divided attention performance. Hypotheses were informed by previous research, which provided preliminary evidence of reduced posterior cerebellar volume and worse divided attention under high working memory demand for individuals with ASD. Past research also suggested a positive association between cerebellar volume and divided attention performance.

Research Question 1

Do adults with ASD show worse performance on divided attention tasks when compared to control participants?

Hypothesis 1

It was hypothesized that adults with ASD would exhibit worse divided attention abilities compared to control participants. Two separate paired samples t-tests were used to compare the proportion of correct items on the PASAT. The first paired samples t-test compared performance on the three-second trial of the task while the second paired samples t-test compared performance on the two- second version. For the ASD group, lower scores were expected on both trials, with worse performance on the two-second trial.

Research Question 2

Do adults with ASD have reduced posterior cerebellar volumes, as compared to control participants?

Hypothesis 2

Adults with ASD were hypothesized to have a smaller posterior cerebellar volume compared to control participants, even after controlling for intracranial volume. The proportion of posterior gray matter to intracranial volume (PCereb/ICV) was calculated for each individual to account for variation in brain size. A paired samples *t*-test was used to compare this value (PCereb/ICV) between the ASD and control participants.

Research Question 3

Is performance on the divided attention task correlated with volume of the gray matter of the posterior cerebellum in adults with ASD and control participants?

Hypothesis 3

A smaller posterior cerebellum was hypothesized to be correlated with a lower proportion correct on the PASAT in both groups. Bivariate correlations were used to compare the posterior cerebellum volume (PCereb/ICV) to the proportion of correct items on the two- second version and the three-second version of the PASAT.

Chapter Three: Statistical Analyses

Descriptive Statistics and Assumptions of Statistical Tests

SPSS statistical software was used to analyze data. Descriptive statistics, including means, standard deviations, ranges, and minimum and maximum values were analyzed for each variable. Data were also examined for outliers. Normality of variables was confirmed using histograms and skew values. The divided attention and cerebellar measures were found to be approximately normally distributed in both groups. When data were combined across the two groups, the three-second version of the divided attention task and the cerebellar data were both negatively skewed. However, the Pearson correlation is robust against violations of normality when degrees of freedom are greater than 25 (Morgan, Leech, Gloeckner, & Barrett, 2004).

Linearity was checked using scatterplots. Results indicated a possible quadratic relation between variables. However, there was no theoretical rationale for a quadratic relation, and the difference in linear and quadratic associations appeared small. Further confirmation of linearity was tested through the F test of change in R^2, using sequential multiple regression. The addition of a quadratic term $(\text{PCereb/ICV})^2$ was added to test for the presence of a curvilinear relation. Results indicated that a linear relation between the cerebellar measure (PCereb/ICV) and divided attention could be assumed, as the quadratic variable did not significantly add to the model for the two-second version of the PASAT ($\Delta R^2 = .016$, F [1,31] = .573, p =.455) or the three-second version ($\Delta R^2 = .027$, F [1,31] = .914, p = .347)

Table 2

Participant WASI Scores

Variable	*n*	*M*	*SD*	Range
Participants completing PASAT				
ASD group	15			
Full Scale IQ		117.60	11.07	92-133
Performance IQ		118.60	9.94	96-129
Control group	19			
Full Scale IQ		119.42	11.93	95-136
Performance IQ		116.42	10.62	95-132
Participants completing MRI				
ASD group	19			
Full Scale IQ		118.05	11.43	92-135
Performance IQ		118.84	9.26	96-129
Control group	21			
Full Scale IQ		120.57	11.91	95-136
Performance IQ		117.62	10.80	95-132

Table 3

Means and Standard Deviations for Main Variables (*N*=34)

Participants	Proportion correct on 3-sec. PASAT	Proportion correct on 2-sec. PASAT	GM/ICV (mm^3)
ASD (*n*=15)	0.73 ± 0.20	0.58 ± 0.21	0.070 ± 0.01
Control (*n*=19)	0.84 ± 0.11	0.67 ± 0.17	0.068 ± 0.01

Main Analysis

Hypothesis 1

Adults with ASD were expected to exhibit worse divided attention abilities compared to control participants. Lower scores were expected on both trials, with worse performance on the two-second trial.

On the three-second task, the ASD group scored significantly lower than controls, $t(14)= -2.27$, $p = .02$, one-tailed. One ASD participant became highly anxious and stopped responding on item 49 out of 60 on the three-second version of the PASAT. Thus, his score and the score from his matched control for this version of the task were omitted for a follow-up analysis, to ensure that these scores were not creating the significant effect. With the omitted pair, there was still a significant difference in scores between groups, $t(13) = -1.94$, $p = .04$, one-tailed.

On the two-second version of the PASAT, there was not a significant difference in performance between groups, $t(14)= -1.61$, $p = .06$, one-tailed. However, the mean proportion correct for control participants (M=0.67) was higher than for ASD participants (M=0.58). Contrary to the hypothesis, participants with ASD scored lower than controls on the three- second version of the task but performed similarly to controls on the two-second version.

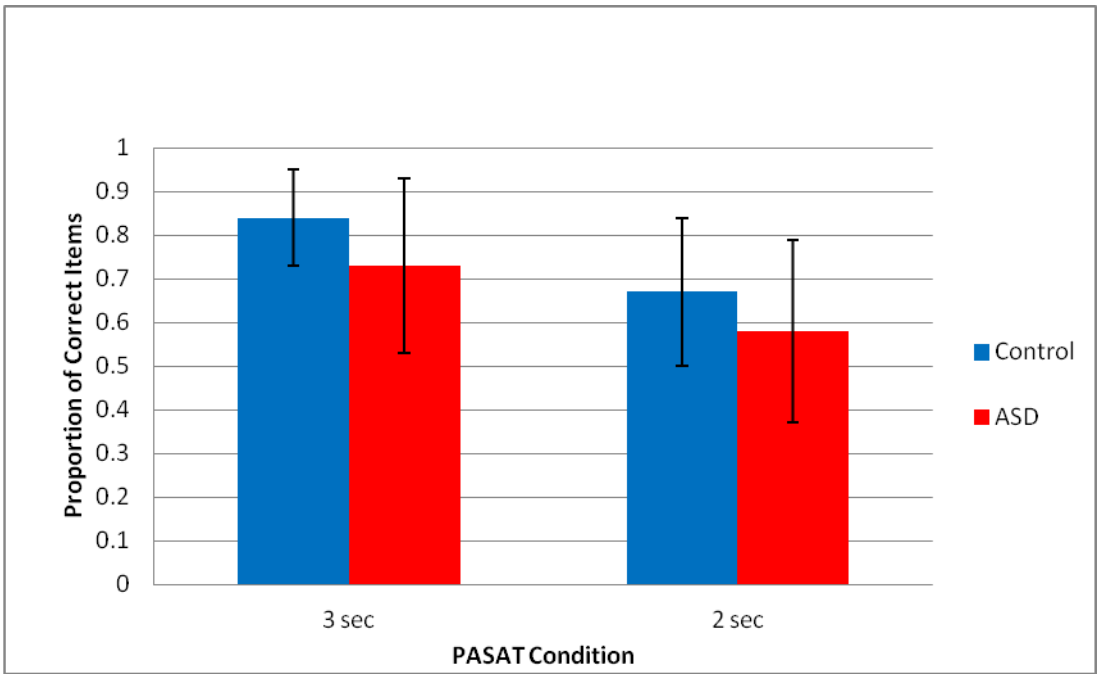


Figure 1. Comparison of group performance on the PASAT. This figure shows the mean proportion of correct items on the three-second and two-second version of the PASAT task. The bars represent standard deviations from the mean.

Hypothesis 2

Adults with ASD were expected to have a smaller posterior cerebellar gray matter volume compared to control participants, even after controlling for intracranial volume. A paired samples *t*-test was used to compare posterior cerebellar gray matter volume (PCereb/ICV) between the ASD and control participants. There was not a significant difference between groups, $t(14) = .763$, $p = .229$, one-tailed. This finding did not support the directional hypothesis of the ASD group having a smaller posterior cerebellar gray matter volume. Additional paired samples *t*-tests found no group differences in

overall posterior cerebellar volume and posterior cerebellar white matter volume. Tests included both uncorrected and corrected volumes, accounting for intracranial volume.

Because there were additional structural MRI data for participants who did not complete the PASAT, a follow-up matched pairs *t*-test was conducted as well. There were 19 matched pairs, based on PIQ within 5 points. There was not a significant difference in scores between matched pairs of control (M = .069 , SD = .007) and ASD participants (M = .070 , SD = .006); $t(18) = .273$, $p = .394$, one-tailed, on posterior cerebellar volume, controlling for intracranial volume.

Hypothesis 3

A smaller posterior cerebellum was hypothesized to be correlated with a lower proportion of correct items on the PASAT. For the three-second version of the task, there was a small to moderate association between task performance and posterior cerebellar volume that was not statistically significant, r (32) = .24, p = .08, one-tailed. For the two-second version of the task, there was a statistically significant association between task performance and posterior cerebellar volume, $r(32) = .31$, p =.04, one-tailed.

