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Rates of Incidental Findings in Brain Magnetic Resonance Imaging in Children

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IMPORTANCE Incidental findings (IFs) are unexpected abnormalities discovered during imaging and can range from normal anatomic variants to findings requiring urgent medical intervention. In the case of brain magnetic resonance imaging (MRI), reliable data about the prevalence and significance of IFs in the general population are limited, making it difficult to anticipate, communicate, and manage these findings.

OBJECTIVES To determine the overall prevalence of IFs in brain MRI in the nonclinical pediatric population as well as the rates of specific findings and findings for which clinical referral is recommended.

DESIGN, SETTING, AND PARTICIPANTS This cohort study was based on the April 2019 release of baseline data from 11 810 children aged 9 to 10 years who were enrolled and completed baseline neuroimaging in the Adolescent Brain Cognitive Development (ABCD) study, the largest US population-based longitudinal observational study of brain development and child health, between September 1, 2016, and November 15, 2018. Participants were enrolled at 21 sites across the US designed to mirror the demographic characteristics of the US population. Baseline structural MRIs were centrally reviewed for IFs by board-certified neuroradiologists and findings were described and categorized (category 1, no abnormal findings; 2, no referral recommended; 3; consider referral; and 4, consider immediate referral). Children were enrolled through a broad school-based recruitment process in which all children of eligible age at selected schools were invited to participate. Exclusion criteria were severe sensory, intellectual, medical, or neurologic disorders that would preclude or interfere with study participation. During the enrollment process, demographic data were monitored to ensure that the study met targets for sex, socioeconomic, ethnic, and racial diversity. Data were analyzed from March 15, 2018, to November 20, 2020.

MAIN OUTCOMES AND MEASURES Percentage of children with IFs in each category and prevalence of specific IFs.

RESULTS A total of 11 679 children (52.1% boys, mean [SD] age, 9.9 [0.62] years) had interpretable baseline structural MRI results. Of these, 2464 participants (21.1%) had IFs, including 2013 children (17.2%) assigned to category 2, 431 (3.7%) assigned to category 3, and 20 (0.2%) assigned to category 4. Overall rates of IFs did not differ significantly between singleton and twin gestations or between monozygotic and dizygotic twins, but heritability analysis showed heritability for the presence or absence of IFs (h^2 = 0.260; 95% CI, 0.135-0.387).

CONCLUSIONS AND RELEVANCE Incidental findings in brain MRI and findings with potential clinical significance are both common in the general pediatric population. By assessing IFs and concurrent developmental and health measures and following these findings over the longitudinal study course, the ABCD study has the potential to determine the significance of many common IFs.

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Incidental findings (IFs) are previously unknown abnormalities discovered during imaging that are unexpected given the reasons for which the imaging was performed. Incidental findings are common in brain magnetic resonance imaging (MRI) in both clinical and research contexts, with 1 recent meta-analysis suggesting a rate of approximately 16% in healthy children.[1] Incidental findings range in clinical significance from normal anatomic variants to findings that may require urgent medical or surgical intervention. Increasing use of high-resolution structural brain MRI has prompted active discussion about whether screening for IFs should be standard in research imaging and how participating individuals should be counseled, given the current uncertainty about the true prevalence and significance of many IFs.[2-4] Knowing the prevalence and significance of IFs in a large population-based nonclinical sample would help frame this discussion and inform the development and refinement of approaches to effectively anticipate, communicate, and manage these findings.

The Adolescent Brain Cognitive Development (ABCD) study[5] is an ongoing longitudinal, multicenter, observational study of a large demographically diverse population of children across the US. The study is unique in its magnitude, participant diversity, and standardization of protocols; to our knowledge, an observational study of this size and scope has never been performed in this field. The overarching goal of the ABCD study is to assess the contributions of genetic and environmental factors to mental and physical health during a period of rapid brain and cognitive development. The study uses state-of-the-art multimodal brain imaging,[6,7] including high-resolution structural MRI of all individuals at the time of enrollment and at subsequent 2-year intervals. In addition, the inclusion of a large sample of twins in the study population allows us to investigate the potential heritability of IFs.

