Factors altering crossed extensor reflex excitability in decerebrate cats : relation of reflex response to pain summative mechanisms
by Mark J Koebbe

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science of Biological Sciences
Montana State University
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Abstract:
The crossed extensor reflex (CER) evoked in decerebrate cats has been classically described as a labile response recruited by the production of the flexor withdrawal reflex (FR) in the ipsilateral limb. Although the two reflexes, the FR and the CER, are related, the CER is more susceptible to a variety of different sensory inputs and shows different characteristics of reflex recruitment. This report provides evidence that the CER in decerebrate preparations may not be as labile as has been previously reported and in addition may recruit activity in a similar manner to the flexion reflex.

Eleven cats were decerebrated at the intercollicular level of the brainstem under ether anesthesia. CERs in the right quadriceps muscle were evoked by stimulation through indwelling electrodes in the left sciatic nerve and inhibited by stimulation of the right sciatic nerve. The CERs were monitored by recordings of isometric tension in the right quadriceps muscle.

CERs in the right quadriceps could be evoked by a single stimulus of the left sciatic nerve under certain prerequisite conditions. The excitability of the CER evoked in the right quadriceps was altered by rotation of the body from side to side (body position), head rotation, mechanoreception, and flexion of the left forelimb.

With the decerebrate cats in an appropriate position to evoke consistent CERs, CERs exhibited several features of recruitment indicative of prolonged central summation. Very low frequencies of stimulation evoked summation of the CER. This is consistent with properties of "windup" observed in the recruitment of the FR, discharges of certain populations of dorsal horn intemeurons, and the perception of noxious stimuli.

These results point out that the excitability of a classical segmental reflex, the CER, are highly affected by descending influences from supraspinal and suprasegmental inputs related to static righting and postural reflexes. Features of the recruitment of the CER suggest that sensory recruitment and reflex recruitment may involve similar mechanisms in certain conditions, although some differences in the duration of the summation of the CER may reflect the modulation by descending and intersegmental inputs.

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A thesis submitted in partial fulfillment
of the requirements for the degree

of

Master of Science

of

Biological Sciences

MONTANA STATE UNIVERSITY
Bozeman, Montana

February, 1985

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APPROVAL

of a thesis submitted by

MARK JOSEPH KOEBBE

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

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ACKNOWLEDGEMENT

The completion of this thesis represents an example in perseverance of an apparently insurmountable goal. Very early this goal appeared to be a certainty, however, several unforseen obstacles made the completion of this objective a difficult task. In finishing this project, I have managed to overcome some trepidation, which has further rekindled my basic interest in scientific research. I can only hope that in the future my interest remains separate of other considerations. For renewing my desire to complete my work many people have played a distinctly supportive role. Because of this, I would like to briefly give them mention.

My association with Dr. Jim McMillan first exposed me to an appreciation of physiology and the neurosciences. I owe a great debt of gratitude to him for supporting me and kindling my interest in research.

This project may never have been completed except for support and a confident attitude from my parents and especially my sister, Julie, without whom I would never have known the mental stamina required to finish a thesis. I am very grateful to Dr. Dwight Phillips and Jim McMillan for supplying rapid and constructive destruction of my writing malaise. I also wish to thank Drs. Robert Moore, Jack Robbins, and Harold Picton for serving as members of my graduate committee. I thank also Tisa Stevenson and Pat Hannon for their encouragement and comradeship in and out of the laboratory.

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ABSTRACT

The crossed extensor reflex (CER) evoked in decerebrate cats has been classically described as a labile response recruited by the production of the flexor withdrawal reflex (FR) in the ipsilateral limb. Although the two reflexes, the FR and the CER, are related, the CER is more susceptible to a variety of different sensory inputs and shows different characteristics of reflex recruitment. This report provides evidence that the CER in decerebrate preparations may not be as labile as has been previously reported and in addition may recruit activity in a similar manner to the flexion reflex.

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With the decerebrate cats in an appropriate position to evoke consistent CERs, CERs exhibited several features of recruitment indicative of prolonged central summation. Very low frequencies of stimulation evoked summation of the CER. This is consistent with properties of "windup" observed in the recruitment of the FR, discharges of certain populations of dorsal horn interneurons, and the perception of noxious stimuli.

These results point out that the excitability of a classical segmental reflex, the CER, are highly affected by descending influences from supraspinal and suprasegmental inputs related to static righting and postural reflexes. Features of the recruitment of the CER suggest that sensory recruitment and reflex recruitment may involve similar mechanisms in certain conditions, although some differences in the duration of the summation of the CER may reflect the modulation by descending and intersegmental inputs.

INTRODUCTION TO THE PRESENT STUDY

The following study is an examination of different sensory inputs which alter the excitability of the crossed extensor reflex (CER). Although previous studies have indicated that the CER is a much more inconsistent (labile) reflex than the flexion reflex (FR) (Creed et al., 1932), the experiments presented are an extension of a serendipitous observation that the rotation of a decerebrate preparation onto its right side, evoked by iterative stimulation of the left sciatic nerve, coincided with a consistent increase in the excitability of the CER recorded from the right quadriceps muscle. In this new position (with the animal on its right side) even a single stimulus of the left sciatic nerve evoked a CER. No previous reports had indicated this degree of excitability of CERs in decerebrate animals (Eccles and Granit, 1929; Pi-Suner and Fulton, 1929).

Since the changes in excitability of the CER were paralleled by postural movements of the entire animal, subsequent experimental manipulations were designed to examine the relationship of the CER to postural and static righting reflexes. These relationships were examined by changing whole body position, rotating the head to either side, flexing or extending the forelimbs, and placement of an opposing surface against the left side when the animal was placed on its right side.

The results of these experiments are considered with respect to previous studies which had indicated an increase in the excitability

of the CER in acute decerebrate animals, but only with certain

manipulations (or stimulation) (Beritoff, 1915; Perl, 1957; Pi-Suner

and Fulton, 1929) or further surgical modifications of the decerebrate

preparation (Eccles and Granit, 1929; Forbes and Cattell, 1924;

Matthes and Ruch, 1933; Rossignol and Gauthier, 1980).

Although both the flexor withdrawal (FR) and crossed extensor

reflexes have been classically related to behavioural responses evoked

by noxious stimulation (Sherrington, 1910), previous studies have

primarily used the flexion reflex to examine recruitment of

nocifensive reflexes (Willis, 1982). Until the present study which

describes CERs evoked by single stimuli, the CER has proven too labile

to study recruitment evoked by low frequency stimulation.

Several recent studies have indicated that recruitment of the

late flexor withdrawal reflex which is evoked by noxious stimulation

of C afferents is dependent on the frequency of stimulation of these

afferents (Iwamoto et al., 1980; Price, 1972; Schouenborg and Sjolund,

1983). These studies have indicated a relationship between the

summation of activity in dorsal horn interneurons and perception of

pain, as well as, recruitment in nocifensive reflex paths. For this

reason the second part of the study used similar low frequencies of

stimulation to evoke summation in the CER. The ability of the CER to

recruit activity in the central nervous system is considered with

respect to the previously mentioned studies of spinal cord summation.

