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Normal Rates of Neuroradiological Findings in Children with High Functioning Autism

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Abstract

Magnetic resonance imaging (MRI) has been used to analyze highly specific volumetric and morphological features of the brains of individuals with autism spectrum disorder (ASD). To date, there are few comprehensive studies examining the prevalence of neuroradiologic findings seen on routine MRI scans in children with ASD. This study examined the prevalence of neuroradiologic findings in children with high functioning ASD, and compared these rates to those in children with Attention-Deficit/Hyperactivity Disorder (ADHD) and children who are typically developing (TD). Results showed that approximately 90% of children had normal MRI scans. There was no significant effect of diagnosis on the total number of neuroradiological findings or the number of specific brain findings. Implications and future research directions are discussed.

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Keywords

Autism; Magnetic resonance imaging; Neuroradiological findings

Introduction

Autism spectrum disorders (ASD) are a group of lifelong neurodevelopmental disorders characterized by impaired social interactions, communication deficits, and restricted and repetitive stereotyped patterns of behavior (DSM-IV, 2000). The prevalence of ASD has soared in the last decade, with an estimated one in 110 children having one of the spectrum disorders, either autism, Asperger Syndrome, or Pervasive Developmental Disorder Not Otherwise Specified (Centers for Disease Control and Prevention 2006). As a result, the demand for medical services to evaluate children with ASD is high, particularly across the disciplines of pediatrics, psychiatry and neurology.

Three major academic organizations, the American Academy of Neurology and Child Neurology Society (AAN: Filipek et al. 2000), the American Academy of Child and Adolescent Psychiatry (AACAP: Volkmar et al. 1999), and the American Academy of Pediatrics (AAP: Johnson and Myers 2007) have each independently concluded that neuroradiologic assessments, such as magnetic resonance imaging (MRI), are not indicated as part of the routine evaluation of children with ASD.

This recommendation is based on prior neuroimaging data indicating that there are no specific brain findings that are more prevalent in ASD compared to other control groups. The data supporting this recommendation, however, come from examinations of small samples (often less than 30 subjects) that were clinically heterogeneous with respect to the presence or absence of intellectual disability, neurological, medical, or genetic disorders (e.g. Damasio et al. 1980; Gaffney and Tsai 1987). Moreover, different imaging methods, such as computerized tomography (CT) or MRI, with the latter including limited scan sequences (e.g., only T1 or T1 and T2 MRI sequences), were used across the studies, thereby restricting the types of brain abnormalities detected. Large scale studies of brain findings in ASD using comprehensive imaging protocols are therefore needed before drawing firm conclusions negating the use of MRI in the evaluation of children with ASD. This type of study would ideally include multiple imaging sequences that generate different image contrasts (e.g. T1, T2, T2*, fluid attenuated inversion recovery (FLAIR), diffusion weighted imaging (DWI)) because each sequence has a specific sensitivity for the various pathologies that may be encountered within the brain. If the prevalence of clinical neuroradiological findings does not differ between children with ASD and other clinical and nonclinical control groups, clinicians will have more definitive data to inform families that MRI scans are not indicated in the evaluation of children with ASD. Alternatively, if a higher prevalence of abnormal findings is found in the ASD group, further research will be necessary to determine their clinical and etiopathological significance.

The first set of imaging studies in ASD involved the use of CT scans. In a group of 17 children and adults with ASD, Damasio et al. (1980) found that 11.8% of the group ASD had intraparenchymal lesions, 5.9% had hydrocephalus, 29.4% had bilateral ventricular

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enlargement, and 52.9% showed mild abnormalities of the ventricular system. Caparulo et al. (1981) reported abnormalities (particularly ventricular) in 18.2% of children with autism (n = 22) and 59% of children with Pervasive Developmental Disorder (PDD) (n = 17), as well as a variety of inconsistent findings in control groups of children with language disorder, ADHD, and Tourette Disorder. Another study using CT reported gross abnormalities such as abnormally enlarged ventricles and porencephalic cysts in 26% of children with autism (n = 27), 33.3% of children with psychosis (n = 9), and 13% of children with intellectual disability (n = 23), whereas no lesions were present in the typically developing group (n = 16) (Gillberg and Svendsen 1983). Prior et al. (1984), however, reported no abnormalities or asymmetries of any kind on CT scans of a sample of nine boys with autism.

