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ORIGINAL PAPER

Neuromodulation, Agency and Autonomy

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Abstract Neuromodulation consists in altering brain activity to restore mental and physical functions in individuals with neuropsychiatric disorders and brain and spinal cord injuries. This can be achieved by delivering electrical stimulation that excites or inhibits neural tissue, by using electrical signals in the brain to move computer cursors or robotic arms, or by displaying brain activity to subjects who regulate that activity by their own responses to it. As enabling prostheses, deep-brain stimulation and brain–computer interfaces (BCIs) are forms of extended embodiment that become integrated into the individual's conception of himself as an autonomous agent. In BCIs and neurofeedback, the success or failure of the techniques depends on the interaction between the learner and the trainer. The restoration of agency and autonomy through neuromodulation thus involves neurophysiological, psychological and social factors.

Keywords Agency · Autonomy · Brain–computer interfaces · Deep-brain stimulation · Neurofeedback · Neuromodulation

Introduction

Neuromodulation consists in altering brain activity to restore mental and physical functions in people with neuropsychiatric disorders and brain and spinal cord injuries. This can be achieved through the use of neural prostheses, which operate in either of two ways. They deliver electrical stimulation that excites or inhibits neural tissue, as in deep-brain stimulation (DBS). Or they use electrical signals generated by the brain to move computer cursors, robotic arms, or paretic limbs, as in brain–computer or brain–machine interfaces (BCIs, BMIs). Neuromodulation also occurs in neurofeedback (NFB), which uses EEG or fMRI to display brain activity to subjects, who then regulate that activity by their own neural and mental responses to it.

These neuromodulating techniques can restore or enhance a person's agency, the capacity to form and execute plans of action. This general capacity consists of specific motor, cognitive, affective, and conative (desire, motivation) capacities, which may be functional or dysfunctional to varying degrees. Still, agency alone is not sufficient to control behavior. One must also be able to identify with or endorse the neural and mental states that produce actions. The requisite sort of control presupposes that the subject undergoing or manipulating these techniques is not simply an agent but an autonomous agent.

I describe the conditions of agency and autonomy and then discuss how they are influenced by DBS, BCIs and NFB for a range of neurological and neuropsychiatric disorders. I argue that, as neural prostheses, DBS and BCIs do not supplant but supplement the agent's mental states in a model of shared control. Rather than undermining the subject's control of his behavior, they enable control by restoring the neural functions mediating the relevant mental and physical capacities. As enabling prostheses, DBS and BCI systems are forms of extended embodiment that become integrated into the individual's body, brain and conception of himself as an autonomous agent. NFB may do more to promote autonomy by enabling individuals to modulate pain perception and other symptoms without a brain implant. After showing how neuromodulation can

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benefit subjects, I consider some of the risks associated with these techniques and how they might cause subjects to experience psychological harm. In BCIs and NFB, the efficacy of the techniques depends on the interaction between the learner (subject) and the trainer (practitioner). Because training is critical for restoring or enhancing the subject's ability to control his thought and behavior, autonomy depends not only on the subject but also on his interaction with the practitioner.

Agency and Autonomy

Deep-brain stimulation can restore some degree of motor control for individuals with Parkinson's disease (PD) and other motor disorders by enabling them to perform voluntary bodily movements. In addition, it can restore some degree of control of thought and action in individuals with obsessive–compulsive disorder (OCD) by reducing or resolving their repetitive behaviors. This technique can also improve mood and motivation in those with major depressive disorder (MDD). BCIs may enable paralyzed individuals to translate intentions into movements or speech. And NFB may help those with debilitating chronic pain to reduce their perception of pain and release this impediment on their actions. Despite restoring or enhancing agency for individuals with these conditions, neuromodulation through DBS and BCIs raises the following question: How can one be the author or originator of an action if a device placed on one's scalp, under the skull, or implanted in one's brain is doing all or most of the causal work in producing that action? We need an account of autonomy to answer this question.

