The Academy convenes a discussion on the regulatory and ethical dimensions of artificially enhancing human cognition

For centuries humans have sought to enhance their natural appearance and abilities through medicine, surgery, exercise, and education. Today, performance enhancement is most often associated with drugs taken by athletes and college students to improve physical and mental performance. However there exists a vast portfolio of performance enhancement approaches, from pharmaceutical drugs to physical or cognitive training to prosthetic devices such as exoskeletons that augment the physical capabilities of military personnel. Recent technological advances have produced devices that directly affect and are integrated with brain function, offering the promise of brain-machine interfaces that might increase human capabilities or compensate for lost motor or cognitive function.

The rapid expansion of the human performance enhancement (HPE) field also raises new ethical dilemmas that must be addressed in order for society to integrate these approaches in a socially responsible manner. On January 21–22, 2016, the Academy convened a multidisciplinary group of scholars from medicine, neuroscience, ethics, law, and economics, along with experts from government agencies and the private sector, to discuss the current state of research and policy discourse on HPE. The discussion focused on the safety, regulation, and ethics of neuromodulation, a process that normalizes (modulates) brain function through the delivery of electrical stimulation or pharmaceutical agents to targeted sites of the body (see sidebar on page 5). Since several workshops over the years have already discussed the use of pharmaceutical agents in the form of nootropics or athletic enhancements, the January 2016 workshop focused on neuromodulation via electrical stimulation. This approach can be used either as a therapy for brain diseases or to augment normal cognitive function. Devices used to augment brain function are commonly referred to as cognitive enhancement devices (CEDs).

While the workshop was not intended to produce consensus recommendations on research projects, policy procedures, or ethical guidelines, the participants identified several topics that require further attention, including regulation by government agencies; safety, efficacy, and labor economics; and other societal implications such as justice, access, fairness, and coercion.

Workshop chair Steven Hyman (Broad Institute of MIT and Harvard; Harvard University)

Clarifying the Regulatory Regime

A presentation by a panelist at the Academy workshop on her recent research[1] highlighted the lack of clarity regarding the regulatory framework for cognitive enhancement devices (CEDs) and the difficulty in determining which regulatory authority or authorities may be best suited to regulate these devices. Many CEDs are readily available to consumers in the form of unregulated "do-it-yourself" (DIY) products and direct-to-consumer (DTC) wearables that purport to enhance cognitive function. It is unclear whether CEDs should be considered medical (i.e., therapeutic) devices since they are marketed to augment healthy cognitive capacities, such as fine-tuning motor skills, changing mood, and improving concentration.

The Food and Drug Administration (FDA), which has primary legal authority to regulate medical devices under the Federal Food Drug and Cosmetic Act,[2] is currently considering whether and how CEDs should in fact be regulated as such. The FDA defines medical devices as any device that is "intended for use in the diagnosis of disease, or in the cure, mitigation, treatment, or prevention of dis-

1. Anna Wexler, "A Pragmatic Analysis of the Regulation of Consumer Transcranial Direct Current Stimulation (tDCS) Devices in the United States," *Journal of Law and the Biosciences* 2 (3) (2015): 669–696.

2. Food and Drug Administration, Federal Food, Drug, and Cosmetic Act (FD&C Act), http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/.

ease . . . or to affect the structure or any function of the body, and which does not achieve any of its primary intended purposes through chemical [and metabolic activity]."[3] The FDA has historically referred to advertising material and claims (therapeutic vs. enhancement) as evidence of intention. Since many CEDs are not explicitly intended for the diagnosis, cure, treatment, or prevention of disease, they do not come under FDA regulation. However, the FDA may still decide that, to the extent that they affect "the structure or any function of the body," they should nevertheless be regulated as medical devices under this definition. Yet the effects of CEDs on brain structure and/or function can be difficult to establish with any degree of certainty (particularly given the lack of funding and studies of using these devices in healthy populations), leading to concern that manufacturers of CEDs would attempt to circumvent FDA regulation again by altering the descriptions of how their products work.

