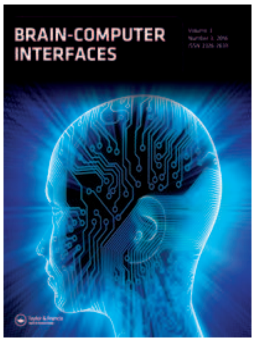

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Beyond 'communication and control': towards ethically complete rationales for brain-computer interface research

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Rapid advances in neural engineering have led to an increasing use of human subjects in brain-computer interface (BCI) research. Here we ask whether the rationales articulated for this research have kept pace with related ethical requirements. To answer this question, we examined the content of peer-reviewed BCI research publications of studies involving human subjects. We analysed the publications for the rationale expressed for the research against a backdrop of journal type and study design. We discuss the results in the context of strategies that neural engineering researchers can adopt to ensure that the ethical dimensions of human subject research are not lost amid the technological drive for results.

Keywords: brain-computer interface; brain-machine interface; neuroethics; research ethics; neural prostheses

Introduction

Neural engineering for brain-computer interfaces (BCI) is a fast-growing field of research at the intersection of neuroscience, computer science, and electrical engineering.[1] Currently, this research aims to produce medical devices for individuals with a variety of injuries and neural disorders such as spinal cord injury, amyotrophic lateral sclerosis (ALS), stroke, and locked-in syndrome. BCI devices involve direct communication between the central nervous system (CNS) and external devices. Unlike transcranial direct current stimulation (tDCS), deep brain stimulation (DBS), and transcranial magnetic stimulation (TMS), which stimulate the brain based on pre-established settings, BCIs measure CNS activity and respond with artificial outputs that replace, restore, enhance, supplement, or improve natural CNS output, either directly through the CNS or via a prosthetic device.[2][1]

The history of BCI technology can be traced back to 1924, and the term 'brain-computer interface' was first used in 1970.[2] Phil Kennedy and Roy Bakay reported the first 'direct brain connection' in a patient with ALS in 1998,[3] and the first clinical trial of BCIs commenced in 2004 with US Food and Drug Administration (FDA) approval (http://www.braingate2.org/). Four participants with tetraplegia were enrolled in this study with promising results. In one of the first papers published as a result of the trial, authors reported that a single participant, a 25-year-old male with a severed spinal cord, had been able to use a neuromotor prosthesis to check email, operate a television, and manipulate a prosthetic hand.[4] Since then, numerous studies have continued to explore and refine BCI technology.

The most difficult – and often most invasive – aspect of BCIs is the method by which they record CNS activity. Current methods include electroencephalography (EEG), electrocorticography (ECoG), single-neuron action potentials (single units), and local field potentials (LFPs). EEG remains the simplest and most often used recording method, while ECoG provides more refined signals but tends to be tested in patients with intractable epilepsy who are already candidates for invasive monitoring.[5]

Potential applications of BCI technology are also diverse. One application is for motor function and rehabilitation in persons with paralysis caused by spinal cord injury or stroke.[4] BCIs can also be utilized as an experimental tool to better understand the adaptive capacity of the nervous system.[6] In addition, entertainment applications are popular [7] and enhancement or augmentation uses are possible.[2,8]

Given the diversity of the field of BCI research, the many recording and stimulating modalities, the multiple possible applications of BCI technology, and an apparent increase in the use of human subjects, in this study we examine published reports of human studies using either the term 'brain-computer interface' or 'brain-machine interface.' Specifically, we are interested in how these self-identified BCI studies justify their research with humans.

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There are many different ways to assess the ethical justification of biomedical research with human subjects, dating back to the Nuremberg Code of 1946. One of the clearest modern formulations of this assessment is Emanuel et al.'s 2000 article, 'What makes clinical research ethical?'[9] They suggest that ethical justification of medical research with human subjects must address the following: (1) value (enhancements of health or knowledge), (2) scientific validity (methodologically rigorous), (3) fair subject selection (subjects chosen based on scientific objectives), (4) favorable risk-benefit ratio (benefit must outweigh risk), (5) independent review (e.g. through an IRB), (6) informed consent, and (7) respect for enrolled subjects (protection of privacy and opportunity to withdraw).

