

This response was submitted to the consultation held by the Nuffield Council on Bioethics on *Novel neurotechnologies: intervening in the brain* between 1 March 2012 and 23 April 2012. The views expressed are solely those of the respondent(s) and not those of the Council.

Foresight , Government Office for Science

NUFFIELD COUNCIL ON BIOETHICS CONSULTATION:

NOVEL NEUROTECHNOLOGIES: INTERVENING IN THE BRAIN

The consultation specifically focuses on the non-pharmacological technologies that intervene in the brain. To a greater or lesser degree, three of Foresight's major reports have potential overlap with this area.

Some of the consultation questions require expert personal judgement on the preferential use, or not of specific technologies, their efficacy and the associated ethical, legal and social issues which, as a GO Science official, falls our remit. Therefore, rather than address the consultation questions directly, I have set out some of the Foresight Programme's findings which the Working Party might wish to consider in their deliberation.

I would also propose that the Working Party might wish to review the three Foresight reports identified below in greater depth to ensure that their full relevance to its work was captured.

Report: Mental Capital and Wellbeing (2008)

<http://www.bis.gov.uk/foresight/our-work/projects/published-projects/mental-capital-and-wellbeing>

Some of the interventions suggested in this report may need to be implemented over many years. This is particularly true of those that seek to change current attitudes and behaviours. However, the evolving values and attitudes of society may themselves affect the viability of certain interventions – for example, due to changes in societal priorities or changes in ethical perspectives. It is impossible to predict how society and its values will change in the future; therefore it is important that decisions concerning interventions that are made today embody sufficient flexibility to adapt to future change.

Brain computer interfaces (BCI)

Nb BCI is specifically highlighted in the consultation

State-of-Science Review: SR-E29 - Brain-Computer Interfaces and Cognitive Neural Prostheses

http://www.bis.gov.uk/assets/foresight/docs/mental-capital/sr-e29_mcw_v2.pdf

It is now becoming possible to control prostheses using advanced techniques that infer intent of the subjects from signals recorded directly in the patient's brain, bypassing parts of the brain or spinal cord that are damaged by diseases such as amyotrophic lateral sclerosis (ALS), stroke or injury. Using

systems incorporating a brain-computer interface (BCI), patients can control prosthetic limbs, computer cursors, or stimulate their own muscles – by thought alone.

In developing such devices, **ethical constraints** would become important. It is one thing to implant electrodes surgically in the brain of a ‘locked-in’ patient in an attempt to give him or her the ability to communicate; it is quite another to carry out brain surgery on a fully-enabled individual in order to position devices intended to ‘improve’ his or her performance. One can expect great advances in brain science in the coming years, while at the same time hoping that ethical limits to human experimentation will continue to be respected as well. The surgery needed to implant electrodes against the motor cortex is minor (as brain surgery goes), and experience with cochlear implants and other devices using electrodes chronically implanted in the head suggests that issues related to infection and longterm performance of electrodes in the brain can be managed. At least in the US, BCI-based prostheses for profoundly disabled patients are likely to gain **regulatory approval** rather easily on humanitarian grounds.

Despite promising results, the current generation of BCIs has significant limitations. Electroencephalographic (EEG) -based systems, in particular, suffer from “long training periods, noisy signals, the continuous professional attention necessary, slow spelling speed, electrode and skin problems with long recording times, and the controlled attention focus required of the subject during spelling”. EEG-based systems (in particular) are also limited by high error rates of communication, even after long training times. In part this may be due to the small amplitude of the EEG, and the susceptibility of EEG recordings to artifacts resulting from body motion, eye blinks, and other effects. In part this may also reflect underlying biological variability. Another limitation is patient acceptance, particularly with invasive BCIs. While some of these limits can be overcome by improved technology, biology poses fundamental limits as well.

The surgery needed to implant electrodes against the motor cortex is minor (as brain surgery goes), and experience with cochlear implants and other devices using electrodes chronically implanted in the head suggests that issues related to infection and long-term performance of electrodes in the brain can be managed. However, for the foreseeable future, BCIs would appear best suited to enhance communication in severely disabled individuals. However, even for those applications, the performance of current devices leaves a lot to be desired – and a variety of other aids is available that may offer considerably better performance to the subject. The growth (and even existence) of a future market for BCI-based assistive devices will depend on the rate of improvement of the technology, which will be constrained by fundamental biological limitations. This uncertainty makes it difficult to predict the extent of the ultimate success of BCI technologies.

