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Brain implants for substituting lost motor function: state of the art and potential impact on lives of motor-impaired seniors

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Abstract

Recent scientific achievements bring the concept of neural prosthetics for reinstating lost motor function closer to medical application. Current research involves severely paralyzed people under 65, but implications for seniors with stroke or trauma-induced impairments are clearly on the horizon. Demographic changes will lead to a shortage of personnel to care for an increasing population of senior citizens, threatening maintenance of an acceptable level of care and urging ways for people to live longer at their home independent from personal assistance. This is particularly challenging when people suffer from disabilities such as partial paralysis after stroke or trauma, where daily personal assistance is required. For some of these people, neural prosthetics can reinstate some lost motor function and/or lost communication, thereby increasing independence and possibly quality of life. In this viewpoint article we present the state of the art in decoding brain activity in the service of Brain-Computer Interfacing (BCI). Although some non-invasive applications produce good results, we focus on brain implants which benefit from better quality brain signals. Fully implantable neural prostheses for home use are not available yet, but clinical trials are being prepared. More sophisticated systems are expected to follow in the years to come, with capabilities of interest for less severe paralysis. Eventually the combination of smart robotics and brain implants is expected to enable people to interact well enough with their environment to live an independent life in spite of motor disabilities.

Introduction

As looming demographic changes are high on the political agendas for many countries, there is an increasing sense of urgency to find new ways of dealing with medical needs in the future (2012 Ageing Report). Funding is aimed at developing strategies to deal with an increasing demand for medical care, some of which are technology oriented with the expectation that care will benefit from sophisticated devices for monitoring and assisting care recipients (Flandorfer 2012, Pearce ea 2012). Such devices can also address the brain. Brain disorders will increasingly impact on our lives, be it due to stroke or cancer, or neurological and psychiatric disabling afflictions such as depression or alcoholism to name a few (Wittchen ea 2011, Yasamy ea 2013). Risks for brain disorders increase with age, and as such will be a dominant topic on the care agenda of the future (Yasamy ea 2013). In this article we focus on a new development that we believe may become relevant to the topic of

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ageing and meeting medical needs for brain disorders. More specifically, we discuss how implant technology can replace some lost brain functions, allowing people to live at home longer. The technology is still in its infancy and is currently developed for severely paralyzed people. In this viewpoint article we explain the basic principles of this Brain-Computer Interface (BCI) concept and present the state of the art. Based on this development we project potential impact on the lives of elderly in the future. Although many other aspects of technological developments will be of importance for seniors, notably for monitoring health, robotic assistance in the home and human interactions, we here focus on the potential and promises of BCI brain implants, arguably one of the biggest challenges in neural engineering.

We first briefly explain how we envision that the BCI implants can be used to improve the lives of seniors. We then present the BCI concept and what we anticipate it will be able to deliver. This is followed by presentation of demographic data to support our expectation that the need for implantable solutions for lost motor functions will drive funding and development in the near future. We close by discussing future prospects. Since BCI brain implants are in direct contact with neurons and serve to compensate for loss of motor function, we refer to them as 'neuroprostheses' in the remainder of the article, recognizing that other uses of the term are possible.

In a broad context, brain implants can perform one or both of two things: read and interpret brain signals, and modulate neural activity. Neuromodulation has grown as a field resulting in various therapeutic solutions for neurological and psychiatric disorders (eg Deep-brain Stimulation devices) (Miocinovic ea 2013). Reading brain signals has been an important topic in neuroscience for decades, but only recently have methods become available for real-time decoding and interpretation (Wolpaw ea 2002). The level of sophistication of decoding increases with more invasive recording techniques because direct measurement capitalizes on the highly refined topographical organization of the human cerebral cortex (Jacobs & Kahana, 2010). The first prototype neuroprostheses are currently under development for restoration of communication in severely paralyzed people, but the increased momentum of neuroprosthetic research holds promise for applications in less severely disabled people. With increasing age, the risk of losing motor function increases due to stroke, a brain tumour or brain trauma. The more disabling cases require daily assistance, for instance to (un)dress and to perform daily household activities, and contribute significantly to the rapidly rising costs of motor disability-related care (Ovbiagele ea 2013). Any solution that promotes independent living and thereby reduces the demand for personalized care would benefit not only the economic burden but also perhaps the quality of life.

