SCIENCE AND SOCIETY

Neuroethics: an agenda for neuroscience and society

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The last decades of the twentieth century saw the rise of modern genetics. Now, many regard the initial decades of the twenty-first century as an era that promises explosive growth in our knowledge of the brain. Just as ethical issues have been a part of discourse in genetics from the outset, we are now paying attention to ethics in neuroscience. But whereas the ethics of genetics was in many ways a new conversation, the philosophical discussion of mental function and behaviour is an ancient tradition that both informs and complicates the emerging field of neuroethics.

Announcing the arrival of neuroethics, the Charles W. Dana Foundation and Stanford University sponsored a highly publicized conference, in which I participated, on May 13–14 2002 in San Francisco. The multidisciplinary sessions included talks by leading scientists on various aspects of neuroscience, with reactions from philosophers, law professors, bioethicists and science educators.

Some participants wondered about an analogy with the 1975 Asilomar conference on the potential hazards of recombinant DNA technology. Unlike Asilomar, however, there is currently no widespread public clamour for self-restraint on the part of the relevant scientific community. If anything, there is a broad-based fascination with the prospects of neuroscience-based innovation, especially as awareness of the ravages of neurological diseases has grown, and as ageing baby boomers hope that science will help them extend their own mental acuity. In addition, early recombinant DNA technology was not nearly as steeped in commercial opportunities as current neuroscience, which operates in the middle of the lucrative environment that is created by modern psychopharmacology.

Free will and mind–body reductionism

In the context of this new interest on neuroethics, there are long-standing issues on the control or alteration of mind and brain that are sure to surface again. There is no better example than free will and determinism, a potential philosophical quagmire that has, since the ancient Greeks, inspired some of the most imaginative intellectual footwork. Does our growing knowledge about the origins and physical basis of mental states, let alone the possibility of controlling them with some specificity, threaten the liberal ideals of freedom and personal responsibility? In short, is neuroscience on the road to showing, once and for all, that mental states reduce to brain states, and even to brain states that could be subject to direct manipulation?

Consider the following results that exemplify what some may find disturbing information that is provided by the new brain science. Using evidence from functional imaging data, investigators found that social judgments about trustworthiness seem to be based on facial representations that involve the extrastriate visual cortices in the fusiform and superior temporal gyri. Perceptual processing is then linked to social judgments, drawing on the amygdala and regions of the prefrontal and somatosensory cortices[1]. Similarly, researchers from Stanford University have obtained evidence that the fusiform region is involved in the preferential response to faces of one's own race[2]. What implications do such data have for the notion of free will?

There are several different concerns here that should not be conflated. First, is the mental reducible to the physical? Second, if the mental is reducible to the physical, does that imply that there is no freedom of the will? Third, if the mental can be controlled by physical manipulation, does this imply that there is no freedom of the will?

Even if the mental is reducible to the physical, it does not follow that free will is an illusion, nor does it follow that cases in which the mental is manipulated cannot be distinguished from cases in which it is not. However, the challenges involved in drawing such distinctions might be formidable.

Let us begin with the problem of mind–body reductionism, one that is vexed with imprecise language, including the notion of reduction itself. Probably the most widely admired contemporary treatment of this and related issues is that from Patricia Churchland. Well before the current enthusiasm for neuroethics, Churchland published her landmark work *Neurophilosophy*[3] in 1989. Churchland canvassed the various meanings of reduction and traced the epistemological debates behind them, noting that the underlying question is which theory of the mind is reducible to which theory of the brain, or vice versa. There is, as she points out, no received view of the interconnections between mental states and behaviour, but the idea that there could be such a theory is neither implausible nor necessarily offensive. As I shall note shortly, philosophers have been living with this possibility for a long time while managing to preserve useful ideas like freedom of the will.

The view that there is something offensive about intertheoretic reduction seems to rest on the view that there is something inherently objectionable about the idea that non-physical brain states can be explained in

terms of neuronal states. Dualists and non-dualists have raised such objections, but they do not seem to be persuasive. For example, the view that the mental and the physical are two distinct substances has a hard time explaining their interaction.

