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The Therapeutic Misconception: A Threat to Valid Parental Consent for Pediatric Neuroimaging Research

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Abstract

Neuroimaging research has brought major advances to child health and well-being. However, because of the vulnerabilities associated with neurological and developmental conditions, the parental need for hope, and the expectation of parents that new medical advances can benefit their child, pediatric neuroimaging research presents significant challenges to the general problem of consent in the context of research involving children. A particular challenge in this domain is created by the presence of therapeutic misconception on the part of parents and other key research stakeholders. This article reviews the concept of therapeutic misconception and its role in pediatric neuroimaging research. It argues that this misconception can compromise consent given by parents for the involvement of their children in research as healthy controls or as persons with neurological and developmental conditions. The article further contends that therapeutic misconception can undermine the research ethics review process for proposed and ongoing neuroimaging studies. Against this backdrop, the article concludes with recommendations for mitigating the effects of therapeutic misconception in pediatric neuroimaging research.

Keywords: consent, institutional review boards, pediatric neuroimaging, regulation of research, research ethics, therapeutic misconception

Introduction

Neuroimaging research has brought major advances to child health and well-being. It has provided physicians with noninvasive neurodiagnostic tools such as computed tomography (CT) and magnetic resonance imaging (MRI). These tools have largely replaced the more invasive techniques of angiography and myelography, and have entirely supplanted extremely noxious procedures, such as pneumoencephalography, in the diagnosis and evaluation of structural lesions of the nervous system. Children have the potential to benefit even more in the future. Neuroimaging research holds the promise of providing techniques that will help us better understand, diagnose, and treat such conditions as mental illness and inborn errors of metabolism affecting the nervous system. Parents, especially of infants and children with severe neurological and developmental conditions, have great hopes and expectations for this research.

However, pediatric neuroimaging research raises many legal and ethical issues. This is true for research that uses established modalities (e.g., MRI) as well as for studies involving new and emerging technologies such as functional MRI (fMRI), magnetic resonance spectroscopy, and

diffusion tensor imaging. As one scholar comments, “neuroimaging pediatric patients is accompanied by all the ethical dilemmas associated with neuroimaging in adults, magnified exponentially” (Hinton, 2002). Because of the substantial vulnerabilities associated with neurological and developmental conditions, the parental need for hope, the expectation of parents that new medical advances can benefit their child, and the societal enthusiasm for new technology, pediatric neuroimaging research presents serious challenges to the general problem of consent for research involving infants and children. Of particular concern is the potential for parents and other research stakeholders to form the sometimes mistaken belief that study enrollment carries the possibility of significant personal medical benefits for child participants. The misapprehension that therapeutic benefits may accrue to individual research participants has been dubbed “therapeutic misconception” (TM) (Appelbaum et al., 1982).

In this article, we shine the spotlight on how TM can pose ethical and legal difficulties for the conduct of pediatric neuroimaging research. This is warranted in view of the largely myopic focus in the bioethics literature on TM in the context of research respecting therapeutic (vs. diagnostic) interventions. The article begins with a description of the promises and limitations of neuroimaging. Next, overviews of the role of parental consent in research involving children and the concept of TM are set out. Against this backdrop, we explore how TM can arise in pediatric neuroimaging research and why this poses a threat to valid parental consent for this form of research. The article concludes with recommendations for mitigating the effects of TM in pediatric neuroimaging research.

Before proceeding further, some comments are in order regarding the article's scope. Although many legal and ethical norms potentially apply to MRI research in the United States and Canada (the two countries of focus here), we concentrate on Title 45, Part 46 of the Code of Federal Regulations (CFR) and its rough equivalent in Canada, the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS), given the prominent role these instruments play in their respective countries. Given this dual jurisdictional focus, and the fact that the United States uses the label “Institutional Review Board (IRB)” and Canada uses the term “Research Ethics Board (REB)” for the bodies that review human research, the more generic label “Research Ethics Committee (REC)” is used to refer to both IRBs and REBs. Finally, this article only addresses research involving children who lack the mental capacity to legally consent to research participation.

