

Target Article

# A Threat to Autonomy? The Intrusion of Predictive Brain Implants

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The world's first-in-human clinical trial using invasive intelligent brain devices—devices that predict specific neuronal events directly to the implanted person—has been completed with significant success. Predicting brain activity before specific outcomes occur brings a raft of unprecedented applications, especially when implants offer advice on how to respond to the neuronal events forecasted. Although these novel predictive and advisory implantable devices offer great potential to positively affect patients following surgery by enhancing quality of life (e.g., provide control over symptoms), substantial ethical concerns remain. The invasive nature of these novel devices is not unique; however, the inclusion of predictive and advisory functionalities within the implants, involving permanent monitoring of brain activity in real time, raises new ethical issues to explore, especially in relation to concerns for patient autonomy. What might be the effects of ongoing monitoring of predictive and advisory brain technologies on a patient's postoperative sense of autonomy? The role played by predictive and advisory implantable brain devices on patient's feelings of autonomy following surgery is completely unknown. The first section of this article addresses this shortcoming by reporting on a pilot study that we conducted with one of the patients implanted with one of these novel brain devices. The second section examines how overreliance on predictive and advisory brain technologies may threaten patients' autonomy. The third section looks into ethical problems concerning how devices delivering automated therapeutic responses might, hypothetically speaking, be used to monitor and control individual's autonomy through inhibition of undesirable behaviors.

**Keywords:** advisory system, automated control, autonomy, brain, brain implants, predictive brain devices, undesirable behaviors

Implantable brain technologies are a rapidly growing therapeutic option around the globe. It has been estimated that more than 100,000 patients worldwide are treated with invasive brain technologies such as deep brain stimulation (DBS) (Medtronic 2013). Yet these numbers are set to increase rapidly. Indeed, implantable brain devices have been traditionally prescribed in the late stages of disease as the last therapeutic alternative, when all other therapeutic options have been exhausted. However, recent studies have demonstrated that the use of implantable brain devices in the early stages of neurological diseases are providing sufficient benefit such that stakeholders are now suggesting early implantation (Schuepbach et al. 2013; Charles et al. 2012). This shift to widespread use of brain implants in the early stages of disease, rather than at later stages, has the potential to quickly revolutionize how medicine treats affected patients, especially by challenging the monopoly of pharmaceutical drugs as the unique and default treatment alternative. In addition, the number of

patients who could benefit from early implantation will expand quickly due to population aging. For instance, the current frequency of Parkinson's disease in Australia is 1 in 350 persons; the incidence is forecast to increase by 80% in the next 20 years as a result of the aging population (Parkinson's Australia 2011). Novel generations of implantable brain technologies promise to improve existing treatments, as well as to expand the range of new treatments available for other common neurological and psychiatric conditions (Yue et al. 2013).

More specifically, the development of novel invasive biomedical technologies such as predictive brain devices and automated therapeutic activation systems (e.g., drug delivery) has the potential to drastically transform the ways medicine can treat prevalent neurological and psychiatric diseases (Halliday and Cook 2009; Phillips and Crook 2010). Predictive brain technologies involve permanently implanting devices designed to forecast specific neuronal events. They can be programmed to advise the implanted

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patient ahead of time of oncoming symptoms or to automatically discharge a therapeutic response. The description of these devices as having *advisory* functionalities refers to the device's capacity to inform in advance a patient how she or he should act in order to avoid specific neuronal events; to some extent, these functionalities provide prescriptive measures to be undertaken. For instance, the world's first-in-human clinical trial using these technologies has been successfully completed in terms of predicting epileptic seizures with an advisory system (Cook, O'Brien, and Berkovic 2013). In short, the invasive brain devices receive and analyze ongoing electroencephalography (EEG) signals recorded directly from brain activity, and then advise the patient by visual or audible information showing the likelihood of a seizure in the minutes or hours ahead. The patient, in turn, may prepare for, or perhaps even prevent, the oncoming seizure by taking antiseizure medications (Kingwell 2013). These novel advisory devices could be a key alternative to control epilepsy outcomes; about 1% of people worldwide (60–65 million) have epilepsy, and 30–40% of cases are not adequately controlled with current treatments (Cook, O'Brien, and Berkovic 2013).

