MOVEMENT SYNERGIES ELICITED BY INTRASPINAL MICROSTIMULATION COMPARED TO STIMULATION OF MUSCLES, NERVES AND ROOTS IN THE CAT

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Abstract
This study tested the idea that there are sets on neurons in the spinal cord responsible for generating elementary synergies (movement primitives) that could have implications for FES. Intraspinal, intramuscular, epineural and spinal root stimulation were compared in the anesthetized cat. Ventral root stimulation produced downward and backward movements of the leg while dorsal root stimulation produced upward and forward movements. Muscle, nerve and spinal cord stimulation generated selective movements in all directions. Muscle stimulation produced the most smoothly graded recruitment curves, but recruitment depended heavily on the location of electrodes relative to the motor point. Intraspinal stimulation within intermediate “movement primitive” regions of the cord activated synergistic groups of muscles, and produced relatively graded recruitment curves. However, the direction of movement often changed as stimulus strength increased. Nerve stimulation produced the largest movements, but the recruitment curves were quite steep, which might make fine control difficult.

Introduction
It has been suggested that electrical stimulation within intermediate laminae of the spinal cord can activate sets of neurons to produce synergistic movements termed “movement primitives” [3]. In addition to electrical stimulation of muscles and nerves, stimuli have also recently been applied to the spinal cord and ventral roots as potential avenues for restoring functional movement [1, 2]. To date, very few studies have compared results using different methods in the same subjects. In addition, many of the basic biomechanical and neurophysiological properties of movements produced by stimulation are poorly understood. This paper compares these properties using electrical stimulation of muscles, nerves, ventral and dorsal roots, and the spinal cord. The results of comparing all these methods in the same preparation should be helpful to understand the concept of movement primitives and to provide some preliminary data for clinical FES.

Methods
Eight adult cats were anesthetized either with halothane (n=5) or pentobarbital (n=3). In 5 animals the following nerves were exposed in the right hindlimb and cuff or epineural electrodes were implanted: tibial nerve (TB), common peroneal nerve (CP), hamstring branches of the sciatic nerve supplying knee flexors (KF) and hip extensors (HE), and femoral nerve branches supplying hip flexors (HF) and knee extensors (KE).

Each animal was positioned in a conventional spinal frame. The right paw was fixed in a foot holder. The foot holder connected to one edge of a 50cm rod that had a joystick-like fulcrum 40cm from the foot holder end. The foot holder was designed to be able to move perpendicularly to the stick to allow all sagittal movements. The other end of the rod was connected to a spring allowing the cat’s right hindlimb to move in a uniform stiffness field in the sagittal plane. The three-dimensional movements of the hip, knee and ankle joints and the paw were monitored using motion tracking sensors (6D-Research™, Skill Technologies, Inc., Phoenix, AZ).

In all cats, bipolar intramuscular EMG electrodes were placed close to the motor points in seven right hindlimb muscles (lateral gastrocnemius (LG), tibialis anterior (TA), vastus lateralis (VL), semimenbranosus (SM), posterior biceps femoris (BF), sartorius (SA), and iliopsoas (IP). The electrodes were insulated except for a 3-mm tip.

In 3 animals, the spinal cord was stimulated through 17-19 microwire electrodes inserted into the right side of the cord. The electrodes were 30-μm diameter, stainless-steel wires (California Fine Wire, Grover City, CA) with 30-70 μm exposed at the tip. They were inserted every 2-3 mm along the L5 to S1 segments with most tips inserted into intermediate locations thought to contain “movement primitive” circuitry [3].

The resting position of the limb was adjusted to approximate a normal standing posture. The following procedures were performed:
1. The muscles were stimulated individually and the kinematics were recorded. The stimulus consisted of a train of monophasic cathodic impulses lasting 0.8 sec. Each pulse had a duration of 300 μs and a frequency of 50 Hz. The stimulation current needed to produce a threshold muscle movement was determined for each muscle using visual observation. We activated each muscle at stimulus intensities of 1.2, 1.5, 2.0, 2.5, 3.0 and 4.0 times threshold (T).
2. Nerves were stimulated individually through epineural or cuff electrodes and the
EMG and kinematics were recorded. For the stimulation of nerves, we used stimulus levels of 1.2, 1.5, 2.0, 2.5, and 3.0 T. Intraspinal electrodes were independently stimulated at stimulus levels of 1.2, 1.5, 2.0, 2.5, and 3.0 T.