Pediatric Neuroimaging Research

The Promise of Neuroimaging

Neuroimaging is concerned with the depiction of structure and function of the nervous system in health and disease. To accomplish this, clinicians and researchers avail themselves of an array of neuroimaging tools including, among others, MRI, and fMRI. Of all the currently available modalities, however, MRI has the best combination of spatial resolution and tissue contrast. This makes it possible, for example, to distinguish cortex, gray matter nuclei, and white matter from each other and from abnormal tissue with great precision. MRI also has tremendous versatility: in

addition to static anatomy, it is able to depict dynamic physiological processes (e.g., perfusion of tissues with blood) and the biochemical composition of brain tissue.

In the clinical realm, neuroimaging can help to diagnose a wide variety of diseases of the nervous system, including hemorrhages, strokes, tumors, infections, and degenerative conditions. Neuroimaging can help clinicians to determine the extent and stage of a disease and its effect on surrounding normal structures. It also permits monitoring of disease and treatment effects. Sometimes neuroimaging is very helpful in predicting patients' future health outcomes.

In clinical pediatric neuroimaging, the effects of growth and development create a moving frame of reference against which the effects of disease and treatment must be evaluated. Naturally, clinicians are very interested in knowing the spectrum of normal and abnormal appearances of the nervous system at all ages. This allows them to make correct diagnoses, optimal treatment plans, and accurate prognoses on behalf of individual patients. However, beyond merely knowing what normal and abnormal brains look like, clinicians also hope to understand normal physiology and pathophysiology in order to get to the root of their patients' problems.

Neuroimaging research holds the promise of providing ever more clear and detailed windows into the developing brain, and of increasing our understanding of developmental neurophysiology. Neuroimaging research has to contend with the same moving frame of reference as clinical neuroimaging, and has the same need for age-appropriate norms. Neuroscientists must conduct research on children if they wish to understand the developing brain. Thus, neuroscientists are creating neuroimaging atlases that account for brain growth in children and allow for meaningful comparisons between healthy children and age-matched children with neurological and psychiatric illnesses (Wilke et al., 2003). Of particular relevance to MRI is the process of myelination that occurs during infancy and early childhood. Myelination causes progressive magnetic resonance signal changes in the developing brain. The relative signal intensities of gray matter and white matter in infants, compared to adults, are effectively reversed. Magnetic resonance fiber tracking studies are documenting the process of myelination in the developing brain and providing a detailed baseline for imaging studies aimed at understanding dysmyelinating and demyelinating diseases (Ben-Bashat et al., 2005). Finally, children learn because their brains develop. This has implications for fMRI. Indeed, functional studies show developmental changes in the patterns of cortical activation that accompany cognitive development and language acquisition in healthy children (Durstun and Casey, 2006), with plasticity in activation patterns still evident in adulthood (Mahncke et al., 2006).

While neuroimaging research is providing society with valuable information about normal developmental processes, it is also beginning to furnish an understanding of abnormal development of the nervous system. For instance, dysfunction of specific brain regions in children with attention-deficit hyperactivity disorder (ADHD) has been shown repeatedly with fMRI (Bush et al., 2005). As well, abnormal patterns of cortical activation have been associated with dyslexia, with converging evidence pointing to a disruption of certain systems and areas of the left hemisphere, along with compensatory engagement of other brain regions (Shaywitz et al., 2006). There are countless other examples.

Limitations of Neuroimaging

There are many things clinical neuroimaging cannot do as of yet. Specifically, it cannot diagnose mental illness. In fact, it cannot guarantee the health of a normal-appearing brain. It does not provide a measure of intelligence and generally cannot accurately predict a child's neurodevelopmental potential. Although there is great interest in the potential applications of fMRI in neuropsychology and psychiatry, this technology is not ready for deployment. We are still far from understanding the activation patterns and the underlying mental processes elicited by fMRI paradigms. Moreover, the influence of a large number of confounding variables (e.g., age, gender, foods, and drugs on research techniques like fMRI) are still poorly understood or inadequately addressed. Research concerning ADHD is illustrative. Despite exciting preliminary advances, "none of the imaging modalities has been accepted in the peer-reviewed literature as a proven method for reliably distinguishing ADHD subjects from other subjects with psychiatric or neurological comorbidities" (Bush et al., 2005).

