**Review**

# Disclosing Incidental Findings in Brain Research: The Rights of Minors in Decision-Making

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MRI is used routinely in research with children to generate new knowledge about brain development. The detection of unexpected brain abnormalities (incidental findings; IFs) in these studies presents unique challenges. While key issues surrounding incidence and significance, duty of care, and burden of disclosure have been addressed substantially for adults, less empirical data and normative analyses exist for minors who participate in minimal risk research. To identify ethical concerns and fill existing gaps, we conducted a comprehensive review of papers that focused explicitly on the discovery of IFs in minors. The discourse in the 21 papers retrieved for this analysis amply covered practical issues such as informed consent and screening, difficulties in ascertaining clinical significance, the economic costs and burden of responsibility on researchers, and risks (physical or psychological). However, we found little discussion about the involvement of minors in decisions about disclosure of IFs in the brain, especially for IFs of low clinical significance. In response, we propose a framework for managing IFs that integrates practical considerations with explicit appreciation of rights along the continuum of maturity. This capacity-adjusted framework emphasizes the importance of involving competent minors and respecting their right to make decisions about disclosure.

**Key Words:** neuroimaging; incidental findings; children; adolescents; neuroethics

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MRI IS COMMONLY used in research with children and adolescents to generate new knowledge about brain development. As the number of these studies increases, so does the detection of unexpected brain abnormalities (incidental findings; IFs). In adult participants, as many as 20–50% are reported to have an IF depending on age; 2–8% of these are significant and require clinical follow-up (1,2). In children, the reported incidence of IFs ranges from 7% to 36% (3–10), but these are largely insignificant. Those that are significant tend to require immediate or urgent follow up (7,11).

Despite the clear likelihood of detecting IFs in children and the potential for intervention, there is an absence of empirical data and normative guidance on managing and disclosing these findings. Unlike the adult IF literature that now amply covers questions about transparency, duty of care, the duty to warn, and burden of disclosure (12), few papers address these issues for the pediatric context and none tackle the difficult challenge of maximizing the autonomy of child participants who may well have adequate competence to express their choice and make decisions about disclosure. Here, we systematically review the literature on IFs in neuroimaging research with children, and draw on the published discourse about decision-making capacities and the rights of children in research to inform a framework for managing IFs in minimal risk neuroimaging research that involves them.

## TERMINOLOGY

We use the terms *child* and *adolescent* or *minor* interchangeably throughout the study to refer to young persons who have not attained legal age for consent to treatments or procedures involved in research, under the applicable law of the jurisdiction in which the research is conducted (13). *Parent* is used to refer to a guardian or surrogate decision-maker legally designated to provide consent for a minor to participate in research.

## METHODS

### *Selection Criteria*

We assembled peer-reviewed primary research papers, review papers, and editorials on incidental findings in children discovered during neuroimaging research. Papers were identified and accessed using a detailed search strategy of Google Scholar, PubMed/Medline, Health Canada, and the library database from the University of British Columbia. We included publications containing the following string of key words: ["pediatric" or "paediatric" or "children"] AND

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Table 1
Ethical Challenges Raised in the Literature, in Order of Frequency*

| Theme | Definition (papers cited) |
|---|---|
| Clinical utility | Ability of brain scans to provide a diagnosis or facilitate medical decision-making about IFs (4,6,8,10,14–23). |
| Identifying and validating IFs | Best practices for detecting and assessing IFs (4,7,8,10,15,16,18,20–22,24–27). |
| Informed consent | Informing parents and children about IFs prior to and during the research study (8,10,14–20,22,24,27,28). |
| Psychological risk | Risks of disclosure of an IF to parent and/or child (e.g. stigma, anxiety) or adverse experiences during the research study (e.g. claustrophobia) (4,8,10,14,16,17,20,22,23,25–28). |
| Disclosure | Best practices informing parents, children, and/or institutional review boards about the discovery of IFs (4,6,8,10,15,16,20,22–25,27). |
| Economic burden | Research costs associated with the managing IFs and medical costs associated with follow-up (4,7,8,10,14,15,17,20,21,24,28). |
| Physical risks | Physical risks resulting from participating in neuroimaging research (e.g. sedation) (8,14,16,17,20,23,25,26,28). |
| Responsibility of investigator | Duty to search for IFs; duty to disclose (4,8,10,15,18,23,24,27). |
| Interpretation of results | Difficulties in interpreting neuroimaging data (e.g. variability of imaging techniques and brain development) (4,8,14,16–18,21,26). |
| Confidentiality | Limitations in confidentiality for the child and potential breaches of privacy associated with research (15–17,23,25,27). |
| Therapeutic misconception | Mistaken belief that study participation confers personal medical benefit (8,10,17,18,20,25). |

*Ethical themes identified in the literature and their definitions.