Currently, predictive brain technologies are being developed to include automated therapeutic responses: for example, a drug delivery system that is not self-administered by the patient but is instead preprogrammed (Yue et al. 2013). Theoretically, these predictive technologies could be used for a range of other pathologies where evidence shows that brain disturbances or changes occur before the onset of preventable symptoms. This could be clinically useful, especially for patients otherwise requiring acute care to either stop or prevent undesirable behaviors. For instance, hypothetically speaking, some forms of aggressive and violent behaviors that are associated with prior brain activity onset could be a target application for predictive automated therapeutic responses in the near future (Franzini et al. 2012; Shih et al. 2009; Marsh Krauss 2000; Jobst et al. 2000).

The invasive nature of these novel brain devices is not unique; however, the inclusion and combination of predictive, advisory and automated functionalities involving permanent monitoring of brain activity in real time creates unprecedented ethical challenges, and may introduce the need for conceptual analysis that is novel. Risks of implanting predictive brain devices may need to be assessed in their own right as distinct from the more conventional risks of neurosurgery insofar as they could implicate substantial harms to a patient's postoperative capacities for self-determination. As such, three preliminary and fundamental questions need to be explored: (1) What might be the effects of ongoing monitoring of predictive and advisory brain technologies on a patient's sense of autonomy? (2) How might overreliance on predictive and advisory brain technologies threaten a patient's autonomy? (3) What are the novel ethical issues ahead, such as how, hypothetically, devices delivering automated therapeutic responses might be used to monitor an individual's brain so as to control undesirable behaviors? However, before

investigating these three questions, we first must briefly clarify some safety issues.

## PRELIMINARY ETHICAL CONCERNS: BEYOND SAFETY ISSUES

As in any other human clinical trial involving innovative medical technology, many traditional safety and efficacy hurdles need to be surmounted before new implantable advisory brain technologies can become a common treatment, especially with automated therapeutic activation systems. Besides the two main ethical criteria—requirements of biosafety (minimizing harm to host neurones) and biotolerability (minimizing chronic inflammatory response)—the new generation of predictive brain implants must involve risks of only low acute traumatic responses, such as vascular leakage and edema (hypoxia, introduction of bloodborne macrophages and serum components), inflammation, astroglial activation (hypertrophy astrogenesis), and microglial activation (phagocytosis) (Marin and Fernandez 2010). These concerns are essential for the safety of the treatment. When the advisory brain devices were for the first time tested in a human clinical trial of 15 participants, postsurgery four significant device-related adverse events (namely, device migration, seroma, device-related infection, device site reaction) were noticed within the first year (Cook, O'Brien, and Berkovic 2013). But beyond these traditional physical safety concerns, there is an urgent need to understand and anticipate the potential inadvertent iatrogenic harms to patients.

In the current medical literature, most of the discussion about implantable brain devices and postoperative psychological harm is focused on abnormal side effects caused by the intervention (i.e., hypersexuality, hypomania, etc.). By contrast, relatively little attention is paid to postoperative iatrogenic harms. In other words, questions of whether (so-called) successfully "treated" individuals might experience difficulties in adjusting to becoming "normal" or "symptom free" have been, for the most part, unexplored. Postoperative iatrogenic harms associated with implantable brain devices are also known as a phenomenon named the Burden of Normality Syndrome (Gilbert 2012; Wilson, Bladin, and Saling 2007). A way to understand risks of postoperative iatrogenic harms on patients and the ethical concerns implicated by these risks is to look at the subjective experience of being implanted with predictive and advisory brain devices. We need to consider, then, how predictive and advisory functionalities may impact affected patients' postoperative sense of autonomy.

## DO PREDICTIVE BRAIN DEVICES THREATEN OR INCREASE AUTONOMY?

First we need to connect the idea of a postoperative sense of autonomy and the concept of autonomy; the former may provide a certain kind of evidence for the latter.

The postoperative sense of autonomy refers to the subjective character of experiencing autonomy by an

individual as potentially distinct from how the person might have felt about him- or herself before the intervention (Atkins 2000; Nagel 1979). It concerns the phenomenology of being autonomous or the feelings associated with an autonomous experience. In that matter, the postoperative sense of autonomy is related to the experience of being implanted with predictive and advisory brain devices. To speak of a postoperative sense of autonomy implies that the relevant patient experience of autonomy has an irreducibly subjective character specific to the implanted individual (Atkins 2000). The postoperative sense of autonomy is fundamental to potential postoperative iatrogenic harms, because it constitutes a patient's first-person point of view and his or her own narrative identity. These subjective experiences enable patients to report restorative or deteriorative feelings of autonomy and self-estrangement following surgery (Gilbert 2013a; Gilbert 2015).

