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Cerebellar vermal volumes and behavioral correlates in children with autism spectrum disorder

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Abstract

Cerebellar histopathological abnormalities have been well documented in autism although findings of structural differences, as determined by magnetic resonance imaging, have been less consistent. This report explores specific cerebellar vermal structures and their relation with symptoms severity and cognitive functioning in young children with autism spectrum disorder (ASD). Children with ASD aged 3 to 4 years were compared with chronological age matched typically developing children (TD) and chronologic and mental age matched children with developmental delay (DD). Volumes of the cerebellum and midsagittal vermal areas were measured from 3-D T1-weighted MR images. Children with ASD had reduced total vermis volumes compared to children with TD after controlling for age, sex, and overall cerebral volume or cerebellum volume. In particular, the vermis lobe VI-VII area was reduced in children with ASD compared to TD children. Children with DD had smaller total vermis areas compared to children with ASD and TD. Within the ASD group, cerebellar measurements were not correlated with symptom severity, or verbal, non-verbal or full scale IQ. Within the DD group, larger cerebellar measurements were correlated with less impairments. The specific relation between altered cerebellar structure and symptom expression in autism remains unclear.

Keywords

Cerebellum; MRI; Vermis; Developmental Delay

1. Introduction

Autism spectrum disorder (ASD) is characterized by impaired social functioning and communication, and a restricted range of activities. A number of neurobiological hypotheses have been put forward to account for autism behaviors that implicate neural and network

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abnormalities in the cerebellum, frontal cortex, medial temporal lobe, in general, and the amygdala and/or hippocampus, superior temporal lobe/sulcus, and brainstem, specifically. While this list is not exhaustive in its scope, it illustrates the pervasive impact of this disorder on neural functioning, the likelihood that multiple brain regions are affected, and the potential for heterogeneity in etiology.

Post-mortem histopathological studies have consistently demonstrated cellular alterations of the cerebellum in individuals with autism. In 21 of 29 autopsy cases reviewed by Palmen et al. (2004), there were decreased numbers of Purkinje cells, the main efferent system for the cerebellum. For a subset of cases, morphological alterations were also present. Histopathological findings suggest that cell loss occurs more consistently in the lateral hemispheres and the vermis, particularly posterior regions (Williams et al., 1980; Ritvo et al., 1986; Fehlow et al., 1993; Bauman & Kemper, 1994; Bailey et al., 1998; Kemper & Bauman, 1998, 2002; Purcell et al., 2001; Lee et al., 2002).

Structural MRI investigations of cerebellum morphometry in ASD have generally demonstrated increases in total cerebellar volume and posterior vermis volume, but reports have been less consistent in direction of effects in other areas. Herbert et al. (2003), Sparks et al. (2002), and Palmen et al. (2005) all found increased cerebellar volume in young children with autism spectrum disorder; however, overall cerebellar volumes were proportional to total enlarged cerebral volume, rather than specific to the cerebellum. Posterior midsagittal vermis areas VI-VII have been found to be decreased (Kates et al., 1998; Carper & Courchesne, 2000; Courchesne et al., 2001; Kaufmann et al., 2003; Akshoomoff et al., 2004). In contrast, anterior vermis has been found to be both normal and increased (Courchesne et al., 2001; Akshoomoff et al., 2004); and the pyramis/uvula/nodulus (vermis volume VIII-X) has been found to be both decreased and normal (Levett et al., 1999; Courchesne et al., 2001).

For this report, we evaluated cerebellar structural abnormalities and examined the correlation between structural differences and symptoms severity and cognitive functioning in children with ASD. Children with ASD aged 3 to 4 years were compared to age matched children with typical development, as well as age and mental age matched children with developmental delay. Brain imaging findings, including overall cerebral and substructure volume relations, and tissue-based chemical alterations for this sample have been previously reported (Sparks et al., 2002; Friedman et al., 2003; Friedman et al., 2006; Munson et al., 2006; Petropoulos et al., 2006; Boger-Megiddo et al., 2007). Based on the existing literature, we hypothesized that ASD children would demonstrate significantly smaller vermal areas and that these changes would be associated with more severe autism symptom expression and lower IQ.

2. Methods

2.1. Participants

The study sample consisted of 3 groups of children 3–4 years of age: 45 children with Autism Spectrum Disorder (ASD), 14 children with developmentally delayed (DD), and 26 children with typically development (TD). In addition, two children with ASD and one TD child had MRI scans with poorly defined cerebellar sub-regions that could not be accurately measured and these children were excluded from all analyses. Children having significant motor or sensory impairment (e.g., blindness, deafness), major physical abnormalities, seizures, history of serious head injury, identifiable neurological disorder, prenatal or perinatal difficulties, metal implants such as prostheses, or taking psychoactive medications on a regular basis were not included. Further, children with developmental delay (without autism) had no known genetic syndrome (e.g., Fragile X, Down syndrome), prenatal or postnatal brain trauma, or a defined disease. Children studied at the University of Washington (UW) were recruited from

local parent advocacy groups, preschools, the Center on Human Development and Disabilities, clinics and hospitals in the greater Seattle area, and the UW Infant and Child Subject Pool.