While most, if not all, of the studies we investigate here will have dealt with these issues in their applications for institutional review board (IRB) approval, whether and how the issues are raised in published reports influence and reflect the overall discourse surrounding the pursuit of better BCI technologies. In particular, while it is routine practice for published research articles to address points 5, 6, and 7 through their ethics statements (where IRB approval entails points 6 and 7), points 1–4 may be omitted despite their centrality to ethical analysis. This kind of omission may reflect the still early stages of learning and internalization of ethical standards by the field, a limitation that affects capacities for critical assessment and ethical accountability and in turn influences the replication, validation, and progress of ethically justified studies.[10]

By analyzing justificatory rationale statements, our goal is to facilitate critical reflection and discourse on these fundamental ethical issues and to enable authors to provide more clarity to their fellow researchers about why this technology is important and for whom. Here, we sought to answer the following questions. (1) Is the rationale provided for BCI studies well aligned with the subject population and degree of study invasiveness? (2) Does the rationale take into account possible uses of BCI technology, clinically or otherwise? And (3) is the rationale sufficiently well-articulated according to benchmarks set by Emanuel et al. given technical advances in the field, new knowledge, and new discoveries to date? The answers to these questions will reveal potentially missing and essential components of modern ethical rationale statements for BCI research.

Methods

We used customized search algorithms to interrogate two databases: the Web of Science database and the PubMed database. Eligibility criteria guiding the creation of search algorithms included: (1) use of one or more iterations of 'brain computer interface' or 'brain machine interface' and (2) use of human subjects. On Web of Science, the search strategy for English article topics in the core collection was: TS (where TS = topic)('brain computer interface' OR 'brain computer interfaces' OR 'brain machine interface' OR 'brain machine interfaces') AND TS = ('clinical study' OR 'clinical trial' OR 'case report' OR 'in human' OR 'pilot study' OR 'feasibility study' OR 'safety study').

On PubMed, an advanced search strategy for English article titles returned the following terms: ('Brain-Computer Interfaces'[Mesh] OR 'brain computer interface' OR 'brain computer interfaces' OR 'brain machine interface' OR 'brain machine interfaces' OR bci[ti]) AND (Clinical Trial[ptyp]).

These search strategies were designed to capture as many publications that (1) used the terms brain computer interfaces or brain machine interfaces and (2) involved in-human studies for eventual treatment or clinical care.

Full text articles available to either the University of Washington or the University of British Columbia library system were retrieved for the period between 2000 and 2015, a 15-year window corresponding to the first published study retrieved by the search strategy (not necessarily the first study of its kind), and the most recent as of January 2016.[2] Search returns were curated for duplicates and irrelevant articles (e.g. not a study involving human subjects).

Articles were classified deductively for type of journal (i.e. discipline or field of journal; Table 1) and number of studies reported. Studies were assessed for number of subjects and classified for subject population (patients, control subjects, or mixed) and invasiveness (i.e. binary yes [surgical intervention for implantation of electrodes, e.g. ECoG], or no [transcutaneous sensing, e.g. EEG]).

Following this analysis, we characterized the rationale for human subject research inductively on the basis of the stated purpose or contribution of the study (i.e. stated importance, contributions, and goals), and for level of detail supporting the rationale (Table 2). Rationales were further analysed thematically after clustering primary themes from the journals accounting for more than 70% of the returns (neurology, neural engineering, and biomedical engineering) into sub-themes based on a second level of analysis. Multiple rationale codes were possible for each article.

Results

The Web of Science search returned 127 results. Seventy-seven final articles representing 78 studies met eligibility criteria. The PubMed research returned 151 results. We retained 133 articles for analysis from this search, representing 139 studies. The final merged dataset comprised 210 unique articles with results from 217

Table 1. Journal types.