[("neuroimaging" OR "brain MRI")] AND [("incidental finding") AND ("ethics")], and manually excluded any returns that were spurious or irrelevant. The search was conducted within a 2-week period in October 2011 and repeated again in November 2012 to ensure the most up-to-date analysis.

### *Content Analysis*

All publications were categorized and coded for the following variables and content: year of publication, type of journal, type of ethical concerns addressed by authors, and proposed recommendations. We used NVivo 8 qualitative research software (QSR International Pty Ltd.) to analyze the content of retrieved publications. An initial coding scheme was developed by one of the authors to identify emerging themes from the ethics-related discourse. A second coder then separately coded all of the text. Coding results were compared for reliability. In the four instances of coding discrepancy, the coders discussed the text selection and reached consensus.

## RESULTS

Twenty-one (21) articles with reference to ethical issues involving incidental findings in pediatric neuroimaging research were retrieved. The earliest article retrieved on this topic was written 10 years ago (14). The majority of the articles (n = 19) were published between 2007 and 2011. Ten papers were published in law/ethics journals, 4 in pediatric and general medicine journals, and 3 in neuroscience journals.

### *Ethical Concerns Identified in the Literature*

The distinct types of ethical concerns addressed in the publications were categorized into themes. In total, 11 themes emerged during the coding process (Table 1). In 14 of the papers, the primary ethical concerns focused on the utility of research scans to diagnose and facilitate medical decision-making about IFs (4,6,8,10,14–23) and detection practices for IFs (n = 14) (4,7,8,10,15,16,18,20–22,24–27). Because research scans are not necessarily optimized for diagnosis, some researchers use clinical grade scans when children are patients enrolled in a study.

The remaining concerns revolved around informed consent (n = 13) (8,10,14–20,22,24,27,28), psychological risks associated with scanning procedures and disclosure of IFs (n = 13) (4,8,10,14,16,17,20,22,23,25–28), the disclosure process itself (n = 12) (4,6,8,10,15,16,20,22–25,27), the economic burden of screening for and following up IFs (n = 11) (4,7,8,10,14,15,17,20,21,24,28), physical risks associated with scans (n = 9) (8,14,16,17,20,23,25,26,28), the burden of responsibility for the principal investigator (n = 8) (4,8,10,15,18,23,24,27), uncertainties in the interpretation of results (n = 8) (4,8,14,16–18,21,26), confidentiality (n = 6) (15–17,23,25,27), and therapeutic misconception (n = 6) (8,10,17,18,20,25).

### *Recommendations Identified In The Literature*

Fourteen of the 21 publications provided recommendations to address the ethical concerns outlined above (Table 2). None addressed the issue of a child's right to know.

## DISCUSSION

The ethical discourse on IFs in neuroimaging research involving minors has focused on practical considerations associated with their discovery. These include methods for identifying and validating IFs, difficulties in ascertaining clinical significance, economic cost, and physical or psychological risk. The general

