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.

**Association of British Neurologists**

Thank you for requesting a response to this document.

In response to the questions:

1) I have been involved with the care of patients who have had deep brain stimulation for Parkinson’s disease, dystonia, and with rare movement disorders such as Myoclonic Dystonia, and Hallervordan-Spatz disease. Such therapies in selected patients can be valuable in improving the motor disability, reducing the burden of care, and reducing the pharmacological cost of the illness through drug withdrawal in many patients. DBS is not a cure.

2) Not applicable

3) These are 2 very separate questions. Might there be a role for DBS in patients with psychological / psychiatric problems that affect the ability to lead a normal life? Such as obsessive/compulsive disorder. This could be argued. However, to allow recreational activity is another issue and in my view is unethical.

4) Has to be safe, with evidence from preliminary studies to suggest a degree of improvement in quality of life. Also potentially reversible. Of reasonable cost.

5) In centres where there is evidence of expertise in managing such therapies. Creating a national database, with vigorous entry and exclusion criteria. Also comprehensive monitoring of agreed outcomes at regular intervals.

6) No experience

7) In the individual who cannot direct their environment, or indicate their desires/needs in order to gain a degree of independence, and allow reduction in disability.

8) Needs to be safe, reliable, addressing an individual need.

9) The device must be used appropriately to meet the needs of the individual in maintaining quality of life and reduction in disability. If patient is believed to be competent, could commands be over-ridden without express authority of the patient?

10) Regulation will be mandatory. This must be patient focused, for the well being of the patient to reduce disability and suffering.

11) See 1.
12) See 1

13) I cannot consider any circumstance where it would be ethical to use neurostimulation if it is not for direct patient benefit.

14) When used for psychiatric states there must be a consensus from more than one psychiatrist that it is appropriate, and reversible. Furthermore, that all other possible interventions have been explored.

15) Regulation is paramount in safe-guarding and protecting the individual and society from abuse of such intervention. I am not familiar with current regulation (if there is any?).

16) As a potential, safe alternative therapy when standard treatments have failed.

17) The potential risks are numerous and require careful consideration. I suggest that the committee refers to published evidence from studies on complications, and morbidity.

The gain is a potential novel mechanism of repleting areas of the brain that require repair and/or reinnervation to allow return of function.

18) Yes, with fundamental religious and philosophical implications. This is a subject of intense debate in western societies and requires open discussion and deliberation.

19) Not appropriate

20) Regulation is paramount for a democratic, ethical society. We must listen to the views of the public in order to make coherent ethical judgements as to the value of an intervention and its source.

Many of the questions asked are of enormous ethical and moral dilemmas.

This format for discussion of such profound interventional advances in therapy has limitations.
11. Have you used neurostimulation and if so, with what consequences? Please describe your experience.

I am a consultant Neurologist with a special interest in Movement Disorders and responsibility for patients undergoing Deep Brain Stimulation procedures at the National Hospital for Neurology & Neurosurgery, Queen Square, London. One to two patients undergo Deep Brain Stimulation procedures each week at this hospital. In an audit of our performance in patients with Parkinson’s disease, patients experience a 56% improvement in their underlying illness severity. There has been no occurrence of symptomatic haemorrhage in over 300 patients receiving operations in our hospital.

There is some evidence that Deep Brain Stimulation, while improving movement symptoms in PD, can have negative effects on clarity of speech and fluency of word production. There are occasions where a compromise position needs to be sought between positive and negative effects of the stimulation. This experience is used as part of the pre-operative selection process to minimise the risk of disabling adverse effects in more vulnerable people. Compulsive behaviours tend to improve following DBS as a result of lowering medication doses. In the acute post operative setting, transient confusion, and behavioural change is not uncommon but can be easily dealt with appropriate clinical and social support.

I do not think there is sufficient evidence to suggest DBS is effective or should be tried in disorders of consciousness.

Informed consent is very rarely an issue in DBS surgery. There are some patients with severe learning difficulties accompanying a congenital disorder such as cerebral palsy that have potential to improve their movement as a result of DBS. In these circumstances, family members, clinicians and advocates rarely have difficulty reaching agreement about the patient’s best interest.

I have only minor experience of TMS which is predominantly used at our centre to investigate plasticity changes in the brain before and after DBS.

12. If you have not used neurostimulation before, under what circumstances would you do so?

Not applicable.

13. Under what circumstances do you think it might be acceptable to use neurostimulation in non-medical context (that is to say, not for the treatment of a disease or disability)?
There remains a considerable demand for DBS among patients disabled by physical symptoms including movement disorders, and chronic pain. It appears that DBS may also have profound effects on some disorders lying at the interface between neurology and psychiatry such as Tourette’s syndrome and Obsessive Compulsive Disorder, and these individuals should be carefully considered by multi-disciplinary teams regarding their suitability for DBS. We have a long waiting list for DBS surgery for these conventional indications, as well as a growing number of research programmes using DBS for “non-controversial” indications.