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REVIEW OF THE LITERATURE

The flexor withdrawal and crossed extensor reflexes have been
described as parts of a coordinated behavioral response to noxious or
painful stimulation (Sherrington, 1910). The flexor withdrawal reflex
is the predominant nocifensive response to noxious stimulation of a
limb or to direct stimulation of nociceptive afferent nerves in that
limb. Ipsilateral flexion of the whole limb can be evoked by
stimulation of a focal area on the limb. Flexion of the entire limb
involves recruitment of synergistic flexor muscles. Extension in the
contralateral limb, the crossed extension reflex (CER), also requires
recruitment originating from the ipsilateral withdrawn limb.

Current texts of medical physiology retain this classical
interpretation of the relationship between the flexion reflex (FR) and
the reciprocal response of the crossed extension reflex (CER)
(Mountcastle, 1980). The FR and CER continue to be considered as
congruent aversive responses to noxious stimulation. Flexion
withdrawal of one limb is accompanied by extension of the
contralateral limb to prevent a loss of equilibrium.

Reflexive (involuntary) and motivated motor responses make use of
a common pool of motorneurons, "the final common path" (Sherrington,
1906a). Sherrington and colleagues (summarized in Creed et al., 1932)
demonstrated that the nature of an evoked reflex is influenced by
various weighted afferent and central nervous inputs to the spinal
cord motorneurons. For example, acute decerebrate preparations

exhibit a pronounced tonic rigidity in extensor (antigravity) muscles (Sherrington, 1898). This rigidity is abolished or diminished by deafferentation (Sherrington, 1898; Denny-Brown, 1929) and by transection of the spinal cord (Liddell et al., 1932b). These findings point out the importance of both afferent and brainstem mechanisms in producing this tonic facilitation in extensor muscles.

Although there are some differences in the characteristics of the flexion withdrawal reflex and the CER, many studies show a strong relationship between the nocifensive FR and the CER. Historically, the CER is described as an "associated" nocifensive reflex which results from a radiation or recruitment of the flexor withdrawal reflex (Sherrington, 1910). More recent studies, recording ventral root reflexes evoked by stimulation of afferent nerve fibers, show a direct association between polysynaptic flexion reflexes and crossed extensor responses (Holmqvist, 1961; Jankowska et al., 1967a).

The FR is more traditionally used as a model of nocifensive responses than the CER. This may be a result of the more labile nature of the CER (Creed et al., 1932; Holmqvist, 1961). The CER in decerebrate cats is not an unequivocable response. The unpredictable nature of the CER in decerebrate cats may be a result of tonic brainstem inhibition and/or variability incurred by the crossed cord path (involvement of more interneurons). For instance, only one known study has reported that CERs can consistently be evoked by single stimuli in otherwise intact acute decerebrate cats (McMillan and Koebbe, 1981). This was seen only under appropriate conditions of body and head position.

Classical Consideration of Different Types of Flexor Reflexes.

Early work with flexor reflexes alluded to differences between
the reflex evoked by noxious stimulation (withdrawal) and that
associated with innocuous inputs (pluck reflex) (Sherrington, 1910).
The types of spinal reflexes evoked depended on the local sign of the
stimulus (where the stimulus was applied) (Sherrington, 1903;
Sherrington, 1906b) as well as the quality of the stimulus (Graham-
Brown and Sherrington, 1912; Sherrington, 1910).

Some major differences have been noted between the withdrawal
types of flexor reflexes and flexions evoked by innocuous stimulation
(Creed et al., 1932). The flexor withdrawal reflex which is evoked by
noxious stimulation radiates to incorporate other synergistic flexor
muscles and even to the opposite side of the cord where it recruits
the CER (Sherrington, 1906a; Sherrington, 1910). Maintained noxious
stimulation can also recruit responses in the fore- and hindlimbs
simultaneously (Sherrington, 1910). Flexor or extensor reflexes are
also evoked by innocuous stimulation of cutaneous afferents from the
surface of the skin overlying the muscle (Hagbarth, 1953). Although
such reflexes may be evoked by a vigorous pinch, this response does
not radiate to synergistic muscles and is confined to the muscles at
one joint.

The ability of nocifensive reflexes to recruit activity in more
than one muscle is apparent in the classically described properties of
reflex fractionation, subliminal fringe, and occlusion. Maximal
stimulation of a single afferent nerve evokes responses in only a

fraction of the motor units to a given muscle. Activation of many

afferents may be required to evoke a maximal reflex in that muscle

(Cooper et al., 1926). Two weak stimuli given simultaneously to an

afferent nerve, each which is incapable of evoking a response

individually, may sum temporally to produce a response. This result

indicates that motorneurons may be activated subliminally by single

stimuli. The combination of two or more such weak stimuli may sum to

recruit motorneurons from this subliminal fringe (Eccles and

Sherrington, 1930; Denny-Brown and Sherrington, 1928). In occlusion

the flexion reflex evoked by simultaneous stimulation of the two

afferents is less than the sum of the two responses to stimulation of

the individual afferents (Cooper et al., 1927). All of these

characteristics of nocifensive reflexes indicate that central

processing of afferent information is required (Liddell and

Sherrington, 1923b; 1925). Such central processing is responsible for

recruiting responses from other synergistic muscles.

Early studies also emphasized the dominance of the FR relative to

other reflexes (Graham-Brown and Sherrington, 1912; Sherrington, 1903;

Sherrington, 1910). Reflexes such as the ipsilateral extensor reflex

(Phillipson's reflex) or the scratch reflex (Sherrington, 1906b),

evoked by innocuous stimulation of skin, can be superceded by noxious

stimulation of skin which evokes an ipsilateral flexion reflex.

Withdrawal reflexes persist for a longer duration than can be

accounted for by the arrival of the afferent volley at the spinal cord

(Creed et al., 1932; Sherrington, 1921). This afterdischarge in motor

nerves was considered an indication of a facilitation mediated by

elements within the spinal cord, reflecting a prolonged central excitatory state (Creed et al., 1932; Liddell and Sherrington, 1923b; 1925). This was demonstrated by using paired stimuli. The response evoked by a second stimulus was always larger and longer in duration than when the response was evoked by a single stimulus. The facilitation of the FR evoked by a single stimulus was dependent on the interval between the first and second stimuli (Sherrington, 1921). Protracted activity in the FR or CER evoked by iterative stimulation (Eccles and Granit, 1929; Liddell and Sherrington, 1923a) indicated prolonged central summation. Excitatory afterdischarges of the FR persist after removing all but one dorsal root. This result demonstrated that the prolonged responses were due to central excitatory processes rather than reiterative excitation by inputs from adjacent dorsal roots (Eccles and Sherrington, 1930).

Relation of Quality of Afferent Input to Flexion Reflexes.

Work in the 1930's began to distinguish differences in the function of different sizes of afferent fibers (Bishop and Heinbecker, 1935). Since noxious input was believed a prerequisite to the withdrawal, or flexor, reflex some investigators suggested a relationship between conduction in both the small myelinated (A-delta) and the unmyelinated (C) fibers, and the flexion reflex (Zotterman, 1939). Later studies demonstrated that small myelinated, or A-delta, and unmyelinated, or C, afferent fibers did indeed respond to noxious stimulation (Burgess and Perl, 1969; Bessou and Perl, 1967).