However, in the long-term (10 years plus), there are certainly grounds for optimism about successful applications of the technology. Within a decade,

assistive devices based on BCIs may have become truly practical for a large number of disabled individuals. Certainly, proof-of-concept for a number of such systems has already been obtained, even though few, if any, of these systems presently remain in use by patients after experiments have concluded. One can hope that this technology will find important applications apart from assisting disabled individuals. Some expert groups have predicted that, in the distant future, very advanced BCIs will become available for greatly enhancing the capabilities of normally-enabled individuals. In developing such devices, ethical constraints would become important. It is one thing to implant electrodes surgically in the brain of a locked-in patient in an attempt to give him or her the ability to communicate; it is quite another to carry out brain surgery on a fully-enabled individual in order to position devices intended to 'improve' his or her performance.

State-of-Science Review: SR-B15 Neurocognition and Neuroimaging in Major Depressive Disorder and Bipolar Depression: Implications for Treatment and Functional Outcome

http://www.bis.gov.uk/assets/foresight/docs/mental-capital/sr-b15_mcw.pdf

Current treatment options in Bipolar disorder (BP) and major depressive disorder (MDD) include **deep-brain stimulation**, where microelectrodes are surgically implanted into disrupted neural circuitry has shown promising effects over one to six months in small groups of patients. However, the complex issues associated with placebo control in such severely affected patients preclude definitive conclusions at the current time, and the nature of the intervention makes it likely that this procedure will only ever be employed in the most extreme cases.

Together, the findings from neurocognitive and neuroimaging studies indicate that MDD and BP depression can be distinguished, at least in part, by indirect and direct measures of brain activity in neural systems that are important for mood stability and executive control. While in their infancy, studies employing these techniques to identify neural system abnormalities that may represent treatment-relevant endophenotypes are promising in MDD, and suggest that identification of neurocognitive and neuroimaging variables that may predict treatment response in BP depression is feasible. It is clear that, in the future, studies employing these newly-developed neurocognitive paradigms with functional neuroimaging techniques may be able to draw us closer to meeting the critical challenges of early and accurate diagnosis and early optimisation of treatment of both MDD and BP depression. This should also prevent relapse and facilitate return to work as well as restoring quality of life in patients with depressive disorders. The final challenge will be to identify endophenotypic markers in order to identify at risk individuals prior to clinical onset.

State-of-Science Review: SR-E10 - Stem Cells in Neural Regeneration and Adult Neurogenesis

http://www.bis.gov.uk/assets/foresight/docs/mental-capital/sr-e10_mcw.pdf

A large number of neurological disorders may be amenable to cellular, including **stem cell, therapies**. These disorders range from acute injuries such as spinal cord trauma and stroke, to more chronic inflammatory and neurodegenerative disorders such as multiple sclerosis and Parkinson's disease. Each of these conditions has its own characteristic pattern and mode of cell death, which in turn presents challenges for their repair using cell therapies. For these therapies, stem cells are an attractive source. Firstly, they are found in the adult brain and thus, in theory, could be used to repair the brain 'from within'. Alternatively, stem cells harvested from a range of sources can be grown to large numbers in the laboratory and their fate potential manipulated in some cases, which would make them attractive for neural grafting in neurological disorders. Of these, Parkinson's disease (PD) and multiple sclerosis (MS) are the most obvious targets, although a range of other disorders have also been considered as possible areas for stem cell therapies. This review briefly discusses the different types of stem cells and their merits and disadvantages, before highlighting the importance of stem cell research for problems of the ageing brain and mental capital, but more especially PD.

PD is a common neurodegenerative disorder that can simplistically be viewed as a movement disorder consequent to a degenerating dopaminergic nigrostriatal pathway. As a result, drug therapies designed to replace dopamine in this pathway are symptomatically successful, but they are not curative and create side effects with chronic use and disease progression. Therefore, there is a need for curative therapy in PD. To date, this has mainly concentrated on replacing the lost dopaminergic neurons.

This search has encompassed many different types of cells, several of which have now reached the level of clinical trials. Of these, the most successful have involved human fetal mesencephalic tissue, although of late the clinical trials with this tissue in advanced PD have proven disappointing. Resolution of these disparate outcomes in patients receiving such transplants is necessary before further cell-based approaches can be undertaken in PD, including stem cells. Nevertheless, it is clear that, as our understanding of stem cells improves, there will come a time when such cells will be thought suitable for translation to the clinic for grafting in patients. In the meantime, sorting out how best to perform neural grafting in patients with PD remains a priority, along with harnessing the potential of stem cells to study PD at a variety of different levels.

