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VERTEBRATE FUSIMOTOR NEURONES AND THEIR INFLUENCES ON MOTOR BEHAVIOR

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Contents

1. Introduction

1.1. EFFERENT MODULATION OF SENSORY ENDINGS

Efferent innervation of sensory end organs and the problem of centrifugal control of the sensitivity of the receptors have interested researchers studying different sensory systems. Granit's early monograph (Granit, 1955a) compared centrifugal control of the spontaneous discharges of the retinal ganglion cells of the visual system with the central effects on the muscle spindle receptors in the skeletal muscles. Granit's work seems to have stimulated studies of centrifugal control of other sensory receptors in the auditory (Galambos, 1956), vestibular (Sala, 1965) and the olfactory systems (Kerr and Hagbarth, 1955). Though Granit has shown both inhibitory and facilitatory centrifugal effects on retinal ganglion cells (Granit, 1955b), the inhibitory effects seem to be dominant (Ogden, 1968). Similarly, the role of the efferents to the auditory and vestibular systems (Klinke and Galley, 1974) appears to be mainly inhibitory to the spontaneously discharging afferents (Galambos, 1956; Sala, 1965; Fex, 1968; Llinas and Precht, 1969; Precht,1975).

1.2. FUSIMOTOR EFFERENTS TO THE MUSCLE SPINDLES

Excitatory effects are the rule in the case of muscle spindle sensory endings in the vertebrate species through efferent "fusimotor" (Hunt and Paintal, 1958) neurones. The central nervous system can, however, exert inhibitory influences by depression of spontaneous fusimotor activity. Subsequent studies in Granit's own laboratory and in many others around the world have focused on the fusimotor control of muscle spindle (Granit, 1970; Matthews, 1972). This paper is a review of the development of efferent control of the muscle spindle from the simple system found in the amphibian and reptilian skeletal muscles to the more complexly developed mammalian fusimotor control. The amphibia possess a simpler arrangement for fusimotion, with the same axon innervating both the extrafusal skeletal muscle fibers and the intrafusal muscle fibers associated with the muscle spindle receptor (Katz, 1949; Gray, 1957; Eyzaguirre, 1957, 1958). In addition to such "skeleto-fusimotor" fibers, the mammalian fusimotor axons arise from separate cell bodies in the central nervous system named gamma motoneurones (Leksell, 1945), which are much smaller than the alpha motoneurones innervating the skeletal muscle fibers through "skeletomotor" axons. The skeleto-fusimotor axons branch intramuscularly and have been known as the "beta axons" to distinguish these motor axons from the alpha (only to skeletal extrafusal muscle) and the gamma (only to the intrafusal muscle) motor axons (Kidd, 1966). Histological features of the muscle spindles and their innervation will not be covered in detail here, and the interested reader is referred to two recent reviews describing the early work (Matthews, 1972; Barker, 1974), while current views on muscle spindle morphology have been discussed in a recent symposium (Homma, 1976). Figure 1 schematically illustrates the currently accepted anatomical features of fusimotor innervation of the amphibian and mammalian muscle spindles. Hunt's review (Hunt, 1974) has covered some comparative aspects of efferent control of muscle spindles, and a subsequent analysis by Smith (1976) has focused on the subject of co-activation of alpha and gamma motoneurones in voluntary movement. The present study will draw attention to the parallels that exist between amphibian and

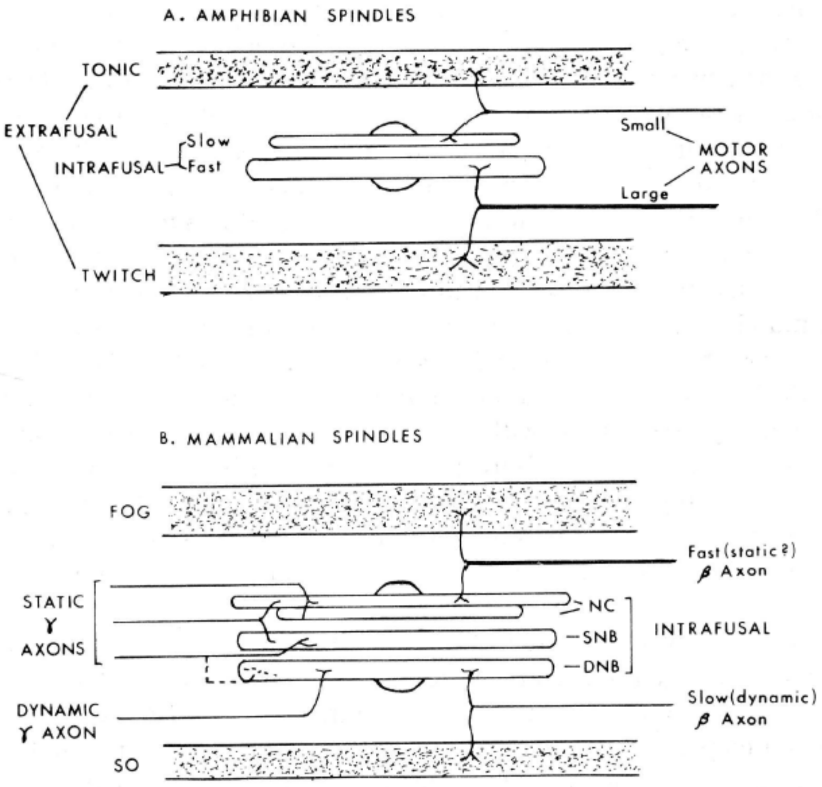

FIG. 1. Schematic illustration of fusimotor innervation in (A) amphibia and (B) mammals. Details of sensory innervation have been omitted for clearness. The amphibian fusimotor axons are collaterals of axons supplying the main (extrafusal) muscle fibers. Large and small diameter motor nerves innervate extrafusal twitch (fast) and tonic (slow) muscles, respectively, and send collaterals to intrafusal muscle fibers with different mechanical characteristics. Similar fusimotor innervation in the mammal is referred to as beta axon innervation. The slow beta axons affect the dynamic responsiveness of the primary sensory endings while the faster beta axons appear to influence the static sensitivity of the sensory endings. These actions are similar to those of dynamic and static fusimotor gamma axons respectively. The extrafusal muscle fibers innervated by the beta axons appear to be of the fatigue-resistant type (FOG—Fast-oxidative-glycolytic; SO—slow-oxidative). Intrafusal fibers: NC—Nuclear chain; SNB—Static Nuclear Bag; DNB—Dynamic Nuclear Bag. The innervation of the DNB by the static gamma axon is shown in dashed line because there is some controversy regarding its occurrence.

mammalian fusimotor systems and their implications for mammalian fusimotor function. In addition, points arising from recent studies involving both normal human subjects and patients with various central nervous system lesions will be reviewed.

2. Functional Differentiation in the Periphery

2.1. THE GAMMA MOTOR INNERVATION OF MAMMALIAN MUSCLE SPINDLES

Leksell's experiments (Leksell, 1945) employing a pressure block of the large diameter (alpha) motor fibers showed conclusively that skeletal muscles are also innervated by smaller diameter efferents which conduct impulses at speeds corresponding to the gamma elevation in the compound action potential and that stimulation of these slow-conducting motor axons increased the rate of impulses from some muscle receptors. Following on this observation, Hunt and co-workers (Hunt, 1951; Hunt and Kuffler, 1951; Kuffler *et al.*, 1951) determined that the function of these smaller diameter efferents is excitatory to the muscle spindle sensory endings. These findings coupled with the results from the experiments of Granit and co-workers (Granit and Kaada, 1952; Granit *et al.*, 1952; Eldred *et al.*, 1953) which showed the supraspinal excitations of the gamma efferents, were instrumental in stimulating research in muscle spindle physiology.

The decade following Hunt's initial experiments on the gamma efferents has been the most rewarding and exciting period in the study of voluntary muscle control (Matthews, 1964), revealing the complexities in the functions of the muscle spindles paralleling their sophisticated morphological features. In fact, the histological features of the intrafusal fibers have been somewhat confusing, with the results coming out of two of the best anatomical laboratories in the world (Boyd, 1962; Barker *et al.*, 1970; Barker, 1974) failing to agree in details of fusimotor innervation pattern. Fortunately, such differences are being resolved (see Homma, 1976) as more data is forthcoming from use of recent techniques in the simultaneous study of anatomical and physiological features of efferent innervation of the intrafusal fibers in the cat muscle spindle (Bessou and Pages, 1975; Boyd, 1976).

It has now become possible to observe through a microscope the mechanical contractions in intrafusal muscle fibers produced by stimulation of fusimotor axons and to record such events cinematographically (Bessou and Pages, 1975; Boyd and Ward, 1975; Boyd, 1976; Boyd *et al.*, 1977). Thus a correlation of morphological features in fusimotor innervation of the mammalian muscle spindle with their physiological characteristics can be achieved. In addition to observations made of intrafusal contractions in response to electrical stimulation of the individual fusimotor axons, the cinematographic recording technique may now be employed to study fusimotor effects on stimulating central nervous structures (Gladden and McWilliam, 1977a, b) and observing intrafusal muscle contractions with the ventral roots intact.

Particular mention must be made of the painstaking but most useful experiments in Laporte's laboratory which showed the types of termination of the "static" gamma efferent (see definition in the following section) on the intrafusal fiber (Barker *et al.*, 1973). This experiment required preparing a cat chronically with all the motor nerves to the tenuissimus muscle severed except for one physiologically identified gamma efferent and sacrificing the animal for histological studies 7–12 days later so that all the severed fibers have had time to degenerate. Equally of significant value have been the experiments which employ tetanic stimulation of single gamma efferents to deplete their intrafusal terminals of glycogen (Brown and Butler, 1973, 1975; Barker *et al.*, 1976) similar to the methods developed for histochemistry of extrafusal muscle fibers (Edström and Kugelberg, 1968).

2.2. STATIC AND DYNAMIC FUSIMOTOR FIBERS

The most important factor in fusimotor function is its effect on the control of muscular activity through its effects on the sensitivity of the stretch receptors. From a control system standpoint, it would be of obvious advantage to possess independent control of the sensitivity of the stretch receptors to a static maintained stretch and to the phasic velocity component of movement (Matthews, 1972). Such an arrangement will ensure that voluntary movements are carried out smoothly (Taylor, 1972; Houk, 1972). It was not known until the early 1960s that the mammalian fusimotor neurones did possess such functional diversity in their peripheral effects. The evidence for separate fusimotor fibers in the cat with independent effects on the position and velocity sensitivities of the primary (Ia) muscle spindle afferent came from Matthews' laboratory (Matthews, 1962; Crowe and Matthews, 1964a, b). These studies involved stimulation of fine filaments in the ventral roots containing single fusimotor fibers to the muscle spindles, the afferents from which were being monitored in the dorsal rootlets while a stretch was applied to the muscle. Fusimotor fibers which produced a marked increase in the rate of nerve impulses from a primary muscle spindle afferent during the dynamic (phasic) part of the stretch were classified as "dynamic" fusimotor fibers (Matthews, 1962). The effects are measured in terms of changes in the "dynamic index" of the Ia afferent response, the dynamic index being defined as the difference between the spindle firing rate just before the completion of a period of dynamic stretching (a ramp stretch) and the rate of discharge occurring 0.5 sec later with the muscle at the final length (Matthews, 1972).

"Static" fusimotor fibers, on the other hand, decrease the dynamic (velocity) sensitivity of the Ia endings, though they are excitatory to the muscle spindle afferents (Fig. 2). Another point of functional difference between the static and dynamic fusimotor fibers is in their effects on the Ia response to a release of the muscle from a previously stretched

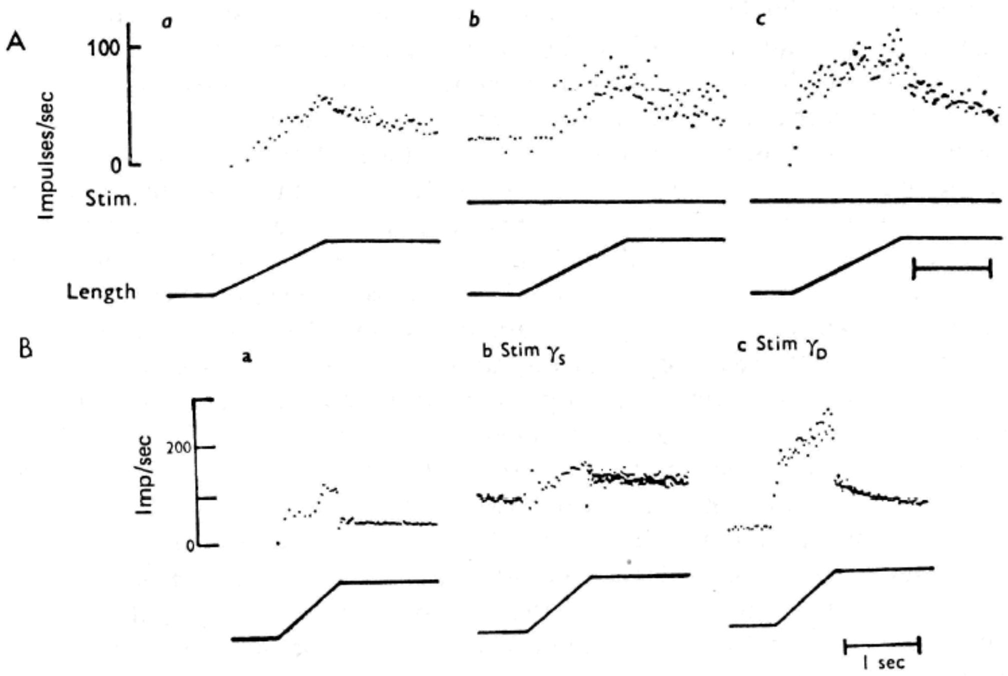

FIG. 2. Effects during muscle stretch: (A) Fusimotor actions in the frog (reproduced with permission from Matthews and Westbury, 1965). (B) Gamma fusimotor actions in the cat (reproduced with permission from Brown and Matthews, 1966). Note the similarity in action of the large motor nerve in the frog and the static gamma axon in the cat on one hand (column b) and of the small motor nerve in the frog and the dynamic gamma axon in the cat on the other (column c). In both cases column a shows the control responses of the spindle afferent (top dotted traces in A and B) to a ramp stretch (bottom traces).