Previous studies have reported on the prevalence of IFs in brain MRIs in the general population, but most have focused on adult populations.[8,9] Of the studies on IFs in a general pediatric population,[10-21] to our knowledge, none have included a cohort as large and demographically diverse as the ABCD study. Moreover, few studies have been based on high-resolution 3-T MRI,[11,13,16,17] which is becoming standard in both the research and clinical settings and allows for increased neuroanatomic detail and better detection of IFs. Herein, we report the prevalence of IFs in the baseline structural MRI from the complete cohort of 11 875 children aged 9 to 10 years enrolled in the ABCD study.

Key Points

Question What are the prevalence and clinical significance of incidental findings on structural brain magnetic resonance imaging in the nonclinical pediatric population?

Findings In this cohort study of 11 679 demographically diverse US children aged 9 to 10 years, 21.1% had incidental findings. Approximately 4% of the scans showed incidental findings for which nonurgent or urgent clinical referral was recommended.

Meaning Incidental findings noted on brain magnetic resonance imaging appear to be common and 4% of children have incidental findings that prompt further clinical evaluation; these estimates of incidental findings' prevalence and significance may provide context for interpreting similar findings on clinical neuroimaging and inform discussions about the appropriateness of screening for brain magnetic resonance imaging findings in the research setting.

Methods

Participants

Between September 1, 2016, and November 15, 2018, 11 875 children aged 9 to 10 years enrolled in the ABCD study. Participants were enrolled at 21 study sites across the US and were selected to represent a demographically diverse sample of US adolescents. This multicenter study was approved by the institutional review boards of all participating institutions, and written informed parental/guardian consent and child assent were obtained from all participants. Participants were enrolled through a broad school-based recruitment process in which all children of eligible age at selected schools were invited to participate.[22,23] Children fulfilled inclusion criteria if they were within the desired enrollment age (age 9-10 years) and able to provide informed assent (child) and consent (parents). Children were excluded on the basis of severe sensory, intellectual, medical, or neurologic disorders that would affect the validity of the collected data or the ability of participants to adhere to the established study protocol.[24] For example, a participant with epilepsy would be excluded if they continued to have 1 or more seizures per month despite medication, but not if their seizures were well controlled and they had normal cognitive function. Contraindication to MRI was also an exclusion criterion. To ensure enrollment reflected epidemiologic diversity, during the multiyear enrollment process, demographic data were dynamically monitored to ensure that the study met targets for sex, socioeconomic, ethnic, and racial diversity.[22,23] The present report is based on imaging from participants whose data are included in the National Institutes of Mental Health Data Archive (NDA) public release of the baseline data from all children enrolled in the ABCD study (NDA 2.0.1). Data were analyzed from March 15, 2018, to November 20, 2020.

Demographic Characteristics

The ABCD cohort was selected to reflect the sociodemographic diversity of the US population. Data analytic approaches can subsequently be used to adjust for remaining demographic differences between the final ABCD sample and the actual population. Specifically, by comparing the final sociodemographic distribution of the ABCD sample with that of the nationally representative sample from the American Community Survey (ACS), a large probabilistic survey of more than 8 million US households conducted by the US Bureau of Census,[25] it is possible to weight the contribution of individuals in the ABCD sample to produce a distribution that closely matches the ACS-based national estimates for demographic characteristics.[26] **Table 1** reports the sociodemographic characteristics of participants in the baseline ABCD cohort

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Table 1. Demographic Information for the 11 677 ABCD Study Participants Who Had Interpretable Baseline Imaging[a]

Variable	No. (%) [adjusted %][b]			*P* value[c]	Adjusted *P* value[c]
	Category 1	Category 2	Categories 3 and 4		
Total	9213 (79.0) [78.8]	2013 (17.2) [17.2]	451 (3.8) [4.0]		
Boys	4756 (51.6) [50.6]	1107 (55.0) [54.1]	224 (49.8) [49.7]	.04	.12
Age, mean (SD), y	9.9 (0.62)	9.9 (0.63)	9.9 (0.62)	.46	.41
Household annual income (%, adjusted %), $					
<50 000	2491 (29.6) [39.1]	542 (29.1) [38.4]	114 (27.6) [37.9]	.60	.75
≥50 000 and <100 000	2397 (28.5) [31.0]	528 (28.3) [31.3]	106 (25.7) [29.4]		
≥100 000	3519 (41.9) [29.9]	794 (42.6) [30.3]	193 (46.7) [32.7]		
Parental highest educational level					
<High school diploma	462 (5.0) [6.2]	98 (4.9) [6.1]	20 (4.4) [5.2]	.85	.44
High school diploma/GED	862 (9.4) [10.8]	196 (9.8) [11.9]	44 (9.8) [12.4]		
Some college	2390 (26.0) [29.7]	520 (25.9) [30.1]	102 (22.7) [25.1]		
Bachelor	2339 (25.4) [24.2]	505 (25.1) [22.2]	121 (26.9) [26.0]		
Postgraduate degree	3152 (34.2) [29.0]	689 (34.3) [29.7]	163 (36.2) [31.4]		
Parents married	6199 (67.8) [61.2]	1368 (68.6) [61.9]	318 (71.3) [62.7]	.46	.94
Race/ethnicity					
Asian	213 (2.3) [3.9]	43 (2.2) [3.5]	12 (2.7) [4.5]	.03	.09
Black	1446 (15.9) [14.6]	278 (14.0) [12.8]	70 (15.7) [13.7]		
Other/mixed[d]	1628 (17.9) [15.0]	326 (16.5) [13.0]	58 (13.0) [11.1]		
White	5791 (63.8) [66.5]	1334 (67.3) [70.8]	306 (68.6) [70.8]		

