

LIMB MOVEMENTS GENERATED BY STIMULATING MUSCLE, NERVE AND SPINAL CORD

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INTRODUCTION

The use of electrical stimulation and neural recording to restore function after spinal cord injury or stroke is a dream that is now gradually becoming a reality through the efforts of many groups around the world (10, 12, 21, 26). We have worked over several years to produce practical devices that can be used reliably in daily activities by people with major disabilities. These devices contain sensors and simple rule bases so that they can sense when a particular motor act is required and generate this action for an appropriate period of time. For example, many people have a condition known as "foot drop" after a stroke or incomplete spinal cord injury. The foot drops and drags on the ground during the swing phase of the step cycle, because the person can not activate the ankle flexors and some other muscle groups adequately. For this condition, a tilt sensor on the leg can sense when the foot is tilted behind the body and about to enter the swing phase (8). This signal triggers stimulation of the common peroneal nerve so that the ankle will flex and clear the ground. When the leg is tilted forward at the end of swing, the stimulation is turned off (27). The device, known as the WalkAide2, is currently undergoing international clinical trials and hopefully will be commercially available in the near future.

Many people with more severe disabilities, including complete spinal cord injury, can walk a limited distance using FES, but the energy required is high and the muscles fatigue readily (10, 12, 14). The fatigue develops in part because the systems that are used generally operate open-loop (but see Ref. 15). In the absence of sensory feedback, stimulation is typically nearly maximal for activation of the required muscle groups and the duration of stimulation is either pre-programmed to a safe (long) duration or determined by the subject using hand switches. This high level of stimulation only exacerbates the problem of fatigue. In contrast, a wheelchair can provide an individual, even with a complete spinal injury, similar or greater speed and endurance for daily activities than able-bodied individuals enjoy. However, muscles atrophy from disuse and a very severe osteoporosis develops (11). Electrical stimulation can reverse these changes to a considerable degree (3), so we developed a wheelchair in which the stationary footrests have been replaced by ones that can rotate (25). Rotation of the footrest (and the legs about the knees) is then coupled to the wheels and provides propulsion of the wheelchair. Propulsion can be generated,

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either by electrical stimulation of the hamstring and quadriceps muscles to flex and extend the knees, or by any residual voluntary control of these muscle groups. For individuals using electrical stimulation the rotation of the footrest is sensed and at preset threshold levels stimulation is switched from extension to flexion and back again. Propulsion of this device, known as the LegPro, requires considerably less energy than for an able-bodied individual to walk a similar distance at a similar speed (25). We hope that daily use of such a device will improve mobility for people who require a wheelchair on a continuing basis, while strengthening their leg muscles, rebuilding bone density and reducing overuse injuries to the arms.

In the past few years several promising techniques have been developed that offer the possibility of greatly improved control strategies. For example, Loeb and his colleagues (7) developed a single-channel microstimulator (Bion). A number of these can be injected using a hypodermic needle into relevant muscles for therapeutic or functional electrical stimulation. Normann et al. (20) developed the Utah electrode array that contains up to 100 microelectrodes in a small area ($\leq 4 \times 4$ mm). This device was originally developed for use in the visual cortex as a visual prosthesis. However, it has now been tested in the auditory cortex (24), in the motor cortex (16) and more recently in the sciatic nerve and the dorsal root ganglion (2, 5). This device can be used for recording as well as stimulation, and so offers the possibility of closed-loop control, using natural sensors. Finally, Mushahwar et al. (17) have implanted arrays of microwires into motoneuronal and interneuronal areas of the spinal cord. These devices may be able to utilize the intrinsic organization of the spinal cord to simplify control of the limb by electrical stimulation. For example, stimulating a single microwire can provide enough antigravity force to support the weight of the hind quarter of the cat (17). Similarly, stimulation through only four wires (two in each leg) can provide alternating flexion and extension for a rudimentary gait cycle (18).

