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Neuroethics: the practical and the philosophical

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Introduction

Almost three decades ago, in the picturesque coastal retreat of Asilomar, California, a group of molecular biologists gathered to discuss the safety of the newly developed recombinant DNA technology. In the years since, concern about the risks of genetic engineering have remained prominent in the public consciousness, as well as commanding the attention of academic bioethicists, government regulators, and biologists themselves. At the start of the 21st century, neuroscience has developed to a point where it, too, may have profound effects on society, extending far beyond the research laboratory or medical clinic.

Like the field of genetics, neuroscience concerns the biological foundations of who we are, of our essence. The relation of self to brain is, if anything, more direct than that of self to genome. Perhaps more important, neural interventions are generally more easily accomplished than genetic interventions. Yet until recently there has been little awareness of the ethical issues arising from neuroscience. Beginning in 2002, neuroscientists began to address these issues in the scientific literature (e.g. 1, 2, 3, 4 and 5) and the field gained a name, 'neuroethics' [6].

Neuroethics encompasses a large and varied set of issues, and initial discussions focused on various different subsets of those issues. Some neuroethical issues concern the practical implications of neurotechnology for individuals and society. Technological progress is making it possible to monitor and manipulate the human mind with ever more precision through a variety of neuroimaging methods and interventions. For the first time it may be possible to breach the privacy of the human mind, and judge people not only by their actions, but also by their thoughts and predilections. The alteration of brain function in normal humans, with the goal of enhancing psychological function, is increasingly feasible and indeed increasingly practiced. At the same time, progress in basic neuroscience is illuminating the relation between mind and brain, a topic of great philosophical importance. Our understanding of why people behave as they do is closely bound up with the content our laws, social mores, and religious beliefs. Neuroscience is providing us with increasingly comprehensive explanations of human behavior in purely material terms. Although the field of neuroethics is young and still evolving rapidly, the time seems ripe for a review in which the key issues of neuroethics, both practical and philosophical, are surveyed and placed in relation to one another.

Brain imaging and brain privacy

Among the neuroscience technologies that present new ethical challenges of a practical nature is functional brain imaging. This includes the familiar false-color images of positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), as well as the electroencephalography-derived methods of event-related potentials (ERPs) and magnetoencephalography (MEG) and optical imaging methods such as near infrared spectroscopy (NIRS). These methods vary in their invasiveness and portability, which constrain the uses to which they can be put, although any one of them can be used to obtain personal information surreptitiously, in a study ostensibly designed for a different purpose. In principle, and increasingly in practice, imaging can be used to infer people's psychological states and traits 1, 3 and 7.

For example, in 'neuromarketing' brain imaging is used to measure limbic system response to a product that may indicate consumers' desire for it. In one recent demonstration, brain activity related to soft drink preference was sensitive to both the taste of the drink and to the brand name, with Coke™ evoking more activity than Pepsi™ only when subjects knew which brand they were tasting [8]. To the extent that neuroimaging can measure unconscious motivation to buy, it provides a valuable new kind of information for marketers.

Another potential use for functional imaging of brain states is lie detection. Although fMRI-based lie detection is far from feasible in real-world situations, researchers have found correlates of deception in the laboratory [9]. ERPs come closer to providing actual brain-based lie detection. They have been used to identify 'guilty knowledge' by distinguishing responses to items that are generally known to be associated with a crime and items that only the perpetrator would know are associated [10]. An example is shown in Figure 1. This method, called Brain Fingerprinting by its developer, has been admitted as evidence in one court trial and is being promoted as a means of screening for terrorists (www.brainwavescience.com).

