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Incidental Findings on Pediatric MR Images of the Brain

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BACKGROUND AND PURPOSE: **Previous studies have addressed the prevalence of incidental findings in symptomatic and healthy adult populations. Our study aims to elucidate the prevalence of incidental findings in a healthy pediatric population.**

METHODS: **We retrospectively reviewed 225 conventional brain MR imaging studies obtained during structural and functional brain imaging research in a cohort of neurologically healthy children (l00 boys [44%] and 125 girls [56%]) ranging in age from younger than 1 month to 18 years. All MR images were reviewed, and two board-certified neuroradiologists categorized the findings by consensus.**

RESULTS: **Incidental abnormalities were detected in 47 subjects (21%), while 79% of the images were normal. Of the 47 abnormalities detected, 17 (36%) required routine clinical referral; a single lesion (2%) required urgent referral. The occurrence of these findings in the male cohort was twice that of the female cohort; however, the percentage of subjects requiring either routine or urgent referral did not differ by sex (male subjects, 34%; female subjects, 39%).**

CONCLUSION: **Although the frequency of clinically important incidental abnormalities was not high in the sample of children studied, the presence and variety of findings in any pediatric group is particularly important for both the welfare of the subject and for research in which knowledge of the subject's neurologic status is vital to the interpretation of the results. Despite the limitations of the study in terms of the age and ethnic distribution, this work highlights the need for the routine involvement of trained radiologists in these studies to ensure that such incidental findings are detected and that appropriate follow-up is provided.**

With the advent of MR imaging as a powerful means of detecting both anatomic and functional information about the brain in health and disease, large numbers of presumably neurologically healthy volunteers have participated in imaging research studies over the past decade. From a research point of view, the confidence in the findings from such studies resides, at least in part, in the confidence that subjects are of the neurologic status intended. However, several groups have reported incidental radiologic findings in symptomatic and healthy adult populations. To our knowledge, the occurrence and management of incidental radiologic findings in a pediatric population, in whom the lifelong implications of such findings may be profound, have not been documented or well established. Moreover, from a subject-welfare point of view, MR imaging studies involving volunteers are frequently performed by persons other than physicians, and a trained radiologist may never review the images. Any unanticipated findings on these images may therefore go unrecognized, and the subjects may not receive the appropriate referral. The goals of the present study were 1) to determine the frequency and severity of incidental findings in a sample population of specifically of children who underwent brain MR imaging for research, and 2) to consider the implications of routinely involving neuroradiologists in these research studies.

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Methods

Subjects

Two board-certified neuroradiologists (R.K., S.W.A.) retrospectively reviewed structural and functional MR images (fMRI) from a cohort of 225 neurologically healthy pediatric subjects. The images were obtained in fMRI research studies of language, spatial discrimination, and higher cognitive function conducted between 1997 and 2000. Subjects were recruited from a variety of sources, including advertisements in local papers and family-oriented magazines and in schools and community organizations, and they were offered compensation for

TABLE 1: Referral Classifications for Incidental Neuroradiologic Findings

Classification	Number	Percentage of Total Images (n = 225)	Percentage of Total Abnormalities (n = 47)
Requiring no referral	28	12%	60%
Requiring routine referral	17	8%	36%
Requiring urgent referral	1	<1%	2%

Note.—Findings were from 225 research MR images obtained in a cohort of neurologically healthy children.

their participation and incentives for successfully completing the examination.

Subjects' ages ranged from younger than 1 month to 18 years. Of the 225 subjects, 100 (44.4%) were male (age range, 0–18 years; 90 [90%] aged 7–17 years), and 125 (55.6%) were female (age range, 4–18 years; 115 [92%] aged 6–16 years). The mean age of all subjects was 11.2 years (median, 10 years). Images in children aged 2–5 years were not available because subjects in this age range were not a focus of our work at that time. Subjects were screened with widely used behavioral questionnaires, such as the Child Behavior Checklist, and with a standard screening interview that was used to rule out neurologic, psychiatric, and cognitive disorders. Many subjects also underwent standardized IQ testing.

Exclusion criteria included implanted metal objects and any other condition in which MR imaging is contraindicated. Subjects were screened for any neurologic, developmental, or psychiatric conditions that could have jeopardized their status as control subjects matched to experimental groups that comprised children with diverse neurodevelopmental, neurogenetic, and neuropsychiatric conditions.

All studies were approved by the institutional review board at the Stanford University Medical Center. Written informed consent for participation was provided by subjects' parents or guardians. Participants and their parents or guardians were informed that the images were obtained for research purposes and not for clinical diagnosis.

