Restoring Standing after Spinal Cord Injury using Intraspinal Microstimulation

Lau B, Guevremont L and Mushahwar VK

Department of Cell Biology and Centre for Neuroscience, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada

Abstract

The aims of this study were to develop open- and closed-loop control strategies for restoring functional standing after spinal cord injury (SCI), and to assess the effectiveness of intraspinal microstimulation (ISMS) in producing kinematically-stable and fatigue-resistant standing. Experiments were conducted in adult anesthetized cats and electrical stimuli were delivered either directly to the spinal cord through fine ISMS wires, or to the muscles through intramuscular (IM) wires implanted bilaterally in the main knee and ankle extensors of the hindlimbs. The ISMS wires targeted regions within the ventral horn of the lumbosacral enlargement shown to elicit extensor synergies in the hindlimbs when stimulated. In both ISMS and IM trials, stimuli were either delivered with predetermined amplitude levels (open-loop) or the amplitudes were modulated based on real-time measurements of ground reaction forces and joint angles (closed-loop). The duration of weight-bearing standing induced by ISMS was 7 times longer than that obtained with IM stimulation using open-loop control, and 3 times longer using closed-loop control. The ISMS-evoked standing was kinematically stable and fatigue-resistant. The results suggest that closed-loop control of ISMS may be an effective method for restoring prolonged functional standing after SCI.

1. INTRODUCTION

The use of functional electrical stimulation (FES) for restoring standing after spinal cord injury (SCI) is a difficult task. Not only is the FES system required to maintain postural stability and bilateral balance, it is also expected to generate fatigue-resistant contractions such that prolonged periods of standing are achieved. The challenges faced by an FES system for standing involve the need to stimulate muscles continuously to sustain upright standing, thus inadvertently increasing the rate of fatigue; and the need to ensure stability in the frontal and sagittal planes [1]. While, to date, anterior/posterior and lateral stability have been primarily managed through the use of a walker, several efforts have been focused on reducing the rate of muscle fatigue. These efforts either utilized customized stimulation waveforms and parameters that improved the motor-unit recruitment order and duration of stimulation of a given set of units [2-4], or closed-loop control paradigms that reduced the occurrences of over-stimulation of muscles (e.g., [5-9]).

The goal of this study was to develop an FES standing system that would address both the postural stability and the fatigue-resistance needed for restoring functional standing. To achieve this goal, closed-loop control of intraspinal microstimulation (ISMS) was employed. Intraspinal microstimulation is an FES method which generates functional leg movements of the hindlimbs of animals through the use of very fine, hair-like wires implanted in the lumbosacral enlargement of the spinal cord [10-13]. This region of the cord is only 5 cm long in humans (3 cm in cats), contains motoneuronal pools innervating all the muscles of the lower extremities, and contains large proportions of the neuronal networks involved in the coordinated activation of synergistic muscles of the legs. Graded force recruitment is generated through ISMS and motor units are activated in a near-normal physiological order [10,14,15]. Furthermore, interleaved ISMS through two microwires generating similar mechanical action significantly reduces the rate of muscle fatigue [16]. Therefore, ISMS may be an attractive option as an FES system for restoring standing after SCI.

2. METHODS

Seven adult cats (2.9-4.5 kg, 5 males, 2
females) were used in the experiments, and some animals were used in more than one testing session. All protocols were approved by the Univ. Alberta Animal Welfare Committee. Electrical stimulation was delivered either through ISMS microwires implanted 2 hrs – 10 days prior to testing (n=4), or through intramuscular (IM) electrodes implanted percutaneously on the day of the experiment (n=9). All experiments were conducted under sodium pentobarbital anesthesia. Six (6) ISMS microwires were implanted in each side of the spinal cord within regions eliciting contractions of the quadriceps (3 wires) and whole limb extensor synergies (3 wires). The IM electrodes were implanted in the vastus lateralis and gastrocnemius lateralis of each limb. The animals were placed in a body harness providing partial weight support, and the hind legs were positioned on force plates to measure the ground reaction force (GRF) generated by each limb. Miniature tilt sensors were placed above the ankle and on the metatarsal region of the foot for instantaneous estimation of ankle and knee joint angles during the standing trials. Stimulation through ISMS microwires was interleaved between 2 quadriceps and 2 extensor synergy microwires in each side of the spinal cord. The stimuli through each microwire consisted of 25 Hz trains of biphasic pulses, 200 µs in width and ranging in amplitude from 20-350 µA. Stimulation through IM electrodes was composed of 50 Hz trains of biphasic pulses, 200 µs in width, and ranging in amplitude from 2-20 mA.