The purpose of this paper is not to provide details of these rehabilitative strategies, but rather to discuss a couple of the more basic issues that remain. Does the spinal cord contain "movement primitives" (9) that can simplify control of multi-joint movements? Also, where is the best site of stimulation to produce reliable movements? These questions are related to some of the many interests Carlo Terzuolo had over his long and productive scientific career. We hope that this paper may help in honoring his life and achievements.

1. Methods for stimulating muscles, nerves, spinal roots and spinal cord

Anesthetized, acutely decerebrated and acutely spinalized cats were suspended from a conventional spinal frame. Motion sensors were placed over the lateral surface of the hip joint, near the knee (lateral epicondyle of the femur), the ankle (the lateral malleolus of the tibia) and the toes (on a foot holder near the metatarsalphalangeal joint). The foot holder connected to one end of a 50 cm rod that had a joystick-like fulcrum 40 cm from the foot holder. The other end of the rod was connected to a spring that allowed the foot to move against a constant stiffness, approximately in the sagittal plane. The position of the apparatus was adjusted so that the

neutral position approximated the normal standing posture of a cat. For movements of the limb by ± 15 cm, the deviation from the sagittal plane was about ± 1 cm. Movements were analyzed using a 6D-Research™ system (Skill Technologies, Inc. Phoenix AZ) by specially written programs in Matlab (Math Works, Inc. Natick MA).

In this preparation we stimulated muscles, nerves, spinal roots and intraspinal-ly (all of which have been used or suggested for use in FES). Fig. 1a shows the results of stimulating 7 different muscle groups through bipolar, wire electrodes. The electrodes were inserted close to the motor points of the lateral gastrocnemius (LG), tibialis anterior (TA), vastus lateralis (VL), semimembranosus (SM), posterior biceps femoris (BF), sartorius (SA) and iliopsoas (IP) muscles. Various intensities were used up to about 4x motor threshold and the movements of the cat's paw are plotted as vectors in polar coordinates from the rest or neutral position. Note that movements of 3-8 cm are typically produced in distinct directions (except for SA and IP, which are both hip flexors) and they are more or less evenly distributed from 0° to 360° . In this Figure the forward direction is 0° , upward is 90° , backward is 180° and downward is 270° . For comparison, Figure 1b shows the effect of stimulating 6 different nerves through cuff or nerve patch electrodes: tibial (TB) common peroneal (CP), hamstring branches of the sciatic nerve supplying knee flexors (KF) and hip extensors (HE) and femoral branches supplying hip flexors (HF) and knee extensors (KE). Again, movements are seen in distinct directions, more or less evenly distributed around the circle. The movements are somewhat larger, with some approaching the range of motion of the cat's limb, presumably because the nerves can more fully stimulate the related muscle groups than a single electrode in the muscles.

In some experiments hook electrodes were used to stimulate individual dorsal and ventral roots from L4 to S1. In contrast to the results with stimulation of muscles and nerves, ventral root stimuli mainly produced movements that were in the downward and backward directions (Fig. 1c). Although most ventral roots contain both flexor and extensor motor neurons, the anti-gravity muscles that produce downward and backward movements are stronger and dominate during whole root stimulation. Stimulation of the dorsal roots produced complimentary movements that were mainly upward and forward (Fig. 1d). This is probably because the stimuli predominantly produced flexor reflexes. Thus, stimulation of both dorsal and ventral roots would be needed to produce movements in all directions. However, stimulation of dorsal roots is not practical in subjects with sensation, since it can produce discomfort and pain. A final point to note is that the vectors changed systematically in the clockwise direction for the ventral roots as the stimulation moved from the L4 roots caudally to the S1 roots. For the dorsal roots, the vectors also changed systematically, although counterclockwise as the electrodes moved caudally. This systematic rotation has not been described previously to our knowledge. It may arise from the fact that the more rostral segments have fibers that innervate muscles and sensory receptors that lie on the anterior surface of the leg. More caudal segments have fibers that innervate those that lie on the posterior surface of the leg.