Neuroprostheses could serve seniors with lost motor function in several ways. First, loss of the ability to communicate due to severe paralysis can be compensated with an implant that allows the user to control a computer by attempting to move a hand or limb (Hochberg ea 2006). The attempt results in a change in neuronal activity in the motor cortex, which can be converted into a control signal to move a cursor or generate a mouse click in dedicated assistive technology software (Leuthardt ea 2004). Neuroprostheses may also provide the ability to control a wheelchair or a remote interactive robot (Millan ea 2010, Andersson ea 2013). Second, people with dysarthria and perhaps also those with expressive aphasia, due to damage in the motor system or in Broca's area respectively, may benefit from neuroprostheses that decode intended speech or sign language from the sensorimotor cortex (Guenther ea 2009, Bleichner ea 2013). Such decoding of attempted speaking could drive a speech computer. Third, people with hemiplegia could benefit from a combination of BCI (for decoding specific attempted movements) and electrical muscle stimulation devices, which would for instance restore the ability to walk or grasp objects (Peckham & Kilgore 2013). None of these devices are commercially available yet, but they are likely to enter the market within a few years (eg Rouse ea 2011). One significant obstacle is the cost of developing neuroprostheses and obtaining FDA approval and CE certification. However, as is discussed below, against the background of impending demographic changes and rising economic burden of health care, the potential for neural prostheses to reduce the demand for care in some of the more care-intensive groups is likely to justify the level of investment. This, in turn, is likely to further stimulate development of more sophisticated BCI systems that can improve the lives of less severely disabled people including many seniors. Crucial to this scenario, however, is the success of the first neuroprostheses in people who need them, outside the laboratory. Here, severely paralyzed people play an important role in that they stand to benefit the most from the research and, in the absence of alternatives, are the most motivated to improve the technology from the user-end.

Demographic changes driving interest in technological solutions

As we witness an increasing number of people from the baby boom generation retire, demographic statistics are starting to paint a gloomy picture. The number of people generating revenue, in the age range of 15-64, is not keeping up with societal needs. The current EU fertility rate of 1.6 children per female (projected to rise to 1.7 in 2060) is too low to maintain a stable size of the working population, which requires a rate of 2.1. In Europe, each working person's income currently supports 0.25 seniors (age over 65) and this will almost double to 0.45 by the year 2030 (2012 Ageing Report). Moreover, since the costs of healthcare increase significantly with age over 65, and since the average life expectancy is still on the rise (from 84 years today with one year every decade to 89 years in 2060), the financial burden on society imposed by seniors will increase dramatically. This increase will need to be financed by a working population that is barely growing, and looks to decline after 2040 (2012 Ageing Report).

Inevitably, the demand for health care and long-term care will increase significantly. Until an age of 45 the demand for both forms of care remains roughly stable, but with every 20 years over that age the costs increase roughly by a factor of 2, while costs of longterm care do so by a factor of 3 after 65. This is due to increasing risk of disability with increasing age. Already medical professionals are pressed for time in performing their profession, with decreasing amounts of time that can be spent on interacting with clients. In order to maintain an acceptable level of medical service, ways need to be adopted to increase efficiency, and to reduce the effort of acquiring and processing information about the physical and mental state of the patient. Moreover, it will be highly beneficial if medical conditions can be dealt with without involvement of medical professionals. If tasks could be performed without their immediate involvement, the services at hand would be more readily available to patients. In a broader perspective, seniors are likely to become dependent on some sort of assistance in

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their daily activities. It is to be expected that development of smart home technologies will increase and encompass more specific purposes such as assisting daily activities in people who need special care. The imminent rise in healthcare costs in coming decades will increase the need for alternative, technical, solutions, the price of which will decline with increasing demand, even if initial costs are high.

Particular challenges in enabling people to remain living independently, are posed by mental disorders and neurological trauma. For instance, many elderly people will suffer from stroke, the leading cause of serious longterm disability in the western world (Roger ea 2012). The risk of suffering from a first stroke doubles every 10 years of age starting at 55. Some 15 % of people over 80 years old will be dealing with consequences of stroke (Roger ea 2012). Many stroke patients will suffer from persistent physical deficits such as paralysis and dysphasia, and perhaps mental problems. They will need special solutions to be able to conduct their daily activities and maintain or regain their independence. Challenges mostly appeal to assistive technology developers, but in some cases, a new approach will be required. For the most severely paralyzed people, rendered incapable of commanding their muscles due to brainstem stroke or motor neuron disease, there are currently no solutions to enable them to communicate at their own will. People with Locked-in syndrome, who are generally mentally intact, can communicate only with great difficulty via a mechanical switch or an eye-tracking device, or only when a caregiver is present to engage in letter board spelling (Laureys ea 2005). It is for these patients that the need for new solutions is recognized best, and acted upon. Development of new technologies to bypass the spinal cord has been pursued for several decades, and recent promising results have fuelled further research on Brain-Computer Interfacing, notably with implantable technologies. In what follows, the state of the art of BCI is presented, with a focus on implants.

