A STUDY OF THE EFFECTS OF DIRECT PYRAMIDAL STIMULATION ON SOME LUMBAR SPINAL MOTONEURON POPULATIONS IN THE DOG

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1962

Submitted to the faculty of the Graduate College of
the Oklahoma State University
in partial fulfillment of the requirements
for the degree of
DOCTOR OF PHILOSOPHY
July, 1967

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PYRAMIDAL STIMULATION ON SOME
LUMBAR SPINAL MOTONEURON
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ACKNOWLEDGEMENTS

The writer wishes to express his appreciation to the members of the faculty of the Department of Physiology and Pharmacology, Oklahoma State University, for their encouragement and support throughout the writer's graduate program. The writer is particularly indebted to Dr. J. E. Breazile for his support of this project and his reading of this manuscript.

The writer is also indebted to Mrs. Rosemary Crow, Librarian, College of Veterinary Medicine, Oklahoma State University, and to Mr. Guy Logsden, Reference Librarian, Oklahoma State University, for their kind help in obtaining the material essential for the review of the literature.

Without the patience and sacrifice of the writer's wife, Nance, this project could not have reached fruition. Her encouragement and sacrifices are gratefully acknowledged.

This project was supported in part by Grant 5 R01 NB05362-03, NINDB and in part by Project S-1240, Agricultural Experiment Station, Oklahoma State University.

Finally, no list of acknowledgements would be complete without mention of the special contribution made by Dr. Karl Frank, Bethesda, Maryland, to the writer's progress. Although not directly connected with this project, Dr. Frank, and the personal contact with him provided a continual source of encouragement and a model for emulation. This acknowledgement in no way implies, nor intends to imply, express approval by Dr. Frank of the work reported herein.

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CHAPTER I

INTRODUCTION

The basic mechanisms for the control of somatic musculature are well developed at the segmental level. The functional and structural bases for maintenance of posture, avoidance of noxious stimuli and stereotyped pacing movements appear to be present within the intraspinal organization. In the phylogenetic development of the central nervous system, a number of higher centers have evolved during the process of progressive encephalization which project onto and influence the activity of these basic intraspinal mechanisms and bring such involuntary, reflex mechanisms under more direct conscious control. These suprasegmental motor control systems provide a greater adaptability of somatic movements to the requirements of the environment of the animal.

In mammalian nervous systems, the development of such suprasegmental motor control systems reaches its peak in the organization of the motor areas of the cerebral cortex and their major efferent projection to the spinal motor nuclei, the pyramidal tract. The pyramidal tract is a system peculiar to the mammalian order and has long been recognized as the classical example of a suprasegmental motor control system. This system of fibers is one of the most prominent fiber tracts in the mammalian central nervous system and because of its prominence and demonstrated importance in motor activity, has been the subject of numerous experimental studies.

Prior to 1941, evidence supporting the role of the cerebral cortex and the pyramidal tract in motor control relied largely upon the elicitation of gross somatic movements in response to electrical stimulation of the motor cortex or its efferent system. The role of these areas and their projections in guiding willed movements was further substantiated by the obvious loss of voluntary control following lesions of this system. Such studies conclusively demonstrated, both structurally and functionally, that this system was highly organized in a somatotopic manner. This type of experimental examination undoubtedly reached its peak with the demonstration that individual muscles, and not different movements, were the basis for this organization.

It remained for Lloyd (99) to demonstrate that, at least in subprimates, the pyramidal system projected onto, and functioned through, the organization of the interneuronal system of the spinal cord. Thus, the pyramidal projections acted as one of several systems which were capable of biasing somatic activity which, at least in large part, was determined at the segmental level. This system of fibers would then be capable of steering the basic spinal activity in the direction which would be required to effect the movements to produce a desired position of the limb in space in orientation to an object.

More recent electrophysiological evidence substantiated anatomical data that a more direct pyramidal control of spinal motoneurons exists in the primate. This provides the basis for the phasic and highly individualized movements, such as the finely controlled manipulative motions, which are characteristic of this mammalian order. The loss of this system in primates is followed by a much more severe and prolonged loss of motor control than in lower mammalian forms. An understanding

of this system therefore has implications in man in whom lesions of this system are occasionally produced by cerebral vascular accidents.

To be certain, the pyramidal system is not the only suprasegmental system capable of controlling willed movements, although, as pointed out above, as one ascends the phylogenetic scale, this tract assumes a greater and greater role in such activity. Even in primates, loss of the pyramidal tract does not completely abolish voluntary motor activity although certain phasic digital manipulations are irretrievably lost.

Although the motor cortex was first mapped in the dog (57), no reports of electrophysiological investigations of the influence of the pyramidal system on spinal motoneurons have yet been made in this species. The purpose of the investigations reported herein was to study the influences of pyramidal tract volleys on spinal motoneuron populations in the dog. In particular, the effect of such activity on motoneuron populations innervating antagonistic muscles effecting movements of the tarsus joint was studied since considerable information is available concerning pyramidal influences on these motoneurons in the cat and primate.

CHAPTER II

REVIEW OF LITERATURE

In view of the extensive literature available concerning the structure and function of the pyramidal tract, an exhaustive review of this material is beyond the scope of the present paper. This review is intended, rather, to be representative of the current state of knowledge of this system. A brief review of studies of electrical stimulation of the cortical areas which give rise to the axons of the pyramidal tract is followed by a review of the anatomy of the pyramidal tract. Representative results of the effects of cortical ablations and pyramidal sections on the motor performance of the different species studied is presented as evidence of changes in voluntary movements resulting from loss of the pyramidal system. Knowledge of the properties of the cortical neurons which contribute their axons to the medullary pyramids and the spinal influences of impulses in these axons is outlined. Finally, a brief review of the basis for the primary experimental tool employed in the present investigations, monosynaptic excitability testing, is presented.

Cortical Stimulation Studies

Since the pioneering work of Fritsch and Hitzig (57), in which they mapped out the excitable cortex of the dog in great precision, numerous investigators have reported the results of electrical stimulation of the

cortex of a variety of species, elucidating the motor areas. In primates, the motor cortex is organized in an area rostral to the central sulcus, the precentral gyrus (67, 175). Electrical stimulation of this area elicits movements of the contralateral limbs (134, 175); ipsilateral limb responses have been reported less frequently (134). The primary sensory cortex of primates is the postcentral gyrus (179) so that the sensory and motor patterns represented on the surface of the cortex are mirror images of one another, becoming adjacent at the areas representing the nose and limb apices along the central sulcus (181). Both flexor and extensor muscles of the extremities are represented in the motor cortex of primates, although flexor muscle responses are more easily elicited by electrical stimulation of the cortex (134) and flexor muscles have a more extensive cortical representation than do extensor muscles (38, 141).

The motor cortex of subprimates, in which a central sulcus has not yet developed, lies in proximity to a possible homologue of the central sulcus, the postcruciate sulcus or "dimple". Thus, the motor cortex of the dog occupies the posterior cruciate and posterior sigmoid gyri (19, 20, 39, 57). This area contains a broad lamina of large pyramidal cells (30). The motor area extends into the cruciate sulcus of the dog (39) and the cat (49, 97). The cruciate sulcus of the cat and dog contain a large population of pyramidal cells (30, 97) and represents a buried region containing an important motor representation (49). As in the primate, contralateral responses are most commonly seen following eletrical stimulation of the motor cortex of carnivores (97), although ipsilateral movements may sometimes be seen (49). Flexion of the extremity is the most readily obtained response but extension and more

complex movements can be elicited by stimulation of different cortical points (49). The primary sensory cortical area of the dog is located in the posterior sigmoid and coronal gyri, with its rostral limit falling 2-4 millimeters caudal to the cruciate sulcus (129). Thus, there is considerable overlap of the sensory cortex with the motor cortex in the dog in contrast with the more complete separation of the two areas in the primate (181), but in general the motor map of the dog is slightly offset rostrad to the sensory map (19, 20, 39, 129).

A second motor map has been delineated in the cortex of the dog on the anterior ectosylvian gyrus (173). Electrical stimulation of this area causes contralateral and sometimes ipsilateral limb movements. The threshold for the effects elicitable from the anterior ectosylvian gyrus is 2 to 4 times higher than for stimulation of the primary motor area (173). This secondary motor area on the anterior ectosylvian gyrus is functionally independent of the primary motor area (173) and lies in proximity to the secondary somatosensory cortex (129).

By recording the tension developed in different muscles in response to cortical stimulation in the monkey, Ruch, et al. (38, 141) found that not only individual muscles but even different parts of the same muscle have a focal point in the cortex from which contraction of that muscle is elicitable at lower threshold and shorter latency relative to other muscles. They conclude that there is a topographical dissociation of cortical points for individual muscles. Thus, the representation in the motor cortex is one of individual muscles and not one of movements (38). No positive correlation between excitable foci in the motor cortex and aggregates of large pyramidal cells has been found (50, 97). The only area in the cortex of the cat which is consistently excitable and consistently contains large pyramidal cells is the cruciate sulcus (97).

The results of cortical stimulation experiments are difficult to interpret from the standpoint of pyramidal function since other descending pathways may be activated as well (see section on Pyramidal Tract: Anatomy). This was conclusively demonstrated by Tower (164, 165, 166) who showed a residual extrapyramidal motor activity which could be elicited by cortical stimulation following transection of the medullary pyramid in both the cat (164, 165) and monkey (166). In the primate, the regions of the cortex from which movements of the extremities can be most easily evoked is the same after as before pyramidal section and the somatotopic organization is the same for both pyramidal and extrapyramidal pathways (21). The threshold for the production of movements by stimulation of the pyramidotomized cortex is higher by at least 50% in both the primate (21) and the cat (72). The movements evoked from the pyramidotomized cortex are similar to those elicited from the normal cortex (21 72), although inhibition of tonic contraction was the most predominant characteristic of stimulation of the pyramidotomized cortex in Tower's experiments (164, 165, 166). This was interpreted as a supraspinal dissociation of cortical excitation and inhibition. The pathways mediating the impulses for extrapyramidal volitional control of movements are not yet completely understood but they probably utilize pathways with a conduction time comparable to that of the pyramidal system (72) in the ventral, ventrolateral and lateral funiculi of the spinal cord (83, 95, 143).

The patterns of movements produced by electrical stimulation of the medullary pyramids are no less difficult to interpret in the form of meaningful patterns than those produced by cortical stimuli. Although the usual movement obtained following pyramidal stimulation is a

brisk flexion of the contralateral hind limb, evoked movements may vary from animal to animal and even from time to time in the same animal. Reciprocal contraction of antagonistic muscles may be seen in response to pyramidal stimulation, although this is not an absolute relationship and co-contraction of antagonists may be seen. The results of movements produced by pyramidal stimulation may be taken as indicative that variations of response to cortical and pyramidal stimulation depend on complex integrative functions at the spinal as well as at the supraspinal level (86).

Pyramidal Tract: Anatomy

The pyramidal tract is a well-defined cortical efferent system composed of fibers of varying sizes. This tract is the classic example of a suprasegmental motor control system. The majority of the larger fibers of the pyramidal tract arise from the cortical regions containing large pyramidal cells (Betz cells) (112); this corresponds to the classical motor cortex and adjoining cortical areas (44, 85, 112). The pericruciate cortex of the cat is the origin of two-thirds of the pyramidal fibers less than 6 microns in diameter and of at least 80% of those fibers larger than 6 microns in the medullary pyramids (44). About 3% of the fibers of the pyramids of the cat are large fibers having a conduction velocity greater than 60 meters per second and these originate from the pericruciate cortex (85). In the cat, a smaller number (10%) of pyramidal fibers originate in more rostral regions, the gyrus proreus and anterior sigmoid gyrus. Thus, nearly all the fibers of the medullary pyramid originate in the rostral one-third of the cortex; contributions from the parietal, temporal and occipital lobes are small or lacking (44).

In their course through the internal capsule, cerebral peduncle and pons there is a somatotopic organization of fibers from these different cortical regions. However, the overlap of fibers from different cortical areas is considerable and increases from rostrad to caudad until, in the pyramid, the only detectable somatotopic localization is some medial concentration of fibers from face areas of the cortex and some lateral concentration of fibers of sensory cortex origin (13).

A constant feature of the pyramidal tract is a decussation in the lower part of the medulla (91). The number of fibers in the pyramids just rostral to the pyramidal decussation varies widely depending upon the species under consideration (90, 91). Man has the largest number of fibers in the pyramids, exceeding 1,000,000, followed by monkeys with approximately 500,000 fibers (90). By comparison, the pyramid of the dog contains approximately 285,000 fibers and that of the cat 186,000 (91). In man, about 4% or 40,000 of the fibers of the pyramids are large diameter fibers, roughly between 10 and 25 microns. The majority of the fibers are between 1 and 5 microns. The histological picture of the pyramids of the dog is similar to that of man but there are fewer large diameter fibers and more intermediate sized fibers. The cat differs from man and dog in that the pyramids contain no large sized fibers (91). All the fibers contained within the medullary pyramids are apparently descending fibers since the presence of ascending fibers in the pyramids has been confirmed by neither anatomical (76) nor electrophysiological (87, 121) investigations.

Cortical and pyramidal lesions in the monkey result in the degeneration of three spinal pathways; a large crossed lateral corticospinal tract and small uncrossed lateral and ventral corticospinal tracts (37,

96). The crossed and uncrossed lateral tracts originate from both the pre- and postcentral gyri and their axons are intermingled in the lateral funiculus of the spinal cord. The ventral uncrossed tract originates from the precentral gyrus (motor cortex) but not the postcentral gyrus (sensory cortex) (96). These spinal tracts exhibit no somatotopic organization of axons originating from the forelimb and hindlimb areas of the cortex (13, 96, 149). Bilateral pyramidal degeneration in the spinal cord of the dog following cortical ablations was reported by Sherrington (148, 149, 150). Four tracts (crossed lateral and ventral tracts and uncrossed lateral and ventral tracts) have been traced to lower lumbar levels in both the dog and cat (19, 36, 116), but the majority of fibers are crossed.

Fibers from all components of the corticospinal system enter the spinal gray matter (36, 96, 116). In the monkey, a few axons of the crossed lateral corticospinal tract recross in the spinal commissures to terminate in the ipsilateral spinal gray matter (18, 71, 96) while the majority of the axons of the uncrossed ventral tract cross in the ventral spinal white commisure to terminate in the contralateral spinal gray matter (96). Other axons of the uncrossed ventral tract terminate ipsilaterally and the uncrossed lateral tract of the monkey remains uncrossed (96). The crossing of the uncrossed ventral tract and recrossing of the crossed lateral tract also occur in the commissures of the spinal cord of the cat (36, 96).

In both man (147) and monkey (37, 96, 125) anatomical evidence of a direct monosynaptic corticomotoneuronal connection between pyramidal tract fibers and spinal motoneurons is available. This system is somatotopically organized (96, 125) and originates chiefly from the

precentral gyrus (96). These direct corticomotoneuronal connections are lacking during the first few days of postnatal life in the monkey, with the bulk of these connections being established in the first 8 months of life (82).

No direct monosynaptic corticomotoneuronal projections exist in the cat (36, 116) or dog (19, 28). In the cat, pyramidal fibers terminate in Rexed's laminae IV-VII (135, 136) throughout the length of the spinal cord (116). Projections from the motor cortex are to the lateral parts of laminae V, VI and the dorsal part of lamina VII while the projection from the sensory cortex is to the medial parts of laminae IV and V and the dorsomedial part of lamina VI (116). This is in accord with Kuyper's findings in the monkey of a motor cortex projection to interneurons and motoneurons and a sensory cortex projection to sensory cell groups (80, 81) with the notable exception of a lack of a direct projection to motoneurons in the cat (36, 116).

In addition to the direct corticospinal projections via the pyramidal tract, numerous projections to subcortical structures which are known to influence spinal control of musculature have been documented. An important contingent of this cortico-subcorticospinal projection system is a somatotopically organized corticorubrospinal system (117, 137, 139). The motor cortex projects onto the ipsilateral nucleus ruber in a somatotopic pattern which agrees with the somatotopic organization of the rubrospinal projection (117, 139); some bilateral projections to the nucleus ruber from the supplementary motor area and gyrus proreus have been noted (137). Functional correlates of this corticorubrospinal system have been demonstrated (159, 167). The corpus striatum also receives cortical projection fibers from all parts of the cortex; these

fibers are probably internal capsule collaterals (174). The projection from the motor cortex to the corpus striatum is a bilateral one with contralateral projection fibers crossing in the corpus callosum (31). Fairly direct corticostriate connections have been confirmed electrophysiologically (92, 140). A modest number of connections have also been traced from the gyrus proreus, supplementary motor area, primary sensorimotor area and secondary sensory area in the cat to the substantia nigra. This projection is chiefly ipsilateral; however, as with the corticorubral projection (137), a few crossed fibers from the gyrus proreus and supplementary motor area have been found (138). Lesions of both the substantia nigra and the corpus striatum have been incriminated as participating in the genesis of motor disturbances (43, 73). The motor cortex also projects to the pontine and medullary reticular formation which give origin to reticulospinal pathways (22, 124) and to the cerebellum via the corticopontine and cortico-olivary pathways (22, 156).

In man and monkey, fibers from the motor cortex project directly to all cranial motor nuclei (79, 80, 81) except those motor nuclei concerned with eye movements (cranial nerves III, IV, VI) (79). In cats, this projection to cranial nerve motor nuclei is an indirect one, probably via interneurons in the reticular formation (171).

Corticofugal fibers to the nuclei gracilis and cuneatus (22) and to sensory cell groups of the trigeminal complex (22, 80, 81) have been described. In the monkey, these projections have been shown to originate primarily from the postcentral gyrus (sensory cortex) and may be considered analogous to the projections from this same area to the dorsal gray of the spinal cord (80, 81). Pyramidal modifications of sensory

information at the level of the spinal cord (106), dorsal column nuclei (1), thalamus (151) and cortically evoked presynaptic inhibition in the trigeminal complex (46, 47, 155) represent the functional correlates of these projections.

Cortical Ablations and Pyramidal Sections

Unilateral ablations of the motor cortex (Brodmann's area 4) in monkeys result in a contralateral hypotonic paresis (45, 146), although spasticity following such lesions has been reported (50). A permanent loss of fine, precise movements is particularly noticeable if the distal extremities are involved (45, 146) and exploratory reactions with the hand and fingers do not recover after area 4 ablations (50). Gross movements, including walking, are still possible (146). Monkeys with bilateral ablations of area 4 have a clumsy, ataxic gait in addition to loss of finer movements (146) but the muscular tonus remains approximately normal (45). The precentral gyrus is thus essential for control of movements directed into the environment which orient the extremity to an object (50). Unilateral ablations of the motor cortex in the dog and cat produce little permanent disturbance in normal movements although placing reactions, tendon reflexes and tone may be depressed (125, 148).

