



Editorial

Neuroenhancement: Enhancing brain and mind in health and in disease

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ARTICLE INFO

Article history:

Accepted 31 August 2013

Available online 12 September 2013

ABSTRACT

Humans have long used cognitive enhancement methods to expand the proficiency and range of the various mental activities that they engage in, including writing to store and retrieve information, and computers that allow them to perform myriad activities that are now commonplace in the internet age. Neuroenhancement describes the use of neuroscience-based techniques for enhancing cognitive function by acting directly on the human brain and nervous system, altering its properties to increase performance. Cognitive neuroscience has now reached the point where it may begin to put theory derived from years of experimentation into practice. This special issue includes 16 articles that employ or examine a variety of neuroenhancement methods currently being developed to increase cognition in healthy people and in patients with neurological or psychiatric illness. This includes transcranial electromagnetic stimulation methods, such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS), along with deep brain stimulation, neurofeedback, behavioral training techniques, and these and other techniques in conjunction with neuroimaging. These methods can be used to improve attention, perception, memory and other forms of cognition in healthy individuals, leading to better performance in many aspects of everyday life. They may also reduce the cost, duration and overall impact of brain and mental illness in patients with neurological and psychiatric illness. Potential disadvantages of these techniques are also discussed. Given that the benefits of neuroenhancement outweigh the potential costs, these methods could potentially reduce suffering and improve quality of life for everyone, while further increasing our knowledge about the mechanisms of human cognition.

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Humans have long used cognitive enhancement methods to expand the proficiency and range of the various mental activities that they engage in. Such techniques include both internally generated procedures as well as external tools. An instance of the former type is the “Method of Loci,” which was developed long ago to help improve memory. Another example is the development of writing, which greatly increased our ability to store and retrieve information, and allowed people to communicate over space and time in a manner that was impossible before its invention. Following the invention of mathematics, external tools such as the abacus and slide rule, and now computers, were all developed in part to enlarge our cognitive repertoire, allowing us to perform mathematical computations more quickly, retrieve larger volumes of information more easily, communicate more rapidly, and perform myriad other activities now commonplace in the internet age.

Although these examples involve the improvement of cognition in healthy individuals, cognitive enhancement can also involve reversing or compensating for cognitive deficits associated with mental and brain illness. Examples include compensating for memory failures in patients

with Alzheimer's Disease and other dementias and restoring speech and other motor functions in stroke patients. When seen in this respect, cognitive enhancement technologies can be viewed as a class of tools essential for the growth and survival of our species. As such they are clearly worthy of investigation and continued development.

Neuroenhancement describes the use of neuroscience-based techniques for enhancing cognitive function. Unlike other external tool-based technologies of cognitive enhancement, neuroenhancement acts directly in the human brain and nervous system, altering its properties to increase performance for a specific cognitive task or set of tasks. A wide variety of neuroenhancement methods have been developed. One that offers significant promise is electromagnetic brain stimulation. Brain stimulation to enhance mental function and relieve symptoms of neurological and psychiatric disease has a long history. Anecdotal reports of brain stimulation date back about 2000 years (Kellaway, 1946). The popularity of electrotherapy peaked in the final years of the 19th century when the claim was made that roughly 10 thousand physicians in the U.S. were certified to make use of electricity as a therapeutic intervention for the nervous system and other organs (Aronowitz, 2007; Bigelow, 1894). With the development of pharmacotherapies, its use waned, with only sporadic research interest in the 20th century. At

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the turn of the millennium, however, factors such as an increased understanding of the mechanisms of neuronal plasticity (Buonomano and Merzenich, 1998; Taub et al., 2002), and a seminal paper on the effects of electrical stimulation on motor evoked potentials (Nitsche and Paulus, 2000) led to a revival of interest in various brain stimulation techniques. Research on brain stimulation was further spurred on by the success of neuroimaging studies in identifying the neural bases of cognitive functions, leading to the possibility of changing cognitive processes by altering brain activity directly. A plethora of cognitive and electromagnetic stimulation techniques are now available and have been the focus of extensive research over the past decade.