Recent studies question the strict relationship between conduction in small afferents, pain, and flexor reflexes. Small afferents can respond to innocuous mechanoreceptive and thermoreceptive stimuli as well as noxious stimulation (Kumazawa and Perl, 1977). Furthermore, group II and III muscle afferents, as well as cutaneous afferents of all sizes, can elicit flexor reflex discharges in ventral roots (Holmqvist and Lundberg, 1961; Holmqvist, 1961). The ability of qualitatively different afferents to evoke flexor reflex responses led Lundberg and colleagues to classify these afferents as flexor reflex afferents (FRAs) (Eccles and Lundberg, 1959; Holmqvist and Lundberg, 1961). Stimulation of high threshold muscle afferents (group II and III), joint afferents, and cutaneous afferents may all evoke flexor responses. While this classification system includes all afferents which can evoke a flexor response into one group, it fails to take into account differences in the qualitative and quantitative aspects of the flexor reflexes evoked by the different classes of afferents.

The relative contributions of different groups of afferent fibers to the FR was clarified by the classic studies of Lloyd in the 1940's (Lloyd, 1943a; 1943b; 1943c). First, he described short and long latency responses related to conduction in large and small myelinated afferents respectively. The early monosynaptic discharge was conclusively associated with activation of the large Ia muscle afferents (Lloyd 1943a; 1946). Polysynaptic reflex discharges with longer latencies were associated with inputs from cutaneous and high threshold muscle afferents (Lloyd 1943a; Lloyd 1943b). These results

suggested that there are significant differences in the flexor

reflexes evoked by the several classes of afferents capable of evoking

flexor reflexes. The polysynaptic discharges evoked by larger

afferents are brief (about 10 ms) (Lloyd, 1943a). Addition of A-delta

(small myelinated) afferents to the afferent volley (stimulus) adds to

the duration and the amplitude of the polysynaptic flexor reflex

(Lloyd, 1943a; Lloyd, 1943b). Stimulation of unmyelinated fibers also

elicits a delayed and prolonged flexor reflex discharge (Burke et al.,

1971; Iwamoto et al., 1980; Koll et al., 1961; Price, 1972;

Schouenborg and Sjolund, 1983). These prolonged discharges associated

with input over high threshold (pain) fibers are more consistent with

the magnitude and duration of the flexor withdrawal reflex than of

flexor reflexes evoked by innocuous stimulation (Brooks and Koizumi,

1953; Iwamoto et al., 1980; Schouenborg and Sjolund, 1983).

The dependence of reflex response on the quality of afferent

input is clearly evidenced by the reversal of reflex patterns under

appropriate conditions. Stimulation of low threshold afferents evokes

a crossed flexor reflex rather than a crossed extensor reflex (Perl,

1957; 1958). Similar low threshold inputs from large muscle afferents

evoked by stretching muscle in the contralateral limb inhibit the CER

evoked in that limb (Perl, 1959). These findings support classical

studies which show that reflexes evoked by innocuous (low threshold)

cutaneous stimuli may depend on the location of the stimulus (local

sign) (Hagbarth, 1953; Sherrington, 1910). For example, bilateral

flexion of the hindlimbs may be evoked by stimulation of cutaneous

afferents of the hindlimb. Crossed flexor reflexes revert to crossed

extension when high threshold cutaneous afferents are stimulated (Perl, 1957). This observation shows the ability of nocifensive responses to supercede reflexes evoked by low threshold stimulation (Sherrington, 1910).

Reflex reversal has recently been related to limb position (Grillner and Rossignol, 1978), and especially to limb position during the walking cycle (Rossignol and Gauthier, 1980). Stimulation of high threshold afferents evokes a crossed flexion reflex when the contralateral limb is extended during the swing phase of the walking cycle (Grillner and Rossignol, 1978). A further examination of this reflex reversal demonstrates that some afferents from muscles and/or joints in the extended limb are required to be intact (Rossignol and Gauthier, 1980). By progressively deafferenting the crossed limb these authors showed that almost complete deafferentation was required to abolish the crossed flexor response. This result is consistent with the importance of low threshold proprioceptive inputs to the limb in which the crossed reflex is evoked (Perl, 1959). CERs evoked by high threshold stimulation after deafferentation of the responding limb are larger than CERs evoked before the limb was deafferented (Rossignol and Gauthier, 1980). This is also consistent with earlier studies which described an increase in the excitability of the CER after deafferentation (Forbes and Cattell, 1924; Eccles and Granit, 1929; Pi-Suner and Fulton, 1929).

Convergence of Afferent Input to the Spinal Cord.

Since flexor reflexes can be evoked by stimulation of several classes of afferents (the FRAs), some authors have suggested that there is a convergence from FRAs onto a common flexor reflex pathway (Holmqvist and Lundberg, 1961). Support for convergence of afferent inputs onto common pathways comes from anatomical studies describing the cellular architecture of the dorsal and ventral horn of the spinal cord (Ralston, 1968a; 1968b; Rethelyi and Szentagothai, 1973; Szentagothai, 1964; Wall, 1967). Recordings from interneurons in the dorsal and ventral horns of the spinal cord also reveal that stimulation of qualitatively different afferent nerves can evoke discharges in single neurons (Kolmodin, 1957; Kolmodin and Skoglund, 1954; Kolmodin and Skoglund, 1960; Price and Mayer, 1974; Price and Wagman, 1970; Wagman and Price, 1969). Additional support for the existence of common paths comes from studies on the presynaptic control of afferent input (or sensory information) evoked by stimulation of different classes of afferent nerves (Mendell and Wall, 1964; Melzack and Wall, 1965).

Anatomical studies have shown that different classes of afferents terminate in different laminae of the spinal cord. The large muscular afferents (Ia and Ib) terminate in more ventral and medial laminae of the spinal cord (Scheibel and Scheibel, 1969; Brown, 1981). The cutaneous afferents, however, project to the dorsal horn (Brown, 1982). Large cutaneous afferents which originate primarily from mechanoreceptors activated by innocuous stimuli synapse primarily in

laminae 3-5 of the dorsal horn (rev. in Brown, 1981). In contrast to the projection of large cutaneous afferents, the small myelinated (A-delta) and unmyelinated (C) afferent fibers synapse only in the first two laminae of the dorsal horn (Kumazawa and Perl, 1978; Light and Perl, 1979; Brown, 1982). Small myelinated afferents, A-delta, which are activated by noxious stimulation (Burgess and Perl, 1967; Christenson and Perl, 1970) terminate in the marginal zone, or lamina 1 (Kumazawa and Perl, 1978), while axons from the unmyelinated (C) afferents project largely to interneurons of the substantia gelatinosa (SG), or laminae 2 (of Rexed) (Light and Perl, 1979). These anatomical studies suggest specific differences in the projection of innocuous and noxious inputs to dorsal horn neurons.

