Decisional Capacity in Research Informed Consent

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Questions

- Is adequate short-term memory necessary to be able to provide informed consent for research?
- Can a patient with a diagnosis of Alzheimer's disease dementia provide informed consent for research?
- Can a patient recovering from a stroke who has significant <u>expressive</u> aphasia (cannot speak or write) have adequate decisional capacity to provide informed consent for research?
- Can a patient recovering from a stroke who has significant receptive aphasia (cannot understand spoken or written language) have adequate decisional capacity to provide informed consent for research?
- If a potential research participant has been found by a judge to be incompetent to complete her last will and testament, can she possibly have adequate decisional capacity to consent to research?

Questions

- If a potential participant was determined Not to have adequate decisional capacity to consent for another research study very recently, should you expect them to be able to consent to yours?
- If you ask a potential participant a question about an important part of the consent form and his initial response is incorrect, should you now determine that he lacks the capacity to provide consent?
- If you determine that a participant lacks decisional capacity to consent, is it okay to have their good friend who accompanied her sign the consent on her behalf?

Informed Consent

•Thanks to Mary-Tara Roth!

Modern Ethical Research Principles

- Past violations of ethical principles contributed to the development of our current regulatory framework
- Belmont Principles: Respect, Beneficence, Justice
 - Ethical underpinnings of our regulations
- Emphasis on:
 - Informed consent prior to research participation
 - Voluntary participation
 - Independent ethics review

Nuremburg Code

Ethics principles for human experimentation set as a result of the Nuremberg trials at the end of the Second World War

"The Voluntary consent of the human subject is absolutely essential."

Nuremburg Code

"This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person, which may possibly come from his participation in the experiment."

Four Characteristics of Valid Informed Consent

- Competent
- Voluntary
- Informed
- Understanding

A Best Practice Recommendation: Informed consent progress note

- Who was involved from the study team?
- Were the subject's family members present?
- Did consent occur and was document signed prior to any research procedures taking place?
- Were there questions? How were they answered?
- How much time was given to the subject?
- Was a signed copy given to the subject?
- And...if there is a possibility of the participant having reduced capacity to provide adequate consent, what, if any, procedures were used to determine the participant's capacity...and how was this determination made?

BUMC Human Research Protection Program Policies and Procedures

- 9.5.1 Additional Requirements for Decisionally-Impaired Persons
 - The use of decisionally-impaired persons as research subjects presents a risk that their disability may compromise their capacity to understand the information presented during the consent process and their ability to make a sound decision as to whether to participate in the research.
 - The investigator must indicate in the submission whether any subject who is cognitively impaired will be recruited, and if so, must describe how the subjects' ability to consent will be assessed, how Legally-Authorized Representatives (LAR) will be identified, and how the consent and assent process will prevent undue influence and coercion...
 - The investigator must explain why inclusion of decisionally-impaired subjects is necessary to answer the study question.
 - If the study population is expected to include persons whose cognitive capacity may fluctuate during the course of the research, the investigator must describe plans for assessing cognitive capacity and obtaining consent from the subject to continue in the research when appropriate.
 - In the case of subjects who are initially able to consent for themselves, it may be appropriate to ask them to identify a research-specific proxy to provide consent in the future.

BUMC Human Research Protection Program Policies and Procedures

9.5.1 Additional Requirements for Decisionally-Impaired Persons (cont.)

- The IRB will approve research on decisionally-impaired persons when:
 - The consent/assent process adequately protects the rights and welfare of these subjects; and
 - The investigator has adequately justified the inclusion of this vulnerable population as necessary to answer the study question, not merely as a convenience for recruitment; and
 - The risks fall into one of the following categories:
 - no greater than minimal risk; or
 - greater than minimal risk and the research holds out the prospect of direct benefit to the subjects; or
 - greater than minimal risk with no prospect of direct benefit to the subjects when BOTH of the following are true:
 - the knowledge likely to be gained through the research will improve the understanding of the condition, disease, or behavior affecting the participant population; and
 - the risks to subjects, including the risks of foregoing available alternative treatments, are not substantially greater than those associated with the available alternative approaches.