Abbreviations: ABCD, Adolescent Brain Cognitive Development; GED, general educational development.

[a] Among the 11 679 participants with interpretable baseline imaging, 2 with category 1 findings did not have complete demographic information and were not included in this analysis.

[b] Percentages are shown for both the raw numbers and the numbers predicted by applying the American Community Survey weights (adjusted %).

[c] Two-sided *P* values reflect randomly subsampling the data to include only 1 member of each family to control for any lack of independence owing to relatedness.

[d] Category without further subcategorization.

stratified according to the IF category assigned to each participant's baseline imaging. For each IF category and sociodemographic dimension, Table 1 presents both the raw percentage of participants and the percentage predicted by applying the ACS weights. The percentage predicted estimates how the US population of children aged 9 to 10 years as a whole would be distributed as a function of IF category and sociodemographic dimension. The ACS weights only match the ABCD sample to the national population with respect to sociodemographic factors and do not guarantee that the sample is representative with respect to other measures.[23]

MRI Acquisition

Of the 11 875 participants enrolled in the study and included in the baseline data release, 65 did not complete MRI, resulting in a total of 11 810 participants who underwent structural neuroimaging. As described in detail elsewhere, MRI protocols were harmonized across the 21 enrollment sites.[6,7] All imaging data were obtained on 3-T scanners using either 32-channel head or 64-channel head/neck coils, depending on availability, and included 3D isovolumetric T1- and T2-weighted sequences. These scans also included prospective motion correction, when available. The imaging parameters varied by MRI manufacturer and are detailed in the published ABCD protocols.[27] All T1 and T2 structural sequences were reformatted in 3 planes and pushed to a centralized server, where they were accessed by clinical neuroradiologists via a specially designed image-review and report-generation web portal.

Neuroradiologic Interpretation

To ensure participant safety, T1 and T2 structural sequences from all MRIs obtained in the study were centrally reviewed by board-certified neuroradiologists and screened for structural abnormalities. Reporting was not based on a prespecified list of potential findings. Instead, all detected anatomic variants and structural abnormalities were reported. To improve reporting consistency, reviewers frequently conferred about the significance of particular findings. All MRI scans were reviewed by 1 of 3 neuroradiologists (including Y.L., L.S., and R.D. [noted in Additional Information]) with subspecialized training in pediatric neuroradiology and a combined 27 years of experience in diagnostic radiology. An individualized report was generated for each scan using a simple categorical scoring system (adapted from Shoemaker et al[28]) to classify findings and identify studies that required follow-up: 0, image artifacts prevent radiology read; 1, no abnormal findings; 2, normal anatomic variant or common incidental finding unlikely to be of clinical significance in a healthy individual, no referral necessary; 3, consider referral; and 4, consider immediate referral.