Being autonomous implies that the mental states that guide a person's behavior are not imposed on her by factors she cannot control and with which she does not identify. Autonomy thus involves more than the ability to act. It also involves the independence and authorship of the conscious and unconscious mental states that move one to act (Kant 1785/1983; Dworkin 1988; Frankfurt 1988, pp. 58–72; Taylor 1991; Mele 1995). These mental states and the actions they produce must be one's own. Neuropsychiatric disorders and brain injuries impair or undermine autonomy by preventing one from acting as one wants to act, or by compelling one to act. The threat to autonomy is not external but internal to the agent.

Autonomy consists of two general capacities: competency; and authenticity. The first involves the specific cognitive and affective capacity to critically reflect on the mental states that issue in one's actions. The second involves the specific cognitive and affective capacity to identify with or endorse these mental states following reflection. The process of critically reflecting on and identifying with one's mental states and actions is what makes them one's own. Mental states with which one does not identify or endorse may be considered "alien" to the agent. An autonomous person is able to neutralize or eradicate these states from the set of cognitive, affective, conative, and motor springs of her actions.

There is an optimal level of this reflective capacity, however. For example, individuals with OCD appear to engage in excessive conscious deliberation about how to act. This interferes with unconscious proceduralized behavior that ordinarily enables one to perform a range of cognitive tasks and motor skills without having to think about performing them (Mallet et al. 2008). Autonomy requires a certain degree of conscious reflection. Yet OCD illustrates that too much reflection can result in a pathology that undermines autonomy. The characteristic features of this disorder suggest that autonomous behavior must to some extent be automatic. It depends on a balance between deliberative (conscious) and automatic (unconscious) processes mediated by interacting cortical, limbic, and subcortical circuits. Ordinarily, each process and circuit constrains and is constrained by the other in preventing behavior that is too deliberative or too automatic. In OCD, dysregulation between these circuits prevents the individual from performing actions he would ordinarily perform as a matter of course. The exaggerated need for control is in fact symptomatic of a loss of control and a form of mental paralysis. The mental states that move one to act in this and other neuropsychiatric disorders are not the sorts of states that one would endorse as the source of one's actions. In this regard, they are not autonomous.

Gerben Meynen points out that those with OCD feel completely alienated from their behavior. They do not consider it their own (Meynen 2010). Similarly, Michael Schormann states: "Patients don't see their obsessions as part of their personality. They see them as something imposed on them, as something they yearn to be rid of" (cited in Abbott 2005, p. 18). Also, patients with severe depression do not identify with the anhedonia and avolition characteristic of the disorder and may perceive these affective states as alien to them. Modulation of neural circuits mediating impaired motor and mental functions through DBS can raise these functions to normal or near-normal levels and thus restore some degree of autonomous agency.

Sabine Muller and Henrik Walter (2010) claim that neuromodulation requires some revision of the concept of autonomy, since it can influence the neural basis of autonomy. With the exception of some cases of intracerebral hemorrhage and hypomania from DBS, overall the effects of this and other forms of neuromodulation on the brain and mind have been salutary. In neuropsychiatric disorders, the neural basis of autonomy is impaired. Electrical stimulation of the right targets can restore function in

the circuits that constitute this basis and thus autonomy itself. Accordingly, there is no need to revise this concept but only to examine the mechanisms behind this restoration. The neural prosthesis promotes control by allowing the thought and behavior the agent wants to have. By regulating dysregulated neural circuits and the mental capacities they mediate, DBS can complement the cognitive capacities of the subject that are intact. These include insight into or understanding of the disorder and the need for treatment. In individuals deemed appropriate candidates for DBS, these capacities are sufficient for them to give informed consent to the technique. Moreover, improving cognitive and affective capacities that might have been impaired can ensure that the subject or patient has the decisional capacity and communicative skills to consent to continued DBS when it has already been effective. So, contrary to what Muller and Walter claim, nothing about the influence of neuromodulation on the brain and mind suggests that we should revise the concept of autonomy.