Similar to the CT scan data, subsequent studies using MRI did not find any lesions that were specific to ASD. Gaffney and Tsai (1987) found that 14% individuals with PDD or autism (n = 14) had mild ventricular abnormalities, and 7.1% had gray matter heterotopias. In a sample of 13 males with high functioning ASD, Piven et al. (1990) reported polymicrogyria, schizencephaly, and macrogyria in 58% of the subjects whereas no abnormalities were present in the comparison group of 13 healthy subjects. Taber et al. (2004) observed a 44% prevalence of dilated Virchow-Robin (V-R) spaces in 16 children diagnosed with autism compared to no gross abnormalities in the TD children (n = 16). Zeegers et al. (2006) reported neuroradiological abnormalities in children under age 3 years with developmental disabilities and found that among the 32 children with autism or PDD, 12.5% (n = 4) had enlarged or asymmetrical ventricles, 6.2% (n = 2) had asymmetrical V-R spaces, 9.4% (n = 3) had white matter lesions, 6.2% (n = 2) had corpus callosum abnormalities, 6.2% (n = 2) had septum pellucidum abnormalities, 3.1% (n = 1) had vermis atrophy, 3.1% (n = 1) had thinning of the corpus callosum, and 3.1% (n = 1) had a Chiari I malformation. A variety of abnormalities were similarly present in the children with learning disability (n = 9) and mental retardation (n = 4), with no specific lesion predominating in any group. Case report studies of ASD reported acrocallosal syndrome (n = 1, Steiner et al. 2004) and left frontal macrogyria, and bilateral opercular polymicrogyria (n = 2, Berthier et al. 1990).

Finally, in the largest scale study thus far, Boddaert et al. (2009) compared MRI findings in 69 children and adolescents with ASD with 77 typically developing (TD) children and adolescents with cervical-facial pathologies. The children were ages 2–16 years and of varying cognitive levels. Three distinct abnormalities were found in the ASD group: white matter signal abnormalities (27.5%), dilated V-R spaces (17.4%), and a variety of temporal lobe abnormalities (29%) including sub-cortical hyperintensity, loss of gray-white matter definition in the temporal poles, and a unilateral nodular temporal lobe mass lesion.

The present study addresses the gap in the field of large scale MRI studies in ASD. The study differs from Boddaert et al. (2009) in several ways. The sample age is narrower (7–13 years), only includes children with normal intelligence, and the findings in ASD are compared to data from a clinical control group of children with Attention-Deficit Hyperactivity Disorder (ADHD) as well as TD children. Similar to Boddaert et al. (2009), multiple MRI sequences were acquired and were independently read by two experienced pediatric neuroradiologists who were blinded to clinical diagnosis.

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Methods

Subjects and Procedures

The sample consisted of 73 children with ASD, 107 children with ADHD, and 144 TD children, ages 7.55–13.41 years. There were 16 sibling pairs who shared the same diagnosis (ASD: two pairs, ADHD: one pair, TD: thirteen pairs) and one set of three TD siblings. Subject characteristics are presented in Table 1. All subjects had MRI scans through previous research studies investigating the neurobiological basis for ASD and ADHD that were conducted by the senior investigator between 2000 and 2009 at our institution. These included studies of motor and behavioral response control in children with ADHD, as well as studies of motor skill learning in children with ASD.

