Yield of MRI brain imaging in children with autism spectrum disorder

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Abstract

Autism spectrum disorder (ASD) is a common neurodevelopmental condition. The American Academy of Paediatrics and American Academy of Neurology do not recommend routine brain magnetic resonance imaging (MRI) in the assessment of ASD. The need for a brain MRI should be decided on atypical features in the clinical history and examination. However, many physicians continue to use MRI brain routinely in the assessment process.

We performed a retrospective review of indications for requesting MRI brain in our institution over a 5-year period to determine. The aim was to identify the yield of MRI imaging in children with ASD and calculate the prevalence of significant neuroimaging abnormalities in children with ASD and identify clinical indications for neuroimaging.

One hundred and eighty-one participants were analysed. An abnormal brain MRI was identified in 7.2% (13/181). Abnormal MRI brain was more likely with an abnormal neurological examination (OR 33.1, p=0.001) or genetic/metabolic abnormality (OR 20, p=0.02). In contrast, abnormal MRI was not shown to be more likely in children with a variety of other indications such as behavioural issues and developmental delay.

Thus, our findings support that MRI should not be a routine investigation in ASD, without additional findings. The decision to arrange MRI brain should be made on a case-by-case basis following careful evaluation of potential risks and benefits. The impact of any findings on the management course of the child should be considered prior to arranging imaging.

What Is Known

- Incidental MRI brain findings are common in children with and without ASD.
- Many children with ASD undergo MRI brain in the absence of neurological co-morbidities.

What is new

- MRI brain abnormalities in ASD are more likely with an abnormal neurological examination and genetic or metabolic conditions.
- Prevalence of significant MRI brain abnormalities in ASD alone is low.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterised by persistent deficits in social communication and social interaction and restricted, repetitive patterns of behaviour, interests, and activities. To meet the diagnostic criteria for ASD according to DSM-5, a child must have persistent deficits in each of the three areas of social communication and interaction plus at least two of four types of restricted, repetitive behaviours [1]. There is a spectrum of cognitive abilities within this definition, from
severe intellectual disability (ID) to average or above average intelligence quotient (IQ). World-wide the prevalence of ASD is variable ranging from 0.7% to 2.9% depending on the cohort studied (age, sex, location and study period) [2-4]. The estimated prevalence of ASD in Ireland is approximately 1.5% in a school population aged 6-11 years [5]. The prevalence has increased especially in the past 20 years due to a combination of factors, including greater public awareness, more accurate diagnostic criteria, and changes in the diagnostic criteria [4].

Guidance from the American Academy of Pediatrics (AAP) and the American Academy of Neurology (AAN) suggest routine magnetic resonance imaging (MRI) brain imaging is not part of the initial evaluation or diagnosis of ASD [6, 7]. According to the AAP, approximately a quarter of children with ASD may show signs of developmental regression in language or social skills, which is not likely attributable to an underlying neurodegenerative cause. The need for a brain MRI should be decided based on the clinical history and examination. Neuroimaging may be indicated in the evaluation of; atypical regression, microcephaly, macrocephaly, seizures, intracranial manifestations of genetic disorders, abnormal neurological examination or other indications [6].

Previous studies have estimated the yield of MRI in ASD to be variable, and often findings not related to the presentation and not helpful in diagnostic work-up [7-9]. However, frequently in clinical practice brain MRI is requested due to a diagnosis of ASD without additional features. Therefore, the aim of this retrospective review was to identify the yield of MRI imaging in children with ASD and calculate the prevalence of significant neuroimaging abnormalities in children with ASD and identify clinical indications for neuroimaging.

Methods

Study Design

We undertook a retrospective review of indications for MRI brain in children < 16 years in Children's Health Ireland at Temple Street, Dublin from January 1st, 2015 to December 31st, 2019. The radiology requesting system (Philips XIRIS) was searched using key words (ASD, autism, autistic and spectrum). Children's Health Ireland at Temple Street is a tertiary referral centre, with facilities to perform MRI under general anesthetic.

Inclusion criteria:

Children under 16 years of age with confirmed or suspected ASD undergoing brain MRI for investigation of ASD.

Exclusion criteria:

Children with a known neurodegenerative disorder, or neuroimaging performed for an acute neurological condition such as meningitis and/or older than 16 years.
Brain MRI findings

All brain MRI images were acquired on a single 1.5 Tesla General Electric HDxt SIGNA scanner. Neuroimaging findings were separated into two groups: normal and abnormal. All abnormal neuroimaging was reviewed by paediatric radiologist (ET). Abnormal findings were defined as white or grey matter signal abnormalities and structural malformations. Incidental findings, which were defined as radiological observations unrelated to the purpose of the examination and unlikely to have a clinical impact or significance were included in the normal group [10]. Examples of incidental findings include arachnoid cyst, developmental venous abnormality, or mucosal thickening.

