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This presentation is based on the opinions of the author alone. It does not represent any individual other than herself or any agency or institution.
Introduction

The focus of this lecture and paper is on the landscape of ethical, legal and social challenges in neurosciences today. I will argue that scholarly research needs to build upon the historical past of ethics in neuroscience, and that the research process will benefit from the early integration of ethics principles. I will use case studies and ongoing research from the Program in Neuroethics at Stanford University and others as a guide. Many examples are from imaging, but that is certainly only one model among many relevant neurotechnologies. I will conclude with some ideas about where I think neuroethics needs to go next, especially given how far and how fast the field has evolved in a short few years.

Neuroethics Needed

As Science Writer Helen Pearson wrote simply in Nature in June 2006 \(^1\): *Neuroethics Needed*. Before I embark on the specific case studies to illuminate why this is the case, allow me to provide a framework for my discussion with a few points. First, adapting Van Rensselaar Potter’s definition of bioethics in *The Birth of Bioethics* \(^2\), a new definition of neuroethics may be viewed as:

*a discipline that aligns the exploration and discovery of neurobiological knowledge with human value systems.*

Second, the normative inquiry that my team at Stanford and I undertake in neuroethics is neither intended to establish definitively what ought to be done nor to provide a single view of best alternatives to difficult ethical, legal, social, and policy challenges in neuroscience.

Rather, we work with the goal of achieving a pragmatic starting point for identification of issues and discussion of scenarios of importance, and resolving them through a negotiated scientific-social process. We seek logical and flexible guidance to the task, and one that empowers, not encumbers the scientific process.

Third, there is a strong historical precedent for ethics in neuroscience from the ancient philosophers to modern day. As shown in the timeline in Slide 2, one key event in the modern history of this discipline is the Nuremberg War Crimes Tribunal following World War II. Another is the era of Tuskegee experiments in the 1970s during which poor black men with syphilis in Alabama were left untreated for the benefit of later neuropathological studies of the disease. These have not only shaped thinking in bioethics but fundamentally ethical conduct in all scientific disciplines.
As the timeline also shows, much work has already been done in creating bridges between the two disciplines of neuroscience and ethics, through work of the International Bioethics Council in 1996 for example, and the recognition by this society of the importance of explicit bridging of ethical and social issues in neuroscience through the work of the former social issues committee, the new dialogues series, and the annual SfN neuroethics lecture.

We are in a new era now, however. Bridges are not enough. With the explosion of methods for probing human thought in health and disease, an integration of ethics and neuroscience is needed to provide the full range of the moral and intellectual space for decision-making. Indeed, as Sir Francis Bacon wrote in 1597, “Knowledge is power (Ipsa Scientia Potestas Est)” The knowledge of neuroscience will be most powerful as we build on lessons learned from the past.

In the second SfN neuroethics lecture, Stephan Chorover (2004) described how the lessons we have learned from genetics are fundamental as neuroscience pursues: "...the meaning of human nature and the power of behavior control." No doubt, one of the great challenges we are tackling today is that of protecting not only the genome but also the “brainome”, a concept that Don Kennedy introduced in the very first SfN Neuroethics lecture in 2003 when he said: “Far more than our genomes, our brains are us collectively defining us as human, and individually marking out the special character of our personal capacities, emotions, and convictions.” The special challenge of protecting the brainome - the need for anticipating and planning to protect it - is the central theme that binds all the cases for discussion next.
Case Studies

Slide 3 shows different phases of research in the life in neuroethics. Naturally, the most evolved are the ones we started on first. Those least evolved are the ones that came into the mix later, or that we have just started to explore.

The ultimate goal of our work is the integration of well-developed research, reference and resource tools to respond to issues identified early in the research process. I would like to present some of the cases through the lens and voice of the entertainment industry whose reach extends far beyond the walls of our laboratories and conference meetings such as this.

Incidental Findings

Slide 4 is a short clip of Alan Alda playing Hawkeye Pierce in the TV comedy-drama MASH ⁴, the story of a Mobile Army Surgical Hospital during the Korean War in the 1950s. While screening for blood type and hepatitis, Hawkeye and his colleagues come across an unexpected and serious finding in a young soldier anxious to donate blood to his friend.