This special issue was developed in part from our recent experiences with the application of transcranial Direct Current Stimulation (tDCS) to enhance attention, learning, and memory in a difficult discovery-learning visual search task (Clark et al., 2012; Coffman et al., 2012a; Falcone et al., 2012). In this series of studies, we showed that tDCS guided by neuroimaging can produce large changes in performance, including an approximate doubling of performance accuracy, d' , and other signal detection measures that lasts at least 24 h after stimulation is ended, with an effect size d of approximately 1.2. We found a dose-response effect, no significant effect of single- vs. double-blinding, nor significant effects of mood or skin sensation on these results. We later showed that anodal tDCS results in significantly increased glutamate and glutamine concentration under the electrode but not elsewhere (Clark et al., 2011), and also increased attention (Coffman et al., 2012b), all suggesting that there is a real effect of tDCS on brain chemistry and function, leading to an increase in attention, learning and performance in this task. Not all tDCS studies have shown such a large effect, but ours was one of the first to use neuroimaging in order to optimize the effects of neurostimulation. In this respect, the combination of neuroimaging and neurostimulation may serve to enhance the application of both techniques: not only may neuroimaging help to enhance the effects of neurostimulation, but neurostimulation may also serve to verify and further clarify the results of neuroimaging studies. In addition, most methods of neuroenhancement are relatively inexpensive. Methods of neurostimulation such as tDCS represent a rapidly growing body of literature (Fig. 1).

Given these developments, we felt that the time was ripe for an examination of current and future trends in research on neuroenhancement in both healthy individuals and clinical populations. This special issue of *NeuroImage* consists of articles invited from leaders in the field of neuroenhancement research. All of the papers describe studies using methods aimed at enhancing brain and mental functions in either health or disease. Our aim was not to be

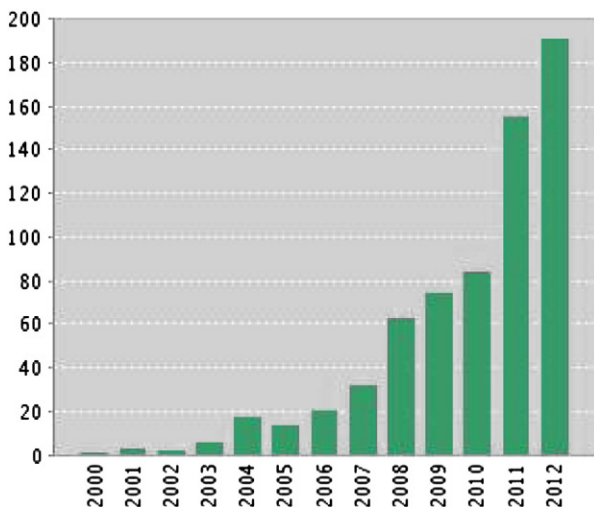


Fig. 1. The number of papers per year including tDCS from 2000 to 2012, from Web of Science.

comprehensive, but to conduct a focused survey of the major neuroenhancement techniques and their use in different populations. Other methods that have been reviewed previously, such as pharmaceutical-based cognitive enhancement (Repantis et al., 2010), effects of basic health and nutrition (Lucke and Partridge, 2013), and other forms of enhancement (Dresler et al., 2013), are not included here.

Overview of papers

We divided the 16 papers in the special issue into five sections. The first 6 papers involve the use of direct current electrical stimulation of the brain, covering both healthy and neuropsychiatric populations. The next two papers describe the use of TMS to enhance cognitive, motor, and affective functions. The subsequent section of 3 papers describes other brain stimulation techniques, including deep brain stimulation and neurofeedback. While most neuroenhancement techniques involve electrical or magnetic stimulation, there has also been considerable recent interest in the use of cognitive training to enhance brain function. The next section of two papers describes the effects of these techniques on cerebral oxygenation, white matter integrity, and brain functional connectivity. The final section of 3 papers covers methodological and integrative issues in the use of neuroenhancement techniques.

