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Discussion Starters

What is the most important innovation in neurosurgical practice that will emerge within the next 10 years?

DISCUSSION STARTERS

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ABSTRACT

Brain computer interfaces BCIs are automated neurostimulators that analyse brain signals and translate them into output. They aim to allow modulation of neurological functioning at cellular and network levels without the need for clinician-performed adjustments. BCIs are beginning to progress from the research and development phase to their introduction into clinical neurosurgery. Some anticipated applications include advanced treatment of cerebral palsy and stroke, aiming to restore function to these patients. In time, they will become one of the most significant innovations in neurosurgery.

Provided here is a review of BCI research to date and their implementation into clinical neuroscience, aiming to highlight the importance of BCIs as a developing treatment modality in neurosurgery in the next decade.
A review of the literature was performed using Pubmed as the primary database. BCI applications, recent technological advancements and current challenges facing these devices were reviewed. Trends in research and development were considered and are discussed. It was found that significant developments have been made in manufacturing BCIs that can interpret cortical processes with adequate spatial and temporal resolution. It was shown that the number of procedures to implant neuromodulators taking place in the UK each year is increasing, with more funding provided for BCI research each year. Further to this, a review of publication data found that neuromodulation devices placed among the top new patent categories in neurosurgery in recent years, a large portion of which were BCIs. These results highlight the continually growing interest in BCI research and their application in neurosurgery.

In conclusion, BCIs will become an increasingly important area of innovation in neurosurgery. Advances in translational neuroscience, imaging technologies and signal analysis will provide clearer insights into disease processes, allowing increasingly complex devices to address current limitations in the treatment of these conditions.

INTRODUCTION

The implementation of brain computer interfaces (BCI) into clinical neurosurgical practice is one of the most important innovations that will further emerge within the next 10 years. Implantable devices interfacing with the nervous system are not new; deep brain stimulation has been approved by the FDA for the management of manage movement and specific psychiatric disorders such as obsessive compulsive disorder (OCD) since 1997 and 2009 respectively. BCIs provide an opportunity to develop highly sophisticated and tailored neuromodulation unlike technologies employed previously. (1) In turn, BCIs will become an important treatment modality in neurosurgery.

MECHANISMS AND CLASSIFICATION

A brain computer interface (BCI) is a computer based device that acquires signals from the brain, analyses them and translates them into commands that are transmitted to an output device to carry out particular functions. They typically consist of 4 components: a device for signal acquisition, signal extraction, signal translation and an output device. (2) Closed-loop BCIs will incorporate advanced sensor technologies capable of chronic neuronal unit recordings, real-time computation capabilities that allow signal classification and interpretation, and more complex effector technologies that can capably reverse or alleviate the neurological conditions they are designed to treat. (3)

BCIs are classified as passive, active or reactive. Passive BCIs decode brain activity in unintentional cognitive states, while active BCIs decode voluntary activity. Reactive BCI interpret brain signals elicited in response to external stimuli in the users environment. (4) Signal acquisition systems are classified as either invasive, non-invasive or partially invasive. The most common modalities currently exploit electroencephalography (EEG) readings and are non-invasive. Invasive electrodes can be placed intracortically relying on electrocorticography (ECoG) to achieve improved signal to noise ratios with more accurate brain activity localisation. (4) Most BCIs translate signals to effector commands, however the incorporation of newer technologies such as transcranial magnetic stimulation has allowed experimental BCIs to stimulate specific brain areas. (4) Over the past 20 years there has been a significant increase in the successful application of BCIs to exert upper extremity control. Current BCIs for this purpose are limited by their need to be connected to an external power source, which will need to be improved if they are to be suitable for introduction to clinical settings. (5) There have been attempts to create algorithms that are able to interpret EEG recordings taken from non-invasive electrodes on the scalp, but such measurements suffer from unwanted signal interference due to their low signal-to-noise ratio. (5)