Determining Decisional Capacity

or....

Not much more than doing a good consenting

Capacity - Definitions

• Competence:

 Technically, a legal term -- not a medical or research term -- used to denote capacity to act on one's own behalf; the ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice. Determined by a judge and not measured or diagnosed or determined by an attorney or clinician.

Decisional Capacity:

• Decisional Capacity is what can be assessed by the attorney or clinician or researcher.

Consent Capacity:

• A specific area of decisional capacity: Includes the specific abilities necessary for a prospective or current research participant to understand and use information relevant to consent.

Specific Areas of Capacity

- Independent Living
- Financial Management
- Treatment Consent
- Testamentary Capacity
- Sexual Consent
- Voting
- Driving
- Research Consent

Specific Areas of Capacity

- It is very possible to have adequate decisional capacity in one domain (e.g., living situation) but not in another (e.g., financial).
- Capacity is a dynamic issue.
 - By definition, many of the causes of diminished capacity are degenerative/progressive diseases and require re-evaluation.
 - Within a single time-point, there are gradations of capacity, based on situational complexity.

Specific Areas of Capacity

 Decisional capacity for research is protocol-specific and situation-specific. Thus a subject may have capacity to consent to a low-risk research protocol in usual circumstances, but not have the capacity to consent to a high-risk protocol or when he or she is confused or under duress.

Important

- Having a diagnosis of dementia (e.g., caused by Alzheimer's disease, CTE, etc.) does NOT necessarily mean that an individual has diminished capacity.
- Having a diagnosis of psychosis (e.g., from schizophrenia, bipolar disorder) does NOT necessarily mean that an individual has diminished capacity.
- Capacity is a functional impairment, not a disease, and these diseases (AD, CTE, Schizophrenia, etc.) have individualized courses and individualized profiles of impairments.

A Model of Decisional Capacity Grisso & Appelbaum

- Four Main Components of Decisional Capacity
 - <u>Understanding</u>
 - ...of the information disclosed about the nature of the research study and its procedures
 - <u>Appreciation</u>
 - ...of the effects of research participation (or failure to participate) on the subject's own situation
 - <u>Reasoning</u>
 - The process of deciding about participation, focusing on subjects' abilities to compare alternatives and their consequences
 - Expression of Choice
 - I want to OR I do not want to
- Appelbaum PS1, Grisso T. Assessing patients' capacities to consent to treatment. N Engl J Med. 1988;319:1635-8.
- Appelbaum PS, Grisso T, Frank E, O'Donnell S, Kupfer DJ. Competence of depressed patients for consent to research. Am J Psychiatry 1999;156:1380-4
- Grisso T, Appelbaum PS. MacArthur Competence Assessment Tool for Treatment (MacCAT-T). Sarasota, FL: Professional Resource Press, 1998

Approaches to Determining Capacity to Provide Research Consent

- Formal Clinical Assessment by third party clinician (e.g., neuropsychologist).
 - Not specific to time and situation of research consent process.
- Formal Capacity Assessment by researcher (e.g., MacArthur Competence Assessment Tool—clinical research; MaCAT-CR)
 - Quantifies responses, based on Applebaum and Grisso's model; long (20 min), not necessary in most situations.

Approaches to Determining Capacity

- Brief measure: UCSD Brief Assessment of Capacity to Consent (UBACC)
 - 10 questions with 0-1-2 responses
 - 5 minutes

 Brief, reliable, but meant to use as a screening method for large numbers of potential participants to identify those needing more comprehensive decisional capacity assessment and/or remediation

Jeste DV, Palmer BW, Appelbaum PS, Golshan S, Glorioso D, Dunn LB, Kim K, Meeks T, Kraemer HC. A new brief instrument for assessing decisional capacity for clinical research. Arch Gen Psychiatry. 2007;64:966-74.

