Introduction

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Amputation of a limb is a surgical intervention used as a last resort to remove irreparably damaged, diseased, or congenitally malformed limbs where retention of the limb is a threat to the well-being of the individual. The procedure traumatically alters the body image, but often leaves sensations that refer to the missing body part, the phantom limb. In 50–80% of cases, these sensations are perceived as painful and referred to as "phantom limb pain" (PLP). Today, it is still not completely understood why the pain occurs, and there are no effective treatments.

A Possible Path for Combatting PLP?

Cortical reorganization has been found to be related to PLP. Amputation of a hand is immediately followed by significant reorganization in the somatosensory pathway and cortex, i.e. the hand area in the brain is invaded by neighboring areas, such that the normal homunculus is shifted. Painful sensations appear to be related to reorganization of the primary somatosensory cortex (S1), and a correlation was demonstrated between the number of sites in the stump from where stimuli evoked referred sensations, the PLP experienced and the amount of cortical reorganization (Grüsser et al., 2001; Knecht et al., 1996). *S*everal studies have demonstrated the favorable effect of enhancing the sensory feedback related to the missed limb to alleviate PLP in the recent years. For example, patients with PLP, who intensively used myoelectric prosthesis (Lotze et al., 1999) or used daily discrimination training of surface electrical stimuli applied to the stump

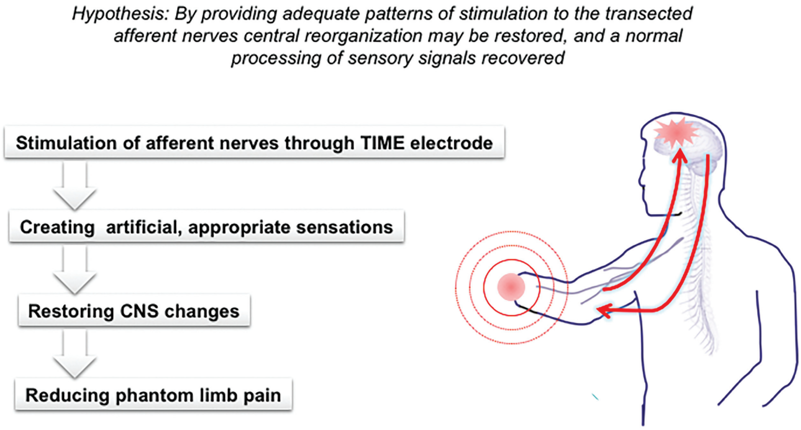

Figure 1 Overview of the main hypothesis of the TIME project.

experienced significant reduction of PLP (Floor et al., 2001). Intrafascicular, electrical stimulation of severed nerves proved to be capable of eliciting tactile or proprioceptive sensations by implanted LIFE electrodes in human subjects (Rossini et al., 2010). Rossini et al. also demonstrated that training for control of a robotic hand (with a limited amount of sensory feedback) significantly reduced PLP in a human amputee volunteer implanted with four LIFE. The reduction in PLP lasted several weeks after the LIFE electrodes were removed and changes in sensorimotor cortex topography were shown electrodes (Rossini et al., 2010). We therefore hypothesized that given appropriate control over a sufficient number of nerve fibers, a neural interface may be able to artificially evoke sensations and eventually relieve PLP (see Figure 1).

Why is a HMI-System is Needed to "Solve" the Problem of PLP?

As anybody who has felt a static electric discharge can attest, electrical impulses can be used to evoke sensations. These sensations are a result of the direct but nonspecific activation of peripheral nerves by the electrical discharge. If this basic principle is refined to specifically and focally activate only those nerve fibers projecting to sensory fibers related to pressure on the skin on the side of the index finger, for example, the evoked sensation would be that of pressure on the side of the hand. Given sufficient control over a large enough set of nerve fibers and types, the neural interface would be able to artificially evoke sensations of touch, vibration, heat, etc., and illusions of limb/finger/joint movement. The holy grail of human-machine interfaces has been considered a device that can directly interface to the body's nervous system. It has been the topic of popular science fiction but is based upon current experimental research in neuroprostheses. It is considered important because almost all interactions between the brain, the body, and the environment are relayed through information flowing through the nervous system. The ability to intercept information from, or artificially place the information into the nervous system can revolutionize the way the brain interacts with the body and the environment. But more importantly, such a technique may provide currently nonexistent treatment modalities to those who have lost or have pathological function due to traumatic injury or disease. Because of the sizes of the cells and constraints on dimensions of devices to minimize tissue damage, the only way to obtain high-density multichannel interfaces to the nervous system is through the application of micro/nanotechnologies to this medical device problem.