Some of the anatomical features of dorsal horn interneurons further indicate the functional separation of noxious and innocuous afferent input. Many of the interneurons in laminae 3 and 4 make no apparent connections with interneurons in laminae 1 and 2 (Brown, 1981). The structure of many laminae 1 and 2 neurons indicates that these cells are largely confined to the lamina in which their cell bodies are located (Light et al., 1979; Price et al., 1979). These results show that interneurons in the different laminae may have specific sensory functions. However, some interneurons in the more ventral laminae of the dorsal horn (lamina 3) may send long dendrites into laminae 1 and 2 (Mannen and Suguira, 1976). These results suggest that different interneurons within the same laminae may respond to specific sensory inputs or may receive convergent inputs from interneurons in more dorsal laminae.

In contrast to the dorsal horn, the anatomical structure of the ventral horn of the spinal cord is considerably more complex. Terminals from long descending tracts, dorsal horn interneurons, and larger afferent collaterals contribute to the extreme complexity of the ventral horn (Rethelyi and Szentagothai, 1973; Wall, 1967). Rethelyi and Szentagothai (1973) have suggested that the ventral horn is a structural homologue of the reticular formation of the brainstem. The convergence of dorsal horn inputs onto interneurons of the ventral laminae of the spinal cord led Wall (1967) to describe a model of cascading inputs. The model basically proposed that interneurons in more dorsal laminae project onto neurons in a more ventral location. Although the anatomical studies described above indicate a functional separation between some laminae of the spinal cord, physiological studies show that ventral horn interneurons respond to a wide variety of converging inputs (Baldissera et al., 1981).

Pioneering studies on the physiology of spinal cord interneurons by Kolmodin and colleagues (Kolmodin, 1957; Kolmodin and Skoglund, 1954; Kolmodin and Skoglund, 1960) first indicated the existence of different functional classes of interneurons located in the dorsal horn (Kolmodin and Skoglund, 1960). Different interneurons were excited by noxious or innocuous stimulation of the foot pads in cats. These investigations also described neurons which were excited by noxious stimulation and inhibited by innocuous stimulation. These early studies showed that some interneurons responded specifically to noxious or innocuous stimulation, while some interneurons received convergent inputs from both noxious and innocuous inputs.

Recent studies describe such interneurons in more specific terms
These studies describe different functional classes of dorsal horn
interneurons. Although these studies use different classification
systems, they all indicate the existence of three classes of
interneurons in the dorsal horn (Chung et al., 1979; Price et al.,
1979; Wall et al., 1979). Class 1 interneurons are specifically
excited by innocuous stimulation, while class 3 neurons are only
excited by noxious stimulation. Class 2 neurons which are excited by
both innocuous and noxious stimuli have been described as wide dynamic
range neurons in previous reports (Price and Mayer, 1974). Such wide
dynamic neurons respond more vigorously when excited by noxious
stimulation.

Brown (1982) has suggested that class 1 type neurons represent
interneurons in laminae 3 and 4 which receive a predominate input from
innocuous mechanoreceptors. Class 3 neurons excited only by noxious
inputs are represented by interneurons of the marginal zone or the SG.
Interneurons at the border of the substantia gelatinosa (lamina 2) and
lamina 3, between the neurons responding to noxious or innocuous
inputs, may be the wide dynamic interneurons described in earlier
studies (Wall et al., 1979).

Cervero et al., (1979a; 1979b) describe a different group of
dorsal horn interneurons which exhibit inverse patterns of responses.
In contrast to class 3 interneurons, class 3 inverse neurons are only
inhibited by noxious inputs. Class 1 inverse neurons are only
inhibited by innocuous stimulation, while class 2 inverse neurons, or
inverse wide dynamic range neurons, are inhibited by both innocuous

and noxious inputs. These results suggest a complementary function for different populations of spinal cord interneurons.

The quantity and quality of afferent input to the spinal cord is regulated by presynaptic inhibition (Schmidt, 1973) or presynaptic facilitation (Mendell, 1972; Mendell and Wall, 1964) in which there is a depolarization or hyperpolarization of the terminals of primary afferents (Eccles et al., 1961; Eccles et al., 1962a; 1962b; 1962c; Mendell and Wall, 1964; Melzack and Wall, 1965). Wall (1962) mapped field potentials within the spinal cord evoked by primary afferent stimulation and identified the substantia gelatinosa as the region of the spinal cord where presynaptic inhibition occurs. A predominance of axoaxonic synapses in the SG has also been associated with presynaptic inhibition within the SG (Ralston, 1968a; Szentagothai, 1964). Primary afferent depolarization (PAD) results in a decrease in the synaptic efficacy of the stimulated primary afferents (Eccles et al., 1961; Eccles et al., 1962b). In contrast to PAD, primary afferent hyperpolarization evoked by stimulation of high threshold afferents may facilitate primary afferent input (Mendell, 1970; Mendell, 1972; Mendell and Wall, 1964; Melzack and Wall, 1965).

Although most reports indicate that PAD (or presynaptic inhibition) is confined to the primary afferents stimulated (Eccles et al., 1962a; Eccles et al., 1963a; 1963b), PAD may be evoked in terminals of different primary afferents under certain conditions (Jankowska et al., 1967a; Anden et al., 1966a; 1966b; Lund et al., 1965; Eccles and Lundberg, 1959). Stimulation of Ia afferents in spinal cats evokes PAD in FRA terminals (Lund et al., 1965).

Stimulation of FRAs can evoke an even larger PAD in the terminals of

larger afferents (Ia) if DOPA is administered to acute spinal cats

(Anden et al., 1966a; Jankowska et al., 1967a). The effect of DOPA on

spinal neurons appears to involve one or more monoaminergic

transmitters released by stimulation of different descending paths

from the brainstem reticular formation (Engberg et al., 1968c;

Krnjevic, 1981). The PAD evoked in FRA terminals by stimulation of Ia

afferents of spinal animals is substantially smaller than the PAD

evoked by Ia afferent stimulation in decerebrate animals (Eccles and

Lundberg, 1959; Lundberg, 1982). These results indicate a reciprocal

interaction of PAD evoked in large and small afferents. This

reciprocal organization may involve the activation of different pools

of interneurons which feedback upon specific terminals of different

primary afferents (Eccles et al., 1962a; Eccles et al., 1963a; 1963b;

Lundberg, 1982).

Other reports suggest that primary afferent hyperpolarization

(PAH) results when high threshold FRAs (unmyelinated C afferents) are

stimulated (Mendell and Wall, 1964; Melzack and Wall, 1965; Mendell,

1970; Mendell, 1972). These authors suggest that such

hyperpolarizations facilitate primary afferent input to spinal cord

interneurons (presynaptic facilitation). Earlier experiments had

indeed shown that artificial hyperpolarization of the spinal cord

facilitates afferent input and reflex activity (Eccles and Krnjevic,

1959; Eccles et al., 1962c; Wall, 1958). These results suggest that

hyperpolarization evoked by stimulation of high threshold afferents

may concurrently facilitate sensory inputs as well as reflex responses.