 What is the purpose of the study that was just described to you? 	
Response (2 = Study investigational drug for memory)	Score
	0
	1
	2
2. What makes you want to consider participating in this study?	
Response (2 - Improve memory and attention, help others)	Score
	0
	1
 De vers hellens ihle is estructive second as estructive investor 	2
3. Do you believe this is primarily research or primarily treatment?	0
Response (2=Research)	Score
	0
	1
4. De seus have in he in it is shown if you de anti-matin and is being	2
4. Do you have to be in this study if you do not want to participate?	Coore
Response (2=No)	Score
5. If you withdraw from this study, will you still be able to receive requi	2 ar treatment
5. If you withdraw from this study, will you still be able to receive regula Response (2 = Yes)	Score Score
	0016
	1
	2
6. If you participate in this study, what are some of the things that you to do?	will be asked
Response (2=At least 2 of the following: answer questions, bring medications to clinic, magnetic resonance imaging, electrocardlogram, blood draw, urine testing)	Score
	0
	1
	2
Please describe some of the risks or discomforts that people may ex if they participate in this study. (Please describe the 2 serious risks a with the study.)	perlence issociated
Response (2 = Heart problems and liver problems)	Score
	0
	1
	2
8. Please describe some of the possible benefits of this study.	
Response (2= Societal and/or personal benefits, may help memory	Score
and attention)	0
	1
	2
9. Is it possible that being in this study will not have any benefit to you	?
Response (2=Yes)	Score
	0
	1
	2
10. Who will pay for your medical care if you are injured as a direct resu of participating in this study?	It
Response (2=The Institution or hospital)	Score
	0
	1
	2

Approaches to Determining Capacity

- •Semi-Structured Questioning based on Specific Consent "Disclosures"
 - •Cons:
 - It can actually be LONGER than the 20 min MaCAT-CR
 - There are no formal scores; relies on "clinical judgement"
 - Not specific to the study or consent form

• Pros:

Individualized to the participant and to the study and consent form

Consent Procedures to Determine Decisional Capacity

Have participant read entire informed consent form (or read it with them or to them) Keep it in front of them...This is NOT a memory test!

Using disclosures, assess decisional capacity

Implement intervention (as necessary)

Repeat assessment & interventional steps (if necessary)

Understanding: Components

- Nature of project (purpose of study plus some procedural elements, such as MRI, Blood test, given investigational drug)
- Primary purpose is research
- Effects on individualized care (the study differs from ordinary clinical diagnostic evaluation and treatment)
- Benefits and risks/discomforts (most important risks/discomforts, most important benefits)
- Ability to withdraw

Example Study: "DIAGNOSE CTE" Disclosures for Understanding Background, purpose, nature of project

1. Purpose of the DIAGNOSE CTE Research Project

Chronic traumatic encephalopathy (CTE) is thought to be caused by repetitive blows to the head, but not everyone with repetitive head trauma gets CTE. Currently, this brain disease can only be diagnosed after death. Therefore, the **purpose of this study is to**:

- **1.** Define the clinical presentation (signs and symptoms) of CTE.
- 2. Develop objective biological tests (biomarkers) to help diagnose CTE during life.
- 3. Try to determine what other factors (such as genes) increase an individual's likelihood of getting CTE.
- 4. Collaborate and share study data with other researchers who are trying to learn more about CTE.

What we learn from this study will hopefully lead to a way to diagnose CTE in living individuals and potentially to treatments in the future.

It is important to note that this research study is <u>not</u> designed to determine if someone has a clinical diagnosis of CTE. That is, this is a research study and will not involve providing a clinical diagnosis or treatment to participants.

- What is the purpose of this study?
 - Should be able to describe the general purpose (e.g., "help diagnose CTE during life")
- Will you be told if you have CTE if you participate?
 - Needs to demonstrate awareness that this is a research study not intended to give a clinical diagnosis or treatment.

Disclosures for Understanding

Background, purpose, nature of project

2. Overview of What Happens in this Research Study

This research study consists of two separate study visits: a Baseline Visit and a Follow-Up Visit. At this time we are only going over the procedures for the 3-day Baseline Visit. The Follow-Up Visit will occur three years after the Baseline Visit.