As the etymology indicates, the concept of autonomy means self-rule or self-government. It has commonly been linked to the concept of freedom, and such cognates as free will, free choice, free decision, and so on. Predictive and advisory functionalities offer the prospect of originating or prescribing decisions to the implanted individual. For instance, if the device alerts a patient that X is about to occur, then the device may also be programmed to prescribe a course of action Y that the patient is expected to initiate, or to implement itself a course of action Y for the patient, in order to prevent X from happening to the patient. On this account, if autonomy refers to a certain idea of freedom, then one could ask how an individual can freely initiate the steps required for a decision if the implanted predictive and advisory brain device appears to be at the inception of the causal chain producing this decision. In other words, how can a free decision coexist or be reconciled with a decision based upon the programmed responses of an advisory brain implant device based on predictions of the brain's prospective causal trajectory? The extended functionalities of these devices raise the protracted problem of whether predictability may be metaphysically incompatible with one being free (Scriven 1965; MacKay 1960). Here our goal is not to explore whether compatibilist and incompatibilist positions of free will and determinism lead to a *cul-de-sac*, but rather to understand how predictive and advisory brain devices could be a potential threat to autonomy.

As Mele suggests, one way to understand autonomy is in terms of control (Mele 1995). According to this account, autonomous decision or autonomous choice requires that an individual exercise control over her or his decision or choice. In that respect, autonomy encompasses self-control or being a self-controlled individual (Mele 1995). We understand that an individual is in control of her or his decisions if she or he identifies or endorses the sort of control behind those decisions. However, is this identification or endorsement of the control sufficient for making the person's decision as one that could rightfully count as having been made autonomously? When the notion of control is articulated in relation to predictive and advisory brain

devices, the question we now must answer is what sort of control over one's resulting treatment decisions is necessary and sufficient for autonomy.

In general, implantable brain devices are not designed to supplant control; rather, they supplement it by tackling a repertoire of diverse symptoms (Glannon 2014). On a first approximation, predictive and advisory functionalities are consistent with autonomy, but only insofar as they restore or sustain optimal levels of control. The ethical concern, which is the focus of this article, is whether a technologically self-controlled individual may experience a sense of autonomy while being fully under the influence of predictive and advisory functionalities. The potential threat to her or his autonomy is that implanted individuals have no control over the predictions and advice produced by these devices while choosing to act in accordance with these predictions and advice. Consequently, the threat to autonomy is not external but rather internal to the individual (Glannon 2014; Muller and Walter 2010).

In bioethics and neuroethics, the concept of autonomy has generally been defended as involving conditions such as (1) intention (volitions), (2) competence (capacity to appreciate right and wrong and determine oneself accordingly), (3) absence of external controlling influences (freedom from external forces), and (4) absence of internal controlling influences (freedom from internal coercive influences) (Beauchamp and Childress 2013; Muller and Walter 2010). Autonomy is a *conditio sine qua non* for evaluating postoperative iatrogenic harms to implanted patients. However, with reversible neurosurgery intervention involving implanted brain devices (e.g., deep brain stimulation), there is an ongoing debate about how we should respect a patient's postoperative autonomy (Muller and Walter 2010; Wardrope 2013; Lipsman and Glannon 2013; Kraemer 2013; Baylis 2013; Gilbert 2013a).

The question that interests us now is how we might understand whether predictive and advisory functionalities could threaten a patient's postoperative sense of autonomy. Specifically, we conducted a pilot study that sought to understand the various ways that patients phenomenologically experienced predictive and advisory brain devices. The accounts explaining patients' experiences will help shed light on how they may potentially compromise patient autonomy.

## WHAT IS IT LIKE TO BE IMPLANTED WITH PREDICTIVE AND ADVISORY BRAIN DEVICES?<sup>1</sup>

We conducted a semistructured interview with a patient who volunteered to be implanted with the first

1. This study pilot was conducted in accordance to Tasmanian Human Research Ethics Committee regulations. Patient Consent and Minimal Risk Ethics Application Approval, entitled "(H0013883) Implantable Seizure Advisory Brain Devices: Ethical Implications," and conformed to Tasmanian Human Research Ethics Committee regulations. Ethical approval was obtained in March 2013.

experimental advisory brain device capable of predicting epilepsy seizure.

Prior to being implanted, the patient had suffered for more than 20 years from severe epilepsy that could not be managed by medication or through other surgical procedures. The patient described seizures as “interrupting his life,” forcing him to “stop what he enjoys in life.” Of note, epilepsy is characterized by the unpredictability of the seizures, a factor that is acknowledged to be a major component of the impairment experienced by patients. The patient’s first experience with the advisory device occurred immediately after the device was turned on: A warning accurately predicted an upcoming seizure. Consequently, with the device, the patient was able to cope and prepare himself by taking clonazepam, a drug that has the capacity to stop seizures.