Presynaptic inhibition (PAD) and presynaptic facilitation (PAH) have been implicated as mechanisms involved in the gating or modulation of sensory (pain) information in the spinal cord (Melzack and Wall, 1965).   In this scheme, common interneurons of the SG either facilitate transmission or inhibit transmission of primary afferent input to higher sensory receiving areas.   Subsequent studies, however, have reported only PAD when high threshold afferents (unmyelinated) are stimulated (Burke et al., 1971; Schmidt, 1973).   These results suggest that the SG is involved in gating sensory inputs to more ventral laminae of the spinal cord, although presynaptic effects may not alone account for this regulation.   Further studies suggest that the duration of responses evoked in dorsal horn cells by stimulation of A-delta or C afferent nerves is more consistent with postsynaptic mechanisms of inhibition or facilitation (Price and Wagman, 1970; Price et al., 1971; Price, 1972).

Physiological analyses of responses of dorsal horn neurons evoked by large and small afferent fibers indicate a convergence of activity from these afferents on dorsal horn neurons (Mendell, 1966; Price and Wagman, 1970; Price et al., 1971; Price et al., 1978; Wagman and Price, 1969).   Stimulation of large afferents alone evokes brief discharges followed by an inhibitory period (depressed background activity) (Price and Wagman, 1970; Wagman and Price, 1969).   The duration of this inhibitory period (200-300 ms) is consistent with the duration of PAD (Price et al., 1971).   If A-delta afferents are included in the afferent volley, a delayed and prolonged discharge follows the inhibitory period.   Stimulation of unmyelinated afferents

also evokes a prolonged response which can be augmented by low

frequencies of stimulation (0.33 hz.) (Mendell, 1966; Price and

Wagman, 1970; Wagman and Price, 1969). This recruitment of excitatory

activity with succeeding stimuli has been termed "windup" (Mendell,

1966; Price, 1972). The relatively prolonged durations of activity

do not support that PAD is solely responsible for this phenomenon

(Price, 1972; Price et al., 1971).

Most interneurons in the lower dorsal horn and in the ventral

horn also have convergent sensory inputs (Wall, 1967). Early studies

showed that both somesthetic and proprioceptive inputs project to

intermediate and ventral horn interneurons (Kolmodin, 1957; Kolmodin

and Skoglund, 1954). Neurons in this region of the spinal cord

respond to interlimb propriospinal inputs (Kolmodin and Skoglund,

1954). Interneurons in the medial intermediate region of the spinal

cord (see Kolmodin and Skoglund, 1960) generally respond to afferents

from more than one synergistic muscle (Kolmodin, 1957). Many of these

interneurons responded to ipsilateral and contralateral proprioceptive

inputs, as well as natural stimulation of cutaneous afferents in the

ipsilateral toe pad. These results are consistent with anatomical

studies which show commissural projections to the contralateral cord

from interneurons in the intermediate zone (laminae 5-7) (Mannen,

1975; Matsushita, 1970).

Interneurons situated more ventrally in the spinal cord respond

to direct afferent inputs from muscular and cutaneous afferents

(Lloyd, 1943a; 1946), other interneurons of the dorsal horn (Wall,

1967; Price et al., 1971), or from descending inputs from the

pyramidal (Fetz, 1968; Lund et al., 1965; Lundberg and Voorhoeve, 1962; Lundberg et al., 1963), reticulospinal (Engberg et al., 1968a; 1968b), and vestibulospinal tracts (Erulkar et al., 1966; Wilson and Peterson, 1978). Like the more ventral laminae of the dorsal horn (Price and Mayer, 1974; Wall, 1967), the ventral horn interneurons also exhibit larger receptive fields (Kolmodin, 1957; Price and Mayer, 1974).

Brainstem Inputs Affecting the Excitability of Spinal Reflexes.

Classical studies indicated that structures in the brainstem altered the excitability of spinal reflexes (Sherrington and Sowton, 1915; Matthes and Ruch, 1933; Creed et al., 1932). These early reports did not examine the specific inputs from the brainstem responsible for the changes in excitability of spinal reflexes, although comparisons between spinal reflexes evoked in spinal and decerebrate animals showed that both the FR and CER were inhibited in decerebrate preparations (Sherrington and Sowton, 1915; Matthes and Ruch, 1933). This inhibition was attenuated by transection of the spinal cord or by lesions of the dorsolateral and/or ventrolateral fasciculi of the spinal cord (Fulton et al., 1930a; 1930b; Liddell et al., 1932a; 1932b). Lesions affecting vestibular inputs to the spinal cord failed to diminish the inhibition of the FR in decerebrate preparations (Liddell et al., 1932a; 1932b). Stretch reflexes evoked in extensor muscles, however, were diminished on the same side as the lesion.

The brainstem in decerebrate animals may affect the excitability of spinal reflexes via two principal systems. First, inputs from the vestibular apparatus are conveyed to the spinal cord by the medial and lateral vestibulospinal tracts (MVST or LVST) (Wilson and Peterson, 1981). The other primary descending system from the brain stem is the reticulospinal system which may include indirect vestibular inputs through bilateral connections of the vestibular nuclei with the reticular formation (Gernandt et al., 1959). Medial and lateral reticulospinal tracts originate from the relatively diffuse nuclei of the reticular formation (Peterson, 1979). Since vestibular inputs project bilaterally to the reticular formation, changes in spinal reflexes evoked by reticular or vestibular inputs are often difficult to distinguish (Gernandt et al., 1959; Gernandt and Gilman, 1959).

Early studies showed that vestibular inputs tonically conferred an increase in the excitability of spinal reflexes involving extensor muscles. Unilateral labyrinthectomy or ablation of the vestibular nuclei does result in a loss of ipsilateral extensor tone. This diminished extensor tone is only seen in acute preparations; chronic animals with unilateral lesions exhibit a return of extensor tone. Even bilateral lesions of the vestibular nuclei only produce temporary deficits in the extensor tone which are not accompanied by a reciprocal increase in the excitability of flexor reflexes (Liddell et al., 1932a). Such results illustrate two features of vestibular control of excitability of spinal reflexes. First, the vestibular system contributes strongly to postural reflexes in extensor muscles, although there is also some compensation for the long term loss of

vestibular inputs on spinal reflexes. Second, the tonic inhibition of the FR does not originate directly from the vestibular inputs. This non-reciprocal control of flexor and extensor reflexes was considered contradictory to the reciprocal patterns of motor control described by Sherrington (1906a).

Further studies by Gernandt and colleagues also showed that vestibulospinal inputs facilitated extensor reflexes evoked by dorsal root stimulation on the ipsilateral side of the spinal cord (Gernandt et al., 1959; Gernandt and Thulin, 1953; Gernandt and Gilman, 1959). Ventral root reflexes evoked by doral root stimulation concurrent with stimulation of the lateral vestibular nucleus were facilitated through short and long latency paths (Gernandt and Gilman, 1959; Gernandt et al., 1959). The longer latency facilitation was attributed to bilateral projections from the vestibular nuclei to the reticular formation or high cervical spinal cord, since this response could be evoked in the contralateral ventral roots. Intracellular recording techniques later revealed facilitation of excitatory postsynaptic potentials in extensor motorneurones evoked by stimulation of the lateral vestibulospinal tract (Wilson and Yoshida, 1969). The latencies of facilitation indicated that both polysynaptic and monosynaptic paths were involved. Wilson and Yoshida (1969) also noted that polysynaptic EPSPs were more commonly evoked in knee extensors. Monosynaptic excitation of motorneurones by LVST stimulation is directed to motorneurones supplying axial extensor muscles (Precht, 1975). Reciprocal inhibition of ipsilateral motorneurones supplying flexor muscles involved two or more synapses

(disynaptic). These results all support a dominant excitatory projection by the lateral vestibulospinal system to ipsilateral extensor motorneurones.

