

For Researchers: Neuroscience and Consent Capacity

In March 2015, the Presidential Commission for the Study of Bioethical Issues (Bioethics Commission) released its report, [*Gray Matters: Topics at the Intersection of Neuroscience, Ethics, and Society*](#) (*Gray Matters*, Vol. 2). By exploring three controversial topics in neuroscience and ethics, including capacity and the consent process, the Bioethics Commission sought to clarify for the public the scientific landscape, identify common ground for productive discourse, and recommend an ethical path forward to support neuroscience's progress. Although potential participants in a broad scope of research can have impaired consent capacity, challenges surrounding consent capacity are especially pronounced in neuroscience research. Neuroscience research often seeks to understand and ameliorate the very disorders and conditions that can be associated with impaired consent capacity. It also can help us better understand the nature of capacity itself.

This primer was designed to help researchers, especially those who conduct neuroscience research, understand and implement the Bioethics Commission's recommendations about responsibly including individuals with potentially impaired consent capacity in research. Researchers can use it to aid ethical decision making and ensure that they have considered and implemented appropriate ethical safeguards. Please see Chapter 3 of *Gray Matters*, Vol. 2, for further reading on the Bioethics Commission's analysis of this topic.

Contemporary neuroscience offers the potential to better understand devastating disorders, or even to ameliorate and prevent them. However, to realize this promise, affected individuals need to be included in related research. Research teams **should responsibly include participants with impaired consent capacity in neuroscience research**, with ethical safeguards in place. Responsible inclusion is crucial to advance research that seeks to alleviate the very disorders that can affect consent capacity (e.g., traumatic brain injury, Alzheimer disease, stroke, schizophrenia, and major depression). Some potential safeguards to help protect participants include:

- using the best available capacity assessment protocols and remaining flexible in modifying consent processes through strategies such as corrective feedback and multimedia techniques;
- respecting preferences expressed by individuals with impaired consent capacity, including assent and dissent;
- using independent monitors to oversee enrollment and consent processes and to help prevent coercion;
- limiting the acceptable level of research risk to which participants with impaired consent capacity can be exposed;

- helping identify legally authorized representatives (LARs) and providing them guidance regarding how to make research decisions on behalf of another individual;
- honoring research advance directives when they are in place and encouraging use of these directives when researchers expect that participants might lose capacity during the course of a study; and
- engaging in thoughtful stakeholder and community engagement to improve understanding of affected communities and alleviate stigma.

Researchers can find further guidance regarding these elements throughout the following sections.

FREQUENTLY ASKED QUESTIONS

1. Should research include participants with impaired consent capacity?

Yes, researchers should responsibly include individuals with impaired consent capacity who stand to benefit from neuroscience research. Participation, with ethical safeguards in place, can ensure progress aimed at understanding and ameliorating neurological disorders and psychiatric conditions.

Neuroscience research can potentially improve prevention, diagnosis, and treatment of disorders that can lead to cognitive impairment. Failing to pursue neuroscience research on certain disorders because potential participants might have impaired consent capacity can do a disservice to current and future patients. To realize the potential of this research, affected individuals, including those who might have impaired, fluctuating, or diminishing consent capacity, need to be included in ethical research with adequate protections in place. Responsible inclusion entails compliance with existing regulations and use of appropriate additional safeguards, which can vary, depending on the nature of the research and the population being studied.

2. Why is research involving participants with impaired consent capacity ethically challenging?

The informed consent process is a primary tool used to prevent and mitigate exploitation in human subjects research. Informed consent helps participants understand what risks and benefits are associated with a particular protocol and make autonomous decisions about whether enrollment is right for them. To give informed consent, however, a person must have the capacity to do so. The underlying abilities that constitute consent capacity include an ability to understand information, appreciate its significance, and use the information to reason and make and express a choice. If a participant has impaired consent capacity and is unable to make such fully informed, autonomous decisions, they might be more vulnerable to exploitation by researchers.

When informed consent is not possible, additional protections can be implemented to prevent exploitation. However, if too many barriers to participation are erected, it can become prohibitively difficult to enroll participants with impaired consent capacity in research. Reconciling the tension between using additional protections to prevent exploitation, while still allowing human subjects research to proceed with all relevant populations, is a perennial challenge in research ethics.