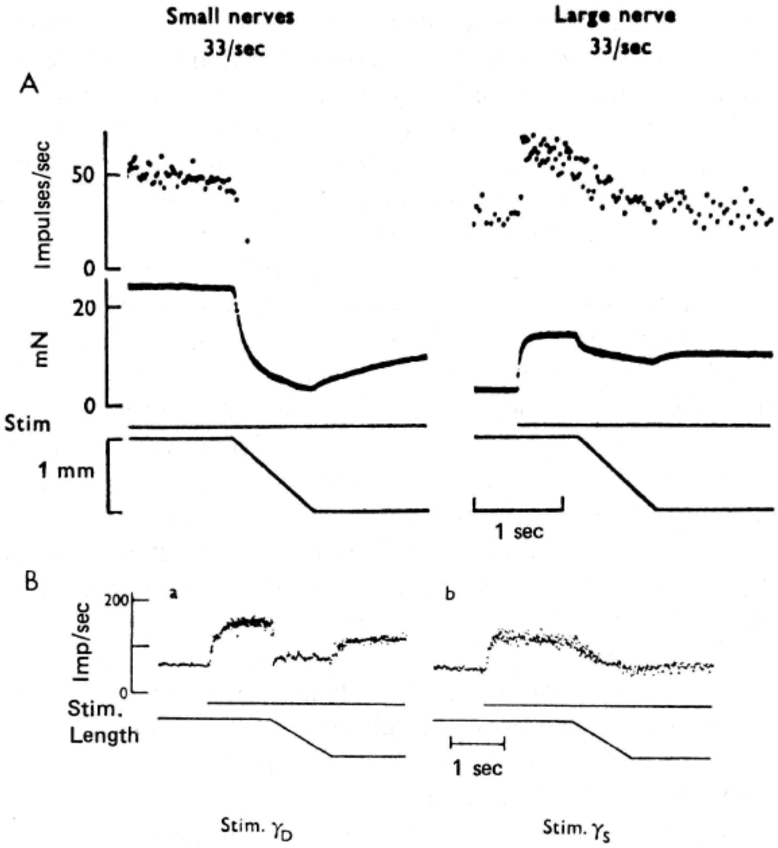

FIG. 3. Effects during release of muscle from a previous stretch: (A) Fusimotor actions in the frog (reproduced with permission from Brown, 1971b). (B) Gamma fusimotor actions in the cat (reproduced with permission from Crowe and Matthews, 1964b). Note the similarity in action between the frog small motor nerve and the cat dynamic gamma axon (column a) on the one hand and between the frog large motor nerve and the cat static gamma axon (column b) on the other. The top dotted traces in A and B are spindle afferent responses whereas the period of stimulations (horizontal bar) and muscle length (negative ramp) are displayed below each record. In A the middle traces refer in addition to muscle tension.

position. While the stimulation of a dynamic fusimotor fiber is insufficient to compensate for the depression or abrupt cessation of Ia discharge during the decrease in muscle length, static fusimotor stimulation permits the Ia response to follow the decrease in muscle length in a smooth graded manner. These features are summarized in Fig. 3.

Static and dynamic fusimotor fibers also differ in their effects on the secondary sensory endings (group II afferents) of the muscle spindle. While the static fusimotor fiber is excitatory to both the primary and secondary endings in a spindle (Appelberg *et al.*, 1966), the dynamic fusimotor fibers have been found to have no effects on the secondary endings unless the passive afferent response by itself displays some phasic sensitivity (Appelberg *et al.*, 1966; Durkovic, 1975). Such sporadic observations have so far been only minor exceptions to the general rule of dynamic fusimotor action being selective to the Ia afferents.

The association of dynamic or velocity sensitivity to stretch with the primary endings and not with the secondary endings (Matthews, 1963; Hunt and Ottoson, 1975) of the muscle spindle is also in line with the mechanical characteristics of the intrafusal fibers on which the two sensory endings are located (Matthews, 1972). Thus, in 1964 the efferent control of mammalian muscle spindle presented a well-designed package containing two types of afferents, two types of efferents and two types of intrafusal muscle fibers to account for the position and velocity sensitivity of the receptors. Further, the control of the velocity sensitivity by dynamic fusimotor neurones was believed to be meant for "damping" any "overshoot" in movement resulting from a stretch reflex (Jansen and Matthews, 1962a). However, all the above-mentioned observations were on muscle spindles subjected to reasonably large amplitudes of muscle stretch (up to 5% of the muscle length).

Further contributions of significance have come from Matthews' laboratory (Goodwin *et al.*, 1975; Hulliger *et al.*, 1977a, b), where the issue of fusimotor effects on the spindle primary endings was reopened for study under conditions of small amplitudes of muscle stretch (under 200 μm). The impetus for such an experimental design came from an earlier study (Matthews and Stein, 1969a) which demonstrated that the spindle primary afferents displayed a non-linearity in their sensitivity (gain) measured as impulses per second per amount of stretch in millimeters. It was shown that the Ia afferent (in the passive spindle) responded with a higher gain for small amplitudes than for larger amplitudes of stretch. The effect of dynamic fusimotor stimulation on the gain of the Ia ending was not found to be significant for small amplitudes of sinusoidal stretch at frequencies in the normal physiological range of up to 20 Hz (Goodwin *et al.*, 1975). On the other hand, static fusimotor stimulation caused a ten-fold reduction in the sensitivity of the Ia ending for small amplitude stretches (Chen and Poppele, 1973; Goodwin *et al.*, 1975). In addition, Goodwin *et al.* (1975, 1976) found that for these low frequencies of sine wave analysis, no effect was detectable on the phase response of the Ia ending to stimulation of either type of fusimotor fiber. Also, it was found that during the peak of a stretch cycle, the effect of combined stimulation of dynamic and static fusimotor fibers was additive (increasing the "gain"), whereas static fiber effects occluded those of dynamic fiber stimulation during the trough of the stretch cycle, i.e. during release of the muscle from a stretch (Hulliger *et al.*, 1977b). The "occlusion" between static and dynamic fusimotor effects when no stretch was applied to the muscle has been reported earlier by Lennerstrand (1968).

The results of studies employing small amplitudes of stretch, however, have not challenged the functional classification of static and dynamic fusimotor fibers which was originally made on the basis of responses of the spindle endings to larger amplitudes of muscle stretch (Matthews, 1962; Crowe and Matthews, 1964a). Although alternative names have been suggested for the mammalian gamma axons, on present evidence it seems best to retain the original classification of (see discussion of Matthews' paper in Homma, 1976) static and dynamic fusimotor fibers. Further, the complexities and controversies surrounding the mechanical behavior and motor innervation patterns of the intrafusal fibers (Emonet-Denand *et al.*, 1977a) do not invalidate these functional classifications of the mammalian gamma efferents. A systematic analysis of fusimotor effects in mammalian muscle spindles was carried out by Emonet-Denand *et al.* (1977a). It was observed that a variety of effects ranging from purely "static" action to purely "dynamic" action could be classified into

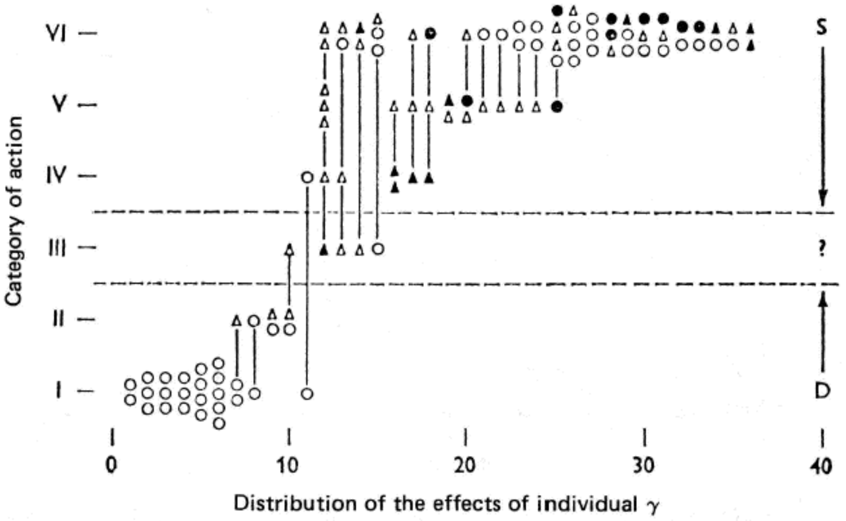

FIG. 4. Variations in static and dynamic fusimotor actions in the cat (reproduced with permission from Emonet-Denand *et al.*, 1977a). Each fusimotor fiber studied is represented along the abscissa and the number of spindle afferents influenced by it along the ordinate. Six categories of differences in fusimotor actions are described.

six categories of fusimotor effects. Roughly a third of the fusimotor effects studied were suggestive of an admixture of static and dynamic actions on muscle spindle endings. However, any particular fusimotor axon was found to produce either predominantly static or predominantly dynamic effects when tested on several spindle endings innervated by it (Fig. 4). Thus, it has been found adequate to maintain the original classification of fusimotor axons into static and dynamic axons.

It has been estimated that the static fusimotor fibers outnumber the dynamic gamma efferents by a ratio of nearly 3:1 (Crowe and Matthews, 1964a; Bessou and Laporte, 1966). A search for differences in conduction velocities (CV), however, has not been positive (Matthews, 1972) with the speeds ranging from 15 to 50 msec^{-1} for the gamma efferents (Boyd and Davey, 1968) compared to 58–92 msec^{-1} for the slow alpha axons and 85–116 msec^{-1} for the fast alpha axons (Burke and Edgerton, 1975).

2.3. FUSIMOTOR CONTROL IN LOWER VERTEBRATES

The study of the efferent innervation in the amphibian muscle spindle has progressed in parallel with the development of the understanding of the mammalian gamma efferents. On present evidence, the amphibia do not seem to possess separate fusimotor neurones in CNS. The motor axons to intrafusal muscle have been found to occur as branches of the the motor fibers innervating the main extrafusal muscle (Gray, 1957; Barker, 1974). Physiological evidence had already been available prior to such anatomical confirmation. Katz, in a series of experiments employing a critical dose of curare to block the extrafusal motor end plates, established that the intrafusal end plates could still drive the spindle afferent discharge (Katz, 1949). However, a differential activation of extrafusal and intrafusal end plates by graded stimuli was not possible, suggesting that these end plates were connected to the same motor axon.

Although the amphibian fusimotion lacks the complex fusimotor innervation displayed by the mammalian muscle spindles, it does have some unique features. The amphibia possess separate fast and slow motor units with different electrical and mechanical properties (Tasaki and Mizutani, 1944; Tasaki and Tsukagoshi, 1944). The fast (large) motor axons (CV 10–40 m sec^{-1}) when stimulated gave rise to a muscle action potential which propagated along the muscle fibers and resulted in a twitch of the muscle as recorded in a myograph. Stimulation of the slow (small) motor axons, on the other hand, did not result in a propagated muscle action potential but only in "small junctional potentials" recordable locally near the end plates (Kuffler and Gerard, 1947; Kuffler and Vaughan Williams, 1953). No appreciable muscle tension resulted from activation of the slow motor axons

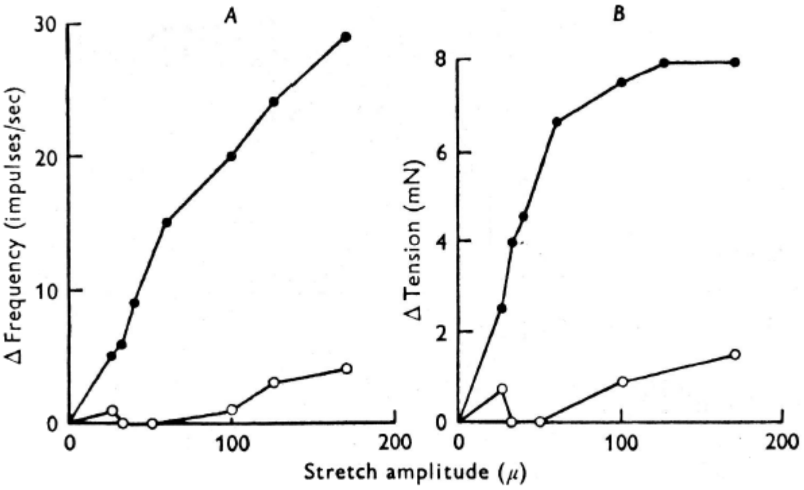

FIG. 5. (A) Responsiveness of a frog muscle spindle afferent to small amplitude square stretches with concomitant stimulation of small motor nerve (filled circles) and large motor nerve (open circles). (B) Corresponding tension developed by the muscle under same conditions (reproduced with permission from Brown, 1971b).