Statistical analysis

Data was analysed using the SPSS version 26.0 (IBM SPSS Statistics, IBM Corporation). Frequencies and percentages were calculated to compare groups. To test for normal distribution, the Shapiro–Wilk test was used. For non-parametric data, quantitative and continuous variables were expressed as median and interquartile range (IQR). Statistical significance was determined at $P$ value less than .05. Binary logistic regression was employed to calculate odds ratios (OR).

Ethical approval

Ethical approval was granted by the local research and ethic committee (ref: CA1912-02)

Results

We identified 210 MRI brain examinations using the search terms. There was a total of 7,177 MRI brain exams performed during the same period. Twenty-nine patients were excluded and 181 were included in the analysis (Fig. 1).

Participant baseline characteristics are described in Table 1. The median age at the time of neuroimaging was 7.9 years (IQR 5.3–11.7 years). General Paediatrics was the most common referring specialty (52.5%, 95/181), followed by Paediatric Neurology (31.5%, 57/181).

Indications for imaging

All indications were recorded (n=28) with majority of children (65.7%, 119/181) had greater than one indication listed on the imaging request. Developmental delay (38.1%, 69/181) and epilepsy (28.7%, 52/181) associated with ASD, were the most common indications followed by behavioural issues (19.3%, 35/181) and abnormal neurological examination (9.9%, 18/181) (Table 1).

Table 1: Association of baseline characteristics and different indications with an abnormal brain MRI result
<table>
<thead>
<tr>
<th></th>
<th>Total n (%)</th>
<th>Normal n (%)</th>
<th>Abnormal n (%)</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>181</td>
<td>168 (93)</td>
<td>13 (7)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-6 years</td>
<td>62 (34)</td>
<td>55 (89)</td>
<td>7 (11)</td>
<td>2.4</td>
<td>0.12</td>
</tr>
<tr>
<td>6-10 years</td>
<td>60 (33)</td>
<td>58 (97)</td>
<td>2 (3)</td>
<td>2</td>
<td>0.16</td>
</tr>
<tr>
<td>10-16 years</td>
<td>59 (33)</td>
<td>55 (93)</td>
<td>4 (7)</td>
<td>0.21</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>151 (83)</td>
<td>139 (92)</td>
<td>12 (8)</td>
<td>2.5</td>
<td>0.39</td>
</tr>
<tr>
<td>Female</td>
<td>30 (17)</td>
<td>29 (97)</td>
<td>1 (3)</td>
<td>0.4</td>
<td>0.37</td>
</tr>
<tr>
<td><strong>Referral source</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General Paediatrics</td>
<td>95 (52)</td>
<td>88 (93)</td>
<td>8 (7)</td>
<td>0.46</td>
<td>0.5</td>
</tr>
<tr>
<td>Neurology</td>
<td>57 (31)</td>
<td>56 (98)</td>
<td>1 (2)</td>
<td>3.68</td>
<td>0.055</td>
</tr>
<tr>
<td>Metabolic medicine</td>
<td>18 (9.9)</td>
<td>15 (83)</td>
<td>3 (17)</td>
<td>2.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Neuro-disability</td>
<td>8 (4.4)</td>
<td>8 (100)</td>
<td>0 (0)</td>
<td>0.65</td>
<td>0.42</td>
</tr>
<tr>
<td>Other</td>
<td>3 (1.7)</td>
<td>2 (67)</td>
<td>1 (33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sedation required</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General anaesthesia</td>
<td>155 (86)</td>
<td>143 (92)</td>
<td>12 (8)</td>
<td>0.51</td>
<td>0.48</td>
</tr>
<tr>
<td>Conscious sedation</td>
<td>13 (7.2)</td>
<td>13 (100)</td>
<td>0 (0)</td>
<td>1.08</td>
<td>0.3</td>
</tr>
<tr>
<td>Walk-in</td>
<td>12 (6.6)</td>
<td>11 (92)</td>
<td>1 (8)</td>
<td>0.05</td>
<td>0.94</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developmental delay</td>
<td>69 (22)</td>
<td>62 (90)</td>
<td>7 (10)</td>
<td>3.85 (0.88-17)</td>
<td>0.07</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>52</td>
<td>49 (94)</td>
<td>3 (6)</td>
<td>4.18 (0.57-16)</td>
<td>0.16</td>
</tr>
</tbody>
</table>
The prevalence of abnormal brain MRI was 7.2% (13/181) (Table 1). Significant findings identified included white matter signal abnormalities, volume loss, cortical heterotopia, and optic atrophy (Table 2). Incidental findings were noted in 21.5% (39/181) including mucosal sinus opacification, enlarged Virchow Robin perivascular spaces, choroid fissure cysts, arachnoid cysts and Rathke cleft cysts.