As shown in Table 1, there were no significant age differences between groups. Group differences in sex were demonstrated using Pearson χ^2 analysis. There were more girls in the DD (57.1%) group relative to ASD (15.6%) and TD (30.7%) groups.

The TD group included 13 children studied at the UW and 13 studied at the NIH. Children recruited for the UW TD group were included if they scored within one standard deviation of normal on the Vineland Adaptive Behavior Scales, and had no parental report of language, social, motor or cognitive delay, emotional or psychiatric disturbances or had not received special services for learning problems or speech. Children in the NIH TD group were assessed via a telephone screen and an on-site structured psychiatric evaluation; children were excluded if they had a history of psychiatric illness, neurological disorder, or developmental delay (Giedd et al., 1996). Written parental/guardian informed consent, approved by the UW Internal Review Board or the NIH Internal Review Board, was obtained for each child participating in the study.

Children with ASD were administered a diagnostic evaluation consisting of the Autism Diagnostic Interview - Revised (ADI-R; Lord et al., 1994) and the Autism Diagnostic Observation Schedule - Generic (ADOS-G; Lord et al; 2000). In addition, experienced clinicians made a clinical judgment of diagnosis based on presence/absence of autism symptoms as defined in the DSM-IV (American Psychiatric Association, 1994) using all available information. Diagnosis of autism was defined as meeting criteria for Autistic Disorder on the ADOS-G and ADI-R (within 2-points) and meeting DSM-IV criteria for Autistic Disorder based on clinical judgment ($n = 30$). Diagnosis of PDD was defined as meeting criteria for ASD on the ADOS-G, meeting criteria for Autistic Disorder on the ADI-R (within 5 points), and meeting DSM-IV criteria for Autistic Disorder or PDD based on clinical judgment ($n = 15$). Comparison children (DD or TD) did not meet DSM-IV criteria for Autistic Disorder or PDD based on clinical judgment. IQ for the children with ASD or DD was evaluated using the Mullen Scales of Early Learning. Children with ASD and DD were also administered the Vineland Adaptive Behavior Scales including the subscales: Adaptive Behavior, Communication, Daily Living, Motor, and Socialization. Participant descriptive demographic information is presented in Table 1. ADOS and IQ scores were not available on the TD group. The ASD group had significantly higher ADOS total scores than the DD group. The ASD and DD groups did not differ in IQ.

2.2. MRI scans

Children with ASD and DD were imaged at the UW during the daytime using continuous intravenous infusion of propofol at 180 to 220 $\mu\text{g}/\text{Kg}$ per minute, as previously described (Amundsen et al., 2005). TD children, scanned both at the UW and at NIH, were scanned late at night during normal sleep. For the UW TD sample, children were sedated on an optional basis with parentally administered benadryl if the child previously had experienced sedation when given this agent ($n = 8$, 25-mg PO). No sedation was used for the NIH TD sample. As prior work has established scanner compatibility between sites and previous published comparisons of cerebral volume and discrete subregion structures were not different between the UW and NIH TD samples, the TD samples were combined for all analyses (Sparks et al., 2002).

Imaging studies at the UW and NIH were performed on a 1.5T GE Signa Scanner. A 3-D SPGR imaging sequence (TR = 33 milliseconds, TE = 3 milliseconds, flip angle = 30 degrees, 22-cm field of view (FOV) and 256×256 matrix) acquired in the coronal plane was used for volume determinations. During acquisition, the effective slice thickness of the 3-mm slice acquisition

was reduced to 1.5-mm through zero-filling in the third phase encoding direction to improve spatial resolution (i.e., the effective partition thickness) with a small loss in contrast (i.e., signal-to-noise ratio). Scanning of TD children at the NIH used an identical GE scanner and similar acquisition parameters with the exception that coronal slice thickness was 2-mm (no zero filling) at a 24-cm FOV.