Brain-Computer Interfaces

Brain-Computer Interfaces (BCIs) are devices that record and amplify brain activity, detect and classify mental events that can be consciously and voluntarily generated by the user. These mental events are converted to a control signal for computer programs or assistive technologies to interact with the environment (Wolpaw ea 2002, Van Gerven ea 2009. The technologies currently developed for severely paralyzed people are initially only relevant to a few seniors. However, as technologies are implemented and further developed, it is to be expected that increasingly sophisticated decoding of brain activity can be achieved. With that, neuroprostheses are likely to offer less severely motor-impaired people, of which many will be elderly, ways to improve independent living and quality of life by reinstating (to one degree or another) mobility and communication.

Reading, decoding and interpreting brain activity

Neurons make use of electrical currents to communicate with each other. Currents are generated to convey signal (an action potential) along the axons from the nucleus to the nerve terminals, and the sum of electrical potentials at the dendrites determines whether action potentials are initiated (Buzsaki 2006). Both sources of electrical potential fluctuations can be detected with electrodes and signal amplifiers. The human brain exhibits a tightly organized distribution of brain functions across the cortex (Penfield & Rasmussen 1957, Cabeza ea 2000). Particularly the regions of the brain that are linked to our senses and our muscles, the 'primary cortices', are located in specific parts of the brain. Primary cortices are characterized by detailed topographical neuronal representations, and are therefore good candidates for decoding mental events from the brain. Much has been learned about the functional topography of the human brain with imaging techniques such as electroencephalography (EEG, for instance Buzsaki 2006) and functional Magnetic Resonance Imaging (Ramsey et al 2002). It is now known that specific mental actions lead to changes in neuronal activity at the mm scale. For instance, simply directing one's visual attention to one of four peripheral directions without moving the eyes invokes different spatial patterns of activity than attending to the other directions, within a few cm of cortical surface (Andersson ea 2013).

Most of the work done on decoding brain activity is based on scalp-EEG. The electrical fluctuations picked up with EEG provide information about mental events. EEG signals can also be converted to signal frequencies and amplitudes, such as the well-known alpha wave (7-13 Hz), a larger amplitude of which typically reflects a state of relaxation. For BCI, several signals have shown to be useful. The most effective ones are the P300, the steady state visual evoked potential (SSVEP) and the sensorimotor rhythm (SMR) (Wolpaw ea 2002). The signal with the highest success rate is the P300, a strong electrical fluctuation that can be measured by multiple electrodes at the top of the head about 300 ms after an infrequently occurring sensory stimulus. The P300 is invoked by having a subject look at a stationary stimulus (for instance a character in an alphabet matrix on a computer screen) and infrequently replacing the stimulus with a brief bright flash or another stimulus. In a typical BCI application based on P300, the screen is filled with rows and columns of icons (characters and keyboard buttons), and by sequentially flashing each icon, one can determine which icon the user is attending to (since only that flash will generate a P300 response). The P300 speller is regarded as the best candidate for commercial exploitation of scalp EEG systems and thus is closest to becoming available at the home for users (Mak ea 2011). More directly relevant for the present article is the SMR, a set of rhythms in the 10-30 Hz range that are generated by the sensorimotor cortex. The amplitudes of these oscillations are high at rest, and decline when the subject moves a limb (Van Gerven ea 2009). The hand and the foot affect different parts of the sensorimotor cortex (several cm apart) and can thus be distinguished in EEG. Even if movements are not generated but attempted (in paralyzed users), the change in amplitude can be detected well enough to obtain some degree of control over a computer. For a more elaborate description see Wolpaw ea 2002.

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In spite of a significant body of research, EEG-based BCI has not quite made much of an impact in the world of assistive technologies (for instance see Future BNCI report), for several reasons. First, the systems are rather cumbersome to initiate on a daily basis since they require skilled electrode placement on the scalp and function a few hours at a time because the conductive liquid or gel dries out, and users report discomforting skin irritation with daily use. Second, the signals are weak due to the attenuation of the electrical signal by the skull, and easily disturbed by electrical fields generated by other (home) devices, causing loss of performance. Third, performance varies greatly across individuals, with a few achieving 100% with P300, but others giving up at little above chance levels (Mak ea 2011).

Fourth, many users find EEG-based BCI mentally quite demanding and may need considerable training to reduce the effort. Attempts are made to improve user friendliness with dry electrodes and sophisticated software but significant improvements are not to be anticipated (Future BNCI report). In coming years some of the hurdles towards commercialization of scalp-EEG BCI may be resolved, but the detail of decoding will remain quite limited due to the effects of the skull on signal quality. However, the techniques developed for non-invasive BCI have had a significant impact on development of implantable systems. Neural prostheses obtain signals from electrodes in direct contact with neurons, which yields very rich signals and a potential for decoding a wide variety of mental events (eg attempted gestures).

