

Neural interface technologies: non-medical applications outside the body

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Lots of excitement, often whipped up by commercial interests, research often at the proof of concept stage, with results that are statistically significant, although often with very variable practical effects: these are all characteristics of the external neural interface field today. Serious developments depend on advancing the mechanistic understanding of neuroplasticity and decoding of brain signals. Long-term effects of stimulating the nervous system should be better understood. Ethical and legal issues also need to be addressed, particularly those related to 'brain hacking' and home-grown applications that have been made possible by the open source/'brain hacking' movement.

Introduction

In addition to neurotechnology-based solutions directed towards medical use, increasing numbers of non-medical applications are being explored and developed due to the perceived low risk of external technologies, their availability and ease of out-of-the-lab use. Technologies for external interfacing with the nervous system can be classified with respect to the direction of the flow of information, either recording activity or stimulating it. Both can interface either directly or indirectly with the nervous system, central or peripheral.

Stimulation

The traditional distinctions between invasive and non-invasive neuro-technologies have become obsolete given the development of relatively inexpensive and easily acquired stimulation technologies that can modify the activity of the central or peripheral nervous system without a need for invasive placement. Transcranial magnetic stimulation (TMS) uses a coil placed on the scalp to apply a magnetic pulse inducing electrical current in the brain region underneath it¹. The most frequent use of TMS is for research into cognitive and motor functions², where disruption of brain region activation was used in order to establish its mechanistic role. More recently, different TMS stimulation protocols have been also shown to enhance cortical activity resulting in enhancement in several cognitive tasks including perception and visual search, attention, memory, language and motor learning³. This suggests at least a theoretical possibility of potential applications of TMS for accelerated skills acquisition in healthy individuals, although in practice the high costs and technical skills required currently limit this technology to the research domain. A cheaper alternative using electrical currents is presented by transcranial electrical stimulation (TES). This family of stimulation mechanisms contains various techniques that vary depending on the nature of the current modulation. For example transcranial direct current stimulation (tDCS) uses small amplitude constant current. Other protocols include transcranial alternating current stimulation (tACS), transcranial pulsed current stimulation (tPCS) and transcranial random noise stimulation (tRNS). In contrast to TMS, TES exerts a non-localised effect on the brain tissue although it is much cheaper and easier to

deploy. There has been excitement about the potential of tDCS technology as a result of a growing number of research articles reporting statistically significant enhancement of attention, learning and memory in adults⁴, with some studies reporting measurable benefits for both cognitive and motor tasks⁵. However, recent efforts seem to be somewhat shifting away from tDCS towards tACS and tRNS, due to the variable effects of the former compounded with its unclear mechanism⁶ and potential suggested mechanistic mode of action of the latter methods⁷. Most applications of TES are in research, although the reported apparent successes in basic cognitive science and translational research, combined with relative ease of access and low costs, have resulted in a rapid increase of its private use in sport, the military and recreation⁸. These are a potential cause for concern in the light of poor understanding of the mechanisms via which TES exerts its effects. Moreover, although TES is generally considered to be well tolerated and mostly safe, the long-term effects have not been well characterised and in some cases, adverse effects, especially in tDCS, such as skin lesions, mania and hypomania have been reported⁹. Effects of chronic, unsupervised self-administration on cognition and behaviour are not known. The field is rapidly changing and uncontrolled, especially its 'do-it yourself' segment, raising a number of safety, regulatory, ethical and legal concerns¹⁰. Nonetheless, a wide range of cognitive enhancements has been reported, including visual perception, memory, reading, decision making, sports performance, dieting and treatment of addictive behaviours, in addition to various applications across a wide range of medical conditions. Therefore, the formation of well-funded guidelines¹¹ could pave the way for potentially exciting opportunities for future applications, for example in e-education¹² or behavioural change.

Emerging non-invasive stimulation technologies, still in very early research stages, have shown significantly improved ability to deliver focussed stimulation of deep brain regions. These include temporally interfering electric fields¹³ and transcranial focused ultrasound¹⁴. Also, transcutaneous vagal nerve stimulation has shown some ability to improve memory consolidation and enhance recognition¹⁵. These technologies offer further opportunities for enhancing stimulation-based applications that may surpass TES in their ability to manipulate brain activity. At the same time, they will pose similar problems and will benefit from regulating the field of non-invasive brain stimulation.

