Are We the Robots? Man-Machine Integration

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ABSTRACT

We experience and interact with the world through our body. The founding father of computer science, Alan Turing, correctly realized that one of the most important features of the human being is the interaction between mind and body. Since the original demonstration that electrical activity of the cortical neurons can be employed to directly control a robotic device, the research on the so-called brain–machine interfaces (BMIs) has impressively grown. For example, current BMIs dedicated to both experimental and clinical studies can translate raw neuronal signals into computational commands to reproduce reaching or grasping in artificial actuators. These developments hold promise for the restoration of limb mobility in paralyzed individuals. However, as we review here, before this goal can be achieved, several hurdles have to be overcome, including developments in real-time computational algorithms and in designing fully implantable and biocompatible devices. Future investigations will have to address the best solutions for restoring sensation to the prosthetic limb, which still remains a major challenge to full integration of the limb into the user's self-image.

INTRODUCTION

At the beginning of the third millennium the development of a revolutionary approach to rehabilitation radically improved the integration between apparently separated fields of research and heavily reshaped the traditional intervention protocols. Building on the last century's most promising technological innovations, this inspired trend confirmed the importance of neuroprosthetics as an interdisciplinary specialty aiming at merging advances in neuropsychology, cognitive neuroscience, and biomedical engineering for creating adaptive devices to overcome the impairments resulting from traumatic or degenerative loss of sensorimotor functionality.

Following long-established procedures, manual interventions have been widely employed in conventional rehabilitation protocols. However this approach is extremely task-specific and time-consuming for both patients and therapists, requires elaborate schemes, and depends drastically both on therapists' experience and patients' compliance (del-Ama et al., 2012). In addition, these procedures do not always address some of the most important features of a proper sensorimotor rehabilitation, including systematic control of feedback and difficulty (Popovic et al., 2003) and monitoring patients’ achievements (Dietz, 2009). Thanks to the most recent technological advances in mechanics, control, and attachment, neuroprosthetics has rapidly grown (Zlotolow and Kozin, 2012). Thus by increasing repeatability, automation, and quantification, robotic-assisted rehabilitation represents one possibility to solve these issues (Prange et al., 2006).

Despite the broad implementation of robotic devices in clinical practices (Marchal-Crespo and Reinkensmeyer, 2009), robotic assistance does not always cope with the difficulties of severe clinical conditions characterized by complete loss of body segments or neural connections, e.g. amputation or spinal cord injury, respectively. As some visionary artists imagined in forward-looking master pieces such as the song “The Robots” realized by the band Kraftwerk in 1978, pioneering studies showed that the signal originating from the neural activity in the brain can be recorded, encoded, and used to control external devices (Fetz and Finocchi.Dv, 1971; Fetz, 1969). This innovative methodology triggered a huge amount of scientific investigations and clinical applications, establishing in fact an innovative field in neuroprosthetics and a new era in rehabilitation. Thus the so-called Brain-Machine Interfaces (BMIs) have been applied to a wide collection of clinical conditions (Lebedev and Nicolelis, 2006) and radically transformed the expectations of both patients and medical doctors, quantitatively increasing the range of possibilities for coping with the patients’ needs and qualitatively improving the rehabilitation protocols. However before BMI techniques can be fully implemented into clinical environments, some important issues have to be clarified and further investigations are necessary.

The main aim of this chapter is to provide detailed information on the state-of-the-art progresses and future directions of neuroprosthetics and BMIs, highlighting the advantages and disadvantages of each technique. In the first section of this chapter we will introduce how BMI systems can provide users with communication and control capabilities independently of muscular activity, explaining that translating the electrical brain activity into commands is a way to restore lost motor functions by allowing the communication between the brain and an external device. In the second section we will summarize the advances in invasive and non-invasive neuroprosthetics, both for rehabilitation and motor substitution, according to the type of disability towards which the intervention is addressed. Here we will review the progresses in innovative prosthetic technology and we will further discuss the future key challenges aimed at improving the life of disabled people. The third section of the chapter will be dedicated to illustrate the development of the BMIs which made it possible to control prosthetic limbs, giving birth to the research and application of neuroprosthetics, including external as well as implanted components. We will take into account recent evidence showing new methodology for accurately predicting and reconstructing natural kinematics from non-invasively recorded brain activity during movements. In addition, we will focus on the therapeutic implementation of functional electrical stimulation, combined with neuroprostheses, as a possibility for restoring lost motor functions by stimulating muscles with either intramuscular or surface electrodes. In the fourth section of the chapter we will mention the significant emerging challenges to implementation of advanced neuroprostheses. Furthermore, we will elucidate the work on the elaboration of biologically-derived and computationally-implemented neural modeling of kinematic learning on the basis of virtual reality technology, focusing on the development of bio-mimetic controllers to control robotic neuroprosthetics. The fifth section of the chapter will be dedicated to provide insights on the work directed towards the restoration of sensations from the prosthetic limb in order to improve what remains still a major challenge in neuroprosthetics: the full integration of the prosthesis into the body representation at the brain level.