This special issue begins with a review of the use of tDCS to enhance attention, learning, and memory in healthy adults (Coffman et al., 2014). We found a large number of tDCS studies that have been successful in augmenting cognitive function, using a variety of tDCS protocols. This method is proving to be highly effective, with a range of effect sizes (d) from -2.2 (for reduced performance resulting from cathodal stimulation) to $+2.5$ (for increased performance from anodal stimulation) across the 37 published studies for which effect size could be estimated, with an average effect size of about $+0.9$ for anodal stimulation. Current modeling studies suggest that tDCS as generally applied lacks precision for anatomical targeting, but may be well-suited for the application of cognitive enhancement in clinical treatment and other community settings, and so may have many practical applications.

One such practical application is to enhance sustained attention or vigilance. Vigilance is the ability to maintain goal-directed behavior for extended periods of time, as required in many work and common daily activities, and is disrupted in a variety of brain mental illnesses. Nelson et al. (2014) examined the effects of applying tDCS to dorsolateral prefrontal cortex for increasing vigilance. TDCS produced increased target detection performance and operator discriminability, along with increased cerebral blood flow velocity and oxygenation when compared with a sham condition, with an effect size d of 2.5, which is quite large. Given the importance of vigilance to efficient operations in many occupations, such as air traffic control (Pop et al., 2012) and surveillance and security (Parasuraman and Galster, 2013), the ability to counter vigilance decrements over time has important implications for ensuring safety in such environments. The beneficial effects of brain stimulation could also be used to reduce symptoms of sustained attention deficits in a variety of brain and mental illnesses such as schizophrenia (Benedict et al., 1994).

Other papers in this issue deal with targeting tDCS on specific brain areas. Many previous studies have focused on tDCS of superficial cerebral cortex. However, an alternative described by Ferrucci and Priori (2014) is transcranial cerebellar direct current stimulation (tcDCS). In a series of studies, tcDCS has been found to modulate motor control, learning, affect and working memory, as well as cerebellar responses to cortical TMS, and other phenomena. They conclude that tcDCS may be useful for studies of cerebellar function, and may also provide benefits for patients with cerebellar dysfunction.

The next three papers in this section focus on the use of tDCS to treat symptoms of brain and mental illness. Modern medicine primarily employs pharmacological manipulation to alter biological processes. While

highly effective for the treatment of many disorders, there are also drawbacks for some patients, including side effects, drug toxicity, and cost, among others. TDCS may provide a useful alternative for the treatment of brain and mental illness. There are few side effects described so far, aside from the possibility of skin irritation and mild headaches in some patients. Some versions of equipment that can be used to produce small, measured currents for tDCS are also very inexpensive, running on batteries. All of these qualities suggest that they may provide a beneficial alternative or adjunctive to the current standard of care.

One example where tDCS may provide a benefit is stroke, which is a common and highly debilitating illness. In patients who survive the initial stroke-inducing event, rehabilitation is often required to improve function. O'Shea et al. hypothesized that combining unilateral tDCS protocols that have previously shown benefits together into a single bilateral protocol might produce a larger, additive effect. To do this, they applied bilateral M1 tDCS, with the anode placed over the healthy hemisphere and the cathode placed over the injured hemisphere, and compared this with two unilateral M1 tDCS protocols, with the anode placed over the healthy hemisphere or the cathode placed over the injured hemisphere and the other electrode placed (cathode or anode, respectively) over the supraorbital ridge. Metrics included changes in reaction times with the paretic (affected by stroke) hand. They also examined effects on motor evoked potentials (MEPs) and neurometabolites using MRS. Contrary to their hypothesis, they found that bilateral M1 stimulation produced no significant changes in MEPs or reaction time. As with other tDCS studies, the work of O'Shea et al. suggests that the placement of both tDCS electrodes should be considered for determining tDCS effects. Their results might have resulted from a direct effect of tDCS over the supraorbital ridge, or from effects on other brain regions lying between this region and M1, which were not stimulated in their bilateral protocol. They did find that the levels of GABA recorded from ipsilesional M1 before treatment predicted reaction time gains from unilateral anodal tDCS, pointing again to the benefits of combining neuroimaging and neurostimulation.