If you choose to be in this study, you will:

- 1. Complete the 3-day Baseline Visit and complete a variety of tests and procedures, including MRI scans, lumbar puncture (or spinal tap), blood draws, and tests of your thinking, memory, mood, behavior, and movement.
- 2. Be available in three years to complete the Follow-Up Study Visit. The Follow-Up Visit will include many of the same tests you will undergo during the Baseline Visit.

- What will you be asked to do if you participate in this study?
 - Should be able to state that there will be various scans, a spinal tap, and other tests.
 - Should state that there will be another set of exams in three years.

Disclosures for Understanding

- Background, purpose, nature of project
- Potential benefits

Potential Benefits of Participation

- 1. You will receive no direct benefit from your participation in this study.
- 2. <u>This study is for research purposes only</u>. However, if you are a patient being examined by healthcare providers for problems with thinking, memory, mood, or behavior, or are concerned about your thinking, memory, mood or behavior, you may benefit from discussing the available results with your healthcare provider.
- 3. Your participation may help the investigators better understand how to diagnose CTE during life, as well as the link between repetitive head impacts in athletes and the development of CTE.
- 4. Additionally, your participation may help guide future studies into CTE risk factors, and may provide additional knowledge relevant to the detection, course, and eventual treatment of CTE, Alzheimer's disease, and other neurodegenerative disorders.
 - What, if any, benefits are there to you for participating?
 - Must state that there are no direct personal benefits.

Disclosures for Understanding

- Background, purpose, nature of project
- Potential benefits
- Risks and discomforts

• Questions:

- What are the possible risks and discomforts from the:
 - MRI scan?
 - Lumbar Puncture?
 - PET Amyloid Scan?
 - PET Tau Scan?
 - Should state something about each of the yellow highlights to right

Magnetic Resonance Imaging (MRI): Risks and Discomforts

During the MRI, you will lie on a table that slides into a hollow tube that is only slightly wider than your body. This may create a feeling of **claustrophobia** (fear of enclosed spaces) and temporary anxiety or discomfort. If you are prone to claustrophobia or feel anxious, let the researchers in charge of the scan know. Additionally, the scanners make loud banging noises as they take images. Earplugs can be used to reduce the noises. You can ask us to stop the scan at any time.

Lumbar Puncture: Risks and Discomforts

In less than 3% of people who have had a lumbar puncture, a **headache** may occur which lasts for 24–48 hours after the procedure. In unusual cases, headaches may be moderately severe. Severe headaches may be treated by something called a "blood-patch" procedure. This would involve the injection of a small amount of your own blood into the lumbar puncture site by an anesthesiologist. This procedure provides immediate relief of lumbar puncture headache.

Amyloid and Tau PET Scans: Risks and Discomforts

The **Tau scan drug is an investigational compound**. The dose of the drug you will receive for this PET scan is quite small and not expected to have a toxic effect. The following side effects have been reported in clinical studies: **diarrhea, headache, and altered taste**. All reported events were **mild** in intensity and **all subjects recovered** from these events. Since the study drug is a new compound that is being studied in clinical trials, you may experience side effects that we do not know about yet.

The drugs used for both of the PET Scans include a small amount of **temporary radiation** that is needed to create the PET scan images. Exposure to radiation is associated with an **increased risk of developing cancer**. The total amount of radiation from each PET scan is about the same that a patient receives from a routine abdominal/pelvis CT scan. It is about 2 to 4 times as much radiation as the average person receives in a year from natural sources (examples include soil, water and sun) and human-made radiation (examples include televisions, smoke detectors, and x- rays).

Appreciation: Components

 Not for personal medical benefit (i.e., purpose of study is not to optimize participant's medical care)

 Withdrawal possible without penalty (i.e., participant can decline to participate OR at a later time, participant can withdraw from study and not be penalized for any reason)

Assessing Appreciation

- Do you have to participate in this study?
- Do you believe you were asked to be in the study for your own personal medical benefit?
- Do you believe you will get a formal diagnosis or treatment?
- Suppose you decided to participate in this study and then changed your mind. What do you believe would be the consequences to you if you decided to no longer participate?
- What are the alternatives to participating in this study?

