Journal of Law and the Biosciences, 328–333
doi:10.1093/jlb/lsu017
Peer Commentary
Advance Access Publication 30 August 2014

Regulation of cognitive enhancement devices: commentary

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ABSTRACT

Maslen et al. (2013) have provided us with a comprehensive overview of the current legislation regulating non-clinical cognitive enhancement devices (CEDs) in the European Union and have proposed a specific model whereby CEDs would be regulated in the same way as medical devices. An alternative model would be to require manufacturers to quantify risks only. Irrespective of the purported 'benefits' of a product, this would allow the consumer freedom of choice to use the product at their will and allow the periodic review of worthwhile indications and unexpected adverse events. Although this departs from the standard Cochrane-type assessment, it takes into account the facts that (i) the evaluation of clinically used cognitive enhancement techniques may not be as rigorous as one might expect, (ii) variations and case-by-case use might be widespread, and (iii) independent variables of significance and useful endpoints may not be obvious *ab initio*. We consider cerebrospinal fluid diversion techniques which are widely used clinically to enhance cognition in patients with normal pressure hydrocephalus despite any large-scale clinical studies demonstrating substantial benefit, and the real risks of paralysis and death from these invasive procedures. The risks of CEDs which have been available for some time need to be kept in perspective: are the risks really more than using conventional cognitive enhancement techniques such as imbibing too caffeinated drinks? Furthermore, the loss of Europe as a market for CEDs which do not comply with the proposed regulatory model implies a potential gain in the market for other parts of the world. This could impact on the ability of companies in Europe being able to compete in an evolving market demand for CEDs. Legislation to regulate CEDs should be guided by the principle of 'do no harm' and allow for innovation and competition.

KEYWORDS: cognitive enhancement devices, medical devices

Cognitive enhancement devices (CEDs) are becoming more widely available, but there has been a paucity of recommendations on how they should be regulated. Many of these devices have been developed for therapeutic use, but as they are perceived to be relatively innocuous and low risk, manufacturers are marketing them to the general public for non-medical use. CEDs have the potential to improve individual quality of life, productivity, and even to reduce the effects of ageing, and thus may be of great benefit to society as a whole. Although no therapeutic claims are being made, the sale of such devices raises questions regarding their efficacy as CEDs and the risk of harm from off-label use of such devices, and the question of how they should be regulated has therefore arisen. Maslen et al. have previously proposed that, within the European Union (EU), such devices should be regulated in the same way as medical devices.[1,2] In their latest version of this thesis, Maslen et al. have provided us with a thorough overview of the current legislation regulating non-clinical CEDs in the EU and a comprehensive defense of their position.[3] They argue that their position is ultimately justifiable because CEDs have similar mechanisms and risk profiles to some medical devices. It is proposed that CEDs with high-risk profiles, eg, the risk of inducing seizures, should be banned outright, whereas CEDs with low-risk profiles would be exempt from regulatory oversight, except when intended for use in vulnerable third parties. This leaves those devices with moderate-risk profiles the mainstay of the regulatory proposals, with the requirement that manufacturers quantify and assess the benefits of such devices in the same way as medical devices and provide comprehensive evidence-based information about their mechanisms, safe use, risks, and benefits.

The most convincing argument in favor of the position put forward by Maslen et al. is the assessment of risk. As with medical devices, and indeed pharmaceuticals, risk is more readily defined than with conventional devices and the authors have kept the actual risks in perspective. Are the risks of many CEDs really more than those involved with the use of conventional cognitive enhancement techniques, such as imbibing caffeinated drinks, and education and training to improve concentration, memory, and critical thinking (even if education and training take the form of a piece of computer software)? Regulation of CEDs can only realistically reduce risk by limiting their availability, and the stance taken by Maslen et al. would appear to achieve this aim with their three-tiered risk profile. Nonetheless, an alternative would be to define the baseline risk that society feels an individual should be allowed to take; recreational climbing or skydiving, for example, poses real risks of death and disability. If there is a potential benefit of CEDs, what risks are we, as a society, comfortable with the individual taking? This would be in line with previous arguments in favor of the use of cognitive-enhancing drugs in presuming that mentally competent adults are responsible for themselves and their own well-being and should be given the freedom to assess the risks and make their own choice.[4] An alternative model, therefore, would be to require manufacturers to

1 Hannah Maslen et al., *Do-It-Yourself Brain Stimulation: A Regulatory Model*, J. Med. Ethics, DOI: 10.1136/medethics-2013-101692.

