MJMR, Vol. 36, No. 1, 2025, pages (214-219).

Open Access
ISSN:2682-4558

Research Article

Brain MRI in Children with Autism Spectrum Disorder

Mohamed Farouk Afify [1], Rehab M. Hasan[2], Mohammed Nagdi Abdel-Hakeem Nagdi[1] and Marwa Waly Eldin Ali[1].

[1] Department of Pediatrics, Faculty of Medicine, Minia University, Egypt
[2] Department of Diagnostic Radiology, Faculty of Medicine, Minia University, Egypt

DOI: 10.21608/MJMR.2024.273523.1682

Abstract

Background: Autism spectrum disorder (ASD) is a neurodevelopmental disorder with onset in early childhood; its key features are deficit in social communication and social interaction accompanied by restricted and repetitive behaviors. Numerous non-invasive imaging techniques have been developed to identify the distinctive brain features of ASD; however, some research revealed an incredibly high frequency of related minor abnormalities or normal variations on brain MRIs of individuals with autism. **Objectives:** evaluation of brain MRI abnormalities/variations in relation to ASD symptoms and severity. **Patients and methods:** This study included 50 children diagnosed with ASD (classic type) according to DSM-5 diagnostic criteria, they had regular follow up visit to Pediatric Neuropsychiatric Clinic at Minia University Children Hospital, from January 2023 to January 2024. All patients were subjected to complete medical history, thorough clinical examination, evaluation of autism symptoms severity by *The Gilliam Autism Rating Scale–Third Edition* (GARS-3), and brain imaging through 3Tesla brain MRI. **Results:** Most children with ASD had normal brain MRI findings. Unsought asymptomatic brain abnormalities that arise while looking for other relevant information are known as incidental findings (Ifs). The most common normal MRI finding/variant in these children were benign enlargement of the subarachnoid space and persistent cavum septum pellucidum. GARS-3 total score, social interaction and communication scores were significantly higher in autistic children with Mega cisterna magna in MRI brain than in other MRI findings, while stereotyping score was higher in children with benign enlargement of the subarachnoid space in brain MRI. **Conclusions:** Brain MRI may be useful in ASD to determine the severity of symptoms, and it may also be beneficial for future research on determining the etiology and pathogenesis of ASD. Brain MRI may be useful in identifying early presymptomatic children with autism spectrum disorders.

Keywords: Autism, Children, MRI findings, symptoms, and severity.

Introduction

Autism spectrum disorder (ASD) is a neuro-developmental disorder with early childhood onset, and characterized by restricted and repetitive behaviors along with difficulty in social communication and social interaction [1, 2]

Globally, the prevalence is 100/10,000, with a 4:1 male predominance. In Egypt, community based countrywide screening revealed an estimated 3.3% of 41,640 children aged 1 to 12 had ASD. Main Types of ASD according to *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) include Autistic disorder, Asperger's Syndrome, Childhood Disintegrative Disorder (CDD), Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS). [3, 4, 5, 6]

Numerous non-invasive imaging techniques have been developed for the early identification of ASD characteristics. Brain magnetic resonance imaging (MRI) is a useful method for

investigating brain structural changes in children with ASD. There is no general consensus on specific neuroimaging features of autism; however, magnetic resonance imaging methods have been helpful in evaluating small structural abnormalities and variants in order to better understand the neuro-pathophysiology of ASD.[7]

Patients and Methods

This study included 50 pediatric patients diagnosed with ASD (classic type) according to DSM-5 diagnostic criteria, they had regular follow up visit to Pediatric Neuropsychiatric

Clinic at Minia University Children Hospital, from January 2023 to January 2024.

Ethical Considerations:

The aim and nature of this study was explained for each parent before participating in the study. Before participants were enrolled, parents gave their informed consent, which allowed them to withdraw from the study avoiding using deceptive practice. This study also was approved by Pediatric Department Council and had approval of the ethical committee of Faculty of Medicine, Minia University No 718:4/2023.

Children aged 4-16 years old with a confirmed diagnosis with autism according to DSM-5 diagnostic criteria were included in this study, [5,6] while children with any systemic diseases, neuro-logical diseases, other psychiatric disorders, and patients who refuse to participate in this study were excluded from this study.

All patients were subjected to:

- Complete medical history, through general and neurological examination
- Evaluation of autism symptoms severity by *Gilliam Autism Rating Scale–Third Edition (GARS-3).* [8, 9]
- Brain imaging using 3Tesla MRI brain diffusion.

