Journal of Clinical and Basic Research
Online ISSN: 2538-3736

Research Article

# Evaluation and Comparison of MRI Findings in Children with Global Developmental Delay and Isolated Neurodevelopmental Delay: A Cross-sectional Study

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**Received** August 14, 2021 **Accepted** October 14, 2021

## ABSTRACT

**Background and objectives:** Neurodevelopmental delay (NDD) is a chronic neurologic problem that adversely affects the quality of life of affected individuals. The aim of this study was to evaluate diagnostic efficacy of MRI for children with NDD by comparing magnetic resonance imaging (MRI) findings of patients with global developmental delay (GDD) and isolated NDD.

**Methods:** A cross-sectional study was designed to enroll all patients with static developmental delay who had been referred to outpatient neurology clinic at Bahrami hospital (Tehran, Iran) between February 2012 and February 2013. The Bayley Scales of Infant and Toddler Development 4th edition, Denver Developmental Screening test, and a self-made questionnaire were used to detect GDD, isolated NDD, and record all necessary information of neurologic examination. Brain MRI was performed based on the guidelines for the selected patients. All abnormal MRI findings were identified and confirmed by a neuro-radiologist.

**Results:** Overall, 140 patients with developmental delay were enrolled in the study. The prevalence of both GDD and isolated NDD was 50%. In addition, abnormal associated neurological symptoms were present in 67.9% of patients. Abnormal MRI findings were significantly more common among patients with GDD compare to patients with isolated NDD (P<0.001). However, positive MRI findings were more common among patients with isolated motor NDD (P=0.007). Microcephaly was the most common abnormal neurologic finding in patients with GDD (P=0.04). Movement disorders were also more frequently seen in patients with GDD than in patietns with isolated NDD (P=0.03).

**Conclusion:** Based on the findings, brain MRI can be considered as a suitable diagnostic modality for GDD but not isolated NDD.

**Keywords:** Global Developmental Delay; Isolated developmental delay; Magnetic Resonance Imaging; Pediatric

**DOI: 10.29252/Jcbr.5.3.52**

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[ DOI: 10.52547/jcbr.5.3.52 ]

## INTRODUCTION

Neurodevelopmental delay (NDD) refers to delays in achievement of developmental skills in infants and young children. Evolution consists of all constructive changes and distinctions that take place in human beings throughout their lives to improve their motor, mental, verbal, and social development. Human evolution is a continuous process associated with development of the brain and the central nervous system (CNS) (1). The brain rapidly grows after birth and completes 90% of its final growth before the age of 6 years (2). This is not only related to the physical parameters of the growth, especially the size, but also includes brain functions. These evolutionary changes can be observed in brain activity and detected by electroencephalography (3, 4). The most important aspect of neurologic examination in children is to assess developmental abilities for early recognition and intervention (5).

Global developmental delay (GDD) is a subset of developmental disorders that is defined by the presence of significant delays in at least two or more major developmental milestones. It may be caused by a group of static or progressive disorders of the CNS (6). The etiology of GDD falls under two general categories: genetic and exogenous factors (7). Brain magnetic resonance imaging (MRI) is widely used to diagnose the specific etiology of developmental delay (8, 9). Abnormal findings are frequently reported from brain MRI of patients with GDD (10-12). This study aimed to compare brain MRI findings of patients with GDD and isolated NDD to determine the diagnostic efficacy of brain MRI for these two diseases.

## MATERIALS AND METHODS

In this cross-sectional study, all children aged below 10 years with the clinical presentation of static isolated NDD or GDD who were referred to the child neurology clinic of Bahrami Children's Hospital (Tehran, Iran) between February 2012 and February 2013 were enrolled. Informed consent was taken from the subjects' parents. Those with a progressive neurologic regression were excluded from the study. The ethics committee of Tehran University of Medical Sciences approved the study.

The Bayley Scales of Infant and Toddler Development 4$^{th}$ edition, Denver Developmental Screening test (DDST), and a self-made questionnaire were used to detect GDD, isolated NDD, and record all necessary information of neurologic examination. Demographic data were collected through interviews with the parents or legal guardians using a standard questionnaire. Brain MRI was performed on the subjects based on the standard and recommended guidelines. All MRI findings were reviewed by a pediatric neurologist and neuroradiologist. The brain MRI findings were then categorized into six groups of normal, non-specific abnormality, congenital abnormality, developmental abnormality, known neurologic syndrome, neurovascular diseases and trauma, and metabolic and neurodegenerative disorders. The frequency of abnormal MRI findings in patients with GDD and isolated NDD was compared. The efficiency of MRI for diagnosis of the underlying cause of GDD and isolated NDD was also evaluated.