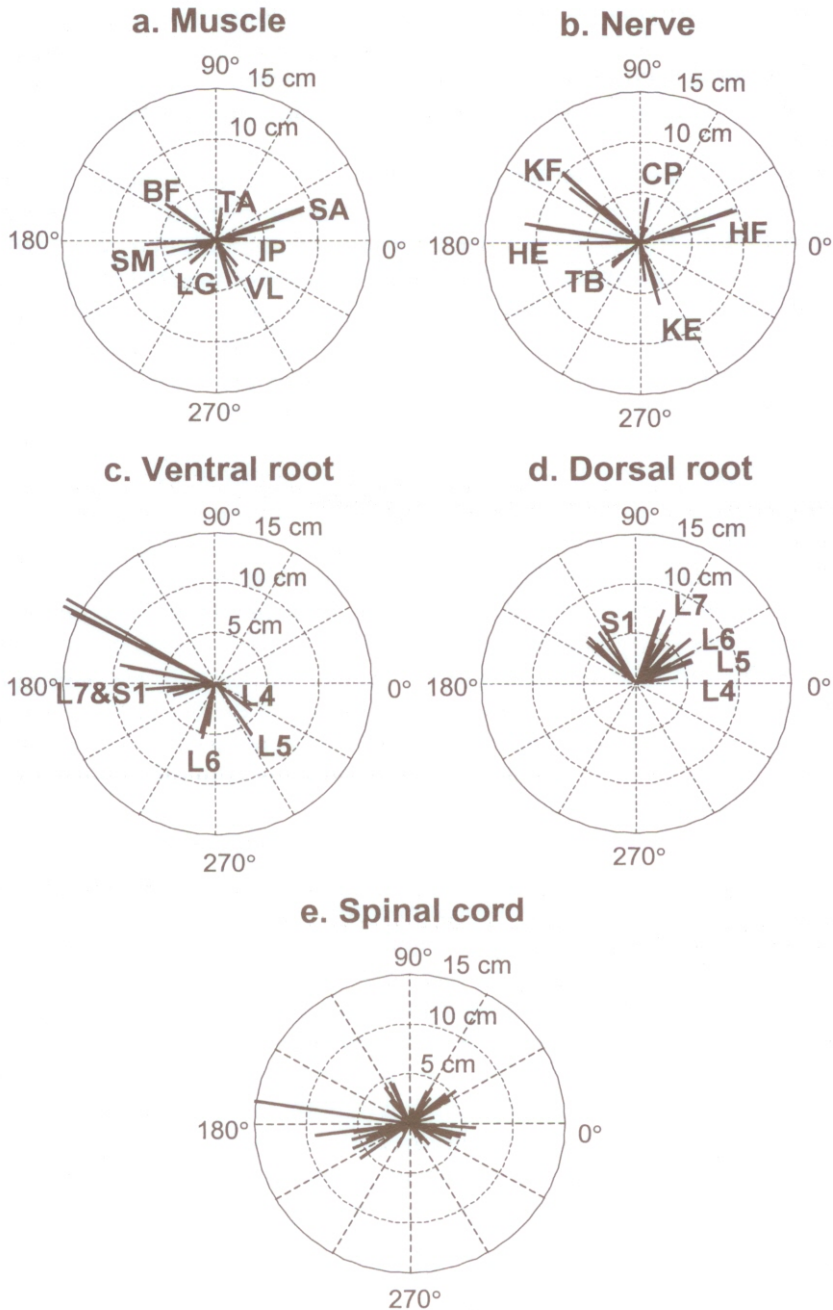


Fig. 1. - Stimulating a) 7 muscles or b) 6 nerves produced movements to distinct regions of the saggital plane from the rest position (center), which approximated the standing posture of the cat. Stimulating various c) ventral roots and d) dorsal roots produced a partial, but complementary range of movements. Stimulating in the e) intermediate areas of the spinal cord produced movements in nearly all directions. Definitions and more details in the text.