1. IMPLEMENTATION OF RECENT TECHNOLOGY INTO THERAPEUTIC REHABILITATION PROTOCOLS

Traumatic injuries of the central nervous system, as well as neurodegenerative disorders, continue to inflict harmful motor deficits in large populations. In 2005 more than 1.5 million people in North America suffered amputations (Ziegler-Graham et al., 2008), with a severely reduced quality of life though preserved cognitive functions (Millan et al., 2010). In the USA alone, spinal cord injury (SCI) is responsible for the occurrence of more than 10000 new cases of permanent paralysis per year (Nobunaga et al., 1999). The annual incidence of stroke in industrialized countries is approximately 2‰ of the inhabitants (Kolominsky-Rabas et al., 2001). In case of stroke survivors, the impairments have a highly disabling impact on the individuals' quality of life. Even after completing standard rehabilitation, approximately 50%-60% of stroke patients still experience some degree of motor impairments (Belda-Lois et al., 2011).

For treating motor outcomes of neurodegenerative diseases several strategies have been proposed, but still result in chronic deficits. One possibility is the pharmaceutical treatment, but for example dopamine administration is affective only in the early, not late, stages of Parkinson's disease. Another possibility is the attempt to restore neural activity, but for example deep brain stimulation can be performed only on 10% of patients and the high risk of mortality is very high (Fuentes et al., 2009). Several alternative approaches have been progressively developed in the recent years, including the use of neuroprosthetic devices, e.g. for stimulating the spinal cord.

The most promising approach is based on the so-called "Brain-Computer Interfaces" (BCIs) and has only recently enlarged its range of application, making it possible to control motor functions such as reaching, grasping, or locomotion. A BCI system can be defined as "a system that measures and analyzes brain signals and converts them in real-time into outputs that do not depend on the normal output pathways of peripheral nerves and muscles" (Wolpaw et al., 2000). Recently, there has been an enormous development in the research field of substitution of lost motor functions. BCIs have rapidly been incorporated into the improvement of neuroprosthetic devices that use neurophysiological signals from undamaged components of the central or peripheral nervous system to allow patients to regain motor capabilities. Indeed, several findings already point to a bright future for neuroprosthetics in many domains of rehabilitation medicine. Translating the electrical brain activity into commands is a way to restore lost motor functions by allowing the communication between the brain and an external device. Clinical practice illustrates that patients who receive robot assisted training in combination with physiotherapy (after stroke) are more likely to achieve better motor functionality with respect to patients trained only with regular physiotherapy or devices (Waldner et al., 2009).

2. BENEFITS AND LIMITATIONS: INVASIVE VERSUS NON-INVASIVE APPLIED NEUROPROSTHETICS

In order to restore motor functions by using an artificial device to overcome the loss of neural activity, the first important step is to integrate the external device with the nervous system. In this vein, since the first experimental demonstrations that the invasively-recorded activity of ensembles of cortical neurons can directly control a robotic manipulator (Chapin et al., 1999; Fetz, 1969), BMI has moved at a stunning pace. Invasive BMIs are based on recordings from populations or few single brain neurons using intracranially implanted electrodes, thus providing an excellent quality of brain signals but with some risks generally associated with invasive procedures, including infection or rejection (Lebedev and Nicolelis, 2006). Implantable brain electrodes and electrocorticography (ECoG) procedures were invented during the 1950s in order to identify the origin of epileptic seizures. Using similar techniques, pioneering animal studies showed that the brain signals can be detected, recorded, and used to control external devices (Nicolelis and Lebedev, 2009). Starting from these revolutionary setups, there has been a huge increase of attempts to integrate such techniques with rehabilitation purposes, but successful results are still very few. In one case a stroke patient suffering from locked-in syndrome was implanted with a device which let him be able to control a cursor on a computer screen (Kennedy and Bakay, 1998). Following the first demonstration of the possibility to control an artificial hand using a device directly implanted on the cerebral cortex (Hochberg et al., 2006), other examples were brought to the scientific community only in the last months. Thus, an innovative prosthetics program achieved the first ECoG-controlled prosthetic arm fitted on a patient with tetraplegia who was implanted with a CyberKinetics 96-electrode Brain Gate chip (CyberKinetics Neurotechnology Systems, Inc., Foxboro, MA), and was able to control not only a robotic arm but also the home lights and television (Zlotolow and Kozin, 2012). Similarly, the residual activity of the neurons in a small portion of the motor cortex has been used to let tetraplegic individuals control a robotic arm and hand in order to perform daily activities such as reaching objects and interact with them (Hochberg et al., 2012).