All three groups were matched for age, but not for gender or IQ. There were significantly more males in the ASD group compared to the ADHD and TD groups. The TD group had a significantly higher full scale IQ (FSIQ) than both the ASD and ADHD groups, and the ADHD group had a higher FSIQ than the ASD group. Likewise, Perceptual Reasoning Index (PRI) and Verbal Comprehension Index (VCI) scores were significantly higher in the TD control group as compared to both the ASD and ADHD groups; these scores were also higher for the ADHD group compared to the ASD group.

In terms of psychiatric comorbidities, results of the DICA showed that 42 subjects with ASD met criteria for one or more of the following co-morbidities: ADHD (n = 20), oppositional defiant disorder (ODD, n = 21), simple or social phobia (n = 17), obsessive–compulsive disorder (n = 11), generalized anxiety disorder (n = 7), past major depressive episode (n = 8), conduct disorder (n = 2), and dysthymic disorder (n = 1). DICA scores and consequently, comorbidity data were not available for nine children in the ASD group. In the ADHD group, 40 children had comorbid ODD (n = 40) and 19 children had simple or social phobia (n = 19). Eight subjects in the TD group had simple phobia.

The screening procedures used for each of the studies from which subjects were originally recruited varied to some degree, but all subjects received detailed diagnostic characterization through a combination of diagnosis specific parent interviews, clinical observation, and the clinical impression of the senior investigator. Thus, slightly different numbers of subjects received each of the diagnostic tests. All subjects were screened and excluded for reading disabilities, known genetic disorders (e.g., Fragile X syndrome), and neurological conditions (e.g., seizures, traumatic brain injury). Additionally, speech and language disorders were excluded in the ADHD and TD groups.

The Autism Diagnostic Observation Schedule (ADOS-G) (Lord et al. 2000) and the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al. 1994) were used to establish the ASD diagnosis. Seventy-one subjects were diagnosed with ASD based on results from the ADI-R and ADOS-G. Two children did not have an ADI-R and were given an ASD diagnosis based on scores from the ADOS-G. Among the ASD group, 32 subjects were diagnosed with high functioning ASD and 41 with Asperger Syndrome. These two ASD subtypes were merged to form the ASD group because of ongoing discussions that these two disorders may not exist as separate entities (Kamp-Becker et al. 2010; Miller and Ozonoff 2000; Mukaddes et

al. 2010; South et al. 2005; Szatmari et al. 1989; Verté et al. 2006) and in order to maximize statistical power.

The ADHD diagnosis was established using the Diagnostic Interview for Children and Adolescents- 4th edition (DICA-IV), a structured psychiatric interview administered to the parent (Reich et al. 1997), as well as two ADHD specific rating scales, the Conners' Rating Scales (Parent version, CPRS-R, Conners 1997) and the DuPaul ADHD Rating Scale (DuPaul et al. 1998). Ninety-nine children were given an ADHD diagnosis based on results of the DICA and both of the ADHD scales; eight children had ADHD based on the results of the DICA and one of these scales. All children with ADHD had T-scores of 65 or greater on Scale L or M of the CPRS-R or had at least six symptoms rated as 2 or 3 on the DuPaul scale. Of the 107 ADHD subjects in the study, 34 were predominantly inattentive, two were predominantly hyperactive-impulsive, 68 were combined subtype and three had an undetermined subtype. Exclusion criteria for the ADHD children consisted of co-morbid conduct disorder, mood disorder, generalized anxiety disorder, separation anxiety disorder, or obsessive–compulsive disorder. Children with ADHD who were taking psychoactive medications, other than stimulants, were also excluded.

The DICA was used to assess psychiatric status in the TD group. This group was free of all lifetime and current psychopathology except simple phobia. One hundred and forty-four children were included in the TD group based on the results of the DICA. The CPRS-R and DuPaul ADHD rating scales were also administered to TD subjects; those with T-scores greater than 60 on the ADHD subscales of the CPRS-R (DSM-IV Inattention, DSM-IV Hyperactivity) were excluded from the study.

