Chapter 1

Introduction

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1.1 The number of people in the UK with serious neurological and mental health disorders is large and rising steadily as life expectancy increases. For example, in the UK there are currently around 127,000 people with Parkinson's disease[1] and approximately 800,000 with dementia (mainly with Alzheimer's disease).[2] In addition, brain damage from stroke is the leading cause of disability in the UK.[3] Conditions associated with old age will increase as populations age; and this poses a problem not only for high income countries such as the UK, but also increasingly for low- and middle-income countries. Other groups of people with serious neurological disorders may also include those who are partially or fully paralysed due to spinal cord injury and those with conditions that cause varying degrees of paralysis, such as motor neurone disease. In Chapter 3 we provide more detail about the number of people affected by neurological and mental health disorders (see paragraphs 3.10 to 3.15).

1.2 We have become very familiar in recent decades with a range of pharmaceutical interventions into the brain, from over-the-counter painkillers, to prescription drugs to treat psychiatric disorders and even illegal mind-altering drugs such as LSD and ecstasy. But we are less familiar with physical interventions into the brain: those which use electrical currents or magnetic fields to stimulate neurological functions or that record brain signals to control external devices, or those that use stem cells to attempt to repair damaged brain tissue. These are the types of interventions we term 'novel neurotechnologies' in this report (see paragraph 1.12)

1.3 While the social and ethical issues concerning psychopharmaceutical drugs have been discussed and debated at great length[4] – although by no means resolved – there has been less consideration of novel neurotechnologies. Yet there is considerable interest in exploring the efficacy of such interventions, especially in addressing neurological conditions that are currently untreatable. Diseases for which neurotechnologies are being developed include Parkinson's disease, stroke, and mental health disorders such as depression and obsessive-compulsive disorder (OCD). Their use to assist the daily lives of those paralysed by brain injury is also being explored. As we shall see, these technologies raise some difficult ethical questions, such as how novel treatments can be made available to individuals who would benefit from them without incurring disproportionate risks. In Europe and the United States, there is a developing debate about the ways in which these devices and procedures should best be regulated to ensure safety and efficacy, to guard against false or misleading claims, to encourage responsible innovation and to ensure that the maximum individual and social benefits are realised.

The historical context

1.4 Attempts to intervene in the brain are far from new. There is a long history of interventions into the brain for what we would now consider 'medical' reasons, dating from as early as the Palaeolithic period where trepanning – removing a piece of the skull to treat conditions such as epilepsy – was used.[5]

1.5 The practice of lobotomy was for a time prevalent in the field of psychiatric neurosurgery. Lobotomy (also known as pre-frontal leucotomy), involved a direct surgical intervention into the brain of those diagnosed with severe mental health disorders, in order to cut or otherwise

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1 Parkinson's UK (2012) *Our plan to cure Parkinson's*, available at: http://www.parkinsons.org.uk/research/our_plan_to_cure_parkinsons.aspx.
2 Alzheimer's Society (2013) *What is dementia?*, available at: http://alzheimers.org.uk/site/scripts/documents_info.php?documentID=106.
3 NHS Choices (2012) *Standards for stroke care*, available at: http://www.nhs.uk/NHSEngland/NSF/Pages/Nationalstrokestrategy.aspx.
4 See, for example, Rose N (2003) Neurochemical selves *Society* **41(1)**: 46-59.
5 Harris JC (2004) The cure of folly *Archives of General Psychiatry* **61(12)**: 1187.

destroy certain key regions in the frontal lobes.[6] This procedure gained widespread popularity after it was developed in 1935 by the Portuguese neurologist Egas Moniz, who later received the 1949 Nobel Prize for medicine for his work in developing this technique. Moniz claimed some remarkable results with this practice, and used it on patients with a wide range of severe mental health disorders from depression to mania; and others, including the British neurologist Sir Wylie McKissock, claimed to be able to replicate these results. The practice became widespread during the 1950s, especially in the United States where it was enthusiastically adopted by the surgeon Walter Freeman. Early reports were optimistic about the results and their implications, as it appeared to offer a way of treating those who were otherwise liable to be confined for years within mental asylums. However, many neurologists expressed doubts about its efficacy, and the procedure was increasingly called into question as evidence emerged of side-effects which left many debilitated by serious brain damage.[7]