2. Evidence concerning "movement primitives" in the spinal cord.

Fig. 1e shows the results of stimulating through intraspinal microwires (30 μm diam., 30-70 μm exposed at the tip; California Fine Wire, Grover City CA). 17-19 wires were placed every 2-3 mm from the L5 to S1 segments at depths of 2.0-3.5 mm. The different depths were chosen because the thickness of the lumbosacral cord varies along its length. The aim was to place the electrodes in intermediate locations that are thought to contain "movement primitives". The locations were verified histologically in most experiments. As for the stimulation of muscles and nerves, all directions could be elicited by spinal stimulation. There was often a preponderance of backward movements because of the strength of these muscle groups, but several clusters of movements are seen in other directions. Some of these clusters represent stimulation of the major muscle groups (Fig. 1a). Thus, some movement primitives may be a consequence of the limited number of major muscle groups in a limb that are activated from interneuronal connections to their motor pools. However, the spinal cord does contain circuitry that will produce coordinated synergies of several muscles, such as the flexor reflex and the extensor thrust (9). The extent to which movement primitives are a consequence of the anatomical and biomechanical organization of the limb and its muscles or a consequence of special spinal circuits remains controversial.

Further evidence relating to this controversy was obtained by stimulating the same points in the spinal cord in a cat at different stimulus intensities. Increasing the intensity up to about 3x threshold for some electrodes merely increased the magnitude of the response without changing its direction, as expected if the electrode was situated in an area generating a movement primitive (4, 13). However, for other electrodes the direction changed dramatically. Increasing the stimulus intensity over the same range produced directional changes for intraspinal electrodes that on average were more than 40° , more than twice that for any of the other sites.

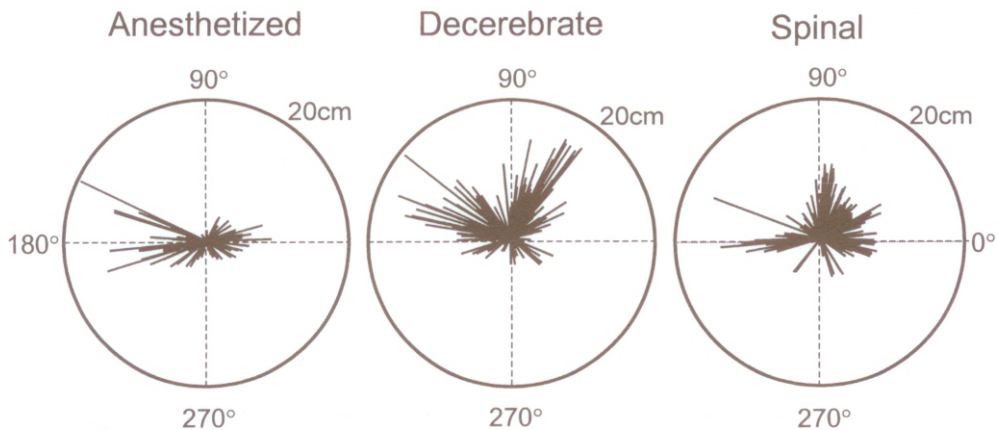


Fig. 2. Directions of movement produced by stimulating the same intraspinal electrodes in a) anesthetized, b) decerebrate and c) spinal states of one cat. Note the dramatic changes in the amplitudes and directions of the movements when the state changes.

Some animals were also studied when anesthetized (Halothane anesthesia) and after acute decerebration (precollicular section) and acute spinalization (T12 section). If the spinal structures represent movement primitives that are activated by supraspinal centers to produce discrete movements, changing the activity in descending pathways would be expected to change the threshold level, but not the direction of movement. In fact, changing the state of the animal changed the threshold for activating movements from intermediate areas of the spinal cord, but often changed the direction of movement dramatically as well. Figure 2 shows that the directions of the responses for stimulating the same sets of electrodes were clearly different from one state to another. For example, in the anesthetized state (a) most of the movements were directed forward and backward, whereas in the decerebrate state (b) the predominant direction is upward. Finally, for the spinal state (c) forward, upward, backward and even a few downward movements are seen.