As suggested by the panelist during her presentation, in the event that the FDA decides that CEDs should not be regulated as medical devices, they could instead be subject to regulation by the Consumer Product Safety Commission (CPSC). The CPSC has the authority to develop certain safety standards for consumer products it deems to be potentially hazardous. A consumer product is defined as any product sold for use in or around the household, mainly for recreational rather than medical purposes. As previously mentioned, a given device can be regulated differently based on intended use claims. For example, a treadmill intended for medical or rehabilitation purposes is considered a medical device and thus is regulated by the FDA, but an identical product that is intended for home or recreational purposes is considered a consumer product and therefore regulated by the CPSC. While cognitive enhancement products could fit the latter intent, there is concern that the CPSC may not be prepared to appropriately regulate these devices, since it does not have the FDA's expertise or resources and is generally perceived to be weaker in terms of enforcement.

Several workshop participants also expressed concern that CPSC regulations focus on the nature of the device itself rather than patterns of use. For example, a product might be safe for adults but not for children, or for use for 15 minutes rather than two to three hours per day. Regulating CEDs based on the end use or the end user would also make it easier for companies to market medical devices in cases where nontherapeutic uses are not approved.

Approaches to Human Cognitive Enhancement via Electrical Stimulation

Neuromodulation devices involving electrical stimulation, whether used for therapy or for enhancement, can be divided into two categories: invasive and noninvasive. Invasive technologies, for the purpose of the workshop discussion, require the physical implantation of devices into the brain. One example is deep brain stimulation (DBS), which requires the surgical implantation of an electrode into the brain to deliver electrical stimulation through specific regions of the brain for the treatment of neuropsychiatric disorders like depression and motor disorders such as Parkinson's disease.

Noninvasive technologies, by contrast, do not require surgical implantation but rely instead on external stimulation delivered to the brain from an instrument placed on or around the head. Examples include transcranial direct current stimulation (tDCS), which uses a pair of electrodes affixed to the head to run a current to superficial layers of the brain, and transcranial magnetic stimulation (TMS), which uses a magnetic coil held above the head to stimulate superficial layers of the brain. Because they bypass the risks associated with surgical implantation such as biological rejection, noninvasive devices may be less likely to be perceived as dangerous. Given their ease of use and ease of construction (particularly in the case of tDCS), noninvasive devices are more prevalent outside of the clinical setting and are often subject to direct-to-consumer (DTC) marketing.

It is important to note that many scholars in the HPE field consider the distinction between "invasive" and "noninvasive" to be problematic. For example, the current induced by TMS and tDCS, not unlike an invasive DBS, can have downstream affects in areas beyond the brain, such as in the spine and musculature. Additionally, the use of noninvasive devices can produce internal and external side effects, including headaches, seizures, and scalp burns. More study is needed to determine whether invasive and noninvasive devices should be considered (due to similar safety risk profiles and cognitive/bodily effects) in parallel when developing ethical, regulatory, and medical guidelines.

3. Food and Drug Administration, "What is a Medical Device?" http://www.fda.gov/AboutFDA/Transparency/Basics/ucm211822.htm.

Recent technological advances have produced devices that directly affect and are integrated with brain function, offering the promise of brain-machine interfaces that might increase human capabilities or compensate for lost motor or cognitive function.

The Federal Trade Commission (FTC) can also play a role in regulating CEDs by highlighting unfair or deceptive business practices. The FTC has filed complaints against companies that have made unsubstantiated cognitive enhancement claims, such as in the case of the brain training product Jungle Rangers.[4] More recently, the FTC entered into a settlement with Lumos Labs, makers of the brain training game Lumosity, for purporting medical benefits.[5] Yet several workshop participants expressed concerns that the FTC may not have ready access to the necessary scientific expertise to make such determinations.

State authorities may also regulate CEDs. For example, in May 2013 the California Department of Public Health shut down the company tDCS Home Device Kit for violating California's Sherman Food, Drug, and Cosmetic Law by selling a misbranded and unapproved medical device.[6]

Monitoring Safety, Efficacy, and Privacy

To date, there are little data on the long-term effectiveness of CEDs. The limited availability of large-scale, longitudinal data makes it difficult if not impossible to determine the true safety and efficacy of the devices currently on the market. Furthermore, studies that show little to no benefit of a particular product often do not get published. To address these problems, one workshop participant suggested the creation of a database that would allow researchers to register, submit, and analyze data on the efficacy of CEDs, similar to the ClinicalTrials.gov website, established by the National Institutes of Health to provide "a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world."[7] Evaluating the safety and efficacy of CEDs would also be greatly facilitated by additional fundamental neuroscience research into how brain function is affected by electrical and magnetic stimulation, particularly in healthy populations.