Findings of potential clinical relevance were assigned to category 3 or 4 based on their perceived clinical acuity, as judged by the neuroradiologist reviewing the study. For example, a large mass that compressed or disrupted nearby brain structures would be assigned to category 4, while a smaller mass, also concerning for neoplasm but not associated with significant mass effect, would be assigned to category 3. In

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Table 2. Distribution of Category 1 to 4 Findings in the 11 679 Participants in the Baseline ABCD Cohort With Interpretable Imaging[a]

Category	Definition	No. (%)			
		Overall	Singleton/sibling (n = 9588)	Twin (n = 2061)	Triplet (n = 30)
1	No abnormal findings	9215 (78.9)	7592 (79.2)	1595 (77.4)	28 (93.3)
2	Normal anatomic variant or common incidental finding unlikely to be of clinical significance in a healthy individual; no referral necessary	2013 (17.2)	1635 (17.1)	376 (18.2)	2 (6.7)
3	Consider referral	431 (3.7)	344 (3.6)	87 (4.2)	0
4	Consider immediate referral	20 (0.2)	17 (0.2)	3 (0.1)	0

[a] Differences among the categories were not significant ($P = .98$). Two-sided P values reflect randomly subsampling the data to include only 1 member of each family to control for any lack of independence owing to relatedness.

addition to the categorical score, the neuroradiology report for each study contained a free-form text box in which any pertinent findings were detailed with images if applicable. For category 3 and 4 studies, this text box also allowed the radiologist to elaborate on findings and provide guidance on recommended clinical or imaging follow-up. The resulting score and report were automatically uploaded to the imaging site, allowing appropriate follow-up to be initiated by the individual identified as the responsible investigator at each enrollment site. For scans with potentially actionable findings (categories 3 and 4), coordinators at the ABCD imaging core liaised with the responsible investigator to ensure appropriate follow-up. The categorical IF score associated with each study is available as part of the NDA 2.0.1 release. However, the free-form text detailing specific findings is considered internal communication and was made available only to relevant investigators to ensure appropriate counseling and follow-up for the participant.

To generate the data reported herein, the number of MRI scans assigned to each category was tallied for the entire study population, as well as for subgroups of singletons, twins, and triplets. To investigate the potential heritability of IFs, overall rates and twin-twin concordance for IFs were compared for monozygotic and dizygotic twin pairs. Furthermore, the prevalence of specific IFs, regardless of IF category or multiplicity of gestation, was calculated.

Interrater Reliability

Two reviewers (Y.L. and L.S.), with a combined 21 years of experience, reviewed 97% (11456 of 11810) of the MRI scans. The third reviewer (R.D.) was only briefly involved. To assess the interrater reliability (IRR) post hoc, the 2 primary reviewers independently categorized a subset of 200 scans from the cohort, enriched for category 3 and 4 scans, but stripped of their original reviews and scores. Of these 200 MRI scans reviewed for IRR, 20 were category 4 (which constitutes all of the category 4 studies in the cohort) and the remainder were randomly chosen from the other categories: 80 from category 3, 50 from category 2, and 50 from category 1. The reviewers were not blinded to the proportion of studies in each category. This approach was chosen to limit the number of studies rereviewed to a practical number, although this subset approach could potentially produce a higher IRR than if a large random sample was rereviewed. Interrater reliability for classification of this stratified subsample of the data was computed using multiple standard statistics, including Cohen κ, polychoric correlation, and Stuart-Maxwell/McNemar tests.

Statistical Analysis

Differences in demographic characteristics between IF categories and differences in the rates of each category between singleton and multiple gestation births were assessed using analysis of variance and χ^2 tests (Table 1 and **Table 2**). To account for nesting of data within families, we performed all analyses randomly retaining 1 member of each family. Polychoric correlations, Cohen κ, and Stuart Maxwell/McNemar tests were conducted to assess IRR. There were 3 families of 2 siblings each in these IRR analyses. We therefore repeated the analyses 8 times, each time retaining 1 member of each family (eTable 2 in the Supplement). In addition, we performed heritability analyses using data from all same-sex twins with valid radiologic reads and zygosity calls, treating radiologic reads as an ordinal variable. P values for all analyses were 2-sided, and $P < .05$ was considered statistically significant. Analyses were conducted in R, version 3.5.3 (R Foundation for Statistical Computing), using the packages polycor, psych, umx, and tableone.