Deep-Brain Stimulation for Neuropsychiatric Disorders

Electrical stimulation of the subthalamic nucleus (STN) or globus pallidus interna (GPi) can enable individuals with limited motor control in advanced PD to perform voluntary physical movements (Benabid 2003, 2007; Odekerken et al. 2013). The fact that modulation of circuits in the basal ganglia operates outside of their conscious awareness does not affect the phenomenology of control, or the feeling of being in control of motor functions. This is because their implicit knowledge that the electrodes are implanted and activated in their brains does not figure in the explicit content of their conscious awareness. Likewise, individuals with OCD and MDD are not aware of the electrodes modulating neural circuits and the cognitive and affective states they mediate. Mechanisms operating at the unconscious level are necessary for them to control their conscious thought and behavior. Most normal brain processes are not transparent to us and operate outside of our conscious awareness. We have no direct access to our efferent system, for example, and only experience the sensory consequences of our unconscious motor plans. Theoretically, it does not matter whether these consequences are produced by a natural or artificial system. Provided that an artificial system connects in the right way with the neural inputs and outputs that mediate behavior, the agent can control her intentions and actions.

Patients with PD may benefit from DBS if they have responded favorably to levodopa. The medication and stimulation are not significantly different in that both can reduce motor symptoms. However, the drugs may cause adverse effects such as dyskinesias in some patients, which make them good candidates for DBS. The differences between medication and stimulation are more pronounced in psychiatric disorders. DBS is an intervention for patients with symptoms that are resistant to psychopharmacology. Unlike pharmaceuticals, DBS is a focused means of neuromodulation that targets a specific structure in an identified neural circuit. This minimizes the distributed and nonspecific action of medications, which can result in compliance-threatening adverse effects such as weight gain. By identifying dysregulated circuits, DBS can contribute to a better understanding of the pathogenesis and maintenance of psychiatric symptoms.

One hypothesis for the pathogenesis of MDD is that it is caused by dysregulation in the reward system in general and the NAcc in particular (Schlaepfer et al. 2008; but see also Mayberg et al. 2005 and Lozano et al. 2008). This impairs the capacity to motivate oneself to act. The characteristic symptom is anhedonia, the inability to experience pleasure from previously pleasurable activities. Modulation of the reward system can alleviate this symptom and restore motivational capacity in many cases. One hypothesis for the pathogenesis of OCD is that it results from a hyperactive meta-cognitive monitoring system caused by dysregulation between or among cortical, limbic, and subcortical circuits. More specifically, it has been hypothesized that the disorder results from hyperactive circuits linking the orbitofrontal cortex, basal ganglia/limbic striatum and thalamus (Modell et al. 1989). This is supported by a more recent hypothesis that OCD is associated with excessive frontostriatal connectivity. It is reflected in the excessive effort of conscious control at the cost of more unreflective skill-driven behavior and nondeliberative responsiveness to the environment (de Haan et al. 2013). The individual misperceives environmental stimuli as threatening, and loses confidence in his ability to perform basic actions. Repetitive and ritualistic behaviors such as checking, washing, and hoarding form a defense mechanism generated by this doubt. Because of its projections to the brain circuits implicated in the disorder, stimulation of the STN or internal capsule in severe forms of OCD can reduce or resolve the symptoms. It can free the conscious mind from unnecessarily attending to motor functions and instead allow it to attend to more demanding cognitive tasks.

Yet DBS can malfunction either from a depleted battery or a lead fracture, resulting in open or short circuits. This may allow symptoms to return and cause the patient to become acutely aware of the disorder and how it impedes his ability to act without excessive deliberation. The return of motor symptoms in PD and cognitive and affective symptoms in OCD and MDD can adversely affect the phenomenology of control. It can reinforce the experience of losing motor skills in the first disorder and the

experience of mental paralysis in the second and third disorders and in each case appear to undermine both agency and autonomy.

In light of the earlier description of OCD as a hyper-reflective pathology, this last claim needs qualification. Despite feeling compelled to act by a hyperactive monitoring system, most patients with OCD retain enough cognitive capacity for insight into their disorder (Meynen 2010). This can motivate them to seek treatment in the form of cognitive-behavioral theory or, in more severe cases, DBS. Many patients with MDD retain enough motivational capacity to seek treatment as well. So, while OCD and MDD may significantly impair control, they do not necessarily undermine it. This indicates that agency and autonomy fall along a continuum of mental capacities and thus are matters of degree. The degree to which one has these capacities depends in turn on the degree of function or dysfunction in the brain circuits that mediate them.