1. Careful history taking included:

Name, age, sex, residency, symptoms and additional data were collected from parents included: Social isolation, interaction, stereotyping movements, hypo/ hyperactivity, motor and sensory symptoms.

Perinatal history of maternal previous abortion, consanguinity, drugs, birth order, and the condition of other siblings.

2. **Thorugh clinical examination.**
3. **Evaluation of autism symptoms severity: by** The Gilliam Autism Rating Scale–Third Edition (GARS-3) [8, 9]
4. **Brain imaging using 3T MRI brain diffusion scanning machine :** the brain images were assessed independently and evaluated by two expert pediatric neuro-radiologist through double blind technique, and their final findings were reported in this study, they assess brain radiological morphology, technical parameters (thickness, TE, TR) were set up to obtain high quality morphological sequencing (T1, T2, FLAIR T2 weight) images mainly that provide adequate anatomical details and high contrast between tissues.

Results

As shown in table (1), there are 16% of autistic children had delayed motor development, 84% had delayed mental development, 52% had sleep disorder. 32% of the studied autistic children not receive medical treatment for the comorbid symptoms of autism (aggressive behavior and sleep disorder), while 44% were on atypical antipsychotic treatment (Risperidone, Aripiprazole), and 24% were on Atomoxetine.

As shown in table (2), mean GARS-3 autism index 106±13.5 and mean GARS-3 raw total score 32.7 ± 6.2, divided into the following subscales; GARS-3 social interaction with mean score 11±3, GARS-3 communication with mean score 10.6±3.2 and GARS-3 stereotyping with mean score 11±3.

As regard MRI findings in studied autistic children (table 3), 54% of autistic children had normal brain MRI, 12% had benign enlargement of the subarachnoid space and persistent cavum septum pellucidum (for each item separately), 8% had faint periventricular faint white matter signal intensity, 6% had ictatic ventricles and 4% had Mega cisterna magna and thin corpus callosum (for each item separately).

GARS-3 total raw score, GARS-3 social interaction score and GARS-3 communication score were significantly higher in autistic

children with Mega cisterna magna (mean ± SD= 43.5±0.7 m 17±0 and 16±0 respectively) than in other findings. As regard stereotyping score, mean was significantly higher in cases with benign enlargement of the subarachnoid space finding in MRI (mean±SD= 14.6±1.8) than in other brain MRI finding.

Table (1): Socio-demographic and Clinical Data of the Autistic Children

Socio-demographic and Clinical data		**Autistic children (n=50)**
Age (years)	**Mean ± SD (Range)**	6.2 ± 2.6 (4-15)
Sex	**Male**	36(72%)
	Female	14(28%)
Residence	**Urban**	*29 (58%)*
	Rural	*21 (42%)*
Weight (kg) Median (IQR)	21.5 (15.7- 42)	
Height (cm) Median (IQR)	115 (111-130)	
BMI Median (IQR)	15(14-25)	
Motor development	**Normal**	42(84%)
	Delayed	8(16%)
Mental development	**Normal**	8(16%)
	Delayed	42(84%)
Sleep disorder	**Present**	26(52%)
	Absent	24(48%)
Medication	**Non medicated**	16(32%)
	Antipsychotic treatment	22(44%)
	On Atomoxetine	12(24%)

Table (2): The Gilliam Autism Rating Scale–Third Edition (GARS-3) Scores of the Autistic Children

GARS-3 Autism Rating Scale	**Autistic Children** (n=50)
GARS-3 autism index Mean ± SD (Range)	**106**±13.5 (81-130**)**
GARS-3 total score Mean ± SD (Range)	**32.7** ± 6.2 (21- 44)
GARS-3 social interaction score Mean ± SD (Range)	**11**±3 (5 -17)
GARS-3 communication score Mean ± SD (Range)	**10.6**±3.2 (4 -16)
GARS-3 Stereotyping score Mean ± SD (Range)	**11**±3 (5-17)

Table (3): Gilliam Total Score and Sub scores as regard MRI Findings of Autistic Children