A more subtle position to take is that mental properties are distinct from physical properties, so that mental experience can, at most, be said to emerge from the physical. Here, a great burden is placed on the idea of emergence, which seems to rule out a comprehensive neurobiological theory. Yet various difficulties infect 'emergentist' views, including that, in at least some cases, they run aground on the intentional fallacy — thoughts about objects are mistaken for the properties of the objects themselves.

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Another set of objections to intertheoretic reduction argue that the logic of nonphysical description is distinct from the logic of physical description — that the relations between the sentences used to describe one domain are different from those that are used to describe another. Here, again, the objections appeal to folk psychology — the commonsense means, at our disposal, to explain behaviour with reference to beliefs, desires, expectations, goals and so on. But if not all cognitive activity operates like language (as is the case for some models of information storage or seemingly intelligent animal communication), then sentential relations need not be the ultimate appeal, and it remains an empirical question whether folk psychology could be improved to the point of radical transformation by neuroscientific insights.

Meanwhile, according to Churchland, we are left with a more or less serviceable theory of the mental — folk psychology. Scientific discoveries in the neurosciences (proceeding, perhaps, from the kinds of examples that I will consider shortly) might require gradual improvements in folk psychology. These improvements, she observes, could proceed so gradually that folk psychology will be seen as having been replaced by, rather than reduced to, a theory of the brain.

Suppose that the reductionist debate continues indefinitely. As the hypothesized ongoing refinement of folk psychology by improved neuroscientific understanding takes place, history gives us reason to believe that the idea of free will will be left standing. To the fledgling student, the issue of freedom and causation has long seemed an enticing and hopeless quandary — the Scylla and Charybdis of psychology. But the most notable thinkers have been unruffled by the matter, often taking a middle-ground position known as 'soft determinism', the view that we are capable of entering into the chain of causes of our thoughts and actions. That is, although my individual psychology and experience shape my preferences, they do not do so in detail, and I am capable of inserting more or less original choices into the chain of causes. So, even knowing the whole of a person's reinforcement history would not be sufficient to predict all of their behaviours. Recent analytic philosophers have gone so far as to call free will and determinism a pseudo-problem — one that subsists only in the linguistic expressions that are available to us.

It is worth recalling in an overview like this paper that the most important precursor of modern neuroscience was William James, the Harvard-trained physician who spent much of his career reflecting on the implications of psychology for philosophy. James' typically vigorous take on the question of free will was to assert what he called 'the will to believe' — that free will could be established by the act of determining to believe in it. What refutation to such a declaration is possible? If either option is equally plausible, he argued, one might as well reach for the more attractive of the two. James' approach is perhaps more compelling in the context of his remarkable *The Principles of Psychology*[4], published in 1890, in which he developed nearly all of what was then known about the brain and nervous system into a coherent psychological theory.

The implications of this information for moral development were of particular importance for James. In this respect, he followed a long line that started with Aristotle. As the original soft determinist, Aristotle argued that subjects are partly responsible for the kind of person they become by, for example, choosing those with whom they associate, a choice that in turn influences their own moral character. James continued a tradition that Aristotle started in the analysis of habit formation. James applied the early lessons of neurophysiology to admonitions about launching strongly and repeatedly on any new behaviour to establish a pattern in neural material that will increase the likelihood that the behaviour will be repeated, gradually with less effort. Within a few years, and influenced by these ideas, John Dewey designed an educational system that was intended to bolster the habits of inquisitiveness and problem-solving skills, the beginning of the 'progressive' education movement in which the development of learning habits are viewed as more important than absorbing factual content.

All of this discussion is by way of pointing out that the ground has long been prepared for anticipated transformations in folk psychology by previous generations of thinkers who observed such changes in their own lifetimes and who seem to have expected them to continue. This is not to say that the process has been or will be without stress, both at the level of theory and at the level of social practices. In the rest of this article, I will allude to examples of these stress points and their implications, proceeding roughly from the more immediate to the science fictional. However farfetched, the most speculative implications are appropriate areas for the ethics of neuroscience. The point of such a discourse is not merely to assess the implications of brain science in topics of more immediate concern, such as changing ideas about legal responsibility, but also to consider the social consequences over the longer term.

