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Review article

# Systematic review of MRI findings in children with developmental delay or cognitive impairment

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**Abstract**

*Aim:* To summarize the reported rates of magnetic resonance imaging (MRI) abnormalities in children with isolated global developmental delay (GDD) or intellectual disability (ID).

*Method:* A literature search was conducted using electronic databases for studies reporting the rate of MRI abnormalities in children with clinically diagnosed ID or GDD and no other neurological signs, symptoms, or previously determined aetiology. All investigations with participants from birth to 18 years were considered. Study quality was evaluated using the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (MAStARI) critical appraisal checklist items.

*Results:* Eighteen cross sectional, and 11 case-controlled studies adhered to inclusion criteria. Reported rates of abnormalities ranged from 0% to 98%. When all subjects with developmental delay from all papers were considered ($n = 2299$) the total percentage found to have abnormalities was 38%. Abnormalities led to an etiological diagnosis for delay in 7.9% of cases.

*Interpretation:* Definitions of abnormalities varied widely between studies, and drastically different rates of abnormalities are reported. Currently available evidence is not of sufficient quality to make firm recommendations on the use of neuroimaging in ID or GDD but MRI should be considered for children that do not have a diagnosis after thorough clinical evaluation.


*Keywords:* Neuroimaging; Intellectual disability; Global developmental delay; Congenital malformation

## 1. Introduction

Developmental delay and intellectual disability are common presentations in general and subspecialty paediatric clinics, with an estimated prevalence of 0.71% for intellectual disability and 3.65% for developmental delay in children 3–17 years of age [1]. Global developmental delay refers to children younger than five years who are found to have significant delay in two or more developmental domains (i.e., gross or fine motor, language, social communication, cognition, or activities of daily living) [2]. Intellectual disability is characterized by deficits in intellectual and adaptive functioning with onset in childhood and is usually reserved for children over the age of six, at which time more reliable tools are available for cognitive assessment [3,4].

Most paediatric organizations advocate for routine screening for developmental impairment, with the goal of early detection, intervention, and etiologic investiga-

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tions [5]. Although impairments are frequently detected, the diagnostic evaluation for underlying etiologies of developmental or cognitive delay is complicated, with continually advancing investigations that often require complex interpretation [6]. There is disagreement as to whether children with developmental impairment of unknown aetiology should routinely undergo neuroimaging. Current published guidelines and practice parameters comment on the lack of consensus regarding recommendations for neuroimaging in investigation of developmental delay or intellectual disability [7]. Magnetic resonance imaging (MRI) is generally recommended as a secondary investigation in the presence of other signs or symptoms, or if diagnosis has not been made after a thorough history, physical exam and initial investigations such as auditory and ophthalmological assessment, genetic studies (comparative genomic hybridization microarray or whole exome sequencing, plus *MECP2*, *FMR1* for fragile X syndrome or other targeted genes as appropriate), thyroid function tests, and tests for treatable inborn errors of metabolism if not completed during newborn screening [2,8]. To the best of our knowledge, there have been no comprehensive systematic reviews of neuroimaging for investigation of developmental impairment in children with isolated delays (i.e. without other signs or symptoms); therefore, clarification of whether imaging is indicated for this presentation is needed.

Neuroimaging has the potential to reveal clinically important information such as congenital brain malformations, evidence of perinatal injury, and features consistent with inborn errors of metabolism or other genetic syndromes [9,10]. Knowledge of such conditions could lead to specific interventions or anticipatory care, as well as provide information about prognosis for the family and care team. On the other hand, conditions associated with abnormal neuroimaging often have other neurological or systemic signs that would constitute a pre-existing indication for imaging. In addition, features seen on MRI are often of questionable significance and do not inform diagnosis or treatment [11]. Furthermore, performing an MRI on a young child may require a general anaesthetic or sedation, which has inherent risks [12].

For children with global developmental delay or intellectual disability, but no additional neurological signs or symptoms, information about the rate and type of abnormalities found when brain MRI is performed would allow for more informed decision making between the care team and family. Without data regarding the likelihood of finding clinically relevant abnormalities, families cannot be appropriately counseled in terms of the risks and potential benefits of an MRI. To address this clinical need, we completed a systematic review of all previous studies reporting MRI abnormalities in children with isolated developmental impairment.

## 2. Methods

### 2.1. Search strategy

A literature search of peer reviewed articles was conducted using the online databases Medline, Embase, PsycINFO, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, and Web of Science, on July 22, 2016. The search included literature published between 1980 and the time of search, and was re-run just prior to the final draft of the review to ensure any new publications were included. Scopus and Web of Science databases provided a search of grey literature in addition to peer reviewed publications.

Search terms were determined by contributing authors with knowledge and clinical experience in paediatric neurology and psychology, with the assistance of a medical research librarian (See Appendix 1 for example of search terms; protocol not previously registered). Multiple keywords and phrases were used to capture the breadth of terminology employed to describe developmental delay and intellectual disability (i.e. developmental abnormalities, cognitive disability, developmental delay, developmental disability, developmental impairment, global developmental delay, mental retardation, intellectual disability, intellectual impairment, and learning disability), and were combined with terms for magnetic resonance imaging. Searches were not limited by language or study type.

A search was also completed of position papers and guidelines from the American Academy of Neurology (AAN), the Canadian Paediatric Society (CPS), and the American Academy of Paediatrics (AAP) for current organizational recommendations regarding the use of MRI in children with developmental impairment. The reference lists of guidelines, position statements, and all selected articles were searched manually for any additional relevant studies.

### 2.2. Inclusion and exclusion criteria

All types of publications, apart from isolated case studies and review articles, were included. Articles were not excluded based on methodological limitations; however, limitations were evaluated and addressed through bias analysis.

Participants were limited to children from birth to 18 years, with clinically diagnosed developmental delay or intellectual disability. Studies using children with isolated learning disabilities, such as dyslexia, were excluded, as were studies on autism spectrum disorder. Participants must have undergone MRI, with the rate of MRI abnormalities reported, for the study to be included. Children with developmental delay or learning disorder that had additional indications for neuroimaging, such as abnormalities in neurological exam,