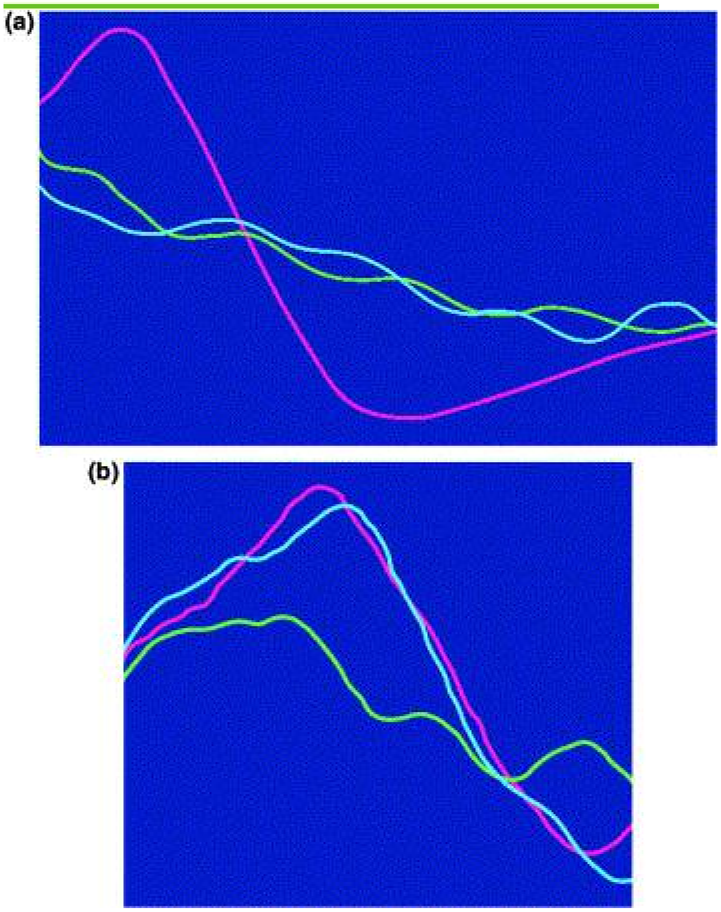

Figure 1. ‘Brain fingerprinting’ is a technique based on event-related potentials (ERPs) that promises to help discriminate criminal perpetrators from those who are innocent, and has also been considered as a means of screening for terrorists. It is based on the finding that information might evoke different ERPs depending on whether the subject recognizes the relevance of the information, and the assumption that the perpetrator of a crime will be familiar with details of the crime that would be unfamiliar to an innocent person. Stimuli that are irrelevant (green) to a crime and stimuli that are known by all to be relevant (red) evoke distinct ERPs that serve as standards against which to compare the ERP evoked by relevant stimuli known only to the perpetrator (blue). **(a)** illustrates the ERPs expected of an innocent person and **(b)** the ERPs expected of someone with a perpetrator's knowledge of the crime.

Psychological traits also have physical correlates that are measurable with current brain imaging technology. Like genotyping, ‘brainotyping’ may be able to reveal mental health vulnerabilities 11 and 12 and predilection for violent crime [13]. Unconscious racial attitudes are manifest in brain activation [14]. Sexual attraction and even the attempt to suppress feelings of attraction have neuroimaging correlates [15]. A growing body of literature has investigated the neural correlates of personality using brain imaging, including extraverion and neuroticism, risk-aversion, pessimism, persistence and empathy (e.g. 16, 17, 18, 19, 20, 21 and 22).

Of course, none of these characteristics can be accurately inferred by imaging (or for that matter, by genotyping) at present. Brain imaging is at best a rough measure of personality, but this is not to say it is uninformative even in its current state of development. The work of Canli and colleagues 16 and 17 on extraversion illustrates this. In their initial experiment, they found that extraversion was correlated with amygdala response to pleasant stimuli, using photographs of puppies, ice cream, sunsets and so on [16]. In a follow-up experiment [17], they confirmed this finding concerning the amygdale with a different type of pleasant stimulus, happy faces (see Figure 2). Although the points are scattered about the regression line, the correlation is nevertheless moderately strong. Such correlations can in principle be used to narrow the range of likely values of a psychological trait on the basis of an individual's brain activity.

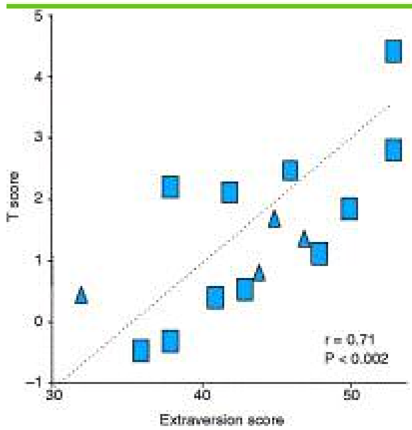

Figure 2. Personality modulates the brain's response to affectively valenced stimuli. The positive correlation of the data shown here demonstrates that the more extraverted an observer is, the more activity (as measured by the T score) will be engendered in their amygdalae by the presentation of a happy face (relative to an emotionally neutral face). Reproduced with permission from [17]. Copyright (2002) AAAS.

