Incidental Findings on Brain Imaging in the General Pediatric Population

Jansen, P.R.; Dremmen, M.; Berg, A. van den; Dekkers, I.A.; Blanken, L.M.E.; Muetzel, R.L.; ... ; White, T.J.H.

CORRESPONDENCE

Incidental Findings on Brain Imaging in the General Pediatric Population

TO THE EDITOR: Incidentally discovered findings on brain magnetic resonance imaging (MRI) in healthy persons pose medical and ethical considerations regarding management.[1] The prevalence of incidental findings on brain MRI has been described in adult populations,[2] but less is known about incidental findings in children. We report the prevalence of incidental findings on brain MRI in a large, single-center neuroimaging study involving a general pediatric population. From April 2013 through November 2015, a total of 3966 children (mean age, 10.1 years; range, 8.6 to 11.9) in the population-based Generation R Study[3] — designed to prospectively identify early environmental and genetic influences on normal and abnormal growth, development, and health during fetal life, childhood, and young adulthood — underwent MRI scanning of the brain on a single 3-Tesla scanner. Scans were systematically reviewed by trained researchers and neuroradiologists for the presence of incidental findings (Table 1).

At least one incidental finding was present in 25.6% of the children (95% confidence interval [CI], 24.2 to 27.0), although the prevalence of findings requiring clinical follow-up was only 0.43% (95% CI, 0.26 to 0.70). The most common findings were cysts of the pineal gland (in 665 children; 16.8%; 95% CI, 15.6 to 18.0), arachnoid cysts (in 86; 2.17%; 95% CI, 1.75 to 2.68), and developmental venous anomalies (in 63; 1.59%; 95% CI, 0.12 to 2.04). Among less frequent findings were Chiari I malformations (in 25 children; 0.63%; 95% CI, 0.42 to 0.94), subependymal heterotopia (in 19; 0.48%; 95% CI, 0.30 to 0.76), and partial agenesis of the corpus callosum (in 2; 0.05%; 95% CI, 0.01 to 0.20). A total of 17 children (0.43%) were referred to a pediatric neurologist for clinical imaging and follow-up; 7 of these children (0.18%) had suspected primary brain tumors, of whom 2 underwent neurosurgical treatment, with the diagnoses confirmed by histopathological examination. The prevalence of asymptomatic brain tumors in our population-based cohort was higher than estimates from cancer registries, which have shown a prevalence in the United States of approximately 35 in 100,000 (0.04%) among persons younger than 20 years of age.[4] However, no reliable statistics are available to estimate the frequency of asymptomatic brain tumors among children.[5]

Our results emphasize the need for careful evaluation of incidental findings on brain scans of asymptomatic children. In addition, it may be prudent to use standardized protocols for managing incidental findings in children, including reporting, disclosure to parents, and subsequent follow-up when necessary.

Philip R. Jansen, M.D.
Marjolein Dremmen, M.D.
Aaike van den Berg, M.D.

Erasmus University Medical Center
Rotterdam, the Netherlands

THIS WEEK'S LETTERS

Table 1. Incidental Findings in the Generation R Study Population (3966 Children).*

Finding	Finding Present	Prevalence	Clinical Referral	Clinical Management
	no. of children	*% (95% CI)*	*no. of children*	
Normal variations				
Cavum septum pellucidum	79	1.99 (1.59–2.49)	0	—
Mega cisterna magna	104	2.62 (2.16–3.18)	0	—
Empty sella configuration	7	0.18 (0.08–0.38)	0	—
Congenital malformations				
Chiari I malformation	25	0.63 (0.42–0.94)	1	MRI follow-up
Partial agenesis of the corpus callosum	2	0.05 (0.01–0.20)	2	Neurologic examination
Agenesis of the septum pellucidum	3	0.08 (0.02–0.24)	0	—
Ventriculomegaly	2	0.05 (0.01–0.20)	1	MRI follow-up
Cysts				
Arachnoid cyst	86	2.17 (1.75–2.68)		—
<3 cm	75	1.89 (1.50–2.38)	0	—
≥3 cm	11	0.28 (0.15–0.51)	2	MRI follow-up
Pineal gland cyst	665	16.8 (15.6–18.0)		
<1 cm	652	16.4 (15.3–17.6)	0	—
≥1 cm	13	0.33 (0.18–0.58)	1	Contrast-enhanced MRI, lumbar puncture
Porencephalic cyst	3	0.08 (0.02–0.24)	0	—
Intraventricular cyst	7	0.18 (0.08–0.38)	1	MRI follow-up
Vascular anomalies				
Developmental venous anomaly	63	1.59 (0.12–2.04)	0	—
Cavernous angioma	7	0.18 (0.08–0.38)	0	—
Capillary telangiectasia	2	0.05 (0.01–0.20)	0	—
Migration disorders				
Subependymal gray-matter heterotopia	19	0.48 (0.30–0.76)	0	—
Transmantle dysplasia	1	0.03 (0.01–0.16)	0	—
Focal cortical dysplasia	1	0.03 (0.01–0.16)	0	—
White-matter abnormalities				
Focal white-matter hyperintensity	7	0.18 (0.08–0.38)	0	—
Radiologically isolated syndrome	1	0.03 (0.01–0.16)	1	Contrast-enhanced MRI
Neoplasms				
Low-grade glioma†	4	0.10 (0.03–0.28)	4	Contrast-enhanced MRI
Dysembryoplastic neuroepithelial tumor†	1	0.03 (0.01–0.16)	1	Contrast-enhanced MRI
Ependymoma‡	1	0.03 (0.01–0.16)	1	Contrast-enhanced MRI, neurosurgery
Craniopharyngioma‡	1	0.03 (0.01–0.16)	1	Contrast-enhanced MRI, neurosurgery
Other: fibrous dysplasia	1	0.03 (0.01–0.16)	1	Computed tomography