Reductionism redux

The legal system is at the frontier of formal social responses to advances in scientific understanding of human behaviour. Numerous law courts have already begun to assess defense strategies involving medications that were alleged to compromise the defendants' *mens rea* — the state of mind required for culpability. A number of such cases have involved people who were undergoing treatment with fluoxetine (Prozac). In these cases, the law courts have focused on expert testimony concerning the causal role of the medication in committing a crime[5].

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As the legal system is inclined to look to the scientific community for guidance in establishing culpability when psychoactive medication is implicated (therefore participating importantly in the modification of folk psychology), it will also do so in cases of traumatic brain injury. Such cases, involving lesions of the prefrontal region, have been observed as leaving the patient with

adequate moral reasoning, but without the capacity to act upon an appropriate conclusion[6]. Improved imaging and diagnostic techniques, particularly if damage to the ventromedial sector can be identified[6], show promise for identifying similar cases that stem from non-traumatic disorders. So, a more subtle approach to offenders whose behaviour can be correlated with trauma in certain neural systems seems inevitable.

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A reasoned respect for the law depends in part on the extent to which findings of culpability are consistent with the best available evidence for self-determination. As Damasio[6] notes, a criminal who is evidently brain damaged has the moral status of a patient whose condition could be brought under a medical rubric. But emerging data indicate that the traditional category of 'criminal insanity' might not necessarily apply to a person who is capable of understanding, but not appreciating, the difference between right and wrong. To use Damasio's terms, cases in which understanding is a function of the reasoning/decision-making system and appreciation is a function of the emotion/feeling system[6]. It seems inevitable that further categories will have to be developed to capture more precise senses of culpability, as has already started to happen in cases that involve psychoactive drugs.

A far different and more speculative problem with the law arises from the possibility that subjects could deliberately forget actions for which they should be held culpable, but for which the evidence is circumstantial. Work by Levy and Anderson suggests that people who have been abused by their parents are able to intentionally repress those memories[7]. Clearly, in these cases, there is a powerful psychological impetus to forget trauma at the hands of those on whom one is dependent. It would be interesting to know if the same mechanism can be used to forget selected events or actions, even without the same emotional drive, and also if physiological indicators like the galvanic skin response can be inhibited. Psychologically sophisticated offenders would be handed a new tool to evade prosecution.

Personal identity

Closely related to these issues about free will are concerns about personal identity. The past few years have already witnessed a vigorous debate about the implications of Prozac and other selective serotonin reuptake inhibitors. These psychopharmacological interventions seem to last longer, and perhaps be more pervasive in their effects on the human personality, than more familiar mind-altering substances with fewer side effects. However, the ethical issues that are raised in connection with the newer psychoactive drugs might not be different from assertions that these or any other alterations of mentation or conduct are 'artificial' and therefore suspect. To make such assertions stick, a background theory of the 'natural' is required, a challenging job in itself. In any case, the decision to use a drug that modifies one's personality may be a free choice, at least in the sense of soft determinism, and therefore an expression of authentic personality.

This view applies as long as the effect of medications ends as they leave the system, and there can be a return to baseline and to the individual choice about continuing using them or not. A more ethically challenging scenario runs as follows: suppose that we have the ability to permanently alter the brainstem nuclei that release serotonin, among other neurotransmitters. In primates, it has been found that the greater the number of a subtype of serotonin receptors, the less aggressive and more social is the animals behaviour[8]. Suppose further that neuronal deficiency can be determined in at least some extremely hostile subjects. For those who have trouble controlling their hostile behaviour, drug therapy would no longer be needed if the number of crucial neurons were increased to the normal range. Old-fashioned psychosurgery, classically in the form of a prefrontal lobotomy, deforms normal structure. Would this newer form of psychosurgery be acceptable if it were seen as helping the brain attain the physiological standard?