Reasoning: Components

- Justifying choice preference (i.e., consequential reasoning – why does the subject want to participate?)
- Relating choice to other option (i.e., comparative reasoning – why is subject's choice better than the alternative?)
- Logical consistency of choice (i.e., is their choice logically consistent with their reasoning responses?)

Assessing Reasoning

- Why do you want to participate?
- Why is your choice better than the alternative?
- How will participating (or not participating) impact your life?
- Determine if the participant's choice seem logically consistent with their responses above?

Expression of Choice

 Participant should express their choice (i.e., "yes, I want to participate" or "no, I decline to participate")

Assessing Expression of Choice

- Now that we have reviewed the consent statement, would you like to participate in this study?
 - Requires clear affirmative response.

Interventional Strategies

- If there seems to be problems with
 - Understanding disclosures
 - Describing appreciation
 - Demonstrating reasoning
 - Clarifying choice
- Don't just stop and determine that the individual lack's capacity.
- Numerous methods can be used to improve decisional capacity performance, including:
 - Repetition of consent information (e.g., using disclosures or oral summaries)
 - Corrective feedback (e.g., correcting errors and providing missed details regarding the study)
 - Simplified consent statements (e.g., one page summary, but this method requires IRB approval)



BUMC Human Research Protection Program Policies and Procedures • 9.5.2 Allowable Legally-Authorized Representatives

- A Legally Authorized Representative (LAR) is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures(s) involved in the research. When the IRB approves for consent to be obtained from a subject's LAR, the following representatives will ordinarily be allowed for research conducted in MA:
 - Court appointed guardian (for any category of research involving decisionallyimpaired persons): In some instances a court may have appointed a guardian who has authority to make decisions that include decisions to participate in research and undergo research procedures, on behalf of a subject who is decisionally impaired.
 - Research proxy (for any category of research involving decisionally-impaired persons): The subject may have designated a research proxy by durable power of attorney, health care proxy, or other legally valid document prior to the subject becoming decisionally impaired. The terms of the designation of a research proxy must specifically include making research decisions for the subject. A general durable power of attorney, healthcare proxy or "living will" does NOT automatically make someone eligible to make research decisions on behalf of a subject or serve as the research proxy. (continued)

Research Proxy

PROXY ASSIGNMENT FOR RESEARCH PARTICIPATION

STUDY TITLE:	*****
PROTOCOL NO .:	<irb #="" protocol=""></irb>
SPONSOR:	*****
INVESTIGATOR:	<site pi=""></site>
SITE:	<site name="">, <address></address></site>

I) Appointment

I, ______(the principal), being a competent adult, at least eighteen years of age or older, of sound mind and under no constraint or undue influence, hereby appoint the following person to be my RESEARCH PROXY under the terms of this document:

Name:	Telephone(s):
Address:	Relationship to you:

In making this appointment, I am giving my Research Proxy the authority to make any decisions related to research participation on my behalf in the event that I should at some future time become incapable of making research participation decisions for myself. By assigning a Research Proxy however, I do not relinquish my rights to refuse participation in any or all activities related to a research study regardless of a designated Research Proxy.

II) Powers Given to Research Proxy

- A. My Research Proxy shall have the authority to make all research participation decisions for me, if I am unable to make research participation decisions for myself. This authority includes whether or not to enroll me or continue my participation in a research study. My proxy is then to have the same authority to make research participation decisions as I would if I had the capacity to make them.
- B. My Research Proxy shall have the authority to act on my behalf only if, when and for as long as a determination has been made that I lack the capacity to make or to communicate research participation decisions for myself.
- C. I shall be notified of any determination that I lack capacity to make or communicate a decision to participate or continue participation in a research study where there is any indication that I am unable to comprehend this notice.
- D. My Research Proxy shall make research participation decisions for me only after consultation with my health care providers and after full consideration of acceptable medical alternatives regarding my diagnosis, prognosis, treatments and their side effects.
- E. My Research Proxy shall make research participation decisions for me only in accordance with their assessment of my wishes, including my religious and moral beliefs, or, if my wishes are unknown, in accordance with my Research Proxy's assessment of my best interests.

