Brain Research 1646 (2016) 25–33

Contents lists available at ScienceDirect

Brain Research

journal homepage: www.elsevier.com/locate/brainres

Review

Brain-machine interface facilitated neurorehabilitation via spinal stimulation after spinal cord injury: Recent progress and future perspectives

Monzurul Alam[a,*,1], Willyam Rodrigues[b,1], Bau Ngoc Pham[c,1], Nitish V. Thakor[a]

[a] *Singapore Institute for Neurotechnology, National University of Singapore, Singapore*
[b] *Faculty of Medicine, Federal University of Alagoas, Brazil*
[c] *Department of Bioengineering, University of California, Los Angeles, United States*

ARTICLE INFO

Article history:
Received 9 January 2016
Received in revised form
24 April 2016
Accepted 19 May 2016
Available online 20 May 2016

Keywords:
Spinal cord injury
Brain-machine interface
Electrical stimulation

ABSTRACT

Restoration of motor function is one of the highest priorities in individuals afflicted with spinal cord injury (SCI). The application of brain-machine interfaces (BMIs) to neuroprostheses provides an innovative approach to treat patients with sensorimotor impairments. A BMI decodes motor intent from cortical signals to control external devices such as a computer cursor or a robotic arm. Recent BMI systems can now use these motor intent signals to directly activate paretic muscles or to modulate the spinal cord in a way that reengage dormant neuromuscular systems below the level of injury. In this perspective, we review the progress made in the development of brain-machine-spinal-cord interfaces (BMSCIs) and highlight their potential for neurorehabilitation after SCI. The advancement and application of these neuroprostheses goes beyond improved motor control. The use of BMSCI may combine repetitive physical training along with intent-driven neuromodulation to promote neurorehabilitation by facilitating activity-dependent plasticity. Strong evidence suggests that proper timing of volitional neuromodulation facilitates long-term potentiation in the neuronal circuits that can promote permanent functional recovery in SCI subjects. However, the effectiveness of these implantable neuroprostheses must take into account the fact that there will be continuous changes in the interface between the signals of intent and the actual trigger to initiate the motor action.

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1. Introduction

Spinal cord Injury (SCI) causes a loss of sensorimotor function due to the compromise of neural tissue integrity in the spinal cord. Traumatic events (automobile accidents, falls, sports injuries etc), diseases (e.g. cancer) and infections can lead to a SCI. Depending on the severity and location of the injury, SCI can lead to

* Corresponding author.
E-mail address: md.malam@connect.polyu.hk (M. Alam).
[1] Authors contributed equally.

http://dx.doi.org/10.1016/j.brainres.2016.05.039
0006-8993/

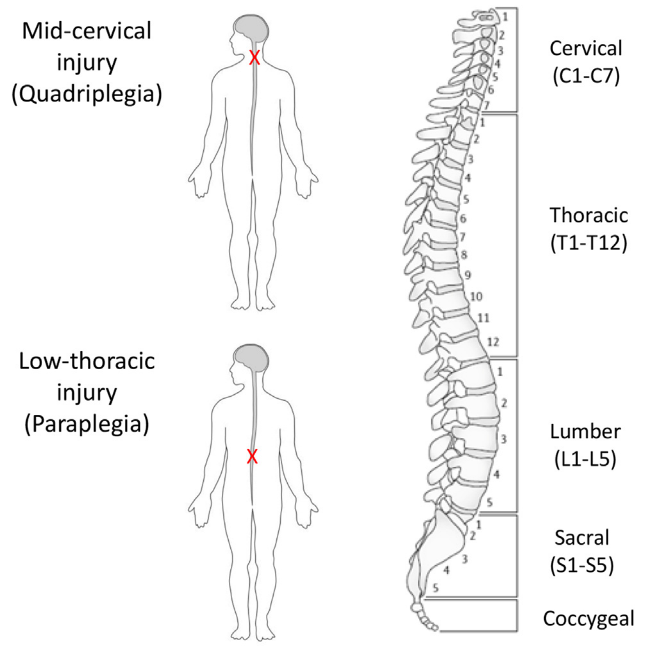

Fig. 1. Different levels of spinal cord injury (SCI). The left panel shows typical injury levels of SCI and the right panel shows the vertebral columns and their corresponding spinal levels. SCI can lead to paraplegia, injury at or below the thoracic spinal cord, commonly resulting lower-limb paralysis with complications including bladder, bowel, and sexual dysfunction. Injury at higher cervical spinal level can lead to quadriplegia, paralyzing all the limbs with complications including difficulty in breathing, speaking, and temperature regulation of the body. (Adapted from Thuret et al., 2006).