There are even greater limitations on the diagnostic utility of research neuroimaging for any given research participant. Occasionally, a research tool like MRI may have unexpected clinical benefit, such as the discovery of an unexpected, serious, treatable condition in a research participant (Mamourian, 2004). However, there are significant limitations to making such discoveries. There are numerous ways to manipulate the MRI scan in order to obtain different kinds of information, and researchers analyze the resultant signals in a highly restricted fashion in order to isolate the specific data of interest. Due to time constraints and the focus on a particular hypothesis, information that would be included in a clinical scan to diagnose diseases is often sacrificed in a research scan. Moreover, the members of the research team who review the scan may lack the necessary training to effectively detect clinical abnormalities.

There are other reasons why a research fMRI scan has limited diagnostic value for an individual participant. Variability in physiological parameters among healthy participants is the rule, rather than the exception in biomedical research. In fact, inter-individual differences in sulcal anatomy are so common that individual participants' scans are often averaged together and warped onto an "ideal" brain (Brett et al., 2004). Therefore, back-extrapolation of a functional pattern derived from a group of participants to an individual is fraught with difficulty.

Keep in mind functional patterns represent a hemodynamic response to neural activity, not the neural activity itself. While the correlation is real and important, the "thinking" is happening beneath the surface on a millisecond scale while the hemodynamic response plods along over a period of several seconds. When a cognitive task elicits a hemodynamic response in a particular part of the brain, it suggests that this part of the brain is involved in, or at least affected by, the task. However, it does not prove that this part of the brain is necessary or sufficient for the task. It may simply be co-activated and functioning in synchrony or may be playing a modulatory role (Rorden and Karnath, 2004).

Most fundamentally, it bears highlighting that researchers gather data from many individuals in order to make valid generalizations about a larger population. They typically attempt to understand a physiological process or a disease, not an individual subject. In the research setting, the

importance of a particular imaging finding or measurement to an individual participant cannot be known as long as this finding or measurement is itself the subject of inquiry. Converging evidence from many studies is needed before one can come to reliable conclusions about the meaning of any such finding or measurement. For all these reasons, fMRI can teach us much about cognitive processes in general, but more work is needed before it can tell us much that is reliable about the cognition of any given individual.

Parental Consent for Research Involving Children

Apart from exceptional circumstances (see 45 CFR 46.116(d); TCPS, Art. 2.1(c)), individuals must not be enrolled in research without valid consent being secured by the researchers. To be valid, consent to participate in research must be free and informed. As well, it must be made by a person possessing the capacity to make this decision, which involves the ability to understand the information presented about the study and to appreciate the consequences of making the decision about whether to participate. Where researchers seek to enroll incompetent children, they must obtain the consent of the children's parents. In order for parental substitute decision-making to have ethical and legal validity, parents' consent must be given voluntarily after they have been properly informed about the research project. This means that they must be given all relevant information concerning the research project, which includes, among other things, a description of reasonably foreseeable harms and benefits that may arise from their child's research participation (45 CFR 46.116(a); TCPS, Art. 2.4(c)). Researchers' obligations extend beyond merely disclosing such information to parents; they must also present the information to parents in a comprehensible manner (45 CFR 46.116; TCPS, Art. 2.4). Thus, researchers must fix their oral and written explanations at comprehension levels appropriate to the particular parents concerned, must be sensitive to parents' emotional/psychological state, must take into account the environment in which the information is presented, and must not rush the consent process (Hadskis, 2007a). For parental consent to be considered voluntary, it must be given by a parent who has not been unduly influenced or coerced (45 CFR 46.116; TCPS, Art. 2.2).