Non-invasive BCI also offers several practical solutions for control and communication between the nervous system and the prosthetic devices, even if there are some costs due to technical issues, required training, and quality of the neural signals. Electroencephalography (EEG) is the most common non-invasive method for recording brain activity (Bortole et al., 2014). One possibility of overcoming such problems is to use adaptive algorithms that constantly update the parameters of the classifiers during training (Wolpaw and McFarland, 2004). Non-invasive EEG techniques can detect the modulations of brain activity correlating with a wide range of conditions, such as sensory processing, movement execution, and cognitive states. These properties have led to development of several classes of EEG-based BMI systems, differentiated in terms of recorded cortical areas, extracted signals' features, and sensory feedback (Lebedev and Nicolelis, 2006). Non-invasive systems use surface EEG to control computers or other devices by encoding the neural response of different origin. This approach is useful for helping paralyzed people (e.g. Locked-in syndrome) to extend communication with the external world. One of the first BMI systems took advantage of the neural activity in response to the presentation of visual stimuli (Sutter, 1992). This system could detect the differences between the cortical activity in the visual cortex related to different symbols (e.g. letters), and therefore identify the letter that the user is looking at and build sequences of symbols (e.g. words). In this way an individual suffering from amyotrophic lateral sclerosis became able to communicate by creating strings of about 12 words in one minute (Sutter, 1992). Another EEG-based BCI system exploits the human ability to voluntarily regulate the so-called slow cortical potentials, i.e. spontaneous brain waves between 0.5 and 10Hz (Brown, 1993; Siniatchkin and Gerber, 2011). Through specific training programs people can learn to control these brain waves and thereby the output associated with them (Birbaumer et al., 1999). Despite its limitations in terms of number of suitable couplings between patterns of brain activity and robotic output, this system has been successfully tested in patients suffering from locked-in syndrome. In particular, the patient showed clear developments in their ability to control a cursor on a computer screen in order to select different symbols. This improved capability significantly increased basic communication skills (Kubler et al., 1999). This system clearly increases the communication capabilities and the interactions with the external world, e.g. providing Internet access to disabled people (Birbaumer et al., 2000).

Non-invasive BCI is an effective tool not only for improving communication and control, but importantly it can be used for re-establishing neural activity. For example it has been very recently shown that EEG activity is a reliable signal to trigger motor rehabilitation after stroke (Pichiorri et al., 2013). In particular, stroke patients were equipped with the EEG cap and could see the projection of a virtual hand shown at the location of their own affected hand. In these conditions patients were asked to imagine to grasp and release objects using the affected hand and the EEG signal resulting from this imagery task triggered the movement of the virtual hand. After the training patients showed restored brain activity, with inter-hemispheric patterns more similar to healthy controls with respect to prior the experiment. Importantly a group of patients which performed the imagery task but did not undergo the BCI setup did not show improvements in inter-hemispheric connections. EEG-based BCIs have been implemented as solutions for patients suffering from both partial (Kubler et al., 2005) and complete paralysis (Piccione et al., 2006; Sellers and Donchin, 2006). These BCIs enable patients to control computer cursors in order to communicate with the external world or to indicate intentions. Electromyography (EMG) works in a similar way and represents an alternative to the existing non-invasive BCIs. In EMG-based systems the voluntary activations of unaffected muscles in partially paralyzed people and amputees is used to control limb prostheses and exoskeletons (Light et al., 2002; Zecca et al., 2002). Currently, these systems are more feasible for daily life situations with respect to EEG-based BCIs, because patients who suffered either amputations (Hargrove et al., 2013) or SCI (Williams and Kirsch, 2004) might have residual muscular activity to allow them to efficiently interact with the external world.