For example, in the neuroscience context, a wide diversity of disorders and injuries can affect an individual's consent capacity, including head trauma, stroke, dementia, neurological cancers, and metabolic disorders, among others. Individuals with psychiatric conditions, including schizophrenia or major depression, and those who use psychoactive medications or addictive substances also might have impaired consent capacity. To make progress in understanding and alleviating the disorders that affect consent capacity, we need to include affected individuals in neuroscience research. But the very individuals who are needed for participation often cannot provide informed consent. Additional safeguards are needed to ensure that they are adequately protected.

3. What are the central ethical considerations related to research involving participants with impaired consent capacity?

Several ethical considerations are relevant when considering enrolling participants with impaired consent capacity in research. Three of these considerations are outlined as follows:

- **Ensuring Access to Research Benefits through Inclusion:** Justice and fairness requires that the benefits of research be distributed equitably across society. To address the conditions that can impair consent capacity, researchers should strive to include individuals with impaired consent capacity ethically in research that might benefit them, with appropriate protections in place. Inclusion of these individuals facilitates access to the benefits of the research. In addition, inclusion demonstrates respect for persons, because individuals with impaired consent capacity still possess desires, values, and certain forms of agency, which can be expressed through measures like assent and dissent, research advance directives, and LARs.
- **Protecting all Research Participants:** Steps should be taken to protect participants with impaired consent capacity from exploitation and undue risk. Some examples of additional protections include limiting the allowable level of risk for studies that enroll such participants or employing independent monitors who oversee consent processes and prevent coercion on the part of researchers or research staff.
- **Avoiding and Alleviating Stigma:** Ethical neuroscience can help mitigate stigma by facilitating a deeper understanding of the neurological disorders and psychiatric conditions that can impair consent capacity. Making assumptions about potential participants' consent

capacity solely on the basis of a diagnosis can perpetuate stigma. These assumptions are particularly prevalent in social attitudes toward those with mental illness diagnoses. Researchers should take steps to avoid this by using validated assessment tools to assess participants' consent capacity before, and if necessary, throughout the research process.

4. How can researchers prevent and mitigate stigma associated with certain diagnoses and with impaired consent capacity?

Equating certain conditions with impaired consent capacity or making unfounded assumptions about individual abilities on the basis of diagnoses can exacerbate or perpetuate stigma. Stakeholder engagement is one important tool that researchers can use to mitigate stigma. Stakeholders include those with or at risk for impaired consent capacity, caregivers, and advocacy groups. Stakeholder engagement can provide information about the lived experiences of those affected by conditions that can affect consent capacity and help dispel common assumptions. In addition, valid and individualized capacity assessment tools help researchers avoid equating diagnoses with impaired consent capacity, thereby reducing the risk of stigma.

5. What are the relevant laws and regulations?

No federal regulations directly address in detail research participation of adults with impaired consent capacity. However, researchers should be aware of certain regulations and guidance documents that can affect their choices and policies with regard to including such participants in their research. Institutional review boards (IRBs) typically are responsible for ensuring that research complies with all regulations. However, researchers should also be familiar with the relevant regulatory landscape.

- **Common Rule:** Subpart A of the U.S. Department of Health and Human Services' (HHS) regulations, Protection of Human Subjects (codified at 45 C.F.R. Part 46), also known as the Common Rule, has been adopted by 18 federal departments and agencies that conduct or fund human subjects research. The Common Rule provides standards for ethical conduct of federally supported human subjects research. It mandates oversight of research by IRBs and requires voluntary informed consent from participants or permission from their LARs for research participation. The Common Rule also requires additional safeguards when participants might be vulnerable for various reasons, including mental disability, but it does not define mental disability or stipulate what these safeguards should be.
- **OHRP Guidance:** The HHS Office for Human Research Protections (OHRP), which is responsible for implementing the Common Rule, offers some guidance and clarification regarding how the federal regulations apply to research involving individuals with impaired consent capacity (see <http://www.hhs.gov/ohrp/policy/faq/informed-consent/index.html>). OHRP notes that an LAR can enroll individuals in research who cannot provide valid informed consent, but that researchers and IRBs must consult state and local laws to

determine who can serve as an LAR. When states do not have laws specifically relevant to surrogate decision making in research, OHRP notes that researchers and IRBs can look to comparable laws regarding medical decision making. In addition, OHRP emphasizes that federal regulations require that IRBs possess the necessary professional competence to review research activities, either through IRB members with relevant experience and expertise or through consultants. This might include expertise or competence about the populations affected by disorders that affect consent capacity, when members of those groups are participants.