1.6 Among those who opposed the relative crudity of lobotomy were neurosurgeons who believed that more refined and careful neurosurgical techniques were more appropriate for the treatment of conditions such as epilepsy or neuropsychiatric disorders. Innovations by surgeons such as William Macewen, who developed a technique for the successful removal of brain tumours, contributed to major advances in the field of brain lesioning in the latter part of the 19th Century and the early part of the 20th Century.[8] This technique, also known as ablative brain surgery, involves cutting lesions in brain tissue. Advances in this field were made possible by parallel innovations. For example, in the early 20th Century the neurosurgeon Harvey Cushing used X-rays to locate brain tumours and the introduction in 1947,[9] by Ernest Spiegel and Henry Wycis, of a stereotactic apparatus made it possible to direct brain lesions much more accurately by locating and targeting particular areas using measured coordinates.[10] With the use of stereotactic apparatus, research and limited clinical application of ablative brain surgery continued in the United States and Europe despite the damage to the reputation of neurosurgery which followed the public recognition that lobotomy had been a medical disaster.

1.7 At the same time, an important new line of research began to be explored in which the localised electrical stimulation of regions of the brain was investigated as an alternative to lesions as a method of treating neurological and mental health disorders. One of the most influential pioneers in this field was the Spanish neuroscientist José Delgado.[11] During the 1950s Delgado, who worked mainly in the United States, implanted electrodes in the skulls of patients in a psychiatric hospital and showed that electrical stimulation of their brains could elicit both motor actions and emotional experiences (for example, fear, rage, and lust), depending on the area stimulated. He also carried out extensive research with implanted electrodes in cats and monkeys, showing, for example, that animals that were habitually aggressive to their subordinates could be calmed by stimulation to certain areas of the brain.[12] Delgado's devices were what he termed 'stimoceivers': they could both monitor the electrical activity of the brain and stimulate the brain electrically. This two-way communication opened the possibility of linking information on patterns of neural activity to calculated interventions to modulate that activity. In his 1969 book, *Physical control of the mind: towards a psychocivilized society*,

6 Valenstein ES (1986) *Great and desperate cures: the rise and decline of psychosurgery and other radical treatments for mental illness*, Volume 24 (New York: Harper Collins). Leucotomies were only one of a whole set of physical treatments that were used at that time, see: Sargant W, Slater E, Kelly D and Dally P (1972) *An introduction to physical methods of treatment in psychiatry* (Edinburgh: Churchill Livingstone).

7 Johnson J (2009) A dark history: memories of lobotomy in the new era of psychosurgery *Medicine Studies* **1(4)**: 367-78.

8 Neuroportraits (2011) *William Macewen*, available at: http://neuroportraits.eu/portrait/william-macewen.

9 Yale Medical History Library (2006) *Harvey Cushing: a journey through his life*, available at: http://www.med.yale.edu/library/historical/cushing/hopkins.html.

10 PL. G (2001) Spiegel and Wycis - the early years *Stereotactic and functional neurosurgery* **77(1-4)**: 11-6.

11 Other important pioneers from this period were Robert Heath, who worked at Tulane University, Carl-Wilhelm Sem-Jacobsen, who worked in Oslo, and Nathalia Bechtereva, who worked in Leningrad. For further discussion, see: Hariz MI, Blomstedt P and Zrinzo L (2010) Deep brain stimulation between 1947 and 1987: the untold story *Neurosurgical Focus* **29(2)**: E1.

