Ethics Review

Ethics Review as a Catalyst for Progress

Allyson C. Rosen[a,b,*], John Wesson Ashford[a,b] and George Perry[c]
[a] *Palo Alto Veterans Affairs Health Care System, Palo Alto, CA, USA*
[b] *Department of Psychiatry & Behavioral Sciences, Stanford University, Stanford, CA, USA*
[c] *The University of Texas at San Antonio, San Antonio, TX, USA*

Abstract. There are several points where ethical decision-making has become paralyzed and inefficient as the field of Alzheimer's disease study has advanced. The focus of this review is to highlight these points and several lines of research that can inform ethical decision-making. The goal is to identify barriers and to move toward solutions. Examples of other fields of study that can be particularly useful for innovative ways to study effective ethical decision-making include implementation science and neuroscience of decision-making, as well as therapeutic investigations of other domains such as the human biology and psychology.

As the research and therapies for Alzheimer's disease (AD) advance, ethical decision-making needs to adapt effectively to protect individuals and society but to avoid paralysis. Ethics is typically defined as a moral code of right and wrong. When there is a new development, there are often new risks to consider, many of which are unknown. In the face of these uncertain risks, there is frequently disagreement about what is right and wrong. At such points, the focus shifts away from the original need or advancement to the impasse in decision-making leading to delays, missed opportunities, and adverse impacts on development. Increasing efforts are devoted to regulation to protect against uncertain risks, but regulatory burden consumes limited resources that would otherwise be available for creativity and innovation. Further, many institutions see new investigators as additional liability rather than treasured talent. Clearly there is a need to identify such ethical quagmires and determine ways to resolve them efficiently.

In this statement, the *Journal of Alzheimer's Disease* is starting a discussion which will take the form of "Ethics Review" to provide support and guidance to move ethical decision-making forward. The goal is to bring together dementia researchers, clinicians, and policy makers so that there can be a greater clarity and constructive discussion in defining risks and benefits from the perspectives of diverse disciplines. Below we describe examples of the process by which such a forum can contribute to advancing research and clinical work in AD.

ANIMAL RESEARCH

Protocols that investigate variables where the integrity of research necessitates compromise of animal comfort can be challenging. Balancing harm and benefit can lead to disagreements depending on the degree to which the institutions value the scientific purpose. For those studies funded by industry, the benefit may be less obvious such as to test a medicine that is functionally equivalent to one in existence but which differs enough to avoid copyright infringement. This benefit is balanced against the animal stress, pain, and intensive resources needed for lab based research. Debates may be less clear around basic science research on the effects of enrichment and stress in awake animals, work which may be valued less than

*Correspondence to: Allyson C. Rosen, Ph.D., Palo Alto VA Medical Center, 3801 Miranda Ave (151Y), Palo Alto, CA 94304-1207, USA. Tel.: +1 650 279 3949; Fax: +1 650 852 3297; E-mail: rosena@psych.stanford.edu.

therapies directed toward potential biological patient benefits.

RESEARCH ON EFFECTIVE AND INEFFECTIVE DECISION-MAKING

There are many reasons why individuals or the structure of a system might be resistant to innovation, and there are now whole fields that can be informative, such as implementation science. There is a phenomenon where clinicians or investigators resist change in practice for reasons that are poorly understood, including resistance to adoption of evidence-based clinical practice. There are examples when evidence for a practice is compelling, such as washing hands to prevent the spread of disease, but clinicians or the public neglect or irrationally refuse to implement it [1]. This reluctance is in contrast to a respect for individual clinicians' judgment when evidence that is not compelling and clinicians may or may not prefer the practice. Implementation science is the study of why there is such resistance to novel therapies, either because of concerns (rational or irrational) about risks or lack of acceptance of evidence of efficacy and potential benefit (which may be sound or biased). The field of implementation science formalizes this study of professional behavior by examining how training and dissemination of novel interventions can most effectively lead to adoption of positive practice change [2]. In considering ethical issues, the goal may be changed from monitoring the fidelity of practice implementation, to timely and focused ethical decision-making as research leads to new risks and benefits. There is now a clear need for a parallel field of study to address these processes of determining right and wrong and implementing those determinations for more efficient advancement in this area of research and clinical science.