Results

Study Categorization

Of the 11 810 MRIs reviewed, 131 (1.1%) were considered category 0 (uninterpretable). Of the remaining 11 679 studies, there was a total IF rate of 21.1% (2464 of 11679) (Table 2). A total of 2013 studies (17.2%) had IFs for which no referral was recommended (category 2), 431 (3.7%) studies had IFs for which nonurgent clinical referral was recommended (category 3), and 20 (0.2%) studies had IFs that warranted immediate clinical referral (category 4). The rate of each IF category was calculated separately for subgroups of singleton, twin, and triplet gestations and did not differ significantly between these groups (Table 2). Furthermore, the overall rate of IFs and the likelihood of both members of a twin pair having IFs did not differ significantly between monozygotic and dizygotic twins (eTable 1 in the Supplement). In addition, we used same-sex twin pairs with valid zygosity calls (456 dizygotic and 339 monozygotic twin pairs) to assess heritability of the radiologic reads. Treating the reads as a 4-level ordinal variable resulted in an estimated narrow-sense heritability $h^2 = 0.211$

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Table 3. Category 3 Findings in 431 Participants[a]

Category 3 incidental finding	No. (%)[b]
Periventricular nodular heterotopia	110 (0.94)
White matter abnormalities concerning for infection, inflammation, or ischemic injury	58 (0.50)
Arachnoid/intraventricular cyst with mass effect	28 (0.24)
Possible glial neoplasm	27 (0.23)
Head and neck findings	26 (0.22)
Large pineal cyst with mass effect	26 (0.22)
Cerebellar tonsillar ectopia (without Chiari I malformation)	25 (0.21)
Parotid lymphoepithelial cysts	22 (0.19)
Chiari I malformation	20 (0.17)
Vascular abnormalities	13 (0.11)
Cerebellar hypoplasia, volume loss, signal abnormality	11 (0.09)
Pituitary abnormality	11 (0.09)
Dilated central canal	10 (0.09)
Ventriculomegaly	7 (0.06)
Focal cortical dysplasia	7 (0.06)
Suspected cavernous malformation	6 (0.05)
Findings suggestive of intracranial hypertension	5 (0.04)
Callosal agenesis/hypogenesis	4 (0.03)[c]
Syrinx	3 (0.03)
Encephalocele	3 (0.03)
Susceptibility artifact concerning for metal in scalp/face	2 (0.02)
Malformations	2 (0.02)
Polymicrogyria	2 (0.02)
Morphologic abnormality of cervical spine	2 (0.02)
Porencephalic cyst	1 (0.01)

[a] Category 3 findings occurred in 3.7% (431 of 11 679) participants. Seventeen participants had more than 1 incidental finding that warranted nonurgent follow-up.

[b] Percentage value based on 11 679 participants.

[c] Two cases of agenesis of the corpus callosum and 2 cases of hypogenesis of the corpus callosum.

(95% CI, 0.097-0.324); treating the radiologic reads as a dichotomous variable (presence or absence of IFs) resulted in an estimated heritability $h^2 = 0.260$ (95% CI, 0.135-0.387).

The 20 category 4 studies for which immediate clinical referral was recommended included 7 masslike regions of signal abnormality concerning for glial neoplasm (eFigure [images A, B, C, D, E, F, and G] in the Supplement); 6 cases of hydrocephalus (eFigure [images H, I, J, K, L, and M] in the Supplement); 3 cases of severe Chiari I malformation with cerebellar tonsillar descent 15 to 24 mm below the foramen magnum, 2 of which demonstrated associated syrinx (eFigure [images N, O, and P] in the Supplement); 1 case of offset of the lateral masses of C1 and C2, suggestive of instability at the craniocervical junction (eFigure [image Q] in the Supplement); 1 sellar/suprasellar mass likely representing an adamantinomatous craniopharyngioma (eFigure [image R] in the Supplement); 1 case of diffuse supratentorial white matter signal abnormality concerning for a toxic/metabolic process (eFigure [image S] in the Supplement); and 1 large, multicystic mass in the right masticator space (eFigure [image T] in the Supplement). The most common findings among the 431 category 3 studies for which routine referral was recommended included periventricular nodular heterotopia (110 cases; 0.9% prevalence), white matter abnormalities (58 cases; 0.5% prevalence), and arachnoid or intraventricular cysts large enough to cause mass effect or potentially cause hydrocephalus (28 cases; 0.2% prevalence). Seventeen participants had more than 1 IF that warranted nonurgent follow-up. A complete list of the category 3 findings is provided in **Table 3**.