New brain tissue grafts are only one sort of medical intervention that is suggested from information about the relationship between neurons and behaviour. Another study leads to the intersection of neuroscience with genetics and prenatal diagnosis. Investigators at the University of Wisconsin reported that members of a group of men who were both abused as children and had an alteration in the gene responsible for producing monoamine oxidase A (MAOA), were nine times more likely to commit criminal or anti-social acts than control subjects[9]. If this or other neurotransmitters are roughly associated with socially offensive behaviour, even under less extreme environmental insults, they could be brought into the controversy over preimplantation genetic diagnosis. Prospective parents might therefore test embryos for the MAOA marker before implantation to avoid giving birth to a child with this particular potential for criminality.

Researchers from Harvard and Beth Israel (Boston) Medical Center are pursuing a more general approach to disorders of brain development[9]. The group reports that they have already identified some of the genetic alterations that result in brains that are too small, abnormally patterned, or show evidence of abnormal location of cortical cells. Specifically, they report that the cerebral cortex of transgenic mice with an alteration in the *β-catenin* gene showed gyri and sulci, which are commonly not found in the brains of lower animals. This group theorizes that β-catenin regulated the proliferation of progenitor cells that lead to a thickened cortical sheet, as is present in human beings[9].

"One can only imagine the pressure to bring to fruition one of the great science-fiction scenarios: genetic engineering … that seeks to enhance mental capacity."

Although it is far to early to assess the relation of the β-catenin regulator to intelligence, results like these may lead us to think about developing diagnostic tests for disorders such as mental retardation or epilepsy. Suppose that this kind of work were to eventually lead to the control of at least some of the mechanisms that control the functional performance of the brain. One can only imagine the pressure to bring to fruition one of the great science-fiction scenarios: genetic engineering that not only corrects for the presence of genes that code for conditions recognized as patent disorders, but actually seeks to enhance mental capacity.

Examples like this suggest that neuroethical debates are unlikely to appear completely separate from more familiar bioethical issues that arise in genetics and reproduction. An example of a controversy that, in retrospect, could have been brought under the ambit of neuroethics, was the use of fetal tissue for implantation into the brains of sufferers from Parkinson's disease and other neurological disorders. In the late 1980s, claims of success made by surgeons in Mexico and Sweden stimulated a debate about the acceptability of using fetal brain tissue in

this way. Unfortunately, the early hopes for the procedure have not been realized, but the incident foreshadowed the current dispute about embryonic stem cells.

Impaired consent

We can add to this list of previous neuroethics issues, experiments with persons whose decision-making capacity, and hence their ability to give valid consent, is impaired. This is a surprisingly old problem to which governments in Europe and the United States tried to regulate as long ago as 1900. Patients in medical institutions, including the mentally ill, have long been the preferred research subjects because they are confined and can be monitored. Historically, experiments involving asylum inmates have not always been confined to conditions from which they suffered. Often they were 'animals of necessity' for experiments that required human models. Gradually the law, policy and public outcry have made persons with mental disorders less desirable subjects[11].

The opportunity to diagnose and treat dementias, led by research on Alzheimer's disease, has renewed attention to the ethics of research on people with impaired or absent decision-making ability. Imaging techniques, sometimes combined with agents intended to provoke neurological processes, have created enormous pressures on the old consensus. Some agreement has crystallized around the proposition that it is possible to devise protection for those with decisional impairments that are consistent with low-risk experimental procedures or for those that, while of higher risk, carry some potential benefit to the patient. However, several stumbling blocks remain. One is the uncertainty of who would authorize such research to be carried out if the patient cannot, a particularly serious issue for incapacitated adults. Many of the lessons that can be learned from basic research with impaired brains, as well as innovative translations of neuroscientific discoveries to clinical medicine, turn on the social question of who would give permission on behalf of those who cannot give it by themselves[12].