- **State Laws:** A patchwork of applicable legal protections exists at the state level, resulting in laws for designating an LAR to facilitate decisions about clinical care that vary by state. For example, laws differ in describing how LARs should make decisions on behalf of patients in the clinical context and who can serve as an LAR. Very few state laws address the assignment of authorized representatives to make decisions about enrollment in research.
- **NIH Guidance:** In 2009, the National Institutes of Health (NIH) released a guidance document that provides researchers and IRBs with points to consider when conducting or reviewing research with individuals who might have impaired consent capacity. The document urges researchers to consider factors such as composition of IRBs, research design, and the use of LARs in making decisions about working with this population (see <http://grants.nih.gov/grants/policy/questionablecapacity.htm>).
- **FDA Draft Guidance:** In 2014, the U.S. Food and Drug Administration (FDA) released a draft guidance document on conducting research with individuals who might have impaired consent capacity that was similar to the 2009 NIH guidance. FDA's guidance leaves decisions about including individuals who might lack consent capacity to the discretion of IRBs and investigators and, like the NIH document, provides several points for consideration in making decisions about research review and design (see <http://www.fda.gov/RegulatoryInformation/Guidances/ucm404975.htm#impaired>).

6. What ethical safeguards can ensure the responsible inclusion of participants with impaired consent capacity?

Respectful and just research policies and practices demand both fair inclusion and additional safeguards for prospective research participants with impaired consent capacity. Relevant safeguards might include assessment of consent capacity, solicitation of assent and respecting dissent, use of independent monitors, potential limits on allowable risk, processes to designate and seek permission of an LAR, research advance directives, and stakeholder engagement.

Consent Capacity Assessment

Researchers should assess consent capacity to avoid making assumptions about prospective participants on the basis of a diagnosed disorder, thus avoiding unfairly labeling and stigmatizing individuals and groups. Robust capacity assessment before research begins (and when indicated, during research) also helps ensure that participants with impaired, fluctuating, or diminishing consent capacity are adequately protected.

An example of an established tool for assessing consent capacity in research is the MacArthur Competency Assessment Tool for Clinical Research (MacCAT-CR). Researchers can tailor the questions in that instrument to a specific research protocol and obtain a score indicating whether the individual has consent capacity. Regardless of which assessment tool is used, however, researchers and IRBs should consider whether a participant's condition, the intervention under study, or other contextual factors indicate a need for assessment and reassessment of consent capacity during the course of a research project.

Modified Informed Consent Processes

An individual's understanding of the information needed to make a decision depends in part on how the information is presented and explained. Modifying informed consent processes by simplifying forms, orally explaining study procedures, or using creative strategies (e.g., multimedia supplements) might improve comprehension among participants with certain cognitive or decisional impairments. Understanding more about the underlying causes of impaired decision making could lead to development and testing of effective consent and assessment strategies (e.g., corrective feedback, repeated explanation, or multimedia consent techniques).

Assent and Dissent

Many participants lacking consent capacity can still express meaningful desires regarding research procedures, including by indicating assent or dissent. Importantly, seeking assent is not the ethical equivalent of obtaining informed consent. Respecting dissent serves as a protective measure to avoid inflicting burdens and maintains the dignity of all persons participating in research. Meaningful expressions of assent and dissent are salient, even if insufficient, evidence of participants' perspectives regarding decisions made on their behalf.

Independent Monitors

An independent monitor is a third-party consultant who can help ensure that the execution of a research protocol meets ethical and legal standards. Independent monitors can oversee enrollment, capacity assessment, and informed consent processes. For example, an independent third-party monitor for consent capacity assessments might be valuable in cases when capacity is in question and difficult to assess. Monitors can be trained to observe both verbal and nonverbal cues. They can monitor assent and dissent of participants with impaired consent capacity

throughout the research project and help determine whether to halt the research with particular individuals on the basis of distress or dissent. Implementation of many of the other additional protections described in this section would be strengthened by the presence of an independent monitor to oversee their use, helping prevent unconscious bias or subtle coercion by researchers.