When asked to discuss his postoperative experience of being informed of upcoming seizures before they occur, the patient described a certain augmentation of his abilities to act without unpredictable and undesirable adverse epileptic events; the patient reported, “I felt more in control when I used the device. I could push on and do what I wanted to do.” On this account, the patient appears to have experienced the effects of a predictive brain device that enabled him to control his seizures and their effects on his life. As a result, this allowed him to act in accordance with his will: to “push on” and do what he “wanted to do.” Here the patient seems to be describing a sense of autonomy understood as control in accord with his volitions. However, the fact that the patient is able to use information to help prevent an otherwise predictable seizure facilitates his sense of autonomy, but more is required for this to really be achieved.

As seen in the preceding discussion, a crucial point to understand about the implanted patient’s postoperative sense of autonomy is whether he identifies himself with the predictive and advisory functionalities of the device. Some critics would view the effects of the device on the patient as being the product of an external force because they are caused by the device that has been implanted into the brain, not by the brain itself. Some could argue that any postoperative change resulting from these external devices might intuitively be interpreted as being inauthentic. When questioned further on how these sudden predictive and advisory functionalities of the device impacted on him, the patient did not report the resulting feeling of being in control as a disruptive change, or a form of discontinuity, or inauthentic; the patient reported, “I don’t think it changed me as a person, but it gave me more confidence.” As such, the patient appeared to explain that the predictive and advisory capacities of the device did not radically change what constituted him as a person, but rather boosted his sense of self-empowerment. From that point of view, it seems the predictive and advisory functionalities have generated changes in the degree of control associated with a sense of autonomy, rather than changes in what constituted him as a person (not in a reductive conception of what constitutes him). A hypothesis to explain this effect is that the phenomenology

of embodiment may be greater due to the invasiveness nature of the devices (Glannon 2014).

By exploring further the patient’s phenomenological narrative accounts of being implanted with the advisory device, we are able to understand that, importantly, these feelings of being in control and confidence appear to substantially become stronger with constant and continuous brain monitoring. In fact, the patient reported: “My family and I felt more at ease when I was out in the community [by myself], [...] I didn’t need to rely on my family so much.” These descriptions are rather clear: With sustained surveillance by the implanted device, the patient experienced novel levels of independence and autonomy. From these self-reports, it seems that the advisory functionalities increased his sense of autonomy by helping to reduce the uncertainty of having a seizure at any time with little or no warning. In that respect, the implanted predictive and advisory functionalities of the device do not seem to intrude on the patient’s postoperative sense of autonomy per se, but rather provide an increased degree of control that enables his capacities to act unimpeded by the constant risk of otherwise unpredictable seizures. The degree of autonomy experienced appears to be directly proportional to the degree of control provided by predictive brain implants.

As a preliminary observation, we note that the patient appears to embrace the predictive functionalities of the device as well as the resulting feelings of control; the patient does not seem to experience this as a sudden enhancement of his abilities or as an abrupt restoration of his “true” or “authentic” sense of autonomy. The patient seems to interpret the permanent brain monitoring and potential upcoming advisory signals as an integral component of his increased degree of control, which leads to his sense of autonomy.

Incidentally, we think that the benefits to patient autonomy through implanted brain devices may involve some risk of postoperative iatrogenic harms. What is more, the paradox of predictive and advisory devices may be that they both increase patient control on the one hand, and diminish patient autonomy on the other hand by advising on what a patient should do. As we have seen earlier, autonomy implies that there is an absence of controlling (3) external and (4) internal influences. Put another way, because advisory and predictable brain implants provide increased degree of control to patients in general, it is not clear whether, by extension, this may not diminish patient autonomy in some respects: in particular by increasing the degree of control *on* patients. These controlling influences can be broken down into two ethical issues, namely, concerns related to overreliance on advisory functionalities, and problems associated with automated therapeutic activation.

#### FROM ADVICE TO INSTRUCTIONS: PROBLEMS WITH OVERRELIANCE AND FALSE EXPECTATIONS

By increasing predictive control concerning a patient’s symptoms, advisory brain devices are a great opportunity to enhance a patient’s quality of life. However, we must

bear in mind that advisory brain devices are not without risk of signal failure, interference, or reading error that could potentially affect the safety of patients. Dysfunctional advisory devices may lead a patient to take too much medication, or not enough, thus increasing the risk of harm to the patient. These possible system failures highlight that without an adequate independent alternative, patients who are exclusively relying on the guidance of devices may become overreliant on these devices.

