Meta-analysis

Incidental Brain MRI Findings in Children: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: The diagnosis of incidental findings on children’s brain magnetic resonance imaging (MRI) suggest various practical issues due to the lifelong effects of such findings may be significant. Therefore, the aim of this study was to investigate the frequency and characteristics of incidental brain MRI findings in children.

Methods: Electronic databases (Scopus, MEDLINE, EMBASE, Google Scholar, and Cochrane) were searched for papers published between 1981 to November 2020, with the following search terms: incidental, findings, brain, magnetic resonance imaging, MRI. We included the studies with the following characteristics: patients with the age of lower than 20 years, being healthy children, MRI was performed using at least a 1.5T magnet, and papers with original design. Two reviewers independently extracted data and evaluated the quality of data extraction. The frequency of incidental findings were pooled. Heterogeneity of the findings of included studies was investigated using the Cochran Q statistic and the I² statistic.

Results: Seven studies reporting frequency of incidental findings in MRI of children were included in our meta-analysis. Incidental findings were found in 17.3% (95% CI, 6.3–39.3) of healthy children, intracranial cysts being the most frequent (19.5%, 95% CI, 9.7–35.4). Furthermore, incidental findings were present in 34.9% of male children (95% CI, 7.2–78.8) and 18.3% of female children (95% CI, 8–36.4).

Conclusion: The frequency of incidental findings is much more prevalent in children than previously reported in young adults. Moreover, the prevalence of incidental findings was more in male children than female children.

Keywords: Child, cyst, Incidental findings, Magnetic Resonance Imaging, Systematic review, Meta-analysis.

Introduction

Magnetic resonance imaging (MRI) of the brain is increasingly performed in both pediatric investigations and clinical evaluations, with constantly increasing image quality due to improvement of performance of hardware and sequence development (1). Performing MRI using higher quality and/or field strength using more sensitive sequences may result in the detection of some subtle brain findings that would not have been previously found. Moreover, with the steadily increasing number of brain MRI scans obtained each year, these technical advances will lead to more needing of patients and physicians to know the best approach for incidental brain findings (2, 3). Incidental findings (IFs) are known as previously undiagnosed abnormalities of potential
clinical significance that are unexpectedly detected and, by definition, unassociated with to the aim of the clinical examination. The diagnosis of IFs suggests various clinical and ethical issues, particularly when you are working in pediatric department, in whom the long-time effects of such findings may be irrecoverable. Detection is potentially harmful because the treatment of IFs can have detrimental as well as beneficial outcomes (4). The information regarding the probability of detection of incidental brain findings is of significance to improve knowledge of clinicians to guide the patients about the risks of these IFs. The clinical significance and the future process of these incidental findings have been investigated in adults but remain largely unknown in the pediatric subjects (5). Previous investigations have assessed pediatric IFs in healthy subjects and in samples of children who underwent MRI for other purposes. Recently, Jansen et al. (6) in a single center investigation of 3966 children, showed that at least 1 IF was found in 25.6% of the children, though the rate of frequency of findings need clinical follow-up was only 0.43%. A systematic review and meta-analysis of the previously published papers has been suggested to provide more estimations of the prevalence of IFs on brain MRI of children and also assess the effect of characteristics of imaging and type of the study on the diagnosis of IFs. In this meta-analysis, we aimed to investigate the rate of frequency and also characteristics of incidental brain MRI findings using previously published papers that assessed these findings in population of children.

Materials and Methods

Before the initiation of this meta-analysis, we provided a detailed questionnaire, including aims and process of collection and also analysis of the extracted data. The final version of the paper was written according to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) and Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA) guidelines. All the process of the preparation of this meta-analysis was performed independent of any company or financial associations.

funnel plot. Heterogeneity among the studies was evaluated using χ2 statistic for the pooled estimates (p<0.05 indicated significant heterogeneity) and I² index. Based on the results of the assessment of heterogeneity, we used random or fixed effects

Search Strategy

The systematic search on incidental brain MRI findings of children was performed on previously published papers between 1981 to November 2020 using advanced search of the following databases: Scopus, MEDLINE, EMBASE, Google Scholar, and Cochrane. Potential studies were assessed using the following keywords: magnetic resonance imaging, MRI, incidental, finding, brain, pediatric, and child. Furthermore, after the primary search of the studies, the reference list of the potential studies were reviewed by the authors.

Inclusion and Exclusion Criteria

We included the studies with the following characteristics: 1) subjects with the age of younger than 21 years, 2) being healthy without any previous diagnosis of the diseases related to the brain, 3) MRI was achieved with a minimum magnet of 1.5T, 4) the original design of the study, and 5) the language of English. We excluded the studies that did not determine age of their subjects

Data Extraction

Data extraction was carried out by to independent physicians according to previous prepared questionnaire and any conflicts were solved by assessment of the data by the third physician. The data-extraction questionnaire was included 4 subsections: 1) general characteristics of the studies, 2) characteristics of children, 3) methodology of MRI, and 4) characteristics of IFs. We extracted the following data: author names, year of publication, country, total number of included subjects, mean age of the children, gender, and frequency of IFs. We assessed the MRI magnet field used (1.5T or 3T) for children. We extracted the number of children and frequency of IFs. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was used to evaluate the quality of the included papers.

Data Synthesis

Before data synthesis, publication bias of the included studies was assessed using Egger test and models to estimate the prevalence of IFs prevalence in children. We used the Comprehensive Meta-Analysis software (CMA, ver. 2) to analyze the extracted data.
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Figure 1. PRISMA flowchart of the literature search and selection of studies that reported incidental brain MRI findings in children.