Children in the study had a full scale IQ (FSIQ) of 80 or higher based on performance on the Wechsler Intellectual Scale for Children WISC-3rd edition (Wechsler 1991) (n = 75) or the WISC-4th edition (Wechsler 2003) (n = 249). Seven subjects had FSIQ scores below 80 with significant discrepancies between IQ sub-indices; these subjects were included on the basis of having either one or both of the Perceptual Reasoning Index (PRI) and Verbal Comprehension Index (VCI) scores above 85.

All studies were approved by the Institutional Review Board. Written informed consent was obtained from each parent/guardian, and assent was obtained from each participating child.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) was performed on one of three available clinical MRI scanners: a 1.5 Tesla (T) Philips Gyroscan NT MRI unit (Philips Medical Systems, Best, The Netherlands) (n = 231), a 3T Philips Gyroscan MRI unit (n = 72), or a 1.5T General Electric MRI scanner (General Electric Healthcare, Milwaukee) (n = 21). There were no significant group differences in the proportion of children receiving 1.5T and 3.0T scans ($p = 0.60$). The standard imaging protocol always included a sagittal T1-weighted, an axial T2-weighted, and an axial FLAIR sequence.

In 84.9% of subjects, data from all three sequences were available for interpretation. For 13.3% and 1.8% of the sample, respectively, data were available for two of the three

sequences (one subject was missing a T1, three were missing a T2, and 39 were missing a FLAIR) or only one sequence (all six subjects were missing T2 and FLAIR scans). In order to keep the study numbers as high as possible, we analyzed all subjects' scans and then conducted a secondary analysis including only those subjects who received all three scan sequences in order to examine any bias that might have been introduced by the absence of additional scan sequences.

The MRI scans were read independently by two board certified pediatric neuroradiologists within our institution's Department of Radiology who were blinded to clinical diagnoses. Prior to reading the scans, the neuroradiologists and the senior investigator established a list of 11 predefined lesion categories as well as operational criteria for systematically coding each of these lesions. These categories were defined based upon a review of the existing literature, incorporating all neuroradiologic findings that have been reported in previous studies. Seven of these predefined lesions were considered abnormal findings: Chiari I malformation, corpus callosum anomalies, enlarged ventricles, focal white matter lesions (including single punctate, multiple punctate, and confluent plaquelike white matter lesions), heterotopia, posterior fossa cyst, and vascular malformation. Four of the predefined categories were considered normal variant findings, i.e., abnormal hippocampal shape, enlarged subarachnoid space, enlarged V-R spaces, and septum pellucidum variants (e.g., a not intact septum pellucidum, the presence of cavum septum pellucidum, and cavum vergae). A twelfth category termed ‘other abnormal findings’ and a thirteenth category termed ‘other normal variant findings’ were created to code any brain findings that did not fit into one of the predefined categories but were considered to be of significance as incidental findings.

The neuroradiologists read the scans for the presence or absence of any of the predefined findings and also commented on additional unclassified findings. The scans were then categorized as normal or abnormal; scans were coded as abnormal if any abnormal finding was present and normal if no brain findings or normal variant brain findings were present. The neuroradiologists adjudicated any discrepancies through case discussion. The types of discrepancies pertained to whether or not one of the pre-specified lesions was present (9/324, 2.78%), and whether or not the finding should be coded in the ‘various findings’ category (17/324, 5.25%).

Data Analyses

Chi-square and one way analysis of variance (ANOVA) tests were used to examine differences in demographic characteristics. Chi-square analyses were used to test the effect of diagnosis (ASD, ADHD, and TD) on the total number of subjects with at least one abnormal brain finding, the total number of abnormal brain findings, and the number of subjects with more than one abnormal finding. These same three data points were calculated for the normal variant brain findings. Data on ‘other abnormal findings’ or ‘other normal variant findings’ were included in these analyses. Chi-square analyses were also performed on the number of brain findings in each of the seven individual abnormal and four individual normal variant predefined categories, but not on the ‘other abnormal findings’ or ‘other normal findings’ categories because of the heterogeneous nature of these two groupings. The

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analyses were repeated for three subgroups of subjects in order to address potential biases due to group composition. These subgroups included subjects who were males, subjects who had all three MRI sequences (T1, T2, FLAIR), and a group in which there were no siblings with a shared diagnosis. This last group was created by randomly removing one of the siblings in each sibling pairs with a shared diagnosis and two of the siblings in a sibling trio with the same diagnosis.

