

# The yield of structural magnetic resonance imaging in autism spectrum disorders

Jiri Lisy<sup>a</sup>, Andrea Efremova<sup>b</sup>, Michal Hrdlicka<sup>b</sup>

**Aims.** The aim of our study was to assess the yield of routine brain magnetic resonance imaging (MRI) performed at our hospital as part of the diagnostic procedures focused on autism.

**Methods.** Our retrospective study involved children who had attended a diagnostic examination focused on autism and underwent brain MRIs between 1998–2015. The International Classification of Diseases, 10<sup>th</sup> edition was used to make clinical diagnoses. In 489 children (404 boys, 85 girls; mean age  $8.0 \pm 4.2$  years), a diagnosis of a pervasive developmental disorder was confirmed. Forty-five children, where the autism diagnosis was ruled out (but other psychiatric diagnoses found), served as a control group (36 boys, 9 girls; mean age  $7.0 \pm 2.4$  years). We can assume that in such a control group, brain abnormalities might occur at a higher frequency than in truly healthy children which would have the effect of reducing the difference between the groups.

**Results.** MRI pathologies were more common in the autistic (45.4 %) compared to the control group (31.8%) but the difference was significant only at the trend level ( $P=0.085$ ). Hypoplasia of the corpus callosum (CC) was significantly more common in the autistic vs. the control group (13.7 vs. 0%;  $P=0.009$ ). In contrast, nonmyelinated areas of white matter were significantly more common in controls (31.8 vs. 17.3%;  $P=0.018$ ). Differences in other parameters were not significant.

**Conclusion.** The occurrence of CC hypoplasia on routine MRI scans could represent a “red flag” for suspicion of autism.

**Key words:** autism spectrum disorders, MRI, brain, corpus callosum

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<sup>a</sup>Department of Radiology, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic

<sup>b</sup>Department of Child Psychiatry, Second Faculty of Medicine, Charles University and University Hospital Motol, Prague, Czech Republic

Corresponding author: Michal Hrdlicka, e-mail: [michal.hrdlicka@fnmotol.cz](mailto:michal.hrdlicka@fnmotol.cz)

## INTRODUCTION

Magnetic resonance imaging (MRI) is a powerful tool in autism research. A recent review by Bölte et al. identified 114 MRI research studies carried out in children<sup>1</sup>. Less is known about the utility of routine MRIs in diagnostic procedures focused on autism spectrum disorders (ASD). Neither the American Academy of Child and Adolescent Psychiatry practice parameters on ASD (ref.<sup>2</sup>) nor the National Institute for Health and Care Excellence clinical guidelines on autism<sup>3</sup> recommend routine MRI scans as part of diagnostic assessments.

There are few reports dealing with routine MRI yield. We identified only five, small or medium-sized, studies, with 33, 55, 70, 70, and 85 children<sup>4-8</sup>. Two of the five studies were methodologically handicapped since some of the children were examined using computed tomography, while others were examined using MRI; both studies reported negative results<sup>4,7</sup>.

Challman et al.<sup>6</sup> reported visible central nervous system (CNS) abnormalities, of varying significance, in 24% of their sample. None of these abnormalities required intervention, and only one MRI scan (in a patient with multiple cortical tubers) contributed to a specific diagnosis. In the Battaglia and Carey study<sup>8</sup>, brain MRIs were

informative in two children (2.3%) with relative macrocrania but no neurological features showing focal-band heterotopia at the level of the right lateral ventricle or partial agenesis of the corpus callosum with right cerebellar hemisphere hypoplasia. Ming et al.<sup>5</sup> found 8 brain parenchymal abnormalities in their sample of 55 patients (14.6%). These abnormalities included two subjects with a Chiari I malformation, one each with a hamartoma, an enlarged vascular space, and a venous angioma, and three with abnormal white matter signals.

In the Czech Republic, some hospitals (including ours) perform routine brain MRIs as part of diagnostic procedures focused on autism. The aim of our retrospective study was to assess the yield of routine MRIs performed at our hospital between 1998–2015.

## METHODS

### Procedure

Our retrospective study involved children who had attended a diagnostic examination focused on autism at the Department of Child Psychiatry between 1998–2015 and whose parents had agreed that a routine MRI (most of which were done under general anesthesia) be part of

the diagnostic process. The study was approved by the Multicenter Ethics Committee of the University Hospital Motol under Reference No. EK-124/17.