The final two papers in this section review the use of tDCS for treating symptoms of neurological illness (Flöel, 2014) and psychiatric illness (Kuo, Paulus and Nitsche, this issue). Flöel (2014) discusses the benefits of tDCS for treating mild cognitive impairment, Alzheimer's Disease, and persistent deficits after stroke. Attempts have also been made to use tDCS with other disorders, such as dystonia and epileptic seizures, but without clear success yet being reported. Flöel points out that administering tDCS in parallel with cognitive or motor therapies often provides more robust outcomes than using either alone, but that efficacy cannot be firmly established without controlled randomized trials. Kuo et al. (2014) review the effects of brain stimulation on neuroplasticity, and its impact on both neurological and psychiatric diseases. Brain stimulation methods have the potential to reduce or increase plasticity, depending on the specific disorder being treated. Among the disorders discussed here are depression, addiction, schizophrenia, anxiety, dementia, tinnitus and pain. They also call for large, controlled, randomized multi-center trials to validate and perfect these techniques.

Aside from tDCS, another method for brain stimulation that has been in use for a longer time is transcranial magnetic stimulation (TMS). There have been a number of excellent reviews of clinical applications of TMS of so we did not pursue this in detail for this special issue. Instead, the next two papers included in this special issue discuss specific applications of TMS for neuroenhancement. TMS was initially used to disrupt cognitive function, in order to validate the causal role for particular cognitive functions of specific brain regions identified by neuroimaging studies. Therefore, increased performance was initially unexpected, but recently has shown promise for enhancement of a variety of cognitive functions. Like tDCS, TMS can be used to alter cortical excitability. Different effects can be accomplished by changing TMS pulse frequency, with low frequency decreasing excitability and high frequency increasing excitability. Some performance increases can be ascribed to confounding

psychological effects: specifically, the effects of the auditory and somatosensory stimulation produced by the TMS coil can interact with the perception of experimental stimuli, and receiving TMS can also increase general arousal, as is true with many medical procedures. Luber and Lisanby (2014) review and summarize 61 papers that involve the use of transcranial magnetic stimulation (TMS) to produce performance enhancements in perceptual discrimination, motor learning, visual search and tasks involving attention, memory, and language in healthy human subjects. They identify two categories of possible enhancement mechanisms, including direct enhancement of activity in cortical regions or networks that support specific cognitive functions, or conversely by "addition-by-subtraction", in which activity in regions that compete with or distract from activity in regions supporting the cognitive process of interest is disrupted. Effects similar to long-term potentiation, Hebbian-like learning process, and modulation of cortical oscillations may be involved depending on the circumstances. Potential applications of TMS cognitive enhancement, including research into cortical function, rehabilitation therapy in neurological and psychiatric illness, and accelerated skill acquisition in healthy individuals are discussed, as are methods of optimizing the magnitude and duration of TMS-induced performance enhancement, such as improvement of targeting through further integration of brain imaging with TMS. They also discuss the integration of TMS with neuroimaging, both for targeting TMS in space and time, and also for examining the effects of TMS on brain function.

The relationship between TMS and Hebbian learning is further explored by Narayana et al. (2014). They examined whether daily TMS is effective for long-term motor sequence learning in healthy adults. They compared 5 Hz TMS vs. sham to right M1 during practice of a digit sequence task with their non-dominant hand, based on Karni et al., 1995. Sequence performance increased significantly more after a month of training in the TMS group, with increases in resting CBF in M1 and other motor areas. This is the first demonstration of the behavioral and neural enhancing effects of TMS on long-term or slow motor learning. They propose that TMS alters the network properties of neural systems through Hebbian learning. They suggest that this could be beneficial for other repetitive physical, behavioral and cognitive therapies.

