heavy use of ganja have shown any systematic decrements in mental abilities suggestive of impairment of brain or cerebral function and cognition (*1–4*).

We also included toxicologic verification of urinary cannabinoid metabolites, observed the inhalation of cannabis by all subjects studied, and analyzed samples of this cannabis for THC. Analysis of cannabis mixed with tobacco (by gas chromatography) yielded a Δ^9-THC content of 4.14 percent (half cannabis, half tobacco); thus the THC content of the pure cannabis exceeds 8.0 percent.

We observed no transient decrements in cognitive functioning that often accompany intermittent or sporadic use of cannabis. The development of tolerance to one or more of the constituents of cannabis may explain this phenomenon.

Although the obtained IQ scores were high, one could speculate that perhaps cannabis had produced a priori declines in IQ scores for all ten subjects, as well as scores on other neuropsychological measures. It was possible for us to obtain early school academic achievement test data on two of our subjects. These data included equivalent IQ conversion scores virtually identical to those we measured for those subjects. We realize that these conversion or equivalent IQ scores derived from early school achievement test data are not to be equated on a one-for-one basis with current scores. However, we do believe that IQ score ranges provide a reasonable degree of equivalency. These achievement test scores were obtained some 15 to 20 years earlier, long before either subject began the use of cannabis, by their report to us.

Finally, we stress the commitment of the ten subjects to their religious sect and way of life. They told us and others (*10*) that members of the church do not use substances (drugs, alcohol, or psychoactive herbs) other than ganja, and we observed them to maintain a regular diet consisting primarily of vegetables, fruit, and small amounts of meat. All ten subjects (as well as other members of the church) appear to be healthy and highly functional individuals adhering to a strict religious doctrine.

JEFFREY SCHAEFFER
Department of Psychiatry and
Biobehavioral Sciences, University of
California School of Medicine,
Los Angeles 90024, and
Neuroscience Associates Incorporated,
Los Angeles 90048
THERESE ANDRYSIAK
J. THOMAS UNGERLEIDER
Department of Psychiatry and
Biobehavioral Sciences, University of
California School of Medicine

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Discharge Patterns of Hindlimb Motoneurons During Normal Cat Locomotion

Abstract. *Long-term recording from single lumbar motoneurons of intact cats revealed activation patterns fundamentally different from those seen in decerebrate preparations. In intact cats, motoneuron bursts showed marked rate modulation without initial doublets. Each unit's frequencygram generally resembled the envelope of the gross electromyogram simultaneously recorded from the corresponding muscle. Average and peak discharge rates increased for faster gaits. These findings suggest that, in cat locomotion, rate modulation is a more important contributor to force regulation than was previously thought.*

A prime objective in the field of motor control is to fully understand the relations between neuronal discharge patterns and movements. Comprehensive studies of the electrical and mechanical properties of hindlimb muscles and their motoneurons, the final output cells of the motor system, arose from the introduction of intracellular techniques (*1*) in anesthetized cat preparations (*2–8*). In contrast, until now, technical difficulties have made it impossible to investigate normal motoneuron firing patterns during locomotion. The only single-unit records obtained previously have come from unidentified motor axons in cut ventral root filaments of decerebrate cats induced to "walk" by being stimulated in the mesencephalic locomotor region of the brainstem (*9–11*).

Motoneurons in walking decerebrate cats typically fire in uniform bursts consisting of an initial doublet [a pair of spikes occurring within a brief interval, usually 3 to 10 msec (*10, 11*)] followed by a train of spikes that stabilize at a nearly constant "preferred discharge rate" (*9*) characteristic for each cell, which does not vary with treadmill speed, strength of stimulation, or duration of step cycle. Discovery of these motoneuron firing patterns had an important influence on current views of the neural control of locomotion (*4–6, 10–12*).

We have developed long-term recording methods in conscious, freely walking, intact cats (*13, 14*) in order to monitor the electrical activity of individual hindlimb motoneurons and to determine unitary axonal conduction velocity and muscle of destination. Records obtained from more than 100 motoneurons revealed striking differences from the characteristic decerebrate cat patterns.