The TIME Prototype System for Treatment of PLP

Our aim was to develop such a Human Machine Interface (HMI) by means of the application of multichannel microstimulation to the nerve stump of an amputee volunteer to manipulate his/her the phantom limb sensations and explore the possibility of using the method as a treatment for clinched fist phantom limb pain.

This book provides an overview of our experiences and results with the design, development, and test of the hardware and software components, and our ambition to safely implant and evaluate the system in an amputee volunteer subject (see Figure 2).

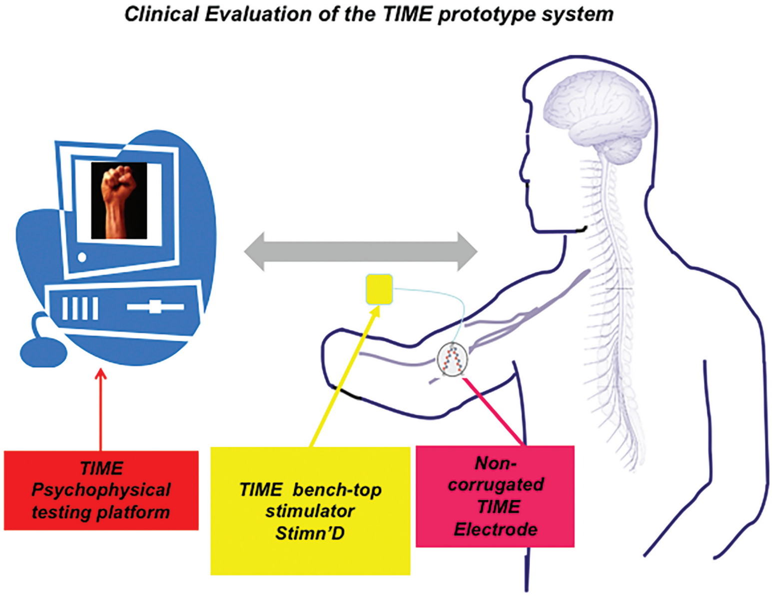

Figure 2 Overview of the TIME prototype system for preclinical evaluation in amputee subjects.

The "TIME prototype system" (see Figure 3) consists of the Thin-film Intrafascicular Multichannel Electrodes (TIME) (Chapter 3), a multichannel stimulator system (Chapter 7), and a psychophysical testing platform (Chapter 8). Theoretical modeling was carried out to drive electrode design (Chapter 4). The TIME electrodes underwent in vivo characterization in animals to test the biocompatibility, stability, and chronic safety (Chapters 5 and 6) before the system was tested in one human volunteer subject (Chapter 9). We also speculate on the future of the TIME electrodes and TIME prototype system (Chapter 10). Finally, to provide the reader with a broad background, we introduce the pathophysiology of pain (Chapter 2) and provide an overview of the current understanding and treatment of phantom limb pain (Chapter 1).

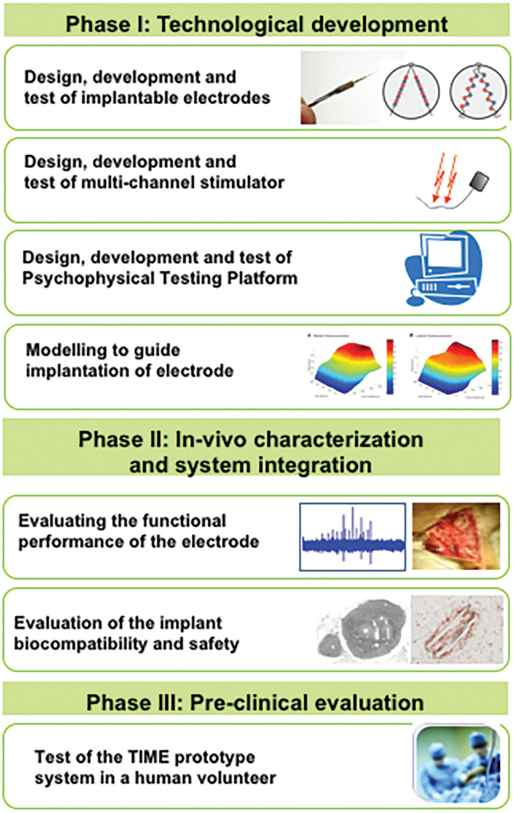

Figure 3 Overview of elements in the development and test of the TIME prototype system for preclinical evaluation in amputee subjects.

References

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