Several features of the anatomical projection of vestibular inputs to the spinal cord are related to vestibulospinal reflexes. Although both the medial and lateral vestibulospinal tracts (LVST) project ipsilaterally to the cervical spinal cord, only LVST axons have been found in the lumbar spinal cord (Wilson and Peterson, 1978). Axons from single neurons in the lateral vestibular nucleus may send collaterals to both cervical and lumbar enlargenments (Abzug et al., 1974). The LVST originates principally from the lateral vestibular nucleus and projects to the ipsilateral spinal cord. Inputs to the lateral vestibular nucleus come primarily from utricular afferents which respond to static position of the head (Peterson, 1970). These results indicate that the lateral vestibular projections to the lumbar cord convey information related to static postural reflexes to both the cervical and lumbar spinal cord.

The pattern of projection of vestibulospinal fibers within the ventral horn of the spinal cord suggests that vestibulospinal reflexes may be subject to modulation by other converging inputs. Vestibulospinal fibers terminate on interneurons in laminae 7-9 in the ventral horn of the spinal cord (Nyberg-Hansen and Mascitti, 1964). Since interneurons in this region of the spinal cord respond to converging inputs from propriospinal and cutaneous inputs (Kolmodin, 1957), vestibular inputs to the lumbar spinal cord of the cat may be modulated by inputs from other sources. A more recent study has

indicated that some interneurons responding to vestibular stimulation were also excited by inputs from segmental primary afferents originating in the contralateral limb (Bruggencate and Lundberg, 1974). Erulkar et al. (1966) indicated that vestibulospinal inputs to the spinal cord were responsible for PAD in interneurons, as well as directly affecting interneurons and motorneurons in the lumbar cord of the cat.

Responses evoked by vestibular stimulation are often difficult to reconcile with behavioural responses attributed to the vestibulospinal reflexes. Responses in extensor muscles of the forelimb evoked by sinusoidal (dynamic) linear accelerations of the head (Anderson et al., 1977) are the opposite of the responses evoked by static tilt (Lindsay et al., 1976). Static tilt to one side elicits extension in the limbs of the side tilted down concurrent with head rotation away from the extended limbs, while the limbs on the upward side are flexed (Precht, 1975; Wilson and Peterson, 1978). Dorsoflexion of the head evokes bilateral forelimb extension and hindlimb flexion concomittant with upward rotation of the eyes. The opposite response is evoked by ventroflexion of the head. Quick movements evoking otolith responses result in transient extension of all limbs (Anderson et al, 1977). This response has been related to bracing movement in anticipation of landing after an unexpected fall (Watts, 1976). This response is lost after connections between neck afferents and the reticular formation are severed (Precht, 1975). These results all indicate that higher order interneurons are involved in the integration or expression of vestibulospinal reflexes. Vestibulospinal reflexes may be

integratively related to reflexes affected by the reticular formation (including the tonic neck reflexes) (Wilson and Peterson, 1981).

The existence of reticular projections affecting the excitability of spinal reflexes was first suggested by Fulton (1926). Early studies showed that the flexor reflex and CER were tonically inhibited in decerebrate animals (Sherrington and Sowton, 1915; Matthes and Ruch, 1933). Liddell and colleagues (Fulton et al., 1930a; 1930b; Liddell et al., 1932a: 1932b) established that tonic effects from the brainstem remained after lesions of vestibular nerve and ablation of the vestibular nuclei. Lesions of the ventrolateral fasciculi of the spinal cord which severed the vestibulospinal tracts failed to completely suppress the inhibition of the flexor reflex. Only complete transection of the spinal cord or lesions of the dorsolateral fasciculus attenuated the brainstem inhibition of the flexor reflex (Liddell et al., 1932a; 1932b).

Later studies characterized general facilitory and inhibitory regions in the brainstem reticular formation (Magoun, 1950). Stimulation of the lateral regions evoked facilitation of spinal reflexes, while stimulation in more medial regions resulted in inhibition of spinal reflexes. A subsequent study showed that generalized effects on spinal reflexes were only evoked with high intensities of stimulation (Sprague and Chambers, 1954). Low levels of stimulation evoked coordinated movements of the whole animal. These studies indicated that certain regions of the reticular formation were responsible for general changes in reflex excitability,

while supporting a complex integrative function for the reticular formation in reflex organization.

The predominant projection from the reticular formation to the lumbosacral spinal cord originates from nuclei located in the medial brainstem (Peterson, 1979). The medial reticulospinal tract, located in the ventromedial fasciculus of the spinal cord projects to all levels of the spinal cord, although most terminals are located rostral to the first lumbar segment of the spinal cord. The lateral reticulospinal tracts, ipsilateral and contralateral, terminate in more dorsal laminae at all levels of the spinal cord (Nyberg-Hansen, 1965). Single lateral reticulospinal fibers terminate in both cervical and lumbar segments of the spinal cord (Peterson et al., 1975). The anatomical projection of these ventrally located reticulospinal tracts indicates a capacity to effect reflex activity at both cervical and lumbar levels of the spinal cord as well as functional distribution to many laminae of the spinal cord.

In contrast to the vestibulospinal system stimulation of the reticulospinal system evokes direct action on both flexor and extensor motorneurons (Grillner and Lund, 1968). Stimulation of the MRST evokes primarily monosynaptic EPSPs or IPSPs in motorneurons supplying the axial musculature. LRST stimulation evokes polysynaptic responses in motorneurons supplying more distal muscles (Wilson and Yoshida, 1969). Although it is often difficult to relate isolated responses in motorneurons or interneurons to the expression of complete behavioural responses, activity in the ventral reticulospinal tracts has been related to short and long spinal propriospinal systems in the spinal

cord (Wilson and Peterson, 1981). The early studies of Lloyd (1941) characterized a long bulbospinal system which involved activation of segmental and intersegmental propriospinal neurons. Later studies showed that both short and long descending propriospinal systems were related to reticular inputs from the brainstem in decerebrate cats (Gernandt and Shimamura, 1961; Shimamura and Livingston, 1963). These results, considered together, suggest a complex interaction between ascending propriospinal and descending propriospinal systems mediated by relays in the reticular formation (Wilson and Peterson, 1981).

A putative reticulospinal pathway in the dorsolateral fasciculus has been physiologically characterized, but has resisted anatomical analysis. These more dorsally located reticulospinal tracts include the descending raphe system (Basbaum et al., 1978) and the dorsal reticulospinal system described by Lundberg and collaberators (Eccles and Lundberg, 1959; Holmqvist and Lundberg, 1961). Although these tracts originate from different regions of the medial brainstem, they travel in anatomically similar locations and project to anatomically similar areas in the dorsal and ventral horns of the spinal cord (Brown, 1981). The terminations of these tracts are located in laminae 1,2,5,6, and 7 of Rexed (Basbaum et al., 1978). Such anatomical connections suggest a function in the control of afferent input as well as reflex activity.

