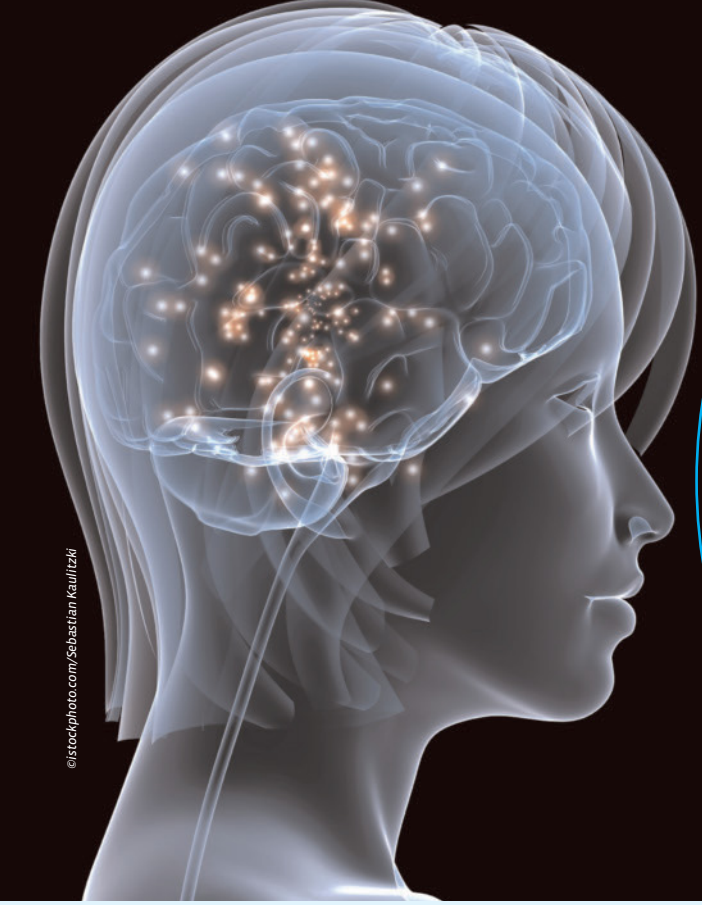

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Expect the Unexpected

Incidental findings create challenges in neuroimaging research

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THE MIND RESEARCH NETWORK (MRN) is an independent, non-profit research institute in New Mexico whose mission is to advance clinical solutions to prevent, diagnose, and treat mental illness and other brain disorders. The success of this organization is based on using multi-modal imaging (MRI, MEG, EEG), genetics, and neuroinformatics to understand disease development and progression.

As an imaging research institute, MRN's local internal review board (IRB) mandated that a neuroradiologist review all readable MR images. Balancing the researcher's needs with a subject's rights in medical research is an ongoing debate. Published literature shows that approximately 40 percent of brain scans identify incidental findings, of which 2 percent to 8 percent are clinically significant and could prompt life-saving interventions if identified early and treated properly.[1,5,6]

In these instances, what is the obligation of researchers and research organizations to identify and respond to these findings? Should a neuroradiologist interpret all readable scans? If so, do all subjects receive their MRI readings, or is the decision regarding participant notification up to each investigator? Who bears the cost of this obligation? The MRN has created a plan to respond to the myriad ethical, legal, and practical implications of dealing with incidental findings in neuroimaging research.

CATEGORIZING FINDINGS

MRN collaborates with more than 40 local investigators and operates 3 MRI machines: Siemens 3T Trio (12-channel headcoil), Siemens Sonata 1.5T (4-channel CP headcoil or 8-channel headcoil), and a Siemens Avanto 1.5T Mobile MRI System (12-channel headcoil). With more than 117 study protocols, MRI sequences vary across studies and investigators.

To meet the IRB mandate for radiological review, at least one anatomical scan is collected during each scan session. In other studies, T1- or T2-weighted images, diffusion tensor imaging (DTI), spectroscopy, and other sequences are run for research purposes, but they are also available for radiological review. In all cases, scans are designed for research purposes only; most do not include a complete clinical scanning protocol.

