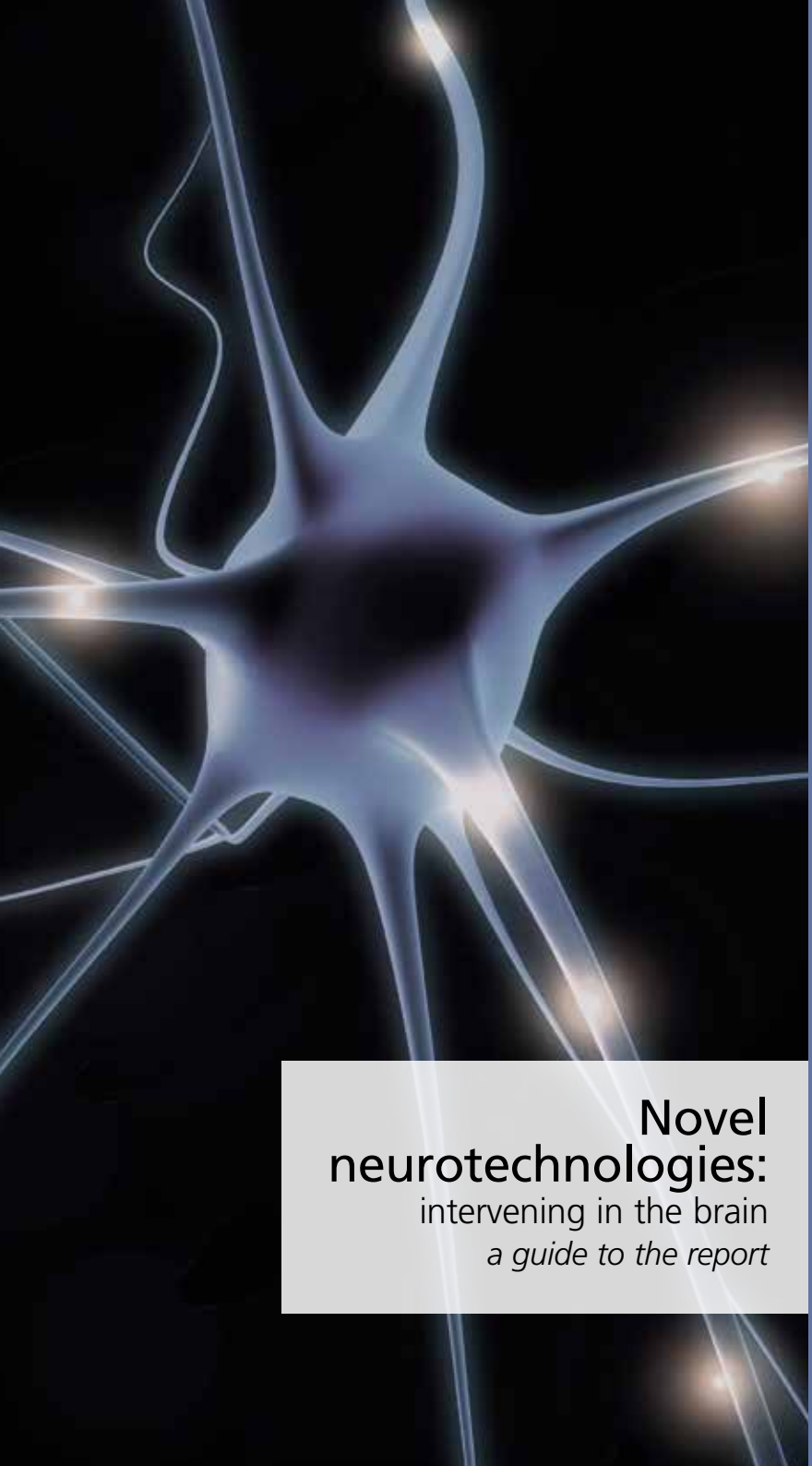
Novel Neurotechnologies



Novel neurotechnologies:
intervening in the brain
a guide to the report

NUFFIELD COUNCIL ON BIOETHICS

The report was produced by an interdisciplinary expert Working Party. In coming to its conclusions, the Working Party consulted a wide range of people, including people with experience of brain interventions, patient organisations, medical professionals and those involved in the research, development, regulation and commercialisation of novel neurotechnologies.