MR Imaging Parameters

MR imaging parameters varied somewhat due to the time course of the retrospective study, but conventional short-TR, short-TE, spin-echo T1-weighted images were available for more than 90% of the subjects. T2-weighted spin-echo or fast spin-echo images obtained by using long TRs and long TEs were available for 64%. Proton density–weighted spin-echo or fast spin-echo images obtained by using long TRs and short TEs were available for 52%, and high-spatial-resolution T1-weighted, three-dimensional, spoiled gradient-recalled echo (SPGR) images were available for 46%.

Classification of Incidental Findings

All findings and classifications thereof were derived by consensus of the two board-certified neuroradiologists. Incidental findings were classified into four categories by using the method described by Bryan et al (1), as follows: 1 indicated that no referral was necessary, that the findings (eg, minimal paranasal sinus disease) were common normal findings in asymptomatic subjects; 2, that routine referral was needed (eg, to assess acute sinusitis or a nonspecific white matter lesion); 3, that urgent referral was required within 1 week (eg, to assess a nonacute intraparenchymal or extraaxial lesion other than small white matter focus); and 4, that immediate referral was required (eg, to assess an acute process with substantial mass effect).

Results

Abnormalities of all categories of clinical importance were detected in 47 (21%) of the 225 studies reviewed, as shown in Table 1. Of these, 18 (38% of abnormalities or 8% of the total subject population) required either routine (17 cases) or urgent (1 case) clinical referral. No cases were in the immediate referral category. Two subjects presented with more than one finding. One of these subjects had acute sinusitis and a posterior fossa arachnoid cyst, and the other subject had a pineal cyst and sphenoid sinusitis.

TABLE 2: Classification of Neuroradiologic Abnormalities

Classification and Abnormality	Number
No referral required	
Chronic sinusitis	21
Arachnoid cyst	2
Frontal venous angioma	2
Mega cisterna magna	2
Ventricular asymmetry	1
Chronic sinusitis with pineal cyst	1
Routine referral required	6
Acute sinusitis	5
Focal white matter lesion of uncertain etiology	3
Tonsillar ectopia	1
Hypoplasia pons	1
Petrous apex lesion	1
Acute sinusitis with arachnoid cyst	
Urgent referral required, cerebellar tonsil lesion uncertain etiology	1

Note.—Abnormalities were detected on 225 conventional research brain MR images in a cohort of neurologically healthy children.

The classification of all detected abnormalities is presented in Table 2. Extracranial abnormalities (eg, sinusitis) were found in 12% of subjects and accounted for 55% of all incidental findings. Intracranial abnormalities (eg, focal white matter lesions and other findings not related to sinus disease) were found in 9% of the subjects and accounted for 45% of the incidental findings. The age distribution of the subjects in whom these abnormalities was found is shown in Table 3.

We further analyzed the data according to sex and found that the incidence of neuroradiologic findings in male subjects was approximately twofold compared with that of the female subjects (Table 4; $\chi^2 = 5.12$; $P < .05$). More than one-third of the male subjects with a detected abnormality required at least routine referral. When we removed the cases of sinusitis that did not require referral from the analysis because of their clinical unimportance, more than one-half of the abnormal findings in both female and male subjects were considered to have required clinical referral (Table 5; $\chi^2 = 4.5$; $P < .05$).

TABLE 3: Distribution of Abnormalities by Subject Age at MR Imaging Examination

Classification and Abnormality	No. of Subjects by Age (y)																	
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
No referral required																		
Chronic sinusitis	0	1	0	0	0	0	1	3	3	2	4	1	4	2	0	0	0	0
Arachnoid cyst	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0
Frontal venous angioma	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0
Mega cisterna magna	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0
Ventricular asymmetry	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chronic sinusitis with pineal cyst	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Routine referral required																		
Acute sinusitis	0	0	0	0	0	0	1	2	0	0	1	0	0	1	1	0	0	0
Focal white matter lesion of uncertain etiology	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	1	1	0
Tonsillar ectopia	0	0	0	0	0	0	0	1	1	0	0	0	0	0	1	0	0	0
Hypoplasia pons	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Petrous apex lesion	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Acute sinusitis with arachnoid cyst	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Urgent referral required, cerebellar tonsil lesion uncertain etiology	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0

TABLE 4: Incidental Findings by Referral Classification and Sex

Classification	Percentage of Total Images		Percentage of Total Abnormalities by Sex	
	Female (n = 125)	Male (n = 100)	Female (n = 18)	Male (n = 29)
Total abnormalities	14% (18)	29% (29)	100% (18)	100% (29)
Requiring no referral	9% (11)	18% (18)	61%	62%
Requiring routine referral	6% (7)	10% (10)	39%	34%
Requiring urgent referral	0% (0)	1% (1)	0%	3%

Note.—Data in parentheses are the number of abnormalities.