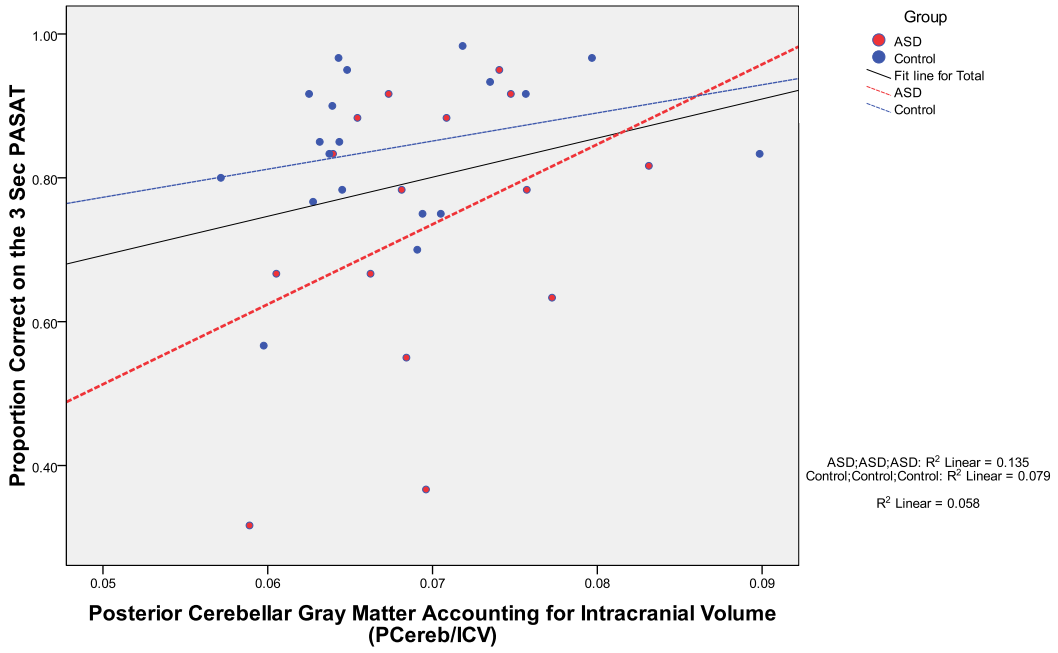


Figure 2. Cerebellar volume and three-second PASAT performance. This figure shows the association between posterior cerebellar volume (PCereb/ICV) and proportion of correct items on the three-second version of the PASAT .

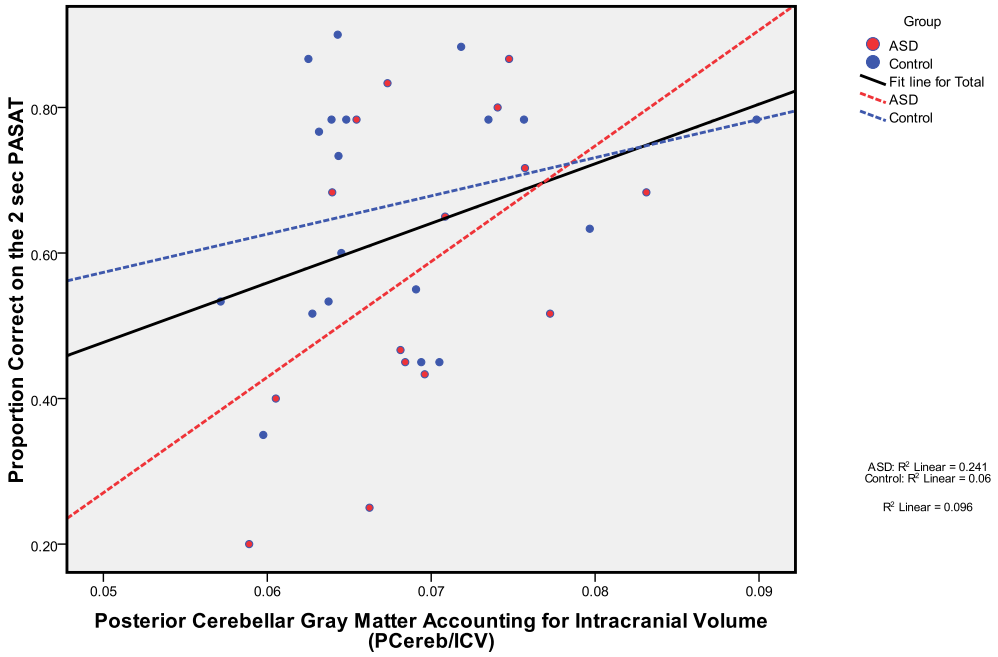


Figure 3. Cerebellar volume and two-second PASAT performance. This figure shows the association between posterior cerebellar volume (PCereb/ICV) and proportion of correct items on the two-second version of the PASAT .

Exploratory Analysis

Within Group Analyses

Follow up analyses included bivariate correlations within the ASD group and control group. Assumptions of the Pearson correlation were checked prior to analysis. Due to worse divided attention performance and past research indicating reduced posterior cerebellar volume, a stronger correlation between volume and performance was expected in the ASD group. However, concerns about inadequate power and small sample size prevented an a priori hypothesis concerning a group interaction effect.

Within the ASD group, there was a moderate correlation between proportion

correct on the three-second task and posterior gray matter that was not statistically significant, $r(13) = .368$, $p = .09$, one-tailed. For the two-second version, there was a significant positive association between proportion correct and posterior gray matter volume, $r(13) = .491$, $p = .03$, one-tailed. For the control group, there was not a significant association between divided attention performance and posterior cerebellar volume for either condition. For the three-second task, the correlation was small, $r(17) = .28$, $p = .12$. For the two-second task, the correlation was also small, $r(17) = .25$, $p = .16$.

Multiple Regression Analyses

Given that the association between divided attention performance and posterior cerebellar volume appeared to differ by group, multiple regression analyses were used to test the significance of this apparent difference. Prior to analysis, the assumptions for multiple regression were examined. Normal distribution of residuals was confirmed using a p-p plot of observed and expected values. Data also met the assumption of multicollinearity.

In order to test for an interaction between group and volume on attention, sequential regression analyses were conducted for both the three-second and two-second version of the PASAT. An a priori power analysis indicated that for a multiple regression with three predictors, 55 subjects are needed to obtain a moderate effect size (f^2=.15) at the level of power of .80 and an alpha of .05. Thus, the actual sample size (N=34) was less than adequate. With these limitations in mind, multiple regression analyses were conducted.

Divided attention (proportion correct on the three-second PASAT) was first regressed on Group (ASD or control) and Posterior Cerebellum (PCereb/ICV_Centered) using simultaneous multiple regression. These two variables accounted for 20.4% of the variance in divided attention on the three-second version of the PASAT (F=3.978 [2,31], p = .029). By itself, group membership had a significant effect on divided attention (b = -.123, t[31] = -2.383, p = .024). However, posterior cerebellar volume (PCereb/ICV_Centered) did not have a significant independent effect on divided attention (b = 6.470, t[31] = 1.784, p = .084). The interaction term (Group_Cerebellum) was added to the equation in the second step of the sequential regression.

The addition of the interaction term did not lead to a statistically significant increase in R^2 (ΔR^2 = .023, F [1,30] = .902, p = .350). Thus, this regression analysis indicated that the effect of posterior cerebellar volume on divided attention performance (i.e., proportion correct on the three-second PASAT) did not differ significantly between groups.

The significance of the interaction was also tested for the two-second condition of the PASAT. Group membership and posterior cerebellar volume accounted for 11.4% of the variance in divided attention on the two-second task (F= 3.117 [2,31], p = .058). By itself, group membership did not have a significant effect on divided attention (b= -.101, t[31] = -1.627, p = .114). However, posterior cerebellar volume (PCereb/ICV_Centered) did have a significant effect on divided attention (b = 9.031, t[31] = 2.075, p = .046). The addition of the interaction term did not lead to a statistically significant increase in R^2 (ΔR^2 = .037, F [1,30] = 1.384, p = .249). The analysis indicated that the effect of posterior

cerebellar volume on divided attention performance (i.e., proportion correct on the two-second PASAT) did not differ significantly between groups, despite correlation analyses indicating a strong association within the ASD group and a weak association within the control group. Inadequate power may have affected the ability to detect a significant group difference in this effect.

Chapter Four: Discussion

Overview of Findings

The current study sought to examine the association between divided attention and posterior cerebellar gray matter volume. Group differences in divided attention performance and posterior cerebellar volume were also examined. The PASAT, one of the most widely administered neuropsychological measures of divided attention, had not previously been used for research purposes with an ASD population. Furthermore, though previous research has found that individuals with ASDs tend to show an overly narrow focus of attention, impaired disengaging and rapidly orienting attention, and impaired shifting attention between sensory modalities, less is known about divided attention abilities in ASD. Divided attention, or the ability to respond to more than one task simultaneously, is an important skill for navigating complex social, communicative, academic, and professional settings. The present study also contributes to research linking brain structure to behavior, which is particularly needed given the behavioral heterogeneity and cerebellar pathology associated with ASDs.

Results showed worse divided attention performance for individuals with ASDs, though the difference was only statistically significant in one condition. When matched on Performance IQ, individuals with ASDs demonstrated a significantly lower proportion correct on the three-second version of the divided attention measure, as compared to control participants. On the two-second version, individuals with ASDs showed a lower mean proportion correct, but the difference was non-significant. Effect sizes were in the

medium range in both conditions, and the power was lower than adequate for detecting a medium effect size.

For the control group, the demands of the two-second condition led to more within-group variability than in the three-second condition. This variability appears to have contributed to the non-significant group difference in the two-second condition, given the similar mean group differences in both conditions. It appears that for both groups the added time pressure of the two-second condition taxed the attentional system more than the three-second task. Of note, when compared to the normative sample, neither group's performance indicated impaired divided attention abilities suggestive of major neuropsychological impairment.

Previous research has found Purkinje cell reduction in autistic posterior cerebella and reduced cerebellar gray matter volume. Thus, a smaller posterior gray matter volume was expected for the ASD group in the current study. However, results indicated no difference in posterior gray matter volume, controlling for intracranial volume, between ASD and control participants. Various participant and methodological factors may have contributed to the non-significant difference. Participants were all of average to superior intelligence and young adult males, and groups were matched for age, nonverbal IQ, and handedness. Thus, it is possible that age and cognitive ability, among other variables, may be important to consider when studying cerebellar differences in ASD. Furthermore, the present study examined a relatively large region (cerebellar lobules VI-X) using both manual and semi-automatic tracing methods. It is possible that a different tracing

methodology allowing for more precise measurement of each subregion may have detected differences.

Results indicated a statistically significant positive association between posterior cerebellar volume and divided attention performance on the two-second condition of the PASAT. However, for the three-second condition, there was a non-significant small to moderate association between variables. Follow-up analyses found medium to strong associations between task performance and posterior cerebellar volume in the ASD group and weak associations between these variables in the control group.

Integration of Findings with Previous Research

Cerebellar Volume

Unexpectedly, the current study found no group differences in posterior cerebellar gray matter volume, overall posterior cerebellar volume, and posterior cerebellar white matter volume. Controlling for intracranial volume did not affect findings. All ASD and control participants were males of average to superior intelligence between the ages of 18 and 26 years with Performance IQ scores between 95 and 132. Groups were matched on handedness and age, and analyses included matched pairs based on Performance IQ within 5 points.