Contents

Introduction

This guide outlines the main themes and recommendations that are discussed in the Nuffield Council on Bioethics' report ***Novel neurotechnologies: intervening in the brain*** (published June 2013).

Serious brain disorders such as Parkinson's disease, dementia, and brain damage caused by stroke already affect many people, and these numbers are set to rise as people live longer.

Procedures that intervene in the brain offer the potential to help people with neurological and mental health conditions, especially those with severe symptoms where other treatments have not worked. They also have other possible applications for enhancement, recreational and military purposes.

This report sets out the potential benefits and risks of a number of technologies that intervene in the brain.

- The report focuses on four particular neurotechnologies, examining their potential uses, potential problems, and the economic influences shaping their availability. An ethical framework is developed around two fundamental considerations: the **need** for medical interventions to treat neurological and mental health conditions and the **uncertainty** about their benefits and risks.
- The report then considers the contexts in which novel neurotechnologies are developed, used, regulated and promoted: through the care of patients, research and innovation, regulation, non-medical uses, and the media. It suggests how the ethical approach might guide the activities of those involved in each of these areas.

What are 'novel neurotechnologies'?

The report focuses on four types of neurotechnologies at different stages of development, ranging from those currently being researched, to established techniques that are being investigated for use in a wider range of conditions.

Illness or injury that causes damage to the brain can lead to impairments of memory, movement or consciousness, as well as conditions such as chronic pain. The brain has only a limited capacity to repair such damage itself.

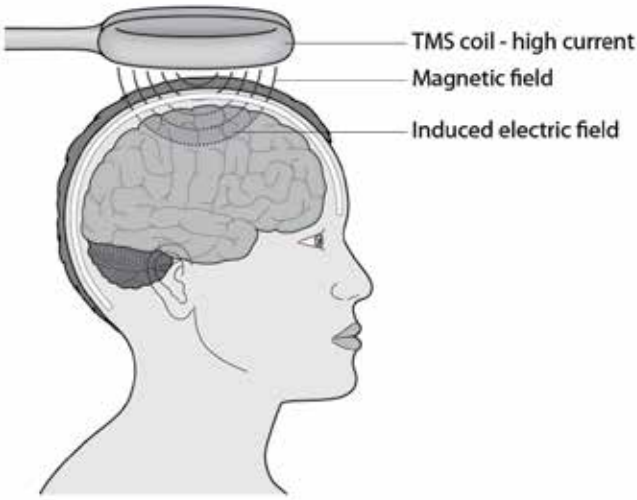
The following novel neurotechnologies have the potential to address some of the distressing and disabling effects of brain damage and mental health disorders by intervening in brain function.

Transcranial brain stimulation (TBS)

What is it? TBS is a term used to describe a group of interventions using devices that stimulate the brain using magnetic fields or weak electrical currents. These are non-invasive in that they involve attaching electrodes to the scalp or placing a magnetic coil next to the head.

What is it used for? TBS technologies are commonly used in research and they are being explored as treatment options for a range of conditions, primarily depression but also addiction, stroke, tinnitus and others. There is also interest in using these devices to enhance mood or learning.

What are the potential risks? TBS can result in minor localised discomfort, or in some cases headaches or temporary memory disturbances.