Activity in the dorsal reticulospinal system in the decerebrate animal has been associated with the tonic inhibition of polysynaptic flexor and crossed extensor reflexes (Eccles and Lundberg, 1959; Holmqvist and Lundberg, 1961). Reflexes evoked in ventral roots by

stimulation of large afferent nerves (Ia) are spared from decerebrate

inhibtion. In fact stimulation of Ia afferents in decerebrate

preparations presynaptically inhibits the transmission evoked by

concurrent stimulation of FRAs (Anden et al., 1966a). Transection of

the spinal cord attenuates the tonic inhibition of polysynaptic FRs

and CERs (Eccles and Lundberg, 1959). Stimulation of FRAs in spinal

animals evokes a presynaptic inhibition (PAD) in the terminals of Ia

afferents (Lund et al., 1965). These effects are further facilitated

by concurrent administration of DOPA to acute spinal preparations

(Anden et al., 1966a; 1966b; Jankowska et al., 1967a; 1967b). Further

studies indicate that the release of polysynaptic reflexes from tonic

inhibition by such methods is associated with spontaneous locomotor

responses (Grillner, 1975). These studies indicate that the

polysynaptic reflexes of flexion and crossed extension may be

integratively related to locomotion as well as nocifensive behavior.

Although it is known that DOPA facilitates polysynaptic reflexes

in the spinal cord, little is known of the mechanism by which this

activity is mediated (Willis, 1982). Part of the problem stems from

the multitude of different reticular paths to the spinal cord. These

paths may release a variety of neurotransmitters. Some early studies

indicated that the effect of DOPA was related to liberation of

norepinepherine or other monoamine neurotransmitters in the spinal

cord, however depletion of norepinepherine terminals by administration

of reserpine does not result in depression of the enhanced

polysynaptic reflexes by subsequent administration of DOPA (Engberg et

al., 1968c). It is likely that more than one neurotransmitter is

involved in the augmented discharge in polysynaptic reflexes associated with the effects of DOPA (Krnjevic, 1981).

The tonic neck reflexes evoked from spindle receptors in the large muscles of the neck (Abrahams, 1977) and joint receptors in the high cervical vertebrae (McCouch et al., 1951) by rotation of the neck or head are mediated through the reticular formation (Wilson and Peterson, 1981). Lindsay et al (1976) distinguished between labyrinthine and tonic neck reflexes by casting the neck of decerebrate cats which allowed examination of labyrinthine effects or by fixing the head and rotating the body around the head. The latter manipulation eliminated vestibular contributions to the reflexes evoked. Rotation of the body evoked extension in the limbs towards which the chin of the animal was pointed. The limbs on the occiput side of the head were flexed. These results supported classical studies by Magnus (1926) who utilized labyrinthectomized animals to isolate similar tonic neck responses. A complex interaction of inputs from the labyrinths and receptors in the neck results in the static righting reflexes observed in decerebrate animals.

METHODS AND MATERIALS

Surgical Techniques

Eleven cats of mixed breeds (1.0-2.1 kg.) were first anesthetized with ethyl ether. The trachea was cannulated with a stainless steel tube in order to prevent reflux of oral contents and to provide access to a ventilation pump which was only used in a few instances when the animal failed to respire during the procedures. In most cases the pump was never required. The common carotid arteries were ligated in the neck to minimize circulation to the upper brain.

The animal was rotated into a prone position for decerebration and subsequent surgical procedures. A trephine and rongeur were used to remove enough cranial bone to expose the cortex, then the neuraxis was transected at the midcollicular level with a blunt spatula, using the bony tentorium as a guide. Bleeding was minimized during the actual decerebration procedure by manual compression of the vertebral arteries against the atlas vertebra. Following transection of the neuraxis, the arterial compression to the vertebrals was applied intermittently, as required to allow perfusion of brainstem structures with minimal bleeding. After several minutes, sufficient clotting occurred to permit uninterrupted perfusion through the vertebral arteries. A ligature placed through the scalp was used to suspend the head in a slightly ventriflexed position so that any transudated fluid

or blood drained to the nasal end of the evacuated cranial cavity rather than along the brainstem.

The sciatic nerve in each of the hindlimbs was exposed in the popliteal fossa and was followed superiorly by dissection along the femur, where it was ligated near the mid point of the femur and cut distal to the ligatures. Branches of the sciatic supplying the hamstring and gluteal muscles in the right leg were cut to prevent coactivation of flexors and hip extensors during stimulation procedures. The right femoral nerve was exposed with the animal in an approximately supine position and all branches were sectioned except those supplying the quadriceps femoris. Identification of the branches to the quadriceps was accomplished by visualizing contractions of these muscles evoked by electrical stimulation of the different nerve branches. Two indwelling electrodes were inserted into each of the severed sciatic nerves just proximal to the ligatures. The .127 mm diameter wire electrodes were fully insulated except for the tips, which were scraped to make good electrical contact. Short pieces of latex surgical tubing were used to enclose the electrode-nerve complex to provide insulation from surrounding tissues.

The cat was then placed in the supine position and the quadriceps muscle and patellar tendon were resected and dissected free from the surrounding tissues. Heavy surgical suture was used to fasten the patellar tendon to an isometric muscle tension transducer. The entire right hindlimb was stabilized vertical to the table by drill bits inserted in the femur at the distal (knee) and proximal (hip) ends of

the bone and clamped to a vertical supporting rod. All structures of
the right hindlimb were oriented vertical to the table.

Stimulation/Recording Techniques

The sciatic nerves were stimulated with square wave pulses
administered through stimulus isolation units. Stimulus frequency,
intensity, and duration for each electrode pair could be adjusted
independently. Stimulus parameters were adjusted to produce a brisk
response from the quadriceps muscle; the levels were varied for
different experimental procedures.

Crossed extension reflexes were monitored by recording isometric
tension from the right quadriceps muscle on an ink-writing curvilinear
oscillograph. The gain of the amplified signal was adjusted to
provide a reasonable visual trace of the evoked response. Paper speed
was varied to facilitate evaluation of different types of responses to
the experimental procedures. Calibrations were obtained at each
setting by suspending a standard unit of weight from the muscle
tension transducer.

Experimental Protocol

In early experiments the threshold intensity sufficient to evoke
the CER was determined at relatively high frequencies of stimulation
(>10 herz). The range of threshold intensities was between 0.05 ma.
and 5.0 ma. With the subsequent observation that CERs could be evoked
by single shocks when animals were on their right side, thresholds
were determined with low and high frequency stimulation. The

intensities required to evoke the CER with single stimuli were between 0.25 and 0.5 ma.