The ultimate trend in rehabilitation and control procedures is the combination of EEG-based and EMG-based BCI. Pioneering this line of research Leeb et al. (2010) fused the recording of EMG and EEG activity in the framework of the hybrid BCI approach. In this way, people could achieve a good control of their hybrid BCI independently of their level of muscular fatigue. Very recently Cheron et al. (2012) used EEG and upper limb EMG, or a hybrid of these two neurophysiological signals, to control assistive exoskeletons used in locomotion based on programmable central pattern generators or dynamic recurrent neural networks. These methods may exploit mechanisms of brain plasticity and assist in the neurorehabilitation of gait in a variety of clinical conditions, including stroke, spinal trauma, multiple sclerosis, and cerebral palsy.

Please insert Figure 1 about here

Figure 1. Schematic representation of the principles (lower panel) and the characteristics of brain-computer interfaces (upper panel). The brain signals are acquired and used by invasive or non-invasive BCIs in order to extract their features and translate them into commands for external devices. The main applications of BCIs are communication skills and interaction with objects.

2.1 Rehabilitation

Initial work on robot-assisted neurorehabilitation for the upper limbs aimed primarily at training the reaching movements with the proximal sections of the extremity. Recent work brought a surge in devices dedicated to arm-hand function, focused on the proximal sections of the missing limb and specifically designed to assist and train movements of the shoulder, elbow, wrist, and fingers. Thanks to these technological advances, a large variety of specific devices is now available for dealing with all phases of neurological rehabilitation, based on the concept that task-oriented repetitive movements can improve motor recovery in patients with neurological or orthopedic injuries. The importance of robotic assistance in rehabilitation is associated with its peculiar utility in helping, enhancing, evaluating, and documenting all the different stages of the neurological rehabilitation procedure.

There are some mandatory requirements for a rehabilitation robot. First, the robot should be adapted to the human limbs in terms of length, range of motion, and number of degrees of freedom (DOFs). Second, in order to rehabilitate several movements, the device should have a high number of DOFs allowing a broad range of movements with many anatomical joint axes of rotation involved. Following these directives many robotic devices have been introduced in clinical environments. Among these, various robots have been dedicated to the rehabilitation of the upper extremities, mostly focused on stroke patients. For example the ARMin II is a robot developed for arm therapy, applicable to the training of activities of daily living. It has a semi-exoskeletal structure with seven active DOF, five adjustable segments to fit different body sizes, and position and force sensors (Staubli et al., 2009). ArmeoPower (Hocoma, Zurich, Switzerland) is a rehabilitative exercise device that allows early rehabilitation of motor abilities and provides arm support in a 3D environment. It is designed for individuals who have experienced strokes, traumatic brain injuries, or other neurological disorders resulting in hand and arm impairment. Similarly to the devices used to address basic research questions in healthy volunteers (Pulliam et al., 2012), recent work showed the importance of integrating virtual environments and robotic prosthetics to train hand and arm movements in post-stroke patients (Adamovich et al., 2009). Adapting a commercially available haptic device incorporated into a virtual environment and implemented in rehabilitation procedures, these authors developed a system which simulated a piano with visual, auditory, and tactile feedback comparable to an actual piano. Arm tracking with the hand Master robot allows patients to train both the arm and hand as a coordinated unit, emphasizing the integration of both transport and manipulation phases.

Robotic hand devices can be used independently by patients in both acute and post-acute settings and, focusing on compensation, they can be valuable adjunctions to conventional approaches. The main feature of such devices is that they are wearable and therefore can be integrated directly into task-specific training. The feasibility of the introduction of robotic devices in several rehabilitation settings is demonstrated by the fact that early efforts with proximal arm robots demonstrated their safety, tolerance by patients, and capability for improving motor control (Burgar et al., 2011; Krebs et al., 1999)

2.2 Substitution

Nowadays, lower extremity prosthetics have developed to the point that a bilateral below-the-knee amputee is able to participate in the Olympics Games and challenge the best runners in the world. Scientific research on the upper extremity has not yet reached the same level and there are still a lot of shortcomings and difficulties with regards to the fact that patients will only use their prosthesis if they consciously perceive a clear advantage (Zlotolow and Kozin, 2012).