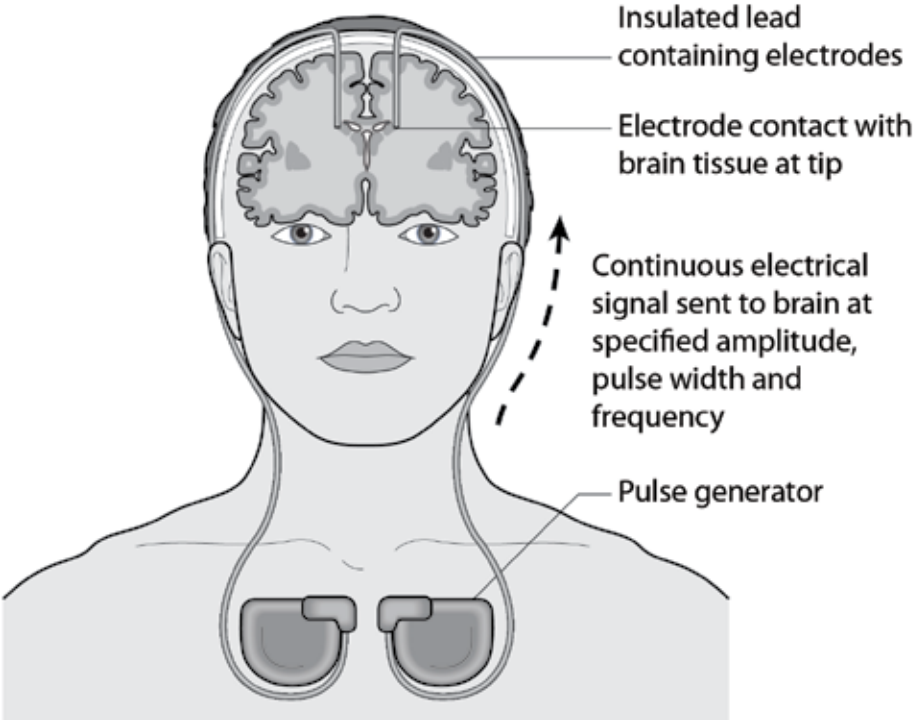
Transcranial magnetic stimulation is one form of TBS.

Deep brain stimulation (DBS)

What is it? DBS is an invasive procedure requiring brain surgery to place electrodes in a specific region deep within the brain. A power source, also implanted in the body, supplies repeated pulses of current to stimulate that part of the brain.

What is it used for? DBS is used to treat Parkinson's disease and movement disorders such as dystonia. Researchers are exploring whether it could also be used to treat psychiatric disorders.

What are the potential risks? Risks resulting from the neurosurgery itself include infection and bleeding in the brain. There is some evidence linking DBS with unintended changes in mood, understanding and behaviour.

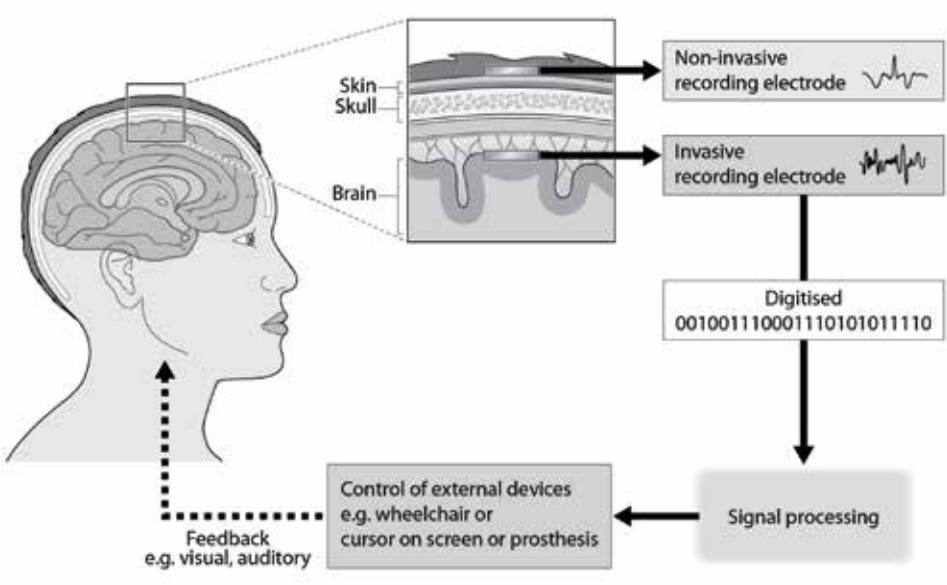


Brain-computer interfaces (BCIs)

What are they? BCIs use electrodes - either implanted in the brain, or resting on the scalp - to record brain signals which are then translated into instructions for operating a computer-controlled device. BCIs give users the opportunity to control devices, for example, by imagining movements.

What are they used for? BCIs are being investigated for use facilitating movement and communication, so they offer significant potential to help paralysed individuals. Currently, invasive BCIs are only being used with patients in research settings. Some non-invasive BCIs are starting to become commercially available, for example as controls for computer games.

What are the potential risks? Invasive BCIs carry risks associated with brain surgery. Most BCIs under investigation are non-invasive and very low risk, though little is yet known about the ways in which they might alter brain function after extended long-term use.