The collected data were entered into SPSS (version 21.0) and expressed as mean ± standard deviation (SD). Furthermore, the chi-square test and the Mann-Whitney U test were used for analysis of qualitative data and non-parametric quantitative data, respectively. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

Overall, 140 patients (75 boys and 65 girls) were enrolled in the study. The mean age of patients was 3.1 ± 1.5 years (age range: 1-10 years). Seventy patients (50%) had GDD and the other 70 patients (50%) had isolated NDD (Table 1). There was no statistically significant difference between patients with GDD and isolated NDD in terms of gender.

[ DOI: 10.52547/jcbr.5.3.52 ]

**Table 1. Prevalence of neurological symptoms in patients with GDD and isolated NDD**

| Neurological symptoms | Number (%) |
|---|---|
| MNDD | 31 (22.1) |
| VNDD | 39 (27.9) |
| Convulsions | 70 (50) |
| Parental Relationship | 59 (42.1) |
| Neurological findings | 95 (67.9) |
| Microcephaly | 61 (43.6) |
| Macrocephaly | 4 (2.9) |
| Skin lesion | 5 (3.6) |
| Organomegaly | 0 |
| Movement disorder | 12 (8.6) |
| Dysmorphism | 7 (5) |
| Atrophy and ventriculomegaly | 37 (26.4) |
| Periventricular leukomalacia | 19 (13.6) |
| Other problems | 26 (18.6) |
| Congenital and evolutionary anomalies | 3 (2.1) |
| Known syndrome | 8 (5.7) |
| Neurovascular diseases and trauma | 31 (22.1) |
| Neurodegenerative and metabolic diseases | 6 (4.3) |

MNDD: Major neurodevelopmental delay
VNDD: Visual and neurodevelopmental delay

Abnormal neurological findings were reported for 67.9% of the patients. There was no statistically significant difference between the two groups in terms of microcephaly (P=0.6) (Table 2).

Positive MRI findings were significantly more frequent in subjects with GDD compared to those with isolated NDD (84.3% vs. 41.4%) (P<0.001). Overall, 62.9% of the patients had positive MRI findings, 37.1% of the patients had normal MRI findings, 28.6% had nonspecific findings, and 22.1% had neurovascular and trauma-related findings. Six patients in the GDD group were diagnosed with metabolic and neurodegenerative disorders, while none of the patients with isolated NDD had such disorder (P=0.02) (Table 2). Moreover, positive MRI findings were present in 56.4% of patients with isolated motor NDD and in 22.6% of patients with isolated NDD.

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**Table 2. The relationship of different factors with GDD and isolated NDD**

| Variables, N (%) | GDD (N= 70) | Isolated NDD (N= 70) | P-value |
|---|---|---|---|
| Atrophy and ventriculomegaly | 28 (40) | 9 (12.9) | < 0.001 |
| Periventricular leukomalacia | 6 (8.7) | 13 (18.6) | 0.1 |
| Neurodegenerative and metabolic diseases | 6 (8.7) | 0 | 0.02 |
| Neurovascular diseases and trauma | 15 (21.4) | 16 (22.9) | 0.8 |
| Known syndrome | 7 (10) | 1 (1.4) | 0.06 |
| Congenital and evolutionary anomalies | 2 (2.9) | 1 (1.4) | 0.5 |
| Parental Relationship | 37 (52.9) | 22 (31.4) | 0.01 |
| Convulsions | 28 (40) | 42 (60) | 0.02 |
| MNDD | 22 (56.4) | - | 0.003 |
| VNDD | 7 (22.6) | - | <0.001 |

MNDD: Major neurodevelopmental delay
VNDD: Visual and neurodevelopmental delay

There was no significant difference between the two groups in terms of congenital or developmental anomalies (P=0.4). Mild to moderate brain atrophy and ventriculomegaly were found in 28 GDD cases (40%) and nine (12.9%) isolated NDD cases (P<0.001). There was no statistically significant between the two groups in terms of periventricular leukomalacia (P=0.1) (Table 2). The relationship of different factors with isolated major neurodevelopmental delay (MNDD) and visual and neurodevelopmental delay (VNDD) presented in (Table 3).

**Table 3. The relationship of different factors with isolated MNDD and VNDD**

| Variables, N (%) | Isolated MNDD (N= 39) | Isolated VNDD (N= 31) | P-value |
|---|---|---|---|
| Neurovascular diseases and trauma | 15 (38.5) | 1 (3.2) | <0.001 |
| Known syndrome | 1 (3.2) | 0 | 0.3 |
| Congenital and evolutionary anomalies | 0 | 1 (3.2) | 0.4 |

## DISCUSSION

This cross-sectional, descriptive study evaluated the efficacy of brain MRI for diagnosis of GDD and isolated NDD in children. Microcephaly and positive MRI findings were significantly more common in subjects with GDD, while a higher proportion of patients with isolated motor NDD had abnormal MRI findings. In a study by Momen et al.(13), abnormal brain MRI findings were observed in 58.6% of patients. These abnormal findings included nonspecific findings in 38 patients (6.6%), congenital malformations and developmental brain disorders in 39 cases (6.7%), detectable syndromes in three patients