No prior structural MRI studies had specifically examined posterior cerebellar volume (i.e., hemispheric and vermis lobules VI-X) in ASDs. However, postmortem findings of Purkinje cell reduction in the posterior cerebellum (Bauman & Kemper, 1985; Kemper & Bauman, 1998; Whitney et al., 2008) and structural imaging findings of

reduced overall cerebellar volumes in adults with ASDs (Courchesne et al., 2001; Hallahan et al., 2009) guided hypotheses.

A closer examination of previous studies indicates participant and methodological factors that likely contributed to differences in findings. Postmortem studies indicating Purkinje cell reduction in posterior cerebella were based on samples of lower functioning individuals with autistic disorder, across a wide age range (i.e., six to 54 years old) (Bauman & Kemper, 1985; Kemper & Bauman, 1998; Whitney et al., 2008). Participants included nonverbal individuals and those who could only follow simple commands. Thus, participant age and cognitive abilities differed substantially from the present study's sample of high-functioning young adult males.

Structural imaging findings also appear to differ markedly based on participant and methodological factors. Age is an important factor to consider, as research indicates atypical white and gray matter trajectories over development in ASDs, marked by early overproduction of white matter and later reduced gray matter (Courchesne et al., 2001). Consistent with these developmental trajectories, larger overall cerebellar volume in children with ASDs ages three to 11 years old (Herbert et al., 2003; Sparks et al., 2002) and reduced overall cerebellar volumes in adolescents and adults with ASDs (Courchesne et al., 2001; Hallahan et al., 2009) have been reported, though cerebellar findings in adults have been inconsistent (Palmen et al., 2004; Piven et al., 1992).

It is possible that cerebellar volume may also differ based on diagnostic classification and cognitive abilities. The two studies finding reduced cerebellar volume in adolescents and adults differed in participant inclusion criteria. Courchesne and

colleagues' (2001) ASD sample included only those with autistic disorder and did not account for cognitive ability, which differed markedly between groups (i.e., autistic nonverbal IQ: 36-122 and control nonverbal IQ: 90 to 144). Hallahan et al.'s (2009) study included participants with autistic disorder, Asperger's, and PDD-NOS and found cerebellar reductions compared to controls, even after correcting for both intracranial volume and IQ (Hallahan et al., 2009). Cerebellar regional abnormalities have also been found, based on cognitive ability. Specifically, individuals with high-functioning autistic disorder had reduced overall cerebellar volume while those with low-functioning autistic disorder had reductions only in the left cerebellum (Hallahan et al., 2009).

Of note, one study reported increased overall cerebellar volume in ASDs, though this group difference was no longer significant when taking into account intracranial volume (Palmen et al., 2004). The participant sample included high-functioning adolescents and young adults with an autism spectrum disorder and controls matched for gender, age, IQ, height, weight, handedness, and parental education. Another study of individuals with high-functioning ASDs and controls with comparable age and IQ found no group differences in lobules VI- VII, based on mid-sagittal ratio measurements (Piven et al., 1992). These two studies are somewhat consistent with the current study's findings of no group differences in posterior cerebellar gray matter, after accounting for IQ, age, gender, and handedness.

Given discrepant findings across studies, many questions remain regarding cerebellar structure in autism spectrum disorders. Image analysis methodology differed across existing studies and included semi-automated model-based segmentation, mid-

sagittal ratio measurements, and manual tracing, which may have contributed to differences in findings. Furthermore, the effect of participant age, IQ, diagnostic category, and symptom severity on cerebellar structure remains unclear and warrants future investigation. Finally, the current study used a relatively gross measure of posterior cerebellar volume, which may not have had significant resolution to detect small differences if they were present.

Divided Attention

The substantial literature on attentional functioning in ASDs has found overly selective attention, impaired shifting attention, and impaired rapid orienting of attention in ASDs (Allen & Courchesne, 2001). However, fewer studies have examined divided attention in ASDs, and there is considerable variability in task type between studies. Based on existing studies, performance on divided attention tasks with high working memory demand appears to be impaired in both single modality auditory (Yerys et al., 2011) and cross-modality auditory and visual paradigms (Casey, Gordon, Mannheim, & Rumsey, 1993; Garcia-Villamisar & Della Sala, 2002; Sinzig, Bruning, Morsch & Lehmkuhl, 2008).

Results of the present study were consistent with previous findings and demonstrated group differences using a reliable, commonly administered neuropsychological measure of divided attention. Participants with ASDs showed worse performance on the PASAT, as evidenced by a statistically significant group difference in the three-second condition and moderate group effect sizes for both conditions.

The finding of weaker divided attention abilities in ASD is consistent with the pattern of overselective attention and impaired disengaging and rapidly orienting attention in this population. Divided attention requires either parallel processing or rapid switching between tasks, and an overselective attentional lens and difficulties with disengaging and orienting of attention likely interfere with these processes. Furthermore, weaker divided attention abilities may reflect a more simplistic attentional system that is resistant to modulation, as suggested by Ciesielski and colleagues (1995). It has been suggested that individuals with ASDs have an alternative compensatory attentional mechanism, which is relatively effective for focused attention tasks but less effective for divided attention situations.

The current study also suggests that weaker divided attention abilities under high working memory demand persist into young adulthood, even in a high-functioning ASD population. Yerys and colleagues (2011) found weaker divided attention abilities in a sample of children with high-functioning ASD, and the present study provides preliminary evidence for continued difficulty in young adulthood. Difficulty with divided attention across development has important implications for social, adaptive, academic, and professional functioning. Processing and integrating social information, balancing competing demands, and keeping track of various deadlines or projects all become difficult under weaker divided attention capability.

Divided Attention and Cerebellar Volume

The current study found partial support for a positive association between divided attention performance and posterior gray matter volume. Results indicated a statistically

significant association on the two-second version of the PASAT when data were combined across groups. No prior studies had examined the relation between divided attention performance and cerebellar structure in ASDs. However, one prior study found an association between selective attention performance and the size of the Crus I, a subregion of the posterior cerebellum (Allen & Courchesne, 2003).

Findings from patient studies (i.e., studies involving patients with focal cerebellar lesions or isolated cerebellar infarcts) suggested that cerebellar pathology was associated with impaired divided attention (Gottwald, Mihajlovic, Wilde, & Mehdorn, 2003; Gottwald, Wilde, Mihajlovic, & Mehdorn, 2004), with one study specifically demonstrating impaired performance on the PASAT (Neau, Anllo, Bonnaud, Ingrand, & Gil, 2000). A voxel-based morphometry study also found an association between PASAT performance and gray matter volume in the right cerebellum for patients with Relapsing Remitting Multiple Sclerosis (Morgen, et al., 2006).

Implications

The findings from the current study have important implications, particularly for a high-functioning ASD population. In particular, weaker divided attention abilities within the context of average or above average intellectual functioning suggest an area of needed intervention or accommodation in order to build skills or reduce frustration. Divided attention involves the abilities to disengage and shift attention and to focus attention simultaneously on more than one task, which have all been found to be impaired in ASD. Thus, skills training for improving divided attention abilities may be particularly challenging, given the unique attentional profile in ASD. A core feature of ASD is

stereotyped and repetitive interests and behaviors, which is reflective of an overly selective lens. Furthermore, an insistence on sameness, difficulty deviating from routine, and problems deciphering nonverbal social cues also characterize ASD and are likely impacted by attentional atypicalities. These skills all require explicit instruction to learn, even for high-functioning individuals with ASDs. Oftentimes, accommodations in academic environments are necessary. Unfortunately, in social situations and professional settings, accommodations are not provided, particularly for individuals with average or above average intelligence who appear otherwise highly capable.

For individuals with ASDs, weaker divided attention has important implications for everyday settings. In order to successfully adapt to social, educational, and professional settings as a young adult and beyond, the ability to adjust to changes in scheduling and to simultaneously juggle deadlines, workplace social politics, and demands from bosses is crucial. On top of managing academic and professional demands, balancing the complexities of friendships, romantic relationships, and everyday adaptive functioning skills also presents challenges. Under this pressure, it is likely that the attentional system can become highly taxed, particularly under time demands. For those individuals with high-functioning ASDs that attend higher education institutions, mentorship programs to aid with adaptive functioning, organization, and social skills are sometimes available and may help accommodate and teach skills. In addition, choosing a profession that complements the attentional profile of weaker divided attention and stronger selective attention may be beneficial. Computer programming, engineering, or research may all be fields where overly selective attention and weaker divided attention is

useful. Individuals who choose professions that require higher divided attention demands may benefit from extra organizational and social skills support.

Limitations and Future Directions

The present study had several limitations, which should be taken into account when interpreting findings. The small sample size, particularly for the divided attention measure, limited the power to detect effects. Results of several tests indicated moderate effect sizes but were not statistically significant. In addition to increasing power, a larger sample size would allow for examination of covariates, or possible factors contributing to variables of interest. For example, participant characteristics including height, weight, and parental education could be examined. Furthermore, future studies with larger sample sizes would allow for comparison across subgroups of autism spectrum disorders, either based on diagnostic categories or symptom severity.

The study included only high-functioning young adult males with average to superior cognitive abilities. Given the heterogeneity within the autism spectrum, it is difficult to generalize findings to individuals with ASDs of different ages, cognitive abilities, and gender. On the other hand, the participant group also varied in specific diagnosis and comorbidity, which may have introduced potential confounds. Several ASD participants had diagnoses of depression, ADHD, and obsessive compulsive disorder, which were not accounted for in the study methodology or statistical analyses. Comorbidity in ASD is very common, with reports indicating that 70% of the ASD population has at least one comorbid disorder (Simonoff et al., 2008). Furthermore, individuals with ASDs are often misdiagnosed with psychiatric disorders that actually

reflect ASD symptoms, rather than a true comorbidity (Ghaziuddin, Weidmer-Mikhail, & Ghaziuddin, 1998; Mandell, Ittenbach, Levy, & Pinto-Martin, 2007). Thus, the current study did not exclude ASD participants with comorbid diagnoses. However, it is possible that this diagnostic comorbidity may have influenced results on both cerebellar and attentional measures. There is some evidence to indicate that clinically significant depression can affect PASAT performance (Arnett et al., 1999; Thornton & Raz, 1997), though there is also evidence of no effect (DeLuca, Johnson, Beldowicz, & Natelson, 1995).