The International Classification of Diseases, 10<sup>th</sup> Ed. (ICD-10) was used to make clinical diagnoses<sup>9</sup>. The diagnosis was based on a clinical examination by experienced child psychiatrists. The assessment was supported in 1998 and 1999 by testing using the Childhood Autism Rating Scale<sup>10</sup>. Since 2000, the third version of the Autism Diagnostic Interview-Revised<sup>11</sup> has been used for assessments. Starting in 2012, the Autism Diagnostic Observation Schedule-Generic<sup>12</sup> was added to assessments; both continue to be used. IQ testing was also performed. The Gesell Developmental Scales was used for younger children, and the Stanford-Binet Intelligence Scale, 4th ed. was used for older children.

MRI scans were obtained using a 1.5 Tesla Philips Gyroscan ACS 15NT and later a 1.5 Tesla Philips Ingenia scanner. The imaging protocol consisted of four pulse sequences: T2 turbo spin echo (T2/TSE) in the axial plane, fluid attenuation inversion recovery (FLAIR) in the axial plane, T1 inversion recovery turbo spin echo (T1/IR-TSE) in the coronal plane, and T1 spin echo (T1/SE) in the sagittal plane. Assessments were done by an experienced neuroradiologist (J.L.) on hard copies of the MRI scans (1998–2002); starting in 2003 assessments were done using digital images. Radiologic assessments described any pathology seen on MRI scans, and categorized scans into three categories: (1) normal; (2) benign pathology (e.g., mega cisterna magna, glial changes, arachnoid cysts); and (3) severe pathology (e.g., septo-optic dysplasia, pilocytic astrocytoma, cavernoma, mesial temporal sclerosis).

The digital MRI images were re-evaluated as part of this study; however, MRI scan hard copies were no longer available. Thus, only some parameters (severe pathology, categorization of the scans, gliosis, arachnoid cysts, and other cysts) that were followed by J.L. since 1998, could be adopted for this study without re-evaluation. Therefore, the number of assessed subjects differs among displayed parameters (see Table 2).

### Participants

From 1998–2015, 489 children were diagnosed as having a pervasive developmental disorder (404 boys, 85 girls). The mean age in the group was  $8.0 \pm 4.2$  years (range 1.7–26.0 years). Diagnoses, based on the ICD-10, included 314 patients with childhood autism, 68 patients

**Table 1.** Categories of MRI findings.

Findings on MRI	ASD	Controls	Statistics
Normal	267 (54.6%)	30 (68.2%)	
Benign pathology	212 (43.4%)	12 (27.3%)	Chi <sup>2</sup> =4.941,
Severe pathology	10 (2.0 %)	2 (4.5%)	df=2, P=0.085
Total	489 (100%)	44 (100%)	

ASD, autism spectrum disorders; MRI, magnetic resonance imaging. Column percentages are given.

with atypical autism, 82 patients with Asperger syndrome, and 4 patients with other childhood disintegrative disorders. Two patients were diagnosed with Rett syndrome, 6 with other pervasive developmental disorders, and 7 with pervasive developmental disorder unspecified. In 322 of 489 autistic patients (65.8% of the autistic group), data on intellectual functioning were available. Of these, 189 of 322 children (58.7%) were diagnosed with mental retardation (MR).

Forty-five children, in whom an ASD diagnosis was ruled out, served as a control group (36 boys, 9 girls; mean age  $7.0 \pm 2.4$  years, range 3.1–12.7). Their diagnoses included specific developmental disorders of speech and language (15 cases), hyperkinetic disorder (13 cases), mental retardation (12 cases), other childhood emotional disorders (5 cases), abnormal personality development (3 cases), and combined vocal and multiple motor tic disorder (one case). Several patients suffered from a combination of diagnoses.

There were no significant differences between the autistic and control groups in age ( $U = 11495.0$ ,  $P=0.619$ ) or gender ( $\chi^2=0.195$ ,  $df=1$ ,  $P=0.659$ ). MR was significantly more common in the autistic group than in the control group (58.7% vs 27.3%;  $\chi^2=15.438$ ,  $df=1$ ,  $P<0.001$ ).

### Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS, version 22.0). Descriptive statistics for the samples were used. For comparing age, gender and frequency of MR and MRI scan categories between the autistic and control groups, the Mann-Whitney U test and the Chi-Square test were used. For comparisons of MRI findings between the autistic and control groups, only findings with a total number >10 were included, and the Chi-Square test was used.