Neuroethical issues: privacy and public understanding

An important practical problem that brain imaging shares with genetics is privacy. It might not be in an individual's best interest to have certain personal information available to others. Another parallel is that with brain imaging, as with tissue sampling for DNA analysis, an individual need not know whether or what kind of personal information will be obtained. The experimental paradigm used by Canli and colleagues to correlate amygdala activation with personality simply required subjects to view pictures and could be administered in the guise of a picture perception study.

Another practical problem raised by progress in neuroimaging is that the public tends to view brain scans as more accurate and objective than in fact they are [23]. Statements like 'the brain does not lie' crop up in popular writing on neuromarking and brain-based lie detection, reflecting a failure to appreciate the many layers of signal processing and statistical analysis that intervene between actual brain function and resulting image or waveform, as well as the complex set of assumptions required to interpret the psychological significance of such images or waveforms.

Brain-based measures do, in principle, have an advantage as indices of psychological states and traits over more familiar behavioral or autonomic measures, being one causal step closer to these states and traits than responses on personality questionnaires or polygraph tracings. For this reason imaging may eventually provide more sensitive and specific measures of psychological processes than are now available. At present, however, such uses must be approached carefully and with a healthy dose of skepticism.

Enhancement: better brains through chemistry

The past two decades have seen the introduction of new antidepressant and antianxiety drugs with fewer side effects [24]. The greater tolerability of these medications, along with increased public awareness of mental illness and aggressive marketing of psychiatric medications to physicians and patients [25] has led to the widespread use of psychopharmacology by people who would not have been considered ill twenty years ago.

There is a substantial literature (which in fact includes literary genres such as essays and memoirs) 26, 27 and 28 on the ways in which Prozac and other selective serotonin reuptake inhibitors (SSRIs) have become a part of life for many. However, there is surprisingly little scientific research on the effects of SSRIs on people who are not depressed. It seems clear that they are not happy pills, shifting depressed people to normalcy and normal people to bliss. Rather, for most people they seem to leave positive affect unchanged but attenuate negative affect 29 and 30, for example reducing the subjectively experienced ‘hassle’ factor of life [30]. They also have subtle effects on social behavior 29 and 31.

In addition to mood, vegetative functions such as sleep, eating, and sex can be influenced pharmacologically and there is a large demand for ways of enhancing these functions. The wakefulness-promoting agent modafinil, approved in the US for treatment of certain sleep disorders, is prescribed off label for a panoply of other conditions [32] and is said to be favored by some ambitious professionals as a way of packing more work into a day [33]. Although a safe and effective appetite suppressant is at present just a goal, such a drug will undoubtedly find a huge market when it comes along. Even after it became clear that the fen-phen combination could cause fatal heart disease and it was pulled from the market, there was a constituency of consumers that fought for continued access to it [34]. Finally, although sildenafil (Viagra) and more recent medications for erectile dysfunction do not achieve their effects by altering brain function, newer neurally active drugs are in development, aimed at improving both male and female libido. If society's experience with sildenafil is any indication, many people without sexual dysfunction will seek these drugs to enhance their sex lives [35].

The treatment of cognitive disorders has also begun to shade into cognitive enhancement for healthy people. Two main cognitive systems have been targeted for enhancement, executive function and memory 4 and 36. Stimulant medication, which has been shown to improve the executive function of individuals with ADHD, also enhances normal performance on a variety of executive function measures 37 and 38. This is not surprising because ADHD probably represents the lower tail of the whole population distribution of executive function rather than a qualitatively different state of functioning, discontinuous with the normal population (NIH Consensus Statement, 1998). Although methyphenidate (Ritalin) and amphetamine (Adderall) are ostensibly prescribed mainly for the treatment of ADHD, sales figures suggest that they are not uncommonly used for enhancement. Methylphenidate is currently widely used by high school and college students. Surveys have estimated that as many as 10% of high school students and 20% of college students have used prescription stimulants such as Ritalin illegally (see D. A. Kapner: www.edc.org/hec/pubs/factsheets/ritalin.html). Figure 3 shows the growth in sales of methylphenidate over a recent 10-year period in the US and worldwide.

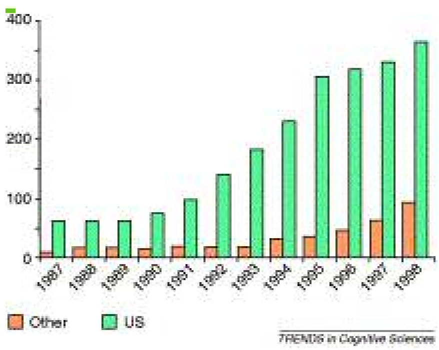

Figure 3. Growth in sales of the attention-enhancing stimulant methylphenidate (Ritalin) over a 10-year period, measured in millions of doses per day.