12 See: John Horgan's account in Scientific American, Inc. (2005) *The forgotten era of brain*, available at: http://www.mesolimbic.com/delgado/brainchips.pdf.

Delgado downplayed ideas of brain control by ‘evil scientists’, but did suggest that neurotechnology was “on the verge of ‘conquering the mind’” and creating “a less cruel, happier and better man”.[13] The work became mired in controversy when it was suggested that the technology might be used for controlling potential criminals and reducing homosexual attraction, and Delgado returned to Spain to work on less invasive methods of neural control that anticipated transcranial magnetic stimulation (TMS) (see paragraph 1.12).

1.8 Despite these developments in ablative surgery and brain stimulation, attention shifted during the 1960s to new pharmacological compounds such as chloropromazine (Largactil), L-3, 4-dihydroxyphenylalanine (L-DOPA), and other neuroleptics which appeared to act directly on the underlying neural causes of mental health conditions. As other drugs were developed that seemed to be safe and effective, and were thought to work on the neurotransmitter systems in the brain, the pharmacological route became the preferred approach for acting on the brain.[14] Of course, there were other approaches – psychoanalytic and behavioural, for example – and some direct interventions into the brain were still used – notably electro-convulsive therapy (ECT) for severe depression and neurosurgery for intractable epilepsy – but by the end of the 1970s, biological psychiatry with its focus on treatment with drugs, appeared to prevail.[15] Coupled with the growing use of ‘minor tranquillisers’ such as Valium for managing the problems of everyday life, and the later rise of new generations of drugs for treating depression, panic disorders and much more, the future of psychiatry seemed to lie with pharmacology. This was not only the case with psychiatry; in neurological diseases such as Parkinson’s and Alzheimer’s disease, the chemical route seemed the obvious one to pursue, and commercial companies devoted much effort to developing new drugs to treat disorders of the brain.

1.9 However, some of these hopes have been disappointed. Several new drugs turned out to be less effective in the long term than had been anticipated.[16] In addition, due to a lack of new molecules to explore and the advent of generics, which provided a disincentive to the pharmaceutical industry to invest in exploratory drug development, the pipeline of psychiatric drugs slowed. Altogether it has proved difficult to translate the great advances in our knowledge of the brain into new and effective compounds.[17] Doubt has also been cast on the safety and efficacy of some of the drugs that had once seemed the obvious first-line treatment for psychiatric and mental illnesses. Moreover, the chronic nature of many neurological and mental health conditions means that the brain adapts to the drugs (as it would to any intervention) leading to loss of efficacy. Despite growing knowledge of the neurological basis of conditions such as dementia, it has proved especially difficult to develop drugs that do more than slow its development.

1.10 One result of this situation has been the impetus to explore altogether new methods of treatment, including the introduction of stem cells into the affected sites in the brain. Another has been the return to techniques for brain intervention which use electrical stimulation, which had, to some degree, been marginalised by psychopharmacology. The central instance of this was the development of deep brain stimulation (DBS), which combined stereotactic techniques from ablative surgery with new technology for brain stimulation involving the insertion of small electrodes into the regions where lesions were used to treat mental health disorders.[18] These surgical techniques have also developed alongside the emergence of new imaging technologies for visualising normal and pathological processes within the living brain, including functional magnetic resonance imaging (fMRI).

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[13] Ibid, at page 71.
[14] Rose N (2003) Neurochemical selves *Society* **41(1)**: 46-59.
[15] NICE (2013) *Depression overview*, available at: http://pathways.nice.org.uk/pathways/depression.
[16] Miller G (2010) Is pharma running out of brainy ideas *Science* **329(5991)**: 502-4.
[17] Hyman SE (2012) Revolution stalled *Science Translational Medicine* **4(155)**: 1-5.
[18] DBS was developed in 1987 by the Grenoble team: Benabid AL, Pollak P, Louveau A, Henry S and de Rougemont J (1987) Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease *Applied Neurophysiology* **50(1-6)**: 344-6.