Motor control is hierarchically organized according to functional-neuroanatomical models. The extent to which agency and autonomy are involved may depend on the level at which a neuromodulating technique is operating. Performing an action automatically engages mainly lower-level subcortical regions. Conscious planning of an action requires deliberation and engages mainly higher-level prefrontal and motor cortices. Yet subcortical structures such as the cerebellum contribute to cognitive and affective processing in coordinating action plans in addition to their role in motor coordination. It is thus misleading to think of different neuroanatomical regions having separate roles corresponding to simple or complex motor functions. While autonomous agency may be associated more with higher-level cognitive and sensorimotor control, it depends on the balanced integrated functioning of higher- and lower-level circuits projecting to and from each other. By restoring this balance in a number of motor control disorders, neuromodulation can ameliorate their symptoms.

It is instructive to consider neuropathologies other than PD and their consequences for agency and autonomy. The symptoms of these disorders can shape expectations about the effects of neuromodulation on control of motor functions. For example, a patient with essential tremor or focal task-specific dystonia retains some degree of control over his behavior. In contrast, a patient with anarchic hand syndrome may lose control over the limb, which moves against the patient's will. The differences in the symptoms caused by these disorders again illustrate how neuromodulation can restore varying degrees of agency and autonomy in patients depending on the extent to which the disorders impair their behavior.

A patient participating in a Toronto-based clinical trial of DBS for treatment-resistant depression experienced a significant reduction in symptoms. He was able to return to work and resume a normal range of activities. When his symptoms returned because the battery for the pulse generator had been depleted, he expressed relief about what he believed was the cause of the symptoms: "I'm just happy it wasn't me, that it was the battery." (Lipsman and Glannon 2012, p. 3) The patient was misattributing the cause of his symptoms to the device rather than the underlying pathophysiology of his disorder. When the device was functioning properly, he wanted to believe that the content and quality of his mental states were under his control and thus very much his own. Yet his comment suggests doubt about whether he was the source of his thought and behavior. For when the device functioned properly, produced the neuromodulating effects, and restored agency, it seems that the agent was not the person in whose brain the device was implanted but rather the device itself. Even if the device ensured that the mental states producing his actions were those he endorsed as the source of those actions, what role would the patient have in regulating this source? Because he regained control of his thought and behavior only when the implanted electrodes functioned properly, they appear to have replaced him as the real agent. Paradoxically, what restores and sustains the neural substrate underlying his ability to motivate himself to act appears to undermine his autonomy. How can one be in control of one's mental states and actions if one implicitly knows that a stimulating device is doing most if not all of the causal work in modulating their neural basis?

The patient can perceive the stimulating system as not replacing but enabling him as an agent. There is shared control between the patient and the device, which works as a neural prosthesis that compensates for impaired mental or motor functions while complementing functions that are intact. It does not supplant these functions but supplements them. When functioning as designed, the technique can restore control by modulating an overactive monitoring system in OCD, an underactive reward system in MDD, and a dysfunctional motor system in PD. Indeed, the modulating effects of DBS in severe psychiatric disorders may allow patients to respond to cognitive-behavioral therapy, which may not be possible prior to the application of the stimulating technique. By modulating activity in dysregulated neural circuits, DBS enables the patient to have the mental states he wants to have and translate them into voluntary actions. In this way, the device becomes integrated into his brain and mind. The device is a form of extended embodiment that becomes a part of his identity. Again, though, if it malfunctions or produces unintended adverse effects, then it can generate the experience of losing control through the patient's awareness of the symptoms. This is significant because it demonstrates that neuromodulation can relieve symptoms but does not

reverse or arrest the underlying pathophysiology of neuropsychiatric disorders. It is the disorder and not the device in the patient's brain that impairs or undermines autonomous agency.

Neuromodulation is consistent with autonomy only insofar as it restores or sustains optimal levels of motor and mental functions. OCD is one illustration of this point. Consider another example. DBS may restore normal levels of mood and motivation in a patient with major depression. Happy about the positive effects, he may want to feel even better and may ask his psychiatrist to increase the voltage of the stimulator. But it could result in a hypomanic or euphoric state in which the patient feels "too good" (Synofzik et al. 2012). This assumes that the patient retains enough insight and understanding that the stimulation has exceeded a salutary level in its effects on mood and inclines him toward a maladaptive or pathological state. It suggests that he would know that the euphoria would likely lead to compulsive or otherwise irrational behavior that would not be in his best interests.