In children with only ASD as the indication for neuroimaging, there was no pathology identified (11/181). Abnormal neurological examination (OR 33.1, p=0.001) and genetic/metabolic abnormality (OR 20, p=0.02) were associated with abnormal brain MRI. Abnormal genetic/metabolic abnormality include abnormal arrayCGH (n=2) and metabolic de-arrangements (raised lactate, high urine 3-hydroxybutyrate and classical galactosemia. Other indications did not have a statistically significant association with abnormal brain MRI (Table 2).
<table>
<thead>
<tr>
<th>MRI finding</th>
<th>Indication for scan (in addition to ASD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased T&lt;sub&gt;2&lt;/sub&gt; signal in the globus pallidi and dentate nuclei bilaterally</td>
<td>Developmental delay and laboratory findings suggesting metabolic disease (succinic semialdehyde dehydrogenase deficiency)</td>
</tr>
<tr>
<td>Several small focal areas of T&lt;sub&gt;2&lt;/sub&gt; hyperintensity in deep white matter</td>
<td>Developmental delay and epilepsy</td>
</tr>
<tr>
<td>Asymmetric high T&lt;sub&gt;2&lt;/sub&gt; and FLAIR signal intensity in the deep white matter posteriorly</td>
<td>Laboratory evidence of a genetic disorder</td>
</tr>
<tr>
<td>Subependymal and adjacent white matter cortical heterotopia</td>
<td>Developmental delay, obesity and confirmed genetic neurodevelopmental disorder</td>
</tr>
<tr>
<td>Patchy white matter T&lt;sub&gt;2&lt;/sub&gt; hyperintensity on a background of hypomyelination</td>
<td>Developmental delay and confirmed metabolic disease</td>
</tr>
<tr>
<td>Porencephalic cyst in adjacent to the body of the right lateral ventricle and periventricular white matter volume loss with T&lt;sub&gt;2&lt;/sub&gt; hyperintensity</td>
<td>Prematurity, intraventricular haemorrhage, abnormal neurological examination (focal spastic weakness)</td>
</tr>
<tr>
<td>Defect in medical aspect of occipital lobe with associated volume loss, consistent with prior infarct</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>Scattered foci of T&lt;sub&gt;2&lt;/sub&gt;/FLAIR hyperintensity in both cerebral hemispheres and adjacent to the posterior horns of both lateral ventricles</td>
<td>Neurocutaneous stigmata</td>
</tr>
<tr>
<td>Minor increased T&lt;sub&gt;2&lt;/sub&gt; FLAIR signal within the posterior periventricular white matter</td>
<td>Abnormal neurological examination (ataxia)</td>
</tr>
<tr>
<td>Progressive left optic nerve atrophy</td>
<td>Epilepsy and abnormal neurological examination (left optic atrophy)</td>
</tr>
<tr>
<td>Mild optic nerve atrophy, cerebellar tonsillar ectopy. Diffuse thickening of skull bone. Effacement of CSF cisterns.</td>
<td>Developmental delay, vision loss</td>
</tr>
<tr>
<td>Areas of T&lt;sub&gt;2&lt;/sub&gt;/FLAIR signal abnormality adjacent to the posterior horns of the lateral ventricles bilaterally, with mild associated volume loss.</td>
<td>Developmental delay, poor social contact, behavioural issues</td>
</tr>
<tr>
<td>Multifocal small regions of parenchymal volume loss and signal abnormality</td>
<td>Microcephaly, developmental delay, behavioural issues</td>
</tr>
</tbody>
</table>

**Discussion**

In our retrospective review of neuroimaging performed in the evaluation of ASD, abnormal brain MRI was identified in 7.2% (13/181). Abnormal MRI brain was more likely with an abnormal neurological examination (OR 33.1, p=0.001) or genetic/metabolic abnormality (OR 20, p=0.02). In contrast, abnormal MRI was not shown to be more likely in children with a variety of other indications such as behavioural...
issues and developmental delay. Thus, our findings support that MRI should not be a routine investigation in ASD, without additional findings.

We identified a 7.2% (13/181) prevalence of abnormal MRI in our cohort which is consistent with previous studies. We analysed incidental findings (39/181) under the normal group, as the findings were not related to presentation. Cooper and colleagues found a 6.5% prevalence of pathology in patients whose MRI request indication was ASD alone [9]. The prevalence was highest in those with ASD and an abnormal neurological examination or pre-existing finding (26.2%) [9]. This mirrors our cohort in which abnormal neurological examination (28%, OR 33.1, p=0.001) and abnormal genetic/metabolic laboratory findings (25%, OR 20, p=0.02) were associated with abnormal MRI findings. Ming and colleagues found a prevalence of 15% of abnormal findings but included incidental findings, which was defined as normal in our study [8]. A recent paper by Rochat and colleagues of 117 children with ASD reported an abnormal MRI brain in 54.7% and minor abnormalities accounted for approximately one third of the abnormal findings [11].