Section of corticospinal fibers at the level of the cerebral peduncle in monkeys also produces a severe impairment of voluntary movement (27, 50, 172). This procedure is followed by complete, or nearly complete, flaccid paralysis of the contralateral extremities (26, 27). Any persisting movements are seen only at proximal joints. Recovery of some skilled movements is possible but may require as long as a year and never reach a level comparable to that seen prior to the pedunculotomy.

The permanent impairment involves both speed and strength of muscular contraction. Bilateral pedunculotomy causes further impairment of the function of the ipsilateral extremities, suggesting some degree of ipsilateral control by the motor cortex (27).

Section of the medullary pyramids in monkeys produces a similar picture of impairment (50, 95, 143). The resulting paresis is not persistent (95, 143) and within a few days following the pyramidotomy, the animals are able to stand and walk (50, 95). Independent finger movements never return and all movements are slower following pyramidotomy (95). Motor deficits following pyramidotomy in the cat are limited to the contralateral extremities (36, 94, 164). The signs of pyramidotomy in the cat diminish after the first few post-surgical days (111) and after one month the only noticeable abnormalities are weak flexor reflexes and a slight delay in contact placing (94). The posture of these animals is usually normal (36, 94) but the flexion phase of the gait may be affected (36, 94, 164). Resistance to passive movement is little changed from normal (36, 94). Extensor muscles are probably not as depressed by pyramidotomy as are flexor muscles though weakness and poor joint fixation may be taken as indications of extensor depression (164). Electromyography indicates a decrease in flexor activity but is not conclusive with regards to extensor activity (94). However, the effect of pyramidotomy on flexors and extensors may be unequal, in accord with the unequal representation of flexors and extensors in the motor cortex (164). The conclusions which can be drawn from the results of pyramidotomy is that movements can be controlled by means of other pathways (94, 143) but that phasic movements are most severely impaired, indicating that the pyramidal tract adds speed and agility to movements so that

movements can be adapted to the spatial characteristics of the stimulus (50, 94, 164).

In addition to pyramidal control of normal, volitional movements, results of transection experiments indicate that the pyramidal tract acts as the final common pathway to the segmental level for impulses mediating involuntary, dyskinetic movements (26, 34, 35).

Pyramidal Tract Neurons: Properties and Activation

Electrical stimulation of the medullary pyramids results in activation of the motor cortex (180). This activation may be recorded from the cortical surface as a potential of variable configuration and amplitude which represents both antidromic activation and orthodromic synaptic activation of cortical cells (130, 180). Much attention has been directed toward the study of single cortical cells activated in this manner. For such studies to be meaningful, cells which are activated antidromically must be distinguished from those which are activated synaptically. The criteria applied to make this distinction are: a) the unit responding to threshold stimuli to the ipsilateral pyramid must respond to single stimuli with an invariable latency and b) the unit must follow faithfully stimulation of the pyramid at repetitive rates of 100/sec. or greater (123, 162). Cells which meet these criteria are designated pyramidal tract neurons (PTNs). PTNs have been isolated from both the pre- and postcruciate cortex of the cat at depths ranging from 800 to 1800 microns beneath the pial surface of the cortex (162).

Not all PTNs respond antidromically to stimulation of the medullary pyramids with brief latency (157, 162). Two populations of PTNs have been distinguished on the basis of antidromic latency. Their latency

of response to pyramidal stimulation corresponds well with two peaks in surface cortical waves and in recordings from the subcortical white matter. It is thus likely that pyramidal stimulation antidromically activates two groups of cells whose axons conduct at different velocities (157). Neurons of the short antidromic latency population are capable of responding to pyramidal stimulation at rates of 250-500/sec. and may be isolated from 1100-1700 microns below the pial surface of the cortex. Those of the longer antidromic latency population often fail to follow stimulus rates higher than 100/sec. and are most often isolated between 700 and 1100 microns below the cortical surface (162). PTNs, especially those of the shorter latency population (162), often, but not always, show an inflection on the rising phase of the spike (123, 127, 154, 162); this inflection presumably corresponds to the A and B, or IS and SD, components of the spike of spinal motoneurons (56, 115). At high stimulus rates, this inflection becomes more prominent and the second component may fail altogether at stimulus frequencies above 250/sec. (162).

Takahashi (157) has recently differentiated these two groups of PTNs on the basis of their membrane properties and antidromic conduction velocities. A close correlation was found between axonal conduction velocity and a) spike duration, b) time to peak of the after-hyperpolarization and c) membrane resistance. The value of each parameter tends to increase with a decrease in conduction velocity. Furthermore, since the specific membrane resistance of slowly and rapidly conducting PTNs is not significantly different and the total membrane resistance would be related to the cell surface area, it appears that slowly conducting cells with a high membrane resistance are smaller in size than rapidly

conducting cells (157), a situation analogous to that existing in spinal motoneurons (75).

Both rapidly and slowly conducting groups of pyramidal fibers can be traced as far caudally as the third lumbar segment in the cat and are found intermingled in the lateral corticospinal tract (84). The majority of the fast group of fibers has a conduction velocity of 50 M/sec. throughout its course from the cortex to the lumbar spinal cord (84, 85). The slow group reaches a maximum of 24 M/sec. from the cortex to the medulla (85) and 14 M/sec. from the medullary pyramids to the lumbar spinal cord (84, 85). This decrease in conduction velocity in the medulla is attributed to a decrease in diameter following collateral distribution to the pons and medulla (85). The range of conduction velocities in the most rapidly conducting pyramidal fibers in man is 72-160 M/sec. (152).

The division of PTNs into two groups on the basis of conduction properties may have the same implications as found in spinal systems and, indeed, may be a general principle governing all motor systems. Activity in small PTN units is probably associated with simple stereotyped movements, postural adjustments and even slow walking (60). Performances of an action requiring movements of a distal part may be associated with an increase in activity of larger units (54, 55, 60). PTNs with high conduction velocity tend to be phasically active in relation to movement while units with low conduction velocity tend to be tonically active in the absence of specific movements and show either increases or decreases of this tonic discharge during movement (54). Thus, large, rapidly conducting pyramidal fibers may terminate in relation to motoneurons controlling distal musculature and control the phasic element of

of motor activity while small, slowly conducting pyramidal fibers may terminate in relation to motoneurons controlling proximal musculature and participate in the tonic phase of pyramidal function (23). In addition, an autonomic function has also been suggested for very small pyramidal fibers (169).

Antidromic conduction over PTN axons after pyramidal stimulation is followed by a sequence of early depression of the PTNs followed by first a facilitation and then a late depression (9, 24, 77, 78). The facilitatory phase is due, at least in large part, to recurrent facilitation of rapidly conducting PTNs induced by impulses in collaterals of slowly conducting PTNs (77, 158). Recurrent inhibition has also been attributed to PTN axon collateral activity (78, 154).

Stimulation of the central end of cut peripheral nerves causes a localized potential change in both the classical sensory and motor cortical areas (110). That the activation of the motor area involves PTN activation has been repeatedly confirmed in studies (29, 123, 162, 163) which show that PTNs receive cutaneous input from broad receptive fields. A majority (72%) of PTNs respond to stimulation not only of the contralateral forepaw but also to stimulation of at least one other paw, and many PTNs have bilateral receptive fields (123). Cutaneous afferents from the contralateral forelimb project through both the dorsal funiculi and the spinocervical tract to both the sensory and motor cortices. The projection over the dorsal funiculi seems to activate the sensory cortex most effectively and the spinocervical tract seems to activate the motor cortex most effectively (118).

Cortical neurons of the motor cortex other than PTNs are activated by group I muscle afferent volleys in contralateral forelimb nerves but

not hindlimb nerves of the barbiturate-anesthetized cat (119). Group I muscle afferents project exclusively through the dorsal funiculi to the caudal part of the motor cortex (118). Extensive convergence of effects not only from muscle groups working at different joints but also effects from antagonistic groups at the same joint have been noted (119). This convergence apparently occurs at or before the level of the thalamic relay (8).

PTNs may be activated also by discharge of PTNs of the opposite hemisphere (10, 123). Electrical stimulation of the opposite hemisphere can evoke PTN firing only when the stimulating electrodes are on a restricted "excitatory" area roughly corresponding to the recording site. Small displacements (0.3 mm) of the electrodes from this excitatory area make the stimulus ineffective in activating PTNs of the opposite hemisphere (10). These effects probably are mediated over the rostral part of the corpus callosum (123).

Short latency responses can be evoked in PTNs by stimulation of the nucleus ventralis lateralis, nucleus ventralis anterior and centrum medianum of the thalamus and by stimulation of the red nucleus (145). Stimulation of the nucleus ventralis lateralis of the thalamus induces EPSPs in PTNs with a latency that suggests monosynaptic or, at the most, disynaptic connections. Such short latency excitation is exerted only on rapidly conducting PTNs; slowly conducting PTNs receive only secondary, long latency influences from this nucleus. This nucleus acts as the thalamic relay for cerebellar influences to PTNs and the electrical stimulation of the brachium conjunctivum results in PTN activation which shows similar characteristics (182). Electrical stimulation of the mesencephalic and diencephalic reticular formation and the bulbar

inhibitory reticular formation causes inhibition of spontaneous and reflexly evoked PTN discharge (29).

Electrical stimulation of the motor cortex evokes a complex wave which can be recorded from the medullary pyramids (120, 122, 183). The initial deflection in this complex wave has a stable amplitude and configuration and is relatively independent of the functional state of the cortex. These waves have a latency as short as 0.4 msec., can be elicited by stimulation of the white matter and follow high stimulus rates (120). These characteristics suggest that these waves represent activity which is initiated directly in the pyramidal tract cell and they are correspondingly called direct or D waves. Landau, et al. (88) found that the lowest threshold responses could be elicited when stimulating electrodes are thrust into the subcortical white matter and that there was a small shift in latency (0.25 msec.) over a distance of about 2 mm as the electrode was withdrawn from the subcortex into the cortex. They concluded that the D wave is primarily elicited by excitation of PTN axons in the subcortex.

The D wave is followed by variable waves which recur at intervals of 2.0-2.5 msec. (122). These variable waves are more susceptible to anoxia and anesthesia than D waves, and do not follow high stimulus rates (120, 183). It is thought that these waves are initiated by synaptic bombardment of PT cells and they are correspondingly called indirect or I waves. Patton and Amassian (120) have shown that D and I waves may be mediated by the same pyramidal units in some cases. They suggest that cortical interneurons activated by a stimulus applied to the surface of the cortex thus not only cause facilitation and/or firing of distant units not directly activated by the stimulus but also permit

re-excitation of directly excited units. The activity of cortical interneurons may thus prolong the period of pyramidal discharge for up to 15-20 msec. after a single cortical stimulus.

The type of response elicited from the pyramids by cortical stimuli may vary depending upon the polarity of the surface cortical stimuli (58). Both anodal and cathodal stimuli evoke both D and I waves, but the D wave evoked by surface-anodal stimulation can be elicited at lower stimulus intensities than the corresponding D wave evoked by surface-cathodal stimulation (58, 65). The D wave evoked by surface-anodal stimuli is relatively stable in amplitude and configuration during repetitive stimulation and is open to synaptic modification; the D wave elicited by surface-cathodal stimuli may be potentiated by repetitive stimulation and is depressed by preceding synaptic volleys. Differences in I waves elicited by anodal or cathodal stimulation are less apparent (58). Thus, the mode of cortical stimulation chosen for use in studies of cortically-evoked activity may play an important role in the responses obtained.

Spinal Influences of Impulses in the Pyramidal Tract

Electrical stimulation of the motor cortex in primates evokes a discharge in contralateral peripheral nerves, the nature of which is dependent on the nature of the cortical stimulus. Single cortical stimuli elicit only a response with a long latency; stimuli applied at a frequency of 10-20 pulses/sec. cause a response, the first deflection of which has a shorter latency than with single stimuli (16). This short latency discharge follows a characteristic time course of waxing and waning, first appearing some 2 seconds after the onset of the

repetitive stimulation. This discharge reaches its maximum amplitude and then, later, disappears (14). The difference in the latency of this early response in the L5 ventral root and the latency of pyramidal impulses arriving at the L5 level is 0.7 msec. This difference in latency includes conduction in the pyramidal collaterals so that the synaptic delay would be less than 0.7 msec. Since this is about the same delay as for the monosynaptic reflex, it is concluded that pyramidal tract fibers activate motoneurons monosynaptically in primates (14, 16, 17). This has been confirmed more recently utilizing the difference in latency between arrival of pyramidal impulses and the latency of the onset of the excitatory postsynaptic potential (EPSP) recorded intracellularly (89). Monosynaptic activation of ipsilateral as well as contralateral forearm muscle motoneurons in the monkey has been reported (15, 16).

Lloyd first showed that activation of motoneurons in the cat required relay through spinal interneurons (98, 99). In the cat, the minimum delay between the arrival of pyramidal impulses and the onset of the EPSP in spinal motoneurons is 3 msec. (64), indicating relay through two or more synapses. In his studies, Lloyd (98, 99) utilized a preparation similar to that used in the studies reported here. He used cats in which the brain stem was transected to avoid antidromic cortical activation and transected a second time at a lower level to avoid activation of other descending pathways by spread of stimulus current. Lloyd's index of influence on spinal motoneurons was the change in amplitude of the monosynaptic reflex discharge (see section on Monosynaptic Excitability Testing) evoked by dorsal root stimulation. He failed to show changes in amplitude with one or two pulse train

stimulation to the pyramid; significant modulation of the monosynaptic discharge required three or more pulses to the pyramid with concomitant summation of pyramidal influences. Facilitation of the monosynaptic discharge was the predominant effect seen and occurred after a latent period of 12 msec. Lloyd's failure to demonstrate an effect with pulse trains of less than three pulses may have been due to barbiturate levels, which, though low, were used to control the irritability of the preparations.

More recent studies utilizing monosynaptic excitability testing to delineate the influences of pyramidal impulses have been carried out on so-called "pyramidal" preparations (5, 131, 133, 168). This type of preparation consists of transverse electrocoagulation of the brain stem sparing only the pyramids. Fibers traversing the medullary pyramids are then activated by electrical stimulation of the motor cortex.

In the "pyramidal" cat, the earliest effect of cortical stimulation on the dorsal root-evoked monosynaptic discharge is seen at stimulus intervals of 7-9 msec. This effect consists of facilitation which continues for up to 30-35 msec.; inhibition of the monosynaptic discharge then occurs and continues up to about 80 msec. (5). In contrast, in the "pyramidal" monkey, the onset of cortical facilitation is seen when the cortical stimulus precedes the test stimulus of the dorsal root by 2.3 msec. This initial brief phase of facilitation is followed by inhibition at cortical stimulus-dorsal root stimulus intervals of 3.6 msec. Facilitation is seen again when the cortical stimulus-dorsal root stimulus intervals are 4.5 msec. (131).

Pyramidal volleys cause effects on the monosynaptic reflex evoked by stimulation of peripheral nerves to flexor muscles of the hind limb

of the "pyramidal" cat which are similar to those found when the dorsal root is the source of the test stimulus. Maximum facilitation of the peroneal nerve-elicited discharge is seen at intervals of 10-15 msec. after the pyramidal volley. Inhibition is not always exerted on peroneal nerve motoneuron populations and facilitation may continue for intervals up to 70-80 msec. following cortical stimulation. Compared with the dorsal root-evoked discharge, pyramidal facilitation of the peroneal nerve-evoked monosynaptic discharge is greater (5, 168).

In contrast to the effect on motoneuron populations innervating flexor muscles of the rear limb, the first effect seen on extensor motoneuron populations in the "pyramidal" cat is an inhibition of the monosynaptic discharge. This inhibition is evident at stimulus intervals of 5-18 msec. and is followed by a period of no effect. Inhibition again becomes evident at intervals of 30-40 msec. and continues up to 60-80 msec. (5). In the "pyramidal" monkey, the pattern of effects of pyramidal volleys on motoneurons supplying both hindlimb flexor and extensor muscle groups is similar. This pattern consists of an early facilitation followed by inhibition which is, in turn, followed by a late facilitation (131).

Uemura and Preston (168) showed that, in the "pyramidal" cat, pyramidal influences consist of inhibition of knee and hip extensor motoneurons and facilitation of motoneurons innervating knee and hip flexors. In primates, pyramidal volleys always produce an early facilitation regardless of the motor nucleus studied. The early facilitation of motoneurons supplying knee and hip flexor muscle groups in primates is followed either by brief inhibition or no effect which, in turn, is followed by facilitation at periods of 3-60 msec. The effect on knee

extensor motoneurons is a brief facilitation followed by inhibition for 9-10 msec.; both phasic and tonic knee extensor motoneurons receive inhibition with phasic knee extensor motoneurons receiving more inhibition than phasic ankle extensor motoneurons. Hip extensor motoneurons receive significantly more inhibition than knee flexor motoneurons. The major difference between pyramidal influences in the cat and in primates is the much shorter latency of effect in primates with the initial effect in primates always being facilitation due to monosynaptic activation of motoneurons by pyramidal tract fibers (14, 16, 17, 89, 168). A closer examination of pyramidal innervation of ankle flexor and extensor motoneurons in the "pyramidal" monkey shows that when the innervation of the lateral head of the gastrocnemius is isolated from that of the soleus muscle, both the gastrocnemius and flexor motor nuclei receive predominantly facilitation while the motor nucleus of the soleus muscle receives predominantly inhibition (133).

The pyramidal influences outlined above have been substantiated in single unit studies in the "pyramidal" cat (4). Single ventral root fibers may be caused to discharge by stimulation of peripheral nerves; the unit may be set either at a low firing level or at a high firing level by the peripheral stimulus. In fibers supplying flexor muscles set at low firing levels, prior pyramidal activation results in a marked facilitation as indicated by an increase in the firing frequency. Some flexor units also show an inhibition when biased at high firing levels. Both inhibition and excitation of fibers supplying the gastrocnemius-soleus complex may be seen (4).

The pattern of reciprocal innervation of motoneurons supplying muscle groups of the cat's hindlimb, such as has evolved from studies

of the "pyramidal" preparation, may be an oversimplification of the problem of pyramidal innervation. Engberg (53) has shown that cortical stimulation facilitates motoneurons supplying the intrinsic muscles of the cat's foot which belong to the extensor group of hindlimb muscles. Recent evidence presented by Asanuma and Sakata (11) indicates that this simple relationship of reciprocal innervation may be a manifestation of complexity in cortical mechanisms. These workers studied the effects of focal stimulation in the depths of the cortex on reflexes to muscles of the forelimb of the cat. They found that there were clusters of "effective points" within the cortex from which either facilitation or inhibition of forelimb reflexes could be evoked. Facilitatory foci were most frequently located more superficially in the cortex than were inhibitory foci and had a lower threshold than did inhibitory foci. While facilitation and inhibition of different reflexes could often be obtained from the same focus there was no meaningful correlation between such zones and the functional relationship of the muscles affected. In agreement with results commonly obtained with surface cortical stimulation (38, 141), cortical facilitation of flexor motoneurons was more commonly seen than facilitation of extensor motoneurons following depth stimulation (11). The effects of stimulation of these "effective points" within the cortex were abolished by transection of the medullary pyramids indicating that the pyramidal tract plays at least a major role in transmitting these effects. The distribution of these "effective points" in the cortex was restricted and extended along the direction of the radial fibers in the cortex; this suggests that the cortical efferent system resembles the cortical afferent systems of the sensory and optic cortices in its vertical columnar structure (11).