(CV 4–8 m $\sec^{-1}$) with single stimuli (Kuffler and Gerard, 1947; Kuffler *et al.*, 1947). The tetanic tensions produced by small nerve stimulation were about 8–10 times smaller than that produced by large nerve stimulation (Tasaki and Tsukagoshi, 1944). Such slow motor units are rare in the mammal, occurring only in some extraocular muscles (Granit, 1970) and are not to be confused with the slow twitch muscle fibers in the mammalian species which do produce a twitch response when stimulated with a single shock. The fast units of the amphibia have hence been referred to as the "twitch" units and the slow motor units as the "tonic" units (Gray, 1957) reflecting on the latter's ability to sustain contractile activity for appreciable lengths of time (Tasaki and Tsukagoshi, 1944) without showing fatigue.

Both the twitch and tonic motor units innervate intrafusal muscle fibers in the amphibia (Fig. 1). Gray (1957) presented anatomical evidence for intrafusal innervation by branches from both large and small motor axons in the frog and this was subsequently confirmed by physiological studies (Eyzaguirre, 1957, 1958).

2.4. A COMPARISON OF MAMMALIAN AND AMPHIBIAN FUSIMOTOR EFFECTS

In an effort to determine whether the effects of fusimotor stimulation on the static and dynamic sensitivities of the amphibian muscle spindle are similar to the effects in the mammalian system, Matthews and Westbury (1965) studied both the twitch and tonic motor innervation in the frog. Using moderately large amplitudes of muscle stretch, it was found that the large motor fiber stimulation increased the overall response of the spindle afferent to a ramp stretch while stimulation of the small motor axon increased specifically the sensitivity to the dynamic (velocity) component of the stretch. These effects compared well with those respectively of static and dynamic fusimotor neurones in the cat (Matthews, 1972). A more detailed study by Brown (1971a, b) later confirmed and extended these observations. Brown (1971b) also showed that the small motor axon stimulation was much more effective during a stretch of the muscle, especially for small amplitudes (Fig. 5), whereas the large motor stimulation permitted the spindle afferent to follow release of the muscle from a previously applied stretch. These features are summarized in Figs 2 and 3 and in Table 1.

The features of skeletofusimotor control of amphibian muscle spindles are best revealed during an active contraction of the muscle under different loads (Murthy and Taylor, 1971a, 1978). With the muscle contracting against springs of various compliances, intrafusal driving is able to maintain spindle discharge during the extrafusal muscle contraction to a degree dependent on the compliance of the load. Even with highly compliant loads which caused a silencing of the spindle discharge during a tetanic stimulation of the motor nerves,

TABLE 1.

	Amphibian	
Nature of effect	Large motor nerve	Small motor nerve
Effect on spindle afferent at constant length ("bias").	Increase in spindle discharge; produces high irregularity in the pattern. Can effectively drive the spindle discharge up to moderate rates.	Increase in spindle discharge; produces less irregularity than the large motor nerve.
Effect on spindle afferent during large amplitude muscle stretch.	Reduces the dynamic responsiveness.	Increases the dynamic responsiveness
Effects during small amplitude muscle stretch.	Fairly ineffective in modulating the spindle discharge.	Considerable increase in the dynamic responsiveness of the spindle ending.
Effects during release of muscle from stretch.	Effective in making the afferent response follow the change in muscle length.	Causes the afferent to considerably depress during the dynamic phase of release.

	Mammalian	
Nature of effect	Static gamma (and fast beta?)	Dynamic gamma (and slow beta?)
Effect on spindle afferent at constant length ("bias").	Considerable increase in both Ia and secondary afferent discharges. Introduces high amount of irregularity in the spindle discharge pattern, significantly more in the case of the primary ending. Also effective in 1 : 1 driving of the afferent discharge.	Moderate increase in Ia afferent discharge; preserves the regularity of spindle discharge pattern compared to that of the deefferented spindle. Ineffective in driving the afferent discharge.
Effect on spindle afferent during large amplitude muscle stretch.	Reduces the dynamic sensitivity of Ia ending.	Increases the dynamic sensitivity of the Ia ending.
Effects during small amplitude muscle stretch.	Reduces the sensitivity of spindle afferents especially of primary. This is more pronounced (ten-fold reduction in gain) at low frequencies of stretch.	Increases the sensitivity of primary ending for high frequencies of stretch but has no significant effects for low frequencies of stretch.
Effects during release of muscle from stretch.	Effective on the primary ending to respond in relation to the decrease in muscle length.	Causes pronounced depression of the primary ending. No effects on the secondary ending.

there occurred a pronounced burst of spindle discharge at the onset of stimulation (Fig. 6). Such a behavior is observed in a positive feedback loop, with the spindle afferents monosynaptically connected to their motoneurones (Holman *et al.*, 1966; Cruce, 1974). The net effect of the initial burst of spindle discharge at the onset of tetanic stimulation will be to speed up the mechanical contraction of extrafusal muscle fibers.

The terms "skeleto-fusimotor axon" and "beta axon" are now frequently employed to refer to such intrafusal innervation by collaterals of extrafusal motor axons. In addition to the amphibia, beta motor innervation has been described for other lower vertebrate species—lizard (Proske, 1969a, b, 1973; Proske and Vaughan, 1968), snake (Fukami, 1970; Hunt and Wylie, 1970; Cliff and Ridge, 1973) and tortoise (Crowe and Ragab, 1970; Proske and Walker, 1975). The reptilian fusimotion has recently been reviewed in detail by Proske and Ridge (1974).

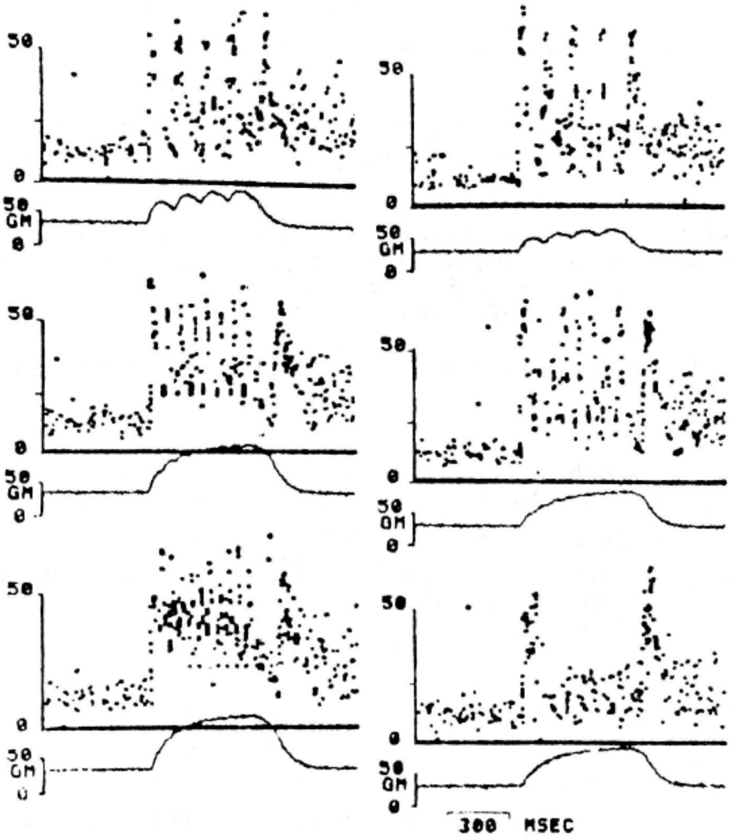

FIG. 6. Responses of a muscle spindle in frog sartorius muscle to twitch motor stimulation at rates of 10, 15 and 20/sec (from above, downward). Lefthand column: isometric conditions; righthand column: spring load of compliance 25 μm g^{-1}. Note the pronounced burst of spindle discharge at the onset of tetani and the second burst due to passive relaxation of the muscle at the termination of the stimuli (reproduced with permission from Murthy and Taylor, 1978).

2.5. BETA INNERVATION IN THE MAMMAL

Initial suggestions of fast alpha motor innervation exclusively of the intrafusal fibers in the cat (Granit *et al.*, 1959) have not been substantiated in later studies (Bessou *et al.*, 1965; Ellaway *et al.*, 1972). The arguments pro and contra on this subject have been reviewed by Matthews (1972) and were reiterated in a recent symposium (Laporte and Emonet-Denand, 1976). On the other hand, beta innervation was first reported for the lumbrical muscles in cat by Bessou *et al.* (1965) who employed critical curarization of extrafusal end plates. This technique demonstrated that for tetanic stimulation of the beta axon (see example in Fig. 7) after administering a critical dose of gallamine, extrafusal muscle contraction occurred only for the first few stimuli whereas the spindle afferent response persisted as long as the stimulation continued. Anatomical evidence soon followed (Adal and Barker, 1965), establishing the presence of beta innervation in the cat. Since then beta innervation has been found to occur in the lumbrical muscles of the rabbit (Emonet-Denand *et al.*, 1970); in the caudal tail muscles of the rat (Kidd, 1964; Andrew and Part, 1974); and also more extensively in the cat hind limb muscles (Ellaway *et al.*, 1971; Emonet-Denand *et al.*, 1975; Emonet-Denand and Laporte, 1975; McWilliam, 1975; Burke and Tsairis, 1977).

Earlier investigations showed that such beta fusimotor effects correspond to the slowly conducting alpha axons (Laporte and Emonet-Denand, 1976) with conduction velocities in the range of 39–92 m sec^{-1} for the cat and 20–40 m sec^{-1} for the rat (Andrew and Part, 1974). Since these studies employed a critical curarization of end plates of large alpha fibers, it was considered that some of the "faster conducting beta axons" may have been missed. Harker *et al.* (1977) applied tetanic stimulation specifically to fast alpha axons (CV 85–110 m sec^{-1}) to a muscle so that the glycogen stored in their terminals were depleted. Subsequent histological studies of glycogen depleted muscle fibers showed that the nuclear

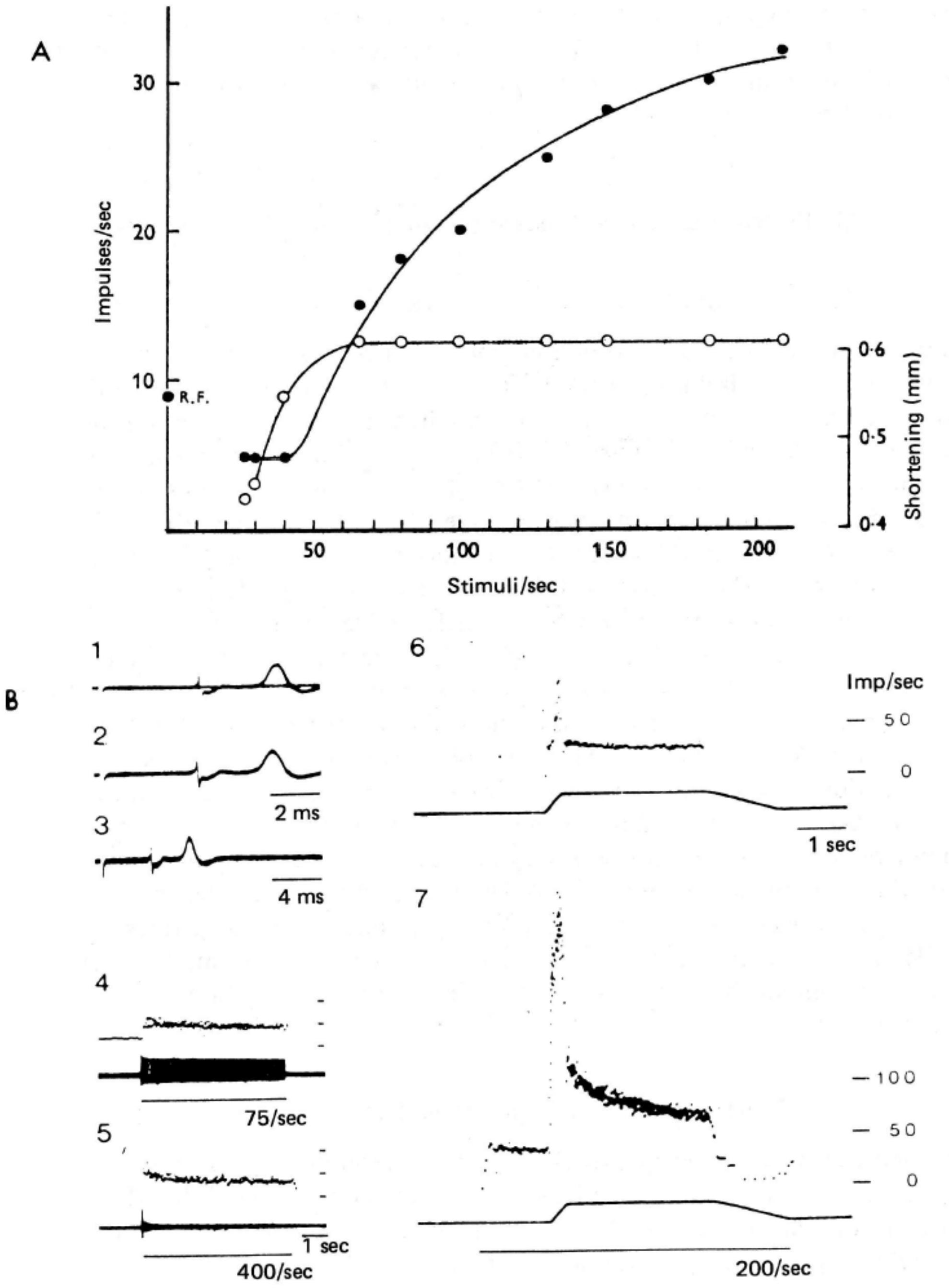

FIG. 7. Actions of a slow beta axon in the cat. (A) Comparison of effects on extrafusal shortening (open circles) and on spindle discharge rate of beta axon stimulation (reproduced with permission from Bessou *et al.*, 1965) (B) 1, 2, 3: action potentials of a single beta axon and its motor unit. Conduction velocity of the axon: 56 m sec^{-1} 4, 5: upper trace: primary ending discharge recorded with an instantaneous frequency meter. Lower trace: muscle action potentials. When the axon was stimulated at 75/sec the discharge of the ending accelerates and at 400/sec resulted in a complete block of the extrafusal neuromuscular junction. The acceleration persisted. 6, 7: responses of the primary ending to a ramp-and-hold stretch of 2 mm followed by a progressive return to the original muscle length. 6: no stimulation; 7: the stimulation of the beta axon at 200/sec elicited a marked increase in the dynamic response of the ending (reproduced with permission from Laporte and Emonet-Denand, 1976).