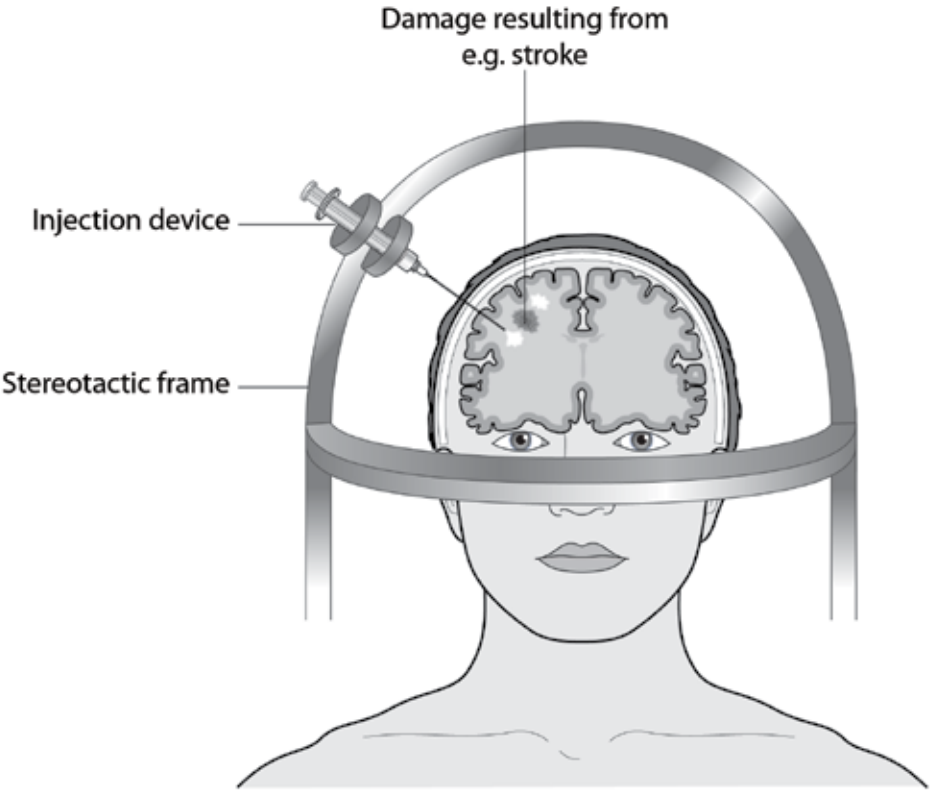


Neural stem cell therapies

What are they? Neural stem therapies involve invasive procedures where stem cells are surgically injected into the brain.

What are they used for? They seek to repair damage caused by stroke or by progressive brain conditions such as Parkinson's disease. Current research into these techniques includes a clinical trial in stroke patients. It is too early to say whether this will provide an effective treatment.

What are the potential risks? Risks resulting from neurosurgery itself include infection or bleeding in the brain. Other possible complications include pain or tumour development if the implanted cells do not grow or integrate as expected. Once the cells are implanted it may not be possible to remove them [Chapter 2].



Economic drivers of innovation

There is a clear need for innovation to deliver effective treatments for disorders affecting the brain, but there are many obstacles to obtaining funding to achieve this.

Why do we need novel neurotechnologies?

The high global incidence of brain disorders has considerable implications for economies. In the UK alone, there are around 800,000 people living with dementia, 300,000 people with disabilities caused by stroke, 127,000 people with Parkinson's disease and millions who live with chronic pain.

Challenges to funding for innovation

Issues that arise in relation to the funding and development pathways of novel neurotechnologies include:

- Private companies and investors are likely to focus on technologies that target the largest or most established markets. The needs of patients with rarer conditions or where health care resources are scarce may therefore receive less attention.
- The long timescales and uncertainties associated with developing stem cell based technologies may be seen by investors as too economically risky.
- Novel neurotechnologies are vulnerable to the 'valley of death' – a lack of funding to support the translation of early stage research into commercially viable products.
- Prioritising fast returns on investment may encourage developers towards practices that might not best meet patients' needs for access to safe and effective treatments, for example, developing elements of devices that might help increase sales, but do not necessarily enhance their benefits to patients.

We conclude...