2 Hannah Maslen et al., *Regulation of Devices for Cognitive Enhancement*, 382 Lancet 938–939 (2013).

3 Hannah Maslen et al., *The Regulation of Cognitive Enhancement Devices: Extending the Medical Model*, 1 J. Law Biosci. 68, 69 (2014), DOI: 10.1093/jlb/1st003.

4 Henry Greely et al., *Towards Responsible Use of Cognitive-Enhancing Drugs by the Healthy*, 456 Nature 702, 705 (2008).

quantify risks only. In this way, irrespective of the purported 'benefits' of a product, the consumer retains freedom of choice to use the product at his/her will, and the model allows periodic review of worthwhile indications and unexpected adverse events. Although this departs from the standard Cochrane-type assessment, it takes into account the facts that the evaluation of clinically used cognitive enhancement techniques may not be as rigorous as one might expect.

Although there are stringent regulations for the evaluation of pharmaceutical cognitive enhancers, the same may not be the case for therapeutic CEDs. Diversion of cerebrospinal fluid (CSF) by the surgical insertion of a ventriculoperitoneal shunt (VPS) is an accepted treatment of normal pressure hydrocephalus (NPH).[5] NPH is characterized by a clinical triad of cognitive decline, gait ataxia (poor balance), and urinary incontinence.[6] In the framework proposed by Maslen et al., the insertion of a VPS is a high-risk procedure as there is a risk of seizures, stroke, paralysis, and death. However, despite such risks there has never been a comprehensive multicenter randomized controlled trial that demonstrates the efficacy of this procedure. When consenting patients for this procedure, there is, therefore, no comprehensive evidence-based information that can be provided to the patient prior to surgery. Nonetheless, this is a widely used procedure in developed countries, with thousands of procedures performed in each year. It may not be practical, therefore, to enforce the provision of evidence-based measures of efficacy to consumers for CEDs for non-therapeutic use. On the other hand, manufacturers could be required to state clearly the lack of such evidence when it does not exist. From a legal perspective, this scenario may be covered by legislation covering trades' description and false or misleading advertising, in which case this would lean more to a *status quo* model, rather than regulating CEDs as medical devices.

Regulation in our view should be careful and limited, so as to maximize the opportunity for potential benefits and minimize harm with the minimal amount of fuss. If a risk-only model were used, there might also be scope for requiring users of risky devices to obtain a license to do so. In this way, people willing to undergo potentially risky but rewarding enhancements could be required to demonstrate sufficient understanding of the risks and the ability to handle them responsibly. This would both ensure informed consent and, if there were a license fee, provide some funding to enable monitoring of CED use. Furthermore, the fact that known and reported risks are displayed but that variably relevant positive data may not be included would reflect the fact that, in situations in which a relatively innovative application of a recognized technology was in view, variations and case-by-case use might be widespread, and independent variables of significance and useful endpoints may not be obvious *ab initio*. Thus, for instance, insertion of a VPS for a patient who had cognitive decline of a non-diagnostic type, associated with some indication of poor CSF drainage, might be worth trying, provided that the patient understood the possible risks. In such a case, there would be uncertainty of improvement and yet the results might be surprising and unpredicted, eg, positive mood change and increased pleasure in social activities, rather than any measurable cognitive improvement.

[5] Glen R. Finney, *Normal Pressure Hydrocephalus*, 84 INT. REV. NEUROBIOL. 263, 281 (2009).

[6] Hakim S & Adams R.D., *The Special Clinical Problem of Symptomatic Hydrocephalus with Normal Cerebrospinal Fluid Pressure: Observations on Cerebrospinal Fluid Hydrodynamics*, 2 J. NEUROL. SCI. 307, 327 (1965).