Examinations of reflex summation were performed with suprathreshold intensities of stimulation (0.5-2.5 ma.) at various frequencies. A typical experimental series consisted of examining responses evoked using slow trains of stimuli at intervals between 7 seconds and 0.1 seconds. Then a conditioning-test paradigm was used. The effects of a conditioning stimulus (C) on the response to a test shock (T) were examined at different C-T intervals.

Inhibition of the CER in response to stimulating the right sciatic nerve was accomplished by using low frequency trains of stimulation. Prolonged CERs were first evoked by iterative stimulation of the left sciatic nerve (10 hz). After the reflex tension had plateaued, stimulation of the right sciatic ensued. Trains of inhibitory stimuli were delivered to the sciatic at frequencies between 0.3 hz and 20 hz.

RESULTS

General Considerations

All the decerebrate animals exhibited the classic signs of tonic extensor rigidity (Sherrington 1898). Rigid extensor tone was observed in all limbs within minutes of the surgical decerebration. Forelimb extensors resisted stretch until adequate force induced the "clasp knife" effect (Sherrington 1906). In a few preparations the rigidity was profound enough to cause axial muscle rigidity in the neck (opisthotonus). Static righting reflexes were also present in the decerebrate cats (Magnus 1926). The extensor tone was more pronounced on the side of the animal in contact with the table.

Several postural reflexes in these acute decerebrate cats were visually observed but not directly recorded on to the oscillograph. Movement of the head to the left or right consistently evoked a rotation of the body to the side in which the head was turned. Postural movements in the forelimbs also were produced by rotating the animal from side to side. Rotation of the cat from right to left evoked a reflex flexion of the left forelimb and extension of the right hind limb. Although the left forelimb would return to an extended posture, the limb could be forcibly flexed with minimal effort. The right forelimb (in contact with the table surface) remained very rigid. Passive flexion of the limb could only be accomplished with considerable force. These observations are

consistent with reflex movements attributed to postural mechanisms and static righting reflexes (Magnus 1926).

Several animals developed clonic contractions in the muscles of the fore- and hindlimbs when the sciatic nerves were stimulated. The frequency of the beats of clonus ranged between 1.5-3.5 herz; this frequency was not related to the frequency of stimulation of the sciatic nerves. Preparations showing a high degree of spontaneous activity seemed more predisposed to developing clonic activity. The clonus often persisted even after prolonged bouts of high intensity and high frequency stimulation.

Influences of Different Sensory Inputs on CER Excitability

Effects of Body Position. In the first two experiments, cats were placed with their left lateral body surface on the table surface with the right hindlimb supported as described in the methods. The CER in these preparations could only be generated by high frequencies of stimulation (>10 herz) (cf. 1). Rotation of the animal so that the right side was on the surface resulted in brisk CERs evoked by single stimuli. Single brief stimuli (1ms) elicited brisk CER "twitches" from the right quadriceps muscle. The same stimuli evoked no demonstrable reflex while the cat was positioned upon the left lateral surface (cf. 1 and 2). Changing the body position also affected the excitability of a sustained CER evoked by high frequency stimulation (10 herz) (cf. 1 and 3). During low frequency stimulation, rotation of the body from left to right evoked different responses (cf.2). First, CERs evoked by single shocks were only seen when the cat was
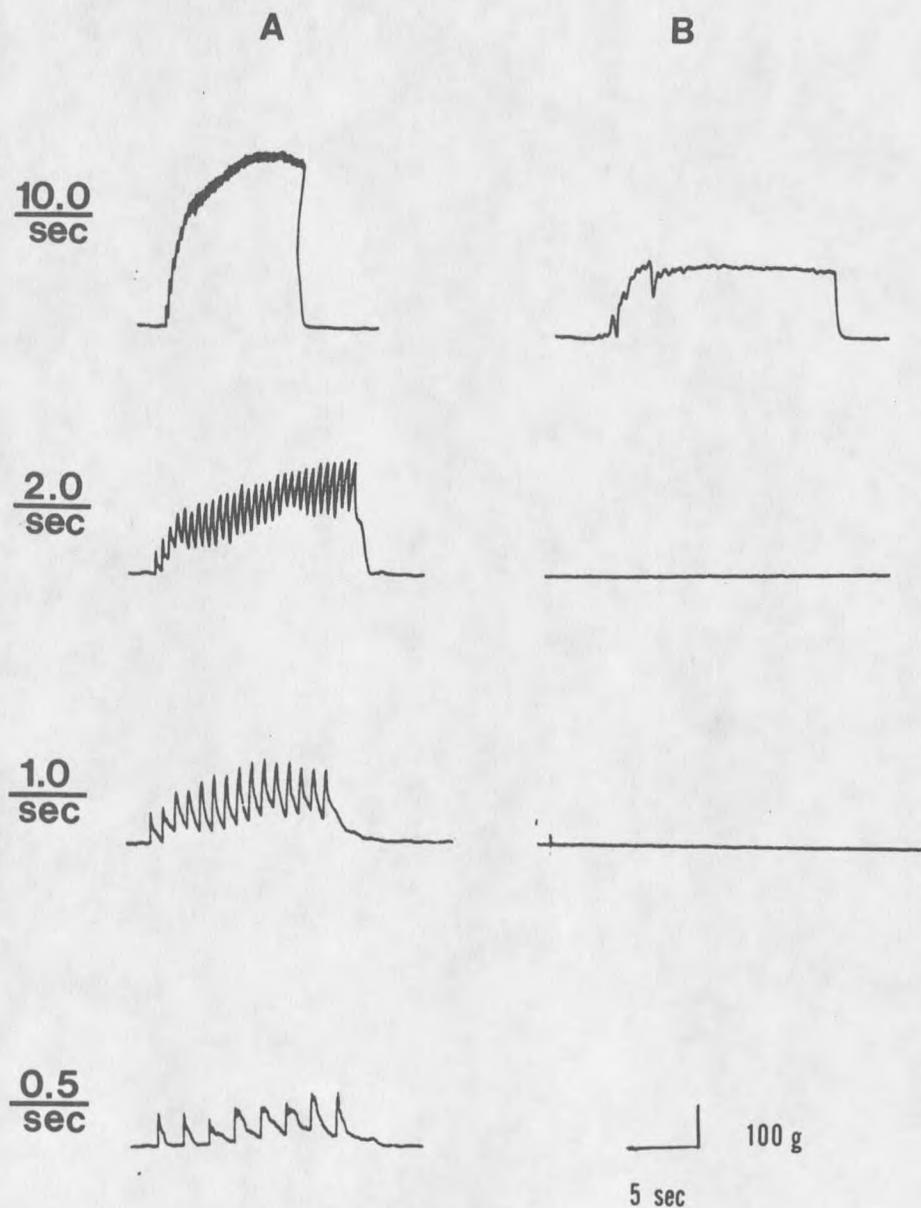
35

FIGURE 1. Effects of body position on CERs evoked by different frequencies of stimulation. These traces represent records of the changes in isometric tension in the right quadriceps muscle evoked by stimulation of the left sciatic nerve (0.5 mA, 1 ms duration). When the animal was on the right body side (Fig. 1A) CERs were evoked at all frequencies of stimulation. However, when the animal was turned onto the left side (Fig. 1B) CERs were only evoked by a frequency of 10 hz.