STUDYING THE PROCESS OF ETHICAL DECISION-MAKING

An example of a good question to study regarding the process of ethical decision-making is how to determine the most effective structure of institutional review boards serving multi-site studies. There has been a call for consolidation of reviews from local to centralized institutional review boards [3]. An example without such consolidation is the institutional review of the Alzheimer Disease Neuroimaging Initiative which is organized to have each local site review their protocol independently which leads to over 50 parallel reviews,

each with its own diverse perspective on ethical issues. An alternative approach is to consolidate review centrally to avoid repeatedly "reinventing the wheel". The second structure may reduce burden to a single review but may instead lead to gridlock as there are many divergent opinions that need to be reconciled. There may also be outsourcing to for-profit reviewing agencies which has its own risks [5]. These are empirical questions that need formal investigation and whose answers should guide policy. It may even be possible to apply neuroscience research on decision-making (e.g., [4]) to learn about the relationship between the institutional environment and differences in tolerance for risk. The payoff for the field of AD is guidance on how to move innovative practices to the field more efficiently and eventually move therapies to practice more rapidly.

PROTECTION OF PRIVACY

With the Alzheimer's Disease Neuroimaging Initiative, AD research is on the cutting edge of gathering and sharing data and making it available to the world of researchers. However, there is a growing awareness that technical advances make the ability to protect privacy more and more difficult. This same issue of protection of privacy appears in several fields, including the human microbiome project [6], a study that also stores large quantities of human samples. Concern about the protection of privacy may lead to a public backlash against all data-sharing in numerous fields. Such a direction would place pressure on AD researchers to restrict access, which has heretofore led to numerous important advances in biological studies of AD. For AD researchers, the public may demand to know what public good can come from this data sharing to justify the risk to privacy when the data being shared do not lead rapidly to cures. The concern is that the risk to privacy, which may become more and more real, does not justify the benefit of data sharing. In contrast the data in the human microbiome project are presently being used in cures, and this benefit would be lost by stopping data sharing. With such an important benefit, there will likely be increased support for continued data sharing and for developing creative technical solutions to protection of privacy.

ADAPTATION TO SOCIETAL CHANGES

Societal changes powerfully affect ethical decision-making. For example, when the PET amyloid ligand

Amyvid became FDA approved and thus available to patients as a clinical measure, the field needed to move beyond what had been the persistent question of whether this information should be disclosed to when and how subjects should be informed [7]. Researchers' fears of provoking emotional distress or patients' difficulty comprehending uncertain results were irrelevant if patients could obtain this information outside of the protected research environment. To withhold results from a patient who could obtain them from a clinician further could lead to additional radiation exposure. One approach to helping clinicians and investigators to adapt to these societal pressures is to disseminate scripts and tools that are effective in explaining results to patients and families. A pilot test of scripted amyloid PET scan results read to patients with mild cognitive impairment showed patients to be both receptive to and capable of understanding such results [8].

CONCLUSION

There are thus several ways debate and study of the process of ethical decision-making around AD research and practice can foster creative solutions. Discussions may not solve these problems but they will identify and target barriers to progress and catalyze solutions. One way to generate consensus is to clearly identify a need within the field such as treating a symptom or enabling research processes such as collaboration and bring it into the light of open discussion. Both points of disagreement and agreement in the field must be specifically defined to avoid overgeneralization. It is also critical to note where empirical data are lacking that could resolve disagreements. Reviews that highlight empirical findings from within or outside of AD research can catalyze resolution of controversial topics. For example the work by Lingler et al. [8] demonstrating the capacity of patients with mild cognitive impairment to understand PET findings has implications for other forms of early detection. Ultimately by studying the processes that hold us back, we can move forward to solve the urgent problems of AD.

ACKNOWLEDGMENTS

REFERENCES

[1] Gawande A (2013) Slow ideas. The New Yorker, July 29, 2013, http://www.newyorker.com/reporting/2013/07/29/130729fa_fact_gawande?currentPage=all
[2] Eccles MP, Mittman BS (2006) Welcome to implementation science. *Implement Sci* **1**, 1.
[3] Human Subjects Research Protections, 76 Fed. Reg. 44,52, 44,512, 44,521 (proposed July 26, 2011).
[4] Suri G, Sheppes G, Gross JJ (2013) Predicting affective choice. *J Exp Psychol Gen* **142**, 627-632.
[5] Zern C (2013) Is the customer always right? Department of Health and Human Services' proposed regulations allow institutional review boards to place customer service ahead of research participants' welfare. *St Louis Univ Public Law Rev* **32**, 411-446.
[6] Hoffmann DE, Fortenberry JD, Ravel J (2013) Are changes to the common rule necessary to address evolving areas of research? A case study focusing on the Human Microbiome Project. *J Law Med Ethics* **41**, 454-469.
[7] Shulman MB, Harkins K, Green RC, Karlawish J (2013) Using AD biomarker research results for clinical care: A survey of ADNI investigators. *Neurology* **81**, 1114-1121.
[8] Lingler J, Roberts J, Schultz R, Klunk W (2012) Development of a standardized approach to disclosing amyloid imaging results in MCI. *Alzheimers Dement* **8**(Suppl), P422.