Particularly with ASD and ADHD, there has been some controversy regarding the validity of comorbid diagnoses. Whether attentional functioning is a primary component of ASD, rather than an additional feature warranting a separate diagnosis is debated. Though the present study assumed that atypical attentional functioning is a component of ASD and did not control for comorbidity of diagnosis, there may be concern about the effect of comorbidity on divided attention performance. To address this, future studies could examine attentional functioning using several groups, including an ASD group, an ADHD group, and an ASD and ADHD comorbid group, in addition to a control group.

Another limitation is that the PASAT is a sensitive but nonspecific measure of neuropsychological functioning. It measures divided attention under high working memory demand in addition to mathematical ability, auditory processing, and verbal expression/speech. Due to the small sample size, controlling for all these variables would not have allowed for adequate power in the model. The PASAT also tests only the auditory modality and does not provide a measure of cross-modality visual and auditory

divided attention. Furthermore, neuropsychological assessments measure functioning in a controlled setting. Thus, though measuring divided attention under high working memory demand is thought to be relevant to real world abilities, it is not a direct measure of everyday functioning.

Finally, limitations related to methodology and participant characteristics likely affected measures of structural volume. Given that participants were all high-functioning young adult males, cognitive abilities, age, and gender may be important variables contributing to cerebellar differences in ASDs. Furthermore, the posterior cerebellum is a large region that includes several subregions (i.e., hemispheric and vermis lobules VI-X). It is possible that there may have been group differences in subregions within the posterior cerebellum but not the total posterior cerebellum. Quantification of the total posterior cerebellum may have resulted in missing differences between these subregions. However, the present study limited quantification to the posterior cerebellum due to time-intensive nature of manual and semi-automatic tracing procedures.

Continued research is needed to address these limitations. Studies with larger sample sizes that allow for consideration of age, gender, cognitive ability, symptom severity, and comorbid diagnoses are particularly necessary, given the heterogeneity of the disorder and the discrepant findings in the literature. In addition, longitudinal studies that include concurrent imaging and behavioral data would also allow for better understanding of brain-behavior relationships across development.

Conclusion

Autism spectrum disorder is one of the most prevalent developmental disabilities, with recent estimates reporting that one in every 88 children meet criteria for the disorder. The etiology remains unknown, but existing research suggests both genetic and environmental risk factors. Functional and structural brain differences are associated with ASDs, and the cerebellum is the most consistently reported site of abnormality. There appears to be an atypical trajectory of white and gray matter growth across development, though whether these structural abnormalities persist in adolescence and adulthood remains a question. There have been inconsistent findings across studies, likely due to differences in methodological and participant characteristics. Attentional abnormalities are also highly reported in ASDs, though divided attention is a less studied area of research. Existing research suggests weaker divided attention abilities in ASDs, particularly under high working memory demand.

The present study helps to clarify and expand upon knowledge of divided attention and brain-behavior relationships in a high-functioning young adult ASD population. Groups were matched for age, handedness, and cognitive abilities. Results indicated partial support for weaker divided attention abilities in ASDs and an association between attentional performance and posterior cerebellar volume. There were no group differences in posterior cerebellar volume. Limitations included a small sample size, which limited the power to detect effects. Possible confounding variables, including diagnostic category, comorbid diagnoses, and educational level, were not examined. Thus, results should be interpreted with these limitations in mind. Future studies are

needed to better understand brain structure and function across development and across the autism spectrum, accounting for age, cognitive ability, and symptom severity, among other variables. The present study provides preliminary support for weaker divided attention abilities under high working memory demand and an association between attentional performance and cerebellar structure.

Appendix A: Literature Review

Autism Spectrum Disorders

History of ASD and Diagnostic Changes

The first clinical accounts of ASD were published by an American psychiatrist Leo Kanner, in 1943, and by an Austrian psychiatrist Hans Asperger, in 1944. Though the two clinicians described similar disorders, they were unaware of each others' work, as Kanner published his account in English while Asperger published in German. In fact, it was not until the 1980s that Asperger's work became known in the English language literature. In 1981, Lorna Wing used the phrase "Asperger's Syndrome" to describe a sample of children with social impairments, and subsequently, Asperger's Syndrome became used to describe individuals of average intelligence but unusual social behaviors.

In Kanner's account of children with "autistic disturbances of affective contact," he described children who appeared emotionally indifferent to other people and rigidly adhered to routines and rituals (1943, p.217). The children Kanner described also exhibited severe language delays. Some were mute while others displayed echolalia, repeating words verbatim without regard to the appropriateness of the conversational context. The adolescents that Asperger described also had difficulties with social communication but appeared to have average or above average intelligence and language skills. Asperger used the phrase "autistic psychopathy" to describe the behaviors he observed. The key features he identified were abnormal prosody, impaired empathy, and restricted interests (Wing, 1981).

Kanner-type autism was first included in the Diagnostic and Statistical Manual (DSM-III, American Psychiatric Association) in 1980 under the name of "Infantile Autism" within a new category called Pervasive Developmental Disorders (PDDs). "Childhood Onset PDD" and "Atypical PDD" were also included in the PDDs category but were not considered to be autism disorders. In 1987, "Infantile Autism" was renamed "Autistic Disorder" in a revised version of the DSM (DSM-III-R, American Psychiatric Association). At this time, autism was conceptualized as a single distinct disorder marked by impaired language and intellectual functioning, in addition to deficits in social reciprocity and repetitive behaviors. However, accounts of individuals who displayed social impairments and restricted interests but had no history of language or cognitive impairments began to emerge in the literature. As a result, the conceptualization of autism began to broaden to include a spectrum of related disorders that shared common features of social impairment and restricted behaviors and interests, rather than a single disorder. In 1994, "Asperger's Disorder" was added to the DSM as a subtype of autism spectrum disorders within the PDDs category (DSM-IV, American Psychiatric Association).

The following version of the DSM (DSM-IV-TR, American Psychiatric Association, 2000) reflected the view of autism as a spectrum of disorders with distinct subcategories. The DSM-IV-TR included ASDs under a wider category of Pervasive Developmental Disorders (PDDs). Within ASDs, there were subtypes of autistic disorder, Asperger's disorder, and pervasive developmental disorder – not otherwise specified (PDD-NOS). A diagnosis of Asperger's disorder required normal development

of language, cognitive skills, and adaptive behavior whereas a diagnosis of autistic disorder required delays in language, social interaction, symbolic play, and restricted interests prior to three years of age. A diagnosis of PDD-NOS was appropriate when an individual exhibited a marked impairment in reciprocal social interaction but did not meet full symptom criteria for autistic disorder or Asperger's disorder.

Previous to the most recent version of the DSM (DSM-V, American Psychiatric Association, 2013), there was considerable controversy about whether autistic disorder, Asperger's disorder, and PDD-NOS represented qualitatively distinct diagnoses or whether the disorders were better understood as a single disorder (ASD) with varying degrees of severity. Though researchers and practitioners agreed that there was wide variability in symptom presentation within ASDs, the categories and diagnostic criteria in the DSM-IV-TR did not adequately identify distinct qualitative differences between groups. Thus, a decision was made to do away with the separate diagnoses in favor of a broader diagnosis of autism spectrum disorder for the DSM-V.

Practitioners showed a low rate of reliability and validity when distinguishing between autistic disorder, Asperger's disorder, and PDD-NOS. Diagnoses tended to be made based on severity, language level, and intelligence rather than on symptom criteria that distinguish between disorders. Though the prevalence of ASD in the population was fairly consistent across studies, the prevalence of subtypes of ASD tended to vary widely from study to study, indicating diagnostic imprecision between clinicians (Lord & Bishop, 2010). Among autistic disorder, Asperger's disorder, and PDD-NOS, when the

patient's language level and intelligence level were controlled, there were wide discrepancies in clinician diagnosis (Rosenberg et al., 2009).

The current DSM-V diagnostic criteria for ASD fall under two symptom domains of social-communication and restricted, repetitive interests. Distinctions between individuals with ASD are based on severity in relation to chronological age and developmental levels (Lord & Bishop, 2010). The revised DSM-V criteria require more symptom behaviors than the DSM-IV-TR, including all three subdomains within the social-communication category (i.e., marked deficits in nonverbal communication, lack of social reciprocity, peer relationships) and two of the three subdomains in the restricted, repetitive behaviors category (i.e., stereotyped motor or verbal behaviors; routines and rituals; and restricted, fixated interests).

Given the diagnostic imprecision in discerning subtypes of ASDs, it was reasonable to eliminate the separate categories of Asperger's disorder, autistic disorder, and PDD-NOS. However, classifying individuals of widely variable symptom presentation under the single diagnosis of autism spectrum disorder is also an inadequate solution. The heterogeneity in intelligence level, adaptive functioning, language, and presentation of social abnormalities within the autism spectrum points to the need for continued research to identify potential subtypes that represent true qualitative distinctions. Research linking neuroanatomical abnormalities to behavioral symptoms within a group of individuals with ASDs could help in the identification of these subtypes.

Prevalence and Etiology

Epidemiological studies have reported increasing prevalence rates since autism was first identified in 1943. Prior to the 1980s, estimates of autism included only Kanner-type autistic disorder, and the rates were approximately one in every 2000 children (Fombonne, 2009; Rutter, 2005). Since then, prevalence rates have included a wider spectrum of disorders. In 2000, an estimated one in every 150 children in the United States had ASD, which is a drastically higher incidence compared to early epidemiological studies (Autism and Developmental Disabilities Monitoring [ADDM], 2012). The most recent estimates report an even higher rate of ASD. In 2012, the rate was one in every 88 children (ADDM, 2012). ASD is five times more common in males, with the prevalence being one in every 54 boys and one in every 252 girls (ADDM, 2012).