Journal type	Journal title
Biomedicine	*Clinical and Translational Science*, *Complementary Therapies in Clinical Practice*, *The Lancet*, *BMC Research Notes*
Neuroscience	*Frontiers in Human Neuroscience*, *Journal of Neuroscience Methods*, *Neuroscience Letters*, *BMC Neuroscience*, *Neuroscience Research*, *Human Brain Mapping*, *European Journal of Neuroscience*, *Brain Research Bulletin*, *Nature Neuroscience*, *Experimental Brain Research*, *Cognitive Brain Research*
Neural engineering	*Journal of Neural Engineering*, *Journal of Neuroengineering and Rehabilitation*, *Neurorehabilitation and Neural Repair*, *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *Eurasip Journal on Applied Signal Processing*, *Frontiers in Neural Circuits*
Neurology	*Clinical Neurophysiology*, *Annals of Neurology*, *Journal of Neurosurgery-Pediatrics*, *Stroke*, *Clinical EEG and Neuroscience*, *Psychophysiology*, *Psychopharmacology Bulletin*, *Neurosurgery*, *International Journal of Psychophysiology*, *Psychiatry Research*, *Epilepsy and Behavior*, *Applied Psychophysiology and Biofeedback*
Biomedical engineering	*IEEE Transactions on Biomedical Engineering*, *Annals of Biomedical Engineering*, *Medical and Biological Engineering and Computing*
Robotics	*International Journal of Robotics Research*, *International Journal of Humanoid Robotics*, *Robotics and Autonomous Systems*
General science	*Proceedings of the National Academy of Sciences of the United States of America*, *PLOS One*, *Scientific World Journal*
Rehabilitation	*Archives of Physical Medicine and Rehabilitation*, *Topics in Stroke Rehabilitation*, *Disability and Rehabilitation: Assistive Technology*, *Neurorehabilitation*
Soft Computing	*Applied Soft Computing*
Computer-human interaction	*ACM Transactions on Computer-Human Interaction*
Engineering	*Computers and Electrical Engineering*, *IEEE International Conference on Rehabilitation Robotics*
Neuroimaging	*Neuroimage*
Aging	*Journal of Clinical Interventions in Aging*
Cognition	*Consciousness and Cognition*
Ergonomics	*Ergonomics*
Artificial intelligence	*Artificial Intelligence and Medicine*

unique studies of BCIs using human subjects, published in 55 different journals.

The journal types represented the disciplines of neurology (n = 12), neuroscience (n = 11), neural engineering (n = 6), rehabilitation (n = 5), biomedicine (n = 4), general science (n = 3), biomedical engineering (n = 3), robotics (n = 3), engineering (n = 2), neuroimaging, aging, cognition, soft computing, ergonomics, and artificial intelligence (n = 1 each).

BCI studies have involved 2822 human subjects (patients, control subjects without impairment, and mixed populations) to date. Of the 217 studies reported in these articles, the majority involved control subjects. Use peaked in 2004, 2006, and 2013 (Figure 1). Since 2012, the numbers of patients and mixed populations have increased, as have the numbers of noninvasive studies (Figure 2).

We found that the most commonly cited rationales for BCI research are technological improvement, motor function, and communication. For example:

> *Technological improvement*: ‘There is a growing interest in brain-computer interfaces (BCI) based on invasive technologies. fMRI [functional magnetic resonance imaging] is exceptionally suited for selecting implant sites since BOLD signals have been shown to correlate well spatially with electric potentials recorded from the brain surface …. In the current study we investigate whether BCI with covert visuospatial attention is feasible with recordings restricted to the accessible regions.’

> *Motor function*: ‘Since physical movements by stroke patients are often not possible due to paralysis, motor imagery, which is the mental rehearsal of physical movement tasks, represents an alternate approach to access the motor system for rehabilitation at all stages of stroke recovery.’

> *Communication*: ‘For patients who suffer from severe paralysis as a result of diseases like amyotrophic lateral sclerosis (ALS) or spinal cord injury, brain-computer interfaces (BCIs) may constitute a way of communicating with the outside world.’

Other rationale codes include scientific knowledge, mental health, safety, independence, and enhancement.

Technological improvement was the most common rationale in neural engineering journals, and motor function was most common in neurology and biomedical engineering journals. The majority of studies with a rationale of technological improvement and communication used control subjects without impairment, while the majority of studies with a rationale of motor function used patients (Figure 3). There was no identifiable relationship between invasiveness of study and study rationale (Figure 4).

Table 2. Study rationale examples.