Securing parents' free and informed consent is a necessary, but insufficient condition for the inclusion of incompetent children in research. Research that would present greater than minimal risk to child participants without direct benefit for the individual participants can only be approved by an REC in the United States in very limited situations (45 CFR 46.406 and 46.407) and, in Canada, it cannot take place under any circumstances (TCPS, Art. 2.5). These regulatory requirements represent an attempt to balance the vulnerabilities associated with inclusion of incompetent children in research against the injustices arising from their wholesale exclusion from the potential benefits of research participation.

The Therapeutic Misconception Generally

TM was first described by Paul Appelbaum and colleagues (Appelbaum et al., 1982) when exploring the problem of informed consent in psychiatric research. They found that many study participants did not understand the difference between participating in a research study and receiving clinical care. Moreover, participants believed that both research and treatment were governed by the same goal (i.e., the best interests of the individual patient-participant). The differences between the

organizing principles of research with its rigid, protocolized nature aimed at producing generalizable data and those of clinical care, focused on the best interest of the individual and continually adapted to the needs and responses of the patient, were not appreciated. In addition, the unknown risks and benefits inherent in research, as compared to standard care where risks and benefits have been established, were not well understood.

The same sorts of misconceptions have been found to exist outside the psychiatric research context. In a recent systematic analysis of the prevalence of TM, Appelbaum and colleagues interviewed 225 research participants in 44 clinical trials across a wide range of medical conditions (Appelbaum et al., 2004). They found that 62 percent of participants demonstrated TM. Others have found that TM can also present problems in the more narrow realm of pediatric research, where the misconception can influence some parents' decisions regarding research participation by their children in clinical trials generally (Stevens and Pletsch, 2002), Phase I oncology trials (Ackerman, 1995), leukemia trials (Kodish et al. 2004), autism studies (Vitiello et al., 2005), and genetic disease research (Henderson et al., 2006).

TM is deeply problematic since it is inconsistent with informed consent requirements and can be viewed as a form of “informational manipulation” that is disrespectful of patient autonomy (Fried, 2001). Indeed, as far back as the 1980s, TM was identified as one of the “two urgent problems in research ethics” (Vanderpool and Weiss, 1987). Given the seriousness of the matter, efforts have been made to elucidate the factors that foster TM (Miller and Joffe, 2006). Outlined below are some of the factors that have been identified.

Participant Factors

Studies have demonstrated TM's connection to the psychology of illness. Potential research participants, especially those with illnesses, need to believe that researchers are concerned with their well-being and that this concern has motivated the offer of research participation (Lidz and Appelbaum, 2002). Many patients believe that access to research means access to new and better treatment. The power and persistence of TM, even when careful attempts were made to explain the differences between research and clinical care, have been attributed to a “unique combination of emotion and reason in individual decision making” (Glannon, 2006). Other psychological phenomena have been acknowledged, including the learned expectancies of patients and coping mechanisms in illness (Appelbaum et al., 2004). Moreover, early empirical research has found that some persons are at greater risk for TM including the elderly, those with lower education, poorer health, and greater optimism regarding their future health, as well as those facing life-threatening conditions (Appelbaum et al., 2004).

The Participant-Researcher Nexus

TM does not simply derive from participant characteristics. Other elements in the research system do a great deal to feed TM. These systemic elements include psychological factors related to the researchers themselves, methods of recruitment, the consent process (including consent forms), and the conflation of the caregiver-researcher roles (Dresser, 2002).

Researchers are generally enthusiastic about research. They do research precisely because they believe it advances medical knowledge and care. This optimism regarding positive research results can shape what is said and how it is said, and can ultimately reinforce the notion of benefit for prospective participants. Moreover, the practical issue of recruiting a sufficient number of participants for statistically-valid studies can color the conversation regarding potential benefit from participation.