The most commonly used method of memory enhancement involves manipulation not of memory circuits *per se* but of cerebrovascular function. Herbal supplements such as Gingko Biloba affect memory mainly by increasing blood flow within the brain [39]. However, a huge research effort is now being directed to the development of memory-boosting drugs 4, 40 and 41. The candidate drugs target various stages in the molecular cascade that underlies memory formation, including the initial induction of long-term potentiation and the later stages of memory consolidation. Although this research is aimed at finding treatments for dementia, there is reason to believe that some of the products under development would enhance normal memory as well, particularly in middle and old age when a degree of increased forgetfulness is normal. As shown in Figure 4, for example, treatment of healthy human subjects with an ampakine, which enhances LTP, improved performance in a dose-dependent manner. Finally, the ability to weaken or prevent the consolidation of unwanted memories constitutes another kind of enhancement that is also under development [42].

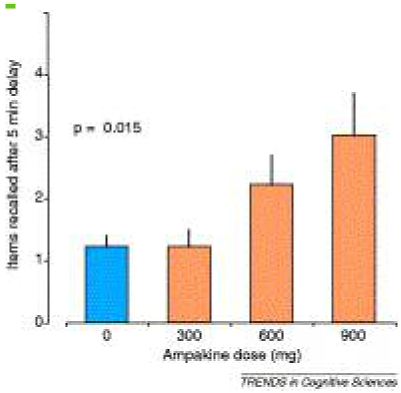

Figure 4. Ampakines, a new class of drug designed to facilitate memory consolidation, are being investigated primarily for the purpose of treating diseases that impair memory. Nevertheless, they are also likely to enhance the memory of healthy individuals for whom normal aging is accompanied by a decline in memory ability. The data shown here demonstrate the dose-dependent effect of an ampakine on the memory performance of healthy elderly research volunteers. Redrawn with permission from [41].

Nonpharmaceutical methods for altering brain function have also evolved rapidly over the past decade and in the future may offer complementary approaches to enhancement. Transcranial magnetic stimulation (TMS) has moved from laboratory to clinic as a means of treating depression [43] and is being explored with healthy subjects as a means to alter mood [44] and cognitive style [45]. More invasive methods such as surgery, brain and vagus nerve stimulation, and brain-machine interfaces may eventually expand our conception of brain enhancement yet further – and possibly our conception of human nature as well [46].

Neuroethical issues: risks to the individual and society

The ethical issues surrounding brain enhancement can be grouped into three general categories. In the first category are health issues: safety, side effects and unintended consequences. Of course, these are a concern with all medications and procedures, but our tolerance for risk is lower for enhancement than for therapy. Furthermore, in comparison with other comparably elective treatments such as cosmetic surgery, brain-based enhancement involves intervening in a complex and poorly understood system, and the likelihood of unanticipated problems is consequently higher.

The second category of ethical issue concerns the social effects of brain enhancement: How will it affect the lives of all of us, including those who may prefer not to enhance our brains? For example, the freedom to remain unenhanced may be difficult to maintain in a society where one's competition is using enhancement. American courts have already heard cases brought by parents who were coerced by schools to medicate their children for attentional dysfunction [47]. Indirect coercion is already likely to be at work in schools where 30% or more of the boys take Ritalin [48]. The military has long used drugs such as amphetamine to enhance the attention of pilots and other personnel on long missions, and the US defense department is a major funder of research on brain–machine interfaces [49]. This raises a concern about a very direct form of coercion, by which troops are ordered to undergo brain enhancement.

Conversely, barriers such as cost will prevent some who would like to enhance from doing so. This would exacerbate the disadvantages already faced by people of low socioeconomic status in education and employment.

Neuroethical issues: undermining personhood

Whereas the effects of enhancement on health and society are important practical issues, enhancement also raises what could be called philosophical issues. This third category includes the many ways in which brain enhancement challenges our understanding of personal effort and accomplishment, autonomy, and the value of people as opposed to things. Have we 'cheated' if we study better with Ritalin, or can we take credit for our improved work? If we fall in love with someone who is on Prozac and then find she is difficult and temperamental off the drug, do we conclude we don't love her after all? Then who was it we loved? Are we treating people (including ourselves) as objects if we chemically upgrade their cognition, temperament or sexual performance? People vary in how troubling they find these scenarios, but at least some see a fundamental metaphysical distinction eroding, the distinction between things (even complex biophysical things), and persons.