It is vital that proportionate regulatory oversight encourages innovation, and directs investment and development towards the production of safe and effective products that meet genuine patient needs.

Effective regulation alone may not be enough to promote equitable access to affordable treatments - innovative approaches to research, funding and commissioning are also needed [Chapter 3].

Responsible research and innovation

There are six key elements to developing a systematic, responsible approach to the development of novel neurotechnologies.

The concept of 'responsible research and innovation' (RRI) has been widely adopted by policy-makers to encourage thinking about the public benefits of science and technology-based research. We identified six key priorities in relation to RRI for novel neurotechnologies:

Clearly identified need: In this case, a need for interventions to improve the lives of those with serious brain disorders. Development for the sake of novelty alone, without clear goals, should be avoided.

Securing safety and efficacy: Protecting patient safety is a central aim of regulation, but risks must be assessed relative to any likely benefits. This highlights the value of assessing efficacy as part of product development.

Generating robust evidence: Small-scale studies, commercial influences, and bias towards publication of positive findings may all hinder the gathering of transparent, robust and balanced evidence. Alternative methods of linking and sharing evidence could help address this.

Continuous reflexive evaluation: Reflecting, and reacting to, the directions towards which research is (potentially) travelling, can help avoid lock-in to innovation pathways that do not serve individual patient or public benefit.

Coordinated interdisciplinary action: Coordination between the diverse professionals involved in novel neurotechnologies – e.g. engineers, surgeons and psychologists – will help to share understandings of, and visions for, how the technology could be developed and used.

Effective and proportionate oversight: A proportionate balance must be struck between oversight that supports innovation, and that which protects patient safety. Sometimes statutory regulation will not be the best means of achieving this [Chapter 6].

Ethical framework

This report sets out a three-part ethical framework to help evaluate and guide policy and practices relating to the development, funding, use, regulation and promotion of novel neurotechnologies.

The brain has a special status in human life that distinguishes it from other organs. It plays a central role in our movement and communication, our ability to make our own decisions, and our understanding of ourselves and our relationships with others – thus in many ways affecting our ability to lead fulfilling lives.

Intervening in the brain therefore raises important ethical and social concerns.

Foundational principles: beneficence and caution

Given the suffering caused by brain disorders and an absence of other suitable treatments, there is a **need** for therapeutic applications of neurotechnologies.

There is **uncertainty** about benefits and risks of these technologies, not only because of their novelty but also a lack of comprehensive understanding of how the brain functions and of the full range of work being done in this field.

The special status of the brain therefore provides both a reason to exercise **beneficence** by finding ways to intervene when injury or illness causes brain disorders, and a reason for **caution** when we are uncertain what the effects of this will be.

Key interests

We identified five key interests that must be considered in relation to novel neurotechnologies:

- Protection of **safety**, taking into account risks alongside expected benefits.
- Promotion of **autonomy** (both in the sense of supporting people's capacity to make their own decisions and in the sense of protecting their sense of who they are).
- Protection of people's **privacy**, bearing in mind that some devices may collect sensitive personal data.
- Promotion of **equity** both in terms of access to innovative products, and in addressing social stigma and discrimination.
- Promoting public understanding of and **trust** in novel neurotechnologies.

Virtues

In describing the kinds of behaviours and approaches that are needed to protect and promote these interests, we highlight three virtues that are especially relevant in guiding the activities of all parties across a wide range of settings and applications of novel neurotechnologies. These virtues are:

Inventiveness – expressed through technological innovation and by identifying ways of providing wider access to therapies.

Humility – acknowledging the limits of current knowledge and of our ability to use technologies to alleviate the harms of brain disorders.

Responsibility – shown by robust research and clinical practices and by avoiding hype in communication about their potential uses.

These virtues should be exemplified in the professional practices of all those involved in the development, funding, use, regulation and promotion of novel neurotechnologies, and supported by the structures and rules of the institutions within which they work [Chapter 4].

Care of patients and research participants

An ethical approach to care is not just about ensuring patient safety - it should also support informed decision-making and protect against harms such as undue privacy infringements or fostering unrealistic hopes.

Decision making, consent and autonomy

Given that novel neurotechnologies often address conditions that themselves impair decision-making abilities, there may be difficulties in gaining informed consent from some patients and research participants. Moreover, the evidence on long-term and unintended effects of intervening in the brain is often not clear, and a lack of alternative treatments may give rise to desperation.