The development of appropriate safety standards will also require much more post-clinical and post-market surveillance to document the side effects of CED use. For example, devices that improve cognitive ability in one area could have negative effects on other cognitive functions.[8] These side effects may not necessarily be reversible and could impact an individual's identity, particularly if traits such as personality or memory are altered. The availability of post-market surveillance data would help regulators and the medical community to determine the level of compensation in function that is considered safe and appropriate for a given technology or device.

Who Should Benefit?

Technological advances in HPE can open up new professions to persons with disabilities, only 16 percent of whom participate in the U.S. workforce.[9] An extreme example cited by one workshop participant was a tetraplegic woman who, in a laboratory setting, was able to control a fighter jet simulator through the use of a brain-controlled prosthetic. Performance enhancement technologies could also, according to one participant, substantially shift the landscape of the workforce by raising the bar for employee performance. One potential concern is perceived or enacted coercion wherein employees feel forced to undergo enhancements in order to be successful and competitive in their careers.

4. Federal Trade Commission, "Makers of Jungle Rangers Computer Game for Kids Settle FTC Charges that They Deceived Consumers with Baseless 'Brain Training' Claims," January 20, 2015, https://www.ftc.gov/news-events/press-releases/2015/01/makers-jungle-rangers-computer-game-kids-settle-ftc-charges-they.

5. Federal Trade Commission, "Lumosity to Pay $2 Million to Settle FTC Deceptive Advertising Charges for its 'Brain Training' Program," January 5, 2016, https://www.ftc.gov/news-events/press-releases/2016/01/lumosity-pay-2-million-settle-ftc-deceptive-advertising-charges.

6. California Health and Safety code, division 104, part 5, Sherman Food, Drug, and Cosmetic Law, effective January 1, 2008, https://www.cdph.ca.gov/services/Documents/fdb%20Sher%20Law.pdf. California Department of Public Health, "CDPH Warns Consumers not to use tDCS Home Device Kit," https://www.cdph.ca.gov/Pages/NR13-029.aspx.

7. ClinicalTrials.gov: A Service of the U.S. National Institutes of Health, https://clinicaltrials.gov/.

8. Teresa Luculano and Roi C. Kadosh, "The Mental Cost of Cognitive Enhancement," *Journal of Neuroscience* 33 (2013): 4482, 4486.

9. American Institutes for Research, *One Size Does Not Fit All: A New Look at the Labor Force Participation of People with Disabilities* (2015), http://www.air.org/sites/default/files/downloads/report/Labor-Force-Participation-People-with-Disabilities-Yin-Sept-2015.pdf.

An additional concern is that the development and sale of cognitive enhancement devices may exacerbate social inequality, as the most potent and effective enhancements are likely to be prohibitively expensive to all but the most wealthy. This would result in a radical exacerbation of a division between the "haves" and "have nots." As one participant noted, "People with disposable income are ready and willing to facilitate an enhancement marketplace." Access would then be deeply reliant on price subsidization, as private companies that have made large investments in HPE technologies seek to recoup their development costs quickly in order to survive in this competitive new market.

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CEDs are increasingly recognized as having potential benefits for elderly populations. For example, neuroenhancement devices and neurocontrolled prosthetics could increase quality of life while reducing health care costs by delaying or even avoiding the need to move a patient to an assisted living facility, or perhaps more importantly facilitating independence of those with disabilities. Recognizing both the potential benefits and the concomitant ethical issues, the President's Council of Advisors on Science and Technology (PCAST) recently advocated for the development of a national research agenda on the issue of cognitive training for the elderly.[10]

At the other end of the age spectrum is the need to establish guidelines for the use of cognitive enhancement devices by children. The potential market for such uses is suggested by the popularity of instructional approaches such as preparatory classes for the Scholastic Aptitude Test and other entrance exams. But the development of CEDs for children would pose an entirely new set of scientific and ethical questions. How much permission should parents be granted, for example, in allowing (or requiring) their children to attend tDCS sessions? Do enhancement interventions imposed by parents close off options for children when they are older? Will the outcomes of such treatments be permanent, or will they be reversed as the child ages? And the primary question is how such devices and their use in the enhancement context impact the developing brain. More studies are needed on these and many other questions.