In addition to the risk of harm to the individual user, other ethical issues arise from the commercial availability of CEDs, including the impact of such technologies on social equality by potentially providing an unfair competitive advantage to the user. Whereas conventional strategies for cognitive enhancement such as education, nutrition, memory training, and even sleep are widely accepted, unconventional strategies with CEDs are more likely to be met with distrust and the feeling that they are somehow a form of cheating by undermining human effort.[7] Of course, such arguments depend on the baseline level of functioning of the individual concerned, as cognitive enhancement is relative: a 10 per cent improvement in short-term memory of one person may be of little consequence, whereas for another it may be the difference between success and failure. In this way, the distinctions between therapeutic and non-therapeutic enhancement are more difficult to discern, and from this standpoint one could argue in favor of treating the CEDs in the same way as medical devices as per Maslen et al.

However, irrespective of the validity of such objections, perhaps the most important ethical concern would be coercion in the use of CEDs by children and members of other vulnerable groups. The framework proposed by Maslen et al. takes this into account elegantly, as they propose that the exemption of low-risk devices from regulation would not apply where CEDs are intended for use by vulnerable third parties, including children. This protection would be maintained if the regulatory model were based on risk assessment only. Nonetheless, there are potential arguments against protection of children. Bostrom and Sandberg have argued that education of children itself has risks, which, although they may be considered to be inherently different from medical risks, are still real and are imposed upon non-consenting children.[8] However, when considering the autonomy of the child in the context of medical consent, regulation to protect them from coercion should be welcomed.

Regulatory requirements on the manufacturer to provide information regarding the risks and benefits of their products are one means of informing the consumer. However, it has been previously proposed in the case of cognitive-enhancing drugs that there is a public health responsibility on physicians and other educators to inform people about the known cognitive-enhancing benefits of healthy eating, adequate sleep, and exercise.[4] One possibility, therefore, is to require CED manufacturers to disseminate such information with their products.

In addition to possibly improving the quality of life of the individual, the potential benefit to society of CEDs is of major importance when considering legislative control of their use. The social and economic benefits of a higher IQ are well known.[9,10] Bostrom and Sandberg have highlighted the potential impact on society, in terms of technological, economic, and cultural development, which might result from the cumulative effect of many individual increments in cognitive function.[8] In order for society

[7] Maratha J. Farah et al., *Neurocognitive enhancement: what can we do and what should we do?* 5 NAT. REV. NEUROSCI. 421, 425 (2004).

[8] Nick Bostrom & Anders Sandbery, *Cognitive Enhancement: Methods, Ethics, Regulatory Challenges*, 15 SCI. ENG. ETHICS 311, 341 (2009).

[9] David S. Salkever, *Updated Estimates of Earnings Benefits from Reduced Exposure of Children to Environmental Lead,* 70 ENVIRON. RES. 1, 6 (1995).

[10] Linda S. Gottfredson, *Life, Death and Intelligence,* 4 J. COG. EDUC. PSYCHOL. 23, 46 (2004).

to benefit, regulatory models will need to take this into account by allowing for, and even cultivating, an environment that promotes innovation.

Technological innovation and translational research may provide us with more CEDs and, provided there is a consumer appetite and demand for such devices, commercial partnerships are necessary and inevitable. Although such funding of scientific research and innovation may have its drawbacks because of potential conflicts when there is a tangible commercial interest, this has long been the situation in the pharmaceutical industry and, arguably, results in more research and development than would otherwise occur through state-funded research alone. This is an essential consideration when legislation that affects research and innovation differs between economic areas. The regulatory framework proposed by Maslen et al. affects CEDs within the EU. It is arguable that if there were an impact on the ability of companies in the EU to compete in this evolving market, then CED development could move elsewhere to the detriment of those within the EU.

It is interesting to consider how CEDs would be considered in jurisdictions outside the EU. For example, it is debatable whether CEDs would fall within the regulatory framework for medical devices in New Zealand and Australia. A 'medical device' is defined by the New Zealand Medicines Act 1981 as 'any device, instrument, apparatus or appliance or other article that is intended to be used in, on, or for human beings for a therapeutic purpose'.[11] Section 4 of the Act further defines 'therapeutic purpose'. It provides that 'unless the context otherwise requires', therapeutic purpose means, amongst several other listed purposes, 'influencing, inhibiting, or modifying a physiological process'.[12] On first glance, this description would appear to encompass some CEDs. However it is likely that, when considered in the broader context of the section and the other specified purposes, the phrase would be interpreted as only encompassing devices intended to be used for the purposes of prevention, diagnosis, or cure in the context of a disease, ailment, defect, injury, or condition.