The increased prevalence of ASD in recent years is concurrent to recent changes in diagnostic criteria that allow for the inclusion of a wider spectrum of autistic behavior, in addition to an increased public awareness of the disorder and methodological differences between studies (Fombonne, 2005; Wing & Potter, 2002). However, the rising prevalence has also raised concerns about possible environmental causes. Prenatal viral exposure, early childhood vaccinations, and antibiotics have all been hypothesized to trigger ASD. Currently, evidence for environmental factors is inconclusive (Miller & Reynolds, 2009), and studies have not yet found convincing evidence for these hypotheses (Fallon, 2005; Kawashima et al., 2000; Libbey, Sweeten, McMahon, & Fujinami, 2005). However, there is some preliminary evidence suggesting environmental

factors, including industrial mercury exposure (Palmer, Blanchard, & Wood, 2009) and prenatal exposure to antidepressants (Croen, Grether, Yoshida, Odouli, & Hendrick, 2011), may contribute to ASD. More research is needed to understand if environmental variables may trigger ASD. It is possible that individuals who have a genetic susceptibility to ASD are more sensitive to prenatal or postnatal exposure to chemical or biological environmental agents, which serve as triggers to the expression of ASD.

A recent meta-analysis (2011) examining 64 studies of prenatal and neonatal risk factors in autism published through March 2007 found that although there was not one clear factor contributing to an ASD diagnosis, a broad number of risk factors associated with compromised health may increase susceptibility to ASD, including umbilical-cord complications, fetal distress, birth injury or trauma, and neonatal anemia. A metaanalysis of prenatal risk factors associated with ASD by the same research group (2009) similarly found evidence for a number of risk factors that could increase risk of ASD, including maternal prenatal medication use, gestational diabetes, and advanced parental age (Gardener, Spiegelman, & Buka, 2009).

The etiology of ASD is unknown. However, research suggests a strong genetic basis, in interaction with environmental factors (Folstein & Rosen-Sheidley, 2001; Moy & Nadler, 2008). Heritability estimates for ASD, calculated from twin concordance rates and recurrence risks in siblings, is above 90%, making ASD one of the most heritable neuropsychiatric disorders (Bonora et al., 2006). The concordance rate of ASD for monozygotic twins is between 60% and 96% (Boyle, Van Naarden Braun, & Yeargin-Allsopp, 2005). In addition, the concordance rate for monozygotic twins is significantly

higher than for dizygotic twins, which is estimated to be between 0% and 24% (Bailey et al., 1995; Boyle et al., 2005; Ritvo, Freeman, Mason-Brothers, Mo, & Ritvo, 1985). The evidence for a genetic component in ASD is strong; however, the genetic model for ASD susceptibility is complex and does not follow a simple monogenic inheritance pattern (Bonora et al., 2006). Further research is needed to better understand the modes of genetic transmission in ASD.

Brain Abnormalities in ASD

There is evidence for neuropathological and structural brain abnormalities in ASD. Several brain regions have been found to be atypical, including the cerebellum, the hippocampus, the amygdala, and the anterior cingulate gyrus (Acosta & Pearl, 2004; Bauman, Anderson, Perry, & Ray, 2006; Folstein & Rowen-Sheidley, 2001). Additionally, there is a reported increase in overall brain volume early in development. Measures of head circumference suggest that at birth, brain volume is not significantly different in ASD. However, by two years of age, overall brain volume appears to be increased, evidenced by measures of head circumference, structural MRI studies, and postmortem studies of children (for review, see Bauman, Anderson, Perry, & Ray, 2006).

Structural MRI studies of children between the ages of two and four years report that the frontal lobes are particularly enlarged, with less change occurring in the occipital lobe (for review, see Carper, Wideman, & Courchesne, 2006). Some researchers interpret this finding to mean that the frontal cortex, which is associated with higher-level tasks, is a primary area of abnormality in ASD. However, other researchers suggest that atypicalities in other cerebral areas may occur prior to two years of age and that further

studies examining brain development in infancy are necessary to understand cerebral development patterns. Following this early brain overgrowth, development appears to slow. By adolescence and adulthood, overall brain volume no longer differs significantly in ASD.

Postmortem and structural MRI studies suggest that areas of the limbic system may develop abnormally in ASD. Serial section studies of adult postmortem brains from one laboratory (Bauman & Kemper, 1985; Bauman & Kemper, 1994) found smaller neuronal cell size, higher cell packing density, and underdeveloped dendritic arbors in the hippocampus, medial amygdala, medial mammillary body, and anterior cingulate gyrus. This pattern is typically associated with early stages of brain development. Thus, these findings suggest that development of limbic areas may be prematurely curtailed in ASD. However, a more recent stereological study of postmortem brains did not replicate findings of atypical neuronal development in limbic structures (Schumann & Amaral, 2005), which points to the need of further research to confirm these preliminary findings.

The Cerebellum

Cerebellar Anatomy

The cerebellum is a highly compact structure, representing only 10% of the brain's volume but containing more neurons than the remainder of the brain combined (Ito, 1984; Williams & Herrup, 1988). The cerebellum is made up of two hemispheres, and the medial gray matter region is called the vermis. The principal neurons of the cerebellar cortex are the Purkinje cells, which integrate incoming information from the

rest of the brain. The Purkinje cells are also the sole source of output from the cerebellar cortex, and they have inhibitory connections with nuclei that are situated deep within the hemispheres. The Purkinje cells inhibit output from these nuclei (the fastigial, globose, emboliform, and dentate) that project to other regions of the brain (Eccles & Szentgothai, 1967).

Classification systems for subregions of the cerebellum are based on anatomical, phylogenetic, and functional divisions (Allen et al., in press; Barlow, 2002). Anatomically, the anterior lobe is located above the primary fissure, the posterior lobe is located below the primary fissure, and the flocculonodular lobe is located below (i.e., inferior) the posterior lobe. Phylogenetically, the flocculonodular lobe is the oldest and is also called the archicerebellum. The anterior lobe (paleocerebellum) is intermediate in development, and the posterior lobe (neocerebellum) is the youngest in development. Functional regions of the cerebellum correspond to medial-lateral divisions, in addition to anterior-posterior divisions. For instance, the spinocerebellum corresponds anatomically to the vermis and the paravermis (i.e., medial cerebellum) and is responsible for limb movements. The cerebrocerebellum corresponds anatomically to the lateral cerebellar hemispheres and is responsible for motor coordination and cognitive functioning. The cerebrocerebellum receives input exclusively from the cerebrum via the pons. The functional division of the vestibulocerebellum corresponds to the flocculonodular lobe and is responsible for balance and eye movements. There is also anterior-posterior localization of functioning. Functional neuroimaging studies have found that the anterior cerebellum is responsible largely for motor tasks whereas the posterior cerebellum is

responsible for higher order tasks, such as selective attention (Allen, Buxton, Wong, & Courchesne, 1997; O'Reilly et al., 2009).

Cerebellar Function

Traditionally, the functional role of the cerebellum was understood to be exclusively one of motor coordination. However, in recent decades, evidence for the cerebellum's role in a wide range of non-motor cognitive and emotional functions has emerged. Despite this accumulating evidence, there is continued controversy about the cerebellum's role in non-motor functioning, and some researchers argue that the existing research is insufficient to demonstrate a non-motor role for the cerebellum (Frank et al., 2007; Glickstein, 2007). However, the opinion that the cerebellum is a purely motor region is becoming a minority viewpoint, as a growing number of studies support the role of the cerebellum in a range of cognitive and emotional functions.

An important study that shifted understanding of cerebellar function was a clinical report of patients with cerebellar lesions, published by Schmahmann and Sherman (1998). The researchers coined the term "cerebellar cognitive affective syndrome" to describe the behavioral changes they observed in patients, including impaired planning, set-shifting, language, and visuospatial skills, as well as flattened affect and disinhibited behavior. The researchers found that lesions to the posterior cerebellum and vermis resulted in pronounced cognitive and behavioral changes whereas lesions to the anterior cerebellum produced only minor changes.

Behavioral deficits in cerebellar patients have been confirmed by more recent studies, as well, and impairments in attention, working memory, verbal fluency, and visuospatial processing are reported (Gottwald et al., 2004; Levinsohn, Cronin-Golomb, & Schmahmann, 2000; Trillenberg, Verleger, Teetzmann, Wascher, & Wessel, 2004). Additionally, functional neuroimaging studies (Allen et al., 1997; Desmond, Gabrieli, Wagner, Ginier, & Glover, 1997; Doyon et al., 2002; Stoodley & Schmahmann, 2009; Xiang et al., 2003) show cerebellar activation during tasks that involve attention, reasoning and problem solving, expressive language, and positive emotion, to name a few.

There is substantial evidence for cerebellar involvement in a wide range of cognitive and emotional functions, in addition to motor functions. However, the exact role that the cerebellum plays in these functions remains unclear. Given the cerebellum's widespread anatomical connections to the rest of the brain, however, it would logically follow that the cerebellum is involved in the modulation of the cognitive, affective, and motor functions associated with these disparate brain regions. The cerebellum's large afferent: efferent ratio of 40:1 and its connection to all major divisions of the brain (Allen et al., 2005; Middleton & Strick, 2001; Schmahmann, 1996) suggests that it plays a role in integrating and analyzing incoming information in order to achieve a coordinated response.

Cerebellar Abnormalities in ASD

Postmortem Studies

Postmortem studies have consistently found cerebellar pathology in autistic brains, with the most commonly reported abnormality being a reduction in the number of Purkinje neurons (Bailey et al. 1998; Fehlow et al. 1993; Kemper and Bauman 1998; Lee et al. 2002; Ritvo et al. 1986; Vargas et al. 2005; Wegiel 2004; Whitney et al. 2008; Williams et al. 1980). It is unclear whether cell reduction is diffuse or concentrated in specific regions of the cerebellum. However, some postmortem studies report that cell reduction is restricted to the posterior cerebellum, while other cerebellar regions are normal (Bauman & Kemper, 1985; Kemper & Bauman, 1998; Whitney et al., 2008). There is also reduction of other cell types within the cerebellum, including granule cells (Bauman & Kemper, 1994; Vargas, Nascimbene, Krishnana, Zimmerman, & Pardo, 2005); however Purkinje cell reduction is the most consistently reported abnormality.