TABLE 5: Incidental Findings by Referral Classification and Sex, with Findings of Sinusitis Removed

Classification	Percentage of Total Images		Percentage of Total Abnormalities	
	Female (n = 125)	Male (n = 100)	Female (n = 3)	Male (n = 17)
Requiring no referral	<1% (1)	7% (7)	33% (1)	41% (7)
Requiring routine referral	2% (2)	9% (9)	67% (2)	53% (9)
Requiring urgent referral	0% (0)	1% (1)	0% (0)	6% (1)

Note.—Findings of sinusitis requiring no referral were removed from the analysis because of their clinical insignificance. Data in parentheses are the number of abnormalities.

Discussion

In 1999, Katzman et al (2) retrospectively studied the prevalence of incidental imaging findings in a healthy asymptomatic population. They reported an 18% incidence of findings in their cohort of 1000 research subjects (54.6% male, 45.4% female; mean age, 30.6 years; age range, 3–83 years). Of the findings they detected, 15.1% required no referral; 1.8%, routine referral; 1.1%, urgent referral; and 0.2%, immediate referral. Other clinical studies have addressed the prevalence of the incidental radiologic finding of sinus disease in adult patients presenting with symptoms such as a chronic cough, seizures, head injuries, and various intracranial diseases (3–6). Variations in incidental findings across age have also been observed, including incidental findings of white matter lesions (7), sinus disease (8), and focal white matter abnormalities (9) in symptomatic subjects.

In the present study, we retrospectively explored the frequency and clinical importance of incidental findings on brain MR images in a neurologically healthy pediatric population involved in fMRI research. Our data broadly replicate those of Katzman et al (2) in adults; for example, our 21% overall prevalence of incidental findings is generally consistent with the 18% of findings overall in healthy adults in the report by Katzman et al, with sinusitis in 12% of the adult cohort. In addition, albeit limited, the ventricular asymmetry found in one of two neonatal subjects is also consistent with the incidence of approximately 45% that Shen and Huang reported (10).

Although the age distribution in our sample was not homogeneous and although the overall incidence of clinically important findings in the total population was relatively small, nearly 10% of subjects had findings that were categorized as requiring at least routine referral. In contrast to findings in older adults, small foci of abnormal signal intensity on MR images

are always of concern in children, whether the findings are in the deep gray matter or in the white matter. For example, small foci of abnormal signal intensity were strongly associated with neurofibromatosis (NF)-1 in a study by DeBella et al (11) in which 43–93% of children with NF-1 presented with such focal signal intensity abnormalities. Consequently, such findings on MR images have been proposed as a diagnostic criterion for NF-1. Our 2.2% incidence of such findings in healthy children is concordant with expected frequencies, although it is less than the incidence in the study by DeBella et al (11). Nevertheless, such findings should prompt further follow-up and routine referral of the subject to a physician or clinical setting.

We also report differences in the prevalence of total incidental findings related to sex. In addition to the twofold increase in the incidence of abnormalities in male subjects compared with female subjects, the male subjects also had a greater variety of incidental findings. Moreover, when we factored out all of the extracerebral findings (eg, sinus disease), the male subjects had a 17% incidence of intracerebral abnormalities, whereas the female subjects had a 3% incidence of such abnormalities. Previous studies have also shown some differences in the prevalence of certain findings across sex (12, 13), with a higher prevalence of pineal cysts reported in young women (14). Although the importance of these sex-related differences is uncertain, MR imaging researchers must be cognizant of such population-related variations.

The disproportionately limited ethnicity of the cohort, which included subjects of primarily European or Asian descent, may be a potential confounding factor in this study. Its effect is unknown at this time. and future multicenter investigations may help to broaden our understanding of the potential geographic, environmental, and genetic effects of the findings.

Conclusion

The prevalence of incidental MR imaging findings in the healthy pediatric population reported here, as well as the prevalence of unidentified bright objects and ventricular asymmetry in the neonatal subjects, are consistent with the results of previous research studies in adults and in clinical studies of adult and children. In addition to these findings, new findings of strong intersex differences and intracerebral abnormalities are other factors that must be taken into account when population variations are considered in fMRI.

Although the MR imaging findings reported here did not compromise the interpretability or validity of the research studies (subjects with intracranial abnormalities were excluded from analyses), even the limited presence of such findings in a cohort of young participants is a matter of medical concern. The findings suggest that researchers must develop specific procedures for managing the brain MR imaging examination that includes proactive involvement of the neuroradiology community both for the detection of abnormalities and for their appropriate follow-up. Such procedures should be applicable at a broad level, in a cost-effective fashion, and in a consistent and clinically appropriate manner.

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