Rationale	Examples
Motor function	'Stroke survivors are typically affected by hand motor impairment. Despite intensive rehabilitation and spontaneous recovery, improvements typically plateau a year after a stroke. Therefore, novel approaches capable of restoring or augmenting lost motor behaviors are needed.' 'In our everyday life, we perform complicated finger motion, such as controlling a smart phone and tablet, operating a remote controller of home electronics, and playing musical instruments. The prediction of three-dimensional finger motion is the most necessary function to interact with environments for quadriplegia.'
Technological improvement	'Given the potential benefits of employing threshold crossings for the control of BCIs, we sought to evaluate neural signal processing improvements to the standard threshold-crossing method.''Brain-computer interface (BCI) systems based on intracortically derived neural signals offer a promising means to control external devices by decoding intended movement-related activity with high temporal and spatial resolution.'
Communication	'A brain-computer interface (BCI) provides a new non-muscular channel for communication and control with external world, which facilitates people who suffer from some sort of locked-in syndrome or amyotrophic lateral sclerosis.''An important aim of BCI is to facilitate the communication of patients with severe motor disabilities, such as amyotrophic lateral sclerosis (ALS), spinal cord injury, stroke and cerebral palsy.'
Scientific knowledge	'The goal of this study was to determine the ECoG features and the cortical regions that are related to sound intensity of continuous music.''Such stimulus-independent activity has important implications for the neural mechanisms underlying episodic memory as well as the development of cognitive neural prosthetics …. Before devices can be engineered using these pre-stimulus signals, however, it is necessary to establish their causal role, if any, during memory encoding.'
Mental Health	'Attention-deficit/hyperactivity disorder (ADHD) is one of the most common child psychiatric disorders. Self-regulation of affected brain regions may be a particularly promising treatment to achieve sustained improvements on the behavioural level.'
Safety	'In America, 60% of adults reported that they have driven a motor vehicle while feeling drowsy, and at least 15–20% of fatal car accidents are fatigue-related.'
Independence	'This is especially important for helping physically disabled people, and could help them achieve greater independence in their lives.'
Enhancement	'We hypothesise that SMR-based neurofeedback training leads to improvements in different cognitive tasks, such as attention, short- and long-term memory tasks, due to a more intense cognitive processing of task-relevant stimuli.'

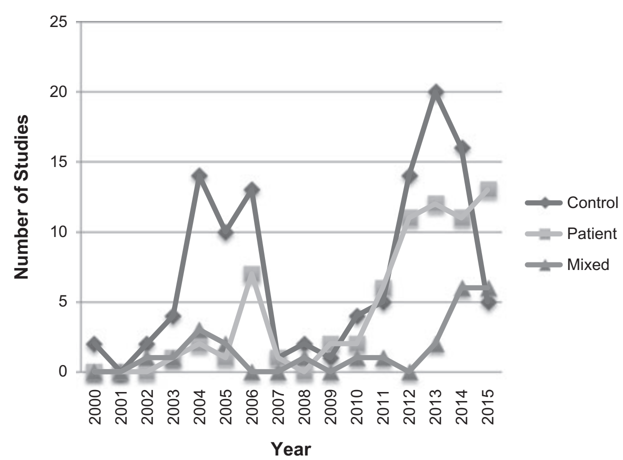

Figure 1. Distribution of populations of human subjects across BCI studies (2000–2015).

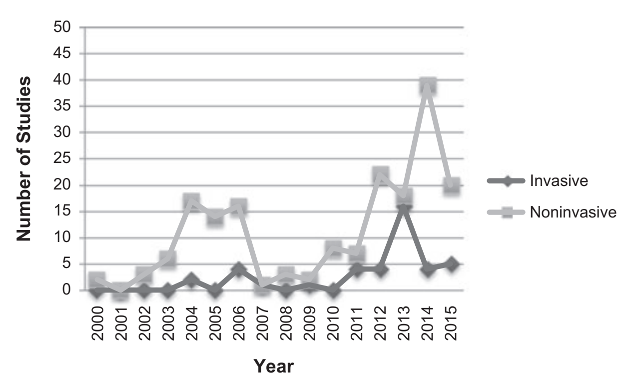

Figure 2. Number of studies classified by invasiveness (2000–2015).