Table 2
Key Recommendations from the Ethics Literature*

| Key recommendations |
|---|
| Research protocols: |
| • Develop a protocol and budget for managing IFs. |
| • Discuss risks and benefits of scanning with institutional review board (IRB) that contains an MRI expert. |
| • Develop a clear strategy to minimize therapeutic misconception. |
| References: (18,21,23,25,27). |
| Consent process: |
| • Clarify the roles of children and parents. |
| • Disclose all known risks, gaps in knowledge of risks, and risk reduction strategies. |
| • Clearly specify how IFs will be handled. |
| • Explain the limitations of MRI research in order to mitigate therapeutic misconception. |
| • Inform that MRI results will not be available for diagnostic purposes. |
| • Discuss neurodevelopmental variance and clinical uncertainty associated with unclear IFs. |
| • Ask for disclosure preferences of parents and participants separately. |
| • Give participants the choice to not be told about IFs, unless they are of a serious nature requiring additional follow-up. |
| • Discuss with older participants the limits of confidentiality prior to initiation of the study. |
| References: (4,7,8,10,14,17,18,22–24,27,28). |
| Scanning: |
| • Establish child-friendly protocols that ensure participants understand the procedure and that fear is minimized. |
| • Rely on established guidelines when sedation is needed (AAP, 1992; ASA, 1996; JCAHO, 2001). |
| • Provide trainees with procedures for reporting IFs. |
| References: (14,21). |
| Validating potential IFs: |
| • Involve neuroradiologists to validate the presence of a suspected IF, when possible. |
| Reference: (10). |
| Disclosure |
| IFs requiring follow-up: |
| • Disclose to both the minor and the parent; parent first in the case of suspected clinically serious IFs. |
| • Discuss with parent best way to disclose information to minor. |
| • Provide referrals for follow-up. |
| References: (10,17,23,27). |
| IFs with low clinical significance: |
| • No disclosure until there is discussion between the researcher and the IRB. |
| • Respect disclosure preferences of parent. |
| • Disclose to both parent and minor if they both agree to receive information about IFs. |
| • Mitigate anxiety or misunderstanding. |
| • Provide referrals for routine follow-up as appropriate. |
| References: (6,10,14,23,27). |
| Collaboration and new directions: |
| • Develop national database of IFs, including incidence data, with free open access for researchers. |
| • Monitor other imaging modalities for IFs. |
| • Develop guidance documents for IFs for funding agencies. |
| References: (21,27). |

*Key recommendations identified in the literature to address ethical concerns related to the discovery of incidental findings in minors.

consensus from the literature is that researchers should anticipate the possibility of IFs in children and develop research protocols to manage them. In keeping with recommendations from both US and Canadian government research sponsors (e.g., NIH and Tri-Council Agencies), families and participants should be informed about IFs with clear clinical significance and an appropriate referral pathway should be provided (29,30). However, guidance on how to disclose IFs with low or uncertain clinical significance is less clear. This is a critical gap given the variability of human brain development and the lack of normative data sets for children (12). The key considerations on who to inform involve questions about the right to know and not know, and whose preference around this right, an adult decision-maker, a minor, or both, should be respected. Below, we address these questions by drawing on the broader ethics literature on the rights of children in research and medical decision-making to inform a framework for disclosing IFs.

Although several authors have discussed child rights within the context of informed consent and decisions to participate in research (8,14,17,20,22,27), few have yet addressed decisions concerning disclosure of unexpected brain anomalies of low actionability. Of the two papers that do address the subject, Wilfond and Carpenter (23) favor disclosing IFs to a parent first and letting the parent decide if and how to tell the child. Wolf et al (27) favor obtaining the disclosure preferences of both the parent and child upfront, disclosing to both when they agree, but respecting parent choice when there is disagreement (i.e. the parent wishes disclosure but the child does not).

Absent from the discussion, however, is guidance regarding the scenario of when a competent minor wishes to know about a nonclinically significant IF and the parent does not. Here, we argue that minors should be included in the disclosure process to the extent of their decision-making capacity. Considerations about autonomy and competence are required to inform ethical guidance that acknowledges their right to be consulted and to participate in matters that affect their health (31).

Over the past 2 decades, a growing global trend in bioethics has come to recognize the developing autonomy and decisional capacity of children through legal and policy frameworks that emphasizes human rights (32). In many countries (e.g., England, Australia, Canada), a minor is able to provide consent for medical treatment without the need for parental permission or knowledge if he or she is judged to be competent (i.e., the Gillick Standard) (33,34). The Gillick standard was originally developed to allow competent minors to make medical decisions concerning their sexual health. Within the context of research, guidelines also now explicitly recognize the emerging autonomy and developing decisional capacity of children through the requirement for assent or dissent to participate in research during the consent process (32). Some bioethicists have argued that the Gillick standard for consent in the medical arena can also be applied within the research context if the research is likely to bring direct benefits to the participants and poses minimal risks to them (35,36). Arguments supporting the use of the Gillick standard for consent in research have centered on addressing issues of children's self-determination and freedom of choice