2.3. Structural measurements

Volumetric measurements of total cerebrum and cerebellum, and midline area measurements of the vermal lobules I-V, VI-VII and VIII-X were performed by a single rater blinded to diagnosis (BFS) using MEASURE, a semi-automated imaging analysis program developed at Johns Hopkins University, which allows simultaneous data visualization and interaction within multiple planes (coronal, axial, sagittal). In previously reported work (Sparks et al., 2002), cerebral and cerebellum volumes were obtained using a stereotaxic grid (Gundersen & Jensen, 1987). In the current study, cerebral and cerebellar measurements were obtained using a semi-automated histogram approach to improve measurement sensitivity for small volume differences (Friedman et al., 2006; Petropoulos et al., 2006). Cerebral volume included the basal ganglia and corpus callosum, and excluded the ventricles, brain stem and cerebellum. At the level of the cerebellar peduncles, the cerebellum and brain stem were separated from the cerebrum by drawing a straight line from the most antero-lateral point of the fourth ventricle to the “notch” that is created by the junction of the brainstem and cerebellum (Figure 1). The cerebellum was segmented using rules previously described in a paper by Aylward and Reiss (1991). The approach used by previous researchers (Aylward & Reiss, 1991; Courchesne et al., 1994) for measuring vermal lobules was employed. The vermian segmentation was performed by an experienced analyst (BFS) supervised by a pediatric neuroradiologist (DWWS). Briefly, a midsagittal slice was reconstructed where the apex of the fourth ventricle, the cerebral aqueduct and the obex were all visible. Divisions between lobes I-V, VI-VII, and VIII-X were traced on this slice, as illustrated in Figures 1a, 1b and 1c. Interrater reliability (DWWS vs. BFS) on ten scans produced the following correlation values: vermal lobes I-V = 0.97, vermal lobes VI-VII = 0.94, and vermal lobes VIII-X = 0.89.

2.4. Data analysis

Because both age and gender are known to affect brain size, data were analyzed with covariance for age and sex to account for any potential influences on comparisons. In addition, in order to account for the influence of brain volume on sub regional analyses, we undertook an additional set of analyses using cerebral volume or cerebellum volume as a covariate in addition to gender and age.

For those measures showing group differences, additional analyses were performed to evaluate the distribution of measurements. Courchesne et al. (1994) suggest that the variability in vermal areas found in ASD represents 2 distinct subpopulations of ASD individuals: those with vermal hypoplasia and those with vermal hyperplasia. To replicate those findings, data were plotted as a probability plot in which observed vermis area values for each subject were plotted against the expected normal distribution. In this type of plot, a unimodal Gaussian distribution would appear as a straight line; whereas a significant Shapiro and Wilk's W statistic would reject the assumption of a normal distribution.

To examine whether individual differences in cerebellar volume or sub region volumes were correlated with symptom severity (ADOS, ADI), IQ (Mullen Scales), or general functioning (Vineland Adaptive Behavior Scales) (e.g., Paradiso et al., 1997; Mostofsky et al., 1998), structural measures were examined separately for the ASD subgroups, which differed in terms of severity of symptoms (Autism Disorder vs. PDD). Correlations with ADOS, ADI, Mullen Scales of Early Learning, and the Vineland Adaptive Behavioral Scales were conducted

separately for the ASD and DD groups for Total Vermis area and Cerebellum volume. Relations with behavioral measures were considered exploratory.

3. Results

3.1. Structural measures

Structural measures for the three groups are shown in Table 2 and statistical comparisons are shown in Table 3. Vermal areas are plotted in Figure 2.

3.1.1. Total vermis—Covarying for age and gender, total vermal area in the ASD group was marginally smaller (at the trend level) compared to the TD group. However, when either controlling for cerebral volume or cerebellar volume, total vermal area was disproportionately smaller in children with ASD (see Table 2,3). Compared to the ASD and TD groups, the children with DD exhibited significantly smaller total vermal area when scaling age and gender. This finding persisted when using cerebral volume as a covariate. In contrast, the total vermis area did not differ between DD and ASD groups when cerebellum volume was added as a covariate.

3.1.2. Vermal subregions—Results of analyses of the vermal subregions are shown in Table 3. Covarying for age and gender, vermal segments VI-VII in the ASD group were smaller compared to the TD group. Significantly smaller areas in the ASD group compared to the TD group were accentuated with the additional covariates of either cerebral volume or cerebellar volume and included both subregions I-V and VI-VII. No differences were found for subregions VIII-X when comparing ASD and TD groups.

Compared to ASD and TD groups, the DD group exhibited significantly reduced volume for regions I-V, VI-VII, and VIII-X when covarying for age and gender. A similar direction of results for both sub-regions was demonstrated when adding cerebral volume as a covariate. In contrast, adding cerebellum as a covariate resulted in a lack of statistical differences for both sub-regions between DD and ASD groups but not between DD and TD groups.

3.2. Distribution of measurements

Using the approach of Courchesne et al. (1994), we examined the distribution of vermal areas within each diagnostic group to assess the occurrence of a bimodal distribution of measurements. There were no deviations from the normal distribution for any of the groups for vermis I-V area (all Shapiro-Wilk's $W > .95$, all $ps = ns$) or vermis VIII-X area (all Shapiro-Wilk's $W > .95$ $ps = ns$). For vermis VI-VII area, both the ASD and TD group deviated from the normality assumption (Shapiro-Wilk's W ASD = .92, $p < .01$, DD = .93, $p = ns$; TD = .91, $p = .03$).