Among the 158 studies isolated for further analysis, the major subtheme to emerge was repetition of the language of communication and control for study justification (27/158). The wording of these rationales was very similar, if not repetitious. For example:

(1) 'Many people with severe motor disabilities require alternative methods for communication and control.'
(2) 'Over the past 15 years, several research groups throughout the world have developed direct

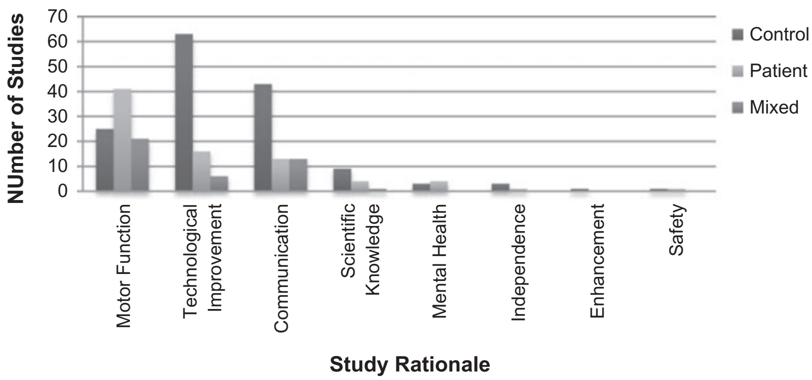

Figure 3. Subject population by study rationale.

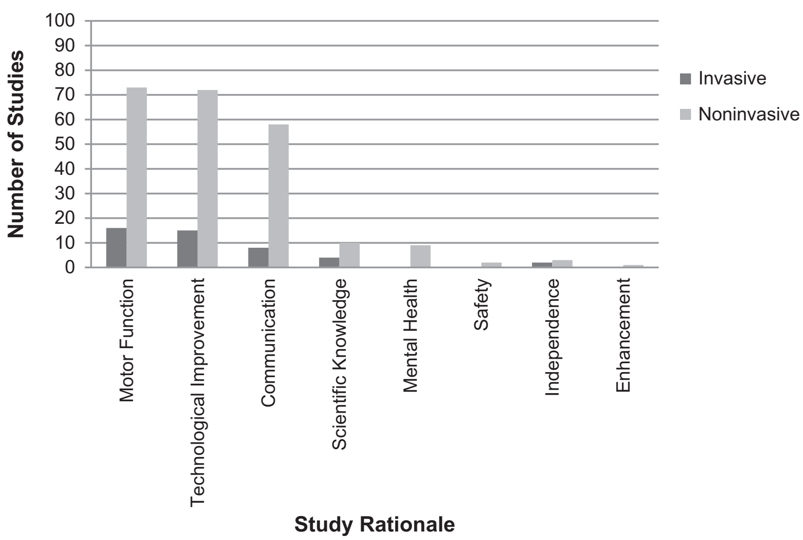

Figure 4. Degree of invasiveness of study by rationale.

brain-computer interface (BCI) devices as possible alternative communication and control solutions for individuals with severe disabilities.'

(3) 'In an effort to provide an alternative communication and control solution for individuals with severe disabilities, an increasing number of research groups are attempting to develop a direct brain-computer interface (BCI).'

(4) 'The main goal of BCI is to improve autonomy of people with severe motor disabilities by new communication and control options.'

These 'communication and control' rationales had similar characteristics beyond word repetition: they (1) identified general target populations or none at all, (2) did not specify clinical applications beyond communication and control, and (3) had minimal detail. These characteristics also emerged as themes across the 158 study data-set.

(1) Target populations

In this data-set, disorders such as ALS and locked-in syndrome and stroke survivors were frequently specified. However, target populations were omitted just as often as they were specified, and the remaining rationales (20% of results) only indicated general populations such as 'severe motor disabilities'. Variants of this general language for target populations include 'severe physical disabilities', 'severely disabled people', 'severe loss of motor function', 'very severe disabilities', 'complete paralysis', 'people with the most severe physical impairments', 'handicapped people', and 'people with paralysis'.

When studies involving patients and invasive methods were isolated, trends slightly differed from the data-set as a whole. The majority of rationales for BCI studies involving patients (n = 43/158) identified specific groups as target populations, such as epilepsy patients, people with tetraplegia, and subacute stroke patients. Some targeted more general groups, such as people with paralysis. Rationales for invasive BCI studies (n = 23/158) focused more on BCI technology than on particular patient populations. Eight studies mentioned specific patient populations, while seven studies omitted target populations and eight studies indicated general populations (e.g. 'people with paralysis').