A different sort of quandary sits on the border between research and therapy. Early detection of lesions associated with Alzheimer's disease might only be the leading edge of diagnostic tools for neurological disorders in the preclinical state, disorders for which there are no effective therapies. In this case the capacity of the patient at the time of testing is not in doubt. A number of those at risk from Alzheimer's disease might request brain imaging. Some clinicians will view testing for risk status as appropriate, arguing that it will facilitate long-term planning, whereas others will urge that any such detection should only take place as part of a clinical trial until a medical intervention is available. Some consensus will be required concerning appropriate counselling in such cases.

In these circumstances, we can learn from history. When pre-symptomatic diagnosis for Huntington's disease became available, some expected a rush to testing. But in the absence of an adequate intervention, many have opted against knowing their genetically determined destiny. If ignorance is not exactly bliss, neither is knowledge in the absence of a solution.

"Gradually the law, policy and public outcry have made persons with mental disorders less desirable [research] subjects."

Manipulations; natural and not

Some neuroscientific discoveries, once they become more widely appreciated, are likely to become objects of popular imagination. Magnetic resonance imaging (MRI) studies conducted by colleagues at Emory University indicate that women who undertook cooperative acts during the Prisoner's Dilemma trials experienced activation of dopamine-rich neurons[13]. The Prisoner's Dilemma is a means to analyze cooperation in which two players win when both cooperate, but if only one of them cooperates, the defector wins more. Businesses that value socially cooperative employees might be interested in using these measures of proclivity on prospective workers as a hiring screen, even though they might not add anything to psychological testing and letters of reference from previous employers. On the other hand, firms interested in more competitive types of employees might use a pre-employment MRI to ferret out those who experience less pleasure from cooperation. It would be interesting to know whether these scans will be received as unacceptably invasive or just part of the job search routine.

A different sort of competitive advantage might be sought by ardent lovers with just enough neuroscientific knowledge to be dangerous. Investigators recently reported that thin, slow cortical fibres are associated with the pleasure that comes from a loving touch[14]. These fibres connect to the somatosensory system and are present at birth, whereas the thicker fibres that rapidly convey sensation develop somewhat later. This Swedish and Canadian team theorizes that an infant is therefore capable of experiencing the emotional effect of parental touching before the tactile sensation itself[14]. Considering the profound psychological depth of these feelings, unscrupulous Lotharios may someday find techniques for thin-fibre stimulation to be important parts of their arsenal.

Aristotle's taxonomic biology, built around the classification of flora and fauna into genus and species, helped give credence to his metaphysical doctrine of natural kinds. Since then, the idea of species mixing has been taken as 'unnatural'. Natural-law philosophy draws the moral implications from this doctrine, with bestiality as a prime example of a crime against nature based on the essential distinctness of natural kinds. When a presidential commission on ethics set out early rules for genetic engineering in the 1980s, the species barrier was cited as one to be respected.

To paraphrase Justice O'Connor's famous remark on the trimester scheme for the regulation of abortion, the species barrier is a standard at war with itself. A pincer movement has been established by the results of comparative genome projects on one side, and the need for animal models with telescoped life spans for critical medical research on the other. Both undermine the commitment to the view that each species has its own unique essence.

Studies that aim to produce genetically altered rodents with human neurons are an interesting example, and might someday test public tolerance of species mixing. Researchers have identified one among presumably many genes linked to human speech. But this particular gene, *FOXP2*, is especially important because it appears to have conferred tremendous evolutionary advantage around 200,000 years ago, when modern humans appeared[15]. To test this claim, the creation of a genetically modified mouse with the *FOXP2* alteration seems to be the obvious next step. Interesting changes in physiology and behaviour would presumably not include a talking mouse, as one of the investigators joked to the media, but at what point, if any, would the public find the presence of human neural tissue in mice to be an intolerable breach of the species barrier? It may only be fortuitous that the creation of mice that are transgenic for the Huntington's disease gene has not already aroused public anxiety about species mixing.

Once again, there are historic analogies to be drawn. Initial discomfort with porcine heart valves and other animal–human tissue grafts have given way to routine, in spite of continuing concern about the introduction of animal viruses into humans. Neural tissue,

however, may push up against what Leon Kass, the chairman of the president's Council on Bioethics, calls 'the wisdom of repugnance,' especially if more than a tiny proportion of neurons is involved. A mouse with a brain that was entirely constructed from human neurons would surely provide remarkable research opportunities, as well as probably prompting a global debate.