Finally, we stress that, whilst our discussion has concentrated on PD, the principles underlying its treatment with cells is the same for all disorders of the CNS including normal ageing. So, the debates surrounding the use of stem cells in PD can equally be applied to a whole range of cell therapies and neurological disorders that will become more acute as the population continues to age and the number of individuals with neurodegenerative disorders and stroke increases. However, the use of such cell therapies in other neurological and psychiatric disorders remains a distant reality at the

present time. This is because a better understanding of the differentiation potential of stem cells needs to be acquired, along with a clearer understanding of the core pathological events in these disorders and how cells could be expected to reverse or modulate those processes.

Report: Brain Science Addiction and Drugs (2005)

<http://www.bis.gov.uk/foresight/our-work/projects/published-projects/brain-science>

<http://www.bis.gov.uk/assets/foresight/docs/brain-science/ethics.pdf>

<http://www.bis.gov.uk/assets/foresight/docs/brain-science/experimental-psychology.pdf>

<http://www.bis.gov.uk/assets/foresight/docs/brain-science/neuroimaging.pdf>

Brain Science Addiction and Drugs comments on the ethical considerations of the use of cognitive enhancement, however this is done in a pharmacological (rather than a neurotechnological) context. However, some of the concerns raised might equally apply to neurotechnological methods. For example, genetic predisposition to addiction and vaccination against drug addiction raise ethical issues, especially those of privacy, personal freedom, discrimination and confidentiality. These concerns must be balanced against the potential benefits for the individual and for society.

Collecting information on possible neurological problems is complex and must meet high ethical standards. Also, finding the right balance between ethical considerations of research on children's brains, and the importance of understanding the development of their brains so we can produce medicines for them, are particular challenges.

BSAD states that cognition enhancement policies should “*seek to minimise harm and also to consider the social and ethical issues*” and that “*We would need to understand the risks of the cognition enhancers to regulate them effectively.*” As indicated above, in this case the context is pharmacological however, the use of neurotechnologies for cognitive enhancement might also bear the same ethical, social and regulatory considerations. For example, pressure to protect information on individuals is very strong and we must ensure the protection and appropriate use of an individual's medical information and also ensure that we have the evidence to support the best decisions for the individual and common good. There are also inherently contentious ethical issues surrounding enhancement of the healthy brain. Also any coerced use of vaccines [or neurotechnologies] raises issues of human rights. Vaccination [use of neurotechnologies] without consent could deprive people of legitimate choices about their own lifestyle, whereas vaccines [or neurotechnologies] could bring many benefits from consensual use as a treatment.

Transcranial magnetic stimulation (TMS)

Much of the knowledge we gain from experimental psychology applies to non-chemical addictions such as gambling as well as to drug use. It also provides insights into future possibilities of direct intervention in the brain, such as **transcranial magnetic stimulation (TMS)** and the use of neural prosthetics to repair brain damage. Although not itself an imaging technique, TMS is increasingly being used in conjunction with neuroimaging techniques to explore the effects of inhibiting and modulating neural circuits. It has been postulated that repeated applications of repetitive TMS (rTMS) could lead to very long-lasting effects on brain function that could have potential therapeutic

value. This has led to trials of rTMS as a treatment for depression, obsessive compulsive disorder, migraine and several varieties of movement disorder. Currently (2005), the results suggest that some positive effects may be obtained, but in no case have the effects been superior to conventional treatments. In the future, increased understanding of how rTMS works and what neural populations are targeted may help improve prospect

TMS can explore the **effects of psychoactive substances** by comparing patterns of task-related brain activation in different populations of users. TMS in this case would be an adjunct to other methods of functional imaging. In addition, TMS can detect connectivity of brain areas, both at rest and during task performance, to test whether the use of psychoactive substances changes the organisation of brain areas. Finally, TMS can reveal how psychoactive substances can lead to changes in neurotransmitter release. In all cases, an important question will be whether the administration of such substances produces long-term effects on brain organisation that outlast the period of treatment.

The main potential contribution in **managing the use of psychoactive substances** is to replace some treatments with rTMS-based methods, which are currently (2005) being tested in patients with depression. As noted above, present studies are suggestive of the possibility of weak effects. However, more studies need to be done to understand which of the infinite number of possible combinations of rTMS applications, in terms of duration of treatment, intensity of TMS pulse, frequency of rTMS, etc., are optimal and to determine the best sites of stimulation to apply the rTMS. The effects of TMS can be seen at connected sites at a distance from the stimulated area.

Report: Cognitive Systems (2003)

<http://www.bis.gov.uk/foresight/our-work/projects/published-projects/cognitive-systems>

Cognitive Systems recognises that “*Like many other potential technologies involving artificial cognitive systems, these medical applications raise numerous ethical, social and legal issues*”. However, the report does not develop what these might be or specifically refer to novel neurotechnologies.