Response to inquiries of the Nuffield Report

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Answers

1. Have you ever used a technology that intervenes in the brain, and with what consequences? Please describe your experience.

Yes, a number of times, inclusive of various forms of neuroimaging (e.g.- computerized tomography - CT, single photon emission computerized tomography- SPECT, magnetic imaging and functional magnetic imaging – MR/fMRI); physiological recording (i.e.- electroencephalography and magetoencephalopgraphy – EEG/MEG), neurofeedback; and transcranial stimulation – TMS. I have used these technologies both in my experimental studies, and have, on occasion, been subjected to these neurotechnologies – both as a research participant, and as a hospital patient. As a neuroscientist and neuroethicists, I've found "being on the other side of the machine" to be rather an interesting experience, in that it affords a subjective value to the event of neurological intervention, that is quite over-and-above the (attempted) approach of non-biased objectivity that one strives to assume and maintain as a researcher.

2. If you have not used a technology that intervenes in the brain before, would you do so if you were ill? Why / why not?

N/A

3. Would you use a technology that intervenes in the brain for non-medical purposes, such as gaming or improving your cognitive skills? Why / why not?

The question essentially focuses upon three core issues: 1) how emergent and/or existing science and technology are viewed, as regards to enabling and/or embellishing (viz. - enhancing) the actions and capabilities of specific aspects of daily life; 2) how parameters of human function, limits and being are operationally defined, with particular regard to notions of ecological stability and flourishing within the niches we - and other species -occupy and create; and 3) what and how are benefits measured and valued with respect to apparent and potential burdens, risks and harms.

Speaking to each in turn, I believe that a historicity of human endeavor reveals and sustains the iterative use of tools to (a) acquire information and knowledge; and (b) employ this knowledge or capacity to augment extant human bio-psychosocial traits, and compensate for abilities that are lacking. This, I feel is a realistic assessment of the reciprocity of tools-to-theory-to-tools heuristics that characterize much of human endeavor, and certainly define neuroscience and neurotechnological progress over the past 50 years. That said, these same heuristics afford some insight to the "nature" of the embodied human who is embedded within environments as part of our ecology. Simply put, there is a perdurable trend for human tool use – and neuroscience and technology have afforded means to better understand the natural world (inclusive of human structure and function) and at the same time exert control of/over it (and here too, inclusive of human structure and function).

Therefore to my view, any genuine evaluation of neurotechnologies must begin from and allow for recognition of an implicit and explicit imperative for their use (driven by social, economic and individual agendas for flourishing). In defining and guiding such use, however, it is important that both technical rectitude and some form of ethical prudence be embraced and enforced, so as to uphold the safety of each and all of these techniques and technologies, as best possible. This provides the groundwork upon which to base – and evaluate - personal/individual, group, and community decisions to use or not use these technologies relative to the benefits, burdens and harms incurred to self and others.

4. What are the most important ethical challenges raised by novel neurotechnologies that intervene in the brain?

I contend that there are 5 major ethical issues and challenges raised by novel neurotechnologies that intervene in the brain; namely, these are:

1. A partial understanding of the full scope of potential burdens, risks and harms that may arise from nascent technology;

2. "Incomplete" science, viz.- an incipient and/or partial understanding of neural mechanisms involved in/subserving processes of cognition, emotion and behaviors;

3. Taken together, these lead to:

(a) possible unanticipated, and/or runaway consequences/effects, and

(b) difficulties in securing fully informed consent to employ these techniques and technologies, in both medical and non-medical situations;

4. Socio-cultural and/or philosophical/theological debates about the "nature" and "limits" of the human being and human capabilities (e.g.- contexts and issues of what constitutes "treatment", "enablement", "enhancement", "normal/abnormal", and concepts such as "cyborgization", and transhumanism);

5. Justice in provision, access and acquisition/use of these techniques and technologies; specifically:

(a) distinctions between commutative and distributive justice

(b) leveraging neurotechnologies upon a pluralist world-stage

(c) addressing, controlling and/or mitigating resultant "bio-power" and "bio-politics".