Overreliance on invasive advisory brain devices may entail the risk of false security. For instance, it has been observed that devices that can continuously inform and guide an individual, such as a global positioning system (GPS) device, may lull a patient into a false sense of security; the effect of this is that relevant individuals neglect other stimuli that may guide them just as well (Langston et al. 2010). In the preceding case report, while reliant on the sustained surveillance of the device, the patient reported that he and his family “felt more at ease when [he] was out in the community” or that the device “gave [him] more confidence.” Sustained brain monitoring may simply encourage patients to behave in ways they would not without brain implants, thus putting patients at an increased risk of harm, given that they feel secure. In this way, these ongoing surveillance neurotechnologies may create a new kind of risk, where a medical monitoring system intentionally designed to make a patient’s life safer is actually responsible for causing iatrogenic harms. In that respect, overreliance on advisory devices may indirectly encourage risky behaviors. Because patients know that the device will permanently advise them on what they should do, they have incentives to be less cautious than they would be without the device.

In addition, the continuous display of monitoring results and corresponding advice may reinforce patients’ expectations for accurate prediction. Patient may come to believe that the predictive signals always accurately advise “what is actually going (or not going) to happen” rather than thinking that brain devices simply advise according to “what could potentially (or not potentially) happen.” Patients must bear in mind that advisory brain devices do not strictly present “EGG data in itself” but rather “EGG data as advice,” which might trigger false expectations. More precisely, we think this overreliance on advisory brain devices may generate decisional vulnerability for patients, which might threaten their capacities to make freely informed decisions on whether and how to proceed with advice received. Under the sustained influence of the device, a patient may lack decisional sovereignty. Where patients’ decisional capacities are strongly influenced by advisory brain devices, they may become passive and less active in their acceptance of the advice received. In other words, there are risks of underestimating how these devices actually produce certain decisions and risks of overestimating how patients initiate these decisions. These unintentional effects of the advisory devices might entail postoperative feelings of powerlessness or a loss of decisional sovereignty, which may result in substantial risk of

harms to a patient’s postoperative autonomy. With a patient being overreliant on advisory brain devices, it is not clear where the realm of decisional autonomy starts and where the realm of advice ends.

#### **AUTOMATED THERAPEUTIC ACTIVATION: NOVEL ETHICAL ISSUES AHEAD**

Researchers are currently developing the next generation of predictive brain devices that will merge with automated therapeutic activation. The future generation of brain devices will be capable of detecting and automatically preventing onset of specific neuronal events in an individual by activating a preemptive therapeutic response. More specifically, the implanted devices will predict and anticipate, for instance, epileptic seizure onsets within a probabilistic framework, thereby enabling a portion of the device to automatically activate a therapeutic response (drug delivery, electric stimulation, optic display, etc.), in order to deter the course of neurological disturbances (Yue et al. 2013). These devices will operate in a continuous-time closed control loop where therapy is responsive to probabilistic severity measurements; in other words, the therapeutic response will be graded from benign to severe as the situation warrants (Osorio et al. 2001).

Initial ethical concerns are that therapeutic delivery will be automatically administered, involving no human decision. The issue is that invasive therapeutic responses may result in error or in unnecessary dosages. However, the ethical advantage of an automated delivery system is that devices will enable administration of treatments in proportion to seizure occurrence, rather than permanent administration, which is the traditional way of being medicated. Chronic administration of drugs often comes with the burden of significant side effects. Pharmaceutical companies set dosing standards based on the whole patient population. By comparison, automated delivery systems, which are calibrated according to patient ongoing needs, would allow some patients to lessen their drug dosage, therefore avoiding, or lessening the degree of, the relevant side effects.

Future predictive devices capable of intervening therapeutically in response to imminent onset of neurological disturbances will allow implanted patients to systematically benefit from treatment without being consulted before each intervention. There will be no need for the patient to consent to each occurrence of the therapeutic activation; the device will operate “autonomously.” In other words, what does it mean to be implanted with a brain device that operates continually on an independent basis, delivering therapeutic responses in the form of drug or electric stimulation or optic display? Does it threaten a patient’s consent in relation to her or his postoperative sense of autonomy?

In terms of informed consent, initially, patients agree to be implanted with an automated predictive device; their consent is not required every time the device induces treatment. Once the device is implanted, a patient about to

suffer from an epileptic seizure will not have the power to stop the device from automatically inducing treatment. In this regard, it would be difficult to see how patient sense of autonomy could be threatened. On the contrary, because the device operates continuously and delivers automated therapeutic responses, a patient's sense of autonomy is preserved rather than compromised.