Twelve cats trained to walk at several speeds on a motorized treadmill had electrodes and transducers implanted under deep pentobarbital anesthesia; they were allowed to recover for several days before recording sessions began. As many as a dozen fine, flexible, insulated wire electrodes (Fig. 1, A and B) were inserted in the fifth lumbar ventral root (L5 VR) through a small laminotomy, an approach recently shown successful for recording from afferent fibers (*15–19*). Root electrodes were of a modified "hatpin" design (*14, 20*): a recording surface was exposed by obliquely cutting a stiff, short iridium or platinum-iridium insulated wire (easily inserted into soft tissue), which was welded to a compliant gold lead (thereby allowing the electrode to "float"). Extracellular recordings from ventral root axons coursing out of the spinal canal were thus made in a region of low relative movement, ensuring secure coupling between electrodes and single motor units. Over a period of several weeks, electrodes appeared to drift slowly and usually sampled new units from day to day. Occasionally a unit identified by criteria shown in Fig. 1 (C and D) could be recorded on three to five consecutive days.

About half of the motor axons contained in L5 VR course along the femoral nerve and supply the anterior thigh muscles. The technique of spike-triggered averaging (*14, 21*) (Fig. 1) was used to determine the axonal conduction velocity and muscle of destination of these motoneurons. Averages were obtained from correlated potentials recorded by electrodes in a cuff implanted around the femoral nerve (*14*) and by indwelling electromyogram (EMG) electrodes sampling each of the anterior thigh muscles. Of 104 discriminated ventral root units, 32 showed correlated femoral nerve potentials (for example, Fig. 1C) and thereby their identity and conduction velocity in the alpha-beta range were ascertained (*22*). Seven units projected to vastus intermedius, four to vastus medialis, four to vastus lateralis, eight to rectus femoris, and nine to sartorius.

Typical features seen for most L5 motoneurons during walking, exemplified in Fig. 2 by a rectus femoris unit, can be generalized as follows: (i) All active motoneurons (flexors as well as extensors) exhibited a single burst of activity per step. A unit was reliably recruited as the rectified, low-pass-filtered EMG of its muscle crossed a given level for each gait speed. (ii) Once a unit was recruited, its frequencygram was continuously modulated, and it resembled the rectified, filtered EMG of the parent muscle. (iii) The first interspike interval was usually longer than the average interval in that burst. Initial doublets were never seen for most units. Fewer than 10 percent of all units exhibited initial doublets during walking. In these units, doublets were generally present only on occasional steps. (iv) Average and peak discharge rates increased for faster gaits (Fig. 2B).

We found the last three features surprising, since they differ systematically from what had been found in decerebrate walking, a state generally believed to arise from activation of the same spinal pattern generator responsible for coordinating normal gait (*12*). The essential differences between decerebrate and normal motoneuron activation patterns during walking are diagrammed in Fig. 2C.

Neither the identity nor the conduction velocity of motoneurons studied previously during decerebrate walking was known, since activity was recorded from cut axons (*9–11*). However, in decerebrate and in anesthetized cats, proprioceptive reflexes generally tend to recruit motoneurons in order of increasing conduction velocity (*23*). In normal cat locomotion, our preliminary data on recruitment threshold versus axonal conduction velocity (range: 70 to 120 m/sec) indicated that motoneurons with the slowest conduction velocities were also activated first. Thus, it is unlikely that the observed differences stemmed from the recruitment of different subpopulations of motor units in normal and decerebrate cats during walking (*24*).

Activation patterns found in conscious cats are of special interest because they may help elucidate three questions central to the field of motor control.

1) What is the extent of supraspinal involvement during normal locomotion? As a consequence of decerebration, the shape of the motoneuron driving function, representing the integration of all descending and segmental inputs onto the presumed spinal pattern generator, appears altered (Fig. 2C). Decerebrate cat motoneurons fire as if driven by an input of rapid onset and invariant plateau, akin to rectangular depolarizing intracellular current injections, which have been shown experimentally to produce this activity pattern (*4–6, 10, 11*). Motoneurons in normal cats appear to follow instead a smoother rising and falling function, whose peak amplitude increases with speed of locomotion. The mechanisms that account for these differences are still unclear since a number of factors may be responsible. Brainstem transection is likely to markedly affect transmission through spinal interneurons that mediate segmental reflexes (*3*), in addition to modifying the descending drive onto alpha and gamma motoneurons (*25*). Furthermore, since in decerebrate cats the hindquarters must be partially supported to ensure stable walking, this reduction in weight-bearing may affect some regulatory reflex components. Head fixation probably suppresses most vestibular inputs as well (*26*).