Neuromodulators have been utilised for the treatment of conditions such as Parkinson's disease and epilepsy for a significant amount of time. (3) Modern deep brain stimulation (DBS) is the closest neurosurgery has come to a true chronically implanted BCI. (3) DBS employs high or low frequency stimulation to elicit neuronal inhibition or excitation, respectively.(6) However, critically, DBS neurostimulators are not a closed-loop circuit and cannot regulate the frequency of their activity autonomously, and thus they are not a true BCI in their current form. (3) DBS is applied continuously, leading to excess power use requiring more frequent battery replacement. (7) BCIs are wholly automated neurostimulators, with the adjustments in output made by the implanted computational component of the device. Smarter closed loop BCI systems will tailor these pulses to what is happening moment-by-moment in the patient's brain. (8)

APPLICATIONS OF BCIs in NEUROSURGERY

Current prospective applications of BCIs focus on the restoration of impaired neurological function, as they progress from research and development to early clinical adaptation. It is intended that they will treat conditions including spinal cord injury, cerebral palsy and stroke. More recently, BCIs have been applied for the prediction of seizures in epilepsy patients. (9) They will eventually be developed for use as neurorestorative treatments for patients with severe neuromuscular disorders. (2) Advances in neural activity decoding technology and targeted external signals have been shown to induce neuroplasticity at this level, allowing reorganisation of synapses, and as such there are potential therapeutic prospects for neurodegenerative diseases. (4,10) Currently BCIs are not in widespread clinical use, but their efficacy has been demonstrated in research. (2)

Many neurosurgical procedures focus on treating a gross structural pathology, such as vascular malformations, aneurysms, and tumours. Many of the conditions BCIs are being developed to treat are more complicated in that they do not have gross structural lesions that can be treated with surgery alone, but rather will require treatment using modulation at cellular, genetic and network levels within the central nervous system.(3)

An example of a condition that has been successfully treated with neuromodulation is essential tremor, which is the most prevalent neurological movement disorder. (5) It a progressive condition which causes involuntary rhythmic movement, particularly of the upper limbs. DBS of the thalamus is a therapeutic option in some cases. ECoG-based closed loop systems have been trialled as a way to modulate essential tremor in DBS patients.(7) BCIs, as they become more suitable for chronic implantation, will become capable of performing these functions in place of current neurostimulators without the need for clinician-performed adjustments.
Spinal cord stimulation (SCS) is another example of neuromodulatory treatment that has come to relative prominence. (11)

Initial neuromodulatory devices for this application were utilised because of their design simplicity, ease of implantation and their potential for significant effects in the management of neurological disease or injury.(11) These interfaces were primitive, with simple electronic circuits designed to deliver pulsed impulses to the spinal cord for pain relief. These have been replaced with more advanced, programmable devices closer to BCIs, as multielectrode spatial arrays are replacing single unit recordings which monitor action potentials from neuronal cell bodies. (11)
The potential applications of BCIs are also being considered in

fields such as psychiatry. There is a growing body of evidence that DBS neuromodulation has a place in treating psychiatric. (12,13) For example, DBS has shown efficacy in the treatment of depression. (14,15) Advanced closed-loop BCIs, which adjust stimulation parameters based on direct measurement of neural activity or biomarkers, are being researched in the hope they can be used to treat psychiatric disease. (16) However care must be taken to ensure negative psychiatric effects do not appear after the implantation of these devices, as a result of non-stimulatory effects that are not yet accounted for. (17,18)

METHODS FOR IMPLANTATION OF BCIs

BCIs will likely be implanted through similar procedures used in the implantation of DBS neurostimulators. Consequently, it is vital that input from neurosurgeons is considered in the design and development of BCIs, particularly with respect to practicality, potential complications and feasibility as treatment for disease. (3) DBS has become the primary stereotactic technique employed for the surgical treatment of Parkinson's disease, dystonia and essential tremor as described. (19) Surgical techniques for DBS neurostimulator implantation involve the use of a stereotactic frame to guide electrodes as they are implanted with high precision. More recently, robotic surgery has been used to implant DBS devices in deep seated targets in the brain with sub-millimetre accuracy. It is likely BCIs will be implemented using these same procedures and availing of advances in robotics and stereotaxis.