TM can also be promoted by factors related to the recruitment and consent processes. Recruitment posters and other recruitment tools and activities convey enthusiasm for research and its benefits. In fact, clinical trials have been described as the source of “recruiting doublespeak” (Hochhauser, 2002). Often, with complex, serious, and life-threatening disease, participation requests are initiated by clinicians whose usual relationship with participants is that of caregiver. The place of consent for medical research is frequently a medical site and the consent is sometimes requested by people wearing white coats or operating room scrubs. Some have also observed that the language of care and benefit appears frequently in discussions about research participation (Weinfurt et al., 2003). Research has demonstrated that the “voices” of caring and research can be misconstrued (Bamberg and Budwig, 1992), which can be a particular problem when the person requesting research participation is also a caregiver (Steinke, 2004). This situation pertains especially with research requiring highly specialized medical knowledge and skill such as in tertiary care centers. With concentrated expertise, the researchers are highly likely to also be the clinicians. These features make it easy to confuse research and clinical care.

Just as the oral aspects of the consent process can foster TM, so too can the forms. Studies looking in depth at the language of consent forms have found “vagueness, inconsistency and overstatement” (King et al., 2005). Others have concluded that the forms often contain language that promotes or does little to deter the TM (Kimmelman and Levenstadt, 2005).

Research Policy

As research ethics has developed, it has identified concerns for the fair distribution of the risks and benefits of human research. Recent research policies have compelled the inclusion of women and other vulnerable groups. Unfortunately, these inclusion policies have sometimes been taken to mean that research necessarily has benefits and prospective participants should not be denied these benefits. Though we acknowledge that, in some instances, individual participants may reap personal medical benefits through their participation in clinical research, it is also true that some research offers no or little chance of obtaining such benefits.

Societal Factors

Contemporary Western society can have a distorted belief in the power of medical research. Public discourse and the media portrayal create a social context for misunderstanding research (Belkin, 2006). Research is marketed to the public so that the public will financially support researchers and research institutions which rely on public funding for their research activities. Whatever is new is often understood to be better. Thus, the research intervention or treatment may be unwisely assumed to be better than the standard care. We do not want to be misunderstood as implying that

the growing emphasis on evidence-based medicine, with its reliance on the scientific method to test the safety and efficacy of existing and future diagnostic/therapeutic strategies, is not a positive cultural shift. However, as this trend unfolds society must remain alert to potential misconceptions about research that can shape how potential research participants interpret and comprehend descriptions of research projects, including their risks and benefits.

Therapeutic Misconception in Pediatric Neuroimaging Research

We have real concerns that TM also resides in pediatric neuroimaging research. The fact that this emerging area of science is well-publicized, together with the existence of a vulnerable and often marginalized population that could benefit enormously from new neuroimaging technologies (e.g., children with profound developmental disability, degenerative neurological conditions, and serious psychiatric disorders), very much situates parents to be influenced by TM when deciding whether to involve their children in neuroimaging research. It bears emphasizing here that we are not claiming it is always wrong-headed for parents to believe that this research will benefit their children. What we are saying is that some of this research possesses possible downstream benefits for other children but scant, if any, potential for direct medical benefits for individual research participants.

If incomplete or distorted information on the matter of personal medical benefits for participants is received by parents, the validity of parental authorization can be brought into question. When discharging their duty to determine whether it is in their child's best interest to participate in research, parents must balance the risks and benefits to their child that are associated with a given study. If parents are laboring under a misapprehension about the existence of a potential benefit or possess an inflated estimate of the possibility that a benefit will materialize for their child, their ability to weigh the risks and benefits will be impaired, thus frustrating attempts to make decisions that are in the best interest of their child.

Parents may not have accurate information about the potential benefits and harms of neuroimaging research for a number of reasons. First, they may be influenced by Contemporary Western society's belief in the power of technology and the phenomenon of believing that whatever is new is better.

Second, marketing efforts may be contributing to the problem. Society has recently witnessed significant marketing of neuroimaging research in relation to social problems such as lying, criminal investigations, and the detection of moral 'deviance', as well as the promotion of certain child care practices (Racine et al., 2005, 2006).