2) How well are normal motoneuron discharge patterns matched to the mechanical events in muscles during locomotion? The occurrence of initial doublets in decerebrate locomotion seemed to fit nicely with a characteristic contractile property demonstrated earlier for mammalian muscle, the "catch" property (*5, 27*). In muscles held isometric, a second spike closely following the initial

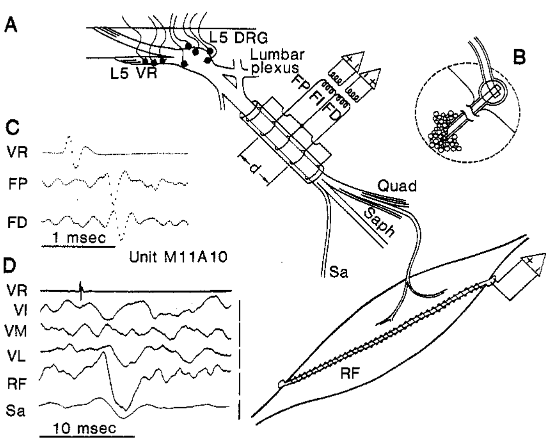

Fig. 1. (A) Location and dimensions of implanted electrodes. "Hatpin" microelectrodes were inserted through the fifth lumbar dorsal root ganglion (*L5 DRG*) or directly into ventral rootlets (*L5 VR*). A recording cuff with five circumferential electrodes was implanted around the femoral nerve (cuff inside diameter, 2.5 mm; length, 24 to 30 mm). The middle and end electrodes, shorted together, acted as indifferent (*FI*) for two tripolar differential sets centered about the proximal (*FP*) and the distal (*FD*) recording electrodes (separation d = 11.5 to 15 mm). The femoral nerve has a cutaneous branch (saphenous, *Saph*) and several motor branches that supply the five muscles of the anterior thigh (quadriceps, *Quad*; sartorius, *Sa*). A bipolar EMG electrode was threaded inside each muscle (only rectus femoris, *RF*, is shown). Indwelling EMG electrodes consisted of two platinum-iridium wires (multistrand, Teflon-coated) wound around a flexible Silastic tube (0.5 mm thick). Insulation was removed from the two wires in multiple alternating locations in order to sample the muscle differentially along its length. (B) Electrode tip size (37- or 50-μm shaft) relative to ventral root axons. (C) The identity of anterior thigh motoneurons was revealed by the technique of spike-triggered averaging (*14, 21*). Each occurrence of a discriminated spike in a microelectrode record triggered the sweep of a signal averager. Records were delayed 5 msec before averaging. As sweeps accumulated, if the axon projected through the femoral nerve cuff electrodes, correlated neural potentials were resolved at fixed latencies from the ventral root spike. (C) shows averaged records from a microelectrode (*L5 VR*; 64 sweeps), the proximal femoral cuff (*FP*; 1024 sweeps), and the distal femoral cuff (*FD*; 1024 sweeps). The latency from *FP* to *FD* rendered the axonal conduction velocity (104 ± 5 m/sec for this unit). (D) Spike-triggered, averaged records of ongoing EMG from the five thigh muscles: vastus intermedius (*VI*), vastus medialis (*VM*), vastus lateralis (*VL*), *RF*, and *Sa*. Each muscle record was averaged for 2048 sweeps. Vertical bars indicate 50-μV calibration for each trace. Although there was some cross-talk in records from neighboring muscles because of electrode design, the EMG potential of this motor unit was detected primarily by the *RF* electrodes, suggesting that the motoneuron projected to *RF*.