Go to “Movies” folder to view MASH video clip (Slide 4)
neuroscience?
The following short clip in Slide 5 provides the answer to this question.

Go to “Movies” folder to view the video clip of the Case of SH (Slide 5)

The video is of SH, a 25 year old medical student, who participated in a functional MRI study of verbal working memory of another medical student within 3 weeks of coming to Stanford. Her MRI at the time, about one year before she gave this seminar and permitted us to record and webstream it, is shown in Slide 6. On this sagittal T1-weighted (left) and this coronal T2-weighted MRI acquired 3T (right), an arteriovenous malformation is visible in the right frontal cortex.

The case of SH is rare but it is a dramatic example of an incidental finding. Such a finding is defined as an anomaly, of the brain for example, that is unrelated to any variables prescribed by a study, whether a subject is recruited for his or her expected good health or for a specific pathology. SH's incidental finding required a number of neurosurgeries to correct. She is back on track with her medical studies now and just published her story in the Annals of Internal Medicine. The full length video of her story may be viewed at http://neuroethics.stanford.edu “The Case of SH.”
My colleagues and I opened a Pandora’s Box in exploring this problem, as illustrated in the 3-dimensional space inspired by Pat Churchland on the Slide 7. Pandora and her box is shown on the left of the scale, a brain scan on the right of the scale, and the three axes on which principal ethical questions may be drawn: incidence, duty of care, privacy.

Slide 7

With respect to incidence, the literature varies, but generally suggests that 1-2% of findings are clinically significant. The data vary substantially with reports of far higher occurrences in studies that draw from the older populations over the age of 65, and much less from, for example, 20 year old ultra healthy air force pilots. Severity also appears to vary with age, with findings albeit rare, highly significant in young populations.

Duty of care is a function of a number of variables, with the greatest weight on the professional training of the PI who may be an MD or not, such as psychology researchers or physicists. Scan parameters, institutional setting and institutional requirements are others.

Privacy in this context has to do with a participant’s right not to know. We have guidance on the privacy axis from the work of two previous groups: The 1999 National Bioethics Advisory Commission and the 2004 National Heart Lung and Blood Institute Working Group on Reporting Genetic Results.

They recommended that research results such as of incidental findings should only be given to subjects if:

a) the findings are scientifically valid and confirmed,
b) the findings have significant implications for the subject’s health, and
c) a course of action exists for intervention and is readily available.

While these recommendations provide a useful starting point they do not fully address the unique conditions for a clinical finding in brain imaging research.

Drawing on these lessons, a binational Working Group on incidental findings – a group of more 50 representatives from neuroscience, bioethics, law and policy from the United States and
Canada – wrangled with many different aspects of the challenge. An updated pathway offering practical and options – tools in the Slide 8.

As shown in Panels A and B, the group concluded that anticipating and being clear to IRBs and research subjects about a plan for handling incidental findings is an unequivocal responsibility. This part is truly straightforward. It may be a cultural shift in as many as 60% of imaging laboratories today, and while it is not trivial, it introduces no risk or extra cost to the scientific process.

In Panel B the majority recommendation for management of an incidental finding beyond the first level is illustrated; a minority favored alternative options, in part until a policy analysis of the cost-benefit of false positives and false negatives is completed, and in part for limitations due to image resolution depending on scan acquisition parameters.

The recommended path continues in the middle column in Panel C where the question of whether to involve physicians in research some or all of the time arises. The all-of-the-time solution can be costly in terms of real dollars, and not always practical given different research settings. The some-of-the-time solution, guided by the discovery of a suspicious appearing brain anomaly, may be most practical overall given all of the variables I have described. Even here, however, physicians must be aware that in their limited role as gatekeepers to follow up of a finding, they may incur a responsibility beyond that of the relationship between the investigator and subject.

In Panel D, there is a return to strong convergence among the members of the Working Group: disclosure should always be made to the subject first, or to his or her guardian in the case of participants with limited decisional capacity.

Ethics analysis to date, therefore, yields the following conclusions about incidental findings:
A singular or strict approach is not appropriate; rather a range of options exists that are morally acceptable.

Clarity upstream and downstream is essential

As the community of neuroimagers and others move forward in gathering more data, it behooves all researchers to have forethought about other already identified and emergent issues such as data base sharing, functional anomalies.

