Informed consent in implantable BCI research: identification of research risks and recommendations for development of best practices

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Perspective

Informed consent in implantable BCI research: identification of research risks and recommendations for development of best practices

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Abstract

Objective. Implantable brain–computer interface (BCI) research promises improvements in human health and enhancements in quality of life. Informed consent of subjects is a central tenet of this research. Rapid advances in neuroscience, and the intimate connection between functioning of the brain and conceptions of the self, make informed consent particularly challenging in BCI research. Identification of safety and research-related risks associated with BCI devices is an important step in ensuring meaningful informed consent.

Approach. This paper highlights a number of BCI research risks, including safety concerns, cognitive and communicative impairments, inappropriate subject expectations, group vulnerabilities, privacy and security, and disruptions of identity.

Main results. Based on identified BCI research risks, best practices are needed for understanding and incorporating BCI-related risks into informed consent protocols.

Significance. Development of best practices should be guided by processes that are: multidisciplinary, systematic and transparent, iterative, relational and exploratory.

Keywords: informed consent, brain–computer interface, research ethics, deep brain stimulation, safety, neuroethics

Introduction

Clinical trials are an increasingly important part of implantable brain–computer interface (BCI) research. After several decades of data from animal studies, safety and efficacy data in humans is a next step in the development of clinical BCI devices for treatment of neurologic conditions like stroke, spinal cord injury (SCI) and amyotrophic lateral sclerosis (ALS). Examples of BCI human studies and trials include: a BCI system for in situ detection and preemptive stimulation of epileptogenicity approved by the Food and Drug Administration in 2013 (Berger et al 2015); trials of BCI-assistive communication and control of robotic devices (Collinger et al 2014, Hochberg et al 2012); adjunctive BCI studies in patients undergoing presurgical epilepsy monitoring (by several groups including, e.g., Leuthardt et al 2004, Vensteensel et al 2010, Wander et al 2013). A literature review of BCI trials in Web of Science finds that at least 75 human subjects have participated in at least 20 implantable BCI studies since 2003 with more than half of this enrollment happening since 2012 (Specker Sullivan and Illes, unpublished).

Informed consent is an ethical and legal requirement for conduct of clinical research (National Commission 1979, 45CFR46). Institutional review boards oversee informed consent processes in clinical research, including BCI research trials. Informed consent processes must include basic elements of: (1) disclosure of information, (2) decisional capacity, and (3) voluntariness (Beauchamp and Childress 2012). Information about a subject’s medical condition, therapeutic
options, and potential risks and benefits of research participation must be disclosed. Subjects must have the capacity to understand, appreciate, and make a reasoned decision to enroll in a research study. Finally, the decision to participate must be voluntary, and hence free of undue influence.

There have been few other examples of the introduction of new, invasive technology to treat brain disorders. The treatment of movement disorders with deep brain stimulation (DBS) is a well-known approach. Thus, the experience in DBS is highly relevant to our discussion of implantable BCI research. Indeed, DBS platforms appear to be a promising approach to early candidates for implantable BCI devices (Carlson et al 2013). Though some early investigators in implantable BCI research have begun to develop and share informed consent processes (Collinger et al 2014), best practices for informed consent in implantable BCI research do not yet exist. As implantable BCI research increasingly moves into clinical trials, now is an opportune time to think broadly and systematically about informed consent in BCI research.

This paper focuses on identifying research risks associated with implantable BCI. Some risks are inherent to any surgical procedure, especially related to an implanted device, but others are specific to the BCI concept. Understanding safety and other research-related risks is a critical part of ensuring meaningful informed consent processes. We begin by describing safety risks of implantable BCI devices related to three principal BCI components: electrodes, power, and data processing. We then identify six types of BCI-related risks—cognitive and communicative impairment, inappropriate expectations, vulnerability, affective impairment, privacy and security, and identity disruption. This preliminary framework of safety and other research-related risks will serve to stimulate discussion about developing best practices for informed consent in implantable BCI research.

Safety risks

Accurate and accessible information about the safety of implantable BCI technology is a prerequisite for meaningful informed consent in BCI research (Hildt 2010, Giordano 2011). The components of implantable BCI are (1) recording and stimulating electrodes, (2) power generation and delivery, and (3) data processing and transfer. Safety risks associated with these BCI components can be grouped into three principal types: implantation, biocompatibility, and longevity (table 1). Though the full spectrum of implantable BCI safety risks is not known, important information about safety risks has begun to emerge. In this section, we provide a brief overview of safety-related risks of implantable BCI.

