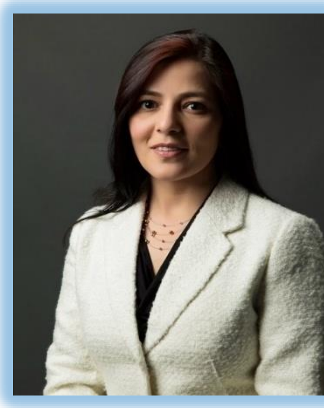

Neuroprostheses

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Executive Editor

Intra Spinal Micro-Stimulation Implant Technology Shows Promise for Clinical Implementation

Intra Spinal Micro-Stimulation Implant for Neuroprosthesis

Recent breakthroughs in neuroprostheses have accelerated a new wave of biomedical technologies including implantable spinal-cord-neuroprostheses that seek to restore standing and walking after paralysis to augment the human body or restore its lost functions [1]. Researchers have extensively studied these technologies in animal models that have shown tremendous promise. One of the therapeutic targets of these neuroprostheses are neural networks of the spinal cord that have been investigated for a number of applications that include restoring paralyzed limbs and mobility deficits, and promoting targeted plasticity and recovery after neural injury and disease [1-3].

Lately, the intra spinal micro-stimulation (ISMS) implant has emerged as an important procedure of neuroprostheses. ISMS comprises of an array of ultra-fine electrodes that are capable of delivering electrical pulses to the ventral horns of the spinal cord [4]. Researchers have shown that depending on the targeted region within the spinal cord, the application of ISMS can generate functional movements of the lower and upper limbs (lumbosacral and cervical implants), breathing (cervical implant) or bladder function (sacral implant) [1]. Further, studies were conducted on stimulation through an individual intraspinal electrode that demonstrated the possibility to activate motor networks including motoneurons, afferent and propriospinal projections, and associated axons spanning multiple spinal cord segments. In further advances made in ISMS, researchers showed that a small number of implanted electrodes can evoke synergistic muscle contractions, which can produce coordinated movements involving single or multiple joints to perform functional tasks [1].

ISMS in the Lumbar Spinal Cord for Overground Walking

The restoration of hind-limb movements after paralysis is a very important medical problem, and new biomedical solutions are sought to address this issue. To this end, ISMS in the lumbosacral spinal cord studied in animals has shown great promise (Figure 1) [5].

Researchers showed that hind limb movements triggered by ISMS in cats resulted in significantly more fatigue resistant compared to those obtained by intramuscular electrical stimulation [3, 5]. It was demonstrated that with ISMS implants, animals were able to stand for ~5x longer durations and walk over-ground for ~10x longer distances than animals with intramuscular implants [3].