Results

The initial search identified 1462 publications, 65 of which were evaluated in full text (see the flow chart in Fig 1). Finally, seven studies were included in our meta-analysis. Table 1 shows the characteristics of the included studies. The funnel plots and Egger’s test revealed no significant publication bias in terms of prevalence of incidental brain MRI findings in children (P=0.32) (Fig. 2).
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**Figure 2.** Funnel plot of results of prevalence of incidental brain MRI findings in children.

Review of the included studies revealed that imaging was performed using either a 1.5T or 3T magnet. All the imaging protocols included a T1-weighted sequence and 4 studies also reported 2D T2-weighted or FLAIR sequences. Four studies were defined as high-resolution MRI. In the included studies, images were mostly reviewed by neuroradiologists, or pediatric neurologist.

Incidental findings were present in 17.3% (95% CI, 6.3–39.3) of healthy children, intracranial cysts being the most frequent (19.5%, 95% CI, 9.7–35.4).

Furthermore, incidental findings were found in 34.9% of male children (95% CI, 7.2–78.8) and 18.3% of female children (95% CI, 8–36.4).

**Table 1.** Characteristics of the included studies in the meta-analysis.

| Author             | Years | Country | Total no. of patients | mean age of patients | Male/Female | Frequency of IF |
|--------------------|-------|---------|-----------------------|----------------------|-------------|-----------------|
| Jansen et al. (6)  | 2017  | Netherlands | 3966                 | 10.1                 | NA          | 102             |
| Monterrey et al. (11) | 2017 | USA     | 168                  | 10.1                 | 2.4         | 109             |
| Kaiser et al. (12) | 2015  | USA     | 114                  | 8.3                  | NA          | 28              |
| Gur et al. (13)    | 2013  | USA     | 1400                 | 14.8                 | 0.9         | 148             |
| Seki et al. (14)   | 2010  | Japan   | 110                  | NA                   | NA          | 40              |
| Kumra et al. (15)  | 2006  | USA     | 60                   | NA                   | NA          | 3               |
| Kim et al. (9)     | 2002  | USA     | 225                  | NA                   | 0.8         | 47              |

**Discussion**

In this systematic review and meta-analysis, we found a prevalence of 17.3% of IFs on brain MRI within a population children of seven studies. Most of these reported IFs were benign and did not require common referral, treatment, hospitalization, or follow-up. Taken together, few studies have examined incidental findings in healthy children, and prior studies have been limited by both the effective resolution of the imaging sequence used and small sample sizes. Furthermore, incidental findings were found in 34.9% of male children and 18.3% of female children.
Figure 3. a) Forest plot of prevalence of incidental brain MRI findings in children. b) Forest plot of prevalence of incidental brain MRI findings in male children. c) Forest plot of prevalence of incidental brain MRI findings in female children.
Due to the increasingly common use of high-resolution brain MRI in pediatric populations, it is essential to determine both a baseline rate for IFs and an approach for their assessment. A recent meta-analysis of 16 adult studies, including nearly 20,000 MRI, showed that the rate of IFs was associated to image resolution (7). In the condition of sequences using high-resolution by present standards, we showed an IF prevalence that was significantly higher than with standard sequences. However, the high-resolution investigations were the most recent ones, which may reveal that the difference could be also due to the MRI scan generation, and not only to the strength of magnet used in MRI devices.

The prevalence of IFs was much higher in our study (17.3%) than in the adult meta-analysis (2.7%), but this comparison is difficult due to differences in studies samples (7). First, the primary characteristics of IFs completely varies. In adults, Vernooij et al. (8) showed that asymptomatic brain infarcts were detected in 7.2%, and cerebral aneurysms, in 1.8%, whereas they were not assessed in population of children. If we do not consider these findings in our study, the prevalence of IFs varies from 16.4% to 9.6%.

Third, imaging protocols considerably change between adult and children (resolution, duration, 3D) and may cause differences in prevalence of IFs. We did not find differences in IFs or subtype of IF regarding to sex, whereas a recent study revealed significant differences in rate of IFs between male and female subjects (9). We found that pineal cysts is the most frequent IF, detected in 19.5% of children. The frequency of these cysts in clinical cohorts is different from 1.8% when cysts are considered as having a diameter of >10 mm up to 57%, most likely these differences are due to the differences in the definition of the cyst versus normal gland in previous studies (10). There are some inconsistency between different studies with respect to the clinical meaning of these cysts. In a recent study, it has been shown that even above 10 mm in diameter, pineal cysts most often remain stable or reveal minimal growth. Therefore, size is probably less associated than mass effect seen on the aqueduct. In the absence of such mass effect, pineal cysts may be seen more times and considered as a previous normal variant.

Taken together, only few anomalies imply the need for cautious assessment by pediatric neuroradiologists. Evaluation of images from research pediatric studies in healthy volunteers, researchers should be aware of the possibility of detection of a brain tumor in about 1 in every 500 children. Our meta-analysis had some limitations. First, we did not perform stratification of the extracted data allowing IFs to be categorized by age, which could be noted because some of the IFs may be present or disappear with age. We may also have some missed data that were not reported in the included studies. Second, the extracted data were not been stratified with regard to ethnicity and this may be a potential bias in our meta-analysis. Third, the effect of differences in study design may change the precision of prevalence of IF and explain the substantial heterogeneity of studies evaluated by Cochran statistics. Fourth, in our meta-analysis, although the comprehensive systematic search was performed to include as many pertinent studies as possible, some publications may have not been included in the study studies, we could not perform any detailed subgroup or meta-regression analyses, and none of our reported results could be corrected for possible confounders.

incidental findings was more in male children than female children.

Declarations

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**Conflict of interest**

There is no conflict of interest.

**Data Availability**

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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