chain intrafusal fibers were depleted (Harker *et al.*, 1977). Thus it appears that the skeletofusimotor (beta) axons in the mammal can also display a dichotomy. The slower conducting beta axons have so far been found to have an action on the spindle similar to the dynamic gamma fusimotor axons when tested with fairly large amplitude stretches. It is conceivable that the faster beta axons may have a peripheral effect similar to the static gamma fibers due to their association with the chain intrafusal fibers (Harker *et al.*, 1977; Emonet-Denand *et al.*, 1977b).

Thus the mammalian gamma fusimotor innervation appears to have evolved in addition to rather than to replace the beta fusimotor innervation of the early vertebrate species. Beta axon effects on mammalian muscle spindles under small amplitudes of muscle stretch remain to be determined.

3. Patterns of Impulse Discharges from Gamma Motoneurones

3.1. SPONTANEOUS RATES OF IMPULSES IN GAMMA EFFERENTS

Understanding of fusimotor gamma efferent functions suffers greatly from the lack of sufficient data on the discharge characteristics of their impulses. Most of our knowledge on peripheral effects of fusimotor fibers has resulted from observations on muscle spindle afferent behavior. Although studies employing stimulation of central nervous structures may be effectively interpreted in this manner, difficulties arise in analysis of the results from stimulating fusimotor fibers themselves. A wide range of frequencies of stimulation up to 640/sec (Lewis and Proske, 1972) have been employed for studying the peripheral effects of the gamma efferents. The experiments that have recorded directly from gamma efferents, either in teased ventral root filaments or in finely divided muscle nerves in the periphery, in order to study effects of reflex activation of gamma motoneurones (Hunt, 1951; Hunt and Paintal, 1958; Voorhoeve, 1960; Voorhoeve and Van Kanten, 1962) or to evaluate effects of stimulating central nervous structures (Granit and Kaada, 1952) have so far been only qualitative. A knowledge of the actual rates of spontaneous fusimotor discharge in various situations is necessary since the efficacy of both cortically elicited (Mortimer and Akert, 1961) and reflexly elicited (Gilman and Ebel, 1970) fusimotor effects has been shown to be a function of the spontaneous fusimotor discharge rates existing prior to the application of such stimuli. Gilman and Ebel (1970) demonstrated that the reactive discharge rate in fusimotor neurones was directly related to their prestimulus discharge rates. Mortimer and Akert (1961) showed that the resting activity in fusimotor neurones was an important factor in determining the magnitude of both excitatory and inhibitory effects elicited on cortical stimulation.

3.2. REGULARITY OF FUSIMOTOR DISCHARGE PATTERNS

In comparing the spontaneous discharges from fusimotor neurones in the decerebrate animals and in spinalized animals, Ellaway and Pascoe (1965) found that there was greater regularity in the interspike intervals of spontaneously discharging fusimotor neurones of the decerebrate preparations. Although there was an abundance of tonically discharging fusimotor neurones in the spinal animal, their discharge was highly irregular. Such increase in irregularity was shown to result in the discharge of the same fusimotor fiber which had been discharging with great regularity in a decerebrate rabbit before spinalization. Ellaway and Pascoe (1965) then concluded that supraspinal influences on fusimotor neurones must exist to regulate their rates of discharge. In a more detailed study, Ellaway (1972) subsequently analyzed the statistical characteristics of the variability in interspike intervals of spontaneous fusimotor neuronal activity in the decerebrate cat. A remarkable amount of regularity was exhibited by the gamma units that were studied, with the coefficient of variation of the impulse intervals (expressed as the ratio of standard deviation of intervals to mean interval) being constant over a considerable range of impulse intervals. The effect of a spinal transection on a flexor fusimotor neurone was shown to be almost a quadrupling of the variability but the mean rate of discharge remained fairly unaffected.

3.3. POSSIBILITY OF DIFFERENCES IN DISCHARGE PATTERNS

Ellaway's study (Ellaway, 1972) has not been able to show any differences in discharge patterns that may be attributable to different fusimotor types. Using currently available techniques, static and dynamic fusimotor fibers can be identified only on the basis of their effects on muscle spindle primary afferents. There have, however, been suggestions of differences between the mean rates of spontaneous discharge in static and dynamic fusimotor neurones identified on the basis of effects of 3,4-dihydroxyphenylalanine (DOPA) (Bergmans and Grillner, 1969). Arbitrarily labeled as A and B group of units, the A units had higher mean spontaneous rates (above 20/sec) in the spinal cat and were depressed by an injection of DOPA. The B units, on the other hand, exhibited very low or no spontaneous activity in the spinal animal but were excited to discharge at a rate of 30/sec after injection of DOPA. Bergmans and Grillner (1969) also determined the A units to be the dynamic fusimotor type and the B units the static gamma efferents. Grigg (1972) and Grigg and Preston (1971) observed significant differences in the rates of spontaneously firing flexor and extensor gamma motoneurones in both the baboon and the cat.

Murthy and co-workers (Gildenberg and Murthy, 1977; Murthy *et al.*, to be published) have recently reopened the issue of possible differences in fusimotor discharge patterns in the cat, similar to the observations by Tokizane and Shimazu (1964) on the discharge patterns of human alpha motor units which showed differences between phasic ("kinetic" in Tokizane's terminology) and tonic alpha motoneurones. While subsequent studies (Person and Kudina, 1972; Kranz and Baumgartner, 1974; Freund *et al.*, 1975) have failed to confirm the precise differences between the phasic and tonic motor units as shown by the Tokizane school, the reasons are likely to be the difficulties in obtaining large samples from human subjects and the necessity to maintain stationary discharge patterns of motor units to obtain reasonably reliable statistical data. Nevertheless, the conclusions of the Tokizane school are that such differences in the discharge patterns as reported by them are indicative of differences in supraspinal control on the alpha motor units (see also discussion in Granit, 1970).

Murthy *et al.* (to be published) studied the discharge patterns of gamma efferents isolated from ventral root filaments of cats lightly anesthetized with sodium pentobarbital. Earlier investigators have shown the qualitative features of spontaneous fusimotor activity under similar conditions of anesthesia (Proske and Lewis, 1972; Gilman, 1976). In addition to observations on spontaneous (background) fusimotor discharge patterns, changes in fusimotor activity were produced by causing them to fire at different mean intervals through

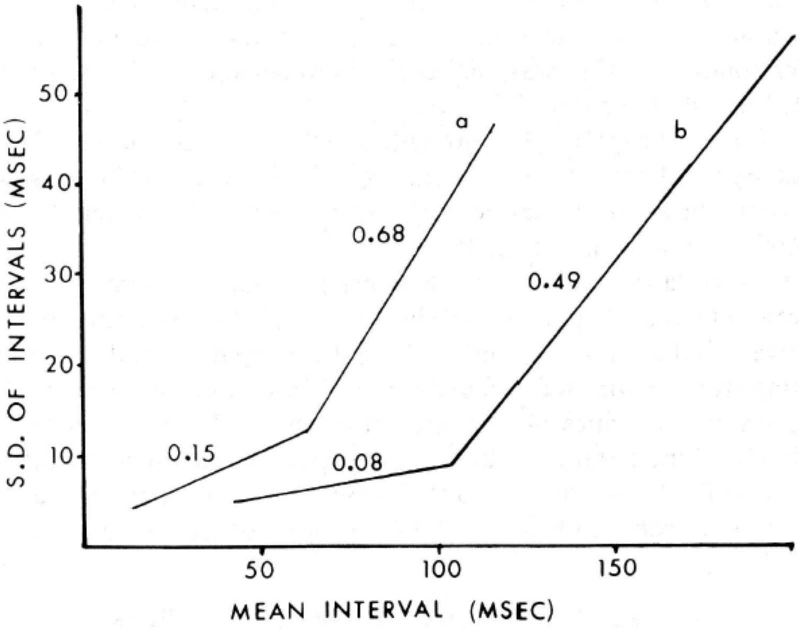

FIG. 8. Firing patterns of gamma efferents in a lightly anesthetized cat. Curves (a) and (b) have been drawn as tangents to best fitting curves for "fast" and "slow" firing units. The data was obtained from individual interspike interval histograms of spontaneously firing gamma motoneurones as well as during reflex activation with natural stimuli. The figures marked alongside the curves represent the mean coefficients of variation (Murthy *et al.*, unpublished data).

application of natural stimuli to activate cutaneous and proprioceptive afferents. Although the majority of the units so studied fired at rates of 10–75 imp sec^{-1}, a few gamma units were found to fire at rates less than 15 imp sec^{-1} (Gildenberg and Murthy, 1977). These units were arbitrarily designated as "fast" and "slow" gamma units respectively because statistical analysis showed the two groups of units to have different coefficients of variation (Fig. 8) for the same mean interspike interval value. The slow gamma units seemed to be more depressed by barbiturate anesthesia but easily activated in intersegmental reflexes.

It would be of interest to learn whether the differences observed by Gildenberg and Murthy (1977) are representative of genuine differences between the two types of fusimotor neurones. Neither in Ellaway's nor in Murthy's experiments has it been practical to identify the fusimotor types. Ellaway's (Ellaway, 1972) statement that a fair sampling of both static and dynamic gamma efferents may have been observed in his experiments remains to be confirmed. On indirect evidence one may suggest that Ellaway's study may have sampled more static fusimotor neurones which are more active in the decerebrate preparation (Jansen, 1966; Matthews and Stein, 1969b). In addition, in the lightly anesthetized cat, Lewis (1973) concluded that static fusimotor actions were more prominent (see also Gladden and McWilliam, 1977b). In any case, differential supraspinal influences on the static and dynamic fusimotor neurones are well known (see following sections of this review). Variations in synaptic activation of gamma motoneurones by different supraspinal pathways may thus be sufficient to contribute to the observed differences in the discharge patterns. Further study in this area is necessary before definitive patterns can be identified.

3.4. RANGE OF INTER-SPIKE INTERVALS

Of significance is the observation that none of the fusimotor neurones has been observed to fire at too high a rate or too low a rate for any appreciable length of time with a mean interval and a "limited" range of firing intervals (Gildenberg and Murthy, 1977). These units were, however, capable of firing at very high or low rates for brief bursts. It is also pertinent to recall here that the range of mean rates observed in spontaneous discharge Patterns (Ellaway, 1972; Gildenberg and Murthy, 1977), i.e. 10–75 imp sec^{-1} is identical with the rates of stimulation at which significant fusimotor effects have recently been described for spindle afferents subjected to small amplitudes (less than 500 μm) of stretch (Hulliger *et al.*, 1977a, b; Chen and Poppele, 1973; Emonet-Denand *et al.*, 1972). Spontaneous gamma activity seems to occur normally at rates of 100 imp sec^{-1} or less when recorded under conditions of supraspinal control (Anderson and Sears, 1970; Fidone and Preston, 1969; Eklund *et al.*, 1964).

It would be of interest to study the correlation between the coefficient of variation in the fusimotor discharge and the regularity of the primary afferents. Primary spindle afferents have already been shown to possess considerable irregularity attributable to static fusimotor activation (Mathews and Stein, 1969b).

Ellaway's study (Ellaway, 1972) also demonstrated that a negative correlation exists between adjacent intervals of spontaneous discharge from fusimotor neurones. In addition, a strong negative correlation was found in interspike intervals immediately after a curtailed interval resulting from antidromic stimulation. The fusimotor neurones were shown to be capable of rephasing their rates of discharge after an antidromic impulse (see also Hunt and Paintal, 1958). Thus, certain amount of autoregulatory capability seems to be inherent in the fusimotor cells themselves. Inhibitory resetting of the spontaneous firing rates of gamma motoneurones can also be effected from motor cortical stimulation.