To further explore the distribution across and within groups, we categorized each subregion in relation to the mean of the TD sample. That is, based on the raw means and SD presented in Table 2, individuals were recoded as having a value greater than +1 SD from the mean, within 1 SD of the mean, or -1 SD or more from the TD mean. Presented in Table 4 and Figure 3, the overall distribution differed across the 3 groups. In all 3 subregions, the DD group compared to the ASD and TD group had a larger proportion of individuals below 1 SD.

3.3. Relation of cerebellum structure to behavior

To evaluate whether individual differences in cerebellar structure were correlated with behavioral differences, we first assessed differences in cerebellar structure between ASD subgroups (AUT vs PDD) differing in symptom severity. There were no significant differences between ASD subgroups for cerebellar volume, total vermal area, sub regional areas vermis I-

V, VI-VII, or VIII-X when including age, gender, and total cerebral volume or age, gender, and cerebellum volume as covariates: cerebellar volume (AUT $M = 1380$ SD 134, PDD $M = 1373$ SD 126), total vermal area (AUT $M = 1016$ SD 112, PDD $M = 1037$ SD 123), sub regional areas vermis I-V (AUT $M = 426$ SD 54, PDD $M = 428$ SD 57), vermis VI-VII (AUT $M = 281$ SD 49, PDD $M = 290$ SD 61), or vermis VIII-X (AUT $M = 308$ SD 48, PDD $M = 319$ SD 50).

Second, we examined the relation between symptom severity, IQ and adaptive functioning in the ASD group. There were no significant correlations between total vermis area or cerebellum volume and symptom severity, IQ or adaptive functioning.

Third, we examined the relation between IQ and adaptive functioning in the DD group. The Vineland Communication Standard Score, Daily Living Standard Score, and Motor Standard Score were correlated with total vermal area ($r_s = .59$ to $.64$, $p_s < .05$). The Social Standard Score was not correlated. Motor Standard Score was also correlated with cerebellum volume ($r = .58$, $p < .05$). Larger vermis total area (or cerebellum volume) was correlated with better scores (i.e., less impairments).

4. Discussion

The primary finding of this study was a significant reduction in midsagittal vermian area, vermal lobes I-V, and vermal lobes VI-VII when adjusted for increases in total cerebral or cerebellum volume in the children with ASD as compared to the children with typical development. Children with developmental delay exhibited cerebellar volumes that were persistently smaller compared to children with typical development and ASD, after controlling for age, gender, and total cerebral volume. These findings are similar to previous reports suggesting hypoplasia of vermis VI-VII in children with autism and children with PDD aged 1.9 to 5.2 years (Akshoomoff et al., 2004) and an overlapping sample of children with autism compared to typical controls aged 2 to 16 years (Courchesne et al., 2001). This pattern of decreased vermal midsagittal area may be a general anatomical finding associated with ASD, consistent with the results of a meta analysis which noted that between 84%- 92% of individuals with ASD exhibited vermal hypoplasia (Courchesne et al., 1994).

As well, we examined whether there existed a bimodal distribution for vermal areas and whether the distributions for the volume of the vermal lobules VI-VII for both the ASD and TD groups deviated from normal. Thus, while we did find evidence of a non-normal distribution, this pattern does not appear to be specific to the ASD sample. As seen in Figure 3, the ASD and TD groups have extreme overlap in absolute (raw) values (Figure 3a) and some overlap in volumes that are corrected for age, gender and cerebrum volume (Figure 3b). Furthermore, while the mean value of the ASD group significantly differed from the TD group, only a small number of individual had volumes that were beyond 1 SD of the mean.

Our findings are in contrast with Akshoomoff's report of increased anterior vermis areas (Akshoomoff et al., 2004). Specifically, we found smaller anterior vermis I-V areas in children with ASD compared to TD (Figure 2). Examining the variability in vermis I-V areas, as compared to the TD mean, 34% of the ASD sample and 71% of the DD sample had values 1 SD below the mean of the TD group, while 6% of the ASD sample and 0% of the DD sample had values 1 SD above the mean of the TD group. There are several demographic differences, as well, between the Akshoomoff sample and ours. Akshoomoff included only *male* children between 1.9 and 5.2 years. Our sample included both male and female children between 3.0 and 4.8 years. More importantly, our analyses used gender, age, and total cerebral volume or cerebellum volume as covariates, whereas Akshoomoff did not. Given that Akshoomoff also found enlarged total brain volume in children with low ($p < .05$) and high ($p = .08$) functioning

autism versus controls; it is possible that their pattern of findings would change if scaled for total cerebral volume.