AN AREA OF INNOVATION IN NEUROSURGERY

Neuromodulation is of great interest as an area of neurosurgical innovation. A rapid increase in the number of neuromodulation device patents began in 1987 with initial DBS technology used to treat Parkinson's disease through subthalamic nucleus stimulation. Most well-regarded patents are currently filed in relation to DBS. (20) Neuromodulation devices were among the top performing patent categories in a review of neurosurgical innovation across 90 countries.(21) 60% of the patents within this field included devices for DBS and BCIs. (21) Figure 1 shows search data illustrating trends across publications on the topics of neuromodulation and specifically BCIs, including clinical trials.

There is clearly an interest in pursuing both advanced BCIs and improved neuromodulation as a whole. The number of procedures for implanting neuromodulators in the UK each year is increasing. (22) Funding has become more readily available for research in neuromodulation due to advances in neuroimaging, implant technology and improved safety and reduced side effects versus older methods, leading to improved public approval. (22)
Development of new neurosurgical treatments will be of great importance in terms of healthcare system improvement, as the financial and services burden from these conditions is significant.

NOTABLE ADVANCES IN BCI TECHNOLOGY

In 2006, Hochberg. et al. (23) made a significant advance in the field of BCIs when their device allowed a tetraplegic man achieved control of a robotic arm for rudimentary functions through the implantation of a microelectrode array in his primary motor cortex. (2,23) Hochberg. et al. (11,23) demonstrated control of robotic prostheses using a BCI implanted in the precentral gyrus of a tetraplegic patient. These effects were maintained for up to 1000 days post-implantation. This was also demonstrated in 2008 in monkeys. (11,24)

Subsequently, in 2012, a collaborative group in the United States reported in Nature that the BrainGate neural interface had successfully allowed two patients to control a robotic arm in 3-dimensional space. (25)

BCIs have undergone rapid improvements in recent years. Notably, ECoG-based BCIs have demonstrated effective interpretation of cortical processes, ascribable to precise spatial and temporal resolution. (26) These implanted BCIs are capable of measuring high frequency activity, which is unfiltered by the skull and surrounding tissues, and is unaffected by movement-derived signal artefacts that equate to noise in the readings. (26) An alternative to ECoG-based BCIs are stereotactic EEG (sEEG) electrodes are placed under stereotactic guidance through small burr holes, and are capable of measuring activity in the deep structures of the brain. They are less precise than ECoG but require lower-risk surgery. (26) However, sEEG relies on external amplification units and extensive wiring. For practical application of this technology as a basis for BCIs, more convenient systems must be developed. (26) It is likely that newer technologies will arise that allow neurosurgeons to take full advantage of sEEG recording's ability to target multiple subcortical foci. Further research involving combinations of sEEG, ECoG and appropriate microarrays may lead to devices that are both subcortical and cortical, with function specific designs. (26)
In the near future, successful BCIs will incorporate neuroplasticity exploitation, and advances in translational neuroscience, hi-fidelity sensor technology and signal processing. It is likely machine learning will become of great importance for the organisational interpretation of the data gathered by these devices. (4)

ADVANCES IN BRAIN IMAGING

An issue still being addressed is that of optimal brain mapping. Electrodes implanted for neurostimulation need to accurately target specific neuronal circuits. With this comes the challenge of accurately positioning the electrode within the brain. (27) Non-invasive brain mapping and brain imaging technologies such as fMRI, PET and rsfMRI have provided great insights into the structural organisation of the brain and the circuits mediating disease states in neurological and psychiatric conditions. For example, they allowed identification of the subgenual anterior cingulate cortex as a target for DBS in the treatment of major depressive disorder. (3)

Due to the nature of BCIs, the signal used requires a combination of both sensitive and specific information, high resolution spatial and temporal information, adequate spatial sampling fidelity with a high signal to noise ratio. (3) This is a difficult balance to achieve with current technology. For example, fMRI lacks the temporality required for such an application, and EEG readings suffer from low signal to noise ratios. (5) Currently, unit recordings provide the highest spatial and temporal resolution. (3)