When extrapolating data on abnormal MRI brain clinicians needs to be cognisant if incidental findings are defined as abnormal or normal in analysis. There is a high rate of incidental findings on MRI brains in the general paediatric population. In our cohort, the prevalence of incidental findings was 21.5%. Studies vary but prevalence of up to one third has been reported [10, 12, 13]. Incidental finding rates between children with ASD and neurotypically developing children appear to be similar, 5.5-68% [14-16]. However, the incidental finding rate in children with ASD may be higher [11, 17] Thus, when ordering a brain MRI scan for a child with ASD families need to be counselled about the higher frequency of incidental findings, which may cause extra anxiety for family and the need to follow-up neuroimaging.

Abnormal MRI findings included white matter signal abnormalities (n=6) and/or volume loss (n=4). As ASD does not have known MRI features, these findings are not diagnostic or suggestive of ASD but rather may indicate a prior injury or an underlying neurological condition. White matter abnormalities have been identified in other ASD cohort but also in developmental delay. Abnormalities, even if radiologically significant, may be clinically incidental [11, 18]. Other groups have hypothesised that white matter signal abnormalities may affect brain connectivity and supported by diffusion tensor imaging techniques [17, 19]. However, much is still to be understood about the genetics, brain connectivity and brain development in ASD.

Although guidelines exist on the role of MRI brain in children with ASD [3, 4, 20], commonly brain MRIs are performed, which are not indicated and do not contribute to the management or prognostication. As highlighted in our cohort, AAP guidelines were not followed when requesting scans [6]. Behavioural issues (19%, 35/181) and developmental delay (22%, 69/181) were the most common listed indications on MRI requests, despite these being common and typical features of ASD. In our cohort, children with ASD alone (11/181), all had normal neuroimaging. Thus, our findings support that brain MRI should not be a routine investigation in ASD, without additional findings. Our data showed an association between abnormal brain MRI and abnormal neurological examination examination (OR 33.1, p=0.001) and
genetic/metabolic abnormality (OR 20, p=0.02). Genetic investigations should be routinely offered to children with ASD as per AAP recommendations and in selective cases metabolic investigations [6]. If these reveal an abnormalities neuroimaging should be considered and is supported by our data. Figure 2 is a suggestive algorithm for selecting ASD patients for brain MRI. This has led to a change of policy in our radiology department, with the data from this study to reject requests which do not meet criteria.

Brain MRI may be required in other cases; however, the presence of ASD should not directly influence the decision to perform imaging. For example, in a child with ASD and focal or refractory epilepsy, brain MRI brain may modify the management of epilepsy, but it is not likely to affect the management of ASD. Of note, in our cohort, 52 had MRI for ASD and epilepsy and 3 were abnormal (6%). Abnormal findings included white matter abnormalities, optic atrophy and previous infarct,

Most children with ASD require a general anaesthetic to successfully carry out a brain MRI exposing them to anaesthesia related risks, and while this risk is minimal in children, it may be significant in toddlers [21]. In addition, the process may be stressful for children with ASD (combination of sensory issues, anxiety, poor communication skills) and for their families.

Our study has a number of limitations. As we studied children with ASD, we were not able to determine the prevalence of similar brain MRI findings in our general child population. The significance of brain MRI findings was determined based on the opinion of the reporting radiologist which may be subjective. The indications for neuroimaging were recorded from radiology requests and may be sensitive to documentation bias. The degree of severity of some presentations such as developmental delay could not be determined.

**Conclusion**

Our study did not show a yield for MRI in the routine investigations of ASD without high risk clinical features which suggest an underlying diagnosis. The decision to arrange MRI brain should be made on a case-by-case basis following careful evaluation of potential risks and benefits. The impact of any findings on the management course of the child should be considered prior to arranging imaging.

**Abbreviations**

**AAN** American Academy of Neurology  
**AAP** American Academy of Pediatrics  
**ASD** Autism Spectrum Disorder  
**ID** Intellectual Disability  
**IQ** Intelligence Quotient
Declarations

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Availability of data and material Data can be provided on request.

Authors’ Contributions: DB, ET, KG and LB conceptualized and designed the study. DB and AF wrote the manuscript, DB collected data, AF analysed data, ET interpreted imaging, LB and KG reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ethical Approval: Ethical approval was granted by the local research and ethic committee.

Consent to participate: N/A

Consent for publication: N/A

References


Figures
Figure 1

Overview of MRI brain examinations identified using keywords
Figure 2

Suggested algorithm for MRI brain in ASD