In this study, we found no relation between cerebellar measures and measures of symptom severity and verbal or nonverbal IQ in the ASD group. However, there was a relation within the DD group with larger vermal area and cerebellum volume being correlated with better daily living skills, better communication, and more typical motor skills. It is unclear why these skills would be correlated within the DD group but not the ASD group. (Scores were not available for the TD sample.) One possibility is that children in the DD group represented the lower end of the normal distribution and thus demonstrate the same relation found in neurotypicals. In neurologically typical individuals, larger cerebellum size has been shown to be correlated with better neuro-physiological functioning, including memory, fine motor dexterity, and IQ (Andreasen et al., 1993; Pardiso et al., 1997).

There have been some structural correlations with neurophysiological findings in ASD. Of note, in a recent report with the same group of children with ASD, we found that larger right amygdala volume, but not hippocampal volume, was predictive of poorer social and communication abilities (Munson et al., 2006). There are several possible explanations to account for the absence of a relation between cerebellar measures and measures of autism symptom severity. First, it is possible that measures that more directly relate to cerebellar function are needed to fully explore the functional significance of these anatomical findings (e.g., manual dexterity such as finger tapping, verbal memory). Second, the cerebellum may mediate general behaviors (such as attention, exploration) that are reflective of the autism phenotype but not directly assessed by the measures in this study.

In contrast to autism, individuals with Williams Syndrome (WMS) show conserved cerebellar volume and disproportionately enlargement of VI-VII and VIII-X despite reduced cerebral volumes (Jernigan & Bellugi, 1990; Reiss et al., 2000; Schmitt et al., 2001). Individuals with WMS are socially motivated, although the disorders share characteristics of abnormalities in motor coordination and gait. Of note, Schaefer et al. (1996) have observed that hypoplasia of cerebellar vermal lobules VI and VII is a diagnostically nonspecific finding that occurs in a number of other developmental disorders. For example, decreases in vermal size have been reported in association with ADHD, fragile X, Schizophrenia, velo-cardio-facial syndrome, and Joubert syndrome (e.g., Holroyd et al., 1991; Mostofsky et al., 1998; Nopoulos et al., 1999; Eliez et al., 2001; Campbell et al., 2006). Thus, cerebellum structures may be genetically unstable, environmentally susceptible, or sensitive to downstream alterations by other affected regions.

What might cause relative decreases in vermal area? It has been suggested that there are two types of cerebellar pathology in autism. First, there may be structural hypoplasia of posterior vermal lobes VI-VII and cerebellar hemispheres related to severe Purkinje neuron loss. Second, hypoplasia may result from a failure to develop appropriate prefrontal – neocerebellar circuitry. The posterior vermis has a long postnatal development period and develops in parallel with frontal and prefrontal structures (Schmahmann, 1991; Ciesielski et al., 1997). Deficits at any levels of the circuitry may result in eventual neuronal loss in the cerebellum.

Although the cerebellar system it has consistently been identified as a region of abnormality in histopathological postmortem studies of autism, the link between anatomical measurements and the autism phenotype is unclear. Future investigations of cerebellar dysmorphology that include targeted functional assessments, are appropriate for across species use, and allow for the assessment of developmental stages of the disorder will provide valuable evidence about the role cerebellar circuitry plays in ASD.

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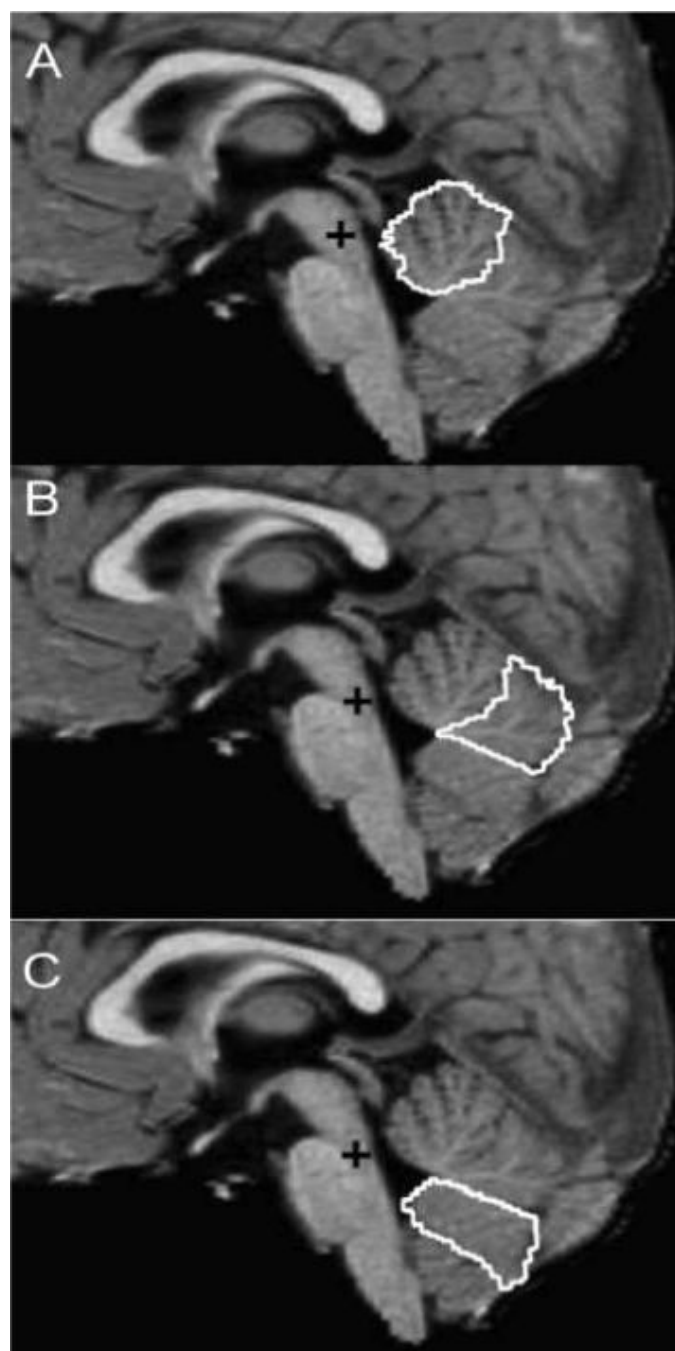