Australia's Therapeutic Goods Act 1989 (Cth) provides separate definitions for 'therapeutic device' and 'medical device'. A 'therapeutic device' is an 'instrument, apparatus, appliance, material, or other article' that is also a 'therapeutic good', which in turn is something that is represented in any way to be, or is likely to be taken to be, for therapeutic use.[13] 'Therapeutic use' is further defined in similar terms to the definition of 'therapeutic purpose' in New Zealand's Medicines Act 1981 and includes 'influencing, inhibiting, or modifying a physiological process in persons'. A 'medical device' is defined as 'an instrument, apparatus, appliance, material, or other article' intended to be used for one of the specified purposes which includes 'investigation, replacement or modification of the anatomy or of a physiological process'.[14] Significantly, the same phrase appears in the definition of a 'medical device' in the third indent of Article 1(2)(a) of the MDD.[15] In a recent preliminary ruling to clarify the scope of that phrase, the European Court of Justice interpreted it in the context

[11] Medicines Act, 1981, s 3A.
[12] Medicines Act, 1981, s 4(d).
[13] Therapeutic Goods Act, 1989, s 3.
[14] Therapeutic Goods Act, 1989, s 41BD.
[15] Directive 93/42/EEC.

of Article 1(2)(a) as a whole as well as the objective of the European legislature in drafting the MDD. It held that a product that 'is *not* conceived by its manufacturer to be used specifically for a medical purpose' does not come within the concept of a 'medical device'.[16] Given this outcome, it is unlikely that a CED would be held to fall within the regulatory framework for medical devices in New Zealand or Australia.

In the unlikely event that CEDs were to fall within the New Zealand/Australian regulatory frameworks, or alternatively if they were to be specifically incorporated into them as Maslen et al. suggest, they would be regulated by two statutory authorities: the Australian Therapeutic Goods Administration (TGA) and the New Zealand Medicines and Medical Device Safety Authority (Medsafe), respectively.[17] The Australian and New Zealand regulatory frameworks are informed by the Global Harmonization Task Force principles,[18] as is the EU framework.[19] Both Australia and New Zealand require a medical device to be classified and assessed according to a device's intended purpose and the potential risk(s) associated with it. The classifications range from Class 1 (low) to successively higher levels of risk, depending on various factors, such as whether the device is invasive and whether it is intended for short-term or long-term use. Medical devices must be registered on the Australian Register of Therapeutic Goods prior to supply in Australia,[20] and in the case of New Zealand, registered on the New Zealand Web Assisted Notification of Devices.[21]

In the future, it is likely that CEDs will be more invasive than are currently available devices, eg, the use of deep brain stimulation devices or brain chip technologies. Organizing legislative frameworks for currently available CEDs will set an important precedent as to how these more invasive, and potentially more risky, devices are regulated. The proposals of Maslen et al. are, therefore, to be welcomed as they go beyond a call for more detailed discussion and debate and provide us with a detailed proposal as to how regulation can be achieved. Irrespective of the model of regulatory legislation used to govern the use of CEDs, the ethos should be guided by the principle of 'do no harm' and allow for innovation and competition where possible in order to maximize the potential gain of such technology.

[16] Case C-219/11, Bain Products GmbH v BioSemi VOF and Others [2012] E.C.J. at [30].

[17] Arrangements to establish a trans-Tasman Australia New Zealand Therapeutic Product Agency to regulate therapeutic products, including medical devices, are currently being developed.

[18] The GHTF was an organization originally founded by representatives of national medical device regulatory authorities of the EU, USA, Japan, Australia, and Canada that sought to achieve international consistency in regulating medical devices to ensure their safety and quality. It is now the International Medical Devices Regulators Forum.

[19] Schedule 1 of the Therapeutic Goods (Medical Devices) Regulations 2002 (SR 2002/236) sets out the essential principles pertaining to medical devices, which are similar to the essential requirements listed in Annex 1 of both the EC council directives on medical devices 93/42/EEC and active implantable medical devices 90/385/EEC.

[20] See Australian Government, *Changes to Premarket Assessment Requirements for Medical Devices: Regulation Impact Statement* (V 2.0, June 26, 2013) at 65.

[21] Medicines (Database of Medical Devices) Regulations 2003 (SR 2003/325).