Prior to enrolling in an imaging study, participants are told a radiologist will review their scans and they will receive a copy of the results. Using customized software, MRN developed a secure, centralized, radiological review process that sends an electronic MRI scan report to the investigator and prepares a hard copy to mail to participants. In most studies the neuroradiologist is not made aware of study enrollment criteria or participant status, therefore some findings are not truly "incidental" (such as multiple sclerosis or traumatic brain injury studies), yet these findings are included in calculations.

The following 5-point Likert scale classifies any incidental findings.[3]

1. normal; no findings

2. no referral necessary; normal findings common in asymptomatic subjects, such as small pineal cyst

3. routine referral; findings not requiring immediate or urgent medical evaluation, but should be reported to the referring physician, such as enlarged ventricles

4. urgent referral required within weeks for any abnormality that will need further yet non-emergent evaluation, such as arteriovenous malformation or mass lesion (meningioma)

5. immediate referral required, as in the case of a large aneurysm or subdural hematoma with mass effect.

NOTIFYING PARTICIPANTS

In addition to the mailed review letters, any findings a neuroradiologist determines needs an urgent or immediate referral – those with a rating of 4 or 5 – are brought to the attention of the facility's medical director, who contacts the participant to explain the results.

To date, we have reviewed approximately 6,000 scans with an overall incidental finding rate of approximately 36 percent. Of the 2,422 reviews with incidental findings 23 percent required no referral, 13 percent were a routine referral, and 0.5 percent required urgent or immediate referral. In the past year, the medical director has contacted approximately 50 subjects regarding clinically significant abnormalities.

In addition to the mailed notification of abnormalities, our system allows subjects and physicians to request copies of scans and reports from prior study participation. This feature is beneficial when a brain abnormality is later discovered, such as recent inquiries involving multiple sclerosis and dementia diagnoses, and a baseline scan is needed to determine disease progression.

Still, our system isn't perfect, and identifying incidental findings on research scans is different than interpreting clinical scans.

A HIGHER RESOLUTION

Many neuroradiologists have been trained to use lower field strength MRIs of 1.5T or lower. Like getting eyeglasses for the first time, things look much clearer using high-definition monitors at 3T. But are we seeing more than necessary? Over twice as many incidental findings are seen using higher resolution equipment.[2]

Not surprisingly, our neuroradiologists require an acclimation period to adjust to scan quality differences. Other challenges also exist, such as a limited number of sequences for interpretation – generally just a high resolution T1 sequence – and there is no clinical information for most cases.

This is a much different experience for radiologists who are used to knowing a diagnosis or clinical symptoms. The information helps focus attention when looking at the scan.

These instances challenge radiologists and research institutes must decide how to handle nonspecific or questionable findings. Without obvious clinical symptoms driving the exam, should these "incidentalomas" be reported as "findings of doubtful clinical significance" or followed up with a repeat MRI?

If one chooses the follow-up option, are you subjecting participants to MRIs for things that may not be clinically relevant?

Another major hurdle is the participant notification system. Radiologists are trained to write complete and detailed reports that are sent to referring physicians for interpretation prior to patient notification. Patients are not given a copy of the report.

A UNIQUE METHOD

At our institute, we take a different approach. All participants are sent a copy of their findings directly, unless they specifically decline. In addition, for urgent or immediate referral cases, our medical director contacts the research participant and investigator immediately, and helps arrange follow-up care.

A problem arises when findings are not urgent, but a referral is still needed. On occasion the participant may be confused after reading the review letter, although a letter is included with phone numbers to call for questions. In this case, some argue that the harm to the research subject outweighs the benefit of providing a copy of the results.

However our experience is similar to published literature that says when given the choice, research participants overwhelmingly request a copy of their scan results.[4] At our organization, participants have the right to request not to receive their results, but none have exercised that right.

Current literature recommendations suggest all imaging research institutes should create a plan to deal with incidental findings.

Our plan fulfills the three major ethical principles of the Belmont Report, which provides the foundation for clinical research in the United States.

1. Respect for people. Subjects have a right to know their MRI scan results, regardless of the findings.

2. Beneficence. Individual subjects know what is best for them, which may now or in the future have benefit for the subject.

3. Justice. Subjects have the right to be treated similarly across different studies.

A cost has been associated with MRN's decision to have a neuroradiologist read MRI scans and notify participants and principle investigators of the results. However, by centralizing the process in our organization, we have minimized costs to researchers and ensured that ethical principles are being met, while enhancing community goodwill.

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