The recording of intracellular potentials in spinal motoneurons in response to pyramidal activation has been reported by a large number of workers (42, 64, 65, 74, 89, 113, 128, 132, 142). Excitatory postsynaptic potentials (EPSPs), inhibitory postsynaptic potentials (IPSPs) and mixed effects have been reported. The EPSPs evoked by pyramidal stimulation in the cat will summate with EPSPs evoked by dorsal root stimulation (113, 132) or with antidromic stimulation (113) to produce firing. In the "pyramidal" monkey, motoneurons may be fired by single pyramidal volleys in the absence of summating influences (132).

Pyramidally evoked EPSPs are usually complex in nature suggesting an asynchronous synaptic barrage. The duration of EPSPs may be as long as 30-40 msec. in some motoneurons. The difference in latency between the earliest arrival of pyramidal impulses at the segment under consideration and the onset of the EPSP support the concept of monosynaptic connections between pyramidal fibers and motoneurons in the primate (17, 89, 132). In the cat, the longer latency of onset of depolarization and a more gentle slope of depolarization are regarded as substantiation of a polysynaptic pyramidal-motoneuronal connection (42, 64).

IPSPs may also be recorded in response to pyramidal volleys (42, 74, 128, 132). IPSPs are more commonly seen in motoneurons supplying extensor muscles. However, as a general rule, EPSPs more commonly predominate in both extensor and flexor motoneurons. Complex potential changes with both depolarizing and hyperpolarizing components may also be seen (42, 74, 128, 132).

Phillips and Porter (128) have shown that, in the baboon, distal muscle groups receive greater monosynaptic excitatory input than do proximal muscle groups. Thus, those motoneurons supplying flexor muscles

of the digits and the wrist receive a greater density of monosynaptic connections from pyramidal fibers than do elbow flexor motoneurons while only about one-half of the motoneurons supplying adductors of the shoulder receive any monosynaptic connections. This has important implications for the control of the very fine movements required for the prehensile, environment-exploring forelimb of this animal. Similarly, motoneurons supplying distal muscle groups in the cat also receive more excitatory input than do proximal muscle group motoneurons. The slope of transient depolarization is significantly greater in distal muscle motoneurons than in proximal muscle motoneurons (42). It has been suggested that rapidly conducting pyramidal fibers terminate primarily on motoneurons supplying distal muscles while the smaller, more slowly conducting pyramidal fibers are the primary source of control of proximal limb muscles. Thus, the larger fibers of the pyramidal tract may be responsible for the phasic element of pyramidal control while the smaller fibers are essentially tonic in function (23).

The depolarization produced by the monosynaptic pyramidal-motoneuronal connections in the primate is normally below the firing threshold of the motoneuron (128). With repetitive activation of these synapses, the amplitude of the evoked EPSP increases although the size of the pyramidal volley does not increase (89, 128). This is probably significant in the normal function of the pyramidal tract (89, 128) since pyramidal tract neurons are capable of high frequency discharge (2, 126). Long duration stimulus pulses (5 msec.) evoke a high frequency discharge in pyramidal tract neurons (66, 89) which probably accounts for the efficacy of long duration pulses in eliciting cortically-evoked movements (2, 89). In the cat, the threshold for cortically

evoked EPSPs in spinal motoneurons is higher than the threshold for repetitive discharge of pyramidal tract neurons. This suggests that considerable summation is necessary to exert even minimal synaptic actions on motoneurons in this species (64).

The effect of pyramidal volleys on gamma-motoneurons parallels that on alpha-motoneurons (42, 93, 114, 176) and the discreteness of cortical representation of gamma-motoneurons is comparable to that of alpha-motoneurons (114). However, in the cat, the threshold and latency of discharge of gamma-motoneurons following pyramidal stimulation is significantly less than that for alpha-motoneuron discharge (93, 176).

Lloyd (98, 99) first showed the activation of spinal interneurons in the cat by pyramidal volleys. His results showed that single pyramidal stimuli activated interneurons and that this activity could be intensified by trains of stimuli applied to the pyramids. More recently, Lundberg and Voorhoeve (107, 108) have shown that pyramidal volleys increase reciprocal Ia inhibition and that inhibition by volleys in group Ib, II and III muscle afferents and in cutaneous afferents is increased by pyramidal activation. Reciprocal Ia IPSPs are enhanced by pyramidal volleys (108). They conclude that this is probably due to facilitation of group Ia inhibitory interneurons resulting in a facilitation of transmission from primary group Ia afferents. This has been confirmed by intracellular recordings from interneurons; interneurons activated by either group I muscle afferents, flexor reflex afferents (FRA) or cutaneous afferents all receive EPSPs following cortical stimulation (105). In addition, pyramidal impulses also activate interneurons mediating presynaptic inhibition of group Ib and cutaneous primary afferents but not group Ia afferents (6, 7, 32, 33). This depolarization of primary

afferent fibers is elicited by stimulation of the sensory cortex (7). This supports Kuypers' (80, 81) contention that the projection from the sensory cortex is predominantly to sensory cell groups.

Monosynaptic Excitability Testing

Large diameter afferent fibers (group I, 12-20 microns in diameter) of muscle nerves arise from primary endings of muscle spindles and from Golgi tendon organs (70). Those afferents arising from the primary endings of muscle spindles are designated as group Ia afferents. These afferents conduct at 105-115 M/sec. (100) and establish monosynaptic connections with motoneurons (51, 102). As Lloyd (102) expresses it: "Some muscles of the limb are linked together in synergy and antagony by monosynaptic reflex connection . . . and yet are unrelated through like reflex connection to other muscles of the limb. Certain other muscles likewise are so bound into groups. In the hind-limb several such groupings exist. Since the monosynaptic reflex paths are reserved uniquely for the mediation of stretch reflexes, the eponym of myotatic applied to such groupings is unequivocally justified, and since action in any one member inevitably must effect the others bound to it by the very nature of their reflex bond, the individuals so bound can be regarded as constituting a unit. Hence the concept of the myotatic unit. At the core of the principle of the myotatic unit is the fact of monosynapticity in reflex interconnection, which ensures that the group of muscles concerned will be coordinated in a manner appropriate to the action in being."

In the rear limb of the cat, two myotatic units concerned with movements of the ankle may be distinguished. The flexor myotatic unit

of the ankle consists of the anterior tibialis and extensor digitorum longus muscles. There is some overlap of this unit with the myotatic unit of the digits since the extensor digitorum longus also participates in the unit controlling the movements of the digits. The extensor myotatic unit of the ankle consists of the medial gastrocnemius, lateral gastrocnemius, soleus and plantaris muscles (101, 102).

Intracellular recordings of the monosynaptic EPSP indicate that synergistic muscles always show a high degree of monosynaptic interconnections. Afferent volleys in the homonymous group Ia afferents generally produce larger EPSPs than do group Ia volleys in heteronymous nerves and tonic motoneurons receive larger monosynaptic EPSPs than do phasic motoneurons (52). Such studies also indicate that some monosynaptic interconnections exist between muscles which are not usually considered to be synergistic in their action (52, 177). These unexpected monosynaptic interconnections may be indicative of co-participation of such muscles in movements more complicated than a simple flexion-extension relationship (177).

Stimulation of a muscle nerve will elicit a monosynaptic reflex discharge which can be used as a test of excitability changes in the homonymous motoneuron population (102) since the influence of group Ia afferent fibers is distributed widely, and possibly completely, throughout the motoneuron pool of a synergic unit (103, 104). The summation of influences from a number of group Ia afferents is required to elicit a monosynaptic reflex discharge (103) but the procedure is sensitive and is capable of indicating the intensity of an effect on the motoneuron pool by volleys in other pathways (102). Implicit in the use of this procedure as a measure of the average excitability of a motoneuron

population is the assumption that changes in motoneuron excitability are linearly related to the number of motoneurons which discharge in response to a test volley (70).

In the use of monosynaptic reflex discharges as a measure of excitability changes, the mean of 20 or more responses must be used because of the variability of the response (70). This temporal variation in the response amplitude is a conspicuous feature of monosynaptic reflex discharges and arises in large part from excitability fluctuations in the motoneuron membranes due to variations in the background activity of interneurons (69). Another inherent problem in the use of this procedure is that the evoked response progressively decreases as the group Ia afferents are stimulated repetitively at frequencies above 0.3 Hz, apparently due to some presynaptic mechanism (48).

CHAPTER III

MATERIALS AND METHODS

Preparation of Animals

The experiments reported in this study were conducted on dogs of varying breed, age, size and sex. A total of 33 animals were studied in these experiments. The initial induction of anesthesia was with thiamylal sodium (Surital, 0.02 mg/kg) administered intravenously to a light stage of surgical anesthesia to allow tracheotomy and intubation. Surital is an ultrashort-acting barbiturate and the animals usually returned to a light stage of anesthesia by the time preliminary preparations and tracheotomy were completed. Return of reflexly and spontaneously evoked motor activity was commonly seen at this point. Anesthesia was subsequently maintained throughout the preliminary stages of surgical preparation by the administration of ether utilizing a positive pressure resuscitator. Following transection of the medulla, animals became comatose and ether anesthesia could be discontinued. At least two hours were allowed to elapse following the discontinuation of ether anesthesia before recordings were made. After the discontinuation of ether anesthesia, somatic motor activity of the preparations was controlled by the intravenous injection of gallamine triethiodide (Flaxedil, 1 mg/kg) at approximately hourly intervals. Deep rectal temperature of the animals was monitored throughout the experiments and maintained at or above 37^{o} C by the application of heating pads to the body surface.

The ventral midline tracheotomy incision was extended rostrally; skin and fascia were dissected away by blunt dissection to expose the anterior thyroidean vein which was ligated and transected. The larynx, pharynx, trachea and esophagus were reflected laterally by blunt dissection to expose the hypoglossal nerve and hyoid apparatus. The hypoglossal nerve was severed and the lingual artery was ligated and transected. The hyoid apparatus was disarticulated and blunt dissection was continued to the level of the longus capitus muscles. Hemostasis was maintained throughout this and subsequent surgical procedures by the use of electrocoagulation in addition to more conventional techniques.

The longus capitus muscles were transected with an electroscalpel at the level of the atlanto-occipital articulation and reflected forward to their origin. Excision of the longus capitus muscles at their origin was completed by the use of the electroscalpel. The exposed surface of the basioccipital bone was cleaned with periosteal elevators rostrally between the tympanic bullae and caudally to the level of the occipital articular surface. The basioccipital bone was then removed with rongeurs from the level of the bullae to the articular surface of the occiput. The lateral extent of the opening was carried to a line just lateral to the medial extent of the tympanic bullae. A flap of dura mater was then removed to expose the ventral surface of the medulla from the corpus trapezoideum to just rostral to the pyramidal decussation.

An opening was made in the pia mater at the level of the corpus trapezoideum over one of the pyramids (usually the right) using the electroscalpel with a fine steel wire tip and low current. The wire tip of the electroscalpel was then introduced into the brain stem at the

level of the corpus trapezoideum and the reduced current was used to extend the lesion laterally and dorsally through the brain stem until the transection of the medulla was complete. As an additional assurance of complete transection, a steel microdissection needle was passed into the medulla and passed laterally and dorsally to sever any remaining structures.

The transection procedure was then repeated at a more caudal level, rostral to the pyramidal decussation. This second transection spared one pyramid, usually the left, and severed all other structures. In most experiments, the medulla between the rostral and caudal transections was removed by aspiration. All lesions were checked by gross examination of transverse sections.

The lumbar spinal cord was then exposed by dorsal laminectomy from about the level of the L2 vertebra to the lumbosacral junction. Hemostasis was controlled throughout this procedure by the use of electrocoagulation techniques. The dura mater overlying the exposed spinal cord was opened and small stainless steel wires were placed through holes made in the cut surface of the dura mater. Small hemostatic forceps were attached to these wires to pull the dura up into a hammock in which the spinal cord could rest. The exposed spinal cord was kept covered by a pool of warm mineral oil.

In preliminary experiments, the dorsal and ventral roots of lumbar segments 5, 6, and 7 were transected to be placed on stimulating and recording electrodes, respectively. In later experiments, the dorsal roots were left intact and the ventral roots of L6, L7 and S1 segments were cut to be placed on recording electrodes.

After completion of the pyramidal and spinal surgery, the animal

was placed in a stereotaxic holder (Baltimore Instruments). The spinous process of the vertebra rostral to the laminectomy was clamped in a spinous process clamp and fastened to the holder frame. The rear of the animal was elevated by a rod passed underneath the pelvis and fixed to the frame; complete immobilization of the rear of the animal was not essential. The animal could then be elevated from the bed of the holder so that respiratory excursions of the abdomen resulted in minimal movements of the spinal cord.

Both rear limbs of the animal were fixed in clamps applied to the tarsal region and attached to the holder frame. A skin incision approximately parallel to the long axis of the thigh was then made over the biceps femoris muscle group. This incision extended from a level about the proximal third of the thigh to just proximal to the stifle. After blunt dissection of the skin from the surface of the muscle, the fleshy belly of the biceps muscle was then divided by blunt dissection parallel to the muscle fibers to minimize hemorrhage. Minor hemorrhage was encountered with this procedure and hemostasis was again maintained with electrocoagulation.

The popliteal fossa was opened and the biceps was retracted to give a clear field. The fat pad of the fossa was removed to expose the sciatic nerve distal to its bifurcation into the tibial and peroneal nerves. The peroneal nerve was then severed near its entrance into the anterior tibialis muscle. The branches of the tibial nerve to the lateral and medial heads of the gastrocnemius muscles were severed and dissected free. The exposed nerves were covered with a pool of warm mineral oil and the dissected nerve branches were placed on bipolar silver stimulating electrodes.

The head of the animal was fixed in a dorsiflexed position by a bar passed through the mouth fixed to the holder frame. The edges of the incision of the retropharyngeal approach to the pyramids were retracted so that bipolar silver ball stimulating electrodes could be applied to the surface of the pyramid using a micromanipulator.

Stimulation

Peripheral nerves or dorsal roots to be stimulated were placed on bipolar silver wire electrodes. Stimuli for these structures were provided by square wave monophasic pulses from a Grass S-4 stimulator applied through an SIU-4 isolation unit. Typically, pulses of 10 microseconds duration at intensities of one to two volts were sufficient to elicit a maximal group Ia afferent volley. Stimulus intensity, in practice, was set to provide a monosynaptic discharge of near maximal amplitude.

Stimuli were applied to the surface of the pyramid through bipolar silver ball electrodes with approximately 2 mm interelectrode spacing. Square wave monophasic pulses for pyramidal stimulation were provided by a Grass SD-5 stimulator. In preliminary experiments utilizing dorsal roots as the source of test stimuli for monosynaptic discharges, 4 msec. duration pulses were applied to the pyramid at an intensity just subthreshold for the discharge of ventral root fibers. In later experiments, 0.2 msec. pulses were applied to the pyramid at an intensity sufficient to give a maximal deflection of the pyramidal tract wave recorded from the cord dorsum in the lumbar enlargement (see section on Recording).

Synchronization pulses were taken from the variable delay circuit

of the S-4 stimulator used for peripheral nerve or dorsal root stimulation. These pulses were used to trigger the SD-5 stimulator used for pyramidal stimulation. Thus, the interval between pyramidal stimulus and test nerve stimulus could be read from a dial on the front of the S-4 stimulator. These dial readings are accurate within $\pm$ 5% (Manufacturer's specifications).

Recording

Activity in pyramidal tract neuron axons in response to stimulation of the medullary pyramid was recorded by means of a monopolar silver ball electrode applied firmly to the dorsolateral cord surface in reference to a stainless steel wire electrode in contact with an exposed muscle surface. Potentials registered by this electrode were amplified by a Grass P-5 preamplifier and displayed on one beam of a dual beam oscilloscope (Tektronix 565). In this manner, the pyramidal volley could be monitored throughout an experiment without interference to other recordings. Records of this activity were recorded on Polaroid film.

Reflexly and pyramidally evoked activity in motoneurons was recorded from the ventral roots of L6, L7 or S1 spinal segments by the use of bipolar silver wire electrodes. These discharges were likewise amplified by a Grass P-5 preamplifier and displayed on the other beam of the dual beam oscilloscope. By the use of the delay circuit and beam brightener of the Tektronix 565, the monosynaptic discharge only of this channel could be selected for display with the rest of the base line being blanked. In this manner, a larger number of test discharges could be recorded on a single sheet of Polaroid film without obliteration of the base line.

The Grass P-5 preamplifier has amplification capabilities of 35, 700 or 28K times with variable attenuation in 10 steps of 3 db/step in each range. This provides a maximum useful sensitivity of 10 microvolts per inch with an oscilloscope sensitivity of 0.3 volts per inch. The half-amplitude frequency response of the P-5 at the low end of the spectrum is variable from 0.1 to 35 Hz in 5 steps and at the high frequency end from 0.1 to 30 kHz in 5 steps. The half-amplitude frequency response was usually set at 35 Hz to 2 kHz for recording monosynaptic discharges and pyramidal tract wave activity. The amplification was set at 28K and the degree of attenuation below this amplification was selected to give an appropriate deflection of the oscilloscope beam.

The Tektronix 565 oscilloscope was equipped with 3A3 dual-trace differential amplifiers so that both monosynaptic discharges or pyramidal tract wave activity could be displayed simultaneously or separately by setting the input selector of this amplifier in the chop, alter or single display mode. The further amplification provided by the 3A3 amplifier was selected to give an adequate deflection of the beam.

In recording pyramidal tract wave activity from the cord dorsum, single oscilloscopic sweeps were recorded on Polaroid film. 1 msec. time marks generated by an RM-181 Tektronix time-mark generator were simultaneously displayed on the second beam of the oscilloscope so that a record of the sweep speed of the oscilloscopic beam could be directly recorded on the same sheet of film. A voltage calibration mark was also recorded directly on the same frame by use of the internal calibrator of the P-5 preamplifier. This calibrator provides a square wave calibration signal variable in 12 steps from 10 microvolts

to 50 millivolts. When the input selector of the P-5 is put into the internal calibrate position, G1 (active lead) is made negative, thus also providing an easy means for the determination of lead polarity.