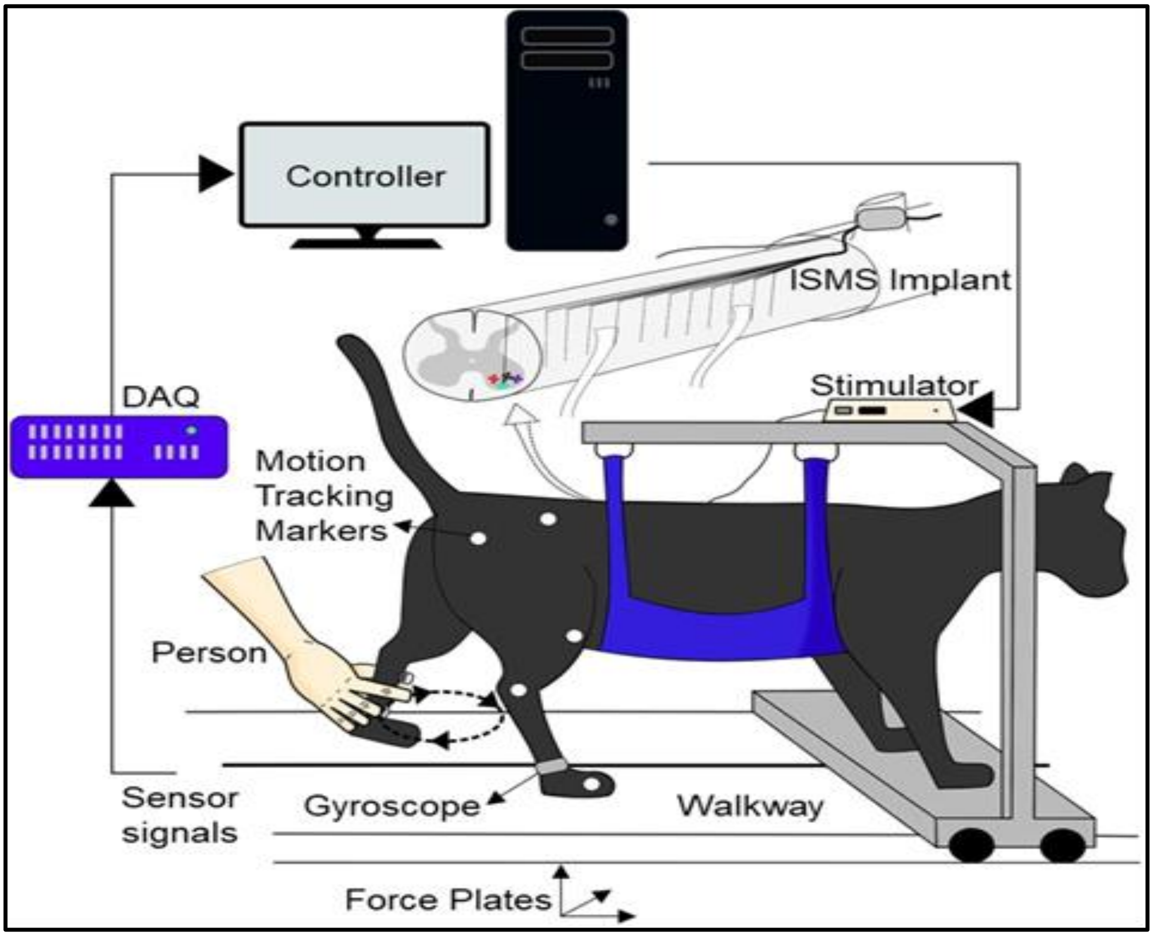

*Figure 1: Illustrations showing the experimental setup for over-ground walking. The process involves sensor signals that come from force plates under the walkway and a gyroscope placed on the tarsals from both hind-limbs. These signals are then converted to digital signals by the data acquisition device (DAQ) and steamed into a Matlab program where an algorithm can control the stimulation to the spinal cord to allow right-hind limb move to the opposite phase of the walking cycle [**Source:** bioRxiv, (2019)].*

Transitioning ISMS from Pre-Clinical World to Clinical One

Transition of ISMS to full clinical implementation is a critically important task that requires understanding about the functional organization of the motor networks to be targeted in the lumbar spinal cord of humans [1]. The existing information regarding the anatomical organization of the motoneuronal cell bodies in the human lumbar spinal cord that innervate the leg muscles (i.e., anatomical map) is not sufficient to reveal the functional organization and connectivity of various motoneuronal pools (i.e., functional map). Further, the required stimulation amplitudes for their activation are also not known [1].

These steps are critical to design and realize a clinical translation path of ISMS as effective neuroprostheses. To this end, researchers recently investigated the organization of the neural networks targeted by these implants in a non-human primate, the macaque monkey. They presented the hypotheses of their study based on preservation of similar functional organization of motor networks in non-human primates (Figure 2) [1].