Aside from transcranial brain stimulation, other methods have been developed to alter or enhance human behavior and alter brain function. Zotev et al. (2014) describe the development of a new multimodal neurofeedback method that combined the simultaneous self-regulation of both hemodynamic and electrophysiological activity. They combined two imaging modalities that are typically used separately for neurofeedback: EEG and fMRI using a novel system for real-time integration of simultaneous real-time fMRI (rt-fMRI) and real-time EEG (rt-EEG) data into real time fMRI and EEG neurofeedback (rtfMRI-EEG-nf). Subjects performed a positive emotion induction task as they regulated BOLD rtfMRI amplitude in the left amygdala and frontal rEEG power asymmetry in the high-beta band. While they found only small effects on mood induction in this study, they suggest that the possible benefits of future rtfMRI-EEG-nf include that the electrophysiological and hemodynamic correlates of brain function can be compared, that performance using one imaging modality (EEG or fMRI) can also be compared and validated based on the other modality, and that with further research, an optimal combination of fMRI and EEG-based neurofeedback could be determined in order to maximize results.

Deep brain stimulation (DBS) is currently widely used for the treatment of movement disorders such as Parkinson's disease. However, it may also have applications for other disorders. Suthana and Fried (2014) discuss the use of invasive, deep brain stimulation targeting the medial temporal lobe and other brain structures for the enhancement of memory function. They review the history of DBS studies in experimental animals and in humans, and more recent DBS studies that have focused specifically on episodic memory effects of DBS. Suthana and Fried also discuss how the anatomical organization of memory structures, the temporal specificity of DBS effects, and the possible mechanisms of DBS action should be considered when planning memory-

enhancement with DBS. They also discuss the possible effects of other neurological illnesses for which DBS is currently administered, and how this might affect outcome of studies that examine memory-enhancement. They discuss recent technical advances in DBS that could further promote the efficacy of DBS for memory enhancement, such as using depth recorded electrophysiological measures to control DBS administration, and applying current administration intermittently when additional assistance with memory encoding or retrieval is needed. Finally, they conclude that the use of consistent methodologies across studies will facilitate systematic comparisons and contribute to the understanding of DBS and its effects on learning and memory and whether it will be a useful therapeutic treatment for patients with memory disorders.

Aside from memory loss, chronic neuropathic pain is extremely debilitating and very common, with few effective treatments (Cooper and Clark, 2013). Moreno-Duarte et al. (2014) compare clinical trials using a variety of transcranial brain stimulation techniques for the treatment of chronic pain from spinal cord injury (SCI), with approximately half of SCI patients reporting chronic pain rated as severe or worse. It has been hypothesized that maladaptive plasticity may be the cause of this and other forms of neuropathic pain. Moreno-Duarte et al. performed a meta-analysis of 9 published studies to see if any neural stimulation techniques have shown sufficient efficacy for the treatment for SCI pain. They compared published results of tDCS, TMS, Cranial Electrotherapy Stimulation (CES), Transcutaneous Electrical Nerve Stimulation (TENS) and Spinal Cord Stimulation (SCS). Of the four studies reporting large benefits, three employed tDCS and one employed CES. TMS also produced a positive effect that the authors concluded was lower than that found in these tDCS and CES studies. They suggest that identifying neurophysiological markers to guide treatment selection and administration, and combining transcranial stimulation with other treatment modalities such as pharmaceuticals, may increase their efficacy for reducing chronic pain. Moreno-Duarte et al. conclude that the lack of significant adverse effects and the apparent efficacious results of tDCS and CES studies suggest that there is potential for the use of transcranial stimulation as a treatment modality. Similar to the conclusions of many other papers included in this special issue, Moreno-Duarte et al. suggest that there is a great need for standardized methods for the application and evaluation of different treatment modalities in order to reduce response variability and also to facilitate their comparison.