MRI finding	Autistic children (n=50)	GARS-3 total score Mean ± SD (Range)	GARS-3 social interaction score Mean ± SD (Range)	GARS-3 communication score Mean ± SD (Range)	GARS-3 Stereotyping score Mean ± SD (Range)
Normal	27(54%)	32±5.6 (21-41)	10.9±2.8 (6-15)	10.3±3 (4-15)	10.5±3.3 (5-17)
Faint white matter signal intensity	4(8%)	23.5±2.8 (21-26)	8.5±4 (5-12)	6.5±0.5 (6-7)	8.5±1.7 (7-10)
Benign enlargement of the subarachnoid space	6(12%)	37.3±7.5 (34-40)	10.3±2.8 (8-14)	12.3±1.3 (11-14)	14.6±1.8 (13-17)
Ictatic ventricles	3(6%)	27.6±1.1 (27-29)	9±1.7 (8-11)	6.6±1.1 (6-8)	12±1.7 (10-13)
Mega cisterna magna	2(4%)	43.5±0.7 (43-44)	17±0 (17-17)	16±0 (16-16)	11±0 (11-11)
Thin corpus callosum	2(4%)	34±0 (34-34)	13±0 (13-13)	9±0 (9-9)	12±0 (12-12)
Persistent cavum septum pellucidum	6(12%)	36.8±3.4 (32-40)	13.3±1 (12-14)	13.6±1 (13-15)	10±1.5 (8-11)
P value		<0.001*	0.007*	<0.001*	0.02*

*_significant at p value <0.05

Discussion

The aim of this study was to evaluate the role of brain MRI in pediatric patients diagnosed with ASD.

This study showed that 54% of studied autistic children had normal brain MRI, and the most frequent radiological variants recorded in studied patients were benign enlargement of the subarachnoid space and persistent cavum septum pellucidum.

These results were in agreement with Rochat et al., (2020) who found that mega cisterna magna, ventricular malformations, and aberrant white matter signal intensity as important incidental findings (IFs) in ASD. Children and adolescents with ASD have a higher prevalence of IFs, which may indicate that neural maldevelopment underlying the ASD, abnormal cortical development, atrophy, corpus callosum anomalies, ventricular anomalies, and mega cisterna magna were among the MRI abnormalities seen in children diagnosed with ASD.[10]

This study was in correspondence with Erbetta et al., (2015) who showed that abnormal brain MRI was in 44% of autistic group, Mega cisterna magna was the primary finding of the brain MRI. These abnormalities are morphologically visible signs of altered brain development. There have been reported psychiatric associations between mega cisterna magna, including schizophrenia, and ASD. Children with low functioning autism may have a high rate of mild neuroradiologic abnormalities, which could further the study of different endophenotypes and complete the clinical evaluation of ASD children. [11]

Byrne et al., (2023) found that 7.2% of children whose only neuroimaging indication was ASD had abnormal brain MRI, which were more frequently associated with abnormal neurological examinations or genetic/metabolic abnormalities. [12]

This study showed that GARS-3 total raw score, GARS-3 social interaction score and GARS-3 communication score were significantly higher in autistic children with Mega cisterna magna (mean was 43.5±0.7, 17±0 and 16±0 respectively) than in other findings.

This was in agreement with Binic et al., (2023) who reported that Mega cisterna magna is usually an unintentional radiographic finding, but it can also be linked to specific mental disorders where patients have poor performance on certain cognitive tasks, such as verbal fluency and memory. The mega cisterna magna is the most prevalent minor abnormality. A minor abnormality such as this is proposed as a marker for brain dysgenesis. Lower performance on speech tests (verbal and semantic fluency) is often associated with cisterna magna enlargements in children with ASD, which interfere with their communication and interaction with the surroundings and caregivers. [13]

As regard stereotyping score, mean was significantly higher in autistic children with benign enlargement of the subarachnoid space in MRI (14.6±1.8) than in other cases.

These results were agreed with Shen et al., (2013) who concluded that infants who suffered from ASD had significantly wide extra-axial fluid by 6–9 months of age. Extra-axial fluid is characterized by an excessive CSF in the subarachnoid space, presence of excessive extra-axial fluid which does not resolve by the second year of life may be a characteristic of infants who develop autism. Furthermore, the longer extra-axial fluid remained elevated, the more severe the ASD symptoms. increased extra-axial fluid during early infancy was associated with both a diagnosis of ASD and increase symptoms severity. Increased extra-axial fluid found at 6 months and continued to be increased through 24 months could be a predictive marker specific to ASD. [14]

These results were in contrast with Peterson et al., (2021) who found that between 3 and 42 years, there were no group differences in extra-axial CSF volume. These findings imply that beyond the age of four, the elevated extra-axial CSF volume in early autistic children returns to normal. [15]

Conclusion:

In conclusion, this study demonstrated that ASD assessment using brain MRI may be useful in determining the symptoms severity and prognosis in presymptomatic children with ASD, and it may also be beneficial for future research on the etiology and pathogenesis of autism.