Unlike DBS for PD, where patients can control the stimulator by turning it on or off and adjusting the voltage, in psychiatric disorders the practitioner usually sets and adjusts the stimulation parameters in regulating the device for the patient. There may be cases in which a patient is allowed to operate the device on his own outside the clinical setting. If the patient voluntarily increased the voltage to induce euphoria and irrationality, then it could result in a loss of control of his thought and behavior. The euphoria could impair or undermine his autonomy once it affected him. Yet if the decision to increase the voltage was the product of normal cognitive and affective states, then becoming euphoric would follow from a voluntary, informed, and autonomous decision. Insofar as he had the cognitive capacity to foresee the euphoria and irrational behavior as the probable consequence of his decision to intensify his mood, his autonomy would transfer from the earlier time when he freely made this decision to the later time when he was euphoric. He need not approve of the behavioral changes prospectively in order for them to be part of his autonomous self but only be able to foresee them as the probable outcome of his action (Merkel et al. 2007; Bublitz and Merkel 2009). The cognitive control he exercised in choosing to increase the voltage would extend from the earlier to the later time. Because of this control, he would autonomously produce and be responsible for his disordered neural and mental state. A decision that resulted in the loss of autonomy could still be an autonomous decision.

It is important to emphasize, however, that the underlying pathophysiology of a neuropsychiatric disorder and the resulting mental impairment can make a patient vulnerable to factors that might interfere with rational decision-making. This underscores the professional responsibility of medical practitioners in discharging their obligations of nonmaleficence and beneficence to not harm and benefit those under their care (Beauchamp and Childress 2008, chapters 4, 5). In providing and monitoring neuromodulation for an individual with MDD, the vulnerability of the patient and the practitioner's medical and ethical obligations may prohibit giving the patient this type of freedom in using the technique. Still, whether these actions should be prohibited or permitted would depend on particular features of the physician–patient relationship and be decided on a case-by-case basis.

Brain–Computer Interfaces for Tetraplegia and Locked-In Syndrome

Brain–computer interfaces are used mainly for patients with tetraplegia resulting from brain and spinal cord injuries (Hochberg et al. 2006, 2012; Leuthardt et al. 2006; Kennedy et al. 2011). This group may include individuals with locked-in syndrome. BCIs do not target dysfunctional neural circuits but instead bypass the site of injury and the usual peripheral nerve and muscle pathways, directing signals from the motor cortex to an output device to generate movements. They translate neural signals into electrical impulses through which individuals can move a computer cursor, produce arm and hand movements through robotic devices, or manipulate a communication system via the P300 brainwave. The original BrainGate Neural Interface System was designed to help people with severe motor impairment from spinal cord injuries to control a computer cursor with their thoughts. Further development of this technology has expanded the range of actual and potential applications.

There are three types of BCIs. Noninvasive techniques consist of EEG sensors on caps or headbands placed on the scalp to read brain signals in motor areas. Invasive techniques come in two types. The first type is electrocorticography (ECoG), in which the electrodes are embedded in a plastic net placed below the dura but above the cortex. The electrodes can read brain signals more clearly than those in a noninvasive system because they are not deflected by the cranium. The second invasive type is a microelectrode array implanted in the gray matter of the motor cortex. Because noninvasive BCIs do not involve intracranial surgery or implants, they do not pose the same risk of infection or changes to surrounding neural tissue as do the invasive forms. But they are external to the brain and thus do not read the relevant neural signals as directly because they are placed at some distance from motor areas and are susceptible to cranial deflection. Also, noninvasive types may detect neural signals from more distributed

neural circuits mediating a wider range of functions and may not be sensitive enough to signals in motor areas to always produce the desired movements. Implanting the microelectrode array directly into the motor cortex can more effectively enable the patient to translate her intention to act into the action. Yet in addition to the risk of infection, another problem with invasive BCIs is how to achieve biocompatibility between the interface and the surrounding neural tissue and remain functional for the lifetime of the patient. Implanted arrays may reorganize and induce changes in this tissue. These changes may be salutary, especially if they promote neuroplasticity and the generation of new neuronal connections that bypass the site of the injury causing loss of motor function. But this will only be determined following a sufficient number of long-term studies of the implants. A safe and effective neural interface that could function for many years would be one in which the surrounding neuropil grew into the electrode tip. This would be more stable and would allow myelinated axons to be recorded using implanted amplifiers (Kennedy et al. 2011). All of these issues are relevant to the ethical question of whether BCIs can benefit or harm subjects in terms of how they might restore or preclude restoration of some degree of autonomous agency.