Innovations in upper extremity prosthetics over the last years have succeeded in improving several critical parameters, including control, functionality, speed, attachment, size, weight, and power (Belter et al., 2013). Most of these advances have been achieved during the Iraq and Afghanistan conflicts, when efforts were focused on improving prostheses for the many soldiers who had to deal with missing or severely compromised limbs (Resnik et al., 2013). Belter and Dollar (2011) made a review comparing several different anthropomorphic prosthetic hands, taking into account not only the technical aspects of each device (identifying metrics such as weight, grip force, and grasp speed), but also the end-user opinion during the clinical use, including the nature and level of the amputation, as well as the motor activity and professional needs. The most advanced prosthetic upper limbs have motors for each finger, interphalangeal and metacarpal articulations (e.g. Contineo Multi-Grasp hand and Michelangelo hand) where the fingers are individually powered and with a great variety of possible pinch and grasp patterns. Other devices are able to gradually increase the strength of grip on an object and offer a fully rotating forearm and wrist flexion/extension (e.g. i-Limb Ultra hand), whereas old terminal devices require manual wrist positioning.

Amputations above the elbow and shoulder are difficult challenges for prosthetic design, because they require the device to implement more functional segments. For an entire-limb replacement the Modular Prosthetic Limb® (MPL) allows 22 DOF with individual finger, thumb, wrist, forearm, and elbow control. The MPL system for control and sensory feedback is designed to accommodate both non-invasive (surface EEG) and invasive (ECoG) interfaces. Thanks to its flexibility in terms of adopted interface and based on its exploitation of the brain signals, the MPL system may be useful not only for amputees but also for SCI patients. In a special report on the role of sensory feedback in upper limb prostheses, (Antfolk et al., 2013) extensively summarized the studies involving upper limb prosthetics, taking into account input and output (vibrotactile, direct nervous stimulation, mechano-tactile, extended physiologic proprioception, electrotactile). The main finding of this report is that the availability of advanced robotic hand devices or multi-fingered prostheses is continuously increasing, their quality in terms of functionality and reliability is progressively enhancing, and the number of experimental studies and clinical applications of prosthetics devices is intended to exponentially grow in the next years. Beyond improvements in function, patients also report improved social integration, self-image, and perception by others. As the field of prosthetics advances, not only functionally but also aesthetically, the users' acceptance threshold will be lowered. Indeed, successful prosthetic care depends not only on technological developments but also on good communication and cooperation among patients, surgeons, and physiotherapists, as well as on the collaboration with the scientists harnessing the power of technology to solve real-life challenges.

3. IMPLEMENTING NEUROPROSTHESES AND FUNCTIONAL ELECTRICAL STIMULATION

The research on new techniques to better integrate brain signals and impaired muscular activity is calling increasing attention to functional electrical stimulation (FES). By means of implanted or surface electrodes, FES is used to trigger muscular contractions using electrical impulses, often coupled together with BCI as a motor neuroprostheses (invasive or not) to facilitate movement (Marquez-Chin et al., 2009). Where viable - not for muscular degeneration- FES artificially compensates the loss of voluntary muscle control and it is also used as an effective therapeutic tool for prevention of muscle atrophy, maintenance of joint mobility, and generation of proprioceptive feedback. FES motor training with surface electrodes is used for supporting the desired movements in order to improve hand functions. For example in the case of SCI survivors the activity from muscles above the level of the lesion can used to control the electrical stimulation of paralyzed limbs (Ferguson et al., 1999).

Following stroke or SCI one of the main issues is to maintain muscular activity of the affected body segments in order to avoid a wide range of secondary impairments due to disuse, including arthritis, osteoporosis, or contractures. Holding promise for achieving these aims, one of the first important advances have been brought by the development of the BION system (Loeb et al., 2001). This system ensembles fully implantable and externally controlled electrodes and is capable to trigger muscular activity. Thanks to these devices it was possible to induce movements of previously paralyzed body segments; however, an external controller was required and external power is necessary to create the stimulation. Therefore, the next step was to avoid the necessity of this external amplifier and render the patient able to internally control muscle contractions. In order to achieve this goal it has been shown that the muscular activity of a preserved body part can function as controller to trigger contractions in an affected limb. In particular, a stroke patient has been successfully implanted with an electromyography-controlled FES device which used the signals recorded at the chest level to control muscular activity of the affected hand (Knutson et al., 2012). Similarly, taking advantage of the ultimate integration between FES-BCI and semi active orthoses, a patient suffering from complete sensory and motor loss due to SCI at the cervical level became able to perform grasp-and-release movements with the previously affected limb, including writing and precision grip, even one year after the training (Rohm et al., 2013). As already suggested by the work of Rohm et al. (2013) the next neuroprosthetic devices will incorporate fully portable active exoskeletons and FES systems, giving birth to new hydrid orthosis devices (Weber et al., 2011). In this direction a new device is in current development: the “OrthoJacket” (Schill et al., 2011). This device combines the advantages of stabilizing the joints together and the possibilities offered by stimulating muscular activity of paralyzed limbs. In addition, it does not require to implant electrodes directly in the muscular fibers, but rather uses surface electrodes to trigger muscular activity. This feature renders the OrthoJacket one of the best candidates to fulfill the requirements for at home motor re-training and for supporting daily activities. Finally, it overcomes the limitations due to the characteristics of the controlling components of previous devices which had to be fixed to the floor or the wheelchair, thereby stationary and suitable only for training in clinics. By increasing portability the OrthoJackect will allow patients to perform rehabilitation exercises at home and to accomplish daily activities independently.