Prospects of Surrogate and Bio Markers

An area of study not quite as far along as incidental findings on the ethics discovery timeline but nearing tools development is surrogate and biomarkers of disease and outcome.

The reader may be familiar with the classic film from the 1960s called Charly, a screenplay based on the book Flowers for Algernon.

In this fiction, the performance of a mouse – Algernon - whose intelligence as measured by maze running is improved significantly by an experimental neurosurgical procedure (Slide 9).

The tremendous success of the mouse predicts a more than improvement of intelligence to near genius in a developmentally delayed protagonist – Charly - who undergoes the same procedure in an N of 1 study. The eventual decline of Algernon’s stellar performance and Algernon’s eventual demise predicts a return to limited intelligence in Charly. Information about this predicted outcome is withheld from him for a host of reasons – scientific hope, investigator interests – but, independently and tragically, he discovers it himself.

The writers of this film probably had no idea what a rich array of ethical issues they stumbled up through this work. The next slide shows a primitive drawing of the Flowers for Algernon Challenge. Simply stated, the challenge describes variability in what a surrogate can or cannot accurately track or predict as future outcome. The best outcome of the challenge is to achieve a surrogate marker that accurately predicts an endpoint of successful intervention and enduring benefit. A more difficult challenge is when the behavior of a surrogate diverges altogether from target or, in the case of Algernon (in green) accurately predicts poor outcome (in orange). The arrow points to the critical ethics juncture.
There are implications for goodness of the predictor, and for the timing of disclosure of the predicted disease or outcome as shown by the timing arrow between the two solid lines. The overall relationship between a surrogate and future outcome, then, raises questions about selection of suitable populations for study, or treatment, allocation of potentially precious therapeutic resources, and even maintenance of therapy when the surrogate may predict its impending failure.

These are challenges to any kind of surrogate, including the fictional mouse model, or of modern imaging biomarkers, the focus of the next.

**Biomarkers for Alzheimer’s Disease:** Tremendous efforts have been devoted to the goal of biomarking Alzheimer’s, including the vast five-year, private-public AD Neuroimaging Initiative partnership (http://loni.ucla.edu/ADNI/).

In May 2006, leaders in neuroscience, ethics and policy came together at Stanford to talk both about the state of the art in technology as well as ethics challenges in five specific related areas. In each, the Algernon challenge comes into play. Short summaries of conclusions are provided here:

Medical and social implications: A combination of tools – imaging, proteomics and others - may ultimately provide the best answers but much work remains to be done. Meaning of brain health and brain disease will depend on and may change with the tools and efficacy of the tools used. Clinical goals and clinical endpoints must be articulated early in the process. Given the type and combination of tools and subsequent interpretations of meaning, there may be unintended challenges for insurance, stigma and disparities of health care that will depend ultimately on the efficacy of the markers that must be anticipated

Differentiating different clinical subtypes of AD: Our discussion of the range of possibilities for differentiating clinical subtypes of AD led to a discussion of populations appropriate for screening, and pros and cons to each. The five different possibilities the group considered are: screen patients who already have some mild cognitive impairment; screen all individuals when they reach the age of 65 years; screen asymptomatic individuals with risk factors; screen everyone who wants a scan. In consideration of the second possibility, imaging tests could be added advantageously to the host of other screening tests such as colonoscopy.
and mammograms that are recommended as people grow older. The greatest concern for this scenario however is that even with prevalence rates for AD approaching 10% in this age range, there will be a significant number of false positives. Considering the last possibility - scan everyone who wants one - the costs to the already fragile health care system, costs both in terms of access and sheer dollars, could be staggering.

Scanning protocols and modalities: The findings of the group for protocols and modalities focused on patient comfort and protection as variables of paramount importance. The Group recommended that acquisition and analysis protocols be standardized, and overall costs of eventual implementation contained. The Group further found that validation studies are especially needed for diagnostic/treatment decision-making, for patients vs. group data, and with respect to diversity of ethnicity, age and co-morbid disease. Management of incidental findings surfaces in this area again.

Research and clinical ethics issues: In the context of research and clinical ethics issues, the question of decisional-capacity emerged as a primary challenge. In the USA, there is a legal opportunity for putting advanced directives for research in place, but most people do not. Perhaps many people probably do not even realize that this option exists. Therefore, the interests of the patient, his or her decision-making guardian and family must be factored into the equation of whether or not to enroll the person in a study or trial.