DISCUSSION

Our experiments do not represent a thorough and complete test of the concept of movement primitives, but the results do not support the concept of movement primitives, at least in its simplest interpretation. Some of the preferred directions may arise from the biomechanics of the limb and its muscles. Others may arise from spinal synergies, such as the flexor reflex and the extensor thrust. Also, the direction of some responses changes dramatically as the state of the spinal cord changes or other factors such as stimulus intensity change. We prefer an interpretation based on the organization of the spinal cord into motor pools. Some interneurons preferentially activate motor neurons of a single muscle or group of closely synergistic muscles. Other interneurons activate broader groupings that form flexor and extensor synergies, but all are dramatically influenced by descending and/or sensory inputs to provide the flexibility required for the variety of movements that animals require for survival.

How do these results relate to the issue raised in the Introduction, namely the generation of reliable movements after spinal cord injury or stroke? Several conclusions can be drawn:

- 1) The results largely rule out the use of spinal roots. Stimulation of ventral roots can not produce a full range of movements and stimulation of dorsal roots may not be effective at tolerable levels in subjects who retain some sensation. Even in the absence of sensation dorsal root stimulation may induce unwanted responses, such as autonomic dysreflexia (6).

- 2) Muscle stimulation (near the motor point where the nerve enters) has advantages and is the most common method of replacing function. Some muscles can be activated from the surface or with Bions injected into the muscle without open surgery. This is the least invasive method and may reduce risks and probably costs. Also, the recruitment curve is more gradual (1), which is an advantage for control. However, a disadvantage is that many electrodes may be needed because of the large

numbers of muscles in the leg, which increases the complexity of the control system. A corollary is that the amount of external equipment needed may reduce the cosmesis of the device and increase the daily hassle. Even with Bions several antennas may be needed to activate units that are implanted in different parts of the leg and a larger battery may be needed to compensate for losses in transmission of signals through the skin.

3) Nerve stimulation has the advantage that fewer electrodes are needed, but they will require surgical implantation (with exceptions such as the common peroneal nerve for foot drop). In these experiments six nerve electrodes were implanted via three incisions in the leg and they were able to control flexion and extension of the hip, knee and ankle. Much less current was needed and the movements were larger than with muscle stimulation, but the recruitment curves were steeper. This approach is appealing, either alone or in combination with muscle stimulation (for muscles such as iliopsoas whose nerve is difficult to reach).

4) Intraspinal stimulation is a promising approach. The data presented here raise some issues, but are all from acute experiments. Clearly, these issues need to be studied in chronic spinal animals and humans. The change in the response with descending inputs will not be an issue for people with a complete spinal cord injury. Sensory inputs may change the responses, but preliminary data from chronic animals have not seen prominent effects (17). For people with an incomplete injury voluntary activation may be used to "boost" the output from given electrodes, so it may be an advantage rather than a disadvantage, if properly controlled (22). Placement of electrodes in motor pools, rather than in intermediate areas of the spinal cord, may provide greater selectivity and less volatility in the responses than found here (17, 19). The pros and cons of intraspinal stimulation can not be assessed without future chronic experiments.

SUMMARY

We have compared the movements generated by stimulation of muscle, nerve, spinal roots and spinal cord in anesthetized, decerebrate and spinalized cats. Each method produced a full range of movements of the cat's hind limb in the sagittal plane against a spring load, except for stimulation of the roots. Stimulation of the dorsal roots produced movements that were mainly up and forward, whereas stimulation of the ventral roots produced complementary movements (down and backward). Results from stimulation in the intermediate areas of the spinal cord were compared to predictions of the "movement primitives" hypothesis. We could not confirm that the directions were independent of stimulus amplitude or the state of descending inputs. Pros and cons of stimulating at some sites were provisionally considered for the reliable control of limb movements with functional electrical stimulation (FES) in clinical conditions.

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