Given that ASD is thought to be caused by genetic factors, in interaction with the environment, the high sensitivity of Purkinje cells to environmental insults is particularly notable. Animal studies have shown that viral infection, mercury, and valproic acid have all been connected to Purkinje cell reduction (Hua, Brun, & Berlin, 1995; Ingram, Peckham, Tisdale, & Rodier, 2000; Pletnikov, Rubin, Moran, & Carbone, 2003; Shi et al., 2009; Sorensen, Larsen, Eide, & Schionning, 2000). Furthermore, immunochemistry studies of the human cerebellum (Whitney et al., 2009; Vargas et al., 2005) suggest that Purkinje cell reduction may occur across development, after normal prenatal periods of neurogenesis, cell migration, and synaptogenesis. The exact timing of cell reduction

remains unknown, but research suggests that Purkinje cell reduction begins prenatally and may progress into the postnatal years, possibly throughout childhood and adolescence. More research is needed to understand if environmental factors influence Purkinje cell reduction in individuals with ASD.

ASD has a strong and complex genetic component, and a large number of candidate genes have been identified. Among these candidate genes is Engrailed 2, a gene involved in cerebellar development. In mice, dysfunction of the Engrailed 2 gene results in cerebellar hypoplasia and Purkinje cell reduction, a condition that is also a key feature of ASD (Kuemerle et al., 1997). Family genetic studies through the Autism Genetic Resource Exchange have found that misexpression or impaired function of Engrailed 2 is associated with susceptibility to ASD (Gharani, 2004; Benayed et al., 2005).

Structural Imaging Studies

Imaging studies allow for in vivo examination of cerebellar structure, which has contributed to understanding of cerebellar anatomy at different stages of development. Differentiating between gray and white matter in the cerebellum is important in order to identify the precise anatomical nature of the abnormality. For instance, white matter in the cerebellum consists largely of input axons from non-cerebellar neurons, specifically projections from the cerebral cortex via the pons.

The trajectory of cerebellar gray and white matter development appears to be atypical in ASD, compared to normal controls. Early in life, cerebellar white matter is reported to be abnormally enlarged. One study reported that two to three year olds with

ASD had 39% larger cerebellar white matter volumes compared to normal controls of the same age (Courchesne et al., 2001). Following this early overgrowth, development of white matter seems to slow. The increase in cerebellar white matter between young children (ages 2 to 3 years) and adolescents (ages 12 to 16 years) with ASD is only 7%. This is in contrast to typical development, where the age-related increase in cerebellar white matter is 50% (Courchesne et al., 2001).

In typical development, there is an apparent increase in cerebellar gray matter from early childhood to middle childhood. One study reported a 12% increase in cerebellar gray matter volume between normal control children ages two to three years and ages six to nine years (Courchesne et al., 2001). However, this age-related change was not observed in children with ASD, who showed a 1% decrease in cerebellar gray matter volume during this same developmental period. From middle childhood (ages six to nine years) to early adolescence (ages 12 to 16 years), cerebellar gray matter has been shown to remain constant in both typically developing individuals and individuals with ASD. In accordance with the lack of developmental gray matter increase, cerebellar gray matter is reportedly reduced in both older children (ages six to nine years) and adolescents (ages 12 to 16 years) with ASD relative to normal controls (Courchesne et al., 2001).

Measures of overall cerebellar volume are somewhat consistent with the reports of early overproduction of white matter and later reduced gray matter. Overall cerebellar volume was reported to be increased in three to four year olds (Sparks et al., 2002) and seven to 11 year olds (Herbert et al., 2003) with ASD, which may reflect this increased

white matter. One study also found increased cerebellar volume in adolescents and young adults ages 15 to 24 years, but this difference was no longer significant when intracranial volume was taken into account (Palmen et al., 2004). However, another study found reduced overall cerebellar volume in adults ages 18 to 58 years (Hallahan et al., 2009) with ASD, which may reflect reduced gray matter volumes. Additional studies examining cerebellar white and gray matter structure at different stages of development will lead to a more complete understanding of the developmental trajectory of anatomical abnormality as it relates to ASD.

Functional Imaging Studies

Functional imaging studies provide valuable insight into how the cerebellum may function abnormally in ASD. There are few studies specifically examining cerebellar function in ASD. However, the existing research does support an atypical functional role for the cerebellum. Functional MRI studies show increased cerebellar activation in response to simple sensory and motor tasks (Allen, Muller, & Courchesne, 2004; Muller et al., 1998; Muller, Pierce, Ambrose, Allen, & Courchesne, 2001). At the same time, studies show decreased cerebellar activation in response to higher-order cognitive functions, including attention (Allen & Courchesne, 2003), facial expression (Critchley et al., 2000), auditory detection (Gomot et al., 2006), semantic processing (Harris et al., 2006), and visual-motor learning (Muller, Kleinhaus, Kemmotsu, Pierce, & Courchesne, 2003). These findings indicate that individuals with ASD may depend highly on the cerebellum for basic sensorimotor tasks but minimally for more complex behaviors.

In contrast to these findings, a recent study indicated a different pattern of cerebellar activation (Gilbert et al., 2008). Though the researchers did not focus on the cerebellum as the primary site for their investigation, the study nonetheless reported abnormalities in cerebellar activation in ASD. Contrary to previous research, individuals with ASD showed reduced left cerebellar hemisphere activation during a simple motor task and increased bilateral cerebellar hemisphere activation during a higher-order cognitive task of letter classification (Gilbert et al., 2008). Further research discerning the functional role of the cerebellum in ASD is necessary to better understand the contradictory findings between studies.

Functional imaging studies of attention are of particular relevance to the proposed study, which seeks to understand the relationship between attentional abnormalities and posterior cerebellar structure. Research suggests that the posterior cerebellum may function differently for individuals with ASD during tasks of attention. In response to a visual selective attention task, individuals with ASD showed minimal cerebellar activation whereas normal control subjects showed bilateral activation of the Crus I (Allen & Courchesne, 2003). The posterior cerebellar hemispheres appear to be involved in visual selective attention in typically functioning individuals, and the apparent reduced activation in these regions in ASD may reflect pathology of the posterior cerebellum. Furthermore, there is preliminary evidence that the structure of the Crus I may be associated with the degree of activation during attentional tasks. Allen and Courchesne (2003) found that the volume of the Crus I (cerebellar hemisphere lobule VIIa) was strongly correlated with activation in this same region during the attention task in both

ASD and control groups. Additionally, in the ASD group, the size of the Crus I correlated with performance accuracy during the attention task. Thus, there is evidence that the Crus I is involved in selective attention, and the volume of the Crus I is associated with performance accuracy and activation of this same region.

Attentional Abnormalities in ASD

Importance of Studying Attention in ASD

Atypicalities in attention are one of the earliest identifiable features in ASD (Elsabbagh et al., 2009). Diagnostic instruments for ASD include measures of attention functioning (Lord, Rutter, DiLavore, & Risi, 2008). For example, in the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994), there are questions that assess attention to voice, which is an aspect of language and communication, and showing and directing attention, which is an aspect of social development and play. Additionally, difficulties with disengaging attention are observed within the first years of life, and researchers suggest that this early deficit affects the input and processing of social stimuli, which may contribute to progressive impairments in social and communication difficulties (Elsabbagh et al., 2009).

Being able to direct attention to objects and people is also important in exploring the world as an infant and beyond, and attentional abnormalities may contribute to an atypical understanding of the social world. Additionally, a focus on parts of objects rather than on objects as functional wholes (e.g., wheels on a car rather than the car as a whole) may reflect an overly selective lens of attention that is related to stereotyped and repetitive interests and behaviors. The abilities to selectively attend to a focus of interest,

maintain attention, disengage attention, and shift attention are essential skills that form the basis for social, communicative, and academic learning. Thus, atypical attention functioning has implications for a wide range of developmental outcomes.

Selective Attention and Stimulus Overselectivity

Selective attention refers to the ability to direct awareness to relevant aspects of the environment and to filter out irrelevant stimuli. Maintaining an appropriate level of selectivity is important in processing and making sense of the world. Overly selective attention refers to directing a disproportionate level of attention to one feature of the environment to the exclusion of other stimuli. This overselectivity could potentially be maladaptive to processing relevant features of the environment and building a coherent picture of one's surroundings. Overly selective attention is prevalent among individuals with ASD and may be a contributing factor to the stereotyped, restricted, and repetitive interests and behaviors that are characteristics of ASD.

The tendency for individuals with ASD to focus disproportionately on one aspect of the environment is referred to as "stimulus overselectivity." Stimulus overselectivity was first described by Lovaas and colleagues in 1971. In the Lovaas et al. (1971) study, children with intellectual disability, children with ASD, and typically developing children were asked to respond to a multi-modal stimulus that included visual, auditory, and tactile features. Typically developing children responded equally to all three modalities, children with ASD mainly responded to only one modality, and children with intellectual disability responded with a moderate level of selectivity in-between the two extremes.

Lovaas and colleagues interpreted these results to indicate that children with ASD exhibited an overly narrow focus of attention.

A number of studies have demonstrated that stimulus overselectivity is indeed prevalent in ASD (for review, see Ploog, 2010). However, stimulus overselectivity is not consistent across the entire ASD population, and there is evidence that suggests that stimulus overselectivity may be more reliably predicted by mental age, rather than by ASD diagnosis (for review, see Ploog, 2010). At the same time, there is supportive evidence that stimulus overselectivity corresponds with severity of ASD, regardless of mental-age (Dickson, Deutsch, Wang, & Dube, 2006; Sonoyama & Kobayashi, 1986). Whether or not stimulus overselectivity is a core deficit in ASD remains unclear. Nonetheless, stimulus overselectivity is a prevalent feature in the ASD population that should be taken into account when considering attentional abnormalities.

One possible reason that some individuals with ASD exhibit overselective attention is due to overarousal from sensory stimuli. In order to cope with overarousal and avoid overstimulation, individuals with ASD may narrow their focus of attention (Easterbrook, 1959; Liss, Saulnier, Fein, & Kinsbourne, 2006). A cluster analysis found that within a subgroup of individuals with ASD, overreactivity, overfocusing, and sensory seeking behaviors were closely associated (Liss, Saulnier, Fein, & Kinsbourne, 2006), indicating that these individuals may respond to sensory overload by narrowing their attentional focus. Further research examining the possible relationship between sensory overarousal, stimulus overselectivity, and repetitive behaviors and interests could help reveal causes of behaviors and point to possible intervention strategies.