Insertion of electrodes into brain tissue is associated with both perioperative and post-operative risks. Electrode insertion causes local mechanical damage to tissue, though the functional impact of this damage is largely unknown (McGie et al 2013b). Systematic data on perioperative BCI risk also is limited (Mak and Wolpaw 2009), though data from DBS suggests that electrode insertion is associated with a 2%–4% chance of brain hemorrhage and 2%–6% chance of infection (Foley 2015). Data on post-operative risks of implanted electrodes is beginning to accumulate. Implanted electrodes induce encapsulation, a foreign body response that can degrade signal detection quality in recording electrodes and require higher levels of current from stimulatory electrodes in order to overcome tissue resistance, with attendant risk of tissue damage and spread of stimulation beyond the intended target (McGie et al 2013). Continued functioning of electrodes after more than five years has been noted (Hochberg et al 2012), but loss of function over time due to electrode encapsulation, corrosion, migration away from an intended target, or other causes are significant concerns within the field.
As with other surgically implanted devices, the required power delivered to the recording, stimulating and data processing systems in BCI devices has associated safety risks. Battery-powered systems rely on wires to travel through tissue (e.g., skull, epidural space, subdural space, or brain parenchyma) in order to bring power to electricity-dependent components, and these interfaces are subject to infection and erosion. Surgical replacement of implanted batteries carries perioperative risk. Advances in battery longevity and rechargeability may reduce the frequency of surgical replacement (by comparison, non-rechargeable DBS batteries currently have a lifespan of approximately 5 years (Larson 2014), though power demands may be greater depending on the design and demands of particular BCI system. Wireless (inductive) power systems may avoid wire–tissue interface risks, and though this technology has been used safely in small trials (McGie et al 2013), long-term safe exposure levels to current and electromagnetic fields of inductive power systems will need to be studied.

Data processing components of implanted BCI have risks that overlap with those of electrode and power components. Implanted processors can induce local tissue reactions or be a nidus of infection, and wires that carry data to or away from a processor generate tissue-interface risks similar to those of power delivery components discussed previously. In addition, processors can generate heat that may cause damage tissue. Rapid obsolescence is a risk of a different kind that is particularly challenging in BCI. Implantable BCI has benefited greatly from rapid advancements in microprocessor computing power over the last several decades. A downside to this advancement is that by the time a BCI device is designed, approved for study, and rigorously evaluated through a clinical trial, the processor capability may be outdated. Rapid obsolescence may reduce what can usefully be learned from a given device and may put those who volunteer for early or proof of concept studies at increased risk if implantation results in exclusion from future studies or use of next generation devices.

### BCI research risks

BCI research involves risks that are not only related to device safety but to other aspects of BCI research and subject decision-making. These include: cognitive and communicative impairment, inappropriate expectations, group...
vulnerability, affective impairment, privacy and security, and identity disruption (table 2).

Cognitive and communicative impairment

Impaired cognition can affect the ability of volunteers to consent to BCI research (Hochberg and Cochrane 2013). Some conditions targeted by BCI, such as ALS or Parkinson’s disease, are comorbid with dementia or other forms of cognitive impairment (Aarsland et al 2005, Consonni et al 2013) that can affect decision-making at study outset. Individuals with these and other conditions may develop cognitive impairment during the course of participation in BCI research. Though the BCI-related side effects on cognition are not yet known, data from DBS suggests that neurostimulation may cause or exacerbate cognitive impairment in some individuals with Parkinson’s disease (Parsons et al 2006). Even when cognition is left intact, impaired communication, such as in ALS or in certain brainstem strokes, can compromise the ability to express decisions about research participation (Clausen 2011).

Inappropriate expectations

Inappropriate expectations can be a barrier to informed consent in BCI research (Haselager et al 2009). One form of inappropriate expectation—the therapeutic misconception—leads individuals to believe they are receiving therapy rather than participating in a trial (Appelbaum et al 1987). The therapeutic misconception has not been formally assessed in BCI research, but it is notable that up to 64.5% of subjects considering participation in a DBS trial for depression were subject to the misconception (Fisher et al 2012). Hypothesized causes for inappropriate expectations in DBS include illness-related desperation (Dunn et al 2011), media hype (Bell et al 2009), and a blurring of the research-therapy distinction (Vlek et al 2012). All of these may have overlap in BCI research as well. In addition, performance may fail to meet participant expectations owing to the physically and psychologically demanding nature of BCI training or due to subjects simply being unable to learn BCI tasks (Kübler and Muller 2007).