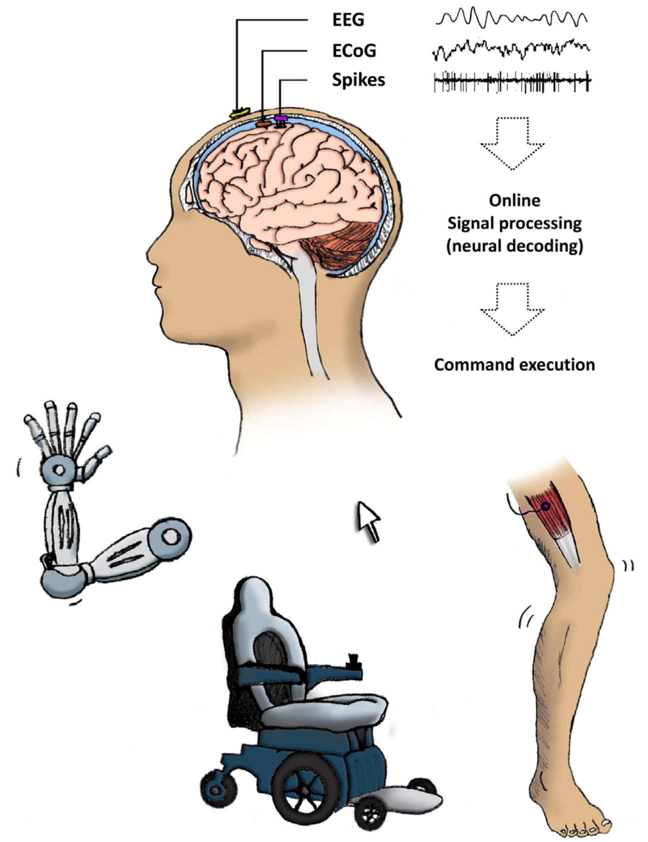

Fig. 2. Different cortical recording modalities and approaches to neuroprostheses. Electroencephalogram (EEG) can non-invasively record population neural activity from the scalp. Electrocorticogram (ECoG) records population neural activity from the surface of the brain (epidurally or subdurally) with better signal quality than EEG. Single or multi-unit (spikes) recordings use electrodes that penetrate into the brain to record signals from single or a few neurons in close proximity. All of these neural signals are processed online to execute tasks, such as controlling a robotic arm, a powered wheelchair, or electrically stimulating particular muscles.

incomplete or complete lower-limb (paraplegia), or both upper- and lower-limb paralysis (quadriplegia). Fig. 1 shows the levels of SCI that commonly occur in patients. The exact epidemiology of SCI is unknown, due to the incidence of SCI not being registered in most countries (Wyndaele and Wyndaele, 2006). It is estimated that the total number of cases of SCI ranges between 236 and 1009 per million worldwide (Cripps et al., 2011).

Currently, there is no complete cure for patients suffering with severe SCI (Thuret et al., 2006; Silva et al., 2014). Current treatments only ameliorate symptoms and complications that arise from complete SCI (Thuret et al., 2006; Simpson et al., 2012). Experimental treatments like stem cell implantations (Tsuji et al., 2010) and tissue regeneration (Joosten, 2012) try to repair damaged spinal cord. Recent studies have demonstrated that these treatments can reconnect transected spinal cords in rodents, but these treatments do not translate to human and nonhuman primates (Sahni and Kessler, 2010; Macaya and Spector, 2012). In contrast, neuromodulatory approaches that target surviving neural tissue have allowed complete SCI subjects to recover adequate functionality after rehabilitation (Harkema et al., 2011; Angeli et al., 2014; Dimitrijevic et al., 2015).

Interruption of the spinal pathways below the lesion after a SCI compromises the body's ability to execute and coordinate movements along with its ability to provide sensory feedback. Despite the disrupted connection between the brain and spinal cord, the brain can still generate appropriate motor commands (Serruya et al., 2002; Collinger et al., 2013a). This phenomenon has inspired treatments that bypass cortical commands over the lesion site to the appropriate descending motor pathways. A neuroprosthesis using a brain-machine-spinal-cord interface (BMSCI) aims to build such a bypass to electronically route this information in real-time. Recent experiments show proof of concept of these bypasses by using brain intention to directly stimulate the limb or spinal cord to reanimate or mimic motor functions (Collinger et al., 2013c; Lobel and Lee, 2014; Bouton et al., 2016). Here we summarize the recent advancements and future challenges of BMSCIs to record and decode brain activity in real-time that enables spinal cord stimulation to restore motor functions in paralyzed SCI patients.

1.1. Brain-machine interface (BMI)

The integration of brain-machine interfaces (BMIs) to neuroprostheses provides an innovative approach to aid patients with sensorimotor deficits. BMI is defined as a device that detects intent, typically motor intent, from the user's brain activity and translates it into an executable action performed by an external device, such as a computer cursor or a robotic arm (for review see Donoghue (2002), Lebedev (2004), Lebedev and Nicolelis (2006), Nicolelis and Lebedev (2009) and Thakor (2013)). BMI works on the principle that neural activities in the brain are associated with intended movement trajectories, even in absence of actual movement (Georgopoulos et al., 1986). Using multichannel neural signal recordings and advanced computer algorithms, it is possible to translate these neuronal activities into executable motor commands (Wessberg et al., 2000). Fig. 2 shows different BMI approaches to neuroprostheses. Different neural signal recording modalities vary in their resolution and accuracy of information transfer. Often times, there is a tradeoff of having increased resolution and accuracy of neural recordings at the expense of increasing invasiveness (Buzsáki et al., 2012). A range of techniques can be used to detect neural activity that includes optical,