For testing the influences of pyramidal tract activity on motoneuron populations, a control record of a monosynaptic discharge evoked by stimulation of the desired test input (dorsal root or peripheral nerve) was recorded from the appropriate ventral root. This control record was unconditioned, i. e., not preceded by stimulation of the medullary pyramid. Thirty superimposed oscilloscopic sweeps of this discharge were recorded on Polaroid film. In making these records, the adjustable beam brightener of the oscilloscope was adjusted to brighten the portion of the sweep at which the monosynaptic discharge occurred. The remainder of the base line could then be blanked by adjustment of the brightness control so that only the desired portion of the sweep was visible. At a lens opening of f8 on the Polaroid camera, Polaroid film (ASA 3,000) would record 30 superimposed sweeps to give an average discharge amplitude. By adjustment of the horizontal position control of the oscilloscope, up to 8 records of monosynaptic discharges could be recorded on the same frame.

Having obtained a control record of an unconditioned monosynaptic discharge, stimulation of the test nerve was then preceded at variable intervals by the application of stimuli to the medullary pyramid. The interval between the conditioning pyramidal stimulus and the test nerve stimulus was selectable by means of the delay circuit of the S-4 stimulator which in turn controlled the triggering of the SD-5 stimulator used as a stimulus source for the pyramid. Thirty superimposed sweeps of the conditioned discharge was recorded at each interval. Both

pyramidal and nerve stimuli were applied at a low frequency, between 1 and 2 stimuli per second. All recordings of this nature were made at least two hours following the discontinuation of ether anesthesia to avoid possible depression of responses.

A Grass AM-3 audio monitor was connected to the second output connector of the P-5 preamplifier to provide an audio signal for monitoring monosynaptic discharges. This audio signal provided a means for counting the number of sweeps of the discharges recorded on film. The audio monitor has an input impedance of 2 megohms which does not appreciably load the P-5 output.

Monosynaptic discharges conditioned by preceding pyramidal volleys were elicited with the delay circuit set to test the motoneuron population at 2 msec. intervals from 0 to 12 msec., at 5 msec. intervals from 15 to 40 msec. and at 10 msec. intervals from 40 to 80 msec. following the pyramidal stimulation. The average amplitude of the discharge at each interval (as indicated by the brightness of the superimposed sweeps) was measured by hand, using drafting dividers, in mm of deflection. The amplitude was then expressed as a percentage of the control discharge amplitude and plotted on a graph as a function of the delay interval between the conditioning pyramidal stimulus and test nerve stimulus. Each 4th to 5th record was an additional unconditioned control to minimize the effect of variations in the recording technique.

CHAPTER IV

RESULTS

Conduction in the Pyramidal Tract of the Dog

Activity in pyramidal tract neuron axons elicited by electrical stimulation of the medullary pyramid was recorded with a monopolar silver ball electrode resting on the dorsolateral cord surface. These potentials showed a sharp rise from the baseline, slower rise to peak and reversal below the baseline in accord with the usual characteristics of monopolar recordings from volume conductors. These potentials, the pyramidal tract wave, could be recorded in greatest amplitude from the dorsolateral cord surface near the dorsal root entry zone, contralateral to the stimulated pyramid. An example of this activity recorded in the lumbar enlargement of the spinal cord of the dog is shown in Figure 1.

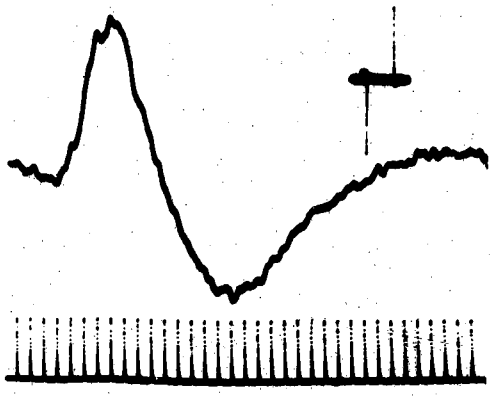

Figure 1. Cord Dorsum Potential in Lumbar Cord in Response to Pyramidal Stimulation

Pyramidal tract waves could be evoked at low threshold stimulus intensities by stimulation of the surface of the medullary pyramid. With good electrode placement on the surface of the pyramid, the threshold stimulus intensity for these waves was 6-8 volts with 0.2 msec. duration square wave pulses. Small displacements of the electrodes laterally from the surface of the pyramid increased the threshold intensity for eliciting these waves 3 to 4 times. The response of the pyramidal tract wave recorded from the lumbar enlargement to increasing pyramidal stimulus intensity expressed in multiples of threshold intensity is shown in Figure 2.

The pyramidal tract wave was stable in configuration and amplitude over a period of several hours, provided no shunting fluids collected around the recording electrode. This activity was capable of following high frequency stimuli (100/sec. or greater) without significant alteration of the configuration or amplitude of the wave. The surface-positive component of the pyramidal tract wave could be recorded from the cord dorsum at reduced amplitude as far caudally as the S3 segment of the spinal cord (Figure 3, A, B, C).

Difficulty arises in the estimation of conduction times from recordings made from a volume conductor, since positive potentials may be recorded before the actual arrival of impulses at the level of the recording electrode (178). In the primate, pyramidal impulses arrive at the level of an electrode applied to the surface of the cord dorsum concurrently with the positive phase of the surface potential, with the majority of the impulses arriving at the electrode at the same latency as the point of reversal of the surface potential from positive to negative (128). In one animal of this series, the dorsal part of the

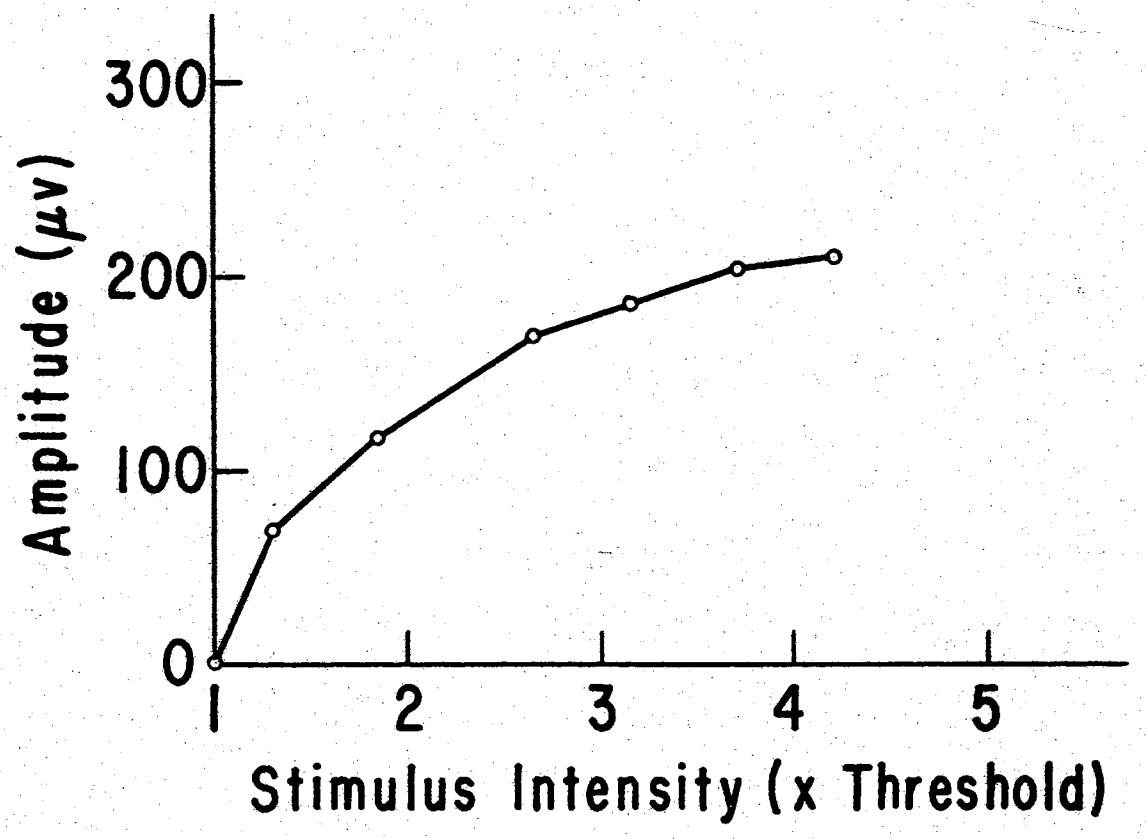

Figure 2. Change in Amplitude of Cord Dorsum Potential in Response to Varying Pyramidal Stimulus Intensity

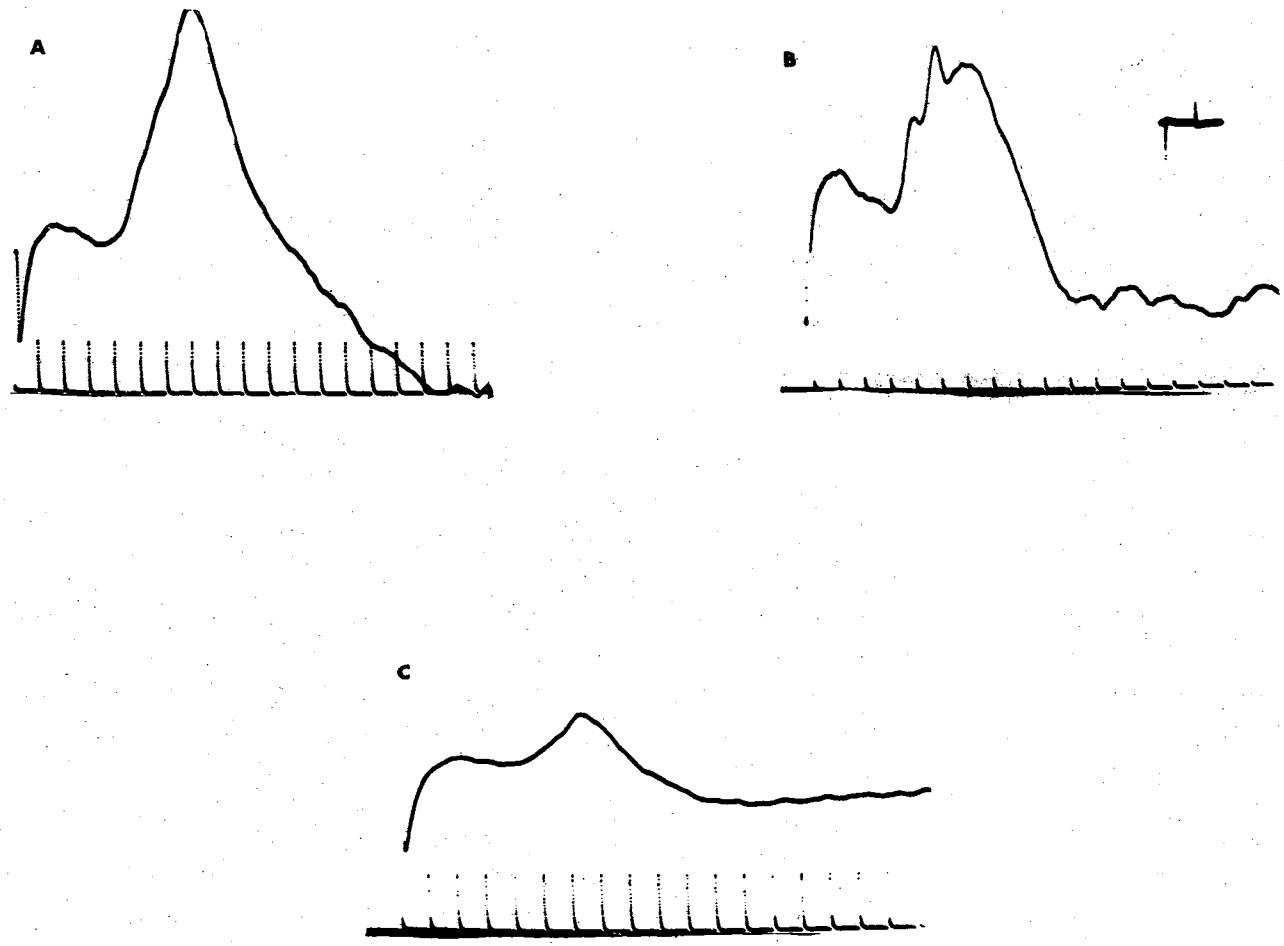

Figure 3. Cord Dorsum Potential in Response to Stimulation of Medullary Pyramid Recorded at Different Levels of the Spinal Cord. A, L4 Segment; B, L7 Segment; C, S3 Segment

lateral funiculus of the spinal cord was dissected free and placed on bipolar silver electrodes. Figure 4 illustrates the activity recorded from the pyramidal tract by this method. The latency of onset of this

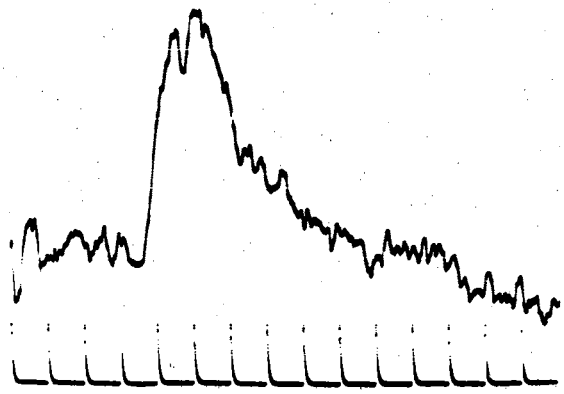

Figure 4. Activity Recorded Directly from the Pyramidal Tract

activity was approximately 3.5 msec. In this animal, this represents a conduction velocity of 89.9 M/sec. The peak activity had a latency of approximately 5 msec., representing a conduction velocity of 63.5 M/sec. In the same animal, the onset of the cord dorsum potential activity recorded at approximately the same level had a latency of 3.13 msec. and peaked at 3.74 msec. These data suggest that impulses arrive at the level of the surface electrode concurrently with the positive phase of the cord dorsum potential, although the onset of the cord dorsum potential preceded activity recorded directly from the tract. In 11 animals, estimating conduction distances as the straight line distance from the interaural line to the recording point, the pyramidal tract wave rose from the baseline at a conduction velocity of 108.8 ± 14.2 M/sec., peaked at 68.9 ± 10.8 M/sec. and reversed from positive to negative at 40.5 ± 11.8 M/sec. (Table I, Appendix).

No second peak characteristic of a more slowly conducting, tonic group of fibers as reported by Lance (84) was seen in recordings made

from the lumbar enlargement. The impulses in these more slowly conducting fibers apparently become temporally dispersed due to the conduction distances involved and do not generate potentials of sufficient magnitude to be recorded with the method used here.

Pyramidal Effects on Contralateral Spinal Motoneuron Populations

Contralateral ventral root fibers could be discharged by pyramidal stimulation with relative ease in the unanesthetized, brain stem-transected preparation, although repetitive stimulation was required for the elicitation of large compound action potentials in the lumbar ventral roots (Figure 5). Typically, 10/sec. stimuli applied to the

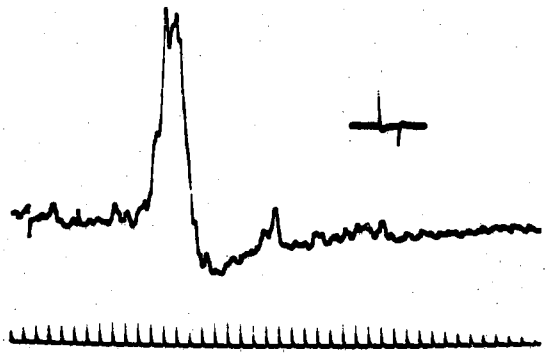

Figure 5. Pyramidal Discharge of Contralateral L6 Ventral Root

pyramid were optimal for the discharge of large compound action potentials.

Ventral root discharge could be effected most easily by stimulus pulses of long duration (4 msec.) applied to the pyramid. Recordings of the pyramidal tract wave activity showed an increase in the amplitude of the falling phase of the positive component of the cord dorsum potential with stimulus pulses of increasing duration. The increase in the later components of the positive phase of this activity in response

to an increase in the duration of the pyramidal stimulus pulse was probably due either to recruitment of more small diameter pyramidal fibers or to repetitive firing of large diameter pyramidal fibers. Long duration pulses of the same order of duration (5 msec.) have been shown to cause repetitive firing of pyramidal tract cells with cortical stimulation (66, 89). The increase in the falling phase of the positive potential is thus likely due to repetitive firing of large, rapidly conducting pyramidal units. The requirement for long duration pulses and repetitive pyramidal stimulation in the discharge of motoneurons is indicative of a requirement for a considerable degree of summation for firing of motoneurons by pyramidal volleys.

In 8 animals in which the discharge of ventral root fibers by pyramidal volleys was studied, the mean latency of discharge of L6 or L7 ventral root fibers was 10.38 ± 1.34 msec. (Table II, Appendix). From calculations made of the latency of the cord dorsum recordings of the pyramidal tract wave, the arrival of the earliest possible pyramidal impulses at approximately this same level is 3.84 ± 0.64 msec. This gives a difference of approximately 6.5 msec. in latency. Allowing for slowed conduction in the terminal ramifications of the pyramidal tract fibers and conduction in the fibers of the ventral root to the point of recording, this allows ample time for relay through several synapses between pyramidal fibers and motoneurons. The interpretation of the difference between latency of pyramidal impulses and motoneuronal discharge involves some uncertainty since, as pointed out above, long duration pulses used for pyramidal stimulation may result in repetitive firing of pyramidal fibers. The more rapidly conducting pyramidal fibers may relay more directly to the motoneurons than these

figures would indicate. However, the requirement for long duration pulses and repetitive stimulation for the discharge of motoneurons is indicative of the need for considerable temporal summation for the firing of motoneurons by pyramidal volleys. This is suggestive of an indirect, multisynaptic influence with a relatively small degree of drive.

For a more detailed examination of pyramidal excitation of spinal motoneurons, the technique of monosynaptic excitability testing at various intervals following pyramidal stimulation was employed. The effect of pyramidal stimulation on the dorsal root-evoked monosynaptic discharge was studied in 7 animals. The results of these studies are summarized in Figure 6 and in Table III, Appendix. The predominant effect of pyramidal volleys on the motoneuron pools studied was one of facilitation. This facilitation reaches its maximal degree at intervals of 10 msec. between the conditioning pyramidal stimulus and the test dorsal root stimulus. This agrees closely with the latency of 10.38 msec. cited above for the discharge of compound action potentials in the lumbar ventral roots. Beyond the maximal facilitation seen at the 10 msec. interval, the conditioned monosynaptic discharge returns toward the baseline, although, even at the 50 msec. interval, the discharge is still elevated above control levels. An example of the change in monosynaptic discharge amplitude at various intervals following pyramidal stimulation is illustrated in Figure 7. The results reported here are comparable to those reported by Lloyd (99) in the cat.