Stimulation amplitude through the ISMS and IM wires was either held at a constant predetermined level (open-loop control), or modulated based on the state of the limbs as determined from on-line measurements of GRF and joint angles (closed-loop or state control). In the latter, if the level of GRF dropped below the lowest threshold deemed safe for weight support, the stimulation amplitude to the knee extensors was increased. If GRF exceeded an upper threshold beyond which unnecessarily excessive force is generated, the stimulation amplitude to the knee extensors was reduced. Similarly, stimulation amplitude to the knee and ankle extensors was modulated up or down based on threshold levels set for the knee and ankle joint angles. Lateral stability of standing was obtained during closed-loop control by setting the same GRF thresholds for the left and right legs. Independent control of stimulation amplitudes in each limb was otherwise used.

Open-loop trials were terminated after achieving 15 min of functional standing or after weight support and/or postural stability (i.e., balanced left and right forces and appropriately proportional knee and ankle joint angles) were lost. Closed-loop trials had no upper time limit and were terminated only after weight support and/or postural stability were lost. The duration of standing evoked by ISMS or IM stimulation, postural stability, rate of force decay, and total injected current were assessed.

3. RESULTS

Various levels of functional standing in the hindlimbs were achieved in all IM trials and in 3 of 4 ISMS trials. In one animal, the prefabricated ISMS microwires were too short and could not reach the target locations for stimulation in the ventral horns of the spinal cord. The results from this animal were excluded from subsequent analyses.

The average duration of standing with full weight support of the hindquarters achieved by open-loop control of interleaved ISMS was 12.1 min, with 2 of 3 animals attaining 15 min of weight-bearing standing (the maximal duration of the experimental protocol for open-loop control). In comparison, the average duration of standing evoked by open-loop control of non-interleaved IM stimulation was 2.6 min. Using closed-loop control, the average duration of standing achieved by ISMS was 20.9 min, with 2 of 3 animals standing for 28.3 and 32.0 min. In comparison, the average duration of standing achieved by closed-loop control of IM stimulation was 4.2 min with the longest duration of weight-bearing standing attained being 8.5 min.

The rate of decay of ground reaction force was 1.7 and 30.7 %body weight/min for open-loop ISMS and IM stimulation, respectively. Closed-loop control improved this rate of decay significantly for IM stimulation but not ISMS. The rate of decay with closed-loop control was 1.6 and 7.6 %body weight/min for ISMS and IM stimulation, respectively. The average amount of current injected throughout the duration of ISMS standing was 1.2 mA during both open- and closed-loop control. In comparison, the average amount of current injected during standing with IM stimulation was 55.1 and 44.5 mA for open- and closed-loop control, respectively. These results suggested that ISMS is capable of producing...
prolonged durations of weight-bearing standing using less than 3% of the current injected with IM stimulation [17, 18].

With open-loop control, bilaterally balanced force production was difficult to achieve using either ISMS or IM stimulation. This was corrected using closed-loop control. Due to the differential fatigue rate in quadriceps lateralis and gastrocnemius lateralis, collapse of the knee joint and hyperextension of the ankle joint was often encountered with open-loop control of IM stimulation. This was not seen in any of the trials with open- or closed-loop control of ISMS. With closed-loop control, collapse of the knee joint and hyperextension of the ankle joint with IM stimulation were corrected, albeit slowly.

**4. DISCUSSION AND CONCLUSIONS**

Our results reaffirmed that closed-loop control can prolong the duration of FES-induced standing by reducing the over-stimulation commonly encountered with open-loop activation of muscles. The results also demonstrated that ISMS produces fatigue-resistant muscle contractions for extended durations, even when used in conjunction with open-loop control strategies. No incidents of knee collapse and ankle hyperextension occurred with open-loop ISMS. This is presumably due to the inherently synergistic activation of muscles obtained through ISMS. Closed-loop control of both ISMS and IM stimulation was capable of balancing the level of force generated in each leg, providing lateral stability of the evoked standing. Due to the steeper force recruitment with IM stimulation relative to ISMS, large oscillations in GRF and joint angles were initially seen with closed-loop control of IM stimulation. This was corrected by reducing the rate of change of the amplitude of current in IM stimulation; however, the cost was a reduction in the response time to a collapsed posture.

In summary, these results demonstrate that closed-loop control of ISMS may be an efficacious means for restoring standing after SCI. Technical improvements in the design of ISMS microwire arrays are needed to avoid incidents of mismatched dimensions.

**References**


**Acknowledgements**

This work was funded in part by the Canadian Institutes of Health, in part by the International Spinal Research Trust and in part by the National Institutes of Health. VKM is an Alberta Heritage Foundation for Medical Research (AHFMR) Senior Scholar.