In line with the virtues of humility and responsibility (see the ethical framework on page 9) it is important that medical professionals involved in providing treatment using novel neurotechnologies are open with patients in ways that include:

- acknowledging and explaining the limits of current knowledge about the treatment outcomes that a patient can expect;
- recognising instances where patients may benefit from counselling from qualified professionals other than their doctors; and
- avoiding characterising treatments as 'last best hope' where this is not justified.

We conclude...

Those providing invasive treatments using neurotechnologies should be required to offer patients independent counselling, before consent is given, to provide an opportunity for patients and those close them to fully explore the implications and uncertainties of the treatment being offered.

Protection from harm

All of the novel neurotechnologies considered in this report involve some potential unintended consequences, but the scale of possible harm varies considerably between the different techniques (see pages 2 - 5).

The lack of clear evidence about the ratio of risks to benefits presents challenges to responsible decision-making about patient care, both in treatment contexts and in the conduct of clinical investigations.

Data collected by some devices (e.g. BCIs or in neurostimulation) about users' brain functions may be valuable for the purposes of providing care or conducting research, but may also be sensitive and stigmatising. This raises concerns about adequate protection of privacy regarding the use of the data, and about the possibility of interference with the function of neurodevices.

We conclude...

NHS services using neurotechnologies should be required to adhere to national guidance on the use of new interventional procedures.

Professional guidelines should be developed to ensure that patients who use private neurostimulation treatment services do so only following appropriate medical assessment.

The Health Research Authority should develop guidance on the use of 'sham' neurosurgery controls in clinical trials of neural stem cell therapies.

Researchers must state in advance what support will be offered to participants if access to neurodevices will finish when the study concludes.

Research or experimental treatment?

It is not always clear whether interventions or devices should be governed by rules that apply to treatment or to research, since the technologies used experimentally may fall in a middle ground between these.

As well as ensuring protection for vulnerable patients, who are the most likely candidates for more experimental treatments, a particular concern is that knowledge and experience gained from experimental procedures should be collected and shared appropriately.

We conclude...

The General Medical Council, Health Research Authority and Medical Research Council should work together to produce professional guidance on responsible conduct in experimental treatment.

Professional bodies such as the Association of British Neurologists, Society of British Neurological Surgeons and the Royal College of Psychiatrists should work together to establish publicly accessible registers to collect and link data on experiences of using novel neurotechnologies in healthcare settings [Chapter 5].

Regulation

There are several key differences between regulation of neurodevices (as used in BCIs, DBS and TBS) and regulation of neural stem cell therapies, giving rise to different challenges.

The development and clinical use of these technologies falls into two distinct areas of regulation:

- The devices used in **TBS, DBS and BCIs** for medical purposes are regulated as medical devices, and can be marketed once they carry a 'CE mark' to indicate compliance with European law.
- **Neural stem cell therapies** are regulated as *advanced therapeutic medicinal products* (ATMPs) - more closely resembling the regulation of pharmaceuticals.

There are some marked differences between these two fields of regulation, such as:

- ATMPs intended for the wider market are centrally approved at European level whereas medical devices are regulated at a national level.
- ATMPs have to undergo clinical trials to demonstrate that they are safe and effective. Medical devices can be marketed once they meet safety and performance standards, but manufacturers do not have to conduct clinical investigations to demonstrate treatment efficacy before receiving a CE mark.
- Clinical investigations of ATMPs and medical devices are overseen by the national regulator; but in the UK, trials of neural stem cell therapies are also overseen by the Gene Therapy Advisory Committee.

These combined factors mean that the journey of ATMPs from research to market is longer and more complex than for medical devices.

Recommendations for regulation of medical devices

The requirements for data about the functioning of medical devices before they are placed on the market are relatively light touch, though invasive devices (as used in DBS) must meet higher thresholds of evidence because they pose greater risks to patients' safety.

One advantage of this system is that devices can get to market relatively quickly, but there is a lack of transparency about the information on which approval decisions are based. The light touch approach to pre-market scrutiny of medical devices makes post-market surveillance for faults and adverse incidents all the more important.

We conclude...

Information relating to the approval of medical devices to enter the market, including the evidence used to show that neurodevices meet regulatory requirements, should be publicly accessible.