Neural Prostheses

Recordings from underneath the skull exhibit much better properties in that the signals are much stronger and are less affected by external electrical noise sources (Jacobs and Kahana, 2010). Moreover, implanted electrodes can fully exploit the topographical organization of the cerebral cortex, allowing for decoding of, for example, multiple arm movement trajectories (Hochberg ea 2012).

Neural prostheses are not new. For several decades systems have been implanted in humans for restoring loss of sensory function and for treatment of neurological and psychiatric disorders. For people with hearing loss, the Cochlear Implant has been shown to be effective (Gaylor ea 2013) and is now widely available. Some 300,000 have been implanted since the early eighties, many of which in young children (as young as 6 months). Deep Brain Simulators (DBS) consist of electrodes implanted deep in the brain, and an electrical stimulator placed under the skin of the chest. DBS is used to alleviate symptoms in Parkinson's Disease, dystonia, essential tremor and more recently also in epilepsy, major depression and obsessive compulsive disorder. Some 80,000 have been implanted since 1997, mostly for Parkinson's Disease for which the treatment is generally effective (Miocinovic ea 2013). The latest system is the retinal implant, which restores vision in people suffering from macular degeneration, implanted in some 30 patients since 2007 (Humayun ea 2012). The technologies for implanting electronic devices in the brain, and the required surgical procedures, have now been refined for several decades, and the complication rates are overall quite low (mainly risks of infection which can generally be treated effectively, and occasionally cerebral hemorrhage), with surgery-caused permanent deficits ranging from 1-5% (eg 1.5 % for grid implants in Van Gompel ea 2008, and for Parkinsons DBS in people aged 21-85 in Boviatsis ea 2010)

Several research projects are currently ongoing to investigate feasibility of implantable systems for BCI. Much of the preliminary research has been conducted in non-human primates (Fetz 1969). In early 2000 several groups succeeded in having primates control a robotic arm without moving their own arm. From multiple needle electrodes inserted into the primary motor cortex, the direction of intended arm movements could be decoded well enough to control a robot arm for self-feeding (Velliste 2008). The first human BCI project that included severely paralyzed patients (Braingate) started in 2004. Four paralyzed people were implanted with a 4 by 4 mm array containing 96 needles (1.5 mm long) in the motor

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cortex. Several managed to control a cursor in computer software. Currently two clinical trials are running with a similar neuroprosthetic system, and both have reported successful direct control over a robot arm during carefully controlled laboratory tests (Hochberg ea 2012, Collinger ea 2013). Another approach was adopted with a so-called neurotrophic electrode unit. Here, signals were obtained from motor cortex neurons that grew into a glass cone containing the electrodes, and were used to decode imagined speech. Several vowels could be distinguished in the participant who was unable to communicate other than by eye blinks (Guenther ea 2009). These results are currently quite limited to a handful of participants (with a bias towards the most successful patients and sessions), and await further confirmation with larger numbers.

Most of the human implant studies have involved needle electrodes but there is a growing interest in electrodes that remain on the surface of the cortex (grids)(Leuthardt ea 2004). Since these electrodes do not penetrate the cortex, they are expected to cause less of a reaction of the brain tissue to the implant. Moreover, preliminary research on such electrodes can be conducted in humans, allowing for investigation of other cortices than the motor cortex, such as regions serving cognitive functions (Vansteensel ea 2010, Jacobs & Kahana 2010). This is possible because electrode grids are frequently implanted in epilepsy patients who do not respond to medication and fail to display a clear source of seizures on scalp EEG. These patients undergo two operations, the first for positioning between 50 and 100 electrodes (embedded in silicon sheets or grids) under the dura, and a second one, typically 1-2 weeks later, for removing the grids as well as the brain tissue from which seizures originate. The recordings obtained during the week between surgeries are used to identify the seizure source. Between clinical procedures, patients can participate in BCI research, where the signal from specific electrodes can be processed and decoded for BCI (Ritaccio ea 2013). Several studies have now appeared, presenting proof of concept with such electrodes where imagined movement and backward counting were successfully used by the epilepsy patient to play a simple computer game (Leuthardt ea 2004, Vansteensel ea 2010). A few paralyzed people have also been implanted with these grids in pilot studies, the latest of whom succeeded in controlling a robotic arm to some extent (Wang ea 2012). With the opportunity to target different brain regions comes the problem that functions are located in slightly different brain regions from one subject to another. Moreover, one faces the challenge of choosing the function that works optimally for a particular individual. These problems can be resolved with the use of high-field MRI scanners: several studies have now shown that the exact locations of brain functions determined with functional MRI, match the best locations for electrodes quite well (Vansteensel ea 2010, Hermes ea 2012). Moreover, at very high field (7 Tesla), realtime feedback is so reliable that subjects can control a robot with it (Andersson ea 2013), indicating that each patient can test before surgery which area/ function would work best for him or her.