Figure 8 and Table IV, Appendix summarize data from 12 animals in which the peroneal nerve served as the site of the test stimulus for eliciting the monosynaptic discharge. Facilitation again is the effect of pyramidal impulses on the motoneuron population of the peroneal

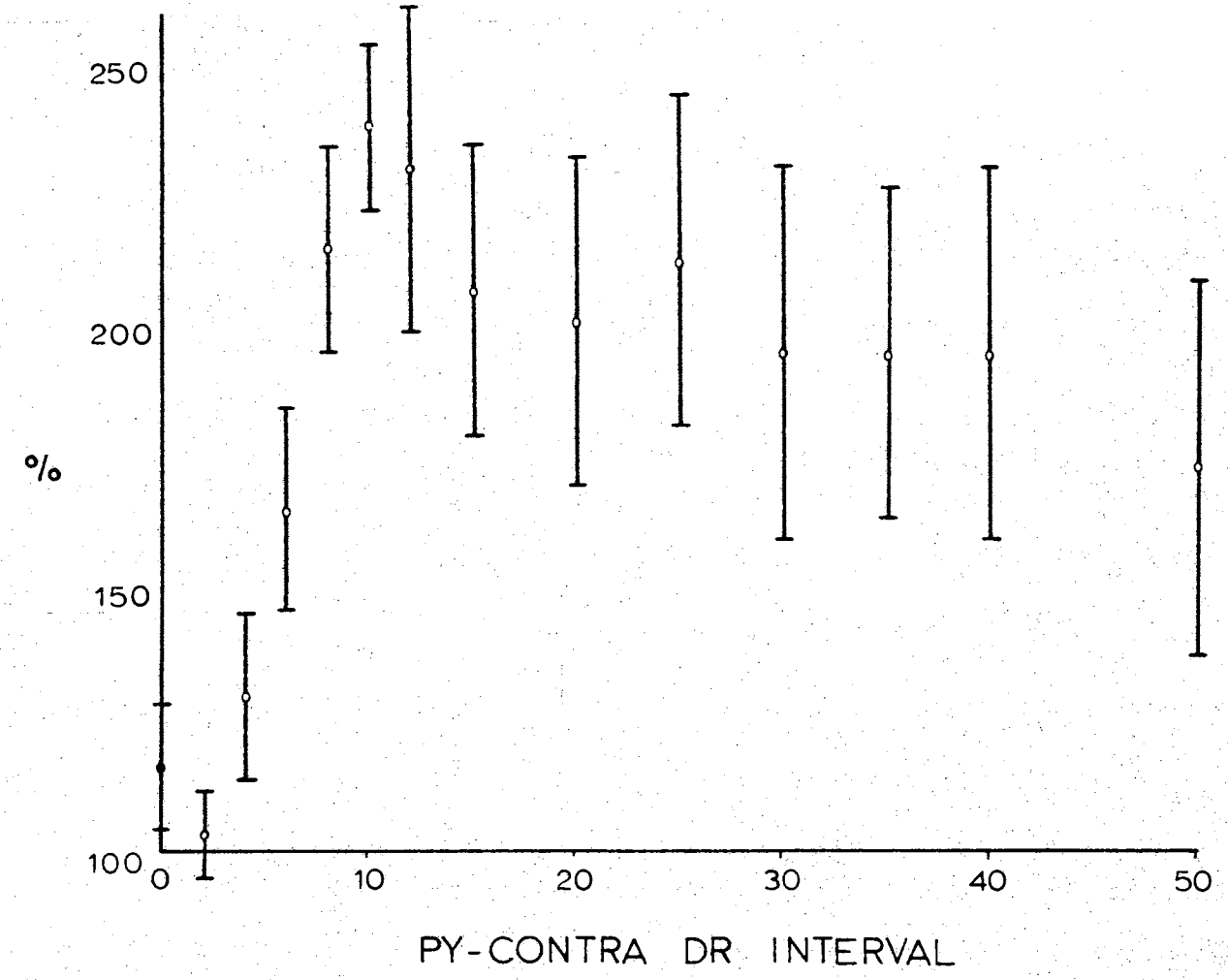

Figure 6. Time Course of Pyramidal Effects on Contralateral Dorsal Root-evoked Monosynaptic Discharge

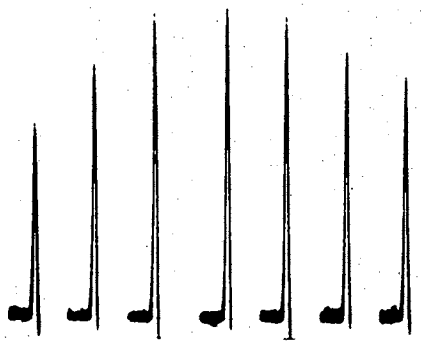

Figure 7. Pyramidal Modulation of Monosynaptic Discharge

nerve, which supplies flexors of the tarsus and extensors of the digits. An increase of the monosynaptic discharge above control levels first occurs at the 2 msec. interval (115.6%, $p < .05$). At intervals from 6 msec. to 60 msec., the increase in the discharge above control levels remains significantly elevated ($p < .001$). At the 80 msec. interval, the discharge is still slightly elevated above control levels (116.7%, $p < .05$).

Compared with the dorsal root-evoked test discharge, the increase in monosynaptic discharge amplitude was less when the peroneal nerve served as the source of test stimuli. A direct comparison between these two preparations is difficult, however, because in early experiments in which the dorsal root served as the site of test stimuli, pyramidal stimulation was effected with pulses of 4 msec. duration. When the peroneal nerve was the source of test afferent volleys, 0.2 msec. duration pulses were used for pyramidal stimulation. If long duration stimulus pulses result in repetitive firing of pyramidal fibers, then a greater summation of pyramidal influences would be expected in the experiments in which such long duration pulses were used.

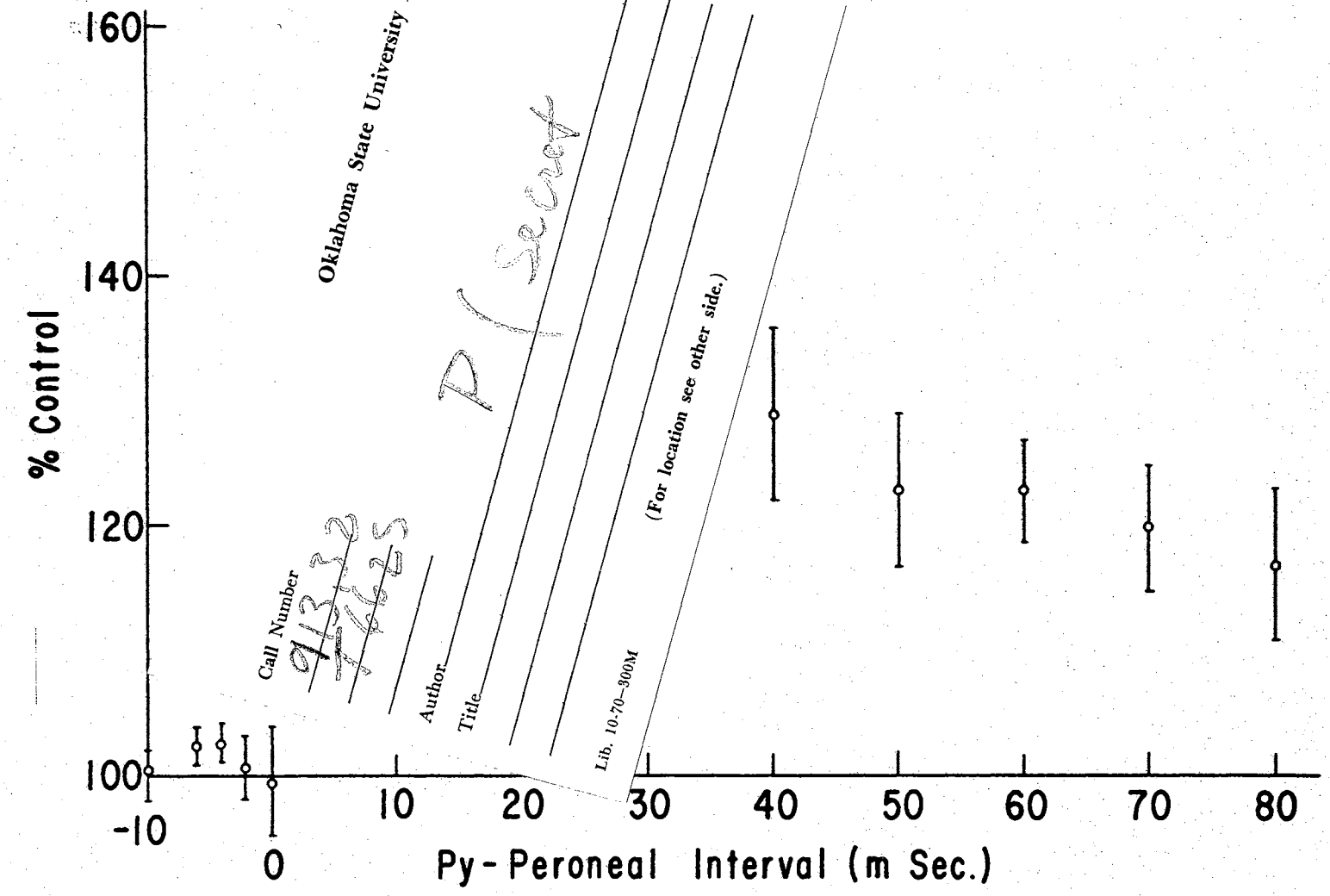

Figure 8. Time Course of Pyramidal Effects on Contralateral Peroneal Nerve-evoked Monosynaptic Discharge

Figure 9 and Table V, Appendix summarize data collected from 10 animals in which the combined nerves to the lateral and medial heads of the gastrocnemius muscle served as the site of test stimuli for eliciting monosynaptic discharges. Again, pyramidal facilitation of this motoneuron population predominates. This facilitation reaches a maximum at intervals of 8-10 msec., then declines toward the control value. The increase of the monosynaptic discharge above control values is highly significant at intervals of 4 to 10 msec. ($p < .001$) and remains significantly elevated ($p < .05$) for interstimulus intervals up to 60 msec. Some elevation above control levels (110%) is evident at the 70 and 80 msec. intervals but the increase is not statistically significant. Changes in the early facilitation of the gastrocnemius population in response to varying pyramidal volley intensities is illustrated in Figure 10.

When the values of the increase in monosynaptic discharge amplitude for the peroneal and gastrocnemius populations are compared (Figure 11), the pyramidally-conditioned test discharge of the gastrocnemius population (broken line) declines more rapidly toward the control value from its initial facilitation than does that of the peroneal population (solid line). However, there was no statistical difference between values for the two populations at any of the intervals studied (Table V, Appendix).

Ipsilateral Influences of Direct Stimulation of the Medullary Pyramid

Motoneurons ipsilateral to the stimulated pyramid could also be discharged by pyramidal stimuli applied at the rate of 10/sec. (Figure 12). In conducting experiments on ipsilateral pyramidal influences,

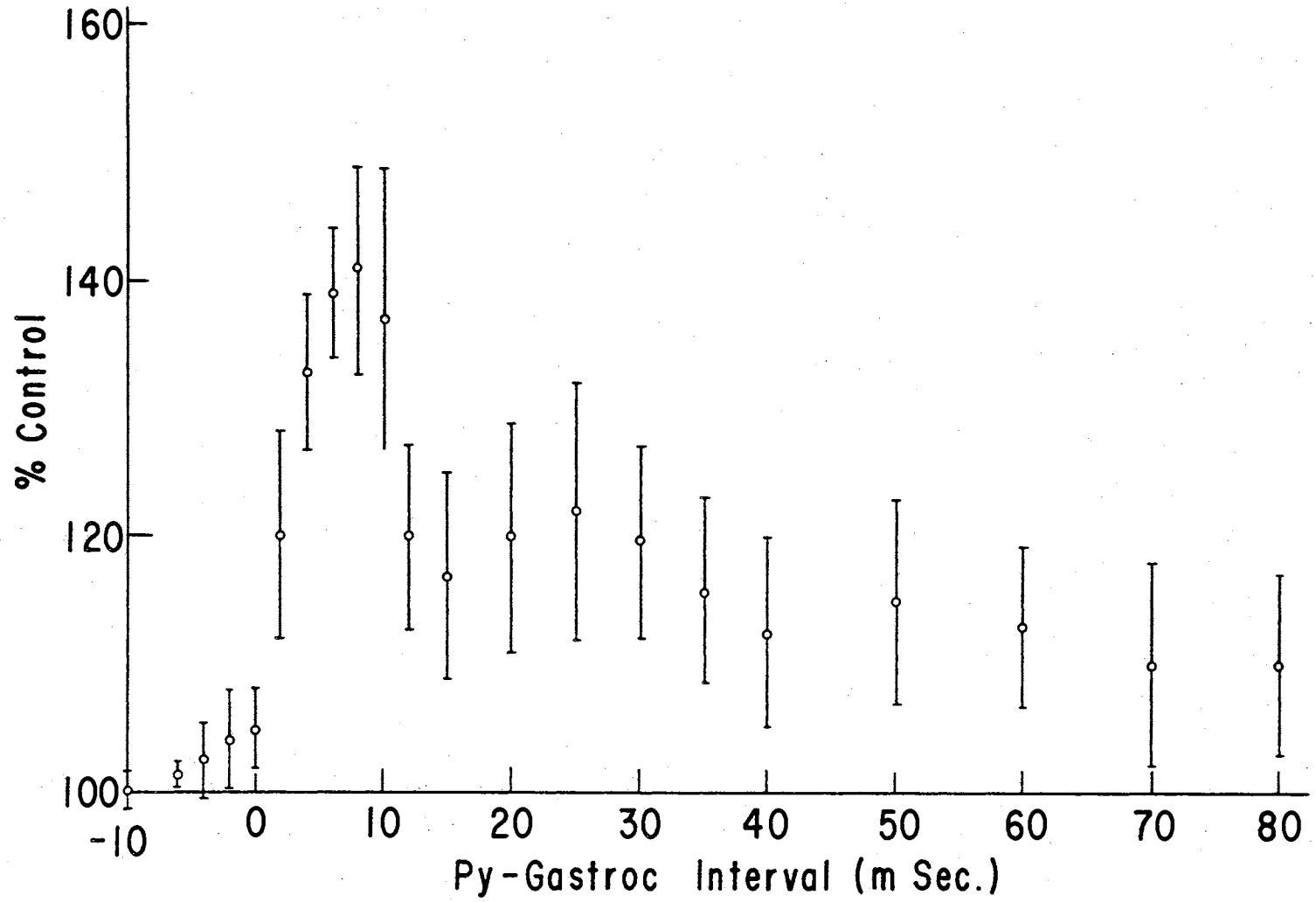

Figure 9. Time Course of Pyramidal Effects on Contralateral Gastrocnemius Nerve-evoked Monosynaptic Discharge

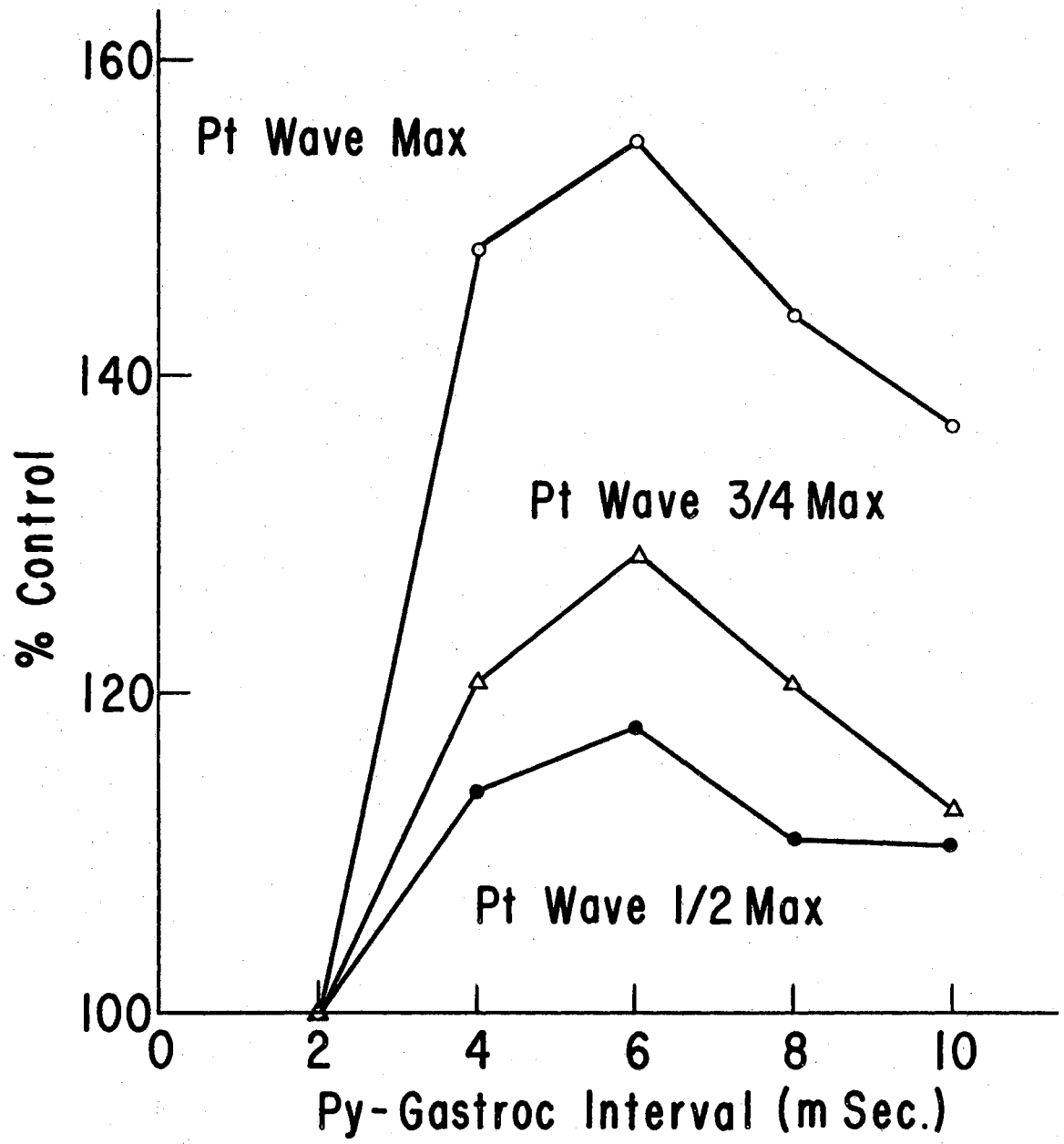

Figure 10. Effect of Variation in Pyramidal Volley on Early Facilitation of Contralateral Gastrocnemius Nerve-evoked Monosynaptic Discharge