Group vulnerability

Target populations of BCI research may be considered vulnerable research groups that require special consideration or protection. For instance, individuals who acquire disabilities over a short time period, such as post-traumatic SCI or traumatic brain injury, may have to decide whether to participate in a BCI study within hours to days of experiencing an injury. As has been noted in stem cell and other

<table>
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<th>BCI research risks</th>
<th>Examples</th>
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<tr>
<td>Cognitive and communicative impairment</td>
<td>Difficulty of assessing potential cognitive side effects of BCI in patients with concomitant neurodegeneration (Kübler and Birbaumer 2008)</td>
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<tr>
<td>Inappropriate expectations</td>
<td>Unrealistic expectations in BCI rehabilitation (Grübler et al 2014)</td>
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<tr>
<td>Group vulnerability</td>
<td>Psychological and informational obstacles to consent in subacute spinal cord injury (Illes et al 2011)</td>
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<tr>
<td>Affective impairment</td>
<td>Anxiety and depression side effects of neurostimulation (Williams and Okun 2013)</td>
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<tr>
<td>Privacy and security</td>
<td>Hacking of wireless brain data transmission (Bonaci et al 2014)</td>
</tr>
<tr>
<td>Identity disruption</td>
<td>Changes to self-perception and personal relationships post-BCI (Klein et al 2015)</td>
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areas of SCI research (Kwon et al. 2012), a short decision window for research participation may generate a kind of decisional vulnerability, as subjects can be desperate to regain lost capabilities and can be unwilling (or psychologically unable) to value a new life lived with disability, and in turn may accept disproportionate levels of research risk. Social stigma may contribute to group vulnerability as family and medical caregivers may undervalue the quality of life experienced by persons with disability (Albrecht and Devlieger 1999).

Affective impairment

Disorders of mood, such as depression or anxiety, can impair cognitive abilities important for informed consent such as attention, executive function, and memory (Porter et al. 2003). While one recent study found that individuals with depression considering DBS performed well across domains of consent-related decisional capacity (Fisher et al. 2012), adverse effects of depression on decision-making are well known (Dunn et al. 2011). Beyond the initial decision to consent to BCI research, mood disorders can affect the ability to make decisions relevant to continued participation. For instance, future BCI systems for treatment of depression may give subjects the ability to change their device settings within pre-set parameters. It is unclear whether allowing individuals to adjust their device settings is always in their best interest, particularly if depression has unappreciated effects on perception of risks and benefits.

Privacy and security

Data collected and processed by BCI devices generates privacy and security risks (McCullagh et al. 2014). BCI devices may allow researchers unprecedented access to information about an individual’s mental life—intentions, desires, biases, proclivities, moods, personality traits—even PIN numbers (Bonaci et al. 2014). Cognitive privacy concerns raised by fMRI and p300 signals as methods of ‘lie detection’ may pale in comparison to what one day may be inferable from voluminous brain signal data recorded by BCI devices. In the near term, risk of device ‘hacking’ is a more relevant worry, particularly if BCI information is wirelessly transmitted. While encryption technology may ameliorate some data security risk, the possibility of someone with malicious intent gaining control of a device may remain a concern, similar to that which prompted a US Vice-President to opt for deactivation of wireless capability of an implanted cardiac defibrillator (Kolata 2013).

Identity disruption

Individuals weighing the decision whether or not to enroll in a BCI trial should consider how being a research participant will affect their sense of self. The motivation to enroll in research, including BCI research, can be the desire to shed features of identity linked to illness (e.g., inability to feed oneself, difficulty with effective communication). But participation in BCI research also has the possibility to disrupt a person’s identity in unwelcome ways. The recent history of DBS provides an instructive example.