[ DOI: 10.52547/jcbr.5.3.52 ]

(0.5%), neurovascular disease or trauma-related findings in 218 patients (37.6%), and metabolic or neurodegenerative disorders in 42 patients (7.2%). The mentioned study concluded that since 60% of the subjects had abnormal brain MRI, this method could be used to diagnose and determine the prognosis of the background disease. In our study, 62.9% of the patients had abnormal brain MRI, but most findings were nonspecific manifestations, neurovascular disease, and trauma-related. This finding is line with findings of some previous studies (14, 15). In a systematic review, the prevalence of abnormal brain MRI was 38% in children, 7.9 % of which led to an etiologic diagnosis (16).

In a research conducted by Pui et al., magnetization transfer and diffusion-weighted imaging were performed on 85 children with GDD and 133 normal children (17). The study reported that abnormal MRI was significantly more common among patients. In addition, 41 children had congenital brain abnormalities, metabolic and chromosomal disorders, and vitamin B12 deficiency-related findings, seven children had genetic disorders, and five children had sequels of previous infectious encephalitis. Although the magnetization transfer ratio and apparent penetration coefficient were abnormal in these children, there was no specific pattern to aid narrowing the differential diagnoses. All 19 children who were eventually classified as idiopathic global DD had normal MRI. Except for non-specific findings of conventional electroencephalogram (62.5%), the diagnostic yield of metabolic screening, cytogenetic testing, and skin/muscle biopsy was low (17).

Trauner et al. evaluated the neurological and MRI findings of children with developmental language disorder (LD)(18). They reported that children with LD not only have significant delayed speech, but also have significant delay in motor milestones, especially walking. Moreover, 12 out of 35 children with LD had positive brain MRI findings, while none of the 27 healthy control children had an abnormal brain MRI. Abnormal findings included ventricular enlargement, loss of central volume, and non-specific white matter signal changes.

In a study by Hart et al., children with developmental delay were slightly more likely to have abnormal MRI findings (19).

In another study on delayed myelination in children with developmental delay , volumetric MRIfindings revealed a significant reduction in the relative content of myelinated white matter corresponding to a 3.2-year myelination delay (20). Although the whole hemisphere was symmetrical, myelin white matter volume was asymmetric in 30% of patients and 10% of controls.

In a study by Plante et al. on MRI findings of boys with specific language impairment (SLI), imaging failed to detect any significant abnormality except for atypical Perisylvian asymmetry in most of the

[ DOI: 10.52547/jcbr.5.3.52 ]

affected individuals. The prevalence of atypical Perisylvian asymmetry in patients with SLI was significantly higher than in controls (P<0.01). These anatomical neurological findings suggested that prenatal abnormal brain development might contribute to SLI (21).

Some studies demonstrated that MRI could provide useful information in most children with cerebral palsy (22, 23). Therefore, a classification system is needed to relate clinical assessments to MRI findings in order to determine the underlying etiologic factors in patients with cerebral palsy.

In a previous study, the volume of the skull, brain, cerebellum, grey and white matter, ventricles, hippocampus, and amygdala was measured in patients with autistic spectrum disorders (ASD) and compared with children with developmental delay (24). The study found no significant difference between these two groups. However, in cases with developmental delay, a significant correlation was found between intellectual function and total brain volume (p=0.02). In a study by Wilmott et al., MRI and diffusion tensor imaging's were used in children with a global developmental delay of unknown cause (25). They found that fasciculus arcuate was absent in a significant number of patients. They also found that abnormal maturation of the inferior longitudinal fasciculus was present in many cases with developmentally delay. This study demonstrated the usefulness of diffusion tensor imaging for determining the central connections in children with developmental delay whose conventional imaging findings are often normal.

## CONCLUSION

Based on the results, a high proportion of patients with GDD and isolated NDD have positive MRI findings. Therefore, this imaging modality can be used for diagnosis and prognosis of patients with developmental delay.

## ACKNOWLEDGMENTS

None.

## DECLARATIONS

### Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

### Ethics approvals and consent to participate

Consent was obtained from the patient's parents for publication after ensuring confidentiality of personal information. The ethics committee of Tehran University of Medical Sciences approved the study, IR.TUMS.CHMC.REC.1394.1077.

### Conflict of interest

The authors declare that there is no conflict of interest regarding publication of this article

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**How to Cite**: Khosroshahi N, Danaeian M, Tavasoli A, Alehossein M, Kamrani K, Khabazi Oskuoei A. Evaluation and Comparison of MRI Findings in Children with Global Developmental Delay and Isolated Neurodevelopmental Delay: A Cross-sectional Study. Journal of Clinical and Basic Research. 2021; 5 (3) :52-59

[ DOI: 10.52547/jcbr.5.3.52 ]