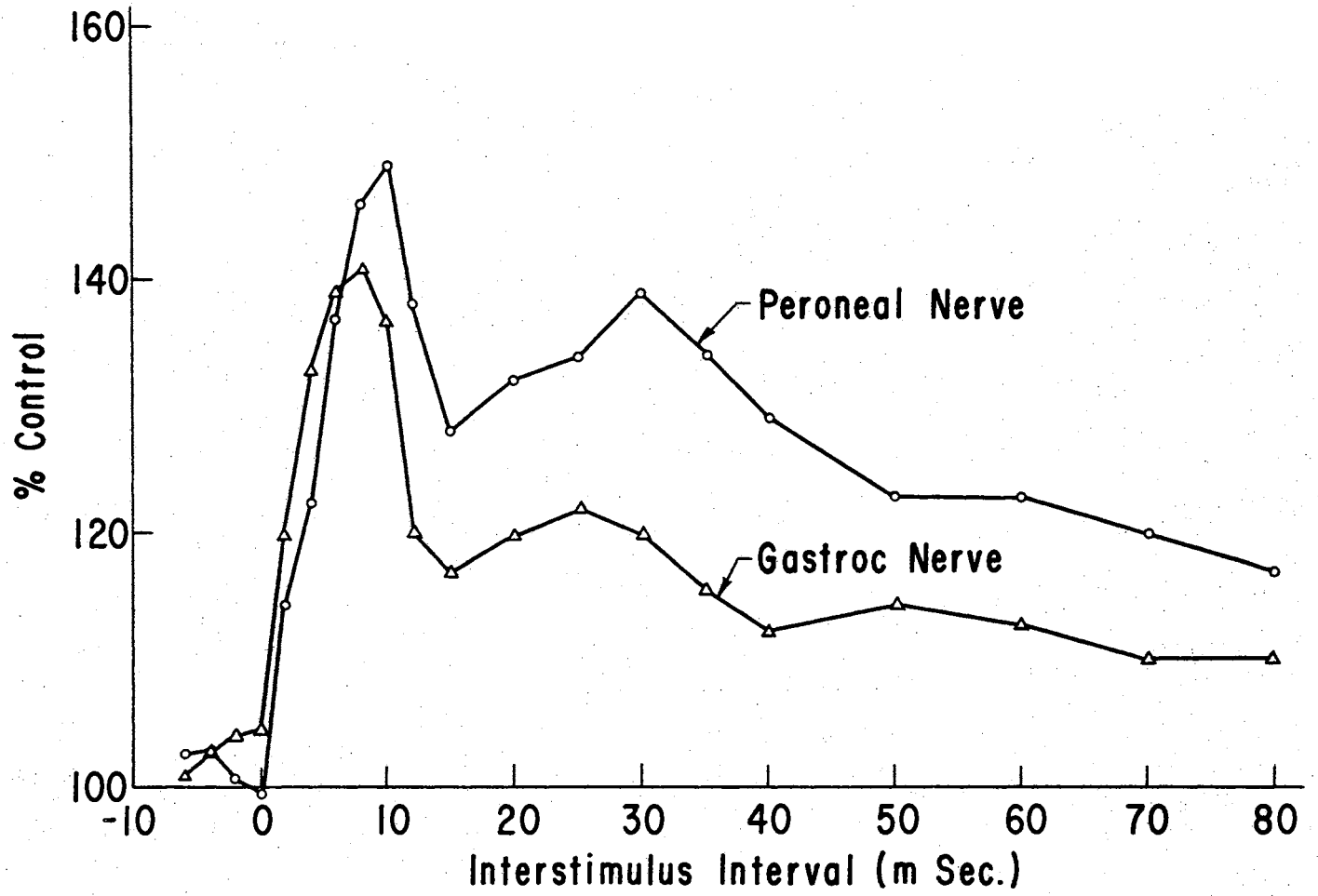

Figure 11. Comparison of Pyramidal Facilitation of Contralateral Peroneal and Gastrocnemius Motoneuron Populations

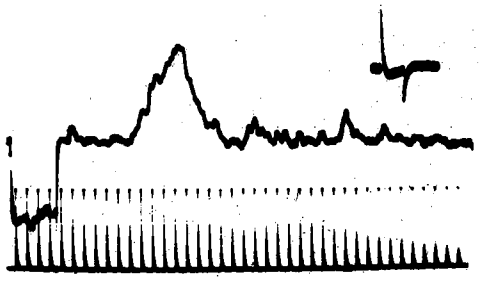

Figure 12. Pyramidal Discharge of Ipsilateral L6 Ventral Root

care was taken to insure a complete transection of the opposite pyramid to avoid the spread of stimulus current and activation of the contralateral pyramid. With a complete transection several centimeters caudal to the point of application of the stimuli to the intact pyramid, activation of ipsilateral ventral root fibers could be attributed to impulses originating in the ipsilateral pyramid.

Figure 13 illustrates data collected from 5 animals in which the influence of pyramidal impulses on the ipsilateral dorsal root-evoked monosynaptic reflex discharge was examined. From this graph, it is evident that the pyramidal activation of ipsilateral motoneurons follows approximately the same time course as does that of contralateral activation.

A more definitive examination of the ipsilateral effects of pyramidal impulses is shown graphically in Figure 14 in which the time course of pyramidal effects on ipsilateral gastrocnemius populations in two different preparations is defined. Although the effect of pyramidal impulses in 4 animals studied was usually one of facilitation on ipsilateral populations, the pattern of effects was not always consistent. In one experiment illustrated (solid line) the earliest effect was a very transient facilitation followed by a prolonged inhibition.

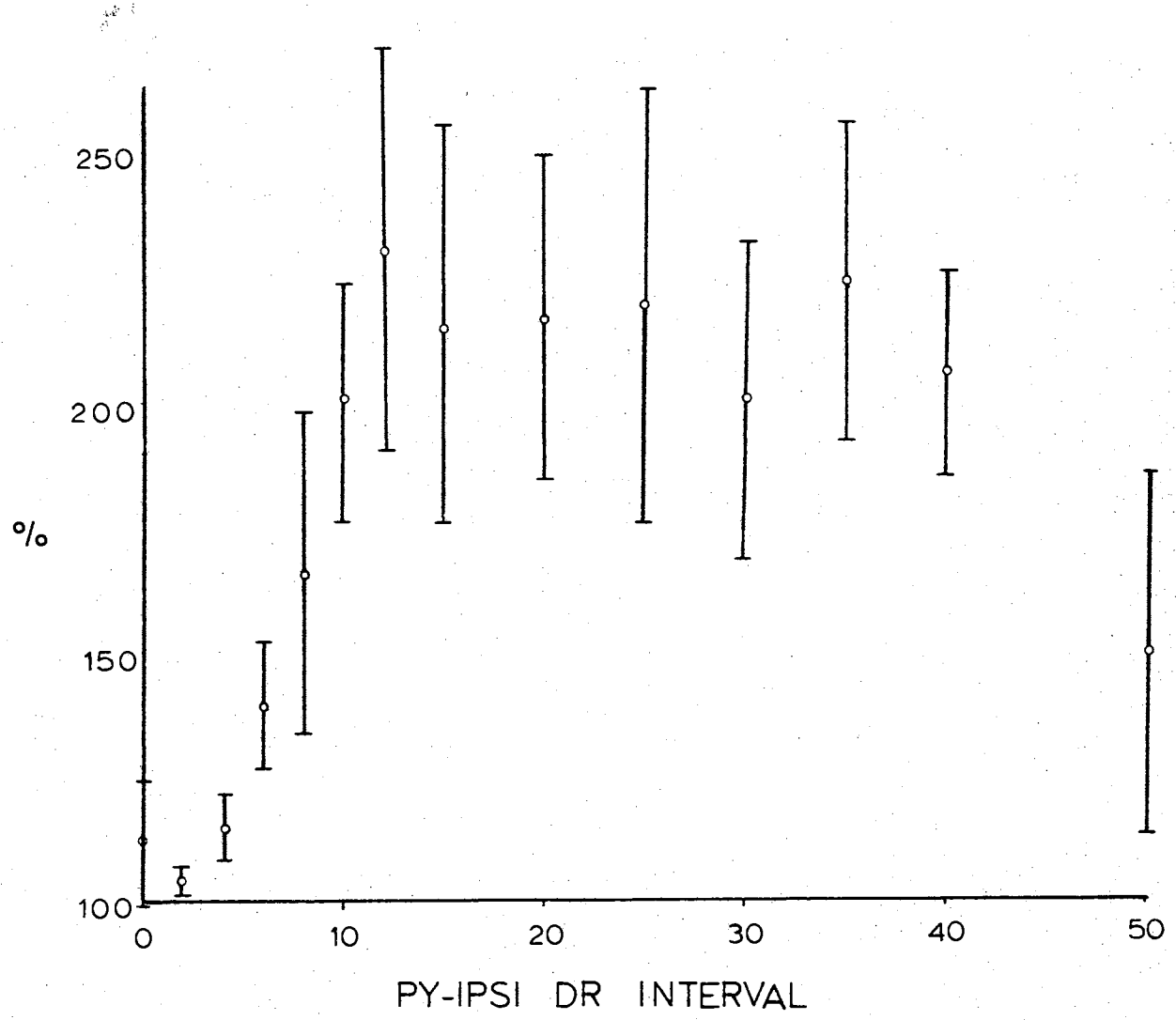

Figure 13. Time Course of Pyramidal Effects on Ipsilateral Dorsal Root-evoked Monosynaptic Discharge

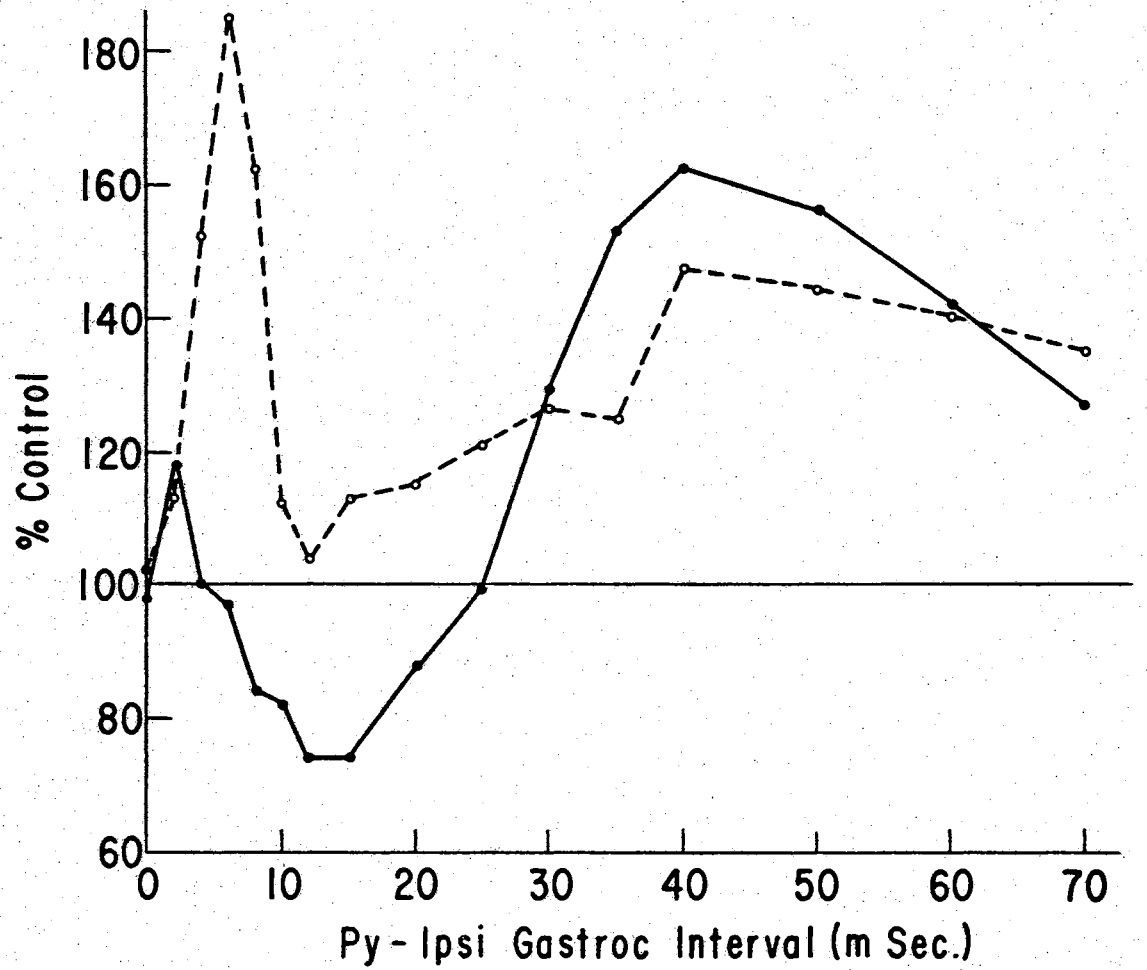

Figure 14. Time Course of Pyramidal Effects on Ipsilateral Gastrocnemius Motoneuron Populations. Two Different Preparations Illustrated

In the other experiment illustrated, the pattern of effects followed that of the contralateral populations. A late facilitation occurring at about the 50 msec. interval is an obvious feature in both preparations.

Ipsilateral peroneal nerve motoneuron populations could also be influenced by impulses originating in the ipsilateral medullary pyramid as shown by the change in monosynaptic discharge amplitude illustrated in Figure 15. Again, the pattern of influences in 3 animals studied was not always consistent. In one experiment illustrated, the influence was predominantly facilitation as with contralateral populations. In the other experiment shown, the early facilitation was followed by a period of prolonged inhibition.

In Figure 16, the upper curve (solid line) illustrates the pyramidal influence on the ipsilateral gastrocnemius population in a preparation with an intact spinal cord. Beginning at the 4 msec. interstimulus interval, the ipsilateral gastrocnemius population was facilitated to levels of approximately 123% of control levels. The lower curve (broken line) in Figure 16 traces the pyramidal influences on the ipsilateral gastrocnemius population in the same preparation following quadrisection of the contralateral spinal cord down to approximately the level of the denticulate ligament, 4-5 segments rostral to the segment from which the recordings were made. This transection, which severs the pyramidal tract contralateral to the stimulated pyramid, completely abolishes the activation of the ipsilateral gastrocnemius population. This data may be interpreted as indicative that pyramidal activation of ipsilateral motoneuron populations is dependent upon an intraspinal mechanism at the segmental level rather than upon direct, uncrossed ipsilateral pyramidal projections.

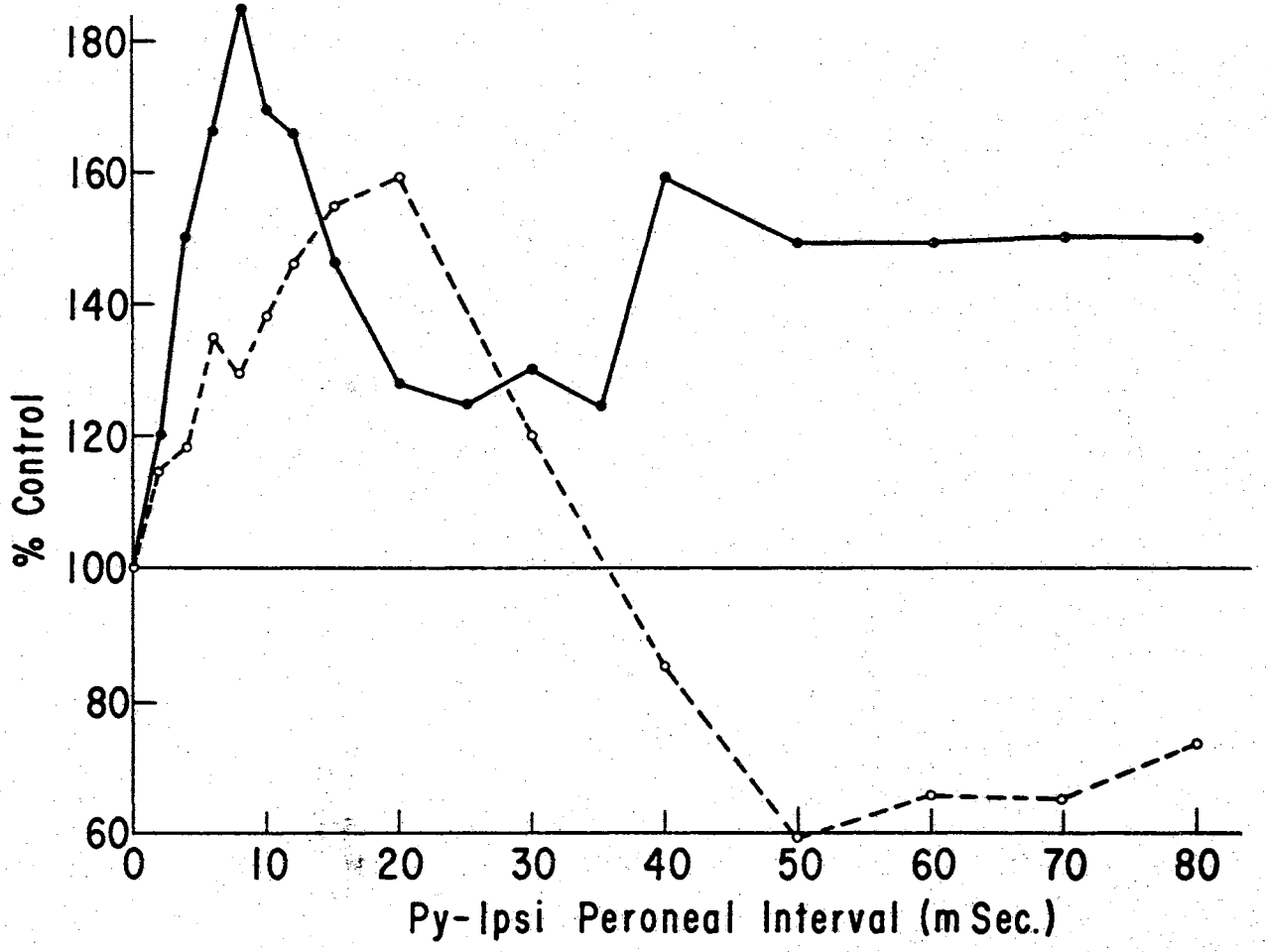

Figure 15. Time Course of Pyramidal Effects on Ipsilateral Peroneal Motoneuron Populations. Two Different Preparations Illustrated