DBS has been sought out by individuals hoping to shed certain symptoms, such as tremor or bradykinesia, that have become an unwelcome part of their identity, both how they view themselves and how others perceive them. In this way, DBS offers the prospect of a positive effect on identity. That being said, a small subset of individuals with DBS develop significant, and sometimes dramatic, changes in personality, such as loss of interest in work, change in expectations of sex and marriage, and unhappiness (Schüpbach et al. 2006). This ‘side effect’ of neural stimulation, though rare, has been interpreted as a kind of threat to personal identity (Witt et al. 2013). Though some have argued that such identity
concerns are largely overblown and misunderstood (Baylis 2013), potentially disruptive and unwanted effects of neural stimulation on an individual’s sense of self can occur and need to be taken seriously. One way to address these concerns is to develop a more sophisticated understanding of how identity can be affected by BCI research (Klein et al) as well as develop ways of measuring changes in identity and interrelated aspects of the self (autonomy, authenticity, sense of agency and responsibility), similar to what has been proposed for DBS (Witt et al 2013).

**Consent framework for implantable BCI**

Having identified important areas of risk in implantable BCI, we now turn toward offering recommendations. Here we suggest five approaches to understanding implantable BCI-related risks for use in developing informed consent best practices: multidisciplinary, systemic and transparent, iterative, relational, and exploratory (table 3). Examples where these approaches have been implemented are included.

**Multidisciplinary**

Current knowledge about BCI human research risks is distributed across multiple disciplines (Haselager et al 2009, Schneider et al 2012). Electrical, mechanical, and computer engineers, mathematicians, computer scientists, neuroscientists, neurosurgeons, neurologists, psychiatrists, neuropsychologists, ethicists and others all possess distinct forms of expertise relevant to understanding BCI risks. Just as multidisciplinary teams come together to overcome design obstacles they must also work together to develop a communal understanding of BCI research risks and find ways to communicate these effectively to subjects. The multidisciplinary team-based approach to assessing candidates for DBS may provide a useful model (Ford and Kubu 2006).

**Systematic and transparent**

Consent practices in BCI can benefit from systematic collection and sharing of risk data. The recent history of DBS is instructive. Early studies on DBS for movement disorders focused on effectiveness and basic measures of safety (e.g., post-operative infection and hemorrhage, overall mortality) (Foley 2015). Important

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**Table 3. Recommendations for implantable BCI informed consent processes.**

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<tr>
<th>Consent process features</th>
<th>Description</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Multidisciplinary</td>
<td>Multiple forms of technical and non-technical expertise should be brought together to explore and elucidate research risks and develop appropriate responses.</td>
<td>Multidisciplinary teams (Ford and Kubu 2006)</td>
</tr>
<tr>
<td>Systematic and transparent</td>
<td>Information relevant to understanding BCI research risks should be made readily available to all conducting human BCI clinical trials.</td>
<td>Study registries (Synofzik 2015)</td>
</tr>
<tr>
<td>Iterative</td>
<td>Informed consent should be understood and instantiated as an ongoing process rather than a discrete event.</td>
<td>Reconsent (Wallace et al 2015)</td>
</tr>
<tr>
<td>Relational</td>
<td>The informed consent process should begin with situating participants within their complex web of social and familial relationships.</td>
<td>Caregiver perspectives (Liberati et al 2015)</td>
</tr>
<tr>
<td>Exploratory</td>
<td>Researchers should actively assist participants in exploring short and long term implications of BCI research participation.</td>
<td>User centered design (Kübler et al 2013)</td>
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</table>
data on safety, particularly non-traditional side effects like personality change, mainly came to attention through case studies and anecdotal reports of DBS researchers (Witt et al. 2013). Expanded use of DBS, particularly in large DBS centers, has facilitated more recent systematic collection of safety data (Kenny et al. 2007, Fenoy and Simpson 2014). Yet DBS for non-approved uses, such as depression and dementia, is typically investigated with small trials or case series. This has led to a call for registries to aggregate data on DBS safety and effectiveness (Schlaepfer and Fins 2010, Synofzik 2015). Development of registries for collection of safety data in BCI research may be even more valuable given the wide range of hardware types, implant locations, and targeted diseases in BCI research. Mechanisms for systematic collection of safety data facilitate transparency, particularly if safety data is tied to failed studies that are not published (Zarin and Tse 2008). Perhaps an even more important form of transparency is that between researcher and subject. Given all that is yet to be discovered about BCI and attendant risks, researchers need to be as transparent as possible about what is and is not currently known, just as they are obligated to be with other emerging medical technologies. In addition, researchers need to be transparent about the source of funding for research; this is particularly important if benefits for research will redound to groups other than current volunteers (e.g., military or gaming).