Responsibility, brain and blame

As cognitive neuroscience expanded from the study of one-trial learning and color vision to decision-making and motivated behavior, its relevance to understanding real-world behavior, and misbehavior, grew. Starting from clinical observations of personality change in patients with ventromedial prefrontal damage, Bechara and others [50] developed experimental tasks in which the ability to make prudent, responsible choices could be quantified and went on to demonstrate that this ability is diminished after ventromedial damage. Subsequent research has enlarged the set of brain regions that play a role in decision-making to include other prefrontal and limbic areas 51, 52 and 53.

Another ability that is essential for prosocial behavior is the ability to take another's viewpoint, and this too has been linked with specific brain systems. Brain imaging has shown that when subjects understand stories or cartoon pictures whose plot or punch line depends on the thoughts or viewpoint of a character, some of the same cortical and limbic brain regions are more active than during similar tasks in which mental states are not relevant [54]. Damage to these areas impairs the ability to understand behavior in terms of the mental states of others 55 and 56. A network encompassing many of the same areas is active in experiments that evoke empathy 20 and 57 or a sense of moral violation [58].

How do these scientific advances affect our understanding of moral and legal responsibility? We do not blame people for acts committed reflexively (e.g. as the result of a literal knee-jerk), in states of diminished awareness or control (e.g. while sleep-walking or under hypnosis) or under duress (e.g. with a gun held to the head), because in these cases we perceive the acts as not resulting from the exercise of free will [59]. The problem with neuroscience accounts of behavior is that everything we do is like a knee-jerk in the following important way: it results from a chain of purely physical events that are as impossible to resist as the laws of physics.

Furthermore, our intuitions about responsibility and blame are more influenced by knowledge of a specific physical mechanism than by the abstract principle that some physical mechanism must be at work. For this reason, we are not inclined to blame Phineas Gage for his bad behavior after an inch-wide, 3 foot-long iron bar was blown through his head, damaging his ventromedial prefrontal cortex [60] and transforming his personality from responsible and polite to slothful and ill-tempered. The challenge arises when we try to draw a principled line between the causes of bad behavior by someone like Gage and bad behavior that lacks *obvious* neurological causes.

Recent neuroscience research has begun to illuminate the more subtle and gradual ways in which the brain can be damaged, beyond the obvious lesions caused by flying iron bars. Most illicit drugs affect these areas and prolonged use has been linked to impaired prefrontal function 61 and 62. Even childhood abuse or severe neglect, which involve neither a direct mechanical insult to the brain nor a foreign substance crossing the blood-brain barrier, damages these systems [63]. There are also genetic factors that influence the function of these systems. For example, psychopathic personality disorder, which is characterized by an absence of empathy or remorse for victims and underlies some of the most abhorrent crimes, is moderately heritable [64] and is accompanied by abnormalities in some of the same prefrontal and limbic systems mentioned earlier in connection with normal social cognition [65]. The physical and mental health of criminal offenders is below that of their non-criminal peers, especially with respect to neuropsychiatric health [66].

Neuroethical issues: rethinking moral and legal responsibility

Society is gradually responding to the emerging neuroscientific view of human behavior. This is evident in our treatment of criminals within the legal system, and also in our social mores and attitudes toward 'bad' but non-criminal behavior such as compulsive drinking, gambling or sex. Within the legal system, evidence of neurological dysfunction is frequently introduced in the penalty phases of criminal trials. We naturally perceive this as relevant to the defendant's responsibility for his or her behavior, and it seems reasonable to punish a person less harshly if they are less responsible. This puts us on a slippery slope, however, once we recognize that all behavior is 100% determined by brain function, which is in turn determined by the interplay of genes and experience.

As ethicists and legal theorists have grappled with neuroscientific accounts of bad behavior, they have increasingly turned to alternative interpretations of responsibility that do not depend on free will 67 and 68, and to so-called 'forward thinking' penal codes, designed not to mete out punishments for previous behavior but to encourage good behavior and protect the public [69]. The 'disease model' of substance addiction, and the extension of the medicalized notion of addiction to other compulsive behaviors such as compulsive gambling and compulsive sex, is another way in which brain-based explanations of behavior have impacted society. The disease model emphasizes the deterministic and physiological nature of the behaviors and thereby reduces their moral stigma.

