ASK THE NEUROETHICIST

Frontotemporal Dementia or Midlife Crisis? Evaluating Capacity and Consent for Participation in Research

BY JUDY ILLES, PHD

Q: Mr. Z., 52 years old, arrives reluctantly at a neurology appointment with his wife, following referral by his primary care physician. Both medical visits were prompted by his wife's complaints about his uncharacteristically erratic behavior — concerns which Mr. Z. deems utterly unnecessary. With great alarm, Mrs. Z. tells the neurologist that her husband has begun unabashedly purchasing services from high-end consorts; moreover, his inconsiderate manner has given way to lewd humor, indecent propositioning of other women, and spontaneous expenditures. Until about 11 months ago, she explains, her husband was loyal and affectionate, and enjoyed an excellent professional reputation as a judge. Mr. Z. expresses little concern about his behavior and demonstrates no insight into the impact of his behavior on his longstanding relationships or of his expenditures on his and his wife's rapidly diminishing savings. The neurologist suspects frontotemporal dementia (FTD). Full neuropsychological testing is pending. Other clinical testing was inconclusive.

The neurologist tells Mr. and Mrs. Z. about a new functional neuroimaging technique being tested at a local academic medical center that promises reasonable sensitivity and specificity in detecting early onset FTD. The study team, with which he is collaborating, has an active three-year protocol that allows for disclosure of individual research results to participants upon their request.

Mr. Z. is especially keen to enroll since, as the neurologist explains, the stimuli are emotionally energizing. Mrs. Z. does not feel that her husband has sufficient insight to appreciate the implications of this decision and the possibility of a positive result. Moreover, she does not want this information herself without better predictive value of the test and hope for treatment or cure.

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AD Advisory Panel

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we are dealt. Congress will need to address funding needs," he said.

The neurologist said that when he received a call from HHS Secretary Sebelius asking whether he wanted to chair the committee, he did not pause to think about the answer.

Dr. Petersen is one of two AD scientists on the council; Jennifer Manly, PhD, an associate professor in the Cognitive Neuroscience Division of the Columbia University Taub Institute for Research on Alzheimer's Disease, is the other. Other members include clinicians, individuals from advocacy groups, health care workers, and caregivers. ["See "Advisory Council Members."]

The Advisory Council will meet quarterly to help officials at the HHS, Veterans Affairs, Department of Defense, and the National Science Foundation address the development of a national plan. The council members will serve a four-year term.

Colleagues in the field are not surprised that Dr. Petersen was appointed to chair the non-federal members of the Advisory Council.

"Ron Petersen is an outstanding choice," said Richard J. Hodes, MD, director of the National Institute on Aging (NIA) in a telephone interview with *Neurology Today*. "He is at the forefront of clinical and translational research and understands the human aspects of this disease." He said that Dr. Petersen is also on NIA's National Advisory Council.

Dr. Hodes said that the NIA has already begun to collect information on the full spectrum of AD supported by the NIH. "*NAPA* has reinforced what we are doing now and this act will accelerate and expand this process," he said. "This committee will provide a more explicit structure of where we are and where we need to be."

Dr. Hodes is one of the 10 federal employees who will also serve on the *NAPA* Advisory Council. Others in the group will include HHS representatives from the Office of the Assistant Secretary for Planning and Evaluation, Office of the Assistant Secretary for Health, Centers for Medicare and Medicaid Services, Centers for Disease Control and Prevention, Administration on Aging, Health Resources and Services Administration, Agency for Healthcare Research and Quality, Substance Abuse and Mental Health Services Administration, Food and Drug Administration, Indian Health Service, and Administration for Children and Families.

Dr. Hodes said that he hopes the new council will "further refine our judgments about research." For instance, the NIH agency has just started to fund research on induced pluripotent stem cells to study AD. He said that there will be a strong effort made to design studies to begin treating at the earliest signs of disease, even before symptoms develop.

Dr. Petersen said he is ready to get to work. "We now understand that Alzheimer's is multi-factorial. We are beginning to figure out what the different biomarkers mean to every stage of the disease. We do have gaps in knowledge. We need to know the cascade of events that take place and how it unfolds. As far as treatments, what works at 65 may not be enough at 85." •

NATIONAL ALZHEIMER'S PROJECT ACT ADVISORY COUNCIL (NON-FEDERAL MEMBERS)

- **Ronald Petersen, MD, PhD**, chair of the National Alzheimer's Project Act Advisory Council, professor of neurology, and the Cadieux Director of the Mayo Alzheimer's Disease Research Center and the Mayo Clinic Study of Aging in Rochester, MN.
- **Anita Albright**, director of the Office of Healthy Aging and Disability in the Massachusetts Department of Public Health.
- **Laurel Coleman**, MD, attending physician at Maine Medical Center and Central Maine Medical Center's Palliative Care Team.
- **Eric J. Hall**, founding president and chief executive officer of the Alzheimer's Foundation of America Inc.
- **David P. Hoffman**, MEd, director of the Bureau of Chronic Disease Prevention and Control, Long-Term Care Restructuring, and Partnership within the Office of Long Term Care in the New York State Department of Health.
- **Harry M. Johns**, president and chief executive officer of the Alzheimer's Association.
- **Jennifer J Manly**, PhD, associate professor in the Cognitive Neuroscience Division of the Columbia University Taub Institute for Research on Alzheimer's Disease and the Aging Brain and the GH Sergievsky Center.
- **Helen M. Matheny**, MS, director of the Alzheimer's Disease Outreach and Registry Program at the Blanchette Rockefeller Neurosciences Institute.
- **David Hyde Pierce**, actor, whose grandfather had AD and who shared care-giving duties with his siblings when his father developed dementia.
- **Laura Trejo**, general manager of the Los Angeles Department of Aging and founder of El Portal: Latino Alzheimer's project and a local provider of long-term services and supports, including Older Americans Act programs.
- **George Vradenburg**, chairs the national advocacy network USAgainstAlzheimer's and the Geoffrey Beene Foundation Alzheimer's Initiative.
- **Geraldine Woolfolk**, former teacher who served as a caregiver for both her mother and father, and has been caring for her husband for the past 11 years.