Results

Types of MRI Findings

Table 2 presents the prevalence of brain findings according to diagnostic group. Among all subjects, 89.8% of subjects had either no MRI findings or only normal variant findings and were therefore categorized as having a normal scan. The number of subjects in the high functioning ASD group exhibiting each abnormal finding was as follows: Chiari I malformation (n = 2), enlarged ventricles (n = 1), and focal white matter lesions (n = 3 of which one had a single punctate lesion, one had multiple punctate lesions, and one had confluent plaque-like lesions). The ‘other abnormal findings’ category (n = 2) included a pineal cyst and a focal gliosis of the globus pallidum. The number of subjects in the high functioning ASD group exhibiting each normal variant finding was as follows: enlarged V-R spaces (n = 2) and a septum pellucidum variant (n = 1). The ‘other normal variant findings’ category (n = 1) included a slight asymmetry in size between the right and left ventricles. Two ASD subjects had two findings. One subject had enlarged ventricles and a Chiari I malformation and another subject had two ‘other findings’, one abnormal and one normal variant, respectively (focal gliosis and slight ventricular asymmetry).

The number of subjects in the ADHD group with abnormal neuroradiologic findings was: Chiari I malformation (n = 1), enlarged ventricles (n = 1), focal white matter lesions (n = 3; two had a single punctate lesion and one had multiple punctate lesions), heterotopia (n = 1), and posterior fossa cyst (n = 4). The ‘other abnormal findings’ (n = 3) category included a right frontal arachnoid cyst, a left choroid plexus cyst, and a FLAIR hyperintense band that extended from the cortex to the periventricular white matter; this band was considered either a gliosis or cortical malformation. The number of subjects in the ADHD group exhibiting normal variant findings was: enlarged subarachnoid space (n = 1), enlarged V-R spaces (n = 4), and septum pellucidum variant (n = 2). In the ADHD group, one subject had three abnormal findings: a single punctate focal white matter lesion, a posterior fossa cyst and an ‘other abnormal finding’ (FLAIR hyperintense band extending from cortex to periventricular white matter). Two subjects each had one abnormal finding and one normal variant finding. Specifically, one subject presented with enlarged V-R spaces and a posterior fossa cyst, and the second presented with enlarged ventricles and an enlarged subarachnoid space.

In the TD group, the number of subjects with abnormal neuroradiologic findings in any of the predefined brain findings was as follows: Chiari I malformations (n = 4), focal white matter lesions (n = 8 of which six had single punctate lesions and two had multiple punctate lesions), heterotopia (n = 2), and posterior fossa cyst (n = 1). One subject had left thalamic gliosis, which was coded as an ‘other abnormal finding’. The number of subjects in the TD

group with normal variant findings was: enlarged V-R spaces (n = 5) and septum pellucidum variants (n = 3). One subject had two findings simultaneously, enlarged V-R spaces (abnormal) and heterotopias (normal). Another subject had two abnormal findings, multiple punctate focal white matter lesions and a Chiari I malformation.

Across all groups, there were no findings in hippocampal shape, no vascular malformations were seen, and the corpus callosum was unremarkable.