Iterative

Informed consent in research is best thought of a process rather than a discrete event (Lidz et al. 1988). The notion of informed consent as a process is particularly important in implantable BCI research. There are several reasons for this. First, implantable BCI research is highly technical and can be hard for subjects to understand. Information may need to be presented through multiple modalities and over time to enhance subject understanding. Second, implantable BCI research can involve extensive and exhaustive training on use of a device, a ‘risk’ that subjects may not fully appreciate at study onset. Though every effort should be made to inform and screen potential subjects, the right to withdraw from the study at any time needs to be respected. In addition, participation in individual training sessions should be viewed as a form of consent (typically implicit) from which subjects can withdraw, though McCullagh et al. (2014) note that subjects may be reluctant to do so out of fear of disappointing researchers. Third, as mentioned previously, BCI is a rapidly evolving field and during the course of a study new information about BCI risks may come to light that is relevant to subjects in ongoing studies and should be disclosed. Fourth, the boundaries between research and therapy in implantable BCI can easily blur, both due to the therapeutic misconception, but also because of lack of clear temporal or clinical endpoints to research. Consent processes in implantable BCI research may need to become iterative: where the decision to participate and how to continue participation is revisited in some fashion. Whether re-consent is needed will depend on the features of individual research projects (Wallace et al. 2015).

Relational

A full appreciation of BCI research risks requires taking account of social and familial relationships. Participation in BCI research can make substantial demands on caregivers (Mak and Wolpaw 2009). Caregivers prepare and undertake travel to frequent medical appointment and training sessions, tend to and troubleshoot hardware at home, and even monitor and report back information to the research team. BCI researchers need to ensure that added responsibilities from study participation do not contribute to caregiver burden, which can be high in conditions like ALS (Chio et al. 2005) and SCI (Post et al. 2005). At times, it may be difficult to separate out the risk to participant from that of the caregiver. For instance, if a
change in study protocol leads to frequent interruptions in caregiver sleep, the caregiver may become too fatigued to attend to other needs of their loved one. As such, caregivers may be motivated to enroll in BCI research independent of the participant. The promise of decreased dependency is implicit in BCI research and could alter central features of the relationship between caregiver and subject (Gharabaghi et al 2014). Conversely, the impact of lost dependency can ramify in unanticipated directions and can become an undesirable outcome of medically successful treatment, as has been noted in other chronic neurologic impairments (Bladin 1992). Given the complexity and high degree of caregiver involvement in BCI research—sometimes out of necessity and often out of participant preference and because of potential changes to their relationship with their loved one—it has been suggested that caregivers also be asked for consent (Mackenzie 2011, Schneider et al 2012). As has been noted in DBS, changes in personality or affect can threaten health and viability of relationships themselves (Samuel and Brosnan 2011). Adequately addressing risks to relationships may require adopting an ethical framework that is principally relational (Sherwin 1998), not one focused on risks to isolated research subjects.

**Exploratory**

Understanding BCI research risks will involve exploration of preferences, values, and meaning with potential subjects. The bar for this exploration is high in implantable BCI research (Klein 2015). Subjects must be able to project themselves forward, sometimes years ahead given the length of BCI studies, and imagine how their lives and identity could change as a consequence of controlling a BCI. What would it feel like to move a robotic hand with only one’s thoughts? Would new forms of control always be empowering or also at times disconcerting? Would BCI control bring responsibilities in tow (‘you can get your own drink!’) and would the impact on familial or other relationships always be welcome? Subjects may need help to engage in the kind of imaginative exercises needed to consider the personal ramifications of participating in BCI research, particularly if subjects possess only a rudimentary understanding of the range of BCI capabilities. In addition, BCI researchers will need to enhance their understanding of what individuals from BCI-targeted populations want out of research participation (Anderson 2004, Collinger et al 2013) and out of BCI devices. Data on end user and public perceptions of BCI is beginning to accumulate (Liberati et al 2015), but more needs to be done.

**Conclusion**

Developing a better understanding of risks in implantable BCI research is an ethical imperative. Many of the risks identified here are not wholly unique to BCI and have important overlap with human subject research in others areas. Nonetheless, the emerging data on safety risks associated with BCI electrodes, power systems, and data processing present some compelling ethical challenges that are important to consider as the field of BCI takes shape, as do risks related to cognitive and communicative impairments, inappropriate subject expectations, group vulnerabilities, privacy and security, and disruptions of identity. We recommend that development of best practices in implantable BCI informed consent continue or strive to be guided by processes that are multidisciplinary, systemic and transparent, iterative, relational, and exploratory.
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