As recently noted, (Giordano, 2012; Giordano & Benedikter, 2012) even a cursory assessment of the contemporary environment of healthcare provision reveals that neo-classical, Smithian assumptions are unrealistic. Goods and resources are limited, and their provision is based upon a multi-factorial and variable calculus that determines the relative distribution of biomedical goods and services. Simply put, even in countries in which there medicine is fully subsidized by the government, it is probable – based upon recent trends in allocation of biomedical resources and services – that everyone will not be able to get such high-tech medical interventions, as these are often only partially covered, and in some cases, not covered at all by the majority of health provision (and/or insurance) plans. So, who will receive state-of-the-art neurotechnological interventions? Will these approaches become part of a new 'boutique neurology and/or psychiatry'? Or, will there be active assertion and effort(s) to increase the utility and use of these interventions, so as to make them more affordable and more widely accessible within the general population of those patients who might require them?

<u>See:</u>

Giordano J. Neurogenetic and neural tissue implantation technology: Neuroethical, legal and social issues. In: Giordano J. (ed.) *Neurotechnology: Premises, Potential and Problems.* Boca Raton: CRc Press 2012, p. 59-68.

Giordano J, Benedikter R. An early - and necessary - flight of the Owl of Minerva: Neuroscience, neurotechnology, human socio-cultural boundaries, and the importance of neuroethics. *J. Evolution and Technol*. 22(1): 14-25. (2012)

5. In what ways, if at all, should the development and use of these technologies be promoted, restricted and/or regulated? Please explain your reasons.

I am optimistic about the potential benefits that neurotechnology may offer. But, it is important to critically evaluate what such developments obtain, mean, and could incur on individual and social levels. A vital first step is the frank, pragmatic evaluation of neuroscientific facts, their contingency, and the tools and tasks that are constructed from them. This pragmatic stance must balance optimism and pessimism, aspirations and anxieties, and the potential for use and misuse, so as to remain prepared for both positive and negative effects, outcomes, and consequences.

I argue that a simple precautionary principle is insufficient and counterintuitive in that potential burdens and risks of any new technique or technology will always tend to be greater than apparent benefits: simply , this is because benefits tend to be proximate – and the "driving force" of the majority of such technological developments - while burdens and risks occur with more protracted use in practice, occurrence and influences of other events, and/or acquisition of new information and knowledge (Giordano, Akhouri and McBride, 2009). Preparedness is an active process that requires engagement of teams of personnel from multiple disciplines in an integrative convergent approach (see, for example, Giordano 2012), a pragmatic assessment of all available information, and use of scenario-gaming, modeling and evaluation. This approach is also important to informing and formulating guidelines and policy; policy enables funds to support research and translate research findings and products to clinically viable assets, and can direct economic resources toward provision of these technologies to accommodate the needs and demographics of the patient population. But, the public must be conjoined to this process if it is to instantiate and empower neurotechnology as a viable social good (Benedikter, Giordano, 2011).

<u>See</u>:

Giordano J, Akhouri R, McBride DK. Implantable nano-neurotechnologies: Ethical, legal and social issues. *J Longterm Effects Med Implants* 5(9): 45-54 (2009)

Benedikter R, Giordano, J**.** The outer and inner transformation of the global sphere through technology: The state of two fields in transition. *New Global Studies;* 5(2); (2011).

Giordano J. Integrative convergence in neuroscience: trajectories, problems and the need for a progressive neurobioethics. In: Vaseashta A, Braman E, Sussman, P. (eds.) *Technological Innovation in Sensing and Detecting Chemical, Biological, Radiological, Nuclear Threats and Ecological Terrorism.* (NATO Science for Peace and Security Series), NY: Springer, 2012.