**Table 2.** Summary of frequent MRI findings in the ASD and the control groups.

MRI Findings	n	ASD	Controls	Statistics	
				Chi <sup>2</sup> *	P
Gliosis	533	56 (11.5%)	2 (5.5%)	1.986	0.159
Arachnoid cysts	533	66 (13.5%)	5 (11.4%)	0.159	0.690
Other cysts	533	17 (3.5%)	2 (4.5%)	0.134	0.714
Nonmyelinated areas of WM	467	73 (17.3%)	14 (31.8%)	5.574	0.018
Hypoplasia of corpus callosum	467	58 (13.7%)	0 (0%)	6.889	0.009
Mega cisterna magna	467	32 (7.6%)	1 (2.3%)	1.700	0.192

ASD, autism spectrum disorders; MRI, magnetic resonance imaging; n, number of assessed subjects in total; WM, white matter

\* df = 1

**Table 3.** Summary of uncommon MRI findings in the ASD and the control groups.

Finding on MRI	ASD		Controls	
	n	% of group	n	% of group
Benign tonsillar ectopia	4	0.8	0	0
Periventricular atrophy	4	0.8	0	0
Cortical atrophy	3	0.6	0	0
Optic nerve atrophy	3	0.6	0	0
Skull deformity	3	0.6	0	0
Optic bulb atrophy	2	0.4	0	0
Cavernoma	2	0.4	0	0
Septo-optic dysplasia	2	0.4	0	0
Capillary telangiectasia	2	0.4	0	0
Cerebellar atrophy	1	0.2	1	2.2
Chiari malformation	1	0.2	1	2.2
Hippocampal malrotation	1	0.2	0	0
Mesial temporal sclerosis	1	0.2	1	2.2
Neurofibromatosis type 1	1	0.2	0	0
Pilocytic astrocytoma	1	0.2	0	0

ASD, autism spectrum disorders; MRI, magnetic resonance imaging; n, number of findings.

## RESULTS

### Overall assessment of MRI scans

MRI pathology was more common in the autistic (45.4%) compared to the control group (31.8%) but the difference was significant only at the trend level ( $P=0.085$ ). For details, see Table 1.

### Frequent findings

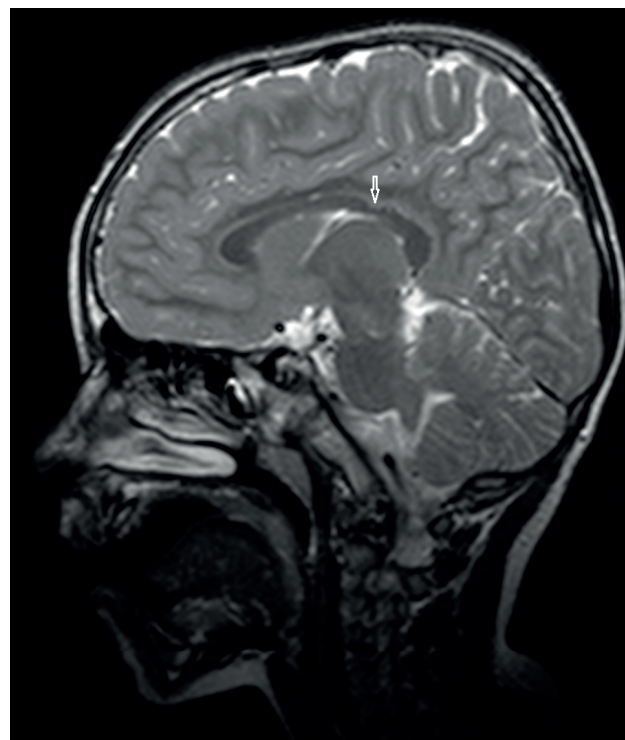
Findings with a total number  $>10$  are summarized in Table 2. Hypoplasia of the corpus callosum (CC) was significantly more common in the ASD compared to the control group (13.7 vs. 0%;  $P=0.009$ ; see Fig. 1). In contrast, nonmyelinated areas of white matter were significantly more common in controls (31.8 vs. 17.3%;  $P=0.018$ ). Arachnoid cysts were seen more frequently in the ASD compared to the control group (see Fig. 2), whereas other cysts were found more frequently in controls than in the ASD group; although, neither were significant. Differences in other variables were also not significant.