However, even if these devices provide effective means of treatment that stand to better the prospects for patient autonomy, there remain questions as to whether individuals under treatment should have a right to set the dispensing system to a voluntary activation setting, or at the very least be given the ability to disengage the automatic setting. In this regard, patients should be apprised of their right to request deactivation of the automated system at any time. As in other cases of invasive brain interventions, the consent process should include explicit explanation to the patient of the conditions under which removal of the device is recommended and the patient's right to request deactivation of any automated response system.

### **CONTROLLING AUTONOMY THROUGH INHIBITION OF UNDESIRABLE BEHAVIORS**

As indicated earlier, predictive brain technologies could in theory be utilized for treating a limited number of other brain disturbances where evidence shows that neuronal changes happen prior to symptoms occurring. As an illustration of how brain activity could be detected and stopped before manifesting itself, we can think of certain forms of aggressive and violent behaviors working in a similar manner to the onset of epilepsy, in particular temporal or frontal lobe seizures (Franzini et al. 2012; Shih et al. 2009; Marsh Krauss 2000; Jobst et al. 2000), as well impulsive sexual urges (De Ridder et al. 2009).

If neurological activity were shut down before it manifests itself in behavior as a result of programmed therapeutic response, this raises questions that may call for a revision to some aspects of our moral and medical approaches to preventing undesirable behaviors, especially in terms of how to manage the autonomy of individuals who manifest such behaviors.

Using automated predictive therapeutic devices as a primary form of inhibition could have a beneficial impact on an individual's capacity to engage effectively in sustained decision making (e.g., avoiding undesirable urges by choosing to act otherwise). One could argue that these devices might be a way for the relevant individuals to control their undesirable urges. And, insofar as their behaviors would be controlled in this way, these individuals might be provided with better chances for achieving a sense of autonomy.

However, the technical possibility of targeting a restricted number of undesirable behaviors with predictive and advisory brain devices raises many ethical questions. Who should be eligible to be offered implantation of such devices? Under what circumstances? Who should be allowed to perform the intervention, under what justifications? Would it be preferable to implant devices

with only advisory functional capabilities as opposed to devices with automated therapeutic activation functional capabilities? Could these devices be offered as a condition of release from custody for certain types of criminals? Should devices with automated therapeutic activation functional capabilities be used as contemporary way to prevent future recidivism? More work is needed to answer these questions. The debate about controlling and preventing autonomy through the use of invasive brain devices should take place before the technology is ready to be implanted in humans.

### **CONCLUSION**

Novel predictive and advisory implantable devices offer great potential to benefit patients following surgery by enhancing and restoring their quality of life and providing control over symptoms. However, there currently is a gap in our knowledge concerning the consequences of advisory and predictive brain devices on patients' postoperative sense of autonomy. From the case study described, it is not possible to draw a general conclusion for the entire population of individuals who have been, or who will be, implanted with predictive brain devices, or to defend an exclusive interpretation of how the predictive effects may positively impact on a patient's postoperative sense of autonomy. This article introduces some preliminary results; more research will need to be conducted concerning patients' experiences of the effects of these predictive devices. Some preliminary questions to consider in relation to potential patients' postoperative sense of autonomy are: What should be done if these patients do not endorse the sort of control induced by these devices? What should be done if the advisory functionalities, in effect, result in an unnecessary intake of medication? What should be done if these devices are remarkably effective at dealing with certain targeted symptoms but patients seems to respond by not being able to cope well with the results of being symptom-free?

Any brain surgery involves a set of ethical concerns (Gilbert and Vranic 2015; Gilbert and Focquaert 2015), especially when links to novel invasive electromaterial technologies (Gilbert et al. 2014; Gilbert 2013b; Gilbert and Dodds 2013). By ensuring that we can better understand the impacts of predictive brain devices on patients' postoperative quality of life, neuroethics will be ideally positioned to assess the novel issues raised by clinical trials and the long-term use of these novel devices in humans. Any clinical trial involving predictive brain devices should collect accounts from patients concerning their postoperative sense of their autonomy. Such conceptual and empirical studies regarding the patient's postoperative sense of her own autonomy do not yet feature in any of the existing medical postoperative evaluation procedures. Implementing such procedures should contribute to articulating any unknown ethical issues related to postoperative iatrogenic harms. By mapping these ethical issues, these studies will articulate how current research trial guidelines can adequately address the protection of patients implanted. If

current guidelines lack the necessary protection, these studies will help to develop new guidelines that will be of significant benefit for promoting long-term use of invasive predictive and advisory brain devices. Also, it will present a significant opportunity to directly frame research ethics surrounding the safe and rapid translation of novel predictive biomedical technologies from the laboratory to the clinic. However, a precautionary approach should be taken at this moment in time, before these devices might be used in a range of new neuronal and psychiatric conditions other than epilepsy.