Mind wars

During the 1940s and 1950s, the bulk of psychological research funding was provided by national security agencies that were interested in gaining an advantage during the cold war. Many of the scandals associated with this research, such as the CIA and army experiments with LSD and other hallucinogens, has become part of our cultural legacy[16]. They have also spawned a legion of conspiracy theorists prepared to entertain any rumored 'mind-control' technology without being inhibited by scientific implausibility. However, national security agencies continue to be interested in the benefits that could be conferred by scientific breakthroughs, as shown by the current attempt of the United States government to control the publication of data deemed related to national security that has been obtained through research supported by federal grants or contracts. Paranoia and naivete about these matters are not the only alternatives.

> "… the species barrier is a standard at war with itself."

One favourite worry of conspiracy theorists is that of long-range surveillance by state authorities. The introduction of increasingly sophisticated imaging technologies, such as functional MRI will probably give such fears a field day. Perhaps these fears would not be without merit. If devices based on these principles could be small and sensitive enough to detect high blood flow in neural systems associated with violence, they would be of great interest for use in airports and other sensitive public spaces. People who activate these alarms could be stopped and interviewed, or simply closely monitored while in the facility through the already ubiquitous video surveillance system. The civil liberties issues at stake here hardly require elaboration.

The potential military applications of neuroscientific developments are rarely mentioned in the literature. Daniel L. Schacter provides an exception; in *The Seven Sins of Memory*[16] he gives an example related to the gene that codes for the *N*-methyl-D-aspartate (NMDA) receptor. As this gene is linked to synaptic plasticity, mice with extra copies of a subtype of NMDA receptors showed superior learning skills. Schacter notes that if NMDA proves to have the memory-improving properties that the early work indicates, it might not only lead to a useful therapy for people with memory disorders, but might also be useful in those with normal memories. Again, we face the question of whether such genetic intervention in brain processes is acceptable, and under what conditions[16].

Particularly striking is Schacter's report of an observation by neurobiologist Tim Tully. A pacifist, Tully acknowledges that memory-enhancing medications would be very attractive in the heat of combat, when complex information about, say, a target-rich bombing mission, must be apprehended by fighter pilots in a short amount of time and many details stored. Schacter's allusion to the national security angle of the fruits of neuroscience, brief as it is, is nonetheless one of the few such references in this literature.

One need not, of course, adopt Tully's view of the matter. As is the case for researchers in other fields, the post-9/11 environment should prompt a discussion about the moral responsibilities of neuroscientists that includes the aims and implications of their work, with particular attention to the agendas of various funding sources. In other words, they will need to join the ranks of atomic physicists and geneticists in fighting a moral crucible. If the neurosciences are indeed poised for their own great leap forward, such will be the burdens of success.

Is neuroethics new?

The frequent references made in this paper both to important historic figures in philosophy and science, and to the longstanding issues and debates, have perhaps tipped the reader to my view that neuroethics is in some ways old wine in a new bottle. There is no reason for surprise here, but some reason for comfort. Ethical problems seem to never be completely new; there are always precursors and therefore analogies to be drawn. And there are prior conceptual schemes to be considered and revised or reformed. If there is an appearance of novelty as ethical issues come to widespread awareness, it is mainly because of peculiar aspects of a particular case that oblige a new analytical approach. In the early days of bioethics, many issues attracted attention because of new technological capabilities, such as the implications of life-extending modalties for the definition of clinical death. With its access to improving technologies, particularly functional imaging, current work in the neurosciences provides rich ground for such cases. Many of those engaged in these efforts will find themselves the subjects of the sort of public attention that was previously experienced by their colleagues in nuclear physics and genetics. Neuroscientists will increasingly be challenged to explain the significance of their work in moral as well as scientific terms.

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Online links

DATABASES

The following terms in this article are linked online to:

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