Overall Prevalence of IFs

Some IFs could be assigned to more than 1 study category, depending on the severity of the finding. For example, a small pineal cyst would be considered a category 2 finding, whereas a large pineal cyst with the potential to cause hydrocephalus would be considered a category 3 finding. When IFs were evaluated without regard to recommendations for clinical follow-up (ie, across all study categories), we were able to assess the overall prevalence of various common structural findings within this large, demographically diverse, pediatric population (**Table 4**). The most common IFs comprised pineal cyst (910 [7.8%] participants); a cystic lesion in the midline posterior fossa (225 [1.9%]), which might represent an arachnoid cyst or mega cisterna magna; and developmental venous anomalies (220 [1.9%]). Other IFs were cavum septum pellucidum (139 [1.2%]); periventricular nodular heterotopia (110 [0.9%]), a malformation of cortical development commonly associated with epilepsy; tonsillar ectopia (48 [0.4%]); Chiari I malformation (23, [0.2%]); and findings concerning for low-grade glioma (34 [0.3%]).

The demographic information presented in Table 1 suggests that, in general, sociodemographic characteristics of participants in the baseline ABCD cohort did not differ systematically with respect to the IF category assigned to participants'

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baseline imaging. The exception was a significantly higher rate of category 2 studies in boys (1107 [55.0%]; $P = .04$) and a significantly lower rate of category 1 studies in participants of White race (5791 [63.8%]; $P = .03$]), although only the former finding persisted when numbers were adjusted based on the ACS weights. To control for any nonindependence introduced by family relationship, the *P* values displayed result from randomly subsampling the data to include 1 member of each family.

Interrater Reliability

The 2 primary reviewers for this study demonstrated a Cohen κ value of 0.76, polychoric correlation of 0.91, and Stuart-Maxwell test *P* value of .26 for classifying a subset of MRI scans into categories 1 to 4. When analyzed based on recommendations for referral, thus combining categories 1 and 2 (the nonreferral categories) and categories 3 and 4 (the referral categories), the Cohen κ value was 0.82, polychoric correlation was 0.96, and McNemar test *P* value was .24. There were 3 families of 2 siblings each in these IRR analyses. To control for any potential bias introduced by relatedness, we repeated the recommendation-for-referral agreement analyses 8 times, each time retaining 1 member of each family. These results are presented in eTable 2 in the Supplement and show ranges of IRR statistics and *P* values similar to those in the original results: Cohen κ, 0.812 to 0.833; polychoric correlation, 0.960 to 0.969; and Stuart-Maxwell test *P* values .09 to .23.

Cohen κ provides a more stringent test than simple percentage agreement by accounting for the level of agreement between raters that might be expected by chance; values of 0.8 or above are considered to reflect strong agreement.[29] The Stuart-Maxwell and McNemar tests of marginal homogeneity for the polytomous and dichotomous groupings provide general assessments of whether the raters differed significantly in their rates of categorizations; in each case, the nonsignificant differences suggest that neither rater was more conservative or liberal in their diagnostic classifications.

Discussion

To our knowledge, the ABCD study is the largest prospective observational cohort study of brain development and child-adolescent health in the US and provides an opportunity to evaluate structural heterogeneity and prevalence of IFs on brain MRI in a demographically diverse cross-section of US adolescents, 3-fold larger than the largest reported imaging cohort.[10] Moreover, as designed, the study is positioned to explore the neurodevelopmental significance of these findings, including their potential genetic and environmental associations.

This analysis was based on structural brain MRIs from 11 679 children aged 9 to 10 years enrolled in the ABCD study, imaged with standardized state-of-the-art protocols, and reviewed by board-certified neuroradiologists using a categorical classification system with high IRR.[29] We found a 21.1% overall rate of IFs. In 17.2% of the participants, no referral was recommended on the basis of the IF review; in 3.7%, routine clinical referral was recommended; and in 0.2%, immediate clinical referral was recommended. Previous studies investigating the prevalence of IFs on brain MRI in the pediatric population (**Table 5**) reported widely variable rates, reflecting underlying heterogeneity in sample sizes, population characteristics, imaging protocols and MRI field strengths, and criteria for identifying and classifying findings. Our overall rate of IFs is similar to some of these studies,[10,15-18] but higher than in some studies in similar populations.[1,11,13,14] A recent meta-analysis[1] of IFs on brain MRI in neuroimaging studies of healthy children published between 1985 and 2018 suggested an overall IF rate of approximately 16% and a rate of IFs requiring follow-up of 2.6%. Again, these rates are somewhat lower than our respective corresponding rates of 21.1% and 3.9%. Our higher rates likely reflect the high-resolution volumetric 3-T imaging used in the ABCD study that provides increased sensitivity for detecting IFs compared with the 2-dimensional and/or lower field strength imaging used in many older studies.