Performance enhancement technologies could substantially shift the landscape of the workforce by raising the bar for employee performance.

Lastly, when DIY brain stimulation devices first emerged in the mid-2000s, many neuroethicists and media observers predicted the immediate and widespread adoption of such devices throughout society. Contrary to those expectations, DIY enhancement devices have remained confined to a small subculture. Nevertheless, it will be important to analyze how extensive the informal economy of off-label experimentation and use will become in the future, especially if the regulatory regime remains unclear.

Conclusion: The Future of Enhancement

As one workshop participant observed, "the great thing about this meeting, as opposed to the last ten years of enhancement meetings, is that we are getting to real world, actionable issues." Although workshop attendees agreed that the technology has not advanced as rapidly as predicted a decade ago, that fact should not deter scholars and policy-makers from investing in research in this field. Just a year prior to the Academy workshop, gene therapy was largely seen as being medically and commercially inviable, yet since that time rapid scientific advances have resulted in five public companies initiating clinical trials on gene therapies for human brain disease.

The workshop did not fully address issues such as the privacy and security of implanted neurostimulation devices, however several critical questions were raised. Who should be ultimately responsible for communications to and from the brain via such devices? Is content in the brain hackable? If so, how much would an individual "own" his or her identity? Are there areas of the brain with which one should not interfere?

10. PCAST, *Report to the President: Independence, Technology, and Connection in Older Age* (March 2016), https://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_independence_tech__aging_report_final_0.pdf.

Suggestions for Future Work

Throughout the Academy workshop, participants suggested opportunities for new scholarship and robust policy discussions on the regulatory, safety, economic, and societal issues surrounding human performance enhancement. Several of these opportunities are described below. Advancing these objectives will require the cooperation of government agencies, companies, university researchers, and medical institutions and practitioners.

- More frequent roundtable discussions with U.S. regulatory agencies, industries, and scientists are needed to develop:
  1. a thorough understanding of the technical fundamentals of the effects of CEDs on brain function;
  2. near-term policy actions to provide a more transparent regulatory landscape and determine the authorities responsible for enforcing regulation and surveillance of CEDs;
  3. separate regulatory policies for devices intended for enhancement and treatment
- Comparisons of regulatory policies with those of international regulatory authorities could also aid in developing a clearer regulatory framework for CEDs in the United States.
- Concerned organizations could consider creating an independent body to evaluate the safety and efficacy data on consumer products and implement a database of these results to establish baseline standards for each individual CEDs.
- Better estimates of the number of innovators, consumers, and DIY users who are developing and using CEDs will be essential for understanding the market potential for these products as well as their potential for unsafe use.
- Studies on the current and future demand-side of the enhancement market are necessary to predict its impact on the social and labor economics of the United States.
- Additional research on invasive forms of modulation is required to compare their effectiveness to noninvasive approaches. The paucity of information is due to limitations of the technology discussed earlier in this report.
- Topics such as genome editing as a foreseeable enhancement tool, autonomy in choice of use, the impact of cognitive training games, and issues with security and privacy regarding the brain-machine interface represent opportunities to bring together government agencies, companies, and academic researchers at future roundtable discussions.

Following the workshop, conversations with several participants demonstrated continued interest in discussions on CEDs as well as the following two activities that would advance the field:

1. Roundtables with scholars, regulators, and ethicists as well as current and potential users of DIY CEDs to break down communication barriers and work together to clarify regulations and safety measures for these devices.
2. Consideration of the possible long-term scenarios that could optimally and thoughtfully deepen long-term developments on issues like autonomy, agency, and identity in the context of neuromodulation and highlight consequences for the individual, institution, and society.

Both activities would foster deep partnerships among government, non-government, and academic organizations that could significantly advance our understanding of the ethical, technical, and social dimensions of current and future approaches to enhancing human capabilities. ■

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