Science and the soul

Most people believe that mind and body are fundamentally different kinds of thing [70]. Yet as neuroscience advances, more and more of human thought, feeling and action is being explained in terms of the functioning of the brain, a physical organ of the body. The reduction of mental to physical processes occurred first in the realms of perception and motor control, where mechanistic models of these processes have been under development for decades. Nevertheless, such models do not seriously threaten our intuitively 'dualist' view of mind and brain. You can still believe in what Arthur Koestler called 'the ghost in the machine' and simply conclude that vision and movement are features of the machine rather than the ghost.

However, as neuroscience begins to reveal the mechanisms of personality, this interpretation becomes strained. The brain imaging work reviewed earlier indicates that important aspects of our individuality, including some of the psychological traits that matter most to us as people, have physical correlates in brain function. Pharmacological influences on these traits also remind us of the physical bases of human personality. If an SSRI can help us take everyday problems in stride, and if a stimulant can help us meet our deadlines and keep our commitments at work, then must not unflappable temperaments and conscientious characters also be features of people's bodies? And if so, is there anything about people that is not a feature of their bodies?

A dualist might answer this question with consciousness or sense of spirituality. Yet neuroscience is making inroads with these mental phenomena too. Neuroscience research on consciousness began with the study of neurological patients who retained perceptual and memory abilities while professing no conscious awareness of perceiving or remembering [71]. From these early observations, research on consciousness has expanded to include brain imaging [72] and animal research [73], all aimed at understanding the neural correlates of conscious awareness. Although this work has not attempted to account for the private, subjective aspects of consciousness sometimes known as 'qualia' [74], it has made progress in accounting for the observable differences between conscious and unconscious cognition. The relation between religious experience and the brain was first noted in the study of patients with temporal lobe epilepsy, whose seizures were sometimes accompanied by intense religious feelings. Recent neuroimaging research has shown a characteristic pattern of brain activation associated with states of religious transcendence, which is common to Buddhist meditation and Christian prayer [75].

Neuroethical issues: edging out the spirit

The idea that there is somehow more to a person than their physical instantiation runs deep in the human psyche and is a central element in virtually all the world's religions. Neuroscience has begun to challenge this view, by showing that not only perception and motor control, but also character, consciousness and sense of spirituality may all be features of the machine. If they are, then why think there's a ghost in there at all?

The incompatibility between the intuitive or religious view of persons and the neuroscience view is likely to have broad social consequences. These are foreshadowed by the highly politicized controversy over evolution and creationism, resulting from the irreconcilable natures of the scientific and fundamentalist Christian views of our origins. Consider, still, that a literal interpretation of Genesis is held by only a minority of religious thinkers, whereas the existence of an immaterial soul is a near universal belief.

Neuroethics: something old and something new

I have argued that interest in neuroethics is timely, much as interest in the ethics of molecular biology was timely in the latter decades of the 20th century. Cognitive neuroscience has already illuminated many aspects of human thought, feeling and behavior, and the technological and theoretical progress reviewed here will undoubtedly be surpassed in coming decades.

Although neuroscience has delivered some genuinely new methods and ideas and will continue to do so, nothing is ever entirely without precedent. In the case of neuroethics, we can draw on our experience with other areas of science and technology, and even our experiences in everyday life, to guide us. For example, as already mentioned, the practical issue of brain privacy has much in common with the privacy concerns that arise in genetics. Likewise, the practical problems of overconfidence in new technologies and long-term safety of pharmaceuticals have ample precedents, even if overconfidence in brain imaging and the long-term effects of psychopharmaceuticals are new problems.

On the philosophical side, the challenges posed by neuroscience are not so much unprecedented as more difficult to ignore and blatant than previous challenges. Are we the same person on Prozac as off? This is a good question, but so is: are we the same person after a glass of wine as before – or even during a vacation as before? Similarly, the impulse to excuse bad behavior may be more powerful when we can see the specific physical mechanisms that caused it, but traditional psychological explanations of behavior also affect our moral judgments.

With brain images adorning websites and magazine articles on everything from children's learning to compulsive gambling, neuroscience is gradually being incorporated into people's understanding of human behavior. The technological fruits of neuroscience are also being gradually incorporated into people's lives. The question is therefore not whether, but rather when and how, neuroscience will shape our future.

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