When the subject's ability to execute certain motor functions depends on the neural interface, the same question that arose with respect to DBS arises here as well: How much of a causal role does the subject play in these actions? She has to imagine, plan, and execute the action by manipulating the interface. The interface is an enabling device that compensates for motor functions that have been lost or severely diminished through brain or spinal cord injury. It supports the cognitive capacity of the patient to form and execute plans of action, albeit to a limited extent. Like DBS in neuropsychiatric disorders, a BCI does not supplant but supplements the neural and mental capacities associated with agency that are intact. The subject's use of the interface constitutes a model of shared control. She can initiate a plan of action by utilizing her neural and mental resources. But she needs the interface to carry out the action plan in moving the cursor or prosthetic limb. Because the interface enables the patient to perform these tasks, she can identify with it as a form of extended embodiment integral to her biological and psychological sense of self. In invasive BCIs, there is somatosensory and proprioceptive feedback from the body to the brain, which reinforces the experience of embodiment (Gallagher 2005). If the patient identifies with the interface and endorses the voluntary actions it enables her to perform, then the BCI is consistent with the idea that the subject's actions are very much her own.

One important difference between a BCI and DBS is that the success of the first technique in generating movement depends on considerable conscious effort by the subject in imagining the action, forming the intention to act, and executing the intention through the interface. Ordinarily, paying too much attention to motor functions can interfere with and distract the conscious mind from attending to more demanding cognitive tasks. But in paralyzed individuals, the loss of motor functions requires conscious attention by the subject to manipulate the interface and produce movement. DBS requires no such effort, only the act of turning the stimulator on or off. One can be motivated to act and perform actions automatically without having to pay attention to the process or how the stimulating system sustains it. Although the range of activity the interface allows is much more limited than that of DBS, a BCI can promote autonomy by making the subject feel that he has regained some control of his behavior. The interface is necessary to execute intentions in the desired movements. But through his brain and mind, the subject initiates and thus has a degree of control over the sequence of events resulting in these movements.

At the same time, though, the expectation of producing movement has the potential to cause psychological harm to the subject by frustrating or defeating that expectation. While the prospect of translating thoughts into actions may provide the subject with the feeling of having some control of his behavior, it may also put a psychological burden on him. The success or failure of generating movements through the interface depends on how effectively the subject can learn to operate it, and some may be more or less capable than others in this regard. The cognitive workload in learning how to manipulate the interface may present challenges that some subjects may not be able to meet. Planning is a critical component in moving a prosthetic limb, since the subject must indicate with his brain and mind where the arm should go before executing the intention to move it. It requires considerable time and patience, and the threshold at which these can be sustained may vary among subjects. This may cause frustration and anxiety and increase the probability of failure for some in trying to achieve their goal. Failure to manipulate the interface and translate brain signals into movements could undermine the feeling of being in control of one's behavior. This experience could negatively affect somatosensory and proprioceptive feedback and change the subject's attitude toward the prosthesis as a form of extended embodiment. Instead, he might perceive it as a foreign object that thwarts his intention to produce movement. The subject is not the only agent in this process. How effective the trainer is in teaching the subject to manipulate the interface can strongly influence whether he succeeds or fails. In this respect, the autonomy of the patient depends on his interaction with the trainer.

A design limitation of implantable devices in BCIs is the wires that are attached to the electrodes. Wireless implants

would be less burdensome for the patient, reduce the risk of infection, and function for longer periods than wired versions, which cannot remain in the brain for more than 30 days. More importantly, they would be functionally superior to wired versions in detecting and responding to neural signals more directly. But they could be more vulnerable to interference from external sources, which could prevent them from functioning or cause them to function in ways that could harm those in whose brains they were implanted. Hackers could disrupt action-potential firing in the device and the transmission of signals from the motor cortex through the interface. A similar type of contamination occurred in 2008 in the US case of a patient with an implanted cardiac defibrillator. There would also be privacy considerations regarding the potential of illicit access to information on the wireless device without the patient's consent. All of these are examples of external interference that could harm the individual by defeating his interest in restoring agency and undermining the autonomy of his actions. In these and other respects, a technology designed to help an individual regain some control of motor functions could instead prevent him from regaining or cause him to lose it.