6. Have you used a BCI, and if so, with what consequences? Please describe your experience.

Yes, as part of an experimental trial to direct cursor movement and acquire computational information in an aviation-simulator/flight simulation paradigm. Clearly, these technologies, while budding, are poised upon a steeply sloping, and rapidly progressing trajectory that incorporates a host of shared technological capacities, and that are likely to be extrapolated and translated into a variety of applications, inclusive of medical, public life (such as adaptive assistive technologies, in both cases) and military scenarios.

7. If you have not used a BCI before, under what circumstances would you do so?

N/A

8. What are your expectations and concerns for BCIs?

With continued progress, BCIs offer great potential for neuroprosthetics, neuro-orthotics, adaptive and assistive living technologies, and educational uses (Hinterberger, 2010; Chhatbar & Saha, 2012). A current concern is if/how BCI's might affect the treatment/enhancement and normality/abnormality discourse, particular as relates to use, viability and value of iterative generations of cochlear implants and how this may influence ontological assertions, claims and conduct of the Deaf community and culture. See below for additional concerns relative to such expected and possible advancements.

<u>See:</u>

Hinterberger T. Possibilities, limits, and implications of brain-computer interfacing technologies. In: Giordano J, Gordijn B. (eds.) *Scientific and Philosophical Perspectives in Neuroethics.* Cambridge: Cambridge University Press, 2010, p. 271-282.

Chhatbar P, Saha S. Neuroprostheses: Implications of the current and future state of the science and technology. In: Giordano J. (ed.) *Neurotechnology: Premises, Potential and Problems.* Boca Raton: CRC Press, 2012, p. 93-106.

9. Are there any particular ethical or social issues associated with BCIs?

See question 4, issues and concerns similar if not identical, however a persistent issue is that of commercialization without stringent direction, regulation or governance of certain forms of BCIs (e.g.- EEG-based neurofeedback);

<u>See:</u>

Plischke H, Du Rousseau D, Giordano J**.** EEG-based neurofeedback: The promise of neurotechnology and need for neuroethically-informed guidelines and policies. *J. Ethics Biol Engineer Med* 4(2): 7-18, (2012)

Giordano J, DuRousseau D. Toward right and good use of brain-machine interfacing neurotechnologies: Ethical issues and implications for guidelines and policy. *Cog. Technol.* 15 (2): 5-10 (2011).

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

We have called for uniform, enforced screening for all BCI neurotechnology products to assess whether products may incur potential risks to the general public (and more specifically to persons with particular pathologic pre-dispositions or conditions- such as seizure disorder, bipolar disorder, and types of impulse and behavioral control disorders). Currently, the manufacture of games, and/or stress-reducing devices that utilize forms of neurofeedback are not uniformly regulated, and so the distribution and use of these technologies and devices fall outside of governmental oversight and control.

We have called for an expanded oversight and regulation of the industry, clinical *and* public use of these technologies and devices, and the level of education and specialized experience of providers, and have argued that at least at present – given currently available evidence of benefits, burdens, risks and harms - BCI neurotechnologies should be primarily used in the clinical setting, and that persons prescribing, coordinating and providing BCI-based interventions should be licensed physicians, or clinical psychologists. Additionally, we call for the provision of explicit language on any/all "over-the-counter" BCI-neurotechnologies that dictates medical clearance for use (as with many other over-the-counter medical products), and 2) warns of possible adverse effects and consequences of use/misuse.

See:

Giordano J, DuRousseau D. Toward right and good use of brain-machine interfacing neurotechnologies: Ethical issues and implications for guidelines and policy. *Cog. Technol.* 15 (2): 5-10 (2011).

11. Have you used neurostimulation and if so, with what consequences? Please describe your experience.

Yes; I have experienced transcranial magnetic stimulation as part of a research protocol involving affect and thematic apperception. It was, in fact, effective in producing an altered (i.e.- improved) mood, and to some extent, heightened sense of clarity and intensity of the visual

scenes presented, both acutely, and with increasing regularity and durability over the course of trial

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

N/A

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)?