The large majority of research on selective attention and ASD uses single modality visual paradigms. These tasks show that individuals with ASD show enhanced processing of visual details. Whether or not this enhanced detail processing is due to a narrow attentional lens, however, is unclear. One study reported that individuals with ASD showed superior visual search skills for a conjunctive target (i.e., a stimulus that is the same color as one distracter and the same form as another distracter) and displayed higher accuracy in detecting differences between similar visual stimuli compared to normal controls subjects (Plaisted, O'Riordan, & Baron-Cohen, 1998). Individuals with ASD have also shown superior performance on the embedded figures task (for review, see Happe & Frith, 2006), which requires focusing on the local aspects of the stimuli and paying less attention to the overall context of the figure. Though individuals with ASD appear to show enhanced local level processing, there is evidence that they also show normal global level processing (Plaisted, Saksida, Alcantara, & Weisblatt, 2003).

Stimulus overselectivity is a well-studied area of research in ASD. A possible direction for future research in the field would include neurobiological correlates, in addition to cognitive, sensory, and behavioral correlates, in order to better understand if an overly selective attentional lens is related to particular brain abnormalities or patterns of behavior. A more comprehensive understanding of neurobehavioral relationships would help identify mechanisms that underlie stimulus overselectivity and help inform knowledge of qualitative differences within the autism spectrum.

Orienting Attention

Orienting attention refers to the ability to move attention rapidly and efficiently between two locations across a spatial field. The three main components of orienting attention are disengaging attention from the original focus of attention, moving attention to a new focus, and re-engaging attention to the new focus. There is evidence that individuals with ASD have impairments in disengagement and moving attention, especially during rapid attention orienting (Casey, Gordon, Mannheim, & Rumsey, 1993; Renner, Klinger, & Klinger, 2006; Townsend et al., 1999; Townsend, Harris et al., 1996; Wainwright & Bryson, 1996; Wainwright-Sharp & Bryson, 1993). Clinical observations of individuals with ASD often report a difficulty in disengaging gaze from an activity of interest. This difficulty with disengagement may be related to the narrow and intense interests that characterize ASD.

A component of orienting attention that is rarely examined is the ability to rapidly orient to a cue that precedes a target. Rapid orienting is relevant to a range of situations, such as reading subtle messages in facial expressions and body language during communication in social situations, as well as in classroom learning situations. Research suggests that rapid orienting attention is impaired in ASD (Townsend, Courchesne, & Egaas, 1996; Townsend, Harris, & Courchesne, 1996) and that this impairment is linked to cerebellar abnormality (Townsend et al., 1999). ASD participants with greater cerebellar vermis hypoplasia were slower to orient attention than ASD participants with less hypoplasia (Harris et al., 1999; Townsend et al., 1999). In addition, patients with

neocerebellar lesions also showed impairments in rapid orienting of attention (Townsend et al., 1999).

Shifting Attention Between Sensory Modalities

The ability to rapidly shift attention between sensory modalities (i.e., visual and auditory) is also a skill that is important in navigating a range of situations. For instance, being able to attend to speech, facial expressions, and objects of joint attention in succession involves the ability to quickly shift attention between modalities. Studies suggest that rapidly shifting attention between sensory modalities is impaired in ASD and that this impairment is associated with cerebellar abnormalities (Akshoomoff & Courchesne, 1992; Courchesne et al., 1994).

Both individuals with ASD and cerebellar patients were impaired in their ability to detect target information in a new focus within 2.5 seconds or less of shifting attention to a different modality relative to normal controls (Akshoomoff & Courchesne, 1992; Courchesne et al., 1994). The impaired performance was not due to component task difficulty, as individuals with ASD and cerebellar patients were unimpaired when responding to stimuli within a single modality and also successfully completed a difficult auditory detection task. In addition, event related potential activity during correct detections (i.e., hits) but not during misses, indicates that misses were due to a lack of covert attention and not due to slowed motor responses.

There were no performance differences between auditory and visual stimuli responses in cerebellar patients and ASD participants (Askshoomoff & Courchesne, 1992; Courchesne et al., 1994), indicating that the impairment is due to rapid shifting

rather than to selective impairment in a particular modality. In addition, selectively attending to one sensory modality while ignoring the other was unimpaired (Akshoomoff & Courchesne, 1992; Courchesne et al., 1994), suggesting that impaired rapid shifting between modalities is not due to difficulty with filtering out irrelevant stimuli.

Rapidly shifting between different sensory modalities is an ability that is important in a number of learning and social communication situations. The impaired rapid shifting in ASD may impact the ability to successfully understand the subtle cues that reciprocal social interactions involve. In addition, rapidly switching between the noises and images of surroundings and understanding a situation as a coherent whole may be difficult for individuals with ASD. As a result, individuals with ASD may turn to stereotyped behaviors and routines in order to cope with their difficulty in rapidly shifting between sensory modalities.

Divided Attention in ASD

Divided attention, or the ability to respond to more than one task simultaneously, has been studied minimally in ASD. However, given the pattern of attentional function and dysfunction in ASD (i.e., stimulus overselectivity and impaired rapid orienting of attention, disengaging attention, and shifting between sensory modalities), there is reason to believe that divided attention is impaired. Divided attention also requires parallel processing or rapid switching between tasks. The stimulus overselectivity literature suggests that parallel processing would be difficult for some individuals with ASD while the orienting and shifting attention literature suggests that rapid switching would be impaired.

The few studies of divided attention in ASD yield inconsistent findings, which may reflect the variability of task types between studies. Tasks requiring visual processing found normal (Bogte et al., 2009) or superior (Rutherford et al., 2007) divided attention abilities in ASD. The Bogte et al. (2009) task required participants to remember one or two visual stimuli and then to perform a visual search to locate these stimuli from an array of distractors. The researchers defined divided attention as the ability to direct attention to all items of the visual display simultaneously. However, it is debatable if this task is a valid measure of divided attention. The task seems to be a simple measure of visual search abilities rather than a measure of the ability to respond to more than one task simultaneously. The Rutherford et al. (2007) task, on the other hand, did require individuals to respond to more than one task simultaneously. The visual dual task involved simultaneously responding to a letter identification task in the center of the screen and a target identification task in the periphery of the screen. The superior performance in the ASD group may be accounted for by reported advantages in visual processing (Happe & Frith, 2006; Plaisted et al., 2003).

Divided Attention under High Working Memory Demand

In contrast to performance on single modality visual divided attention tasks, performance on divided attention tasks with an auditory component appears to be impaired in ASD. In particular, there is evidence of impaired divided attention under high working memory demand in both auditory paradigms (Yerys et al., 2011) and cross-modality visual and auditory paradigms (Garcia-Villamisar & Della Sala, 2002; Sinzig, Bruning, Morsch & Lehmkuhl, 2008). Working memory tasks that do not require

divided attention appear to be intact (Garcia-Villamisar & Della Sala, 2002; Kenworthy et al., 2008, Yerys et al., 2009).

Children with high-functioning ASD performed significantly worse on the Consonant Trigrams Test compared to matched controls (Yerys et al., 2011). The CTT requires listening to a sequence of letters and numbers, keeping the letters in working memory, performing a subtraction task for the numbers, and then reciting the letter sequence. Within the ASD group, CTT performance was significantly correlated to parent-reports of working memory, measured by the Brief Rating Inventory of Executive Functioning (BRIEF; Gioia, Isquith, Guy, & Kenworthy, 2000).

Better auditory divided attention under high working memory demand was also associated with less severe social and communication symptoms of autism in a large archival sample of children with high-functioning ASD (Kenworthy, Black, Harrison, Della Rosa, & Wallace, 2009). Better performance on the Score! DT Divided Attention subtest of the Test of Everyday Attention for Children (TEA-Ch; Manly, Robertson, Anderson, & Nimmo-Smith, 1999) was negatively correlated with communication symptoms and reciprocal social interaction symptoms, as measured by composite scores derived from the ADOS and ADI-R. The Score! DT subtest requires simultaneously attending to a news broadcast for an animal name and counting randomly presented beeps, which requires dual attention and working memory demands.

Children with ASD performed more poorly on a cross-modality visual and auditory divided attention task compared to typically developing children (Sinzig, Bruning, Morsch & Lehmkuhl, 2008). The divided attention task required responding to

both the visual target of a square and also to an auditory sequence. Adults with ASD also showed impaired cross-modality divided attention (Casey et al., 1993; Garcia-Villamisar & Della Sala, 2002). Participants showed impaired performance on a dual task involving simultaneously performing a digit recall task and a visuomotor tracking task, compared to controls (Garcia-Villamisar & Della Sala, 2002). There were no group differences in single task performance of the digit recall task and tracking task. The Casey et al. (1993) study measured divided attention through a paradigm (Posner & Boise, 1971) that involved simultaneous responding to visual and auditory continuous performance tasks (CPT). Individuals with ASD detected fewer targets (i.e., made more omission errors) than normal controls, regardless of whether the targets were visual or auditory. There was no significant difference in group performance in the percentage of false alarms (i.e., commission errors).

There is also evidence for aberrant brain activity during performance of cross-modality divided attention tasks with high working memory demands (Ciesielski, Knight, Prince, Harris, & Handmaker, 1995). Ciesielski and colleagues (1995) found an atypical pattern of event-related potentials (i.e., ERPs) in participants with high-functioning ASD during attention tasks. In normal control participants, the ERP associated with voluntary attention gradually modulated in response to attentional demands, with the highest activity during focused auditory and focused visual attention conditions, intermediate in response to the divided attention condition, and smallest in response to unattended stimuli. In individuals with ASD, however, the ERP associated with voluntary attention

was decreased or absent, which suggests a decreased ability to selectively inhibit irrelevant stimuli.

Though the differences were not statistically significant, the largest discrepancy in performance between the control and ASD group was during the divided attention task. Individuals with ASD had a lower percentage of correct responses, a higher number of false alarms, and slower reaction times. At the same time, the differences in ERP activity were greatest during the divided attention tasks. The pattern of activity in ASD participants suggests a more simplistic attentional system that is resistant to modulation. The authors interpret these results as evidence for an alternative compensatory attentional mechanism, which is relatively effective for focused attention tasks but less effective for divided attention situations.

There are relatively few studies examining divided attention in ASD, and the diversity of paradigms used to measure performance make findings difficult to interpret. However, there is evidence that divided attention under high working memory demand in both single modality auditory and cross-modality paradigms is impaired. There is a need for more research, using a reliable measure of divided attention, in order to better understand divided attention abilities in ASD.