These are still very early days for understanding the impact of predictive and advisory brain technologies on patients' postoperative sense of their autonomy. Phenomenological narrative accounts are not enough to understand all ethical issues ahead, but do provide a starting point for framing questions regarding how patients interpret, and relate to, implanted predictive and advisory functionalities. This work helps to comprehend and anticipate potential inadvertent iatrogenic harms to patients. Future work should engage with a larger number of patients.

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## REFERENCES

- Atkins, K. 2000. Autonomy and the subjective character of experience. *Journal of Applied Philosophy* 7(1): 71–79.
- Baylis, F. 2013. "I am who I am": On the perceived threats to personal identity from deep brain stimulation. *Neuroethics* 6: 513–26
- Beauchamp, T. L., and J. F. Childress. 2013. *Principles of biomedical ethics* (7th edition). Oxford, UK: Oxford University Press.
- Charles, et al. 2012. Deep brain stimulation in early Parkinson's disease: Enrollment experience from a pilot trial. *Parkinsonism and Related Disorders* 18(3): 268–73.
- Cook, M., T. J. O'Brien, S. F. Berkovic, et al. 2013. Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: A first-in-man study. *Lancet Neurology* 12(6): 563–71.
- De Ridder, D., B. Langguth, M. Plazier, and T. Menovsky. 2009. Moral dysfunction: Theoretical model and potential neurosurgical treatments. In *The moral brain, Essays on the evolutionary and neuroscientific aspects of morality*, ed. J. Verplaetse, J. de Schrijver, S. Vanneste, and J. Braeckman, 155–83. Luxemburg and Berlin: Springer Science + Business Media.
- Franzini, A., G. Messina, R. Cordella, C. Marras, and Broggi. 2010. Deep brain stimulation of the posteromedial hypothalamus: indications, long-term results, and neurophysiological considerations. *Neurosurgical Focus* 29(2): E13. doi:10.3171/2010.5.FOCUS1094
- Gilbert, F. 2012. The burden of normality: From 'chronically ill' to 'symptom free'. New ethical challenges for deep brain stimulation postoperative treatment. *Journal of Medical Ethics* 38:408–12. doi:10.1136/medethics-2011-100044
- Gilbert, F. 2013a. Deep brain stimulation for treatment resistant depression: Postoperative feelings of self-estrangement, suicide attempt and impulsive-aggressive behaviours. *Neuroethics* 6(3): 473–81. doi: 10.1007/s12152-013-9178-8.
- Gilbert, F. 2013b. Deep brain stimulation and postoperative suicidability among treatment resistant patients: Should eligibility protocols exclude patients with history of suicide attempts and anger/impulsivity? *American Journal of Bioethics: Neuroscience* 4(1): 28–35.
- Gilbert, F. 2015. Self-estrangement and deep brain stimulation: Ethical issues related to forced explantation. *Neuroethics* 8(2): 107–14. doi:10.1007/s12152-014-9224-1
- Gilbert, F. and S. Dodds. 2013. Is there a moral obligation to develop brain implants involving nanobionics technologies? Ethical issues for clinical trials. *Nanoethics: Ethics for Technologies that Converge at the Nanoscale*. 8: 49–56 DOI 10.1007/s11569-013-0177-3
- Gilbert, F., A. Harris, and R. Kapsa. 2014. Controlling brain cells with light: Ethical considerations for optogenetics trials. *AJOB Neuroscience* 5(3): 3–11. DOI:10.1080/21507740.2014.911213
- Gilbert, F. and F. Focquaert. 2015. Rethinking responsibility in offenders with acquired pedophilia: Punishment or treatment? *The International Journal of Law and Psychiatry* 38(1): 51–60. DOI: 10.1016/j.ijlp.2015.01.007
- Gilbert, F. and A. Vranic. 2015. Pedophilia, invasive brain intervention and punishment. *Journal of Bioethical Inquiry* 12(3): 521–526. DOI:10.1007/s11673-015-9647-3
- Glannon, W. 2014. Neuromodulation, agency and autonomy. *Brain Topography* 27: 46–54.
- Halliday, A. J., and M. J. Cook. 2009. Polymer-based drug delivery devices for neurological disorders. *CNS Neurol Disord Drug Targets* 8: 205–21.
- Kingwell, K. 2013. Implantable device advises patients with epilepsy of seizure likelihood. *Nature Reviews Neurology* 9: 297; published online May 21. doi:10.1038/nrneuro.2013.94
- Kraemer, F. 2013. Me, myself and my brain implant: Deep brain stimulation raises questions of personal authenticity and alienation. *Neuroethics* 6: 483–97.
- Jobst, B. C., A. M. Seigel, V. M. Thadani, D. W. Roberts, H. C. Rhodes, and P. D. Williamson. 2000. Intractable seizures of frontal lobe origin: clinical characteristics, localizing signs, and results of surgery. *Epilepsia* 41: 1139–52.