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DR. ILLES RESPONDS: A critical question in this case relates to the capacity to consent: If the focus of a study is to precisely target mechanisms that compromise consent, how can Mr. Z. agree to participate? Does Mr. Z. have sufficient capacity to consent? Does the option of learning the results affect this assessment? The second relates to his autonomy. Where does Mr. Z.'s autonomy end and the need for surrogate decision-making begin in a case like this? Should his wife's evaluation of the risks of disclosure trump Mr. Z.'s?

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> 'Mrs. Z.'s objection to her husband's participation in the research raises the question of who can act as a surrogate decision-maker and when, especially in the trajectory of neurodegenerative disease, that authority will need to be invoked eventually.'

The legal recognition of decision-making capacity in medical ethics refers to a person's ability to make rational decisions about personal health care given the competence to do so. Legal guidelines exist to ensure that a patient is aware of an intervention, as well as its risks and costs. They protect both patients and physicians in this regard.

Ethical guidelines in medical and research ethics promote the values of autonomy — respect for persons and truth-telling. Both are achieved by a process during which a study or intervention is explained to the patient, and all relevant information is disclosed, including risks, benefits, anticipated outcomes, and alternatives. The explanation should be comprehensible and meaningful to the prospective patient/participant who should be given the opportunity to ask questions, explore the alternatives, and involve others if desired.

The criteria for assessing whether these goals have been achieved involve, first, the rationale for the information. Does the person know why a study is being proposed? Does he or she have all the facts needed to make a decision? The second assessment involves comprehension. Does the patient understand the information presented? Does he or she have the capacity and the time needed to reason and deliberate? The third criterion is voluntariness: Is the decision the person's own? Does he or she know about the continuity of care, even if the decision is to decline a procedure or participation in a study? Together, these criteria recognize the patient's right to self-determination through a process of dialogue and deliberation where the patient brings values, beliefs, a social context, and personal goals to the equation, and the physician or researcher brings professional expertise, recommendations, and options.

For this case, given the neurologist's possible conflict of interest, two models of consent are particularly relevant. The *reasonable person model* recognizes that reasonable people can have different preferences. Physicians must provide information necessary for a patient to make treatment or other decisions reflecting these preferences. The *transparency model* requires that physicians make their thought processes transparent to patients, but they are obligated to discuss only the factors that play a role in their thinking and recommendations. It would seem that a combination of both applies here.

Mrs. Z.'s objection to her husband's participation in the research raises the question of who can act as a surrogate decision-maker and when, especially in the trajectory of neurodegenerative disease, that authority will need to be invoked eventually. As presented, the case does not tell us whether she, a living parent, adult child, or even a sibling has been designated. But we could assume that Mr. Z., as a judge, is knowledgeable about the legal aspects of surrogate decision-making, has an advanced directive for medical care, and has designated Mrs. Z. to serve in this role.

The surrogate's role is to represent the patient's values and goals in decision-making, and offer judgment for a person who was once competent. Risks and benefits are balanced in the context of a patient's known preferences. An alternative model for decision-making, acting in the best interest of a person, assumes that the individual was never competent. The role of a surrogate then is to balance risks and benefits. Either way, the goal is to determine which approach will result in the best outcome.

Capacity for informed consent is not static and cognition, personality, as well as preferences may change with mental state and brain health — all hallmarks of neurodegenerative diseases that lead to dementia. The ability to agree to research in the face of the diminishing ability to provide consent is a vexing problem at best. That an imaging study might further inform the extent of capacity adds a layer of circularity for which strategies have been suggested but good solutions still remain elusive.

We don't know enough about Mr. Z.'s capacity under the current conditions to assess his capacity to consent to the research — so immediately trumping his autonomy may be inappropriate, even if FTD is ultimately the diagnosis. His wife is realistically hesitant to embrace the imaging protocol, even though many patients and family members have reported the desire to medicalize a neurologic or neuropsychiatric condition via imaging for which tangible evidence is otherwise unavailable.

Mr. Z. demonstrates enough capacity in the here and now to be urged, at least, to wait and see. Further clinical testing and evaluation for research with a tool such as the Delis-Kaplan Executive Function System would provide valuable information. Neither he nor the researchers will be harmed by a delay since the potential for harm with immediate action exceeds foreseeable benefit. Waiting is the virtuous path. •

Dr. Illes is the Canada Research Chair in Neuroethics and professor of neurology at the University of British Columbia, as well as the founder and governing board member of the International Neuroethics Society.

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