The next two papers focus on the possibility of using cognitive training methods to stimulate brain structural and functional changes that lead to cognitive enhancement. Such techniques are of interest because they may complement the other brain stimulation techniques discussed in this special issue. It is also possible that brain stimulation may interact synergistically with cognitive training to lead to even greater neuro-cognitive enhancement. In the first paper, McKendrick et al. (2014) examined the effects of working memory training on brain function and behavior. They monitored subjects using near infrared spectroscopy (NIRS) while they performed a dual verbal-spatial working memory task. Subjects were either assigned to an adaptive condition whose working memory load was adjusted based on performance, and others to a yoked condition whose working memory load was determined based on the performance of trainees in the adaptive condition. Changes in cerebral hemodynamics of the left DLPFC and right VLPFC were found to be associated with time spent in training. Adaptive vs. yoked training showed differences in rostral prefrontal cortex. McKendrick et al. interpreted these results in terms of decreased proactive interference, increased neural efficiency, reduced mental workload for stimulus processing, and increased working memory capacity with training.

In the second paper, Strenziok et al. (2014) examined the effects of extensive video game training on performance, white matter integrity, and brain functional connectivity in healthy older adults. Methods to ameliorate age-related cognitive decline must demonstrate that any positive effects of training transfer to everyday cognitive functioning—so-called “far transfer.” Strenziok and colleagues used video game

training to test the hypothesis that far transfer is associated with altered attentional control demands mediated by the dorsal attention network and trained sensory cortex. They randomly assigned healthy older adults to six weeks of training on three games shown previously to influence brain function and structure: Brain Fitness (BF—auditory perception), Space Fortress (SF—visuomotor/working memory), or Rise of Nations (RON—strategic reasoning). Before and after training, cognitive performance, diffusion-derived white matter integrity, and functional connectivity of the superior parietal cortex (SPC) were assessed. They found the strongest effects from BF training, which transferred to everyday problem solving and reasoning and selectively changed integrity of occipito-temporal white matter associated with improvement on untrained everyday problem solving. The authors also showed that both BF and SF training also lead to changes in functional connectivity between SPC and inferior temporal lobe (ITL).

The final papers in this special issue examined methodological and integrative issues of neuroenhancement. Two of these papers describe studies of the interaction between brain tissue and applied electric fields. Antal et al. (2014) examined the influence of concurrent tDCS on BOLD fMRI, to see if the passage of current through the brain has any direct influence on BOLD fMRI. They used two post-mortem subjects, in order to eliminate the contribution of changes in functional neuronal responses to current, leaving the direct effects of applied current on T2* images. TDCS induced signal change in a variety of brain regions. The precise location of signal change depended on the location and polarity of the electrodes. In agreement with modeling studies, they found that the strongest effects of applied current were located near the scalp electrodes, and at the borders of CSF filled spaces. Alternating current, or tACS, showed no effects. These results of tDCS might be explained in part from the known interaction between an applied current and a static magnetic field in a conductive medium, related to Lorentz forces (Feynman et al., 2006). However, the mechanisms of the T2* effects observed in this study have yet to be fully explained.

In another study of the interaction between brain tissue and applied electric fields, Wagner et al. (2014) examined the electrical properties of brain tissue to help guide the application of electromagnetic brain stimulation methods. Prior studies have relied on ex-vivo impedance measurements of brain tissue, which might be influenced by changes in tissue properties after extraction. Here, Wagner et al. obtained impedance measures of brain tissue in-vivo during neuro-surgical procedures. These were used to construct models of fields generated by TMS and DBS and conductance-based models of neurons exposed to stimulation. They show evidence for frequency dependent resistive and capacitive properties not typically included in previous models. They suggest that there may be a significant influence of brain tissue properties on neurostimulatory fields and on neural responses to stimulation, including stimulation threshold, ionic currents, and membrane dynamics. The findings of both this study and that of Antal et al. (2014) highlight the importance of obtaining objective neuroimaging data to better understand and model the effects of brain stimulation.