The challenges of shared databases also require considerable ethics forethought and planning, since data acquired today may have countless uses that neuroscientists cannot even anticipate for the future. Acceptability of such future studies to subjects or their guardians, and re-contact must be handled openly during the process of obtaining informed consent.

Education, counseling and communication: The Group could not think of a single type of stakeholder that would not benefit from education about the content of research, utilization of technology and professional responsibility. In other words, everyone will benefit, and this includes the eventual commercializers of these methods – neuroscience entrepreneurs - a topic that will be addressed in detail below.

Ethics Analysis: The goal of predicting disease with biomarkers and surrogate end points is to improve upon the human condition by providing reliable information about treatment outcome, rate of decline, and possibly therapeutic benefit to slow or even halt disease. These worthy goals are challenged by the still relatively immature state of the technology. Given the momentum and progress in neuroscience, however, these challenges call for proactive consideration about how culture and values differ in terms of what defines benefit and risk, who will benefit and who is at risk, what methods must be in place to assure the maximum safety, comfort and protection of subjects and patients, and educational and policy needs.

Commercialization of Cognitive Neuroscience

Let me introduce the commercialization challenge by quickly reviewing some data that Matt Kirschen, John Gabrieli and I published in 2002. Slide 10 illustrates proportions of functional
MRI studies per year, alone or in combination with other imaging techniques, of different levels of functional complexity.

Slide 10

We coded each of the 3426 studies and found that in early years studies were largely dedicated to methods development and sensorimotor processing shown in red. We see studies, such as those of memory and language, introduced beginning in 1993. The studies that we coded for integrated complex higher cognitive processing, including those with ethical content, are shown in blue and yellow. They were first introduced in 1995 and increased significantly through 2001.

Slide 11

These are studies like those of Green et al.\textsuperscript{14} on moral judgment as correlated with changing blood oxygenation as subjects solved existential thought problems, Canli et al.\textsuperscript{15} of personality, and more recently by DeMartino et al.\textsuperscript{16} in the area of neuroeconomics involving what the authors call rational decision-making (Slide 11).
We also published overall trends with fMRI in 2002, updated them in 2004 and Matthew Kirschen spent the better part of the past September 2006 updating the graph with about 1500 new data points, at least up to 2005, the last full year indexed in PubMed (Slide 12). Overall, we are looking at about 8700 fMRI and CNS papers over 15 years. The number published in the first 10 years of the technology is equal to the number published in the past 2 years alone. Some other general observations for the past few years, as we would predict: there are proportionally many more papers in the thematic categories for complex higher order cognition - deception, judgment and consciousness - than ever before.

In a follow-on study, my group and I conducted focus groups and one-on-one interviews what on issues of greatest immediate concern for investigators involved in human neuroscience research such as the examples shown above. We predicted that it would be transfer to clinical practice, but this hypothesis was quite wrong.

From a detailed content analysis of responses from neuroscientists and those of other professional groups, it was transfer of the technology to outside the clinical setting and associated researcher obligations. This is summarized in Slide 13 with the checks illustrating most frequently occurring themes of 333 coded units for the 6 focus groups.
To illustrate this finding, one narrative offered by a neuroscientist from our transcripts captured the findings perfectly:

“… eventually we’ll be able to know a lot more about people through understanding more about how their brains work. And I think it would be terribly unfortunate if that resulted in some sort of long-lived cookies about somebody’s predilections or somebody’s emotional states or somebody’s tendency to anger or whatever. …”

“it strikes me that this is a domain that offers enough that’s novel in the area of information about one’s own persona that we ought to be thinking very seriously about.”

If images can capture function that correlate with selective functions, then means to obliterate them must exist as well - transiently certainly, with transcranial magnetic stimulation and perhaps in perpetuity with beta blockers.

This last video slide (Slide 14) provides some fiction related to the latter theme. It is an infomercial for a company portrayed in the movie Eternal Sunshine of the Spotless Mind in which a young man seeks to have selective memories of a failed romantic relationship erased. He engages the company of Lacuna, Inc that uses a procedure reminiscent of transcranial magnetic stimulation to accomplish this goal.