What to expect in the future

All of the human BCI implant studies concern experimental systems. Most of the participants were, or are, able to speak. Goal of the needle array studies is to restore kinetic control (physical movement of a device) in people who are paralyzed from the neck down. The brain signals can, however, readily be used to operate a computer. The described studies

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essentially show that we are capable of decoding intended movements (Hochberg ea 2012, Collinger ea 2013), cognitive events (Vansteensel ea 2010), or internal speech (Guenther ea 2009) to some extent, quite well at this point. However, we are still far away from commercial exploitation of this capability. To date, there is as of yet no implantable device for signal amplification of larger numbers of (needle) electrodes that is approved for chronic human use. Current brain implants operate with external amplifiers and require skilled operation to get the system to work, and much more development is required before a system can operate autonomously and without failure at the home of the user, and without requiring significant training for the caregivers to manage it. Moreover although high levels of decoding can be achieved under controlled circumstances, it is not known how reliable the system is when used at home, notably in terms of false detection rate (errors can pose serious safety issues with robotic limbs). It is, however, quite likely that the research required to get these advanced BCI systems closer to commercial availability will be conducted in years to come, especially since the US Brain Initiative is promoting development of human brain implants (DARPA subnets call 2013 (,http://www.darpa.mil/NewsEvents/Releases/2013/10/25.aspx). To prove that neuroprostheses can function at the home, a simple system would suffice. In fact, a single on/off switch is sufficient to operate a computer and any connected device, and there are many assistive technology solutions available for single (mechanical) switch operation. At the University Medical Center in Utrecht, Netherlands, a pilot study is initiated in 2013 to implant a basic switch device in people with Locked-in syndrome (www.neuroprosthesis.eu). The aim is to provide the ability to generate mouse clicks with very high reliability. It is expected that participants can obtain a means of communication that is not available to them with any of the existing assistive technologies.

It is to be expected that once the concept of decoding brain activity for function restoration is validated in an at home application, research on (and commercial interest in) more versatile systems will follow. One can envision BCI systems that can translate intended movements into actions in computer programs, or into physical actions executed by robots, either attached to the body or separate, into movements of a environment-aware wheelchair (Millan ea 2010) or eventually movements of one’s own libs (Peckham ea 2013). The implantable BCI systems will be designed to control any robotic device, especially those that are developed for daily activities in the home. Rather than developing complete systems, the BCI’s will benefit from the rapid development in home robotics that can be expected to accelerate in the coming decades given the arguments we presented earlier. Thus, standards will need to be devised to allow any BCI system to interface with robotic devices and with more classical assistive technology devices. The primary brain region targeted currently is the primary motor cortex because of its detailed topographical organization and because signals for movements are generated here, even if signals do not result in movements due to paralysis. Other brain regions may prove to be good candidates also, notably those involved in planning movements and speech or those that are amenable to attentional control such as sensory cortices (Andersson ea 2013). BCI systems may also become an option for speech rehabilitation, for instance by translating internal speech to computer-generated speech.

In summary, we expect a rapid increase in development of neuroprostheses for people with motor disabilities that will link to home assistive technologies and robotics to facilitate independent living at home. After initially targeting severely paralyzed people, developing applications for disabled seniors will become attractive for industry, which in turn can play a crucial role in technological progress. Many current developments in material- and neuroscience are likely to find their way into neuroprostheses, including new ways to measure and stimulate neurons, such as optical and chemical technologies. All are likely to reduce the invasiveness of devices and improve capabilities. It may seem science fiction now, but the need for timely solutions to the ageing problem may well see a rapid emergence of a new field of restorative neurotechnology. An overarching issue is the attitude of people towards the use of robotics, which is rather conservative when they are considered in care for children and seniors (Special eurobarometer 382). When BCI systems become fully operational and claims of their added value to daily life can be substantiated, people may come to regard robots in care more acceptable, at least for people with motor disabilities. Perhaps the larger challenge is to prepare for the impact of impending socioeconomic changes on care for seniors, and to engage future seniors in a discussion on what it takes for robots to serve our needs in this context (Flandorfer 2012).

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