The rates of specific IFs in our study were in general agreement with those reported by previous studies. We found pineal cysts in 7.8% of participants, which is higher than the 2.43% reported by Gur et al,[11] but lower than the 16.7% reported by Jansen et al.[10] We found an enlarged posterior fossa cerebrospinal fluid space, which could be compatible with mega cisterna magna or a posterior fossa arachnoid cyst (a largely subjective distinction), in 1.9% of participants, which is slightly lower than the 2.62% rate reported by Jansen et al.[10]

Table 4. Prevalence of Common Incidental Findings in 11 679 Participants, Regardless of Categorization

Incidental finding	No. (%)
Pineal cyst	910 (7.8)
Posterior fossa arachnoid cyst vs mega cisternal magna	225 (1.9)
Developmental venous anomaly	220 (1.9)
Nonspecific white matter lesions concerning for sequela of infection, inflammation, ischemia, dysmyelination, or demyelination	188 (1.6)
Mastoid effusions	141 (1.2)
Cavum septum pellucidum	139 (1.2)
Arachnoid cyst	128 (1.1)
Periventricular nodular heterotopia	110 (0.9)
Tonsillar ectopia	48 (0.4)
Choroidal fissure cysts	41 (0.4)
Cavum vellum interpositum cysts	34 (0.3)
Ventriculomegaly	34 (0.3)
Possible glial neoplasm	34 (0.3)
Parotid lymphoepithelial cysts	27 (0.2)
Chiari I malformation	23 (0.2)
Dilated central canal	14 (0.1)
Hydrocephalus	8 (0.07)
Focal cortical dysplasia	7 (0.06)
Cavernous malformation	6 (0.05)
Hypogenesis of the corpus callosum	4 (0.03)
Encephalocele	4 (0.03)
Syrinx	3 (0.03)
Agenesis of the corpus callosum	2 (0.02)
Polymicrogyria	2 (0.02)

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Table 5. Studies on Incidental Findings on Brain MRI in Pediatric Populations

Study	Pediatric population	No. of participants	Incidental finding rate (rate requiring follow-up)	MR images rereviewed for IFs instead of reports	3-T MRI	High resolution
Jansen et al,[10] 2017	Yes	3966	25.6 (0.43)	Yes	Yes	Unknown
Gur et al,[11] 2013	Yes, "generally good health"	1400	10.57 (0.85)[a]	Yes	Yes	Yes
Sullivan et al,[13] 2017	Yes	833	11.8 (0.5)	Yes	Yes	Yes
Seki et al,[14] 2010	Yes	110	10.9 (2.7)[a]	Yes	No	Unknown
Kim et al,[15] 2002	Yes	225	21 (8)[b]	Yes	Variable	Variable
Hartwigsen et al,[16] 2010	Yes	206	19 (10.2)	Yes	Yes	Yes, T1
Kaiser et al,[17] 2015	Yes	114	23.2 (12.5)[b]	Yes	Yes	Yes
Potchen et al,[18] 2013	Yes	96	21 (NR)[a]	Yes	No	No
Gupta et al,[21] 2008	No (all pediatric, but some with medical illness)	666	25.7 (8.7)[b]	No	No	Unknown
Yilmaz et al,[19] 2014	No (all pediatric, but all have chronic headache)	449	8.9 (NR)	No	No	No
Bayram et al,[20] 2013	No (all pediatric, but all have chronic headache)	527	22.1 (NR)	Yes	No	No
Graf et al,[12] 2010	No (all pediatric, but all have chronic headache)	400	21.5 (NR)[b]	No	NR	NR

Abbreviations: IFs, incidental findings; MRI, magnetic resonance imaging; NR, not reported.

[a] Excluded sinus disease as a reportable incidental finding.

[b] Included sinus disease as a reportable incidental finding.

