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An MRI Study of Increased Cortical Thickness in Autism

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Abstract

Objective: In light of the postmortem evidence of cortical abnormalities in autism, this investigation was conducted to examine cortical thickness in this disorder. **Method:** Sulcal and gyral thickness was measured for the total brain and for all lobes using MRI scans acquired from 17 children with autism and 14 healthy controls. **Results:** Increases in total cerebral sulcal and gyral thickness were observed in children with autism when compared with controls. Similar findings were noted in the temporal, and parietal lobes but not in the frontal and occipital. **Conclusions:** These preliminary findings indicate that increased cortical thickness may contribute to the increased grey matter volume and total brain size that have been observed in autism and may also be related to anomalies in cortical connectivity.

Increased brain size is one of the most consistent neurobiologic findings in autism,[1-2] and appears to be associated with cortical grey matter enlargement involving mostly the frontal and temporal lobes.[3] While increase in cerebral and lobar size have been reported, the exact pathophysiology of these volumetric alterations remains to be determined.[3,4] Cortical and lobar grey matter volumes are correlated with brain surface and cortical thickness, as observed in normal population and in individuals with neuropsychiatric disorders.[5] Hence, an increase in cortical volume in autism could be related to an increase in either its surface area, its thickness or both.[4,5] A recent preliminary investigation of the gyrification patterns in autism revealed an increase in cortical folding in the frontal lobe suggesting a possible increase in total cerebral surface area.[4] In light of these observations, this study was conducted to examine cortical thickness in a group of children with autism.

Methods

Subjects were 17 boys with autism and 14 healthy male controls between 8 and 12 years of age. The diagnosis of autism was established through the administration of the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS). Children with secondary autism such as tuberous sclerosis were excluded. Control subjects were screened by face-to face interview, and individuals with family history of any neuropsychiatric disorder, such as autism, learning disability, affective disorders, and schizophrenia, were not included. Potential subjects with a history of birth asphyxia, head injury, or a seizure disorder were excluded. All control subjects had a full scale IQ (FSIQ)>70 and no learning disability as assessed by the Wide Range Achievement Test-R. Exclusions were based on history and physical examination as well as laboratory testing when indicated. The WISC-III was administered to measure FSIQ, verbal IQ, and performance IQ (PIQ).

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Methodology of the study was approved by the Institutional Review Board. Written informed consent was obtained from parents and assent was obtained from all children.

Scans were obtained on a GE 1.5 Tesla Signa scanner. A T_1-weighted SPGR sequence was first acquired with the following parameters: slice thickness=1.5mm, slice numbers=124; TE 5ms; TR 25ms; flip angle 40, NEX 1; FOV 24cm; matrix 256×192. Proton density and T_2-weighted images were then obtained with the following parameters: slice thickness=5mm; TE 17ms for PD or 102ms for T_2; TR 2500ms; NEX 1; FOV 24cm; matrix 256×192. MRI data were identified by scan number to retain blindness, and analyzed using Brain research: Analysis of images, Networks and Systems software[7] (BRAINS) while applying previously published methodologies of cortical thickness and total brain volume (TBV) measurements.[6,7] The initial step of surface analysis in BRAINS is the creation of a triangle-based isosurface using the parametric center of the cortex as the outer boundary of the brain. Cortical thickness is calculated from vectors that are normal to each triangular surface, and the shortest distance to the 50% grey matter and 50% white matter is defined as the thickness.[6]

All measurements from autistic subjects were compared with controls using Student's t- test. Pearson's correlations coefficients were used to examine the relationships between TBV, IQ measures and cortical thickness. Spearman's rho correlation coefficients were used to examine the associations between ADI-R and ADOS scores with cortical thickness measurements. A two-tailed statistical significance level was set at $p<0.05$.

Results

No age differences were observed between the autistic (M=10.5±1.5 years; range:8.1- 12.9 years) and control groups (M=10.7±1.4 years; range:8.9-13.0 years). However, the autistic sample had a lower FSIQ (M=90.7±18.4; range:64-128) when compared with controls (M=110.9±12.2; range 91-130)($t=-3.498$; df =29; $p<0.005$). Children with autism had a mean score of 55.9 on the ADI-R (SD= 9.6; range 41-67) and 15.6 on the ADOS (SD=2.7; range 11-19). Differences in cortical thickness were found between the two groups and results are summarized in Table 1. No differences in TBV or in any of the global volumetric measures were observed between the two groups (Table 1). No association was found between TBV and IQ measures in either the autistic group or controls. Similarly, no relationship was found between cortical thickness and IQ measures in either group except for PIQ in the autistic group (rho= -0.500; p=0.041). Additionally, no significant correlations were found between cortical thickness and clinical features as measured by ADI-R and ADOS items.