See response to question 3.

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

Please see response to question 4.

As well, it is important to note that with advancing frontiers of neuroscientific and neurotechnological capability, philosophical foundations and ethical boundaries that define and guide the utility and use of these tools and approaches in society are challenged. What should be done if and when an intervention such as neurostimulation (or any other neurotechnology) both mitigates pathologic signs and symptoms, and also induces changes in personality traits and personal identity? There is evidence that neurostimulation procedures can, and often do exert such effects, yet, there is no reason to assume that these changes will necessarily be negative (or positive, for that matter).

Thus, important ethical questions might be whether neurotechnologic interventions such as transcranial or deep brain stimulation threaten, diminish or augment certain personality traits and personal identity, and how such alterations affect the patient, as well as her personal and professional relationships. How will these effects be judged – and by whom? What ethical constructs might be best suited to direct decisions about whether to use neurostimulation technologies given such potential changes? This is not a straw man argument. While negotiating the benefits, risks and burdens of any intervention is axiomatic to clinical decision-making, the first three major points outlined in response to question 4, above, that arise from the unique nature of neuroscience and neurotechnology (i.e.- incipient and/or partial understanding of neural mechanisms involved cognition, emotion and behaviors; partial understanding of the full scope of potential burdens, risks and harms of new technology; and runaway consequences/effects, and resultant issues surrounding fully informed consent) are crucial to discussions and decisions about the use of neurostimulation– and any advanced – neurotechnologies.

<u>See:</u>

Jotterand F, Giordano J. Transcranial magnetic stimulation, deep brain stimulation and personal identity: Ethical questions and neuroethical approaches for medical practice. In: Giordano J. (ed.) *Neurotechnology: Premises, Potential and Problems.* Boca Raton: CRC Press, 2012, p. 107-124.

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

As discussed in response to question 10, it is important that policy and regulation be well-informed, and that such information must avoid over-simplification, exaggeration, or miscommunication of potential capabilities, mechanisms, effects, as well as risks and/or harms of the technique and technologies in question. Any and all guidelines and policies must be based upon the most current factual information, accurately represent this information, and seek to direct the use and application of these technologies in ways that responsibly uphold the good of individuals and the public. This requires stringent assessment of what these technologies can actually do, how they can be used (i.e.- technical rectitude), and evaluating the ways that, and for whom such technologies *should* be used (i.e.- ethico-legal probity; see also, response to question 2, above).

See:

Plischke H, Du Rousseau D, Giordano J. EEG-based neurofeedback: The promise of neurotechnology and need for neuroethically-informed guidelines and policies. *J. Ethics Biol Engineer Med* 4(2): 7-18, (2012).

16. Under what circumstances would you use neural stem cell therapy?

Neural stem cells therapy could be employed to repair, regenerate, re-model and re-direct the viable structure and function of specific neural networks that are involved in, and/or subserve particular cognitive and/or behavioral abilities, and which have been insulted by trauma, disease, decline or congenital malformation.

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

Neural stem cell therapy (NSCT) can incur risks of: 1) mutagenesis and possible anaplastic variation, and 2) possible aberrant activity and irreversibility when using NSCs, due in part to: a) the inherent properties of the donor material, and b) the effects of host tissue factors upon implanted matter. These possibilities might be respectively mitigated through the use of lentiviral vectors (Meloni, Malley, Faucon-Biguet, 2010) Philippe et al., 2006), and co-implanted real-time biosensors that are linked to devices (such as molecular scaffolds or carriers) that can suppress local neuronal activity via the release of restrictor/regulator ligands (Giordano, Akhouri, McBride, 2009) , and in these ways might potentiate benefits of NSCT in the prevention, treatment and rehabilitation and/or management of previously intractable neurological diseases and injury. Such possibilities have been further augmented by the conjoinment of genetic, nanoscale, and computational technologies in neuroscientific applications.