Authors' contributions:

- **Study concept and design**: Mohamed Farouk Afify, Rehab M. Hasan, Mohammed Nagdi Abdel-Hakeem Nagdi, Marwa Waly Eldin Ali Waly Eldin.
- **Analysis and interpretation of data:** Mohamed Farouk Afify *, Rehab M. Hasan*, Mohammed Nagdi Abdel-Hakeem Nagdi *, Marwa Waly Eldin Ali ***.**
- **Drafting of the manuscript**: Mohamed Farouk Afify, Rehab M. Hasan, Marwa Waly Eldin Ali.
- **Critical revision of the manuscript for important intellectual content:** Mohamed Farouk Afify, Marwa Waly Eldin Ali.
- **Statistical analysis interpretation:** Mohamed Farouk Afify, Rehab M. Hasan, Mohammed Nagdi Abdel-Hakeem Nagdi, , Marwa Waly Eldin Ali .

Author details:

- **Corresponding Author**: Mohammed Nagdi Abdel-Hakeem Nagdi, Pediatrics Department, Faculty of Medicine, Minia University, Egypt.
- Mohamed Farouk Afify, professor of Pediatrics, Pediatrics Department, Faculty of Medicine, Minia University, Egypt, 01223458960, afifimfa@gmail.com
- Rehab M. Hasan, Lecturer of Diagnostic Radiology, Faculty of Medicine, Minia University, Egypt, 01011911299, dr.mohamed.1989@gmail.com
- Marwa Waly Eldin Ali, Lecturer of Pediatrics, Pediatrics Department, Faculty of Medicine, Minia University, Egypt, 01026521115, Marwa.Walieldeen@mu.edu.eg.com

References

1. Bridgemohan, C.F., Autism Spectrum Disorder.In: Nelson Textbook of Pediatrics, 21st Edition, edited by KLIEGMAN, ST GEME, BLUM, SHAH, TASKER, WILSON. Copyright © 2020 Elsevier Inc, 1725:1749.
2. Lord C, Brugha TS, Charman T., et al., Autism spectrum disorder. Nature reviews Disease primers, (2020)6 (1): 1-23.
3. Metwally, A.M., Helmy, M.A., Salah El-Din, E.M. et al., National screening for

   Egyptian children aged 1 year up to 12 years at high risk of Autism and its

determinants: a step for determining what ASD surveillance needs. BMC Psychiatry (2023). 23: 471
4. Zeidan J, Fombonne E, Scorah J., et al., Global prevalence of autism: A systematic review update. Autism Res. (2022)15 (5): 778-790
5. American Psychiatric Association Diagnostic and statistical manual of mental disorders 5th edition (DSM-5®). American Psychiatric Pub.:(2013) p. 50-59.
6. Posar A, Resca F, Visconti P., Autism according to diagnostic and statistical manual of mental disorders 5th edition: The need for further improvements. J Pediatr Neurosci, (2015) 10 (2): 146-8.
7. Rafiee, F., et al., Brain MRI in Autism Spectrum Disorder: Narrative Review and Recent Advances. J Magn Reson Imaging, 55 (6): 1613-1624.
8. Chlebowski, C., Green, J. A., Barton, M. L., et al., Using the childhood autism rating scale to diagnose autism spectrum disorders. Journal of autism and developmental disorders, (2022) 40 (7): 787–799.
9. Karren, B. C., et al., A Test Review: Gilliam, J. E. Gilliam Autism Rating Scale–Third Edition (GARS-3). Journal of Psychoeducational Assessment, (2017)35 (3): 342–346.
10. Rochat MJ, Distefano G, Maffei M,. et al., Brain Magnetic Resonance Findings in 117 Children with Autism Spectrum Disorder under 5 Years Old. Brain Sci., (2020)10 (10): 741.
11. Erbetta, A., et al., Low-Functioning Autism and Nonsyndromic Intellectual Disability: Magnetic Resonance Imaging (MRI) Findings. Journal of Child Neurology, (2015) 30 (12): 1658-1663.
12. Byrne, D., et al., Yield of brain MRI in children with autism spectrum disorder. European Journal of Pediatrics, (2023),182 (8): 3603-3609.
13. Binic, I., Petrović JM, Stojanovic A., et al., Structural brain MRI studies in autism spectrum disorder. Eur Psychiatry, (2023) 66 (Suppl 1): S914
14. Shen MD, Nordahl CW, Young GS., et al., Early brain enlargement and elevated extra-axial fluid in infants who develop autism spectrum disorder. Brain,. (2013) 136 (Pt 9): 2825-35.
15. Peterson M, Prigge MBD, Bigler ED., et al., Evidence for normal extra-axial cerebrospinal fluid volume in autistic males from middle childhood to adulthood. NeuroImage, (2021) 240: p. 118387.