Approvals based on evidence relating to a similar neurodevice on the market, rather than clinical investigations of the new device, must be justified by the devices being sufficiently similar in effect.

It should be compulsory for medical professionals to report any problems encountered in the use of neurodevices, supported by a scheme identifying newly approved devices. Information regarding adverse incidents and trends should be publicly accessible.

Recommendations for regulation of ATMPs

Given the health risks posed to patients if a neural stem cell therapy does not work as expected, robust regulation is vital. However, delays and regulatory complexity may present challenges and costs to developers and disincentives to investors.

We conclude...

There should be a responsible and proportionate approach to oversight that supports careful and appropriate scientific progress. Recent developments to streamline and reduce delays in the governance of stem cell therapies, and to promote dialogue between regulators and developers, are encouraging.

Regulating therapies for individual patients and rare conditions

There are several exceptional means by which patients can be treated with neurotechnologies that have not been generally approved to be used for their particular condition. These can offer valuable opportunities to address unmet health needs. However, oversight must be sufficiently robust for patients with rare conditions not to be exposed to disproportionate risks.

We conclude...

Where neurodevices or ATMPs are approved for use on exceptional or non-routine grounds, it is important that the regulatory authorities have mechanisms for collecting information on when and why these treatments have been used and what the outcomes were and that this information can be shared to improve future good practice [Chapter 7].

Non-medical uses: enhancement, gaming, military

There is a potentially large market for novel neurotechnologies outside health care. These raise a number of ethical and social concerns.

Research into the use of non-invasive TBS and BCI devices for 'enhancement' or gaming purposes is ongoing, and in some cases, products are being sold to consumers. Though these technologies do not present serious risks, their use for these purposes do not bring clear social benefits either. There is a need to understand better what the long-term effects of frequent private use of these devices might be, without research itself contributing to unnecessary interventions in the brain.

Understanding the possible effects on the developing brain is particularly important as children and young people might be especially likely to use BCI games or to be encouraged to use neurodevices for educational 'enhancement' purposes. Furthermore, false or misleading claims about the benefits that novel neurotechnologies might offer risk exploiting consumers and undermining wider public trust in neurotechnologies.

Enhancement – current knowledge

Some small studies using non-invasive TBS procedures have reported improvements in participants' performance in, for example, memory or language tasks. Whether and how these effects could be said to be 'enhancements' or would translate into practical benefits in the real world is unclear, as most studies are very limited in scale and the effects are small and transient.

Gaming – current knowledge

Non-invasive BCIs that record brain activity using electrodes placed on the scalp or forehead are being developed to enable players to control action in computer games. Some devices that claim to use BCIs are on the market, but these are currently limited in their functionality, and there are some doubts as to whether all of these are genuinely using brain signals, or are responding to facial movements.

We conclude...

Institutional ethics committees should monitor proposals for research into non-medical uses of novel neurotechnologies to ensure their value and quality. Evidence gathered about non-medical uses should be made available via publicly accessible registers.

For the purposes of regulation, the European Commission should consider designating neurostimulation devices as medical devices, irrespective of the purpose for which they are marketed.

The UK Departments of Education and the Royal College of Paediatrics and Child Health should issue advice to teachers and parents about the current evidence on the effectiveness of neurodevices for 'enhancement'.

Observational research of children who already use neurotechnologies for gaming or learning is needed to assess the benefits and risks including effects on the developing brain.

Military - current knowledge

Aside from uses in treating war injuries, for example using BCIs for prosthetic limbs, military research is also being conducted into the possible use of neurotechnologies for non-medical applications, including:

- BCIs to enhance fighters' effectiveness by improving perception and learning capabilities.
- BCIs to allow the remote control of weapons by brain signals.
- The use of neurostimulation or BCIs for interrogation purposes.

Existing international conventions outlawing the use of biological and chemical weapons in war do not cover the use of neurodevices. However, the use of coercion in interrogation of prisoners is prohibited under international humanitarian law.

We conclude...

Advice should be issued to personnel in the armed forces and intelligence services highlighting that the use of neurodevices in interrogation is prohibited under the Geneva Conventions.

Postgraduate teaching of neuroscientists should include ethical training, including awareness of the potential dual-use of neurotechnologies for hostile as well as peaceful purposes [Chapter 8].