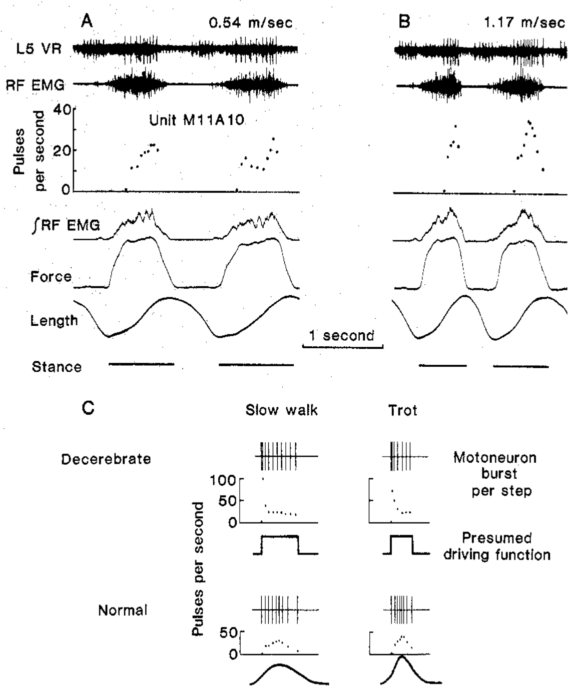

Fig. 2. (A and B) Raw record obtained from an *L5 VR* microelectrode (top trace) included a motoneuron active during extension (large spikes). This was the unit of Fig. 1, assumed to innervate *RF*. There was a second unit active during flexion (smaller spikes). Other traces: simultaneously recorded *RF EMG*; instantaneous frequencygram of the discriminated extensor motoneuron; rectified, low-pass filtered *RF EMG*; force generated by the five anterior thigh muscles, recorded by a force transducer implanted on the patellar ligament (*8*); and length recorded by a distensible gauge (*16*) implanted in parallel with *RF* (lengthening upward). Records are shown for two different treadmill speeds. (C) Schematic comparison of motoneuron firing patterns in decerebrate and normal cats. Decerebrate cat data are from figure 6 of (*10*). Normal cat data are averages for a vastus medialis motoneuron from ten typical steps at each speed. In decerebrate cats, bursts start with a doublet followed by a train at a uniform rate. In normal cats doublets usually do not occur, and the frequencygram is more modulated. At faster gaits (trot) decerebrate bursts are briefer but the preferred discharge rate is unchanged; normal cats show increased firing rates at faster gaits. In decerebrate cats, motoneurons appear to follow a rectangular step input of invariant amplitude, regardless of gait speed. Normal motoneurons fire as if driven by a gradually rising and falling function whose amplitude depends on gait speed.

one can mediate a substantial increase in the total tension produced by a motor unit, an increase that can persist throughout the duration of a burst even if the unit subsequently fires at a lower rate. A recent search for "optimal" patterns of muscle activation (*6, 28*) has confirmed that closely spaced doublets followed by low-frequency trains are the most efficient way of maximizing tension output. However, whereas isometric conditions are an adequate model of maintained posture, muscles rarely operate isometrically during locomotion: extensor muscles often lengthen considerably during the generation of active force (Fig. 2), while flexor muscles often shorten against minimal loads when active. It will be of interest to study the effect of such length changes on the tension output of single units subjected to discharge patterns like those seen during walking.

3) What is the relative importance of motor unit rate coding, compared with recruitment of additional units, in the regulation of force? In decerebrate cats, motoneuron discharge rates settled at stable plateaus in spite of increased reflex activation (*29*) or increased brainstem stimulation (*9*), indicating that over most of the operating range of a muscle, further increases in tension had to be mediated by the recruitment of additional motor units. Our data imply that rate-coding of already recruited units is a more important mechanism of tension production during normal walking than was previously thought (*4–6, 29, 30*). Rather than maximize the rate of rise of tension or the tension output per motoneuron impulse, a priority of normal locomotor programs may be to regulate motoneuron firing in a way that matches closely and takes advantage of the full dynamic range of each active motor unit.

J. A. HOFFER
M. J. O'DONOVAN*
C. A. PRATT†
G. E. LOEB

Laboratory of Neural Control, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20205

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31. We thank M. Chapman for training and caring for the cats and L. D. Abraham, R. E. Burke, and Z. Seltzer for comments on the manuscript.

* Present address: Department of Biology, Yale University, New Haven, Conn. 06511.

† Present address: Department of Physical Education, Health and Recreation Studies, Purdue University, West Lafayette, Ind. 47906.

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