4. Segmental and Intersegmental Reflex Effects

4.1. SPONTANEOUS ACTIVITY OF GAMMA MOTONEURONES

Fusimotor neurones have been observed to be spontaneously active, i.e. in the absence of any identifiable stimuli, in many experimental preparations—in the decerebrate cat or rabbit (Diete-Spiff, 1961; Jansen and Matthews, 1962a; Jansen and Rudjord, 1965), in the spinal animal (Hunt, 1951; Hunt and Paintal, 1958; Alnaes *et al.*, 1965), in anesthetized preparations (Gilman and Ebel, 1970; Proske and Lewis, 1972) and even in deafferented, isolated spinal segments (Lindsley and Eldred, 1960). The gamma units not spontaneously active may be excited in various reflexes.

Results of most studies on gamma motoneurones are likely to be biased by data of effects pertaining only to the spontaneously active gamma efferents. Jansen and Rudjord (1965), from their observations on recording from spindle afferents in a decerebrate cat, came to the conclusion that in this preparation spontaneous fusimotor activity was more prominent in the extensor muscle than in the flexor. Spinalization appeared to reverse this feature. Dynamic gamma motoneurones were more spontaneously active in the spinal animal (Alnaes *et al.*, 1965), while there is probably a dominance of the static fusimotor activity in the decerebrate preparation (Jansen and Matthews, 1962a, b). Thus, a larger sampling of extensor static fusimotor neurones may have been studied in decerebrate animal preparations and a greater proportion of flexor dynamic fusimotor neurones may have been observed in the spinal animal (Jansen, 1966). It is not clear how much these observations reflect the fact that the static fusimotor innervation dominates over the dynamic fusimotor fibers by a ratio of 2 to 3:1 in the intact animal (Crowe and Matthews, 1964a; Emonet-Denand *et al.*, 1977a; Bessou and Laporte, 1966).

Spinalization also reduces the level of spontaneous activity in some gamma motoneurones (Barnes, 1964; Diete-Spiff *et al.*, 1962). In a chronic spinal preparation gamma motoneurone activity may be absent even 5–6 months after the transection (Maksimova and Afelt, 1970, cited by Nesmeyanova, 1977).

Another factor of importance in ensuring spontaneous fusimotor activity is the integrity of afferent inflow (Hunt, 1951). Subsequent investigators have recognized this feature, but in most studies fairly extensive peripheral denervation of ipsilateral limb musculature has had to be done for the sake of convenience in experimentation. This is particularly true in studies on decerebrate animals which demonstrate rigidity in extensor muscles. With preservation of afferent inflow, one may be in a position to document more realistically the balancing of various synaptic influences on static versus dynamic fusimotor neurones. Improvements in present experimental techniques are necessary to confirm earlier observations of selective reflex or supraspinal activations of fusimotor neurones.

4.2. REFLEX EXCITABILITY OF FUSIMOTOR NEURONES

One of the earliest known features of the gamma motoneurones has been their readiness to respond to reflex activation, possessing a considerably lower threshold for various synaptic inputs compared to that of the alpha motoneurones (Hunt, 1951; Hunt and Paintal, 1958; Kobayashi *et al.*, 1952). The lower threshold of smaller motoneurones for reflex activation is considered to be due to their higher input resistance (Henneman, 1957; Kernell, 1966).

Investigations of reflex activation of gamma motoneurones have been carried out with the use of four different recording techniques:

(1) Intracellular recording from gamma motoneurones in the spinal cord (Eccles *et al.*, 1960; Grillner *et al.*, 1969; Appelberg *et al.*, 1977).

(2) Recording of unit activity in teased ventral rootlets.

(3) Recording of efferent unit activity in peripheral muscle nerves.

(4) Recording of muscle spindle discharge in dorsal rootlets and evaluating fusimotor effects based upon the responses of the muscle spindle endings.

Investigators have often found it frustrating to attempt intracellular recording from gamma motoneurones due to their small size. Hence, most studies have employed other recording techniques listed above.

4.3. CUTANEOUS INPUTS

Reflex effects originating from cutaneous afferents have been observed more prominently on gamma motoneurones by many investigators, particularly on application of noxious stimuli (Hunt, 1951; Hunt and Paintal, 1958). The majority of studies have employed electrical stimulation of the sural nerve at fairly high strengths to activate cutaneous afferent fibers of group III and group IV diameter. This has often resulted in nonspecific and mixed reflex effects on gamma motoneurones (Hunt and Paintal, 1958). Initial observations suggested a pattern of reflex effects similar to that of the flexor reflex afferents on alpha motoneurones (Hunt, 1951). Subsequent studies employing natural stimuli have demonstrated both excitatory and inhibitory effects from discrete skin areas (Eldred and Hagbarth, 1954; Hunt and Paintal, 1958). In the spinal cat, intravenous infusion of DOPA causes excitatory effects of cutaneous afferent stimulation in presumed static fusimotor neurones of a flexor muscle (Bergmans and Grillner, 1969) in contrast to the status before the injection of DOPA when such excitatory effects were more effective on presumed dynamic fusimotor neurones (see following section on effects of drugs).

Mixed reflex effects on lumbar gamma motoneurones can be seen on electrical stimulation of the ipsilateral sural nerve at strengths above the threshold for group III fibers: (1) by prolonged stimulation at the same frequency; and (2) by increasing the frequency of stimuli (Murthy *et al.*, 1977). Similar differences in effects due to afferents from the skin have also been found to be directed to different types of alpha motor units in the same muscle (Kanda *et al.*, 1977). These investigators determined that either electrical or natural stimulation applied to the cutaneous afferents selectively excited the less fatiguable slow motor units and inhibited the larger alpha motor units in ankle extensor muscles.

These observations serve well to emphasize the need for application of cutaneous stimuli more precisely by naturally elicited afferent activity as demonstrated by Eldred and Hagbarth (1954). Eldred and Hagbarth also showed that the cutaneous reflex effects on gamma motoneurones follow the same patterns as for alpha motoneurones of both extensor and flexor muscles (Hagbarth, 1952)—facilitatory effects from the skin over the same muscle and inhibitory from other skin areas. Appelberg (1973) later concluded that such facilitatory effects are mostly directed toward static fusimotor neurones. More recently, Appelberg *et al.* (1977) have used intracellular recording techniques to show that low threshold skin afferents project excitation to identified dynamic gamma motoneurones. The same cells were inhibited by high threshold skin afferents.

Recording from lumbar gamma motoneurones in high-spinal cats, Sato and Hasegawa (1977) found a strong reflex effect on their spontaneous discharge rates on cooling or warming the ipsilateral footpad. The reflex pathway was strong enough to contribute reproducible responses to alternate cooling and warming using a thermode. Though Sato and Hasegawa (1977) have been unable to identify the type of gamma efferents responding to such thermal stimuli, it was noted that these exhibited spontaneous activity in the spinal animal. Hence, the possibility of these being dynamic fusimotor neurones is to be considered.

In general, it may be said that reflex effects on gamma motoneurones from specific cutaneous afferents should be considerable. This is demonstrated by the effectiveness of single stimuli to cutaneous nerves in eliciting multiple impulses from gamma efferents (Hunt and Paintal, 1958) resulting in significant activation of spindle endings (Proske and Lewis, 1972; Lewis, 1973). Granit (1975) has recently reiterated the importance of skin and joint senses for finer control of movements. Such cutaneous effects may last for quite a length of time after single stimuli (Tanji and Kato, 1972a).

4.4. AUTOGENETIC EFFECTS FROM MUSCLE RECEPTORS

Employing intracellular recording techniques, Eccles *et al.* (1960) showed that gamma motoneurones do not receive monosynaptic excitation from group I afferents, thus differing from the alpha motoneurones. However, inhibitory postsynaptic potentials (IPSP's) with di- and trisynaptic latencies have been recorded from extensor alpha and gamma motoneurones by Grillner *et al.* (1969) on stimulating muscle nerves at group I strength.

4.4.1. *Effects due to group I afferents*

After a period of controversy in which autogenetic inhibition of gamma motoneurones have been repeatedly suggested and denied in different studies (Hunt, 1951; Hunt and

Paintal, 1958; Eldred *et al.*, 1953; Brown *et al.*, 1968; Matthews, 1972), autogenetic reflex effects on gamma motoneurones evoked by stretch of the muscles they innervate must now be considered to be firmly established though they are weak (Fromm and North, 1974, 1976; Fromm *et al.*, 1974; Trott, 1976) and demonstrable only with vibratory stimuli to the muscle. Low amplitude and high frequency muscle vibration is a selective stimulus to the Ia afferents from the muscle spindles (Brown *et al.*, 1967). In decerebrate preparations (with extensive denervation of the hindlimb musculature), observations have been made on activity in ankle extensor fusimotor fibers, the majority of them innervating the medial gastrocnemius. Whereas Trott (1976) obtained mostly excitatory autogenetic reflex effects on vibrating the ankle extensors (19 out of 27 gamma efferents were excited while the rest showed no effect), Fromm and Noth (1974, 1976) observed inhibitory effects also (14 out of 63 units). In both cases, a considerable number of units (8 out of 27 in Trott's study against 28 out of 63 in Fromm's) showed no effect. The reasons for such variability are not clear. It is quite possible that loss of afferent information because of extensive denervation of the hindlimb muscles has contributed at least in part to such differences in reflex effects.

Recently, however, Ellaway *et al.* (1976) have demonstrated that autogenetic excitation may be observed in fusimotor neurones to ankle extensors on application of a brief stretch to the muscle (50 μm amplitude, 3 msec rise time and 5 msec decay). Such brief, small amplitude stretching of the muscles has been known to be a selective stimulus for primary spindle endings (Lundberg and Winsbury, 1960; Stuart *et al.*, 1970). The reflex effects for such stimuli were too weak to be noticeable on a single oscilloscope sweep but may be observed in poststimulus histograms built up over a number of repetitions of the stimulus. It also appears that such reflexes may employ polysynaptic pathways.

The possibility that observed autogenetic inhibitory effects on gamma motoneurones are due to Ib afferents from golgi tendon organs is demonstrated by the observation that electrical stimulation at group I strength more effectively reveals this inhibitory effect than does muscle vibration (Ellaway and Trott, 1976a, b, 1978). Ellaway and Trott (1978) have performed a comprehensive analysis of such autogenetic reflex effects on gamma motoneurones and determined that autogenetic effects on ankle extensor fusimotor neurones included both excitation and inhibition when tested with brief stretches of the muscle which primarily excited the Ia afferents. Both excitatory and inhibitory effects were observed with long central delays due to polysynaptic transmission and the excitatory effects displaying a lower threshold but longer latency.

Ellaway (1971, 1976) has studied the organization of recurrent inhibition of gamma motoneurones mediated by the Renshaw cells. Though impulses in gamma axons themselves might evoke such recurrent inhibitory effects (Kato and Fukushima, 1974), a major contribution appears to result from collaterals of the alpha axons (Ellaway, 1971). These inhibitory effects were observed in both static and dynamic fusimotor neurones. Ellaway (1976) has reviewed at length the controversial features of observed recurrent inhibitory effects on gamma motoneurones.

4.4.2. *Effects due to group II afferents*

A stronger reflex inhibition of extensor gamma efferents was seen by Fromm *et al.* (1976) on vibrating the antagonist muscles. These investigators observed inhibition by group II fibers on electrical stimulation of the antagonist muscle nerve in addition to the vibration-induced group I inhibition from the antagonist. In tests using L-DOPA in the spinalized animals, it was concluded that autogenetic inhibitory actions were seen in static fusimotor fibers and the excitatory effects were directed to dynamic fusimotor fibers (Fromm and Noth, 1974; Fromm *et al.*, 1976). Fidone and Preston (1971) observed an inhibition of ankle extensor gamma efferents to stimulation of the peroneal nerve (antagonist muscle nerve) at a strength just maximal for eliciting a monosynaptic reflex.

The group II afferents from secondary endings of the muscle spindle have been traditionally grouped with the "flexor reflex afferents" (FRA) on the basis of effects observed on alpha motoneurones due to electrical stimulation of peripheral nerves (Eccles and

Lundberg, 1959). Recent evidence from tests employing natural stimuli clearly favors an excitatory role for the spindle secondary afferents even for extensors (Matthews, 1969, 1972; McGrath and Matthews, 1973). Similar tests have to be employed to determine group II effects on gamma motoneurones. Apart from the inhibitory effects of group II afferents from antagonists referred to above (Fromm *et al.*, 1976) intracellular recording from gamma motoneurones (Bergmans and Grillner, 1969) showed excitatory effects on flexor gamma motoneurones and mixed effects on extensor gamma motoneurones (Grillner, 1969).

Recording intracellularly from identified dynamic gamma motoneurones, Appelberg *et al.* (1977) have been able to show autogenetic excitatory effects originating from group II muscle afferents and exhibiting a central delay of 2 msec. It would be of interest to determine whether this pathway is powerful enough to override possible inhibitory effects from Ib afferent input (Appelberg *et al.*, 1977; Ellaway and Trott, 1976a, b).

Granit (1969) has described a strong autogenetic effect on the muscle spindle endings produced by muscle stretch in a cat where the decerebration had been done by a cut at the precollicular level, sparing the superior colliculus and its connections to the caudal structures. This autogenetic reflex on fusimotor neurones disappeared after the cut was made at the intercollicular level (the Sherringtonian decerebrate animal). Since a precollicular preparation exhibits clonic muscle behavior, Granit considers the observed reflex effects to be directed to the dynamic fusimotor neurones of the ankle extensor muscles. The possibility of spindle group II afferents contributing to this observation (as suggested by the study of Appelberg *et al.*, 1977) needs to be considered.