Group Differences in MRI Findings

Three way Chi-square analyses revealed no significant differences between diagnostic groups in the total number of abnormal findings, the number of subjects with one abnormal finding, or the number of subjects with more than one abnormal finding. Likewise, no significant differences across the three study groups were found in any of the seven predefined abnormal findings categories. A trend level difference was found for the prevalence of posterior fossa cysts ($p = 0.07$), which was present in four subjects in the ADHD group, one subject in the TD group, and no subjects in the ASD group. No significant differences were found in the post hoc two way Chi-square analyses directly testing differences in the prevalence of posterior fossa cysts between the ADHD and ASD groups, the ADHD and TD groups, and the ASD and TD groups (all $p > 0.05$). Likewise, no significant differences between the three diagnostic groups were found in the total number of normal variant findings, the number of subjects with one normal variant finding, the number of subjects with more than one normal variant finding, or in any of the four predefined normal variant findings categories.

For each of the three subgroup follow-up analyses (males, subjects with all three MRI sequences, and removal of siblings with shared diagnosis), there were no significant differences in the total number of abnormal findings, number of subjects with one abnormal finding, or number of subjects with more than one abnormal finding ($p > 0.05$ for all analyses). Likewise, there were no significant differences between diagnostic groups in any of the seven predefined abnormal lesion categories for any of the subgroup analyses ($p > 0.05$ for all analyses). In the normal variant findings category, there were no significant differences in the total number of normal variant findings, number of subjects with one normal variant finding, or number of subjects with more than one normal variant finding ($p > 0.05$ for all analyses). Lastly, there were no significant differences between diagnostic groups for any of the four predefined normal lesion categories ($p > 0.05$ for all analyses).

Discussion

This study examined the prevalence of neuroradiologic findings in a large cohort of 7–13 year old children with either ASD, ADHD, or no psychopathology who were recruited for previous research studies over a nine year period. The study methods were stringent in the use of a homogenous and narrow age group of ASD subjects, well-established instruments to characterize the clinical and control groups, inclusion of multi-sequence MRI imaging protocols, and the systematic review of all images by two experienced pediatric neuroradiologists who were blinded to diagnoses. Our data showed that there were no

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significant differences in the prevalence of neuroradiologic findings in the ASD group compared to the ADHD and TD groups.

Prior data on the number and type of MRI findings in ASD are inconsistent, most likely due to clinical variability in subject profiles both within and across studies, small subject populations, and limited imaging protocols. These factors limit the comparability of these prior studies with our findings. Aside from the present study, Boddaert et al. (2009) has conducted the only large scale MRI study of ASD that included a complete range of MRI sequences (T1, T2, FLAIR). Their findings indicated a greater prevalence of white matter hyperintensities, temporal lobe abnormalities, and dilated V-R spaces in ASD subjects, compared to a TD control group. These lesions are not specific to ASD and are present in other neurological (Bax et al. 2006), metabolic (Matheus et al. 2004), and genetic disorders (Van der Knaap et al. 2004). The discrepant neuroradiological findings between Boddaert et al. (2009) and our study may relate to differences in patient characteristics.

A limitation of this study is that the findings apply only to a narrow age of children with high functioning ASD and are not generalizable to all children with ASD. Given the clinical heterogeneity of ASD, the field is moving in the direction of investigating the neurobiological basis of more clinically homogenous subgroups of children with ASD (e.g., high functioning autism: Goldberg et al. 2011; low functioning autism: Scott et al. 2009). Another limitation is that the ASD and control groups were unmatched on gender and IQ, with a higher percentage of males in the ASD group and a higher mean IQ in the TD group. The effect of the gender mismatch was examined through the analysis of a male only subgroup, which replicated the findings of the larger mixed gender group, although with somewhat diminished statistical potential. In addition, although there was a statistically significant difference in IQ between diagnostic groups, all subjects had IQs of 80 or above. These issues are therefore estimated to have a limited effect on the study's findings.