Recording

The most frequently used technologies for recording brain activity have been electroencephalography (EEG); magnetoencephalography (MEG); and functional magnetic resonance imaging (fMRI); recording, respectively, electrical activity of large populations of neurons; magnetic fields produced by such electric currents; and the relative amount of oxygenated blood flow into a volume of neural tissue. They are pivotal for the field of cognitive neuroscience, concerned with unravelling the neural correlates of cognitive functions, and they have been used extensively in research on brain function. Their use has stimulated development of new areas such as neuroergonomics¹⁶, which investigates the relationship of the brain's activity to human behaviour in everyday settings, relating, for example, to mental workload, stress, fatigue or drowsiness. EEG, MEG and fMRI have also benefited rapidly expanding closed-loop brain computer interfaces¹⁷ and neurofeedback¹⁸. The need for such out-

of-the-lab uses of neurotechnologies motivated research in neuroengineering to come up with more affordable, easy-to-use and portable solutions. Most notable attempts include dry EEG electrodes¹⁹, used as alternatives to conventional electrodes using gel or paste, with several commercially available headsets offering significantly cheaper and wireless solutions to those that are willing to accept the signal quality trade-offs²⁰. These are still based on a galvanic coupling and hence require contact with scalp of the user. Capacitive electrodes offer the possibility of non-contact recording of biopotentials²¹ (EEG but also ECG and EMG), which could, for example, be used in clothing or car upholstery for pervasive monitoring²². Functional Near-Infrared Spectroscopy (fNIRS) has received increasing attention for its potential portability in imaging modalities monitoring hemodynamic responses related to brain activity²³. Also, the recent development of wearable MEG offers the possibility of using this sensing modality in applications not requiring the participant to remain motionless²⁴. Other sensing modalities that indirectly capture signals related to the operation of the peripheral nervous system have been used in various neurotechnology applications. These include Galvanic Skin Response sensors (GSR), used for example to identify distractions for drivers²⁵, mental workload or stress²⁶ and electromyography (EMG) sensors for gaming and gesture-based communication and human computer interaction²⁷. An interesting alternative to the EMG sensors is provided by acoustic myography sensors which measure muscle contraction using sounds generated by muscle activity²⁸. Many such sensors are used in combinations, for example with electrocardiography (ECG) to assess heart rate variability or with eye tracking or pupillometry to provide more robust estimates of a subject's cognitive or affective state²⁹. There is an increased research focus on developing and applying wearable sensors.³⁰ These include wearable chemical sensors that base their operation on accessing bodily fluids such as saliva, sweat or tears. The electrochemical sensors may be placed either directly on the skin or in fabric. Tattoo biosensors have been developed for sensing lactate, glucose and alcohol. Sweat electrolyte and sensors offer the ability to monitor concentrations of various ions, such as sodium, potassium, calcium or ammonium and may be used to assess the chemical and physical state of the body. Monitoring of glucose content in tears via sensors integrated onto contact lenses offers an attractive alternative for non-invasive monitoring of diabetes. However, such wearable non-invasive chemical sensors face multiple challenges. In addition to those shared with other flexible wearables, the secreted bodily fluids that are their point of measurement often contain diluted and highly variable concentrations of analytes. Here, focusing on the development of hormone sensing may be advantageous as many of these have similar concentrations in secreted biofluids to those found in blood. Apart from opening new dimensions for continuous health monitoring, non-invasive chemical sensors could offer exciting opportunities for monitoring states such as fatigue or exertion and could provide very detailed information to optimise athletic performance in competitive sports. Nevertheless, the multiple challenges have stemmed the commercialisation of such products so far, with few exceptions³¹.

Further opportunities will arise from ubiquitous availability of stretchable sensors that could be placed on the skin or weaved into fabric to create intelligent garments³², fuelled by the parallel push towards the 'Internet of Everything'. Their low costs, ease

of deployment and small size and power consumption stimulate various applications related to lifestyle or sports performance monitoring. However, their signal quality is often variable and they face significant challenges in improving detection of the underlying physiological or mental states. This is due to several factors, including: the nature of the signal transduction at the skin-sensor surface; the complexity of the relationship between signals captured, physiological processes and activity of the brain; and the challenges related to the intended out-of-lab use.