ETHICAL ISSUES IN NEUROMODULATORY THERAPIES

Ethical concerns have been voiced regarding the potential for misuse of devices that interface with, essentially, the human mind. The field of neuroethics has emerged in the past two decades to monitor the development of brain-interfacing technologies and ensure the development and use of BCIs is guided by appropriate ethical principles. (28) Potential uses and misuses, regarding whether BCIs should be developed solely for the motives of treatment, cure or rehabilitation, or for enhanced cognition, will be at the core of debates between neuroethicists over the coming years. (1)

CONCLUSION

In conclusion, in the near future, improvement of BCIs through developments in our understanding of neurophysiological functioning, production of advanced devices and optimisation of the software and hardware will see BCIs become widely used in neurosurgical practice. BCIs aim to restore function to patients with devastating conditions such as stroke, spinal cord injury and neurodegenerative disorders. Rather than simply removing the pathologies underlying a disease, BCIs provide a way through which complex neurophysiology can be interacted with and altered with the goal of improving the long-term outcomes for these patients. Neuromodulation is a field with relatively high public awareness for which there is an intense curiosity due to its potential to treat severely morbid conditions. However, numerous issues must be addressed before BCIs can be more widely used in a neurosurgical clinical setting.

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APPENDIX 1: HISTORICAL PUBMED DATA REGARDING THE NUMBER OF PUBLICATIONS PER YEAR RELATING TO NEUROMODULATION AND BCIS

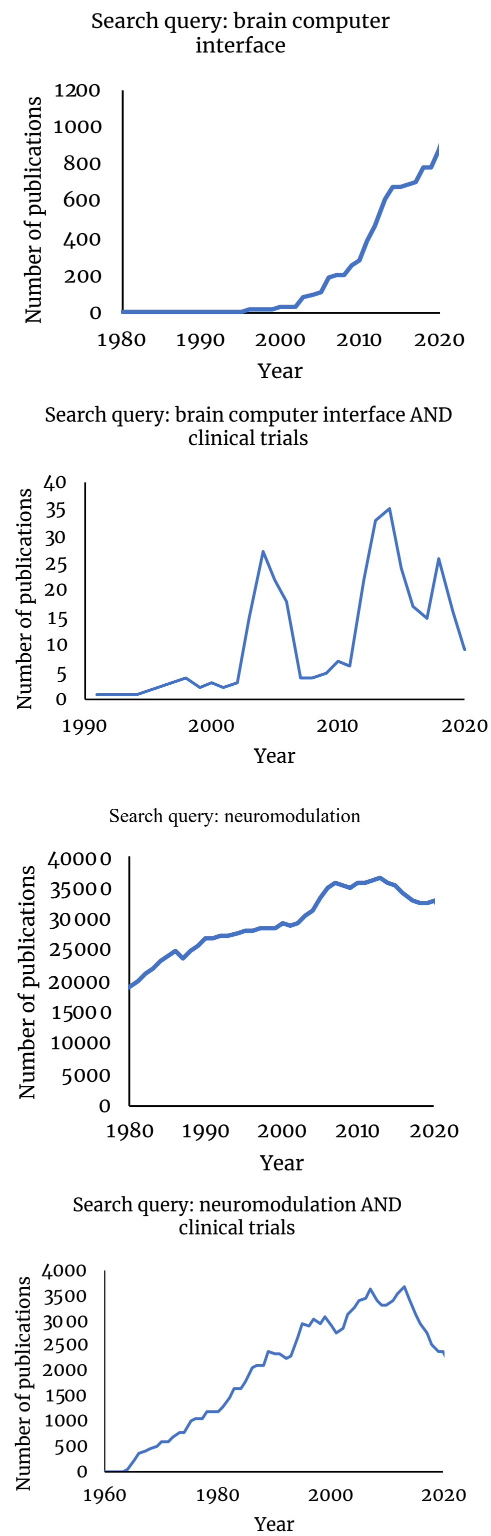

Figure 1: Graphs a–d illustrate historical PubMed data regarding the numbers of publications per year relating to neuromodulation and BCIs. It also illustrates the increasing numbers of clinical trials being conducted within both categories.

(a) Search results for "Brain Computer Interface"

(b) Search results for "Brain Computer Interface AND Clinical Trials"

(c) Search results for "Neuromodulation"

(d) Search results for "Neuromodulation AND Clinical Trials"

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