Figure 1. Representative midsagittal MRI of a subject with ASD showing vermal subregions: Figure 1a depicts vermal lobules I-V; Figure 1b depicts vermal lobules VI-VII; Figure 1c depicts vermal lobules VIII-X.

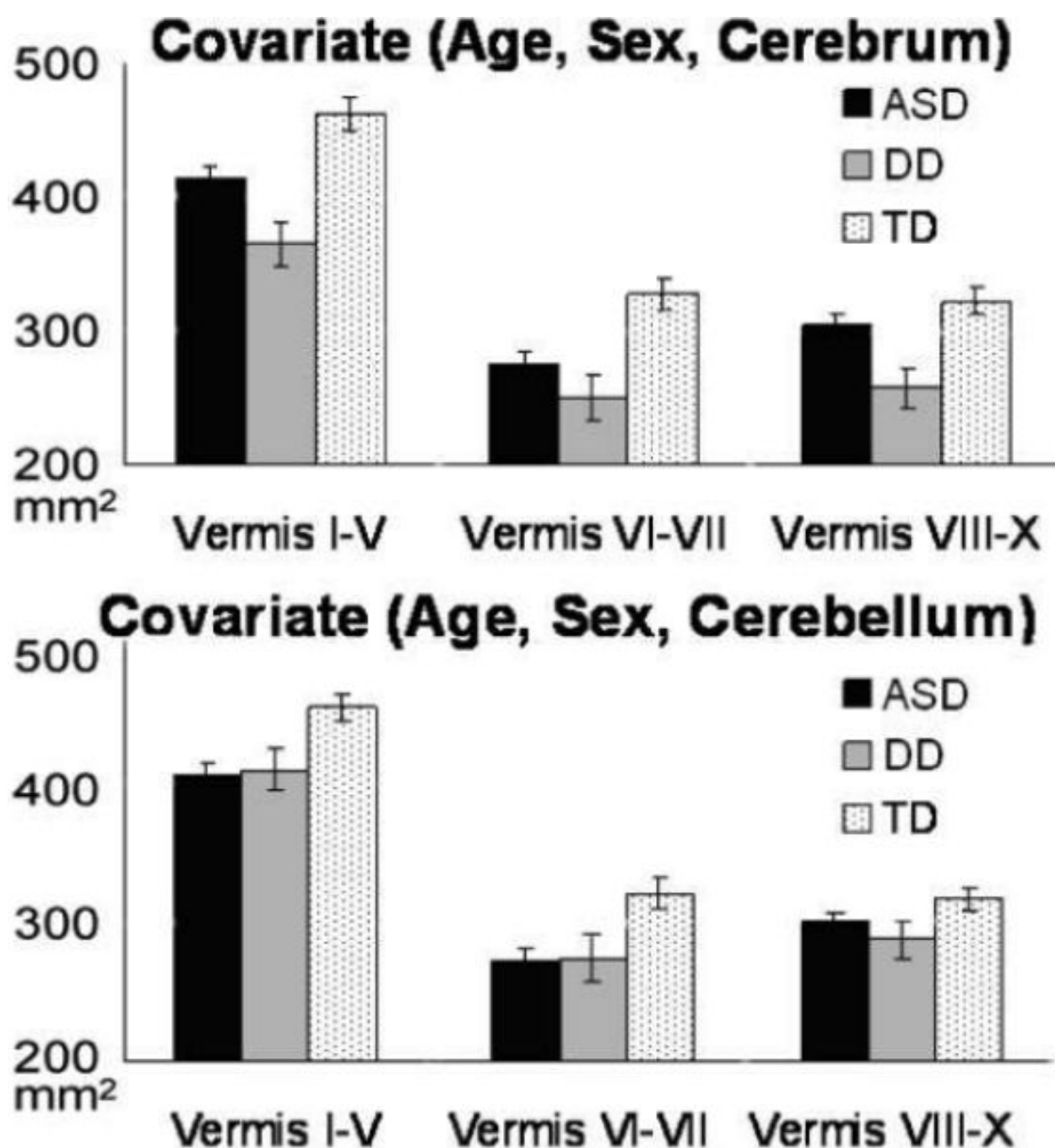


Figure 2.
Adjusted means and standard deviations (bars) for vermal areas when age, sex, and cerebrum or age, sex and cerebellum were used as covariates.