Closed-Loop Neurotechnology Applications

Various so-called closed-loop solutions integrate technologies for recording and modifying or stimulating nervous system activity in a continuous interaction. Most popular of these are brain computer interfaces³³ which record some brain activity and provide the input to the user, usually via modifying information presented through natural sensory channels. EEG has been adopted as the most popular method of choice in BCIs. Proofs of principle have been also demonstrated for brain computer Interfaces based on sensing brain activity with fMRI^{34,35} and MEG³⁶. The latter two are of theoretical interest, as these modalities overcome some of the limitations of EEG in their ability to decode mental states from brain activity, in practice. Currently they lack portability, although development of wearable MEG sensors³⁷ may open potentially interesting avenues for MEG based BCI solutions. fNIRS, which similarly to fMRI records metabolic processes related to neural activity, has been used more extensively, partly due to its greater potential for portability³⁸. There is a current trend in exploring various types of hybrid systems, or brain/neuronal computer interaction (BNCIs) technologies, where hybridisation may involve different forms. These include different BCI paradigms, such as event related potentials (P300); steady state visually evoked potentials (SSVEP); and event related desynchronization (ERD)³⁹. They can use different modalities of brain activity recording, such as EEG and fNIRS⁴⁰, or EEG and wearables⁴¹. The reason for the increased success of such solutions may be pragmatic, linked to the inherent limitations of decoding brain activity, or fundamental, arising from embodied cognition, and more research is needed in order to guide their development. Other hybrids involve combining various recording modalities with more direct stimulation of the nervous system than via natural sensory modalities (such as the senses), for example using fNIRS in combination with tDCS⁴², or in combination with virtual reality, neuromodulation and brain imaging⁴³. Although such applications are still primarily driven by clinical needs, interest in applications for cognitive enhancement will inevitably result in applications beyond healthcare, such as 'edutainment'. There is an ongoing research into creation of novel BCI paradigms that would address some of the challenges facing this technology, for example improving information transmission rates⁴⁴.

A recent 'roadmap' for BNCI technologies, supported by the European Commission,⁴⁵ identified a range of potential non-medical applications under the broad headings of –'enhance', 'supplement' and 'research', with an increased focus on research and industrial innovation. Applications range from assistive technologies and education, to entertainment, sporting performance, security, marketing and research.

In contrast to original 'active' BCI systems which were designed in order to allow the user to control the external world via computer, 'passive' BCI paradigms invert the direction of control⁴⁶. The register brain activity and the closed loop of interactions are designed respectively to estimate the cognitive or affective state of the user and to either modulate it or the environment, according to a predetermined goal. Such systems can be used for adjusting applications to the user, for example: by adjusting cognitive loads ; estimating the user's intentions⁴⁷; monitoring and alleviating stress and fatigue; or by modulating affect or mood, for example by adjusting musical output⁴⁸; to advance human computer interaction applications;⁴⁹ or improve well-being. An emerging area within BCI is that of affective systems, which estimate users' moods or affective states. Many such applications have been developed for adaptive gaming^{50 51}. For example, in one demonstration it was shown that game players have better experiences and make greater improvements if the game difficulty is adapted to their mental state instead of their performance level⁵².

Other application areas explored include navigation and driving aids⁵³, where biosignals such as blink and heart rate as well as EEG-derived indices were used in order to monitor lapses in attention or vigilance. Analogous future opportunities could see development of BCI-based eEducation tools adaptable to pupils' capabilities and the fluctuation of their cognitive engagement⁵⁴. Another emerging area of BCI application is in collective performance, for example in assisting group decision making⁵⁵. There has been also a lot of interest in artistic applications of BCI technologies, for example generating music or painting⁵⁶, with applications exploring active, passive and collective BCI variants. One example of artistic performance involved use of auditory neurofeedback in a physical installation. Users' brainwaves that were indicative of levels of either relaxation (alpha waves) or alertness (beta oscillations) were used to generate sounds on steel squares hanging from the ceiling. The sounds were either in the form of a slow rhythm if the users were relaxed or clattering steel if they were alert.