Nowadays, several FES-based actuating systems have been proposed to aid motor task practice and training, including virtual reality feedback systems (Merians et al., 2006) and robotic assistive device (Alon et al., 2007). In order to investigate the integration between BMI and FES systems, Marquez-Chin et al. (2009) tested two SCI patients on a neuroprostheses for grasping. Both patients suffered from a bilateral loss of the grasp function, but the first one had subdural ECoG electrodes implanted, while the second one underwent to four-week long FES training paradigm and wore a neuroprosthesis for generating palmar and lateral grasp (using a Compex Motion transcutaneous electrical stimulator). After some training, both patients demonstrated a significant increase in grasping, actuating the desired hand movements and picking up different objects by executing previously impaired movements (Marquez-Chin et al., 2009). These findings support the notion that neuroprostheses based on FES are reliable and non-invasive possibilities for restoring lost motor function (Millan et al., 2010). The clinical applications of the FES-BCI joint approach range from neurological disorders at the cortical level to motor impairments due to lesions of the corticospinal tract. In the case of stroke the FES-BCI is used to restore hand motor function as a neuroprosthetic and assistive tool in a rehabilitative capacity. In the case of SCI, the FES-BCI works as a motor substitution tool for upper limb motility. In both SCI and stroke patients it has been demonstrated that, by stimulating muscles, the FES training performed by the users can produce neuroplasticity changes in the motor representations at the brain level, a fundamental feature that further supports the effectiveness of such systems.

As a final remark, it is important to note that several examples of muscular stimulation systems based on surface electrodes are currently available on the market. Though the non-invasive systems are rapidly developing, they are currently limited due to insufficient selectivity in terms of selectivity in muscular stimulation, difficulties with reproduction of movements, limited excitability of deeper muscle groups, and also pain sensations (Mattia et al., 2012). On the other hand, implantable electrode stimulation systems have been developed (Keith et al., 1989). However, they inherently bear the risks of infections and associated with surgical interventions. The full implementation of robotically-assisted therapy in standard clinical practice will depend on the ability of future research to address such issues relative to both non-invasive and invasive FES-BCI.

4. THE NEURAL BASIS OF PROSTHETICS

Control is the process of acting on a dynamical system in order to achieve a goal. The brain operates as a biological controller to perform difficult tasks such as locomotion and manipulation, and it is able to manage nonlinearities, such as noise, delays, and external perturbations. The human hand includes multiple joints, thereby allowing for an infinite number of different finger trajectories critical in daily tasks. Such flexibility results in a complex brain-spinal cord-hand coordination system, based on a neural control scheme required at the brain level -and communication pathways through the spinal cord- to select, plan, and execute particular trajectories in order to properly accomplish the requirements of the manual tasks (e.g., accuracy), supporting the central role of the spinal cord.

Evidence in animal models of SCI showed that the firing rate of individual neurons can be modulated as a function of the sensory feedback associated with the neuronal firing (Fetz and Finocchi.Dv, 1971; Fetz and Baker, 1973; Fetz and Finocchio, 1975). Recently, several studies in rodents (e.g. Talwar et al., 2002) and in primates (e.g. Serruya et al., 2002; Taylor et al., 2002), have demonstrated that animals can learn to take advantage of the brain signals to control the movement of a computer cursor on a screen, and also the 1- and 3-dimensional movements of a robotic arm (Chapin et al., 1999; Wessberg et al., 2000). These findings support the notion that motor recovery can be improved by bypassing the SCI and using the brain signals to directly control external devices. One of the first attempts to bypass human SCI and restore voluntary motility included the implementation of an interface between the residual cortical and subcortical activity and an artificial device able to perform specific mechanic movements (Schmidt, 1980). Modern BMI systems for upper limb prosthetics are focused on predicting arm movements during reaching and grasping in the form of endpoint trajectories or wrist, elbow and shoulder angles and velocities in monkeys and humans (Carmena et al., 2003).