1.11 Thus the hope for the future is that the new understanding of these recalcitrant disorders provided by these and other recent developments in neuroscience can be used to inform new therapeutic interventions in the brain. Such interventions could both avoid the perils of the older neurosurgical interventions and provide better treatments than current pharmacological therapies offer.

Novel neurotechnologies in this report

1.12 This report focuses on the issues which are most characteristic of interventions that involve new neurotechnologies. It does not discuss the significance of brain imaging techniques such as fMRI, important though these are. Equally, we do not discuss refinements of older surgical techniques, such as the use of ablative radiosurgery or the use of new psychopharmaceuticals. Instead, we concentrate on technologies that are either radically new, or where new knowledge and practices are combined with recently-established technologies to develop novel therapeutic interventions in the brain. Thus this report focuses on the following four categories of technologies:

- **Transcranial brain stimulation**, which encompasses a range of non-invasive interventions using devices to apply either weak electrical fields or electromagnetic pulses to the scalp to affect the brain's neural activity.
- **Deep brain stimulation**, which also uses a device to administer electrical current to stimulate neural activity, but through the use of electrodes that are inserted into the brain directly.
- **Brain-computer interfaces**, which use electrodes (either implanted in the brain, or resting on the scalp) to record brain signals that are translated into commands to operate computer-controlled devices.
- **Neural stem cell therapies**, where stem cells are injected into the brain in order to replace or stimulate regeneration of lost or damaged brain tissue.

1.13 Applications of neural stem cell therapies and assistive brain-computer interfaces are still confined to experimental uses and research settings. Transcranial brain stimulation (TBS) techniques have been used as research tools for some time, but are now being translated from the laboratory into clinical practice. DBS has become an established therapy for Parkinson's disease, but its use is now being extended to a number of other conditions. As such, the technologies discussed in this report occupy a spectrum of maturity as emerging therapeutic interventions. We discuss each of these technologies in detail in Chapter 2.

Ethical and social considerations

1.14 Our attention is focused on ethical, legal and social issues to which these four categories of novel neurotechnologies give rise. These technologies encompass a wide variety of applications, ranging from highly invasive surgical interventions used to ameliorate the effects of serious brain disorders, to non-invasive brain-computer interfaces (BCIs) that might provide assistance to individuals with impaired motor control. Although this report focuses primarily on therapeutic applications of novel neurotechnologies, non-therapeutic applications in relation to cognitive enhancement, gaming and military applications will also be considered (see Chapter 8).

1.15 This report evaluates the potential individual and social benefits and risks arising from the development and use of this diverse range of technologies. This evaluation begins in Chapter 4, with an ethical framework. This focuses solely on therapeutic applications of novel neurotechnologies, as it is here that there is the greatest potential for social benefit, where research and usage are most advanced and therefore, in our view, where the most pressing and least speculative ethical concerns arise. This is not to say that non-therapeutic applications do not pose their own challenges, but these are sufficiently distinct that we discuss them separately (see Chapter 8).

1.16 Ethical issues raised by novel neurotechnologies are not wholly exceptional or unique. However, we suggest that the brain has a special status in founding the capacities and abilities which are central to our existence, and this provides both a reason to intervene – in order to try to restore what has been lost when the brain ceases to function as it should – and a reason for great caution when we are uncertain what the effects of doing so will be. These two competing considerations provide the foundation of our ethical framework.

1.17 In articulating what negotiating this tension between need and uncertainty entails in the context of developing and using novel neurotechnologies, we identify a cluster of five interests that warrant particular attention. These include safety, autonomy, privacy, equity and trust. Finally we suggest that, in seeking to protect and promote these interests, three virtues in particular should guide actors across a wide range of settings and applications of novel neurotechnologies. These virtues are inventiveness, humility and responsibility.