In 3 animals, the right dorsal and ventral roots from L4 to S1 were exposed. Dorsal roots were sequentially cut peripherally and hook electrodes were placed on each root. The roots were stimulated at levels of 1.2, 1.5, 2.0 and 3.0 T. Each ventral root was also stimulated at stimulus levels of 1.2, 1.5, 2.0 and 3.0 T.

Results

As an example of the motion analysis, Fig. 1 shows the trajectory of the hip, knee, ankle and paw when BF was stimulated with 3 T. The distance of the paw movement was 6.3 cm from the rest to the extreme position. The direction was 143° with respect to the forward direction.

![Fig. 1. Sagittal trajectory of the hindlimb during stimulation of BF muscle.](image)

In the same way, vectors induced by stimulation of muscles, nerves, ventral and dorsal roots and spinal cord were analyzed and plotted in polar coordinates. Fig. 2a-e show typical results elicited from single animals. Stimulation of either muscles or nerves evoked distinct, reproducible movements to 6 separate directions. Intraspinal stimulation was able to induce movements to all directions. Ventral root stimulation produced only downward and backward movements. In contrast, dorsal root stimulation produced only upward and forward movements. Interestingly, vectors produced by microstimulation of intermediate spinal cord regions often changed abruptly depending on the stimulus level, which was very different from muscle, nerve and root stimulation (Fig. 3).

![Fig. 2. Lines radiating from the center of the polar graphs represent the vectors from rest to extreme position during stimulation for all stimulus strengths.](image)

The threshold current for muscle stimulation was $1437 \pm 434 \mu A$, whereas those for nerve, spinal cord, and root stimulation were less than $130 \mu A$. Thus, muscle stimulation required over an order of magnitude higher currents to induce a minimal movement.
maximal directional changes produced by varying the level of stimulus intensity. Maximal degree differences by spinal cord stimulation (41 ± 37°) were significantly larger than those obtained by the other four stimulation locations (p<0.01).

We also compared recruitment curves for stimulation of muscles, nerves, spinal cord, and roots in terms of amplitude and direction (Fig. 3). Using repeated measures ANOVA, the following results were obtained:
1. The recruitment curves elicited by intramuscular stimulation had the most gradual slope and those elicited by nerve and root stimulation had the steepest slopes. 2. The recruitment curves elicited by intraspinal stimulation curve were intermediate. However, the coefficient of variation of movements induced by muscle stimulation was significantly larger than that of nerve stimulation-induced movements.

Discussion
When stimulation pulses were applied through intraspinal electrodes targeting “movement primitive” regions in the lumbar enlargement, movements were activated with low stimulus intensity. The generated movement vectors demonstrated that single muscles or synergistic muscle groups can be activated [4]. This may not be surprising because individual motoneuronal pools exist as a cluster along the lumbo-sacral segments. However, movement recruitment curves obtained by stimulating intermediate gray matter regions were rather variable depending on electrode location. Furthermore, the direction of movement vectors could dramatically change depending on stimulus strength. Presumably, these stimuli activated a large number of interneurons, whose state may change, as well as neighboring motoneuron pools. Therefore, generating reproducible and selective movements by targeting “movement primitive” locations may be a challenging aspect for intraspinal stimulation.

Application of FES to persons with paraplegia has predominately addressed the restoration of standing and walking [5]. Intramuscular or surface electrodes are the most commonly used. Disadvantages of these electrodes include the high currents required to stimulate the motor units. The electrodes are also exposed to high mechanical stresses and motion, which can result in lead breakage and electrode migration.

One difficulty commonly associated with direct neural stimulation is that of topological selectivity of activation because nerves typically contain axons that innervate multiple different muscle groups. However, this issue may be circumvented since we have found that flexor and extensor muscles of the hip, knee and ankle can be activated selectively through nerve branches. Since nerve stimulation produced more than 80% of the limits of the passive range of motion (not shown), this approach has the potential to reproduce whole, lower limb movements. In addition, the stimulus current required to activate nerve axons using epineural or cuff electrodes was much lower than muscle stimulation. One disadvantage of nerve stimulation is the relatively narrow range of stimulation intensity generating minimal to maximal movements.

Since ventral roots are composed of mixed nerve groups, selectivity is relatively poor compared to single nerve or muscle stimulation and mainly extensor movements are produced. Therefore, stimulation of ventral roots alone will not induce good functional movements such as walking. However, stimulation of ventral roots can produce strong extensor activity and may be a good candidate to restore standing or leg powered cycling for ergometer exercise in which extensor muscles are predominantly used.

References

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