Slide 14

In his 2005 SfN lecture, Tom Murray shared his deeply personal story illustrating the potential for and the risks and benefits of suppressing memory using beta blockers such as propanolol. On the one hand, devices or drugs that could achieve this effect may impede memory consolidation of a tragic event, providing relief to those who suffer, for example, from post-traumatic stress and other disorders of mental health. At the same time they raise gnarly ethical issues about isolating what we integrate and carry forward as life experiences and thus tampering with the very essence of our consciousness and human identity.
If *Eternal Sunshine* was anything but science fiction, the film clip I showed you would be an egregious example of neurohuxtering. But there are many serious companies and prospects for neurotechnology today. In work I have conducted with Margaret Eaton and others, we identified more than 20 companies actively commercializing aspects of cognitive function (Slide 15). Some are funded through federal grants such as small business innovation research grants (SBIRs) from NIH and DARPA. Some of these companies are strictly tool developers, others focus on diagnosis, including devices that enable turn-key assessment of cognitive function by non-specialists. Others are innovating new marketing tools.

### Technology Development

<table>
<thead>
<tr>
<th>Type of Service</th>
<th>Industry Examples</th>
</tr>
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<tbody>
<tr>
<td>Acquisition Tools</td>
<td>Brain Resource Company, Corteva Solutions, GE Healthcare</td>
</tr>
<tr>
<td>Marketing and Strategy Services</td>
<td>Brigham Institute for Therapeutics, Neurosens</td>
</tr>
</tbody>
</table>

Slide 15

Health care market is still the biggest market. The World Health Organization estimates that in Europe, brain disorders that such companies are targeting cause 35% of the burden of disease, a percentage that is increasing. In the U.S., the market is $100 billion annually for Alzheimer’s disease alone; $56 billion for traumatic brain injury.

As commercialized neuroscience is in the public eye, so is the commercialization of personalized medicine. Health care and brain products are for sale today. Drugs for the treatment of central nervous system disorders are well regulated and may offer powerful choices for consumers in a range of health care systems. Direct to consumer marketing of neuro-products other than drugs, like CT and MR imaging for screening, are not regulated at all. We have examined this in print and radio ads, and most recently on the Internet. In work with Eric Racine, we have shown that this regulatory gap is being exploited, and we believe presents new risks to individuals to whom information about benefit as well as possible harm is not wholly conveyed. Selling to the healthy wealthy consumer who may be curious and is able to spend out of pocket dollars is one issue, but the challenge is especially vexing as many brain products and services are marketed directly to the very people who are most vulnerable: those desperate for a cure for a neurologic disease or seeking relief from mental illness.
In the context of the recently popular topic of commercializing imaging outside medicine such as for lie detection, some people think that it will take us to new heights from where polygraphy left off. Some people do not. But we can all agree that this is an era in which we hear a great deal about homeland security where applications of this technology may well find a home. If anyone has stood in a long security line and overheard, as I did, a passenger say “This is the gate where you get your brain scanned,” you will appreciate that public perception is as important as technology development as this episode in the history of neuroscience unfolds.

Slide 16 shows that the media, however well intentioned, fuels this kind of bantering, if not belief, with increasing coverage of new technology such as MRI as one example, but with an optimism that is not always well matched with cautions about limitations as the headline suggests in the British newspaper The Guardian in 2003: “The brain can’t lie: Brain scans reveal how you think and even how you might behave”. Singh et al. have new data on how the media can even be paradoxically out of synch with major trends in research and research funding, at least with respect to neurogenetic diseases like autism.

Where does an ethics analysis of commercialization lead of such data lead? It leads us to consider both the immediate and long-term challenges of this progress (Slide 17). In the short term, initial validity, communication of benefits as well as limitations, quality control, and fair access for all are key if benefits are truly to be realized. In the longer term, sustained validity, especially for small business developments, use and unintended uses are prevailing challenges.
Stakeholder Engagement

In 2003 Racine et al. \textsuperscript{22} first explored the view that the perspectives of all stakeholders are important to technology development and transfer – a move away from traditionally unidirectional information and methods flow from the bench to the bedside as shown in Slide 18 to a cycle of knowledge shown in Slide 19.