Another ethical issue arises from the prospect of using BCIs to enable communication for individuals who had lost their natural ability to speak (Birbaumer et al. 2008; Leuthardt et al. 2011). The technique could be used for this purpose by patients with locked-in syndrome, who are fully aware but almost entirely paralyzed. The condition usually results from a lesion in the ventral pons of the brainstem, and eyelid movement is often the only intact voluntary motor function. Still, it is unclear to what extent patients using such a device could effectively communicate their thoughts. Unless the speech capacity of BCIs was developed to a high level of sophistication, they could entail a risk of harm for those trying to communicate through them. Suppose that a patient who was fully conscious but paralyzed and unable to speak was asked by family members and health care providers if she wanted to continue or discontinue life-sustaining artificial hydration and nutrition. Would the interface enable the patient to express more than a "yes" or "no" response to this question? Would it allow her to make her wishes clear and show that she fully understood the question and the consequences of the action? It is doubtful that the level of communication through the interface would be high enough to meet criteria of informed consent (Beauchamp and Childress 2008, chapter 4). This requires clear evidence of understanding the goals and probable consequences of a proposed intervention, as well as clear expression of the patient's wishes regarding the intervention. Lack of clarity in the expression of the patient's wishes could lead to actions she would not want. The potential for harm in this use of a BCI could be just as great as the potential for benefit. These are some of the scientific and ethical issues that need to be worked out before BCIs are considered for use in a greater number of individuals with severely compromised motor and language functions.

Neurofeedback for Chronic Intractable Pain

Neurofeedback uses EEG or fMRI to monitor brain activity in real-time and provide information about this activity to subjects. The subject learns to manipulate this information in modulating activity in regions of the brain associated with disorders such as ADHD, epilepsy, depression, and chronic pain (Arns et al. 2009; Linden et al. 2012; Tan et al. 2009; Weiskopf 2012). The ability to modulate brain function in these regions may enable subjects to alleviate symptoms associated with these disorders. For example, given proper training some individuals with chronic intractable pain can modulate activity in the rostral anterior cingulate cortex (rACC), which is involved in pain perception and regulation. One study using fMRI showed that individuals who learned to modulate rACC activation reported a decrease in their experience of chronic pain (de Charms et al. 2005). By controlling activity in this brain region, they were able to control pain perception. NFB may enable individuals with ADHD to modulate prefrontal cortical areas and dopaminergic pathways and become more focused on cognitive tasks. In addition, for some individuals with epilepsy, the technique may enable them to prevent seizures by altering electrical activity in the temporal lobe at the onset of an aura. Learning how to modulate brain activity in NFB involves both conscious and unconscious processes. Subjects must have the conscious cognitive capacity to know how to manipulate the information presented to them about their brain and expect a positive outcome in order to alter the neural processes and produce a therapeutic effect. Once they have learned how to do this, the process becomes unconscious, a form of operant or classical conditioning. The salutary effects on the subject's brain and mind are attributable to both conscious expectation mechanisms and unconscious conditioning mechanisms. As Linden and coauthors describe it, mind–brain interaction in NFB consists in "a holistic approach that overcomes bio-psychological dualisms" (Linden et al. 2012, p. 9). The patient's conscious and unconscious mind induces changes in his brain and behavior.