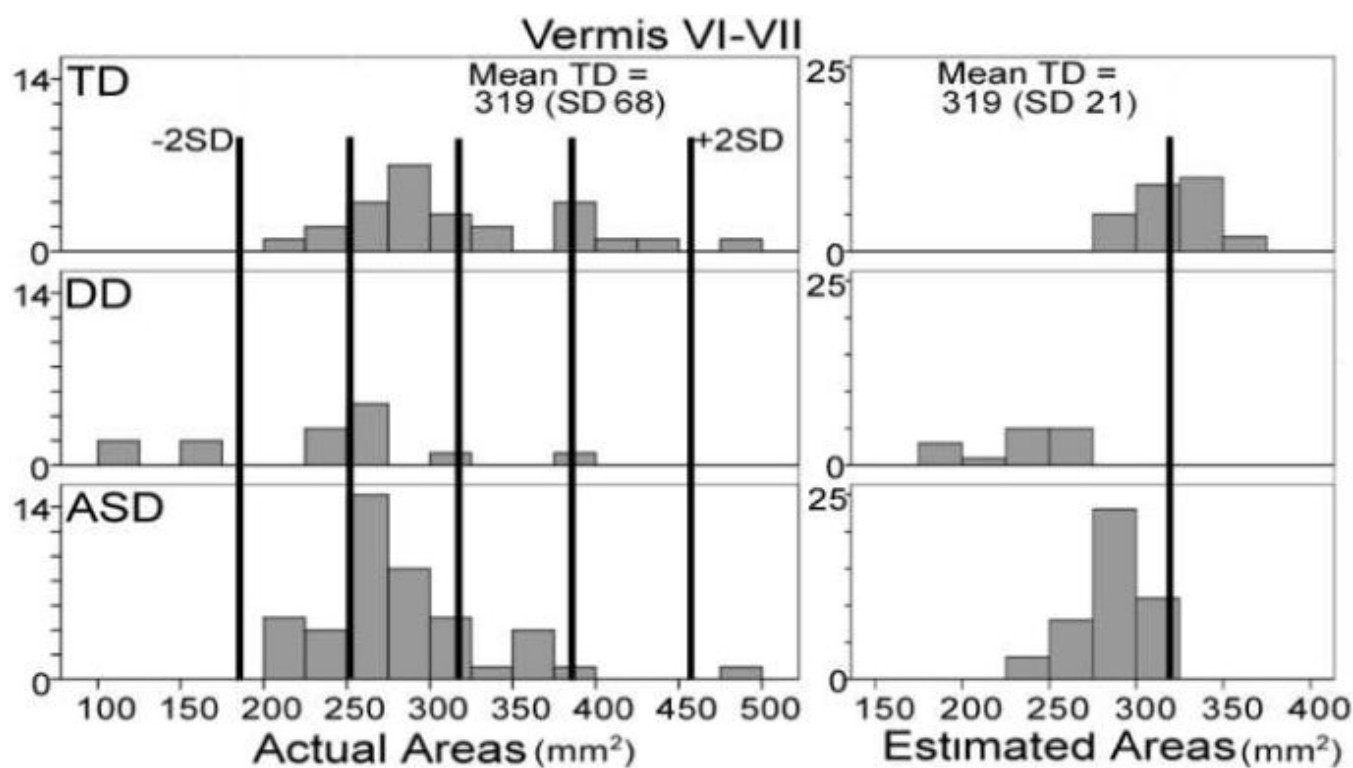


Figure 3.
Distribution of actual and estimated areas for Vermis VI-VII. Black vertical bars represent 1 SD of TD mean. The DD group compared to the ASD and TD group had a larger proportion of individuals below 1 SD.

Table 1

Descriptive information on participants (mean, standard deviation in parentheses and range).