### Rare findings

Uncommon findings are summarized in Table 3. No statistical comparisons between the autistic and control groups were performed because of the small number of cases.

## DISCUSSION

Our study showed that the frequency of MRI abnormalities was higher in the autistic group compared to the control group (45% vs. 32%, see Table 1). To understand why the result failed to reach significance, we must understand that the control group was not a group of fully



**Fig. 1.** Focal hypoplasia in the posterior body of the corpus callosum, 5-year-old autistic boy, MRI T2/TSE in the sagittal plane.



**Fig. 2.** Right-sided frontal arachnoid cyst in a 14-year-old autistic boy, MRI T2/TSE in the axial plane.

healthy children. The control children were not free of psychiatric diagnoses, i.e., these were children who had been sent for diagnostic examination with a suspicion of autism and in whom the ASD diagnosis was excluded, however, other psychiatric diagnoses were made. We can



assume that in such a control group, brain abnormalities might occur at a higher frequency than in truly healthy children which would have the effect of reducing the difference between the groups. This was the first limitation of our study; however, there was no other way, in a retrospective study, to have a control group where autism was precisely excluded.

The frequency of abnormal MRI findings (45%) was higher than in any other study regarding MRI abnormalities. The next closest was 24% in a study by Challman et al.<sup>6</sup> and 14.6% in a study by Ming et al.<sup>5</sup>; although, the definition of an "abnormality" varied among the studies. In our study, mild pathological changes (including congenital variations) were observed in 43.4%, which was much higher than the 2% with really severe pathological involvement.

We believe that the most important finding of our study was that CC hypoplasia was significantly more common in ASD than the control group (13.7 vs. 0%). Classification of CC hypoplasia used the classification scheme developed by R. Hanna<sup>13</sup>, CC hypoplasia in our study included both hypoplasia without dysplasia and the "apple core" form. Our data showed that CC hypoplasia seemed to be a finding rather specific for the ASD group (with a zero frequency in the control group); as such, its occurrence during routine MRI scanning, could represent a "red flag" for suspicion of autism. The decrease of CC volume in ASD individuals is well known from MRI research studies, e.g., a meta-analysis by Stanfield et al.<sup>14</sup> identified five studies on reduced CC in ASD and a review by Chen et al.<sup>15</sup> found four studies. However, we are not aware of such observations during routine MRIs. CC involvement in the etiology of autism has also been confirmed in studies of autism connectivity<sup>16,17</sup>.

Findings with non-significantly higher frequencies in the autistic group vs. the control group were arachnoid cysts (13.5%); its frequency was also higher than in the population of healthy children. Previous studies described a 1.4% prevalence of arachnoid cysts in adults<sup>18</sup> and 1–3% in children<sup>19</sup>. This observation could possibly be associated with the neurodevelopmental background of autism<sup>20</sup>.

The clinical benefits of our study will likely center around the value of routine MRIs as part of the diagnostic process focused on autism. We believe that the 12 observed cases having a severe MRI pathology, especially those involving brain tumors (two cavernomas, one pilocytic astrocytoma; 0.61% of the sample), provides rather strong evidence suggesting that it is indeed a valuable diagnostic tool.

The major limitation of our study was its retrospective nature. This limitation also led to the control group being much smaller than the autistic group. As previously mentioned, the control children were not free from psychiatric diagnoses. It is worth noting that the rate of MR was higher in the autistic group than in the control group. The advantages of the retrospective manner of our study meant that we were able to collect consecutive data from an extended period (18 years); thus, we obtained, to our knowledge, the largest sample published on yield of rou-

tine MRI in autism. Additionally, our study appears to be the only study with a control group.

## CONCLUSION

The study proved that the frequency of MRI abnormalities during routine MRI scanning was marginally higher in autistic children than in controls. We believe the occurrence of CC hypoplasia could represent a "red flag" for suspicion of autism.

## ABBREVIATIONS

ASD, autism spectrum disorders; CNS, central nervous system; CC, corpus callosum; ICD-10, International Classification of Diseases, 10<sup>th</sup> edition; MR, mental retardation; MRI, magnetic resonance imaging.

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**Author contributions:** JL: assessed the MRI scans and drafted the manuscript; AE: collected data, contributed to the design of the study, and commented on the manuscript. MH: conceived the study, performed statistical analysis, and commented on the manuscript.

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