* Children may have more than one incidental finding. A total of 940 children had one incidental finding, 73 had two incidental findings, and 2 had three incidental findings. CI denotes confidence interval, and MRI magnetic resonance imaging.
† Radiologic diagnosis was by means of MRI.
‡ The finding was confirmed by means of histopathological analysis.

Ilona A. Dekkers, M.D.
Leiden University Medical Center
Leiden, the Netherlands
Laura M.E. Blanken, M.D., Ph.D.
Ryan L. Muetzel, Ph.D.
Koen Bolhuis, M.D.
Rosa M. Mulder, M.Sc.
Desana Kocevska, M.D.
Toyah A. Jansen, M.Sc.
Marie-Claire Y. de Wit, M.D., Ph.D.
Rinze F. Neuteboom, M.D., Ph.D.
Erasmus University Medical Center
Rotterdam, the Netherlands
Tinca J.C. Polderman, Ph.D.
VU University
Amsterdam, the Netherlands
Danielle Posthuma, Ph.D.
VU University Medical Center
Amsterdam, the Netherlands
Vincent W.V. Jaddoe, M.D., Ph.D.
Frank C. Verhulst, M.D., Ph.D.
Henning Tiemeier, M.D., Ph.D.
Aad van der Lugt, M.D., Ph.D.
Tonya J.H. White, M.D., Ph.D.
Erasmus University Medical Center
Rotterdam, the Netherlands
t.white@erasmusmc.nl

Supported by the Sophia Children's Hospital Research Foundation (project S14-27) and the Netherlands Organization for Health Research and Development (TOP project 91211021).

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Illes J, Kirschen MP, Edwards E, et al. Incidental findings in brain imaging research. Science 2006;311:783-4.
2. Morris Z, Whiteley WN, Longstreth WT Jr, et al. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. BMJ 2009;339:b3016.
3. Jaddoe VW, van Duijn CM, van der Heijden AJ, et al. The Generation R Study: design and cohort update 2010. Eur J Epidemiol 2010;25:823-41.
4. Porter KR, McCarthy BJ, Freels S, Kim Y, Davis FG. Prevalence estimates for primary brain tumors in the United States by age, gender, behavior, and histology. Neuro Oncol 2010;12:520-7.
5. Maher CO, Piatt JH Jr, Section on Neurologic Surgery. Incidental findings on brain and spine imaging in children. Pediatrics 2015;135(4):e1084-e1096.

DOI: 10.1056/NEJMc1710724

Instantaneous Wave-free Ratio versus Fractional Flow Reserve

TO THE EDITOR: Davies et al. (May 11 issue)[1] report on the DEFINE-FLAIR trial (Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation). In the same issue, Götberg et al.[2] report on the iFR-SWEDEHEART trial (Instantaneous Wave-free Ratio versus Fractional Flow Reserve in Patients with Stable Angina Pectoris or Acute Coronary Syndrome). The revascularization rate was lower in the instantaneous wave-free ratio (iFR) group than in the fractional flow reserve (FFR) group in both trials (47.5% and 53.4% in the DEFINE-FLAIR trial; 53.0% and 56.5% in the iFR-SWEDEHEART trial).

In the ADVISE II study (Adenosine Vasodilator Independent Stenosis Evaluation II), an iFR cutoff value of 0.89, as compared with FFR, had a specificity of 87.8% and a sensitivity of 73.0%.[3] Conceivably, revascularization of some lesions that would be warranted according to an FFR-guided strategy would be deferred with an iFR-guided strategy. Although an iFR-guided revascularization strategy was noninferior to FFR-guided revascularization in the trials reported by Davies et al. and Götberg et al., outcomes in patients with iFR-guided deferral of revascularization were not reported.

In the FAME 2 trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation 2), among patients with an FFR higher than 0.80 in all vessels who were enrolled in a registry and received the best available medical therapy, the rate of major adverse cardiovascular events was 3%; this rate was lower than that among patients who were randomly assigned to both the medical-therapy and percutaneous coronary intervention (PCI) groups in this trial.[4] It would be interesting to know whether the patients in the DEFINE-FLAIR and iFR-SWEDEHEART trials who had an FFR higher than 0.80 or an iFR higher than 0.89 and for whom intervention was deferred had similar outcomes. If indeed the clinical outcomes were similar, interventional cardiologists would have more confidence in deferring revascularization if the iFR is higher than 0.89, and these findings would help to encourage transition from a hybrid iFR–FFR approach to a pure iFR-guided strategy.[5]

Sourabh Aggarwal, M.B., B.S.
Gregory Pavlides, M.D., M.P.H.
University of Nebraska Medical Center
Omaha, NE
drsourabh79@gmail.com

No potential conflict of interest relevant to this letter was reported.