- Langston, R. F., J. A. Ainge, J. J. Couey, C. B. Canto, T. L. Bjerknes, M. P. Witter, E. I. Moser, and M.-B. Moser. 2010. Space and direction are already represented in specific neurons when rat pups navigate a location for the first time. *Science* 328(5985): 1576–80. doi:10.1126/science.1188210
- Lipsman, N., and W. Glannon. 2013. Brain, mind and machine: What are the implication of deep brain stimulation for perceptions of personal identity, agency and free will? *Bioethics* 27: 465–70.
- MacKay, D. M. 1960. On the logical indeterminacy of a free choice. *Mind, New Series* 69(273): 33.
- Marin, C., and E. Fernandez. 2010. Biocompatibility of intracortical microelectrodes: Current status and future prospects. *Frontiers in Neuroengineering* 3(8). Epub.
- Marsh, L., and G. L. Krauss. 2000. Aggression and violence in patients with epilepsy. *Epilepsy Behavior* 1(3): 160–68.
- Medtronic. 2013. Deep brain stimulation for movement disorders. Available at: <http://professional.medtronic.com/therapies/deep-brain-stimulation/index.htm> (accessed March 7, 2013).
- Mele, A. R. 1995. *Autonomous agents: From self-control to autonomy*. New York, NY: Oxford University Press
- Muller, S., and H. Walter. 2010. Reviewing autonomy: Implications of the neurosciences and the free will debate for the principle of respect for the patient's autonomy. *Cambridge Quarterly of Healthcare Ethics* 19: 205–17.
- Nagel, T. 1979. What is it like to be a bat? In *Moral questions*, 165–80. Cambridge, UK: Cambridge University Press.
- Osorio, I., M. G. Frei, G. Mark, B. F. J. Manly, S. Sunderam, N. C. Bhavaraju, and S. B. Wilkinson. 2001. An introduction to contingent (closed-loop) brain electrical stimulation for seizure blockage, to ultra-short-term clinical trials, and to multidimensional statistical analysis of therapeutic efficacy. *Journal of Clinical Neurophysiology* 18(6): 533–44.
- Parkinson's Australia. 2011. Living with Parkinson's disease—Update. Available at: [http://www.parkinsons.org.au/ACT/AEReport\\_2011.pdf](http://www.parkinsons.org.au/ACT/AEReport_2011.pdf) (accessed March 2013).
- Phillips, B. W., and J. M. Crook. 2010. Pluripotent human stem cells: A novel tool in drug discovery. *BioDrugs* 24(2): 99–108.
- Schuepbach, W. M. M., J. Rau, K. Knudsen, J. Volkmann, et al. 2013. Neurostimulation for Parkinson's disease with early motor complications. *New England Journal of Medicine* 368: 610–22. doi:10.1056/NEJMoa1205158
- Scriven, M. 1965. An essential unpredictability in human behavior. Voice of America Forum Lectures: Philosophy of science series. [Reprinted (1965) in expanded form in *Scientific psychology*, ed. Wolman, B. B. and E. Nagel. 411–25. Basic Books.]
- Shih J. J., T. LeslieMazwi, G. Falcao, and J. Van Gerpen. 2009. Behavior in frontal lobe epilepsy: A video-eeg and ictal spect case study. *Neurology* 73(21): 1804–6.
- Wardrope, A. 2013. Authenticity and autonomy in deep-brain stimulation. *Journal of Medical Ethics* 40(8): 563–66. doi:10.1136/medethics-2013-101419
- Wilson, J. S., P. F. Bladin, and M. M. Saling. 2007. The burden of normality: A framework for rehabilitation after epilepsy surgery. *Epilepsia* 48(suppl. 9): 13–16.
- Yue, Z., S. E. Moulton, M. Cook, S. O'Leary, and G. G. Wallace. 2013. Controlled delivery for neuro-bionic devices. *Advanced Drug Delivery Reviews* 65(4): 559–69.