	ASD	DD	TYP	
Subjects	45 (38 males)	14 (6 males)	26 (18 males)	$\chi^2 = 9.6, df = 2,$ $P < .008$
Age at MRI (mo.)	47.33 (4) 38 to 54 mo.	47.5 (6) 40 to 58 mo.	46.9 (6) 36 to 56 mo.	$F(2,82) = 1.0,$ $P = .91$
ADOS Total (Social + Comm.)	14.8 (4) 8 to 21	2.8 (2) 1 to 8	NA	$F(1,57) = 132,$ $P < .001$
Mullen IQ	59.0 (21) 30 to 104	56.9 (14) 29 to 79	NA	$F(1,56) = .13,$ $P = .72$
Mullen Verbal IQ	53.2 (25) 18 to 108	54.4 (16) 20 to 82	NA	$F(1,56) = .03,$ $P = .87$
Mullen Non Verbal IQ	64.8 (18) 36 to 104	59.8 (15) 38 to 93	NA	$F(1,57) = .91,$ $P = .34$

Table 2
Raw group means (+/- SD) for brain regions in children with autism spectrum disorder (ASD), typical development (TD), and developmental delay (DD).

	Total Vermis (mm ²)	Vermis I-V (mm ²)	Vermis VI-VII (mm ²)	Vermis VIII-X (mm ²)	Cerebellum (ml)	Cerebrum (ml)
ASD	1023 (114)	426 (54)	284 (53)	312 (48)	1377.71 (129.9)	11730.19 (937.3)
TD	1087 (134)	452 (58)	319 (68)	316 (45)	1289.17 (138.8)	10872.60 (1020.8)
DD	820 (246)	343 (104)	235 (76)	242 (83)	1020.77 (353.9)	10492.86 (1289.2)

Table 3

Group comparison of brain regions for children with autism spectrum disorder (ASD), typical development (TD), and delayed development (DD).

Group Comparisons ^a		ANCOVA (age & sex)	ANCOVA (age, sex, cerebral vol.)	ANCOVA (age, sex, cerebellum vol.)
Total Vermis		$F_{(2,80)} = 12.8,$ $p < .0001$	$F_{(2,79)} = 15.0,$ $p < .0001$	$F_{(2,79)} = 10.1,$ $p < .0001$
	ASD vs. TD	$p = .064$	$p = .001$	$p < .001$
	ASD vs. DD	$p < .001$	$p = .010$	$p = .879$
	TD vs. DD	$p < .001$	$p < .001$	$p = .004$
Vermis I-V		$F_{(2,80)} = 11.1,$ $p < .0001$	$F_{(2,79)} = 12.8,$ $p < .0001$	$F_{(2,79)} = 8.7,$ $p < .0001$
	ASD vs. TD	$p = .096$	$p = .003$	$p < .001$
	ASD vs. DD	$p = .001$	$p = .018$	$p = .861$
	TD vs. DD	$p < .001$	$p < .001$	$p = .014$
Vermis VI-VII		$F_{(2,80)} = 7.7,$ $p = .001$	$F_{(2,79)} = 9.4,$ $p < .0001$	$F_{(2,79)} = 6.3,$ $p = .003$
	ASD vs. TD	$p = .020$	$p = .001$	$p = .001$
	ASD vs. DD	$p = .032$	$p = .023$	$p = .946$
	TD vs. DD	$p < .001$	$p < .001$	$p = .030$
Vermis VIII-X		$F_{(2,80)} = 8.0,$ $p = .001$	$F_{(2,79)} = 7.0,$ $p = .002$	$F_{(2,79)} = 2.1,$ $p = .129$
	ASD vs. TD	$p = .690$	$p = .179$	$p = .119$
	ASD vs. DD	$p = .001$	$p = .010$	$p = .527$
	TD vs. DD	$p < .001$	$p < .001$	$p = .086$
Cerebellum		$F_{(2,80)} = 14.0,$ $p < .0001$	$F_{(2,79)} = 10.8,$ $p < .0001$	
	ASD vs. TD	$p = .105$	$p = .755$	
	ASD vs. DD	$p < .001$	$p < .001$	
	TD vs. DD	$p < .001$	$p < .001$	
Cerebrum		$F_{(2,80)} = 6.9,$ $p = .002$		
	ASD vs. TD	$p = .003$		
	ASD vs. DD	$p = .004$		
	TD vs. DD	$p = .526$		

^aPost Hoc adjustment for multiple comparison using least significant differences.

Table 4

Distribution of individual area measurements relative to the mean of the typically developing group.

	- 1 SD	-.99 to .99 SD	+ 1 SD
Vermis I-V	$\chi^2 = 17.4$, df = 4, $p = .002$		
ASD	12	30	3
DD	10	4	0
TD	3	19	4
Vermis VI-VII	$\chi^2 = 20.26$, df = 4, $p < .001$		
ASD	10	34	1
DD	8	5	1
TD	3	16	7
Vermis VIII-X	$\chi^2 = 11.2$, df = 4, $p = .02$		
ASD	9	29	7
DD	8	5	1
TD	3	19	4