Third, in some cases, the media may simply be reflecting distorted social beliefs and conveying a misleading picture of the potential benefits of research in general and pediatric neuroimaging research in particular. For example, MRI and fMRI in adolescents, school-aged children, and infants have generated immense public media hype in recent years. There has been a tendency by the media to present the findings of fMRI in an uncritical and sensationalist fashion, creating the impression that neuroimaging now offers the definitive view into the human mind. A review of media portrayals of neuroimaging has dramatically demonstrated how much positive 'spin' is put on new and emerging technologies such as neuroimaging (Racine et al., 2005).

Fourth, parents may receive misinformation from advocacy groups that present overly optimistic views of research benefits (Racine et al., 2005, 2006).

Fifth, researchers may also be playing a role in parents' misapprehension of information. The scientific community has been accused of overstating the explicative power of fMRI (Racine and Illes, 2006). Researchers may also unwittingly misinform parents by virtue of having internalized an overly confident view of the insight that is currently provided by neuroimaging. After all, researchers are embedded in a society that believes in the benefits of research and have also been trained in a professional culture that is rooted in these benefits. Their belief in and optimism about the value of research in general and the specific projects in which they engage can shape what is said and how it is communicated which in turn can mislead parents.

Information imparted by researchers to parents during the consent process may actively foster or at least not minimize potentially inflated diagnostic expectations. For example, some parents may believe that their child's participation in any fMRI experiment will necessarily reveal a clinically-significant medical condition if it exists, such as a tumor. However, as alluded to above, the likelihood of such discoveries may be low in a given study, particularly where a diagnostic scan is not being carried out and/or the researcher who reviews the scan is not trained to detect clinical conditions. Even if these limitations are expressly disclosed in a consent form, TM may still be promoted by environmental cues. For instance, MRI scanners are almost invariably located in hospitals and those persons charged with disclosing information about the study typically possess all the trappings of caregivers (e.g., white coats and badges indicating or suggesting that they are health care professionals).

Sixth, parental susceptibility to TM may also be a function of their particular circumstances. The need for relief from the burden of care for their child and/or their profound desire for the child to be helped could also make them prone to TM. Parents of children with severe neurological or developmental conditions can become quite desperate (particularly in light of the failure of society to provide appropriate support for them and their children), and both desperation and hope may cause them to exaggerate the potential for benefits and deemphasize neuroimaging research risks.

Recognizing and Mitigating the Therapeutic Misconception: A Role for Research Committees

The principal mandate of an REC is to protect the rights, safety, and welfare of individuals who participate in research projects conducted under the auspices of the institution with which the REC is affiliated. Since the presence of TM on the part of research participants can run afoul of the "respect-for-persons principle and the requirement of informed consent" and thus lead to participants being "wronged and harmed" (Dresser, 2002), it seems indisputable that the effective management of TM falls squarely within an REC's bailiwick.

While we accept that RECs can greatly assist with the TM issue, it bears emphasizing that REC members can themselves labor under such misconceptions when reviewing MRI research. The potential for TM to compromise the REC review process is indeed unsettling given the REC's lofty charge of protecting participants. This potential exists because of the nature of the information on which RECs base their decisions and because of the composition of these boards. RECs render their

decisions after deliberating on the information that has been put before them, which typically consists solely of documentation submitted to the board by the very persons who are proposing the research. This material sets out the researcher's opinion regarding the study's attendant risks and benefits for participants, and the researcher's express or implied opinion on why the benefits of the research would outweigh any harm that might be occasioned. If it is unreasonable to expect researchers to be able to shroud themselves in impartiality when communicating the benefits and harms of MRI research to parents, perhaps less still can this be expected when they are communicating such matters to the very body that will decide whether the research will proceed as proposed or at all (Hadskis, 2007b). If the only information before an REC regarding an MRI study is tainted by TM, there is a real danger that the REC's review of the project will be substantially compromised.