- F. My Research Proxy shall have the right to receive any and all medical information necessary to make informed decisions regarding my research participation, including any confidential medical information that I would be entitled to receive.
- G. If I object to a research participation decision including dissent of any research procedures made by my Research Proxy, my decision shall prevail.
- H. The decisions made by my Research Proxy on my behalf shall have the same priority as my decisions would have, if I were competent, over decisions by any other person, including a person acting pursuant to a Durable Power of Attorney, except for any limitation I state below or specific Court Order overriding this Research Proxy assignment. *Optional Limitations*:

III) Revocation

This Research Proxy shall be revoked upon any one of the following events:

- A. my execution of a subsequent Research Proxy;
- B. my divorces or legal separation from my spouse where my spouse is named as my Research Proxy; C. my notification to my Research Proxy or a health care provider orally or in writing or by any other
- c. my nonneation to my Research Proxy of a health care provider orally of m writing or by any of act evidencing a specific intent to revoke the Research Proxy;
- D. by veto of my Health Care Agent (if designated); or
- E. revocation by the designated Research Proxy.

IV) Statement of Research Proxy

I have been named by the principal as the principal's Research Proxy in this document. I attest that I not under any constraint or undue influence to encourage the principal to enroll or continue research participation. I have read this document carefully and accept the appointment.

Research Proxy Signature

Printed Name of Research Proxy

V) Principal Signature

I hereby sign my name on this date, _____, to this Research Proxy in the presence of two witnesses:

Principal Signature

Printed Name of Principal

VI) Witnesses

I, the undersigned, have witnessed the signing of this document by the principal or at the direction of the
principal and state that the principal appears to be at least eighteen years of age, of sound mind and
under no constraint or undue influence. I have not been named as a Research Proxy or alternative agent
in this document.

Witness Signature

Printed Name of Witness

I, the undersigned, have witnessed the signing of this document by the principal or at the direction of the
principal and state that the principal appears to be at least eighteen years of age, of sound mind and
under no constraint or undue influence. I have not been named as a Research Proxy or alternative agent
in this document.

BUMC Human Research Protection Program Policies and Procedures

• 9.5.2 Allowable Legally-Authorized Representatives (Continued)

- General healthcare proxy (only for research involving decisionally-impaired persons that holds out the prospect of direct benefit to the subjects): The subject's general healthcare proxy may serve as the LAR to consent for this type of research. The study records must clearly document how the healthcare proxy determination was made.
- Next of kin (only for research involving decisionally-impaired persons that holds out the prospect of direct benefit to subjects or for minimal risk research where not obtaining the consent of the subject meets the waiver criteria in Section 8.4.3. The subject's next of kin may serve as the LAR to consent for these types of research. The sequence of kinship is as follows: spouse, adult child, parent, adult sibling. When a potential subject has a spouse, the spouse is the next of kin. If the spouse is incapable of being the LAR or is unavailable, the adult child may serve as the LAR, and so on, down the line of kinship. The study records must clearly document how the next of kin determination was made.

Return of the Questions

- Is adequate short-term memory necessary to be able to provide informed consent for research?
- Can a patient with a diagnosis of Alzheimer's disease dementia provide informed consent for research?
- Can a patient recovering from a stroke who has significant <u>expressive</u> aphasia (cannot speak or write) have adequate decisional capacity to provide informed consent for research?
- Can a patient recovering from a stroke who has significant receptive aphasia (cannot understand spoken or written language) have adequate decisional capacity to provide informed consent for research?
- If a potential research participant has been found by a judge to be incompetent to complete her last will and testament, can she possibly have adequate decisional capacity to consent to research?

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- If a potential participant was determined Not to have adequate decisional capacity to consent for another research study very recently, should you expect them to be able to consent to yours?
- If you ask a potential participant a question about an important part of the consent form and his initial response is incorrect, should you now determine that he lacks the capacity to provide consent?
- If you determine that a participant lacks decisional capacity to consent, is it okay to have their good friend who accompanied her sign the consent on her behalf?