See:

Meloni R, Mallet, J, Faucon-Biguet N. Brain gene transfer and brain implants. *Studies in Ethics, Law, and Technology* 4(3): (2010).

Philippe S, Sarkisa C, Barkats M, Mammeri H, Ladroue C, Petit C, Mallet J, Serguera C. Lentiviral vectors with a defective integrase allow efficient and sustained transgene expression in vitro and in vivo. *Proc Nat Acad Sci.* 103, 17684-9. (2006)

Giordano J, Akhouri R, McBride DK. Implantable nano-neurotechnologies: Ethical, legal and social issues. *J Longterm Effects Med Implants* 5(9): 45-54 (2009)

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

Perhaps glaringly the most influential issue regarding NSCT is the continued debate over the use of embryonic stem cells, in general. Obviously, this issue bears upon any consideration and context of NSCT, and thus cannot be disregarded as it continues to affect the scope and conduct of SCT research and use, at least to some extent. Of course, the variety of (non-embryonic) stem cell lines that are currently at least putatively viable for NSCT afford a side-step to those issues and concerns generated from the use of embryonic/fetal stem cells. More specifically, however, a number of ethical issues are centered upon NSCT, those explicated in response to question 4 (above), as well as concerns about "identity" given the extent of implanted "non-self" (ie- xenotransplanted) tissue, shifting constructs of personal and community ontologies, and definitions of normality.

See:

Boer GJ. Transplantation and xenotransplantation. In: Giordano J, Gordijn B. (eds.) *Scientific and Philosophical Perspectives in Neuroethics.* Cambridge: Cambridge University Press, 2010, p. 190-215.

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

I maintain that given the present state of the science (i.e.- the potential for failure, risks and harms), consideration of NSCs for anything beyond medical purposes is difficult to justify, and problematic to ethically support or sustain, even from a position of total (non-trumping) respect for individual autonomy and freedom of choice. A best-interest standard would tend to mitigate such use in light of an inability to accurately assess benefit-risk-harm ratios with sufficient accuracy to empower patients' fair choice(s).

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

As discussed in previous responses, any and all guidelines, regulations, directives, policies and laws should be informed by, and based upon detailed and pragmatic address, assessment and pre4sentation of the factual capabilities, and limitations of NSC technology and techniques. Clearly, however, the potential promise – as well as the ongoing difficulties - of this nascent technology compel ongoing research so as to examine, evaluate and define those approaches that are most effective, safe and of greatest utility in alleviating the effects of identified pathologies.

Working in our group, Misti Ault Andersen, Dan Degerman, Nicholas Fitz (now of the National Neuroethics Core at the University of British Columbia, Canada) and Daniel Howlader are collaborating with Roland Benedikter of Stanford University, California, to examine those ways that NSC research – and other neurotechnological developments – are being undertaken in the United States, Western European countries (eg- United Kingdom, Germany, etc) and non-western nations (e.g.- China, India, Korea) in an attempt to both (a) gauge respective paths and extent of scientific progress, and (b) assess and analyze differing ethical approaches to the scope, conduct and translation of this research within these respective countries, and (c) how such distinctions in research practices, ethics and policies may affect medical, social and economic balances upon the world stage.

<u>See:</u>

Anderson M, Fitz N, Howlader D. Neurotechnology research and the world stage: ethics, biopower and policy. In: Giordano J. (ed.) *Neurotechnology: Premises, Potential and Problems.* Boca Raton: CRC Press, 2012, p. 287-300.

Giordano J, Benedikter R. An early - and necessary - flight of the Owl of Minerva: Neuroscience, neurotechnology, human socio-cultural boundaries, and the importance of neuroethics. *J. Evolution and Technol.* 22(1): 14-25. (2012)