Future studies with larger sample sizes can address the hypothesis that phenotypically different patient groups may have different underlying brain findings with study designs that include heterogeneous profiles of children with respect to ASD subtype and severity, cognitive level, and presence of medical comorbidities. Given the complexity of the ASD phenotype and the difficulty in recruiting homogeneous populations, a first step may be to conduct a multi-site ‘data sharing’ study whereby researchers pool structural MRI scans across different laboratories and apply standardized neuroimaging methods to delineate specific lesions. Brain findings can subsequently be correlated with clinical measures (e.g., sociocognitive, linguistic, motor) across different patient subgroups (Belmonte et al. 2008). Findings from such a retrospective study may lead to hypothesis driven investigations of brain lesions using newer technologies, such as ultra high-resolution anatomical MRI sequences, and functional MRI techniques such as diffusion tensor imaging, connectivity MRI, perfusion weighted MRI, and multi-nuclear quantitative magnetic resonance spectroscopy. These methods may increase the sensitivity and specificity of MRI in the anatomical and functional evaluation of subjects with ASD.

Over the past two decades, MRI and postmortem data have significantly advanced our knowledge of the neurobiology of ASD. These data have implicated abnormalities, although

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somewhat inconsistently, in key brain regions such as the amygdala, cerebellum, and callosum, as well as abnormal patterns of brain growth and functional connectivity amongst brain regions (see review by Stigler et al. 2011). However, there continues to be little evidence that directly connects abnormal brain findings to the clinical profile of patients with ASD. Studies investigating neuroradiologic brain lesions using MRI may provide one research avenue that can help reveal such connections, if direct links between brain anatomy and behavior do indeed exist.

The discussion about whether MRI scans are clinically relevant in the assessment of youth with ASD is an ongoing issue. MRI scans are costly and pose risks including claustrophobia, panic attacks, and side effects of anesthesia if required as is often the case with very young children and/or lower functioning children with ASD. Therefore, more robust data supporting the use of MRI are needed if the medical community is to recommend their regular use. This includes data indicating that certain brain findings are more prevalent in ASD and that these findings are correlated with clinical or etiopathologic aspects of the disorder. Findings from the current study do not demonstrate clinically significant MRI abnormalities in children with ASD. The diagnosis of ASD is currently based only on clinical findings. Clinicians caring for children with ASD now have more rigorous data to share with parents regarding the AAN, AAP, and AACAP recommendations discouraging the use of clinical neuroimaging assessments in the evaluation of children with ASD.

In summary, this study examined the prevalence of neuroradiologic findings in children with high functioning ASD, children with ADHD, and TD children and found no brain findings that were preferentially associated with high functioning ASD. Multi-site studies using rigorous ASD assessments and advanced anatomic and functional MRI protocols are needed to determine whether specific subgroups of ASD may have distinct brain findings. In the interim, the evidence does not support the regular use of clinical MRI scans for the evaluation of children with ASD.

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Table 1

Subject characteristics

	ASD[a] (n = 73)	ADHD[b] (n = 107)	TD[c] (n = 144)	Test statistic	*p* value
Age (SD) in years	10.20 (1.65)	10.32 (1.34)	10.39 (1.24)	F = 0.47	0.62
Number (%) of males	62 (84.93)	64 (59.81)	75 (52.08)	χ^2 = 22.53	<0.001
Full scale IQ (SD)	101.89 (16.21)	107.03 (13.28)	114.56 (11.07)	F = 24.85	<0.001
Perceptual reasoning index (SD)	88.04 (15.42)	106.00 (12.96)	111.65 (12.32)	F = 77.57	<0.001
Verbal comprehension index (SD)	106.21 (21.46)	112.99 (15.45)	118.45 (13.55)	F = 14.01	<0.001

Three way group comparisons were performed using Chi-square or one way analysis of variance. Posthoc bivariate analyses were performed using Chi-square and *t* tests

ASD versus Control, % Male: χ^2 = 22.46, $p < 0.001$, FSIQ: $t = 6.77$, $p < 0.001$, PRI: t = 12.22, $p < 0.001$, VCI: $t = 5.13$, $p < 0.001$