The goal is that by having a grasp of how providers and patients might use technology and the impact it would have on physicians’ practice patterns and patients’ self-image and compliance with treatment, R&D can be better prioritized and better targeted. In the knowledge cycle, the interdisciplinary professional community seeks a common voice and language, the media pursues a stronger partnership between science and journalism, and the critical voice of patients, caregivers and stakeholders is sought seamlessly and genuinely.

As Gaskell wrote in Science in 2005 \textsuperscript{23}:

“The public expect and want science and technology to solve problems, but they also want a say in deciding which problems are worth solving.”
[It is a matter] “… of seeing the public as participants in science policy with whom a shared vision of socially viable science and technological innovation can be achieved.”

Some Examples of Studies of Stakeholder Engagement and Related Issues

**Major Depression:** In one study, Illes, Arnow et al.\textsuperscript{24} showed that patients with major depression are eager for and open to the prospect of imaging to aid in their diagnosis. Indeed, in 91% of 72 inpatients and outpatients indicated a high desirability for and high receptivity to functional MRI. The study revealed main effects from patients who reported that scans would improve understanding of their condition, and mitigate effects of stigma and of self-blame, and we are now analyzing the data to explore the relationships of these effects with treatment choice and compliance. Further work will enable studies of patients with other forms of mood and thought disorders and explore their attitudes towards this technology and others including new devices, deep brain stimulation, and even the re-emergence of ECT.

**Pediatric Neuroethics:** Many questions about the future of functional imaging also apply to pediatric neuroethics, where true prospects for predicting development and outcome perinatally and in early childhood exist (Slide 20). But benefit will only outweigh the risks of stigma, labeling and limited or poorly evolved resources if the interests of our pediatric constituents and their families are understood, and the ethics issues are sorted out before the technology is brought forward. Gardner and his colleagues\textsuperscript{25} hope, for example, that a new group of professionals – neuroeducators – who have expertise both in pedagogy and in neuroscience will emerge in response to research and clinical translational capabilities of imaging. Neuroeducators could usher complex new technology and information into the lives of these individuals more effectively and constructively than ever before.

Slide 20

The technology, and not entirely remote possibilities for population screening, could have also a special impact on socioeconomically disadvantaged children in our society, for example,
especially given some of Farah’s data on the effects of poverty on the developing brain and implications for public policy.

New imaging studies of patients in limited states of consciousness such as those by Schiff et al. and just recently by Owen et al. are pushing the envelope both on the technology and ethics side (Slide 21). These studies are a sine qua non of where critical ethics thinking is needed right alongside protocol design and certainly before dissemination of results. In a true collision between science, well-intentioned neuroscientists, the media, and the public, the most desperate families were given, or at least took hope from what they heard and read about signs of cognitive function in patients in varying states of consciousness.

Each time one of these small N studies came out, imagers and ethicists alike have received requests from families for scans for loved ones, but have had little to offer in return beyond existing standards of medical practice.

**Ethics Analysis:** These frontier applications, as different as they are, may hold great promise in the areas of mental health, neurodevelopmental and CNS disorders, especially if they lead to interventions that can be tailored to meet stakeholder - individual, community and society - needs. They represent areas where understanding of those needs is imperative to meet that goal. However, they also all raise important questions about the meaning of the data for the individual, what the person can do, and what the professional community can do for the person. In depression and for children - perhaps a great deal. For patients in limited states of consciousness - that is less clear at this time. In disorders of consciousness specifically, we have to understand and establish motivation for testing and endpoints if this neurotechnology were to be rolled out clinically. Is the goal to obtain data that will tell a caregiver that the patient will recover, even to pre-trauma cognitive function and familiar personality, or that it is time to take measures and harvest her organs? The issues are further complicated by new clinical neuroethics studies by Lansberg et al. showing significant effects of professional training of physicians on expected outcomes. Those with specialty neurointensive training tend to be far more optimistic than those without.

There are anecdotal cases of miraculous recoveries and we should not ignore them, but the science requires large scale, multi-modality, longitudinal efforts if it is to bring forward the
benefits intended and mitigate, among other things, the substantial consequences of positive and negative information to which we do not yet have the tools to respond.

Next Frontiers

*International Neuroethics*: There are currently 12 countries around the world today with known or peer-reviewed activity in neuroethics (Slide 22).