Discussion

To our knowledge, this is the first neuroimaging investigation reporting abnormal cortical thickness in autism, which is consistent with evidence from neuropathological studies describing areas of increased cortical thickness.[8] Findings here were most obvious in the temporal lobe, which is concordant with several investigations reporting various anomalies in this structure in autism including decreased size of the left planum temporal, bilateral reduction of temporal perfusion, and abnormal activation of the superior temporal sulcus in response to vocal sounds.[9,10]

In the present investigation, gyral thickness was increased compared to the sulcal one in both patients and controls which is consistent with normal human brain cytoarchitecture.[5,7] This regional differentiation is important since sulcal and gyral areas have distinct histologic and neurochemical characteristics with different functional specializations.[7] Findings are also in support of the aberrant cerebral connectivity observed in this disorder[11] since convolutional maturation and cortical architecture are interrelated[4,5,7] and are important markers of cerebral development and neuronal connections.[4,5,7] In fact, neural pathways trajectories differ

depending on their localization with tangential orientation and long connections in sulcal regions in contrast to vertical and shorter paths in gyral areas.[7] Hence, surface architecture as determined by a complex gyrification process may reflect on the development of the underlying neural circuitry.[4,5,7]

Cortical thickness findings of the current study should be considered with caution taking in consideration the preliminary nature of this investigation and the inability to control for all confounding factors such as TBV and IQ measures due to the small sample size. Additionally, the lack of relationship between IQ and TBV observed here is consistent with several investigations examining the association of cognitive functioning and volumetric measurements[1,2] but is not concordant with evidence from developmental studies of healthy and intellectually disabled individuals indicating the existence of positive correlations between brain size and IQ.[12] Finally, the non-significant increase in TBV in the patient group when compared with controls is inconsistent with several previous reports of brain enlargement in children with autism,[1-3] and could be related to the small sample size or to the possible age-related changes observed in this disorder.[1,3] Larger studies examining cortical architecture as well as TBV and their relationships with cognitive measures and clinical features are warranted before final conclusions can be made.

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Table 1

Cortical Thickness Measurements

	Autistic(N=17)		Controls(N=14)		(df 29)	
	Mean	SD	Mean	SD	t	p
Cerebrum						
TCT	5.11	0.52	4.8	0.19	2.294	0.032
Gyral Thickness	5.76	0.58	5.42	0.31	2.055	0.050
Sulcal Thickness	4.36	0.53	4.06	0.26	2.005	0.056
Frontal lobe						
TCT	5.51	0.60	5.27	0.28	1.505	0.146
Gyral Thickness	6.23	0.66	5.98	0.42	1.300	0.205
Sulcal Thickness	4.49	0.62	4.43	0.31	1.326	0.197
Parietal lobe						
TCT	5.52	0.68	4.78	0.20	2.070	0.052
Gyral Thickness	5.88	0.84	5.52	0.36	1.648	0.113
Sulcal Thickness	4.42	0.60	4.10	0.30	1.876	0.072
Temporal lobe						
TCT	5.18	0.64	4.62	0.32	3.069	0.005
Gyral Thickness	5.98	0.82	5.34	0.44	2.711	0.012
Sulcal Thickness	4.28	0.60	3.74	0.32	3.135	0.004
Occipital lobe						
TCT	4.27	0.55	4.04	0.32	1.376	0.179
Gyral Thickness	4.43	0.86	4.08	0.61	1.265	0.216
Sulcal Thickness	4.12	0.43	3.96	0.30	1.186	0.245
Brain volume						
TBV	1368.9	119.9	1338.7	85.9	0.729	0.436
Total Grey Matter	878.85	89.63	854.22	59.14	0.881	0.386
Total White Matter	490.04	37.18	484.46	39.65	0.405	0.689
Total CSF	144.57	29.51	136.70	23.79	0.796	0.433
TBV/ICV	1.79	0.12	1.76	0.13	0.476	0.620

TCT: Total cortical thickness (gyral and sulcal); TBV: Total Brain Volume; CSF: Cerebral spinal fluid; TBV/ICV: Ratio TBV/ Intra