Our 1.2% rate of cavum septum pellucidum is similar to the 1.14% reported by Gur et al,[11] but slightly lower than the 1.99% reported by Jansen et al.[10]

We report a 0.9% rate of periventricular nodular heterotopia, a malformation of cortical development commonly associated with epilepsy, the incidence of which is not well established in the general population. Jansen et al[10] reported a lower rate of 0.48%. In addition, 0.3% of our participants had findings suggestive of glial neoplasm. In approximately one-third of these cases, findings were of sufficient concern that immediate referral was recommended; in the remaining two-thirds of the cases, findings were sufficiently nonspecific to recommend routine clinical referral. This rate of possible glial neoplasm is consistent with that reported by cancer registries in populations younger than 20 years.[30]

In our study, we found a 0.2% rate of Chiari I malformation and a 0.4% rate of tonsillar ectopia. We did not use strict measurement cutoffs to differentiate between these 2 conditions; rather, Chiari I malformation was diagnosed when tonsillar ectopia was sufficiently severe to produce a triangular morphology of the cerebellar tonsils with crowding of the foramen magnum, with or without associated syrinx. Across the literature, reported rates of Chiari I malformation range from 0.45%[9] to 0.6%,[10] likely reflecting variability in the definition of this condition and similar to our combined rate of Chiari I malformation and tonsillar ectopia.

One of the unique aspects of the ABCD study is the inclusion of a large number of twins in the study sample (n = 2061), which allowed us to investigate the heritability of IFs. We found that the overall rates of IFs did not differ significantly between twin and singleton gestations, and the likelihood of both members of a twin pair having IFs did not differ significantly between monozygotic and dizygotic twins; however, direct estimation of narrow-sense heritability[31] treating the radiologic categories (or the presence or absence of IFs) as ordinal variables showed evidence of statistically significant heritability. Our study was not sufficiently powered to evaluate the heritability of specific IFs, but we assume that the low overall heritability we observed may be related to specific types of findings. Other genetic analyses, such as genome-wide association studies, of participants with more common findings may ultimately clarify which of the findings we described have a significant genetic component.

At a basic level, our results provide information about the rates of IFs in a large, demographically diverse pediatric population. No cross-sectional sample can be considered representative of the larger population across all dimensions; however, as Table 1 reports, the raw rates of each IF category in our sample are similar to the rates predicted when the ABCD participants are weighted so that their sociodemographic characteristics exactly match those of the ACS of more than 8 million US households.[26] Overall, our findings support earlier smaller studies that suggested a relatively high rate of IFs in the general pediatric population, but suggest that only 4% of the children had findings of potential clinical significance. Specifically, our results suggest that 1 in 25 children have findings on structural brain MRI that warrant clinical referral and 1 in 500 have a finding that warrants urgent clinical referral.

Limitations

This study has limitations. As originally designed, the ABCD study does not have a protocol in place to collect outcomes data on clinical follow-up initiated as a result of these referrals. Collecting such data would be an important addition to the study and would help us understand the clinical importance of the IFs we describe.

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Conclusions

From a clinical perspective, knowing the prevalence of specific IFs can help contextualize the importance of similar findings on clinical imaging. From a research perspective, knowing the overall rate of IFs can help in counseling research participants during the informed consent process. Perhaps more importantly, knowing the value of routine neuroradiologic screening of research brain MRIs can inform ongoing discussions about the appropriateness of making such screening standard practice, particularly in large-scale studies like ABCD. Our experience with the ABCD study suggests that it is feasible to perform neuroradiologic screening using a centralized and standardized system, even at large scale, with report turnaround times of less than 2 weeks. Such standardized screening systems are relatively uncommon in the research community; however, the results of another study of a more heterogeneous, primarily adult, research population[2,28] supports our experience with the ABCD cohort.

In addition, the clinical or neurodevelopmental importance of many of the common nonurgent findings that we documented herein has yet to be determined. For example, the higher rates of category 2 IFs that we observed in boys and lower rates of category 1 IFs in White children suggests that there may be some association between sociodemographic factors and the prevalence of IFs. The rich data set being collected for each ABCD participant, including genetic, sociodemographic, neuroimaging, neurocognitive, and biophysical measures, will allow investigators to explore whether these IFs are associated with more subtle quantitative findings on structural or functional brain imaging, sociodemographic factors, or measures of child health and brain development. The longitudinal nature of the ABCD study will also provide a unique opportunity to both determine the incidence of new findings and evaluate how existing IFs evolve over the 10-year study period.

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but died before it was submitted. A listing of participating sites and a complete listing of the study investigators can be found at https://abcdstudy.org/. The ABCD data repository grows and changes over time. The ABCD data used in this report came from National Institute of Mental Health Data Archive doi:10.15154/1504041; other dois can be found at https://nda.nih.gov/study.html?id=721. Coding for these analyses is available at https://github.com/ABCD-STUDY.

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