ADHD versus Control, % Male: χ^2 = 1.48, $p = 0.223$, FSIQ: $t = 4.95$, $p < 0.001$, PRI: $t = -3.51$, $p < 0.001$, VCI: t = minus;2.97, $p = 0.003$

ASD versus ADHD, % Male: χ^2 = 13.04, $p < 0.001$, FSIQ: $t = -2.27$, $p = 0.024$, PRI: $t = -8.45$, $p < 0.001$, VCI: $t = 2.47$, $p = 0.015$

[a]High functioning autism spectrum disorders

[b]Attention deficit hyperactivity disorder

[c]Typically developing

Table 2

Prevalence of MRI findings in children with high functioning autism spectrum disorder (ASD), Attention-deficit hyperactivity disorder (ADHD), and children who are typically developing (TD)

	ASD (n = 73)	ADHD (n = 107)	TD (n = 144)	Chi-square (χ^2)	*p* value
Abnormal findings					
Total number (%) of abnormal findings	8 (11.0%)	13 (12.1%)	16 (11.1%)	0.09	0.96
Number (%) of subjects with 1 abnormal finding	7 (9.6%)	11 (10.3%)	15 (10.4%)	0.04	0.98
Number (%) of subjects with >1 abnormal finding	1 (1.4%)	1 (0.9%)	1 (0.6%)	0.24	0.89
Chiari I malformation	2 (2.7%)	1 (0.9%)	4 (2.8%)	1.14	0.57
Corpus callosum anomalies	0	0	0	n/a	n/a
Enlarged ventricles	1 (1.4%)	1 (0.9%)	0	1.74	0.42
Focal white matter lesion(s):	3 (4.1%)	3 (2.8%)	8 (5.6%)	1.14	0.57
Punctate, single	1 (1.4%)	2 (1.9%)	6 (4.2%)	1.89	0.39
Punctate, multiple	1 (1.4%)	1 (0.9%)	2 (1.4%)	0.12	0.94
Confluent, plaque-like	1 (1.4%)	0	0	3.45	0.18
Heterotopia	0	1 (0.9%)	2 (1.4%)	1.02	0.60
Posterior fossa cysta	0	4 (3.7%)	1 (0.7%)	5.22	0.07
Vascular malformation	0	0	0	n/a	n/a
Other abnormal findings[b]	2 (2.7%)[c]	3 (3.8%)[d]	1 (0.7%)[e]	n/a	n/a
Normal variant findings					
Total number (%) of normal variants findings	4 (5.5%)	7 (6.5%)	8 (5.6%)	0.13	0.94
Number (%) of subjects with 1 normal variant finding	4 (5.5%)	7 (6.5%)	8 (5.6%)	0.13	0.94
Number (%) of subjects with <1 normal variant finding	0	0	0	n/a	n/a
Abnormal hippocampal shape	0	0	0	n/a	n/a
Enlarged subarachnoid space	0	1 (0.9%)	0	2.03	0.36
Enlarged Virchow Robin space	2 (2.7%)	4 (3.7%)	5 (3.5%)	0.14	0.93
Septum pellucidum variants	1 (1.4%)	2 (1.9%)	3 (2.1%)	0.14	0.93
Other normal variant findings[b]	1 (1.4%)[f]	0	0	n/a	n/a

[a] Posthoc bivariate analyses were performed using Chi-square tests for this category: ASD versus Control: $\chi^2 = 0.509$, $p = 0.48$, ASD versus ADHD: $\chi^2 = 2.79$, $p = 0.095$, and ADHD versus Control: $\chi^2 = 2.913$, $p = 0.088$

[b] Chi-square analysis was not performed on this category due to the heterogeneous nature of the brain findings

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[c] Pineal cyst, focal gliosis of the globus pallidum

[d] Right frontal arachnoid cyst, left choroid plexus cyst, FLAIR hyperintense band extending from cortex to periventricular white matter

[e] Left thalamic gliosis

[f] Right ventricle slightly wider than left