4.4.3. *Positive feedback with beta efferent modulation*

In discussing autogenetic effects on alpha motoneurones originating from muscle spindle afferents in the same muscle, one must also consider the autogenetic effects from Ia afferents projecting to alpha motoneurones which send collaterals to both extrafusal and intrafusal muscle fibers (beta innervation). Burke and Tsairis (1977) have recently observed that such a motoneurone to soleus displayed a Ia EPSP. It has already been discussed above that such beta innervation in the mammal is now considered to be present in a significant proportion.

It is of interest to point out here that such beta efferent axons are found to innervate the less fatiguable extrafusal muscle fibers—slow oxidative (type S) and the fast oxidative glycolytic (type FR) fibers (Burke and Tsairis, 1977; Laporte, 1978). Motoneurones with such motor units are known to receive the strongest monosynaptic excitation from Ia afferents (Burke, 1973). The implications of this positive feedback system for mammalian motor control remains to be determined (see also discussion in Section 8.4).

4.4.4. *Group III and group IV afferents*

Muscle receptors with afferent fibers of diameter in the group III and IV class are known to be responsive only to intense pressure applied to the belly of the muscle and to nociceptive stimuli (Paintal, 1960). These receptors are also excited by algesic chemicals (bradykinin, histamine, potassium) injected intra-arterially into the muscle (Mense, 1977). Hong *et al.* (1978) have determined that such intra-arterial injection of algesic compounds into the ankle extensors produce reflex excitatory effects on gamma motoneurones to the same muscles. Thus additional autogenetic excitatory pathways on gamma motoneurones appear to exist with the inputs from nociceptive muscle afferents.

4.5. EFFECTS FROM JOINT AFFERENTS

The effects of joint afferents are not known in detail and the only data we have so far is from studies employing electrical stimulation of the posterior articular nerve to the knee joint. Intracellular recording has again revealed a reflex pattern similar to that on alpha motoneurones (Grillner *et al.*, 1969) from flexor reflex afferents. Similar effects have also been seen on recording gamma activity in peripheral muscle nerves (Voorhoeve and Van

Kanten, 1962). The contributions from joint afferents to reflex responses are not well understood. Recent experiments have demonstrated that joint afferents are activated by mechanical vibration similar to that used by other investigators to excite Ia afferents (Millar, 1973). In addition, joint afferents respond well to active contraction of the muscles that are attached to that joint, presumably through mechanical forces exerted on the joint capsule by such contractions (Millar, 1973; Grigg, 1976; Grigg and Greenspan, 1977). In the light of such evidence, reflex effects observed in previous studies, using vibratory stimuli or involving contractions of muscles and where the articular nerves had been intact, should be reviewed to consider possible effects originating from joint afferents. The joint afferents have often been found to be inactive at intermediate joint angles, especially when the position is static (Burgess and Clark, 1969; Clark and Burgess, 1975). However, in a recent study, observation of an adequate number of intermediate range joint afferents has been reported (Ferrell, 1977).

Grigg *et al.* (1978) have used natural stimulation of knee joint afferents to show a positive feedback on alpha motoneurones innervating thigh muscles. The effects were shown to be due to afferents in the posterior articular nerve. Hence, fusimotor reflexes due to joint afferents need to be re-evaluated in view of the current knowledge from results of these experiments.

Convergence of reflex effects from three separate joints (knee, ankle and hip) may occur on a single flexor gamma motoneurone, as evidenced by local pressure being applied at these joints (Murthy *et al.*, 1977).

4.6. INFLUENCES OF VISCERAL AFFERENTS

4.6.1. *Bladder afferents*

The ease with which gamma motoneurones are reflexly influenced has also been observed on excitation of various types of afferents from the viscera. Abdullah and Eldred (1959) first described an increase of flexor gamma activity on distension of the bladder. Evans and McPherson (1959), however, observed that on gradual distention of the bladder the muscle tone at first increased for low intravesical pressures but fell as the pressure increased. Later while recording directly from gamma efferents, Evans (1963) confirmed such complex effects of inhibition and excitation on fusimotor neurones originating from the visceral afferents stimulated by bladder distention. Evans (1963) also observed inhibitory effects from such visceral afferent inputs on extensor gamma motoneurones in addition to the effects on flexor gamma motoneurones. Visceral inhibition of the knee jerk (Dusser de Barenne and Ward, 1937) probably results from such reflexes on gamma motoneurones. The above effects were seen mostly in decerebrate or anesthetized animals. In the acute spinal cat, however, such inhibitory effects from the pelvic afferents could not be demonstrated, but in the chronic spinal cat, these visceral inhibitory effects on gamma motoneurones recovered when the bladder was capable of contracting (McPherson, 1966).

Such inhibitory reflex effects on gamma motoneurones from visceral afferents in the bladder have also been suggested in the human (Marsden *et al.*, 1969) based upon the effects of micturition on the force of tonic vibration reflexes (TVR). A phase of increase in the force attributable to TVR accompanies the abdominal contractions during micturition, followed by a phase of decreased amplitude of TVR, presumed to result from the increased bladder pressure which reflexly causes inhibition of the gamma motoneurones (Evans, 1963). Though biphasic excitatory and inhibitory effects similar to those on the TVR (Marsden *et al.*, 1969) are seen in human monosynaptic reflexes (H-reflex and tendon jerk) during micturition (Pedersen and Mai, 1975), these latter investigators do not consider an effect attributable to inhibition of the gamma activity. They base their conclusion on the observation that changes in H- and T-reflexes were uniform.

4.6.2. *Effects from pulmonary receptors*

Type J pulmonary receptors (Paintal, 1969) which are located near the alveoli close to the pulmonary capillaries ("Juxta pulmonary capillary receptors") have been suggested to exercise bilateral nonreciprocal inhibitory effects on flexor extensor motoneurones of the limb muscles (Deshpande and Devanandan, 1970). The natural stimulus for these J-receptors is thought to be lung congestion which would result in termination of exercise by inhibiting reflex activity in limb musculature (Paintal, 1969). These J-receptors which send slowly conducting afferents through the vagus nerve are activated by intra- right atrial injection of the drug phenyldiguanide (PDG). Following on these observations, inhibitory effects originating from these vagal afferents on the gamma motoneurones of the hindlimb flexors and extensors have been demonstrated (Schiemann and Schomburg, 1972; Eldred and Ginzel, 1972; Ginzel, 1973a; Ginzel and Eldred, 1973). Similar inhibition resulting from PDG activated J-receptors has been observed nonreciprocally in alpha and gamma motoneurones of both expiratory and inspiratory intercostal muscles (Schmidt and Wellhöner, 1970), but in this case inhibition appears to be predominantly on the "rhythmic gamma motoneurones". Very little, if any, depression of "tonic gamma" activity results through reflex inhibition from the vagal afferents. The effects appear to be mediated supraspinally, perhaps from the brainstem reticular formation (see further discussion in Section 6 under Effect of Drugs). These experiments show that there exists a mechanism for bilateral nonreciprocal inhibition of the motor system. This is a powerful physiological tool that has not yet been properly used to study motor functions. It would be of interest to find whether there is a selective depression of the static or dynamic fusimotor neurones, and also whether the threshold for gamma reflex is lower than that for the reflex effects on alpha motoneurones.

4.6.3. *Effects due to other afferents from the viscera*

Inhibitory reflex actions from other visceral afferents have been reported. The effect of systemic administration of nicotine, though exhibiting motor effects similar to those from injections of PDG, is thought to result from excitation of pulmonary arterial baroreceptors (Ginzel, 1973b). Increase of carotid sinus pressure causes gamma inhibition through the excitation of baroreceptors (Schulte *et al.*, 1959a), while the carotid chemoreceptors appear to be excitatory to gamma motoneurones (Schulte *et al.*, 1959b). All these studies were done before the discovery of the static and dynamic fusimotor neurones and must be reinvestigated for specific effects on static versus dynamic gamma efferents.

In general, visceral afferents appear to possess powerful, long-lasting inhibitory effects on both alpha and gamma motoneurones as evidenced from effects on decerebrate rigidity (Ginzel and Eldred, 1969), and monosynaptic and polysynaptic reflexes (Evans and McPherson, 1959; McPherson and Skorpil, 1966; Deshpande and Devanandan, 1970).

4.7. LONG-SPINAL REFLEX EFFECTS

Activation of gamma motoneurones innervating the hindlimb muscles by proprioceptive and cutaneous afferents to the cervical segments has been known since the early experiments in Granit's laboratory (Eldred *et al.*, 1953) when hind limb muscle spindles were shown to be influenced by flexion of the neck. Such long-spinal reflexes have been employed by many investigators as a test for confirmation of gamma activity. Quantitative studies of changes in gamma efferent discharge rates for such stimuli have been demonstrated in lightly anesthetized preparations with or without cerebellar control (Gilman and Ebel, 1970; Gilman, 1976).

Recently it has been observed that such activation of lumbar gamma motoneurones in a long-spinal reflex may be powerful enough to occur on a stretch applied to a single contralateral dorsal neck muscle (Murthy *et al.*, 1978a). The excitation to the gamma motoneurone is observed to occur earlier than the activation of alpha motoneurones which are coactivated under sufficiently light barbiturate anesthesia. Such long-spinal reflex excitation has so far been noticed in identified knee flexor gamma motoneurones (Fig. 9) and some unidentified gamma motoneurones isolated in lumbar ventral root filaments. The type of fusimotor neurones so observed is, however, not known.

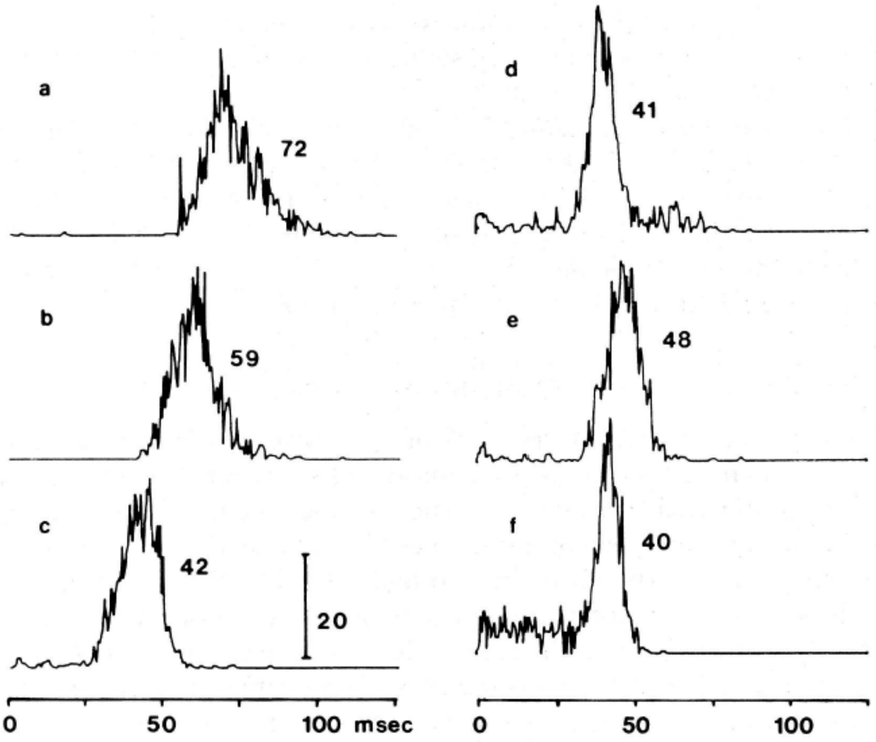

FIG. 9. Interspike interval histograms of a semitendinosus gamma motoneurone showing: (a) spontaneous activity and excitation through (b) ipsilateral ankle extension, (c) contralateral ankle extension, and stretch of contralateral dorsal neck muscles, (d) occipitoscapularis and (e) splenius. The long spinal effects are long-lasting as indicated by (e) which was obtained 2 min after release of the stretch applied to the occipitoscapularis in (d) (reproduced with permission from Murthy *et al.*, 1978a).

Such powerful long-spinal reflex effects have significance for postural control. The propriospinal and spino-bulbo-spinal pathways for such crossed interlimb reflexes probably overlap with those that have been demonstrated with electrical stimulation of forelimb and neck muscle nerves (Lloyd, 1942; Lloyd and McIntyre, 1948; Shimamura and Akert, 1965). The importance of neck muscle proprioceptors for postural control situations is well known (Magnus, 1926; Abrahams, 1972). Judging from an earlier (Lloyd and McIntyre, 1948) observation that such long-spinal effects are mediated by high threshold muscle afferents, it seems likely that the secondary afferents of the neck muscle spindles would be involved. It is also pertinent for this observation that the dorsal neck muscles appear to possess a greater number of afferent fibers of group II diameter (Richmond *et al.*, 1976).

Such descending long-spinal pathways (coursing through the lateral funiculus) have monosynaptic connections to the interneurones in lamina VII and to motoneurones in lamina IX of the lumbar segments (Jankowska *et al.*, 1974). The concerned interneurones are those mediating Ia reciprocal inhibition, thus giving rise to a mechanism of "alpha–gamma" linked reciprocal inhibition (Hultborn *et al.*, 1976).