The Cerebellum and Divided Attention – Patient Studies

Patient studies show evidence of cerebellar damage being linked to impaired divided attention performance. One research group reported that patients with focal cerebellar lesions (i.e., lesions restricted to the cerebellum) showed deficits in a cross-modal (visual and auditory) dual task measure, compared to control participants

(Gottwald, Mihajlovic, Wilde, & Mehdorn, 2003; Gottwald, Wilde, Mihajlovic, & Mehdorn, 2004). The Gottwald et al. (2003) study included a sample of 16 cerebellar patients and 16 healthy control participants. The latter study by Gottwald and colleagues (2004) included the original sample of 32 participants but also included five additional cerebellar patients and five additional healthy control participants. In the Gottwald et al. (2004) study, the total of 21 cerebellar patients included five patients with vermis damage and 15 patients with deep cerebellar nuclei damage. The Gottwald et al. (2003) study did not report location of cerebellar damage.

Cerebellar patients missed a significant amount of target stimuli (i.e., omission errors) and falsely responded to more non-targets than control participants (i.e., commission errors) but did not differ in reaction time (Gottwald et al., 2003). In the Gottwald et al. (2004) study, normative percentile ranks were used for statistical comparisons. Because no norms were available for false alarms (i.e., commission errors) in the Divided Attention test, no statistical test was performed. Normative percentile ranks were available for omission errors. Patients missed significantly more target stimuli (i.e., omission errors, measured by normative percentile rank) than the control group. Patients also showed a larger variability in reaction time during the divided attention task, compared to the control group. These results suggest that the cerebellum may play an important role in the ability to perform cross-modality divided attention tasks.

Patients with isolated cerebellar infarcts also showed impaired performance on the PASAT, compared to a control group, matched on age, sex, and educational level (Neau

et al., 2000). The cerebellar patient sample included four patients with superior cerebellar artery territory (SCA) infarcts, one with an anterior inferior cerebellar artery (AICA) territory infarct, and 10 patients with posterior inferior cerebellar artery territory (PICA) infarcts. The PASAT was administered at the rate of one digit every four seconds. The cerebellar patient group had significantly fewer correct responses on the task, compared to the control group. Within the small sample of cerebellar patients, there were no PASAT performance differences between the PICA and the SCA patients.

Imaging studies of the PASAT in Multiple Sclerosis research also provide evidence for cerebellar involvement in divided attention. An fMRI study of individuals with Relapsing Remitting Multiple Sclerosis (RRMS) showed increased activation of the Crus II during performance of the PASAT, relative to controls, despite no significant difference in task performance (Lesage et al., 2010). Lesage and colleagues (2010) interpret this finding to suggest that the areas of the cerebellar cortex that are connected to the prefrontal cortex play a key part in compensating for neural effects of RRMS (i.e., white matter degeneration, diffuse neural pathology) while performing tasks that require acquired cognitive skills in individuals with RRMS. Additionally, an fMRI study of patients with early RRMS and control participants suggests that there may be functional changes early in MS to compensate for the disease, including greater activation in the right cerebellum in patients (Audoin et al., 2003).

There is also evidence that cerebellar structure is related to performance on the PASAT. A voxel-based morphometry study found that lower scores on the PASAT were correlated with decreased global gray matter volume, including decreased gray matter

volume in the right cerebellum, bilateral prefrontal cortex, precentral gyrus, and superior parietal cortex for patients with RRMS (Morgen, et al., 2006).

The Cerebellum and Divided Attention – Neurotypical Studies

Imaging studies in neurotypical participants help to pinpoint which cerebellar regions may be involved in the cognitive operations of the PASAT. Compared to patient studies, imaging studies of healthy participants allow for the isolation of cognitive operations, apart from the speech and motor components of the task.

Two studies that accounted for listening and speech production (i.e., included a control condition of simply repeating the numbers) found bilateral cerebellar activation during the PASAT in neurotypical participants (Forn et al., 2008; Lockwood, Linn, Szymanski, Coad, & Wack, 2004). Another fMRI study that also used a control condition to account for motor and speech components of the task found activation of the medial cerebellar cortical lobule VII (Hayter, Langdon, & Ramnani, 2007). Left cerebellar activation was also found in neurotypical participants, after accounting for non-cognitive aspects of the task (Audoin et al., 2005). Imaging studies that did not account for listening and speech production during the PASAT found bilateral cerebellar activation (Cardinal, Wilson, Giesser, Drain, & Sicotte, 2008) and activation of the medial cerebellar lobule VII (Ito, 2008).

One research group examined cerebellar activation in response to covert and overt completion of the PASAT task (Forn et al., 2006; Form et al., 2008). During the covert condition, participants were instructed to silently complete to task. During the overt condition, participants were instructed to respond verbally. Administering the covert and

overt versions of the PASAT allowed for the isolation of activation due to the cognitive aspects of the task, compared to the initiation of speech production. While the overt condition activated a larger region of the cerebellum, the covert condition also activated the cerebellum bilaterally. Thus, the cerebellum appears to be active during the completion of the PASAT, even when there is no speech production involved. The areas of the cerebellum that were activated during the overt version but not the covert version appear to be due to speech initiation and production.

Summary

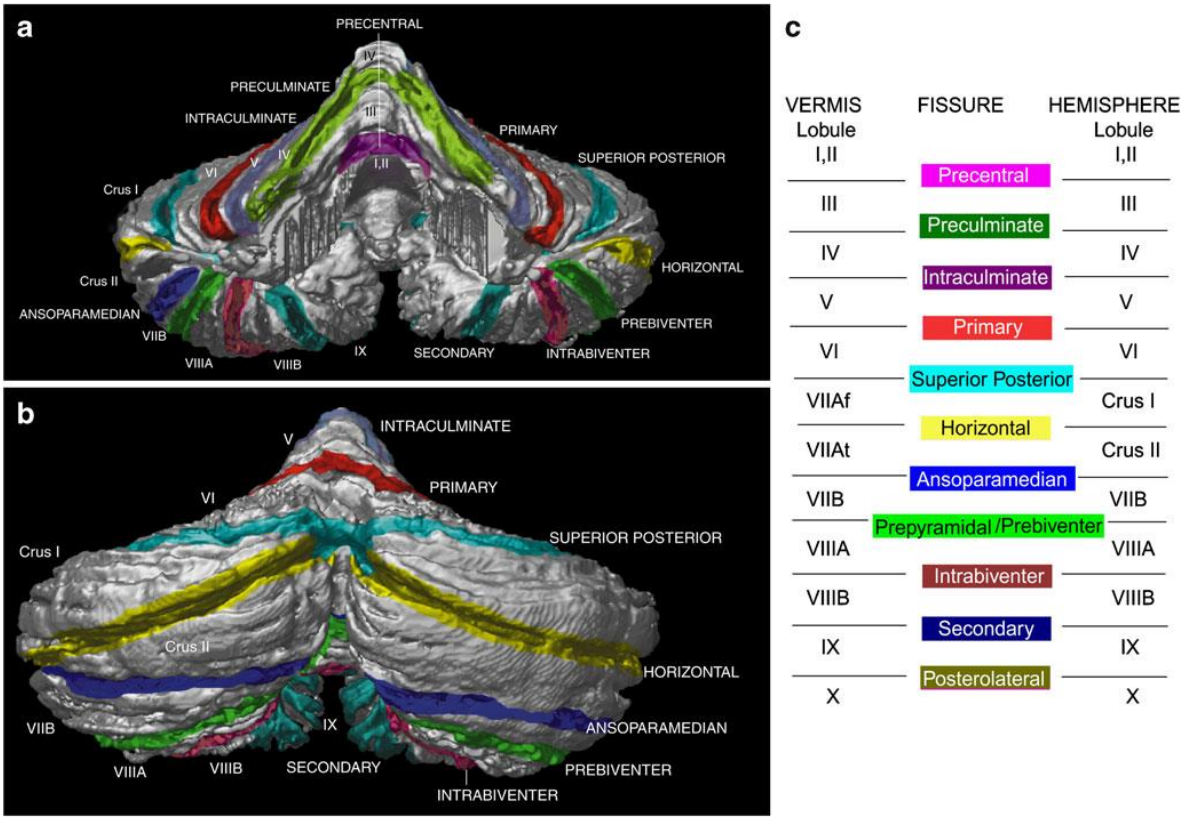
Autism spectrum disorders are neurodevelopmental disorders that are estimated to affect one in every 88 children. The etiology of ASD remains unknown, but research suggests a strong genetic component, in interaction with environmental variables. There are several brain regions that have been reported to be abnormal in ASD. However, the most reliably reported region of pathology is the cerebellum. Purkinje cell reduction is the most commonly reported abnormality, and there is evidence that this cell reduction may be particularly concentrated in the posterior cerebellar hemispheres, which are associated with higher-level cognitive functions like attention. The cerebellum is thought to serve an integrative role, by processing incoming information from a number of brain regions and helping to make functions more coordinated and efficient. Damage to the cerebellum could thus disrupt the efficiency and coordination of a number of motor, cognitive, and emotional functions.

Attention abnormalities are one of the earliest identifiable features of ASD and are thought to contribute to social-communicative deficits and restricted and repetitive

behaviors and interests. Individuals with ASD tend to show an overly narrow focus of attention, impaired disengaging and rapidly orienting attention, and impaired shifting attention between sensory modalities. An area of attention that has been minimally studied is divided attention, or the ability to respond to more than one task simultaneously. However, a small number of studies provide preliminary evidence that divided attention is impaired in ASD. Furthermore, imaging studies of patients with cerebellar lesions suggest that divided attention impairment is associated with cerebellar dysfunction.

The current study seeks to examine the relationship between posterior cerebellar volume and divided attention performance in ASD. Research linking neuroanatomical abnormalities to behavioral symptoms within a group of individuals with ASD is particularly necessary, given the variability of behavioral features within ASD. Examining neurobehavioral relationships will contribute to a more complete understanding of how specific brain abnormalities relate to behavioral functions. Lesion studies and imaging studies suggest a relationship between reduced volume of the cerebellum and impaired attentional performance. Thus, the current study predicts that reduced posterior cerebellar volume will be associated with impairments in a divided attention task.

Appendix B: Illustration



Source: From The role of the cerebellum in cognition and emotion (p. 246) by Schmahmann, 2010

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