Consumer and marketing research has also seen increased interest in using neurotechnologies to advance understanding of consumer behaviour⁵⁷.

Neurofeedback (NF) constitutes a family of closely related technologies to BCI. NF operates using fundamentally analogous components and closed loop principles to those of BCI but, in contrast to BCI, it aims to explicitly modify specific brain activity, by visualising it for the user and relying on the user's ability to consciously modify it. Explorations of nonclinical applications of neurofeedback include performance enhancement⁵⁸, for example enhancing artistic creativity⁵⁹, improving sporting performance⁶⁰ or increasing cognitive activity among elderly people.

Challenges and opportunities

The applications reviewed in the previous section offer very exciting opportunities. However, similarly to clinical applications, research in neurotechnologies must overcome number of challenges for this potential to be realised. Perhaps the most significant of these is that, despite an ever-growing amount of knowledge in cognitive neuroscience, our ability to decode the brain activity in non-controlled, real-life situations is still not sufficiently robust. This is in part related to our lack of

understanding of a relationship between cortical dynamics, the main source of central nervous system signals for external neurotechnologies, and the cognitive activity they support, confounded by significant variability between subjects and the inherent inability to isolate specific cognitive processes of interest in realistic out-of-the-lab situations. Many applications of neurotechnologies depend on, or promote, neuroplasticity and advancing the mechanistic understanding of its action and the effective means of its manipulation will be crucial for advancing such technologies. Practical challenges facing neurotechnologies include dealing with various artifacts (or interferences) related to recording modality and advancement of equipment that must strike compromises between ease of use, subject comfort, portability and quality of signals^{61 62}. Over recent years there has been a rapid increase in efforts to commercialise non-invasive neurotechnologies and several products are available on the market. An increasing number of cheap commercial TES systems can now be easily purchased⁶³ and given the continuing interest in cognitive enhancement outside academia it is expected that these will continue to proliferate. In terms of sensing devices, a number of companies are selling EEG systems and the availability of inexpensive commercial headsets using dry electrodes has contributed to the marked increase in BCI studies⁶⁴. There is also a smaller number of commercially available wireless wearable fNIRS systems, although their number will continue to grow as the technology improves towards greater portability and miniaturisation⁶⁵. By far the most dynamic commercialisation is taking place for wearable sensors⁶⁶.

The European Commission has funded two projects, the Future BNCI Project (2010-2011) and BNCI Horizon 2020 (2013-2014) which published their respective roadmaps for neurotechnologies, capturing snapshots of the state of the art and identifying promising directions and opportunities^{67 68}. These documents show trends in the development of neurotechnologies and expectations for their advancement. Some forms of hybrid BCIs have already been identified as promising and since these reports, research intensified in this direction. Particularly promising novel extensions are combinations with external stimulating devices, particularly those novel technologies that offer more focal – or localised - stimulation. These also pose regulatory challenges as their wide availability creates opportunities for home use leading to potential risks of self-medication, or self-experimentation resulting in detrimental immediate or long-term side-effects which are currently not well documented. Further ethical, regulatory and privacy issues may emerge if research into EEG fingerprinting shows that these signals can be used for biometric purposes.

In sensing technologies, portable MEG may transpire to be a disruptive development, as well as dry non-contact biopotential electrodes. However, time and further research is needed to evaluate their implications. In spite of a number of commercially available dry electrode EEG headsets, there is still a need to develop a truly wearable wireless robust EEG system supporting reliable long-term performance for out-of-the-lab use.

Improving the long-term system performance will also depend on a sustained effort into decoding brain signals and collaboration between cognitive neuroscientists and engineers, incorporating the theories and models of brain function into proposed signal processing solutions. Changing the mindset from that of a signal processing problem to that of modelling the brain activity that underlies cognitive processes, may offer

significant advances. These include improving the effectiveness of neurotechnological applications as well as the additional benefit of providing novel experimental paradigms to test theories and hypotheses about brain function.

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