Slide 22

Going global will open up the world of neuroethics from everything spanning consent – individual, communal or tribal – to perceptions of and interventions for neurologic and psychiatric disease that are multicultural and multidimensional. Our own early work has focused on two issues in particular: public engagement and, with Gladys Maestre at the University of Zulea in Venezuela and Matthew Kirschen at Stanford on different perspectives and ethics principles that guide views on enhancement with drugs and devices 31.

We surveyed 186 medical and nursing students and learned from them that drugs are acceptable forms of enhancement for attention, cognition and mood. Acceptability of devices is more variable, and neither is acceptable for altering personality. The ethics principles dominating these findings are beneficience, safety and risk-benefit for drugs, and risks of unintended use for devices. We will be continuing this work in North America, as well as at a new international field site in Tokyo, Japan.

*Regenerative Medicine*: Regenerative medicine in the CNS represents a unique challenge to neuroscience and ethics. Early discussion has focused on source and scarcity of human embryonic material and even on issues of personhood Grisolia suggests when he wrote 32:

“How much can we reweave the cerebral tapestry without creating a new self, a new identity?”

Human-animal chimeras such as human neurons transplanted into mouse brain as shown here may give pause and good reasons for critical ethics thinking early in the research process. As Hank Greely has said, “The centaur has left the barn.” 33 However implausible that changes in morally relevant mental capacities that yield a moral confusion of sorts between humans and animals will ever be witnessed, ethics analysis by Ruth Faden, Guy McKhann and others 34 has begun. They assert particular cautions for neural engraftment into
certain species such as great apes, and have made specific recommendations regarding the proportion of engrafted human cells into animal species and sites of integration.

**Brain-Machine Interfaces:** The prospect of humanoid robotics may be a new horizon for neuroethics that has already gained momentum on the international scene in Europe and Japan. For example, Kawato, Kamitani and Kumura at ATR and Honda have shown that fMRI signals of a human performing the hand motions of rock-scissor-paper in a scanner can drive a robotic hand to do the same with only minimal time delay. Will telerobotic machines, operated by remote signals associated with thinking, acquire autonomy, the ability to self-regulate, self-motivate?

**Conclusions**

The cases I have reviewed are naturally only a sampling of this *Brave Neuro World* suggested by this cover of *The Nation* in Slide 23.

I have not touched upon many issues such as the neurobiology of religion, imaging genomics, addiction and agency, or the ethical future of nanomedicine. Each case that I did discuss, however, those well underway in the world of neuroethics such as incidental findings, biomarkers, commercialization, and those emerging – pediatric neuroethics, regenerative medicine, and brain machine interfaces, illustrate many different types of neurochallenges for neuroethics. They all embody:

> The need for planning and anticipating ethical issues at the bench, at the bedside, and in the public domain as critical steps.

> Disclosure and consent, especially in the face of new and unknown capabilities, communication of benefit and promise, risk and limitations as key principles.

> Fairness, privacy and access as fundamental values.
The challenges draw out expanded professional roles that have surfaced for the neuroscience community. They include (Slide 24):

> Responsiveness – duty of care within and outside the research setting
> A new partnership with society that promotes public understanding and democratic debate
> Proactive thinking.

Slide 24

A broad landscape of neuroethics touches all of neuroscience. It is important to continue to build on history from the wide range of disciplines that can contribute to this one and to get involved: join the Neuroethics Society; help build capacity in the next generation; contribute by publishing in new journals such as the American Journal of Bioethics – Neuroscience.

Advances in neuroscience must be informed by an ethically coherent agenda based on the needs of the neuroscience community. Neuroethics must keep up with the pulse of neuroscience and deliver knowledge that ensures the highest integrity of research, subject protection, and better care and quality of life for patients suffering from diseases of the CNS. As neuroethicists, we will continue to identify challenges in neuroscience. More importantly, we will develop the tools to address them: tools that are flexible, practical, useful and, therefore, welcome. Delivering those tools, in fact, is a commitment with which I close this paper.

Thank you.

*****
3. Bacon F. *Knowledge is power (Ipse Scientia Potestas Est)* 1597.
8. NHLBI. Reporting Genetic Results in Research Studies Meeting Summary. Paper presented at: Working Group on Reporting Genetic Results in Research Studies Meeting Summary, 2004; Bethesda, MD.