(2) Clinical applications

The most common rationales in the data-set were motor function and technological improvement. The majority of rationales for BCI studies involving patients (n = 43/158) focused on clinical applications of technology (for motor function or communication), such as decoding motor intentions to control prosthetic devices and using BCI-based neurofeedback to facilitate stroke rehabilitation. By contrast, only four of the rationales for invasive studies (n = 23/158) were coded as 'motor function', while 50% were coded as 'technological improvement' and focused on the benefits of intracortical recording modalities such as ECoG. For example:

> 'An alternate BCI methodology has been studied in epilepsy patients undergoing invasive monitoring for seizure localization. Electrocorticography (ECoG), which is recorded from electrodes placed on the surface of the brain, has been shown to be a powerful and practical alternative to these other modalities. ECoG has higher spatial resolution than EEG, broader bandwidth, higher amplitude, and far less vulnerability to artifacts such as EMG.'

(3) Rationale detail

Rationales also varied by detail. Maximally detailed rationales described the need for research in the context of the daily lives of persons in the target population of the study:

> 'Most individuals with tetraplegia depend on caregivers for mobility and physical interaction with their environment. The use of computers as a resource for communication and productivity is hindered by slow, unreliable or cumbersome input methods such as mouth sticks to type on a computer keyboard, EMG switches to make sequential selections in alphabet-scanning software or head/eye tracking systems to point to on-screen items in specialized assistive software. Individuals with anarthria resulting from, for example, brainstem stroke or amyotrophic lateral sclerosis (ALS) often rely on eye movements alone for communication, conveying one letter at a time to an attendant holding an alphabet board. In addition, individuals with tetraplegia may incur disability-related lifetime health care and living costs on the order of $1.8–3.2 million in the United States (National Spinal Cord Injury Statistical Center 2009). These burdens could be reduced by improving tools for communication and independence.'

By contrast, minimally detailed rationales relied on general or abstract statements of patient need:

> 'Recent advances in neurotechnology have established the potential for creating direct connections between the human brain and external devices to restore communication or environmental control to people with paralysis.'

The frequency of maximally and minimally detailed rationales did not correspond to either the use of patients or invasive study design.

Discussion

We sought to examine the rationale for BCI studies given documented positive trends in neural engineering and the concomitant rise in numbers of BCI studies involving human participants.[4–8,11] The methods we implemented were designed to yield the most comprehensive, if not a closed, set of relevant publications for analysis. We found more than 200 unique publications and studies. From them, we describe a bimodal distribution of human subject use with over 2822 control and patient participants in the 15-year period ending in 2016. The peaks in the distribution of human use corresponded to the initial clinical BrainGate trial approved in 2004 under an Investigational Device Exemption (IDE) from the FDA and the first major paper from the study published in 2006, and BrainGate2, approved under an additional IDE from the FDA in 2009. Overall, human subject use has increased over time.

Study rationales, the focus here, intersected tightly with types of journals and subject populations. Rationales in neural engineering journals focus on technological improvement of BCIs, while those in biomedical engineering and neurology journals highlighted the opportunities for BCIs to improve motor function. Unsurprisingly, patients tend to be involved in studies with the rationale of motor function, while volunteers without impairment are involved in studies focused on technological improvement.

When study rationales from neurology, neural engineering, and biomedical engineering journals were isolated for further analysis, we found significant repetition of communication and control language. The origin of this language can be attributed to several papers by Wolpaw et al., beginning in 1991 and more recently in 2002.[12,13] In the abstract of the 1991 paper, the authors write that: 'This study began development of a new communication and control modality for individuals with severe motor deficits.' Studies using this rationale reference one of the Wolpaw et al. articles without citing further studies of potential end users' needs in the areas of communication and control.[3] While repetition of this rationale is not problematic per se, in the context of the three other subthemes of target populations, clinical applications, and level of rationale detail, it does indicate a notable trend: rationale language used to justify BCI research often does not engage with literature on preferences of persons with disabilities, omits particular clinical applications, and lacks sufficient detail for a complete ethical justification.