Communication and the media

The reporting of novel neurotechnologies should be accurate and evidence-based, and should take account of the personal and social impacts of misrepresenting or overstating their potential.

The ways in which science and technology are presented in the media helps to shape public understanding and expectations. This in turn can affect attitudes, opinions, policy and perhaps investment decisions.

There are obvious benefits to engaging the media with scientific issues: reaching new and potentially large audiences, promoting awareness, driving interest and possible investment in new technologies, for example. We welcome the recent increasing commitment to communication of science and technology. However, there are concerns about media coverage of new technologies in general. These include:

- headlines that misrepresent research findings;
- inaccuracy, mistakes or lack of detail in reporting studies;
- misuse of 'balance' – i.e. presenting a minority view in a way that creates a false impression of balance of opinion amongst scientists or the public;
- focussing only on, or overstating, the possible benefits of a technology (and not reporting negative results, risks, long term uncertainties);
- over-reliance on a narrow range of sources; and
- uncritical reproduction of press releases.

The resulting misapprehensions of novel neurotechnologies amongst the public can be problematic for a number of reasons:

- They may instil false hope amongst patients by failing to report the limits or risks of current applications.
- They can affect patients' ability to make informed treatment choices.
- They could result in a loss of public trust in novel neurotechnologies.
- They could reinforce a notion that we are 'just' our brains.

The role of scientists, press officers and journalists

Scientists and press officers in research institutions are increasingly involved in public communications about science, but they face political, economic and institutional pressures to demonstrate important practical and economic impacts of their work. This, together with intense competition for science funding, can lead to a bias in favour of positive or newsworthy results.

Science journalists are working in an increasingly competitive and fast-paced media environment. Expanding workloads mean less time to seek out and research new stories, which may go hand in hand with an increasing reliance on PR material. There is a trend for brief and rapid responses to new developments, accelerated by advances in social media.

Responsible communication

All of the factors described above may in combination contribute to a 'spiral' of hype.

Responsible reporting of novel neurotechnologies should be accurate and avoid undue speculation. Importantly it should take account of the possible impacts that framing stories in certain ways could have for patients and families.

We conclude...

Researchers, press officers and journalists involved in the communication of the use of novel neurotechnologies should reflect on how their representations might contribute to hype, and exercise caution when describing the possible applications of a technology.

Policy makers and higher education funding councils should consider the effects of the 'impact agenda' in university funding in contributing to hype about novel neurotechnologies.

Companies and universities developing and promoting these products should consider their corresponding responsibilities carefully when seeking investment or promoting their products [Chapter 9].

Summary

Conditions affecting the brain such as Parkinson's disease, dementia, stroke, chronic pain and depression affect many people. Technologies that intervene in the brain offer potential to help people with such conditions, especially those with severe symptoms where other treatments have proved ineffective. The technologies also have potential application in military contexts, and to commercial developers looking to exploit their use for enhancement and gaming purposes.

This report looks at the benefits and risks presented by the development and use of a number of technologies that intervene in the brain. It considers the issues raised in relation to role of the brain in our self-perception, behaviour and personal relationships, the privacy of data about our brain activity, and the possible unintended effects of altering brain functions. Underlying these personal issues are also the wider social challenges of how regulation and innovation may be directed to developing safe and effective therapies and ensuring equitable access.

The report sets out an ethical framework to guide the practices of those involved in the development, regulation, use and promotion of novel neurotechnologies. The framework is based around two fundamental considerations: the need for medical interventions to treat brain conditions, and uncertainty about their benefits and risks. It suggests that the virtues of *inventiveness, humility and responsibility* capture the kinds of behaviours and attitudes that are most important in protecting and promoting the kinds of interests engaged by novel neurotechnologies.

Recommendations are made as to how this ethical approach might guide policy and practice in a number of areas including:

- Care of patients and research participants
- Responsible research and innovation
- Regulation of medical technologies
- Non-medical applications
- Communication and the media

The full report and this guide are available to download or order from the Council's website: www.nuffieldbioethics.org

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Nuffield Council on Bioethics
28 Bedford Square
London WC1B 3JS

Telephone: +44 (0)20 7681 9619
Email: bioethics@nuffieldbioethics.org
Website: www.nuffieldbioethics.org