The reliability of the quality of the brain signals to be used in BMI systems and of the recording techniques is demonstrated by the high accuracy (up to 99%) with which a single-movement-specific neural firing pattern can be recognized using staining techniques in awake animals (Ben Hamed et al., 2007) Not only simple movements but also complex, combined motor schemas are recognizable by BMI systems. Some important studies used intracortical electrodes in monkeys to show that it is possible to encode grasp aperture and finger movements during natural grasping motions (Artemiadis et al., 2007; Vargas-Irwin et al., 2010). Furthermore, in a recent study Aggarwal et al. (2008) demonstrated the asynchronous decoding of individual and combined finger movements. Single-unit activities were recorded sequentially from a population of neurons in the hand primary motor cortex of trained primates during flexion and extension movements of individual fingers and wrist, respectively. The detection accuracy of the BMI system was within 90% and 99% for individuated fingers and wrist. The average decoding accuracy was still 92.5% when combined movements of two fingers were analyzed. In humans, recent studies have shown the possibility of decoding kinematic parameters of movement during individuated finger movements, and simple grasping motion from local motor potentials extracted from ECoG signals (Acharya et al., 2010; Kubanek et al., 2009).

Taken together, these results demonstrate that it is possible to asynchronously decode dexterous finger movements from a neuronal ensemble with high accuracy. Agashe and Contreras-Vidal (2011) presented a methodology to accurately predict and reconstruct natural hand kinematics from non-invasively recorded scalp EEG signals during grasping. EEG and hand kinematics were recorded simultaneously while subjects performed a grasping task. The task involved making a decision to select an object, planning the goal of the movement, programming the movement, and executing the grasp in conjunction with specification of the appropriate hand trajectory. The authors used a specific decoder, basing its performance on a correct combination of time-domain amplitude modulation of EEG signals. Trajectories of the joint angles were reconstructed for metacarpophalangeal joints of the fingers. The high decoding accuracy detected during the study indicated that this technique may be suitable for use with a closed-loop real-time BMI to control grasping motion in prosthetics with high DOF. This demonstrates the first successful decoding of hand re-shaping kinematics from non-invasive neural signals.

This line of research takes an important step towards the development of a BMI for direct control of multi-fingered hand prostheses. When considering the multiple DOFs involved in the control of dexterous robotic hands and fingers, both specialists in neuroscience and robotics focused on adaptive robot controllers (Conforto et al., 2009; Reinhart and Steil, 2009). One fundamental problem is that the brain -as any other robotic controller aiming to command complex kinematic mechanisms- is able to learn internal models of forward and inverse sensorimotor transformations (e.g. inverse kinematic) for reaching and grasping (Gentili et al., 2011). This is a problem because the mapping between sensory and motor information is generally highly non-linear and depends on the constraints imposed by the physical features of the human or robotic hand/finger. One possible solution of this issue is the so-called inverse kinematics. It refers to the use of the kinematics equations of a robot to determine the joint parameters that provide a desired position of the end-effector. “Motion planning” refers to the specification of a movement pathway to achieve a desired task. Inverse kinematics transforms the motion plan into joint actuator trajectories for the robot. Gentili et al. (2011) propose a cortical neural model that is able to learn to control the inverse kinematics of an anthropomorphic simulated robot finger named Shadow Hand. The neural model specifically reproduces the main kinematic features of human finger movements and grip production. At the first step, there is an exploration phase, where endogenously generated random motor commands are used to activate the finger while the corresponding sensorial consequences (e.g. visual) allow training the neural model to learn the inverse kinematic of the actuator. This neural model is based on biological neural network modeling, including specific brain structures/functions both at the cortical (Bullock et al., 1993; Gentili et al., 2012) and cerebellar level (Contreras-Vidal et al., 1997; Porrill and Dean, 2007). The learning period of the model is based on the integration of five different sensorimotor data: i) neural drive conveying information about motor command for actual performance; ii) proprioceptive information providing the current state of the finger (e.g., angular position); iii) visual information related to the finger and the localization of the targets in the 3D space; iv) task and goal-related information involved in motor planning; v) motor accuracy elaborated by the cerebellum. The results revealed that the neural model was able to control the anthropomorphic finger in order to perform accurate and robust 3D reaching movements (with various levels of complexity) towards spatial targets with kinematics comparable to those previously observed in humans (Gentili et al., 2011).