5. Supraspinal Control of Fusimotor Functions

Granit (1970) and Matthews (1972) have extensively reviewed earlier literature relating to studies of supraspinal influences on fusimotor neurones. Most of the studies have used electrical stimulation of various supraspinal structures for effects on muscle spindle afferent discharge. Such a technique has the advantage of permitting identification of static and dynamic gamma effects when the observed effects on CNS stimulation are superimposed on the spindle response to a simultaneously applied ramp (dynamic) stretch. Some investigators have also observed supraspinal effects on efferent activity recorded either in teased ventral root filaments or in peripheral muscle nerves. The following discussions will mainly deal with data obtained most recently and refer to earlier work only as necessary. In most cases, the threshold of stimulating current necessary to elicit gamma effects is lower than that necessary to recruit alpha motoneurones. Effects (excitatory or inhibitory) have been observed on stimulation of a number of supraspinal structures scattered throughout the brain.

One of the reasons for observation of mixed supraspinal effects on fusimotor neurones must be the different levels of anesthesia from use of barbiturate and volatile anesthetics which depress or excite the fusimotor neurones to different levels (see Section 6.3). As mentioned earlier in this review, the level of spontaneous fusimotor activity has a direct influence on the magnitude of the response to various supraspinally or reflexly evoked effects (Mortimer and Akert, 1961; Gilman and Ebel, 1970).

5.1. EFFECTS FROM THE BRAINSTEM STRUCTURES

Effects of stimulating midbrain structures on hind limb muscle spindles and on lumbar gamma efferents were among the first demonstrated supraspinal effects on the fusimotor neurones (Granit and Kaada, 1952). The whole of the reticular formation appears to be quite effective in activating fusimotor neurones (Eldred and Fujimori, 1958). The characteristic features of brainstem effects are two-fold (Granit, 1970)—a driving effect on the spindle discharge through a fast pathway and a slow and diffuse effect that could outlast the stimulus (Granit and Holmgren, 1955). Also, the former effect occurs in a reciprocal manner on both flexors and extensors while the latter diffuse effects are nonreciprocally organized (Shimazu *et al.*, 1962). As can be expected, these supraspinal effects are very much dependent upon the level of anesthesia (Vedel and Mouillac-Baudevin, 1969a). The diffuse nonreciprocal effects appear to be more powerful. It is not clear whether such would be the case in the intact animal. It, however, indicates that the reticular formation has a powerful mechanism to override any background influences. Granit (1970, 1975) has discussed various examples of these slow and long-lasting effects on spindle afferents under the subject of "arousal". In the anesthetized animal, this mechanism can be activated by pinna twist (Granit *et al.*, 1952; Schomburg, 1968, 1970; Schomburg and Henatsch, 1968), though the type of effects (excitatory or inhibitory) on gamma motoneurones resulting from such a stimulus depends upon the functional state of the reticular formation corresponding to different levels of anesthesia (Schomburg, 1968; Schomburg and Schiemann, 1971). Extensor fusimotor activity is influenced by pinna stimulation in the following manner: (1) under sufficiently light pentobarbital anesthesia, gamma activity is enhanced; (2) under moderately deeper pentobarbital anesthesia, however, the effect is a depression of fusimotor activity; and (3) maximum excitatory effects on gamma motoneurones occur on pinna stimulation in the decerebrate unanesthetized animal (Schomburg, 1968; Schomburg and Henatsch, 1968). Because of its effectiveness, the pinna stimulus is commonly used as a test for identification of fusimotor activity and also of excitability of the brainstem structures.

Schomburg and Schiemann (1971) also observed effects mediated by the reticular formation influencing both the respiratory patterns and hindlimb fusimotor activity and showed that the fusimotor effects were not due to the changes in the respiratory system but, both effects were being mediated in parallel from the brainstem. It is quite likely that the effects from the viscera (described earlier in Section 4.6) on the alpha and gamma motoneurones are mediated by the same structures of the bulbar reticular formation through spino-bulbo-spinal pathways since these effects display similar diffuse long-lasting characteristics.

Fast monosynaptic pathways from the brainstem structures have been shown to project to lumbar alpha and gamma motoneurones (Willis *et al.*, 1966; Lund and Pompeiano, 1968; Grillner and Lund, 1968; Grillner *et al.*, 1969; Grillner, 1969b) through reticulospinal and vestibulospinal tracts. The reticulospinal connections originating from the pontine reticular formation were tested by stimulating the ipsilateral medial longitudinal fascicles (MLF) projecting to flexor static gamma motoneurones (Grillner, 1969b). The vestibulospinal effects originate from the lateral vestibular (Deiter's) nucleus and appear to project to the extensor static gamma motoneurones. Effects of stimulating Deiters' nucleus have earlier been shown by Carli *et al.* (1967) to affect both primary and secondary spindle endings of the hindlimb extensor muscles. The fast descending system from the brainstem with a monosynaptic connection appears to project only to the static fusimotor neurones and not to the dynamic fusimotor neurones (Grillner, 1969b). These vestibulospinal effects on gamma motoneurones are discussed in detail by Pompeiano (1972) and Grillner and Hongo (1972).

The differences in supraspinal control in an unanesthetized animal, either decerebrated at the intercollicular level or spinalized, have been recognized for quite some time (see discussion by Granit, 1970, p. 234). It seems that static fusimotor neurones are more spontaneously active in the animal with decerebration at the intercollicular level (Jansen and Matthews, 1962a), while in the spinal animal the dynamic fusimotor activity is spontaneously present (Alnaes *et al.*, 1965). However, in the spinal cat, static fusimotor activity may be induced by an injection of DOPA (Bergmans and Grillner, 1968, 1969; Grillner, 1969b). These observations have suggested a role for the descending noradrenergic reticulospinal pathways (Carlsson *et al.*, 1964) originating from cell bodies in the pontine reticular formation (Dahlström and Fuxe, 1965) in altering the balance between static and dynamic fusimotor control.

Granit (1969) has described a precollicular preparation in which the superior colliculus is left intact with its connections to caudal structures. Such a preparation appears to exhibit more dynamic gamma activity than static gamma activity. Further, these dynamic fusimotor neurones (of an ankle extensor) seem to be excited by the stretch of the muscle they innervated, resulting in a long-lasting clonic response (Denny-Brown, 1929). Thus, it is clear that the brainstem structures have strong influences on both dynamic and static fusimotor neurones.

The effects on dynamic fusimotor neurones appear to be mostly from bulbar reticular formation, while stimulation of pontine reticular formation has a greater effect on the static fusimotor activity (Vedel and Mouillac-Baudevin, 1969b). It was also confirmed that these effects from the reticular formation are not mediated by the rubrospinal pathways but by the reticulospinal and vestibulospinal pathways coursing in the ipsilateral ventral and ventrolateral funiculi of the spinal cord.

Effects from the red nucleus have been studied extensively in the cat by Appelberg and co-workers (Appelberg, 1962; Appelberg and Emonet-Denand, 1965; Appelberg and Jeneskog, 1975). The influence of the rubrospinal pathways seems to be to enhance the dynamic fusimotor action in flexor muscles and depress the static fusimotor effects (Appelberg *et al.*, 1975). Control from rubral cells may also be exerted through reticulospinal pathways in selectively increasing the static sensitivity of the muscle spindles (Appelberg and Jeneskog, 1972). In addition, restricted areas within the red nucleus may also enhance static fusimotor activity in different muscles. The control of dynamic fusimotor fibers by the rubrospinal pathways have been thought to occur via a relay in the inferior olivary nucleus (Appelberg, 1967; Appelberg and Molander, 1967). Koeze *et al.* (1974) have obtained static fusimotor effects on stimulation of the red nucleus in the primate.

5.2. INFLUENCES FROM THE CEREBELLUM AND THE VESTIBULAR SYSTEM

Influences on spinal gamma motoneurones mediated via Deiters' nucleus and the vestibulospinal pathways (Pompeiano, 1972; Grillner and Hongo, 1972) have already been briefly discussed in the previous section. Gamma efferents may also be influenced by natural stimulation of the vestibular apparatus (Poppele, 1967) as well as electrical stimulation of the VIIIth cranial nerve (Diete-Spiff *et al.*, 1967). These effects, however, are not mediated by the vestibulospinal pathways but considered to be executed via the reticulospinal tract. It appears that the threshold for fusimotor effects obtained by VIIIth nerve stimulation is less than that for effects from descending vestibular nucleus or from the reticular formation, with such effects typically outlasting the stimulus (Diete-Spiff *et al.*, 1967).

In the decerebrate animal, marked extensor rigidity occurs through overactivity of the static fusimotor fibers (gamma rigidity), possibly under the influence of Deiters' nucleus

(Pompeiano, 1972). Such rigidity disappears on disrupting the gamma loop by deafferentation (Sherrington, 1898). However, cooling the anterior lobe of the cerebellum in such decerebrate, deafferented preparations causes a return of the rigidity by direct excitation of the alpha motoneurones (alpha rigidity) (Granit, 1970; Gilman *et al.*, 1976). In addition, cerebellar ablation depresses static fusimotor effects on the muscle spindle endings (Granit *et al.*, 1955; Gilman and McDonald, 1967a, b; Gilman, 1969). The alteration in the dynamic sensitivity of primary endings observed on stimulation of the anterior lobe of the cerebellum (Jansen and Matthews, 1962a) may thus be due to excitation of the static fusimotor efferents which would depress the dynamic sensitivity of the spindle Ia afferents. Loss of cerebellar control would then lead to oscillatory behavior in voluntary movements (Glaser and Higgins, 1966).

5.3. CORTICAL INFLUENCES

Fusimotor effects resulting from stimulation of the motor cortex or the pyramidal tract have been found to be generally excitatory to hindlimb flexors and inhibitory to the extensors (Granit and Kaada, 1952; Mortimer and Akert, 1961; Kato *et al.*, 1964; Fidone and Preston, 1969, 1971). Fidone and Preston (1969), however, reported that roughly a third of the fusimotor neurones to each muscle showed opposite effects to pyramidal stimulation. While the dominant effects were on static fusimotor neurones, i.e. flexor static gamma units excited and extensor static gamma units inhibited, Fidone and Preston (1969) concluded that the opposite effects in each muscle were directed to the dynamic fusimotor neurones. Under halothane anesthesia, however, mixed effects (excitation or inhibition) may be evoked from stimulation of the same cortical area or from the pyramidal tract, in both extensors and flexors, depending upon the depth of anesthesia (Vedel and Mouillac-Baudevin, 1970). Facilitation of dynamic fusimotor effects to ankle extensors were initially reported (Vedel, 1966). The motor cortical effects were further shown to be not mediated through the red nucleus but by the pyramidal tract (Vedel and Mouillac-Baudevin, 1970).

Yokota and Voorhoeve (1969) monitored the spindle Ia and secondary afferents in forelimb muscles to determine whether cortical influences were more specifically organized with regard to the delicate functions of forelimb muscles. Stimulation of forelimb area of the motor cortex was found to influence both static and dynamic fusimotor effects to the forelimb muscles. Yokota and Voorhoeve (1969) were also able to show through a simultaneous recording of pyramidal tract discharges that most of these effects are mediated by the fast conducting pyramidal fibers.

In all these studies referred to above, fusimotor effects have been obtained at low thresholds before effects on alpha motoneurones were noticeable (Fidone and Preston, 1969; Yokota and Voorhoeve, 1969; Laursen and Wiesendanger, 1966). Considerable interest in direct cortical control of spinal motoneurones has resulted since Koeze *et al.* (1968) demonstrated that the cortico-motoneuronal (CM) projection to alpha motoneurones had a monosynaptic part that was stronger than the projections to fusimotor neurones in the hand muscles of the baboon. The primate digit muscles should be expected to have much specialized organization of alpha and gamma motoneuronal control because the range of sophisticated and delicate movements of which these muscles are capable. Koeze *et al.* (1968) established that certain instances of cortical activation exist when the fusimotor excitation occurred independently of the CM excitation to alpha motoneurones. Thus, separate and independent cortical projections to alpha and gamma motoneurones are present. This feature could be confirmed by applying near-threshold stimuli to the cortex so that the monosynaptic pathways to the alpha motoneurones are not activated, but cause temporal summation through polysynaptic pathways, i.e. either cortico-rubrospinal or cortico-interneuronal (Koeze *et al.*, 1968). These cortical effects have all been found to be short-lasting, unlike the effects from the reticular formation which have been described in the previous section.

The cortico-fusimotor excitations to the forearm and hand muscles in the baboon involve latencies for monosynaptic connections (EPSP's) for the I-volley due to repetitive firing of the corticospinal tract cells but not to the D-volley (Clough *et al.*, 1971). A number of forelimb fusimotor neurones also do not respond to cortical stimulation. Inhibitory effects were also found to project from the motor cortex via pyramidal fibers, giving rise to IPSP's with short latency corresponding to disynaptic pathway (Clough *et al.*, 1971; Grigg and Preston, 1971).

Though Vedel and Mouillac-Baudevin (1970) consider motor cortical effects in the cat to project to dynamic fusimotor neurones also, recent experiments by Koeze (1973) have not shown any convincing effects attributable to dynamic fusimotor activation in the baboon. Thus, the dominant effect of corticospinal fibers seems to be exerted on static fusimotor neurones. Both excitation and inhibition have been noticed (Koeze, 1968, 1973). According to Koeze (1973) such excitatory and inhibitory effects project from anatomically close cortical areas.