Limits on Acceptable Levels of Risk

Limiting the level of risk to which participants with impaired consent capacity are exposed in research can help protect them from exploitation. Limits on risk help prevent participants from bearing unreasonable risks of harm solely for the benefit of others, without the ability to provide informed consent. In the case of research involving children, regulations generally only allow research to proceed if it poses no more than minimal risk or offers a possibility of direct benefit to participants. Certain experts have recommended a similar framework for participants with impaired consent capacity, but others advocate for risk to be capped at higher levels. The determination remains at the discretion of IRBs.

Legally Authorized Representatives

Participants with impaired consent capacity can be enrolled in certain kinds of research by an LAR. Sometimes referred to as surrogates or proxy decision makers, LARs have the legal power to make decisions on behalf of others. State laws dictate who can serve as an LAR, how much decision-making power an LAR has, what kinds of decisions the LAR can make, and what processes and procedures are required to establish an LAR. Using an LAR is an important way to facilitate inclusion of participants with impaired consent capacity in research, thus ensuring the just distribution of the benefits that might accrue to individuals who share the disorder under study. Using an LAR also is a reasonable way to help protect participants from exploitation, because loved ones or caregivers who have been designated as LARs are often the best proxy for representing participant interests.

State laws vary regarding who can serve as an LAR. In the majority of states, health care proxies or those holding a durable power of attorney for health care previously appointed by individuals when they were capable, are deemed the most appropriate LARs. State laws usually include a list of possible LARs in a hierarchy, including those with health care power of attorney, followed by the individual's next of kin (e.g., a spouse, adult child, parent, or sibling). The majority of state laws describe LARs as having authority for medical decision making, but do not indicate whether the LAR's decision-making power applies to research participation. Medical decisions are presumed in the majority of cases to be compatible with the best medical interests of the individual, whereas research enrollment entails procedures or interventions performed for reasons other than the individual's medical interests. Although OHRP guidance indicates that state laws about appointing LARs for medical care might be relevant, uncertainty remains regarding whether laws specific to medical decisions can or should extend to research decisions.

Research Advance Directives

In certain cases, individuals can prepare an advance directive that specifies their willingness to participate in certain kinds of research before their consent capacity becomes impaired, to be consulted and honored by an LAR. An advance directive is the designation of a proxy decision maker and a set of written instructions articulated by an individual to direct the actions of others in the future, in case the individual becomes unable to make his or her own decisions. Honoring an individual's preferences as delineated on an advance directive demonstrates respect for that individual. It facilitates inclusion of participants with impaired consent capacity while also avoiding exploitation by respecting their stated preexisting wishes.

One type of advance directive included in the laws of all 50 U.S. states is appointment of a power of attorney for health care, sometimes referred to as a health care agent. Similarly, research advance directives, although uncommon, would be especially helpful as part of the informed consent process for research in which the prospective participants' consent capacity might predictably become impaired at a later date. For example, the NIH Clinical Center's advance directive for both health care and medical research provides individuals with an opportunity to select broad categories of research in which they would be willing to participate; delineate values, goals, and limitations that should guide their participation in research; and designate a power of attorney to make research decisions.

Stakeholder Engagement

Stakeholder and community engagement can help improve informed consent processes, build relationships and trust among researchers and affected communities, and increase the likelihood that research findings are relevant for affected communities. Community engagement is particularly important for research that involves underrepresented and potentially stigmatized groups. Many individuals and groups have a stake in research design, implementation, and results. Increasingly, standard practice in different research areas—especially those with contentious past and present social, political, and ethical implications—is to employ different techniques to identify stakeholders, as well as incorporate and address their perspectives and concerns during the research process.

Many approaches to engaging stakeholders with an interest in neuroscience research exist, including explicit attention to IRB composition, formal advisory groups, participatory research methods, large public or community meetings, and empirical research designed to elicit stakeholder perspectives. IRBs can include members or consultants who can contribute understanding of the experiences of those with impaired consent capacity, including current or former patients, family members, patient advocates, or experts in specific patient populations or LAR decision making. Funding agencies (e.g., NIH) encourage forms of stakeholder engagement in research beyond those that pertain to IRB composition.

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This primer offers practical advice to researchers, especially those who conduct neuroscience research, to responsibly include participants with impaired consent capacity in research and employ additional protections. To learn more about this ethical challenge and the Bioethics Commission's analysis and recommendations, access Chapter 3 of *Gray Matters*, Vol. 2, at http://bioethics.gov/sites/default/files/GrayMatter_V2_508.pdf.