In a sense, NFB enables a subject to have a greater degree of control of brain activity mediating certain perceptions and behaviors than DBS or BCIs. This is because the neurophysiological and neuropsychological effects are produced by subjects with only the information provided by EEG or fMRI. They do not require the aid of a prosthesis placed on the scalp, under the skull, or implanted in

the brain. The range of behaviors that can be controlled in NFB may be more limited than it is with DBS. But the subject in NFB plays a more active role in producing the neuromodulating effects, and these involve a broader range of conditions than the impaired motor skills that BCIs are designed to partly restore. While the effects of NFB on brain activity and perception are partly due to unconscious conditioning mechanisms, this does not imply that they are beyond the subject's control. A neural or mental process that does not require constant conscious deliberation can still be within one's control if it promotes voluntary behavior. Besides, the subject in NFB must consciously initiate the process in learning how to manipulate the information before unconscious conditioning takes over. The critical first part of the process thus requires conscious cognitive effort. Equally important, how effectively the subject uses NFB to modulate brain activity depends on how well the practitioner trains him to do it. So, as with BCIs, the interaction between the subject and the practitioner is critical to the success or failure of the technique and to restoring and maintaining the subject's agency and autonomy.

Yet even with proper training, some subjects may have difficulty in learning how to use information about their brain to alter its activity and reduce symptoms caused by a disorder. Not all subjects are equally adept in doing this. Some might become frustrated and impatient and fail to produce any modulating effects from the information they receive about their brains. The cognitive task of manipulating the technique may be too difficult for some to carry it out successfully. This may reinforce a perceived lack of control over their condition. It could generate the experience that they are being controlled by rather than being in control of their symptoms. For patients with intractable chronic pain, this may exacerbate their perception of pain.

Using information about the brain to modulate its activity involves more than the practitioner explaining and the subject knowing about the mechanical and neurophysiological features of the technique. It is a biopsychosocial process. The interaction between the learner and trainer is a social encounter framed by beliefs and expectations (Benedetti 2011). How the trainer motivates and instills confidence in the subject in making him believe that he can modulate brain activity and reduce pain or other somatic perceptions can make a significant difference as to whether the subject can achieve these goals. This can influence the subject's therapeutic expectation about the process and increase the probability of producing therapeutic effects. Conceived within a biopsychosocial model, the role of the trainer is critical in effecting a therapeutic outcome and thereby promoting the agency and autonomy of the subject.

Conclusion

Deep-brain stimulation, BCIs, and NFB involve different forms of neuromodulation. They enable subjects with neuropsychiatric disorders or brain injuries to regain varying degrees of control of their thought and behavior. While DBS involves less conscious control than the other two techniques, it can modulate a broader range of neural and mental functions. The fact that DBS operates largely outside of one's conscious awareness does not threaten control because the capacity to regulate how one thinks and acts consists of both conscious and unconscious processes at neural and mental levels. Conscious cognitive effort is critical in BCIs because the subject must form and execute an intention to act through the interface in order to produce movement. The electrodes and microelectrode array implanted in the brains of subjects using DBS or BCIs are part of a system of shared control that can be perceived by the subject as a form of extended embodiment. NFB arguably involves the greatest degree of control among these three types of neuromodulation because there are no devices implanted in the brain of the subject. She must rely on her own cognitive and affective skills in responding to information about her brain to achieve a positive effect. Even here, though, conscious expectation and unconscious conditional responses in addition to the subject's effort are necessary to produce this effect.

Some might raise the question of whether there are significant differences in bodily representation between neural prostheses and devices external to the brain utilized to produce or facilitate mental and bodily actions. These would include speech-generating devices, wheelchairs, or even tools used in daily life. The difference in extended embodiment between these devices and neural prostheses may be one of degree rather than kind, and this hinges on the extent to which they enable one to initiate and execute action plans. Because the neural prostheses I have discussed play a more critical role in restoring normal thought and behavior for those with physical and mental paralysis, the phenomenology of embodiment seems greater in cases where the device is internal rather than external to the brain.

Neuromodulation may also depend on factors external to the brain, specifically the learner–trainer interaction. This interaction, and particularly the role of the trainer, is critical in producing beneficial outcomes and promoting autonomy for individuals using BCIs and NFB. Considered as a form of the doctor–patient relationship, the interaction between the subject and the practitioner, or therapist, is a social encounter. Fabrizio Benedetti (2011, p. 269) points out that "the therapist has a central role in triggering all those mechanisms that take place in the patient's brain, from seeking and hopeful behavior to expectation and

placebo responses". Neuromodulation can be construed as a process that occurs within a biopsychosocial context. In neurophysiological, psychological, and social respects, the three neuromodulating techniques that I have described and discussed can have salutary effects on the brain and mind and restore and maintain the autonomous agency of the subject.

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