There is hope that well selected individuals may have improvements in cognition in response to DBS however this is not likely to be applicable to the vast majority of patients with dementia. Nevertheless the current demand for DBS is high and it should not in any way be forced to compete or be considered alongside experimental research of performance enhancement. I do not think that the introduction of DBS for people who do not have significant disability can be justified in any way.

14. Are there any particular ethical or social issues associated with neurostimulation?

There are many ethical issues. Our hospital is hosting an International meeting on Deep Brain Stimulation on 11-12 October 2012. Most of the major opinion leaders and pioneers of DBS will be speaking. Up to one third of the meeting will focus on Ethics. Details can be obtained via www.ucl.ac.uk/ion/departments/sobell/Research/UFN/Workshop2012

15. What would robust and effective regulation of research in this area look like? Is more or less regulation needed? Please justify your response.

Centres that have experience in movement disorders and have a proven track record of safety and effective outcomes from functional neurosurgery should be freed from the repetitive funding bureaucracy that currently surrounds NHS commissioning, and decisions regarding the appropriateness of DBS for conventional indications should be made on clinical grounds focussing on each patient’s best interest. Audit figures should be requested to ensure a centre is performing to an expected standard.

DBS as part of research programmes requires different regulation. Human research using devices as interventional therapies should be subject to the same regulations as pharmaceuticals i.e. regulated by a competent authority such as the MHRA. The difficulty arises when a single exposure to a non-invasive technique such as TMS requires to be considered as a study rather than a therapy. Investigators need to justify this position at ethics meetings as part of the approvals process. I have no experience of unexpected adverse events occurring as a result of TMS.

Questions

Prepared by: Dr R Barker, University of Cambridge on behalf of the ABN
16. Under what circumstances would you use neural stem cell therapy?

I think there is a very clear case to be made for using these cells when one is only trying to target selective populations of specific cells—e.g., motor neurones in Motor Neurone Disease or dopamine cells in Parkinson’s disease. I think that using these cells in diseases which have a distributed pathology of multiple networks of neurones are less likely to be targets for stem cells unless they are being used to offer support to networks of cells rather than cell replacement. Thus, I think they may find a place in Huntington’s disease, but not in stroke or Alzheimer’s disease.

17. What do you think of the risks and benefits of neural stem cell therapy?

I think the risks are:

(a) From the surgery itself (which is very minor)
(b) Overgrowth of the cells, which I think is unlikely given what we can do with the derivation of these cells nowadays
(c) Infection which again I think is minimal
(d) Migration and integration into “normal” circuits which is unknown and could be a problem
(e) Immune rejection
(f) Hype around what can be achieved in the first into man trials
(g) The occurrence of the disease in the grafted cells especially in case of iPS cell derived cells.

The benefits are:

(a) The capacity to repair an aberrant network and by so doing alter the natural history of the condition, without necessarily curing it
(b) Reducing the need for drug therapies and the side-effects associated with them and the financial savings that this will bring with it
(c) Treating diseases that have no treatments at the moment (e.g. MND)
(d) The ability to set up an iterative process to look at this experimental therapeutic approach and by which one can expand the repertoire of cells and disease that could be treated and how this can best be done in small experimental trials.

18. Are there any particular ethical or social issues associated with neural stem cell therapy?

The ethical problems are:
(a) Where the cells come from which is dependent on that source e.g. ES versus iPS versus bone marrow
(b) The scientific basis for doing the trial i.e. is there sufficient pre-clinical data to allow a clinical trial to be undertaken
(c) The ability of the patient with a neurological condition to give informed consent for experimental invasive trials of this nature
(d) The issues of trial design with such therapies and the interpretation of the data so obtained.

The societal issues are really to do with how we view the status of embryos and fetuses; what are we prepared to try in patients with incurable CNS disease; and where will this the of work end up given the history of psychosurgery.

19. How do you feel about neural stem cell therapy being used for non-medical purposes one day, for example for human enhancement?

I think this should not be allowed. The therapy should only be used to treat patients with defined, evolving neurological conditions for which there is a plausible and logical reason to use the cells for repair.

20. What would robust and effective regulation of research in this area look like? Is more or less regulation needed? Please justify your response.

I think that this work does need to be regulated and that in the UK we do this very well, as we take on board the views of all interested parties and move forward slowly with a consensus position. I think that it is imperative that when trials with stem cells are being discussed that the quality of the preclinical data in terms of efficacy and mode of action is especially scrutinised, rather than just issues to do with safety and the GMP standard of the prepared product. I say this, because there is a tendency for the regulatory agencies to naturally worry about the latter and forget the former, such that several trials have, or are taking place, where the cells are safe and of a GMP standard but there is no expectation that they will work based on the animal data which, whilst a poor imitation of the clinic, is nevertheless a vital part of the equation in deciding whether to move into patients.