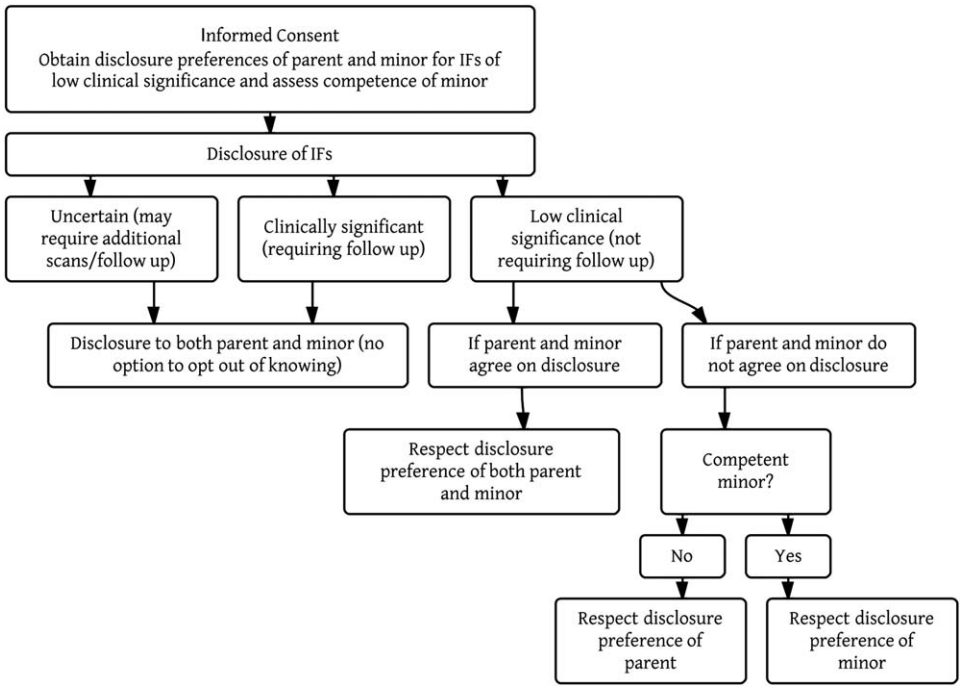


**Figure 1.** Capacity-adjusted framework for decision-making about IFs in neuroimaging research that involves children and adolescents.

effectively (35), as well as on weighing of societal benefit and risk to the individual appropriately (36). Based on these criteria, neuroimaging research, which is generally considered minimal risk and which, however serendipitously may benefit participant health through early detection of an IF, qualifies (37). Empirical research studies have also demonstrated that many adolescents do not differ from adults in their ability to understand therapy or research procedures, consider risks and benefits, and participate in informed decisions (35,38–40); although see (41). Consistent with the empirical data, the ethics discourse on informed consent involving children also recognizes the nonlinear association between a child's chronological age and level of competence (35,42,43). In light of these arguments for expanding the rights of minors in decisions about research and the analyses presented here, we propose that the capacity of child participants be taken into consideration when making decisions about who to inform about potential IFs. We note and respect, however, opposing views (44), as well as the position taken by, the American Academy of Pediatrics that upholds obtaining parental permission first and foremost, and the minor's assent when developmentally appropriate (45).

In applying our recommendation, we suggest that the competence of children be evaluated either through the development of a validated assessment tool or through interview during the informed consent process by a trained researcher. To our knowledge, a standardized tool for children has yet to be developed; the adult competence assessment tools such as the MacCAT-CR can serve as a basis for this effort (46). Meanwhile, institutional protocols and procedures for assessing competence by interview may well vary, and should be optimized to the context and nature of the study at hand. Minors who demonstrate competence should be included along the full trajectory of disclosure and, while effort during the process of consent should be made to attain consensus between minors and parents, minor's preferences should be respected over those of the parent. In the case of young children or youth lacking competence, disclosure preferences should default to those of the parent (Fig. 1).

Mitigating needless anxiety of participants, regardless of age, is a critical concern in any discussion of IFs. Concerns over the psychological impact of knowledge about an incidental brain finding, even those of uncertain or low clinical significance, may be especially salient for children and adolescents as they strive to achieve independence and a sense of self (47–49). A pipeline to a qualified professional able to review research scans, such as a neuroradiologist, radiologist, neurologist, or neurosurgeon, is essential (50). Erring on the side of caution in cases of uncertainty should be the norm. It is essential that nonclinical investigators coordinate with a designated clinician who is affiliated with the research to answer medical questions and provide information for follow-up during the disclosure process.

In conclusion, over the past decade, ethicists and investigators whose research focuses on children have made significant progress in advancing guidance on the management of IFs. Here, we attempt to expand on these efforts to include considerations about the rights of minors in the disclosure process for IFs. We argue that competent minors should be given the right to make decisions about disclosure within the context of minimal risk neuroimaging research studies and, in the case of IFs of expected low clinical significance, their preferences should be the dominant guide to disclosure.

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