5. FUTURE PERSPECTIVES

Attempting to create a mental image of the missing limb by early prosthetic fitting is an important direction for the research in neuroprosthetics. This line of research is both timely and challenging because some data show that in children with congenital absence of limbs the body sensorimotor representations in the brain do not include the missing body parts. Such alterations can explain why most of the children reject their prosthesis, probably because their own familiar limb, although incomplete, is still more functional to them. Due to the absence of sensory feedback from the prosthetic limb, children rarely incorporate the prosthetic limb into their body schema. By restoring the sensations from the missing limb and therefore repairing the sensorimotor loop, future research will help patients to better accept, integrate, and use neuroprostheses. Some work in this direction has already started, however some issues remain to be clarified. For example, it has been shown that electrotactile and vibrotactile feedback -together with tactile re-innervation- can be successfully integrated (Kaczmarek et al., 1991; Marasco et al., 2009). However, patients need to be specifically trained to associate the stimulation due to the occurring physical events with the state of the prostheses (Antfolk et al., 2013). The attempt to reproduce the original sensations associated with the lost limb will be one of the main challenges for future researchers.

Another crucial aspect is the timing of the sensory feedback. Short latencies between the event occurring at the prosthesis and the perceived sensation (within 300ms) is important for the brain to develop the sense of ownership of the prosthesis and to allow its incorporation within the body schema (Shimada et al., 2009). Emerging insights into the procedures to be followed for better integrating prostheses with the body schema highlight the importance of timely closing the loop between exteroceptive and proprioceptive information for a proper functioning of the prosthesis and recovery of the function (Antfolk et al., 2013). One possibility to “recover” sensory information or provide sensory substitution is provided by the use of invasively implanted electrodes (Berg et al., 2013; Tabot et al., 2013). For example, trying to close the informational loop between brain and machines a Brain-Machine-Brain interface can allow active tactile exploration during BMI control using intracortical microstimulation (O'Doherty et al., 2011). In this study two monkeys were intracortically implanted in the primary motor cortex and the primary sensory cortex. The task required searching a single object with particular artificial tactile properties using a computer cursor or a joystick to explore a virtual space. As resulted, artificial tactile feedback was delivered when the actuator, controlled by cortical ensemble activity, entered the feedback zone and continued in the response zone. A particular interleaved scheme of recording and stimulating was implemented to achieve concurrent afferent and efferent operations and both the afferent and efferent channels bypassed the monkeys’ body and created a specific communication loop between brain and an external device. However, despite the reliability of intracortical stimulation for mimicking the sensory feedback of a prosthetic limb in animal models, such technique does not seem easily implementable in standard therapeutic protocols for humans. Indeed none of the prostheses used in clinical practice is designed following this principle and the use of visual, vibrotactile and electro-tactile feedback remains still the most promising technique.

CONCLUSION

Ambroise Parè, the official royal surgeon in France during the 16th century, was the creator of artificial limb. He realized that surviving amputees would prefer to die rather than live without a limb, so he began to design artificial limbs (Hernigou, 2013). This is not the first example of prostheses. Even in Ancient Greece and Roman Empire there were examples of substitutive prostheses. From then on, clearly, scientists have made great strides, almost finding the way to restore sensory information to amputees, but some additional work is still required.

The hand is the main structure for physically manipulating objects and interacting with the environment, that is why so many researchers are involved in the development of prostheses to restore motor function, from hand kinematics to the original sensations. However, before implementing new therapeutic protocol, it is necessary to introduce methods for providing the brain with feedback from the actuators and to design and build artificial prostheses that can be controlled directly by brain-derived signals. BMIs can be seen as extremely useful platforms to enhance the investigation on several neural mechanisms and the implementation of rehabilitation therapies. By reaching these milestones, future BMIs will be able to drive and control revolutionary prostheses that will feel and act like the human body segments.

Thanks to the multidisciplinary interactions between different fields of research and application, neuroprosthetics is constantly progressing and improving. The number of opportunities is continuously increasing and the impact of the neuroprosthetic research will soon be clear, not only to specialists. In this direction a challenging project aiming at restoring full mobility in tetraplegic patients by using BMI in a whole-body exoskeleton, will be play an important role in the opening ceremony of the FIFA World Cup in Brazil 2014 (Nicolelis, 2012). If the progress to date is any indication, amputees of the future will find their dreams limited only by their imagination.

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KEY TERMS AND DEFINITIONS

Rehabilitation
BCI: Brain-Computer Interface
BMI: Brain-Machine Integration
FES: Functional Electrical Stimulation
Robotics
Neuroscience
Sensorimotor
Therapy