The backgrounds of the persons who typically sit on RECs are unlikely to meaningfully mitigate this danger. Included in their memberships are persons with scientific expertise as well as individuals who are not engaged in scientific research (45 CFR 46.107; TCPS, Art. 1.3). Notwithstanding the variety of backgrounds represented on RECs, these boards are commonly dominated by scientific members who, as argued above, may be predisposed to TM due to their strong beliefs about the benefits of biomedical research generally. Other REC members may not effectively function as a counterbalance because, as one scholar has noted, "non-research members of [RECs] are dependent on their research members for information about current research practices and the likely effect of the particular experimental interventions proposed" (McNeill, 1993). Consequently, these members tend to defer to the scientific members on matters such as the specific risks and benefits that attend research. This is not to say that scientific members will not provide valuable information about MRI research risks and benefits; we merely contend that this information may be coloured by their deep commitment to research. Of course, in view of the highly specialized nature of MRI research, if none of the scientific members hold expertise in such research, the ability to elucidate helpful information on attendant risks and benefits may be significantly restricted.

Despite their susceptibility to TM, RECs can still play a central role in diminishing the likelihood that such misconceptions will impair the validity of consent for MRI research. However, their ability to do so would be greatly enhanced by implementing a number of strategies. First, RECs can adopt policies and procedures that will increase the chance that complete and accurate information concerning the benefits and risks of MRI research is considered by the REC before they render their decisions. Toward this end, researchers should not only be instructed by RECs to provide probability estimates for any potential benefits that are being claimed, but also to furnish credible support for such estimates. In terms of the identification of MRI research risks, this can be facilitated by requiring researchers to clearly respond to REC prompts regarding risks that can attend MRI research participation. Moreover, REC chairs should ensure that, at a minimum, an ad hoc REC member with expertise in MRI research is present when MRI studies are reviewed. In the event that the REC frequently reviews such research, a member with appropriate expertise should be included within the REC's regular membership.

Second, RECs need to inform themselves about TM, including the subtle ways that it can operate in a given study and how its impact can be minimized. There are many ways for RECs to become

educated. For instance, REC administrators should stay abreast of articles and other resources dealing with the general topic of TM and disseminate this material to REC members. To learn more about its impact in the specific context of pediatric MRI research, RECs should employ the seldom-used consultation mechanisms (Coleman, 2003) contained in the regulatory instruments (45 CFR 46.107(f); TCPS, Art. 1.3) to, at least on occasion, invite parents of children who have previously participated in MRI research to speak to the REC. These parents could address such matters as their motivations for authorizing their child's participation, their understanding of what benefits and risks attended the research, and their appreciation of any limitations concerning the potential for their child to benefit from the study.

Third, RECs should specifically instruct researchers to detail in their REC submissions, perhaps in a separate section, all of the measures that they will take throughout the informed consent process (i.e., from recruitment efforts to consent form completion and beyond) to obviate the development of TM on the part of parents. RECs should also devote sufficient time at their review meetings to carefully evaluate whether the measures suggested by the researcher are appropriate and sufficiently comprehensive. The review should not be limited to identifying problematic language that is buried in consent forms. As others have suggested, researchers should be expected to ensure that discussions about the study with prospective participants (and, where relevant, their substitute decision-makers) are conducted by persons who are not involved in the prospective participants' clinical care and that other steps should be taken to give them "stark, bold, and dramatic signs that research is different from clinical care" (Dresser, 2002).

Conclusion

TM has largely only been identified as a concern for clinical trials research. However, there is a pressing need for the concept to be included in discussion and debate on the rapidly expanding area of diagnostic research. Most crucially, this dialogue must encompass the specific context of parental consent for pediatric neuroimaging research. While there is an imperative to conduct pediatric neuroimaging studies in order to benefit children, a concomitant duty exists to protect children from exploitation, particularly those with serious disorders such as neurological or developmental conditions. TM can only be effectively ameliorated by enhanced awareness that parents, researchers, RECs, the media, and the general public can labor under this misconception, and by developing strategies aimed at ensuring that all research stakeholders are furnished with full and clear communication about the potential harms and benefits of participation in pediatric neuroimaging research.

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Notes

Title 45, *Code of Federal Regulations*, Part 46, Subpart A ("Common Rule").

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