In the final paper of this special issue, Brem et al. (2014) discuss how enhancement of some cognitive functions both in patients and in healthy individuals might come at the cost of reducing other cognitive functions. They suggest a variety of mechanisms by which transcranial stimulation could affect cognitive function, including changes in the distribution and/or amplitude of processing power, reduction of neuronal interference processes, and/or changes in how fast processing power can be re-distributed. They propose a “net zero-sum model”, based on the principle of conservation of energy in closed systems. To support this idea, they give examples of brain stimulation and brain lesion studies that have found enhancement of one area of cognition concurrent with lessening of another. They argue that the net-zero sum concept may be helpful for guiding future studies, by proving an estimate of cost–benefit ratio.

Conclusions

This special issue presents a variety of neuroenhancement methods, including neurostimulation and behavioral treatments examined with neuroimaging. Across these studies, there are a variety of findings and conclusions in common. First, it appears that neuroenhancement shows a great deal of promise. Human history has been punctuated by the development of tools for cognitive enhancement that have increased our capabilities, such as writing, mathematics and computers, which are now fundamental to our survival. Without them, our lives and place in the world would be significantly changed. Neuroenhancement can be seen as only the latest example of the continuing development of such tools, but ones that work directly on our nervous systems, to improve our cognitive function and increase our capabilities. The papers included here show that neuroenhancement has great promise for providing real-world applications for enhancing cognitive function in health and disease. As Brem et al. suggest, these enhancements might also come with some costs. This may be true to some degree for all forms of cognitive enhancement, including older ones such as written language. Anything that alters a specific area of cognition may lead to broader, long lasting changes in cognition and brain physiology. Objective, empirical research will help to determine what the cost of such changes might be, allowing cost/benefit analyses to be performed and intelligent decisions to be made by individuals and medical professionals. Such analyses should also inform debates on the ethics of neuroenhancement, particularly in healthy individuals (Farah et al., 2004).

One common suggestion across the papers included here is that the combination of imaging and/or treatment modalities, which we call “multimodal neuroenhancement,” is often more powerful than the use of single methods alone. This special issue includes a variety of examples, such as combining different forms of neuroenhancement, combining neuroenhancement with neuroimaging, and combining multiple methods of neuroimaging for neurofeedback. Employing multiple technologies together may add to the expense, time and complexity of studies and treatment protocols. However, if the results of cost–benefit analyses show that the added benefits outweigh the costs, then multimodal neuroenhancement may be preferred.

An overwhelming number of review papers included here mention that the comparison across studies is made more difficult by the lack of common protocols for the application of neuroenhancement technologies, and the lack of common reporting measures of cognitive enhancement. A minimal, common set of procedures and metrics should be put into place, which neuroenhancement studies would incorporate. This would include randomized assignment to treatment conditions, the addition of a sham control condition, and reporting statistical measures including effect size. Additionally, there is broad consensus of the need for large-scale, multi-institution clinical trials of neuroenhancement, such as is currently used to evaluate pharmaceuticals. While expensive and labor intensive, such studies offer the hope of improved methods of treatment for brain and mental illness, at a potentially reduced cost when compared with current methods of treatment.

We hope that this special issue of *NeuroImage* will help to promote the further development of methods for neuroenhancement. Neuroimaging has now reached the point where it may begin to put theory derived from years of experimentation into practice. Improved attention, perception, memory and other forms of cognition may lead to better performance at work, school and in other aspects of everyday life. It may also reduce the cost, duration and overall impact of illness. Such benefits of neuroenhancement could reduce suffering and improve quality of life for everyone, while also further increasing our knowledge about the mechanisms of human cognition.

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