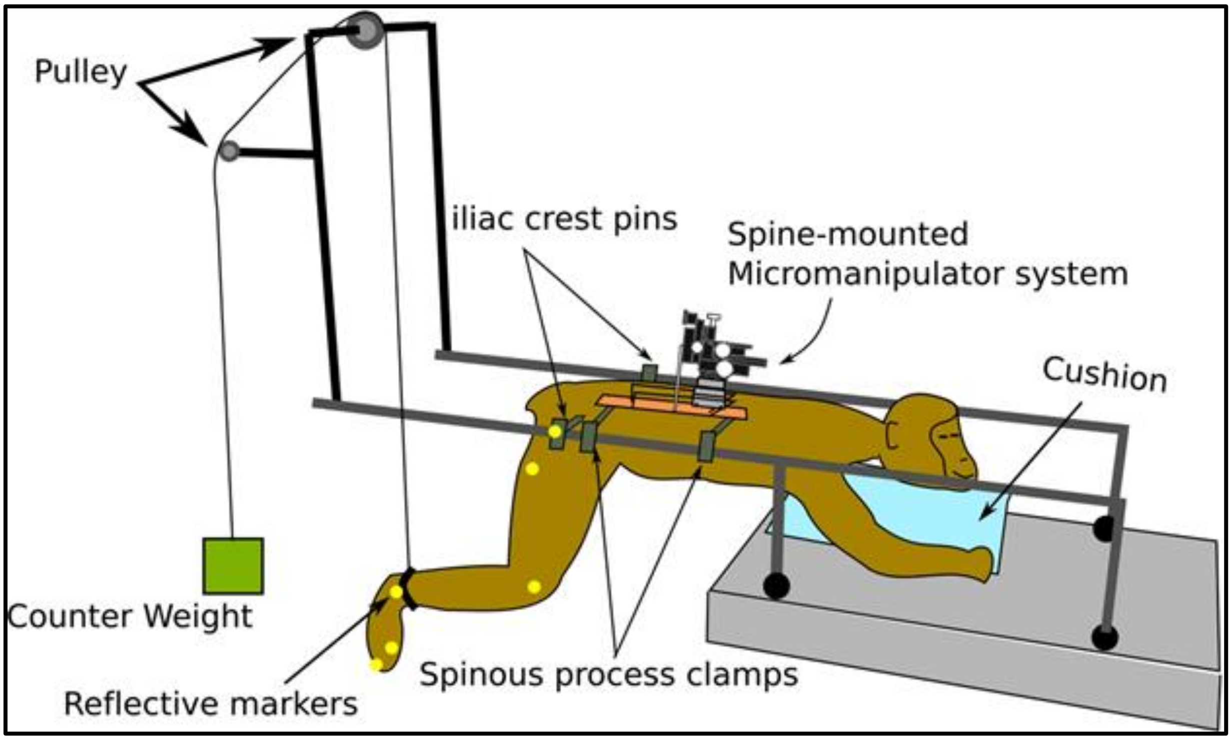

*Figure 2: Experimental setup showing the concepts of functional mapping of the lumbosacral spinal cord in non-human primates [**Source:** Scientific Reports, (2019)].*

Concluding Remarks

Research advances made in spinal-cord neuroprostheses have shown tremendous promise for clinically improving lower limb mobility after spinal cord injury (SCI). For example, researchers have shown that by targeting the motor networks in the ventral horns of the spinal cord, ISMS can specifically result in various coordinated leg movements that are necessary for functional tasks such as walking over-ground. In this regard, preclinical studies have indicated the potential of ISMS to produce beneficial outcomes of standing and walking even after a chronic complete SCI. Therefore, it is believed that ISMS has the potential to restore walking for people with more severe SCIs than may be possible with any other existing procedure such as epidural stimulation. Further, to achieve the goal of clinical implementation of ISMS implants, the knowledge of the functional organization of the motor inter-neuronal networks in the lumbosacral spinal cord of humans is critical. This involves the knowledge of exact location of the spinal cord to place the implant for successful targeting of the leg movements that are required for functional standing and walking. This will enable the optimized design of the implant. Future technical design considerations are expected to include the number of microelectrodes in the array, spacing between the microelectrodes, and targeting depth and length of the microelectrodes. We anticipate that further R&D advances in specifications of the clinical microelectrode and stimulator would pave the way to safely deliver the current intensities that are required for producing the pre-requisite functional movements.

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