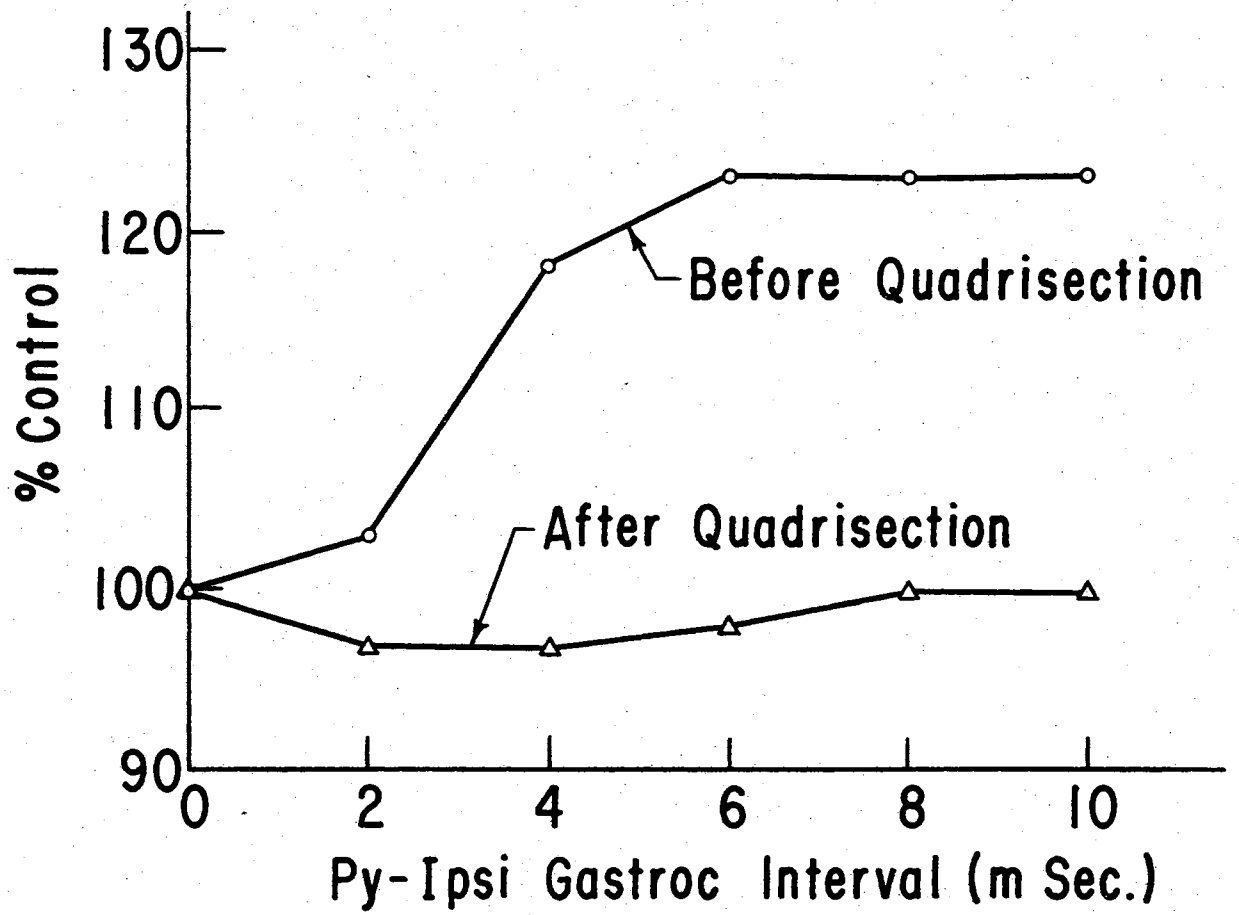

Figure 16. Change in Pyramidal Effects on Ipsilateral Gastrocenemius Nerve-evoked Monosynaptic Discharge Following Quadrisection of Contralateral Spinal Cord

The upper curve (solid line) of Figure 17 shows the ipsilateral facilitation of the peroneal population in a preparation with an intact spinal cord. Following quadrisection of the contralateral spinal cord, this pattern of facilitation was changed to that shown by the lower curve (broken line) of Figure 17. In this experiment, the quadrisection included most of the dorsal funiculus and the dorsal part of the lateral funiculus and was made 2-3 segments rostral to the segment from which the recordings were made. In this experiment, contralateral section of the cord did not completely abolish the ipsilateral facilitation of the peroneal population. The early facilitation was decreased from a maximum of 184% of control to a maximum of 154% of control at the 8 msec. interval. The late facilitation in the intact spinal cord declines to approximately 130% at the 20-35 msec. intervals, then shows a late facilitation at 40 and 50 msec. back to 150-160% of control levels. The section of the contralateral pyramidal tract abolished this late facilitation; at the 20 msec. interval, the test discharge returned to the control level and at the 40 msec. interval was slightly below control levels (90%).

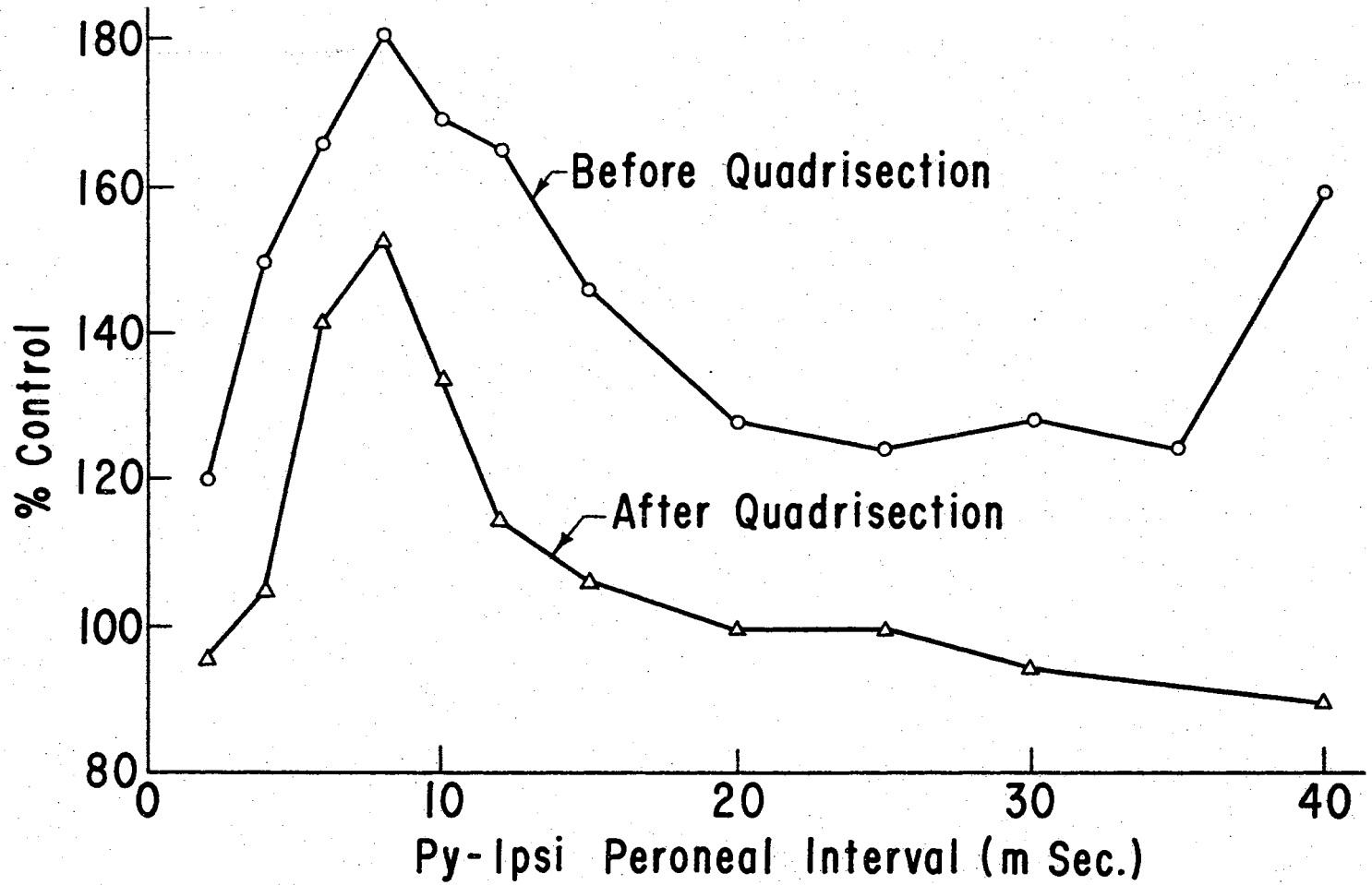

Figure 17. Change in Pyramidal Effects on Ipsilateral Peroneal Nerve-evoked Monosynaptic Discharge Following Quadrisection of Contralateral Spinal Cord

CHAPTER V

DISCUSSION

Activity recorded from the cord dorsum in the lumbar enlargement in response to pyramidal stimulation in the dog had the same general characteristics as that previously reported in the cat (84) and monkey (128). This activity could be elicited by stimulation of the surface of the medullary pyramid at low threshold stimulus intensities. Small displacements of the electrodes laterally from the surface of the pyramid resulted in significant increases in the threshold stimulus intensity. This suggests that the activity was indeed conducted by pyramidal fibers descending from the stimulated pyramid. The ability of this activity to follow high frequency stimuli (100/sec. or greater) is evidence that the activity recorded is due to directly excited fibers in the spinal cord and not due to synaptically relayed activity.

The cord dorsum potential was very stable throughout the duration of an individual experiment and could be monitored during an experiment without interfering with other recordings of the influences of pyramidal volleys on spinal motoneuron populations. This tract wave therefore provided a good index for maintaining the pyramidal volley at a constant level during an experiment and allows somewhat more consistent direct comparison between different preparations.

The pyramidal tract wave could be recorded from the cord dorsum, although at reduced amplitude, as far caudally as the third sacral

segment of the spinal cord of the dog (Figure 3, A, B, C). Only the positive phase of the cord dorsum potential was evident at this level; no significant reversal of the potential from positive to negative was seen at the third sacral segment (Figure 3, C). Allowing for current spread through the volume conductor of the spinal cord, this may be interpreted as suggestive that at least the larger fibers of the pyramidal tract of the dog extend well into the lower lumbar levels. This interpretation is in agreement with anatomical data (28).

The estimation of conduction times from recordings made in a volume conductor is difficult. Positive potentials may be recorded which precede the actual arrival of impulses at the level of the recording electrode (178). Phillips and Porter (128) correlated the cord dorsum potential with the arrival of impulses in the pyramidal tract of the primate at the same level by recording from single pyramidal tract fibers using microelectrode techniques. They found that the earliest pyramidal impulses arrive at the same level of the spinal cord concurrent with the positive phase of the cord dorsum potential. They also found that the majority of pyramidal impulses had about the same latency as did the reversal of the cord dorsum potential from positive to negative (128). These findings are characteristic of recordings made in a volume conductor (178).

In the one experiment of this study in which activity was recorded directly from the pyramidal tract, it was found that pyramidal impulses in the dog arrive at the lumbar enlargement concurrent with the positive phase of the cord dorsum potential. The latency of onset of activity recorded directly from the pyramidal tract was 3.5 msec. The cord dorsum potential recorded at the same level in the same preparation

had a latency of onset of 3.13 msec. The peak of the activity recorded directly from the pyramidal tract had a latency of 5 msec. These data suggest that measurement of latencies of the cord dorsum potential should provide at least a reasonable measurement of conduction velocities in the pyramidal tract of the dog. Conduction distances in these experiments were estimated as the straight line distance from the interaural line to the recording point on the cord dorsum. Utilizing the measurements of latency of the cord dorsum potential, the latency of onset of this potential corresponds to a conduction velocity of 108.8 $\pm$ 14.2 M/sec. Latency measurements made relative to the peak of the cord dorsum potential correspond to a conduction velocity of 68.9 $\pm$ 10.8 M/sec. The direct recordings from the pyramidal tract in one experiment indicates a maximum conduction velocity of 89.9 M/sec. Thus, measurements of latency of the peak of the cord dorsum potential appears to provide a good estimate of conduction velocities in a majority of the more rapidly conducting pyramidal tract fibers of the dog, although the data from the direct recording suggest that this estimate may be somewhat low for maximum conduction velocities.

Lance (84) found that, in the cat, cord dorsum potential recordings of pyramidal tract activity in the cervical enlargement showed a second peak following the initial deflection of the cord dorsum potential. In the experiments reported here, no second peak of this nature was found in the lumbar enlargement of the dog. Lance (84) correlated this second peak in the cord dorsum potential with activity in slowly conducting fibers in the pyramidal tract of the cat. His studies showed that this activity could not be recorded in the cord dorsum potential caudal to the C7 segment. Correlating these results with

activity recorded directly from the pyramidal tract, it was found that at greater conduction distances the impulses in the more slowly conducting fibers of the pyramidal tract become temporally dispersed. With temporal dispersion at the conduction distances involved in the lumbar enlargement, these impulses do not generate potentials of sufficient magnitude to be recorded in the cord dorsum potential. This second, more slowly conducting group of fibers in the pyramidal tract of the cat corresponds to the tonic fiber group (54, 157). Their presence in the pyramidal tract of the dog was not confirmed in the present investigation, but their absence should not be presumed.

Stimulus pulses of long duration (4 msec.) caused an increase in the amplitude of the falling phase of the positive component of the cord dorsum potential. This increase in the positive potential is likely due to: a) recruitment of small diameter fibers, or b) repetitive firing of large diameter fibers. With cortical stimulation, long duration pulses (5 msec.) are known to cause repetitive firing of pyramidal tract cells in other species (66, 89). Repetitive firing of axons in response to prolonged depolarization has been show (160) and the conditions for repetitive discharge of axons have been computed from the Hodgkin-Huxley model (3, 40, 41). Thus, it is likely that the increase in the positive phase of the cord dorsum potential may be due to repetitive firing of large diameter pyramidal tract axons. Discharge of ventral root fibers could be effected most readily with pyramidal stimulus pulses of long duration. This is especially true for the discharge of large compound action potentials in the lumbar ventral roots. Since long duration stimulus pulses may result in repetitive firing of pyramidal units, this suggests that the discharge of a large proportion of the motoneuron population requires considerable temporal summation.

The difference between latency of onset of the pyramidal tract wave in the lumbar enlargement and the discharge of ventral root fibers was approximately 6.5 msec. The interpretation of this difference in latency regarding synaptic relay of pyramidal drive to motoneurons in the dog spinal cord is uncertain. If repetitive firing of pyramidal units is occurring, the delay cited (6.5 msec.) is probably of greater magnitude than is actually the case. In the cat, the difference in latency between pyramidal impulses and the onset of the EPSP recorded in lumbar motoneurons is of the order of 3 msec. (64). One might expect the delay between pyramidal fibers and motoneurons in the dog to be approximately of the same order. The data strongly suggest that the connection between pyramidal fibers and motoneurons in the dog, as in the cat, is an indirect one involving several synapses. No ventral root discharges characteristic of a monosynaptic connection, such as is seen in the primate (14, 16, 17) was noted in the animals studied in the present investigation.

The effect of pyramidal impulses on the dorsal root-evoked monosynaptic discharge is similar to that reported by Lloyd (99) in the cat. This effect is predominantly one of facilitation. A major difference between these results and those reported by Lloyd in the cat is that the effects noted here were elicited by single pulse pyramidal stimuli. Lloyd reported that trains of three or more pulses were required to elicit significant changes in the amplitude of the test monosynaptic discharge. This difference is possibly due to the fact that Lloyd used barbiturates to control the excitability of his preparations, although the levels of barbiturates were low. Another difference in the results reported is that of latency of these influences. Lloyd

reported a latent period of 12 msec. In these studies in the dog, some change in monosynaptic discharge amplitude was noted as early as 4 msec. Correcting for a dorsal root test stimulus to ventral root discharge recording interval of the monosynaptic discharge of approximately 2 msec., this would represent approximately a 6 msec. latency of significant onset of effects. With a latency of pyramidal impulses at the same lumbar level of 3.8 msec., this would allow approximately 2 msec. for relay between pyramidal fibers and motoneurons. This difference in latency is sufficient to allow for relay through at least two synapses, assuming a synaptic delay of 0.5 to 1 msec.

The measurement of delay between pyramidal fibers and motoneurons is not an absolute determination since uncertainty arises from the interpretation of the cord dorsum potential. This value (2 msec.) is suggestive, however, of the magnitude of delay. This delay between pyramidal fibers and motoneurons is of the same order of delay as that found in the cat, but is a somewhat shorter delay than that reported for the cat (64). This may be correlated with a ventral shift in pyramidal terminations in the spinal cord gray of the dog as compared with the pyramidal terminations in the cat spinal cord (28). In the dog, pyramidal fibers terminate in lamina VIII in the spinal cord. This is in contrast to the pyramidal terminations in lamina VII of the spinal cord gray in the cat (116). On this basis, a somewhat more direct relay between pyramidal fibers and motoneurons might be expected in the dog than in the cat. In other animals of the Order Carnivora (raccoon) a further ventral shift of pyramidal fiber terminations into lamina IX in the cervical enlargement of the spinal cord has been shown. It is suggested that pyramidal tract connections to motoneurons supplying

musculature of the extremities may be determined by the physiological use of the musculature rather than by a strict phylogenetic development of these connections (28) since the raccoon shows considerable digital dexterity. A more definitive examination of the delay between pyramidal tract fibers and spinal motoneurons in carnivores other than the cat would be desirable.

Highly significant increases of the monosynaptic discharge above control levels resulting from pyramidal volleys is seen when the monosynaptic discharge is evoked by peroneal nerve stimulation. This increase above control levels first occurs at the 2 msec. interstimulus interval (115.6%, $p < .05$). With an average test stimulus to recording interval of approximately 3.8 msec., this represents a latency of onset of effects of approximately 6 msec. Again, this allows approximately 2 msec. for relay between pyramidal fibers and motoneurons of the peroneal population. At intervals up to 60 msec., the facilitation of peroneal populations is highly significant ($p < .001$). A direct comparison between the degree of facilitation of peroneal populations and the facilitation noted on the dorsal root-evoked monosynaptic discharge is difficult. If repetitive firing of pyramidal units due to long duration stimulus pulses is occurring, greater temporal summation of pyramidal influences would be expected in experiments in which such pulses were used for pyramidal stimulation and, therefore, a greater degree of facilitation. Four msec. duration pyramidal stimulus pulses were used in experiments in which pyramidal effects on the dorsal root-evoked monosynaptic discharge was studied. Facilitation in these experiments was greater than the facilitation of peroneal nerve motoneuron populations where 0.2 msec. duration stimulus pulses were used. The effects

noted here on peroneal motoneuron populations are similar to those reported by other workers for the "pyramidal" cat preparation (5, 131, 133, 168).