1.18 Our ethical framework is intended to guide the activities of all actors involved in funding, developing, regulating, using and promoting novel neurotechnologies. In many cases those living with serious neurological or mental health conditions will have few other therapeutic options for treating or ameliorating their conditions other than those potentially offered by novel neurotechnologies. As a result, there are also ethical dimensions to the economic drivers (discussed in Chapter 3) and regulatory frameworks (discussed in Chapter 7) which determine whether these technologies progress from research to marketable commercial applications, since both impact on the availability of, and access to, these technologies. A further social context with significant ethical ramifications is the media presentation, and 'hyping', of the capabilities and promises of novel neurotechnologies (discussed in Chapter 9).

1.19 Our discussions of the social and ethical issues raised by novel neurotechnologies over subsequent chapters adopt the following structure. **Chapter 2** describes in some detail the four categories of neurotechnologies that are the subject of this report. It outlines their state of development on the pathway to therapeutic application, what these applications are, the mechanisms by which they achieve therapeutic (or assistive) effects, and any unintended consequences of their use. **Chapter 3** addresses the demand for, and availability of, therapeutic applications of these technologies in the context of the economic pressures and incentives that influence whether they reach the stage of development that permits them to be marketed for widespread use. This provides the background to our ethical framework, the key elements of which we have outlined above and which are described fully in **Chapter 4**. The chapters that follow the ethical framework consider the contexts in which novel neurotechnologies are developed, used, regulated and promoted. Each applies our framework – and the principles, interests and virtues identified therein – to the practices of a wide range of actors and organisations, and to the mechanisms of oversight that govern and shape them, making recommendations as appropriate.

1.20 **Chapter 5** focuses on ethical issues raised by the care of patients using novel neurotechnologies and of participants in clinical research. **Chapter 6** introduces the concept of Responsible Research and Innovation (RRI) and identifies the elements that are of greatest priority for RRI in this field. **Chapter 7** describes different regulatory frameworks applicable in the UK to neurodevices and neural stem cell therapies and applies the values set out in our ethical framework to identify possible gaps, or areas of disproportionate burden, in the current system of oversight. We then widen our scope to look beyond the solely therapeutic applications of these technologies. **Chapter 8** describes the potential for novel neurotechnologies to be applied to enhancement, recreational and military purposes. Finally, in **Chapter 9** we address issues arising from communication about novel neurotechnologies, the harm that misinformation and hype might cause, and the respective responsibilities of researchers and journalists to communicate with responsibility and humility. **Chapter 10** draws together cross-cutting themes that emerge from the preceding chapters and recommendations arising.

A Freudian ending: man as a "prosthetic god"

1.21 In *Civilization and its discontents*, Sigmund Freud famously wrote "Man has, as it were, become a kind of prosthetic God. When he puts on all his auxiliary organs he is truly magnificent; but those organs have not grown on to him and they still give him much trouble at times. [...] Future ages will bring with them new and possibly unimaginably great advances in this field of civilization and will increase man's likeness to God still more. But in the interests of our present investigation, we will not forget that present-day man does not feel happy in his God-like character."[19]

1.22 Some see in neurotechnologies the emergence of new ways for humans to escape the limitations of their bodies and minds, the sub-optimal legacy of our evolved history. These ideas, that humans are 'hybridising' with machines, becoming cyborg-like fusions of machine and organism, excite enthusiasm and repugnance in equal measure. Nowhere are they more problematic, and intriguing, than when the human brain and mind are at stake. Neurotechnologies offer us both prospects – to become Delgado's psychocivilised citizens or to enable us to achieve undreamed levels of control and remediation over the most severe and troublesome medical conditions that affect our species. While much of our report will focus on more prosaic issues of regulation, efficacy, and safety, we will not ignore these more fundamental social and ethical questions raised by the development of these novel neurotechnologies.

[19] Freud S (1961) *Civilization and its discontents* (New York: W.W. Norton & Co.).