As often as particular populations were specified in the rationale of many studies, they were omitted as frequently in others. We speculate that this finding may be attributed to the multi-use potential of BCIs, wherein a technical paper with control subjects will not necessarily need to identify a potential use. When rationales for BCI studies with patients were isolated, they did have a greater percentage with specified target populations and clinical applications. By contrast, few rationales for invasive research specified target populations. Instead, these rationales focused on the technological improvement aspects of BCI studies, foregrounding technical problems with BCI devices that the research aimed to solve. This phenomenon correlates with a recent study showing that BCI researchers focus on quantitative measures of the technological success of BCIs to the exclusion of qualitative measures of user experience with BCIs.[14]

Rationales for studies involving patients and invasive studies ranged from maximally to minimally detailed. Maximally detailed rationales specified a target population and explained the need for BCI technology in terms of individual experiences; minimally detailed rationales described a general target population, if one was specified at all, and did not explain why this population might need BCI technology. Yet the ethics of research with human subjects requires that such research be justified based on benefit, and the lack of specified target populations and potential clinical applications makes it difficult to assess the justification of studies with minimally detailed rationales.[9]

Complete ethical justification of studies with human subjects requires rationales that identify particular target populations and clinical applications in sufficient detail. While BCI devices are currently being studied for a range of similar uses (e.g. motor rehabilitation, control of motor prostheses), the reasons these devices are important varies between different target populations.[15] Individuals with paralysis due to stroke are often in need of rehabilitation, while leisure devices may be a priority for individuals with locked-in syndrome.[16,17] Persons with spinal cord injury may desire the ability to independently operate their own assistive devices and may prioritize bladder control over ambulation.[18–20] A recent study found that ALS patients have different attitudes towards BCIs than other patient populations.[21] Without specifying *whom* the BCI is aimed for and *why* this type of BCI is needed, the justification of BCI research is incomplete.

We recognize that even though the search strategy for this work was implemented in two databases, the constraints on databases imposed by categorization and indexing limit the retrieval of 100% of all BCI studies with human subjects aimed at clinical use. Nonetheless, given the rigor of the strategy itself, we obtained a representative sample for analysis. In addition, we recognize that there are inevitable biases in thematic analysis and it is possible that other coders might have clustered study rationales differently. Here too, the rigor of the analytic approach yields a valid categorization of study rationales for consideration by the field and open dialogue.

To conclude, we suggest that the existence or further development of BCI technology is no longer an end in itself. Sufficient justifications for BCI research with human subjects must take into account the elevated ethics requirements for articulating aims and rationale that comes with a more advanced field.[22] As with the requirement of ethical reproducibility in biomedical research that mandates transparent and proportional ethics reporting,[10] this call for ethically complete rationales promotes transparent reporting of research ethics methods in proportion to the complexity and risk of BCI research.

Therefore, we propose that the rationale and articulated published rationale statements for future BCI research using human subjects should include the following four components:

(1) A statement explaining the choice of subject.
(2) A statement of risk-benefit.
(3) Citations supporting claims about target population desires, needs, and/or values.
(4) Recognition of the multiple possible uses of the BCI device being tested, including related opportunities and caveats.

We further emphasize the importance of delivering maximum detail about the engagement of humans with technology (i.e. how and why does this engagement take place?), and the rejection of technological advance as its own justification without further rationale. We recognize that researcher exposure to the ethical dimensions of research may vary across the spectrum of relevant disciplines spanning engineering and medicine.[23] Our goal is to advance these practical ethics recommendations for easy adoption and integration into neural engineering research, from the very conceptualization of BCI human use studies, through the publication of results in the academic literature and dissemination of their meaning in the public sphere.

Notes

1. In this paper we do not strictly define a brain-computer interface. There is continuing disagreement among researchers about which technologies are brain-computer

interfaces, and we are most interested in how the term is used, not how it is defined. For our purposes here, nevertheless, we do consider BCIs in the context of the spectrum of technologies that measure CNS activity and respond with artificial outputs.

2. While studies of brain-computer interfaces with human subjects were conducted prior to 2000, these studies were not included in the analysis if they were not retrieved by the search strategy. This approach ensured that the composition of the data-set was free of bias about what constitutes a brain-computer interface.
3. The 1991 article was not returned by our search strategy because it was not categorized either as a clinical trial by PubMed or as a brain computer/machine interface study by Web of Science.

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