In light of data obtained from "pyramidal" cats, the finding of facilitation of extensor motoneuron populations by pyramidal volleys is somewhat surprising. Preston, et al. (5, 131, 133, 168) have consistently demonstrated, in the "pyramidal" cat, that motor cortex stimulation results in inhibition of extensor motoneuron populations. Inhibition is not exerted on all extensor units in the "pyramidal" cat, however. Agnew and Preston (4) found that, in studying single extensor units, some units of the gastrocnemius complex were facilitated and others were inhibited. The results of intracellular recordings from motoneurons in the cat in response to pyramidal activation demonstrates that EPSPs predominate in both flexor and extensor motoneurons (42, 74, 128, 132). In the cat, transient depolarization of motoneurons in response to pyramidal activation is not significantly different between flexor and extensor motoneurons (42). Thus, facilitation of extensor motoneuron populations is not entirely unexpected.

Recent evidence presented by Asanuma and Sakata (11) suggests that the differences noted here between stimulation of the motor cortex and direct pyramidal stimulation could be a reflection of cortical mechanisms. Microstimulation in the depths of the cortex indicates a cortical organization into minimal building blocks. From different cortical zones, effects on different motoneuron populations can be elicited. In some zones, effects on more than one motoneuron population can be found. The effects elicited from such overlapping zones do not reflect a simple reciprocal relationship such as might be expected if the system were

organized exclusively at the spinal level. This is in direct contrast to data obtained from "pyramidal" animals using surface cortical stimulation in which a relatively simple reciprocal innervation of antagonists, i. e., facilitation of flexors and inhibition of extensors, has been shown. Minimal building blocks in the cortex found by Asanuma receive their input from cutaneous afferents located in the skin over the path of action of the muscle supplied by the cortical zone (12). The cortex is thus organized into minimal input-output units which are probably related to the tactile placing reaction.

Kato, et al. (74) found that, in the cat, direct pyramidal stimulation resulted in inhibition of motoneurons supplying the tibial nerve. This population of motoneurons would include all the neurons supplying all the physiological extensors of the distal part of the rear limb. This would represent, therefore, a very heterogeneous population of motoneurons. No explanation for the differences between Kato's studies and the studies reported here can be offered other than the speculation that the observed differences may result from differences between species or from differences in the types of motoneuron populations studied. The gastrocnemius complex of the cat contains a well-developed tonic head, the soleus muscle (61). The gastrocnemius complex of the dog does not contain a well-developed tonic head homologous to the soleus muscle of the cat. In the "pyramidal" monkey, a differentiation between motor cortex effects on tonic and phasic extensor motoneurons has been shown (133). In this preparation, both lateral and medial heads of the gastrocnemius muscle as well as flexor motor nuclei receive predominantly facilitation from the motor cortex. The motor nucleus of the soleus muscle, a distinct tonic head of the triceps surae, receives

predominantly inhibition from the motor cortex. The differences between the results reported here in the dog and those reported by Kato (74) in the cat may be due to a differentiation in pyramidal effects on tonic and phasic extensor motoneurons rather than a distinct species difference, though the latter may well be the case.

Direct control of both flexor and extensor motoneurons by the pyramidal system would allow a more favorable control of movements than would a simple reciprocal innervation of antagonists. The results reported from "pyramidal" preparations (5, 131, 133, 168) and by Kato (74) indicate such a reciprocal control. Such control would seem to lead to very stereotyped movements rather than the highly individualized movements which are possible with pyramidal control.

There also exists the possibility that the inhibitory effects elicited by cortical stimulation in the "pyramidal" preparation is mediated by a pathway other than the pyramidal tract. Such a possibility is suggested by Agnew and Preston (4) and by the work of Tower (164, 166). Tower found that stimulation of the motor cortex following pyramidotomy abolished pyramidal motor function but demonstrated the preservation of inhibition of tonic or reflexly evoked motor activity. This suggests that the excitatory and inhibitory effects of cortical activity are partially dissociated at a supraspinal level. Cortical excitation, Tower suggests, is transmitted by way of the pyramidal tract while cortical inhibition must be relayed, at least in large part, through some other supraspinal centers. In the "pyramidal" preparation, all descending cerebral pathways other than the pyramidal tract have been severed in the upper medulla at the level of the corpus trapezoideum. There still exists, however, the possibility of an

intact corticoreticulospinal system (22, 124). Corticofugal fibers terminate only in the medial two-thirds of the reticular formation (22) which is known to give rise to reticulospinal pathways (161) capable of inhibiting motor activity (109).

Some differentiation in the effects of pyramidal stimulation on flexor and extensor motoneuron populations was seen in these studies. Early pyramidal facilitation of extensor motoneuron populations declined more rapidly than did the facilitation of flexor motoneuron populations although this difference was not statistically significant. There was little difference in the early facilitation when the two populations were compared; facilitation of each population was to approximately the same level above control values.

A distinct feature seen in the graphs depicting the time course of pyramidal influences on both flexor and extensor motoneuron populations (Figures 8, 9, 11) is that a late facilitation is seen at about the 25 to 30 msec. interstimulus interval. This facilitation is not very powerful but does delay the return of the test monosynaptic discharge toward the control level. This late facilitation may be due either to a) relay from the same pyramidal fibers through interneuronal chains of varying lengths or to b) bombardment of motoneurons through interneuronal chains by a second, more slowly conducting group of pyramidal fibers.

Motoneurons of different sizes show a differentiation in their thresholds of firing to inputs of different origins including activation by suprasegmental system. Somjen, et al. (153) have found that size is a chief determinant of the excitability of a motoneuron. Excitability predetermines the order of discharge in a motoneuron pool

regardless of the source of excitation to the motoneurons and the neuronal circuits which transmit this excitation. The converse, in general, is also true, i. e., inhibitibility of motoneurons is in direct proportion to motoneuron soma size (62, 63). On this basis, the discharge zone of a motoneuron population may be defined as consisting of all motoneurons whose thresholds are below a certain level. Since threshold is determined by cell size, large cells have a higher threshold and make up the subliminal fringe of a motoneuron population. Facilitation of the population then represents an expansion of the discharge zone due to additional excitation impinging on the population and exceeding the threshold of the larger neurons of the population. The distribution of sizes in the population thus provides the capability of an anatomically built-in grading mechanism which responds automatically to any input and discharges an appropriately sized output. Small motor units are more frequently active than are larger motor units and, as the drive to a motoneuron population increases, not only are more motor units brought into play but also an increase in the size of motor units discharged is effected. Thus, as the drive to a motoneuron population increases, the graded output of the population, in terms of muscle tension exerted, remains relatively linear (62).

From this viewpoint, the results presented here probably represent not only an increase in the total number of motor units discharged by the temporal summation of pyramidal excitation and group Ia afferent excitation, but also an increase in the size of motor units discharged. For example, at about the 8 to 10 msec. interval following pyramidal stimulation, a near maximal number of motor units is being discharged by the combined excitation. Also, at this interval, the larger motor

units of the population are being brought into the discharge zone. Beyond the 10 msec. interval, as the test monosynaptic discharge declines toward the control level reflecting decreased pyramidal facilitation, the larger motor units progressively drop out of the discharge zone. Progressive recruitment of larger motor units into the discharge zone in response to increasing pyramidal facilitation has been demonstrated (153). Control of motoneurons in this manner would allow a fine control over the development of muscle tension.

In the cat (36, 116), monkey (96) and dog (28) pyramidal fibers terminate bilaterally. In the monkey (96), some axons in the crossed lateral corticospinal tract recross in the spinal commissures to terminate ipsilaterally. Fibers from both the ventral and lateral uncrossed tracts also terminate ipsilaterally. This same pattern of terminations has been observed in the cat (36). Recent evidence (28) indicates pyramidal terminations ipsilaterally in Rexed's laminae V-VIII in the dog. Bilateral degeneration of pyramidal fibers in the dog spinal cord had been demonstrated by Sherrington in 1885 (148).

Movements of the ipsilateral extremities are occasionally seen in response to cortical stimulation (49). The representation of ipsilateral movements in response to cortical stimulation in monkeys was reported by Bucy (25). Monkeys also show a more severe impairment of motor control following bilateral pedunculotomy than that produced by unilateral pedunculotomy (27), further suggesting ipsilateral pyramidal control. Similar evidence indicates that innervation of motoneurons from the ipsilateral cortex in man plays a minor role in motor control (26). Evarts (55) has also recorded PTN discharge in relation to ipsilateral movements in the monkey and a small percentage of the PTN units studied could be

related to ipsilateral movements. Ipsilateral pyramidal projections in the monkey have been shown to make monosynaptic connections with spinal motoneurons (15). Ipsilateral responses in the monkey persist following hemisection of the contralateral spinal cord (15, 25) indicating that, in the monkey, the ipsilateral activation of motoneurons by the pyramidal system is not dependent upon a segmental mechanism (17, 25).

The pattern of ipsilateral influences of pyramidal impulses found in the studies reported here was inconsistent. The usual pattern of ipsilateral pyramidal effects was one of facilitation. However, an early inhibition of ipsilateral gastrocnemius motoneurons followed by a later facilitation was seen in one experiment. Likewise, an early facilitation of ipsilateral peroneal motoneurons followed by a late inhibition was seen in another preparation. A similar variability has been reported for crossed spinal reflexes evoked by stimulation of flexor reflex afferents (FRA) (68). Such crossed effects have relatively short latencies and show various combinations of facilitation and inhibition to both extensor and flexor motor nuclei. The possibility exists that the ipsilateral effects reported here may be mediated by commissural interneurons which mediate crossed reflex actions from the FRA. This speculation deserves further study.

Landau (86) obtained ipsilateral movements in the cat in response to direct pyramidal stimulation. The movements noted by him usually consisted of transient inhibition of decerebrate rigidity. He found that transection of the contralateral pyramidal tract abolished ipsilateral movements in response to direct pyramidal stimulation. This suggests that ipsilateral movements elicited by pyramidal volleys are mediated by way of an intraspinal mechanism in the cat.

Transection of the contralateral pyramidal tract 4 to 5 segments rostral to the segment from which recordings were made completely abolished the activation of ipsilateral gastrocnemius motoneurons (Figure 16). Severing the contralateral pyramidal tract 2 to 3 segments rostral to the segment studied in another preparation did not completely abolish pyramidal effects on ipsilateral peroneal motoneurons (Figure 17). In the latter experiment, the early facilitation was decreased while the late facilitation beyond the 20 msec. interstimulus interval was abolished. This failure of section of the contralateral pyramidal tract to completely abolish the early facilitatory influences of ipsilateral pyramidal stimulation might be due to uncrossed, direct pyramidal projections or to fibers remaining in the other pyramid following the pyramidal transection in the medulla. A third explanation might be sought in the fact that the spinal cord transection was made only 2 to 3 segments rostral to the segment under study. Motoneurons project their dendritic systems in the longitudinal direction in the spinal cord (144, 170) and this system may extend into adjoining segments (144). Such projections might receive pyramidal fibers or commissural spinal interneurons which cross in the spinal commissures rostral to the spinal transection. The results of spinal cord quadrisections on ipsilateral pyramidal effects, though not conclusive, tend to substantiate Landau's (86) conclusions that ipsilateral pyramidal activation of spinal motoneurons in subprimates is dependent upon a segmental mechanism.

CHAPTER VI

SUMMARY AND CONCLUSIONS

In the present investigation, pyramidal influences in the spinal cord of the dog, a species heretofore not studied in this respect, have been reported. These influences were evoked by direct electrical stimulation of the medullary pyramids. This approach was selected in order to avoid the complicating factors of cortical mechanisms. Transection of the medulla at the level of the corpus trapezoideum produced a comatose preparation and allowed the use of a chemically unanesthetized animal, to avoid possible anesthetic depression of responses. A second transection in the caudal medulla, leaving only one pyramid intact and severing all other medullary structures, assured that current spread from the pyramidal stimulus did not activate other descending pathways; pyramidal function thus could be studied in isolation.

Evoked activity in the axons of pyramidal tract neurons was recorded as a surface potential by means of a monopolar electrode applied to the dorsum of the spinal cord. Although this method does not allow the accurate determination of conduction velocities in the most rapidly conducting fibers of the pyramidal tract due to positive potentials which precede the arrival of impulses, it was estimated that a majority of the faster fibers of the pyramidal tract of the dog were conducting at a velocity of approximately 70 M/sec. This is of the same order as maximum conduction velocities previously reported in the cat (84).

Recordings from the isolated pyramidal tract in one experiment indicated a maximum conduction velocity of approximately 90 M/sec., suggesting that determinations obtained from cord dorsum recordings were somewhat low for maximum conduction velocities. This maximum conduction velocity would be somewhat higher than the maximum conduction velocities reported for the cat, and would be in agreement with anatomical data which indicates that the pyramid of the dog contains larger diameter fibers than does that of the cat (91). It is suggested that accurate determinations of the conduction properties of pyramidal tract neuron axons in a series of non-feline carnivores would be enlightening as to the phylogenetic development of the pyramidal system.

The time course of pyramidal influences on lumbar spinal motoneuron populations was followed by the use of monosynaptic excitability testing. It was found that pyramidal volleys initiated by direct pyramidal stimulation facilitate motoneuron populations innervating both flexor and extensor muscle groups of the rear limb. This suggests that pyramidal control of the musculature of the extremities is not organized in a simple reciprocal fashion such as would be expected if this system were organized exclusively at the spinal level. This is in contrast with previous investigations reported in the cat.

Pyramidal effects on ipsilateral, as well as contralateral, motoneuron populations were found. Changes in ipsilateral pyramidal influences following transection of the crossed lateral pyramidal tract suggest that intraspinal mechanisms play at least a major role in mediating these effects. Identification of these intraspinal mechanisms is suggested as an area for future research.

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TABLE I

CONDUCTION IN THE PYRAMIDAL TRACT OF THE DOG CALCULATED FROM CORD DORSUM POTENTIALS

Conduction Distance (cm)	Latency, Onset (msec)	Latency, Peak (msec)	Latency, Reversal (msec)	Conduction Velocity, Onset (M/sec)	Conduction Velocity, Peak (M/sec)	Conduction Velocity, Reversal (M/sec)
38	3.33	6.22	13.77	114.1	61.1	27.6
37	3.33	4.88	11.33	111.1	75.8	32.6
41	4.44	6.66	12.44	92.3	61.6	32.9
38	2.86	4.38	6.28	132.9	86.7	60.5
40	3.55	7.10	10.66	112.7	56.3	37.5
41	3.33	5.33	6.86	123.1	76.9	59.8
41	3.79	5.58	7.79	108.2	73.5	52.6
41	4.00	6.10	11.37	102.5	67.2	36.1
40	3.37	4.84	9.47	118.7	82.6	42.2
40	4.84	7.26	12.10	82.6	55.1	33.1
36.5	3.68	6.00	12.00	99.2	60.8	30.4
Mean	3.84	5.94	10.61	108.8	68.9	40.5
	± .64	± .89	± 2.6	± 14.2	±10.8	±11.8

TABLE II

DISCHARGE OF LUMBAR VENTRAL ROOT FIBERS BY 10/SEC. PYRAMIDAL STIMULATION

Conduction Distance (cm)	Discharge Latency (msec)
39.0	7.0
37.5	10.5
33.5	10.5
39.5	11.0
43.5	11.0
40.5	11.0
45.0	11.0
36.5	11.0
Mean	10.38 $\pm$ 1.34

TABLE III

ACTIVATION OF MOTONEURON POPULATIONS BY DIRECT PYRAMIDAL STIMULATION: TIME COURSE OF EFFECTS ON DORSAL ROOT-EVOKED MONOSYNAPTIC DISCHARGE

Time Interval (msec)	% Control	SE
0	116.7	12.7
2	103.2	6.4
4	132.5	17.6
6	166.7	22.1
8	216.1	19.6
10	241.4	13.9
12	231.3	29.1
15	209.5	29.9
20	202.6	31.9
25	214.0	33.4
30	196.4	35.2
35	195.4	36.0
40	196.0	35.8
50	174.2	30.5

TABLE IV

TIME COURSE OF EFFECTS OF DIRECT PYRAMIDAL STIMULATION ON CONTRALATERAL PERONEAL NERVE MOTONEURON POPULATIONS

Time Interval (msec)	% Control	SD	SE	vs. Control p<
-6	102.4	3.8	1.7	NS
-4	103.3	2.6	1.7	NS
-2	100.7	4.3	2.5	NS
0	98.7	13.5	4.3	NS
2	115.6	21.1	6.1	.05
4	123.4	28.3	8.2	.005
6	137.5	27.5	8.3	.001
8	146.1	33.3	10.4	.001
10	149.1	17.4	5.2	.001
12	138.5	20.8	7.3	.001
15	128.1	14.3	5.0	.001
20	132.5	24.2	7.6	.001
25	133.9	24.4	7.6	.001
30	139.4	40.9	12.9	.001
35	133.9	24.9	7.9	.001
40	129.4	21.8	6.9	.001
50	123.6	20.3	6.4	.001
60	123.0	12.0	4.0	.001
70	120.5	13.7	4.8	.05
80	116.7	14.9	5.6	NS

TABLE V

TIME COURSE OF EFFECTS OF DIRECT PYRAMIDAL STIMULATION ON CONTRALATERAL GASTROCNEMIUS MOTONEURON POPULATIONS

Time Interval (msec)	% Control	SD	SE	vs. Control p<	vs. Peroneal p<
-6	101.5	2.2	.98	NS	NS
-4	102.4	7.8	3.5	NS	NS
-2	104.0	9.3	4.1	NS	NS
0	106.7	9.3	2.9	NS	NS
2	120.8	26.6	8.4	.005	NS
4	133.6	19.9	6.3	.001	NS
6	139.4	18.8	5.9	.001	NS
8	141.8	27.5	8.7	.001	NS
10	137.2	33.0	10.4	.001	NS
12	120.6	18.2	6.4	.005	NS
15	116.7	23.3	8.2	.05	NS
20	120.2	23.9	8.4	.005	NS
25	122.5	27.5	9.7	.005	NS
30	119.9	19.7	7.0	.005	NS
35	115.6	19.0	7.2	.05	NS
40	112.6	19.9	7.4	.05	NS
50	115.0	21.2	8.0	.05	NS
60	113.7	15.2	5.8	.05	NS
70	110.0	20.4	7.7	NS	NS
80	110.4	18.3	6.9	NS	NS

TABLE VI

IPSILATERAL ACTIVATION OF MOTONEURON POPULATIONS BY DIRECT PYRAMIDAL STIMULATION: TIME COURSE OF EFFECTS ON DORSAL ROOT-EVOKED MONOSYNAPTIC DISCHARGE

Time Interval (msec)	% Control	SE
0	112.7	12.7
2	105.7	1.9
4	115.7	7.3
6	139.5	13.6
8	166.1	34.2
10	201.6	28.1
12	230.9	39.9
15	215.3	36.8
20	217.3	34.7
25	219.7	44.7
30	201.7	35.4
35	225.7	33.6
40	206.5	22.3
50	152.6	47.6

VITA

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