Mortimer and Akert (1961) were able to compile a cortical map in the sensorimotor area from the activation of lumbar gamma motoneurones in the cat and the monkey. A number of these fusimotor units were "driven" by the cortical stimuli. Of interest is the finding that the cortical effects were well correlated with the spontaneous rates of fusimotor activity, i.e. the higher the rate of spontaneous discharge of the gamma efferent, the greater is the effect (both excitatory and inhibitory) of cortical stimulation.

On the basis of an observation of a lack of effect of dorsal root section on the latencies or thresholds for cortically elicited foot movements in monkeys, Lewis and Porter (1971) emphasize the inadequacy of the indirect gamma route for initiating voluntary movements (see also Phillips, 1969). It would, however, be of interest to study the dynamics of such movements when deprived of the gamma control through dorsal root sections.

In a study of possible differences in cortical activation of alpha and gamma motoneurones, Van der Meulen and Ghez (1970) have demonstrated the dependence of fusimotor connections on propriospinal fibers that can survive lesioning of all the major descending tracts.

5.4. EFFECTS FROM THE BASAL GANGLIA, THALAMUS AND THE SUBSTANTIA NIGRA

A nonreciprocal depression of muscle spindle discharge has also been observed on low frequency stimulation of the *n. centrum medianum*, *n. ventralis posterolateralis*, and ventrolateral nucleus in the thalamus, and also of the basal ganglia (Hongo *et al.*, 1963; Yanagisawa *et al.*, 1963). Such fusimotor effects have been found infrequently to occur concomitantly with the slow waves (EEG spindles) in the electroencephalogram (Euler and Söderberg, 1956; Buchwald and Eldred, 1961). High frequency stimulation of the same areas in the thalamus and basal ganglia produced a facilitation of the spindle discharge (Hongo *et al.*, 1963). Vedel and his collaborators investigated in detail the effects of stimulating the caudate nucleus (Vedel, 1975; Vedel and Coulmance, 1975). Predominantly, static fusimotor effects to extensors and dynamic fusimotor effects to flexors have been seen although there were some variations attributable to different levels of halothane anesthesia. Vedel's experiments also demonstrate that static and dynamic fusimotor effects may be elicited in two successive trials of stimulation of the same area from the same afferent ending. The reasons for such complex effects may be the differences in temporal summation of impulses.

Interest in thalamic effects and in influences of basal ganglia on the fusimotor efferents has stemmed from the observation of motor abnormalities in extrapyramidal disorders. The tremor and rigidity exhibited by Parkinsonian patients have thus been investigated by many workers (see following sections in this review) to evaluate the role of the gamma system in Parkinsonism (Rushworth, 1961). Since lesions of the thalamic nuclei are employed to relieve Parkinsonian symptoms, the effects from the thalamic structures are of importance. Both reciprocal effects and nonreciprocal effects have been observed in flexor and extensor gamma motoneurones on stimulation of the thalamus or of basal ganglia. Langfitt *et al.* (1963) have suggested that the beneficial effects of thalamotomy or pallidotomy in relieving Parkinsonian rigidity may result from the blocking of the nonreciprocal effects exerted by these nuclei. Thus, lesions placed in these nuclei may permit cortical control to be exerted in a more reciprocally organized manner.

Lieberman *et al.* (1974) have recently studied the effect of cryogenic lesions of the ventrolateral nucleus or of the pulvinar in the cat. Using a cryoprobe placed stereotaxically in the appropriate locations, it was shown that lesions (produced with a probe tip temperature of −20°C) in the ventrolateral nucleus caused significant depression of fusimotor activity as inferred through effects on the muscle spindle response. Lesions in the pulvinar had no apparent effect on the muscle spindle sensitivity.

Hassler (1966) considers both static and dynamic fusimotor neurones to be involved in the Parkinsonian abnormalities resulting from a neuronal cell loss in the substantia nigra (Hassler, 1938; Greenfield and Bosanquet, 1953). Wagner (1965) and Wagner and Kalmring (1968) studied the effects of stimulating the substantia nigra on cat hindlimb muscle spindles. Stimulation of the rostral quarter and anterior margin of the substantia nigra produced inhibition of static fusimotor activity while stimulation of the caudal part of the nigral structure enhanced dynamic fusimotor effects (Wagner and Kalmring, 1968). Inhibitory effects on gamma motoneurones similar to those obtained from the rostral part of the substantia nigra have also been obtained on stimulation of the pallidum or the entopeduncular nucleus (Wagner, 1965). Hence, a surgical relief of Parkinsonian abnormalities may be achieved by interrupting the connections between the pallidum or the entopeduncular nucleus and the pyramidal tract.

Thus, a dopaminergic pathway from the caudal part of the substantia nigra may control the fusimotor neurones in the intact animal (Hassler and Wagner, 1975). The loss of such control in the Parkinsonian patients manifests in a depression of phasic stretch reflexes (tendon jerk) and slowness of initiating movements (Hassler, 1973). The nigrostriatal and pallidonigral connections may form part of the same system that becomes prominent in extrapyramidal abnormalities.

6. Drugs Affecting Fusimotor Activity

Several drugs have been employed either to block or to excite the fusimotor activity selectively. Drugs which produce a gamma block have been of particular interest in many investigations due to the clinical importance of such a technique in relieving spasticity or rigidity resulting from an overactive gamma system. The excitatory action of drugs, on the other hand, have been mostly useful in basic laboratory investigations and have been helpful in differentiating the static and dynamic fusimotor actions (Bergmans and Grillner, 1969). Matthews (1972) has reviewed some of the peripheral actions of drugs on gamma efferent activity.

6.1. PERIPHERAL EFFECTS

The fact that smaller diameter nerve fibers are more susceptible to conduction block resulting from the action of local anesthetics applied directly on peripheral nerves (Gasser and Erlanger, 1929) has been made use of by Matthews and Rushworth (1958) in producing a selective paralysis of fusimotor excitation to a muscle. It has also been shown that when applied to a peripheral muscle nerve in appropriate concentrations, procaine blocks conduction in gamma efferents first before either the alpha efferents or the spindle afferents (Ia and II) are affected (Matthews and Rushworth, 1958). Similar preferential action of other drugs on gamma efferents in ventral roots has also been reported. Nathan and Sears (1961) confirmed the action of procaine applied to ventral roots. While the action of procaine is reversible, an acute conduction block results from the use of phenol or ethyl alcohol (Iggo and Walsh, 1960; Nathan *et al.*, 1965). Hence, these drugs have clinical use for relieving symptoms of spasticity or rigidity (Rushworth, 1961; Walshe, 1924).

Selective block of the action of alpha motoneurones, on the other hand, may be achieved by preferentially blocking the extrafusal motor endplates with curare or other neuromuscular blocking drugs. Katz (1949) established that the safety factor of the intrafusal endplates in the frog muscle to such neuromuscular blocking drugs is greater than that for the extrafusal endplates, though in the amphibia these are innervated by branches of the same axon. This feature also has been found to be true for the slow beta axon innervation in the cat (Bessou *et al.*, 1965). Similarly, the gamma motor endplates are also more resistant to neuromuscular blocking agents. Emonet-Denand and Houk (1968) demonstrated that among the two types of gamma axons (dynamic and static), the endplates of the dynamic fusimotor efferents were more susceptible, suggesting a differential action of curare at neuromuscular junctions of the two types of fusimotor fibers (see also Takano, 1964). This feature has yet to be made proper use of in studies involving selective block of the intrafusal endplates.

Selective excitatory action of dynamic fusimotor endplates may, however, be mimicked (Matthews, 1972) by application of the drug suxamethonium or succinylcholine (SCh). The effects are observed in the form of an increase of the dynamic sensitivity of the Ia ending. Though there is excitation of the secondary ending also, this is not as impressive as the action on the primary ending (Fehr, 1965). The effect of SCh probably results from direct action on intrafusal muscle fibers. Brown has shown that in the frog SCh has similar preferential excitatory action on muscle spindles in the slow muscles innervated by the tonic motor axons but not in fast muscles innervated by the twitch motor fibers (Brown, 1971a).

The antispasticity drug dantrolene sodium causes skeletal muscle relaxation by affecting the excitation contraction coupling mechanism in the extrafusal muscle fibers (Ellis and Bryant, 1972; Ellis and Carpenter, 1972). A suggestion was made that this drug might also cause a reduction of muscle spindle bias by interfering with intrafusal fusimotor effects (Zorychta *et al.*, 1971). However, such an effect has since been shown to be negligible compared with the effects on extrafusal contractile tension (Takano, 1976a; Knutsson and Martensson, 1976).

6.2. CENTRAL EFFECTS

The convulsive effects of tetanus toxins occur due to a blockade of central inhibitory synaptic transmission (Brooks *et al.*, 1957). In addition to releasing the alpha motoneurones from inhibition, fusimotor activity is also increased (Kano and Takano, 1969; Takano and Kano, 1973) by the action of the toxin. The disinhibitory action is similar to the action of strychnine (Curtis, 1968) which blocks postsynaptic inhibitory processes as in recurrent inhibition of alpha motoneurones by Renshaw cells. The action of picrotoxin, on the other hand, appears to be exerted on presynaptic inhibitory processes (Curtis, 1968). Tanji and Kato (1972b) on the basis of their observation of a disinhibition by picrotoxin of fusimotor reflexes elicited by stimulation of sural nerves concluded that this might be a presynaptic inhibitory mechanism. Strychnine did not have an effect on the reflex inhibition of gamma motoneurones by cutaneous nerve volleys (Tanji and Kato, 1972b).

Catechol (1,2-dihydroxybenzene) also produces convulsive behavior of the muscles in which involvement of fusimotor neurones has been found through indirect recording from muscle spindle afferents (Angel *et al.*, 1976). The alpha rigidity can be selectively produced with concomitant depression of gamma motoneurones by drugs which inhibit monoaminergic transmission—reserpine, haloperidol or phenoxybenzamine—or by drugs like physostigmine which facilitate cholinergic transmission (Steg, 1964). Conversely gamma rigidity can be produced by L-DOPA which facilitates monoaminergic transmission with decrease in alpha motoneurone discharges (Roos and Steg, 1964). It was subsequently shown by Bergmans and Grillner (1969) that such effects of L-DOPA occur selectively to enhance static fusimotor activity in the spinal cat. In the decerebrate rat similar increase in static fusimotor activity was obtained with intravenous administration of D-amphetamine (Sorenson *et al.*, 1978). Part of this effect was probably due to direct effects on the "mesencephalic locomotor region" (Grillner and Shik, 1973) which is located in the brainstem, close to cells containing catecholamine (Steeves *et al.*, 1975). The gamma rigidity can be also induced by atropine which inhibits cholinergic transmission (Arvidsson *et al.*, 1967). Thus, monoaminergic and cholinergic pathways may be organized for reversible control of alpha and gamma motoneurones from the brainstem (Steg, 1966; Jurna, 1976).

Fusimotor control may also be affected through the serotonergic pathways. Intravenous injections of 5-hydroxytryptophan (5-HTP), the metabolic precursor of 5-hydroxytryptamine (5-HT), in the spinal animal has been found to cause an increase in static fusimotor activity (Ahlman *et al.*, 1971; Ellaway and Trott, 1974), but the observed facilitation of the stretch reflex may not be entirely due to the enhancement of fusimotor action (Ellaway and Trott, 1975). In deafferented spinal cats, both alpha and gamma motoneurones were observed to be activated by serotonin precursors, an effect which could be reversed by 5-HT antagonists, cinanserin and methysergide (Myslinski and Anderson, 1978). The effects of 5-HTP on fusimotor neurones can be mimicked by the hallucinogenic drug LSD-25 (Dixon *et al.*, 1969). The general effect of these drugs, in addition to increasing static fusimotor activity, may also be to regularize their discharge patterns (Dixon *et al.*, 1969). The static fusimotor control by noradrenergic and serotonergic pathways is considered to be independent based upon the observation that the reserpine syndrome is not relieved by administration of 5-HTP but by the administration of L-DOPA (Carlsson, 1975).

Most of the drugs that have been investigated for relief or production of spasticity and rigidity have central actions. This list includes the phenothiazine derivatives (Maxwell and Sumpter, 1974)—benzoctamine (Tacitin^R), a psychoactive drug; chlorpromazine; baclofen (Lioresal^R), a GABA derivative; and diazepam (Martins, 1975) which reduce gamma activity, as also the tremorogenic agents—metrazol (Jami, 1973, 1974) and harmaline (Lamarre and Weis, 1973). The effects of benzoctamine appear to be mostly on noradrenergic neurones, while the effects of chlorpromazine are directed on dopaminergic neurones (Baltzer and Bein, 1973). To this long list of centrally acting drugs must also be added the drugs such as nicotine (Ginzel *et al.*, 1970, 1975) and phenyldiguanide (Schiemann and Schomburg, 1972; Eldred and Ginzel, 1972; Ginzel and Eldred, 1973; Ginzel, 1973) which, though acting peripherally on sensory receptors in the viscera, produce their action on the spinal motoneurones in a viscerosomatic reflex via reticular formation and bulbospinal pathways. These drug-induced viscero-fusimotor effects last for a considerable length of time.

6.3. EFFECTS OF ANESTHETICS

The observations of differential fusimotor effects due to different levels of anesthesia have been reiterated at various points in this review. This has been specifically studied under volatile anesthesia using halothane in Vedel's laboratory (Vedel, 1975; Vedel and Coulmance, 1975; see also Koeze, 1973). The volatile anesthetics in general appear to increase

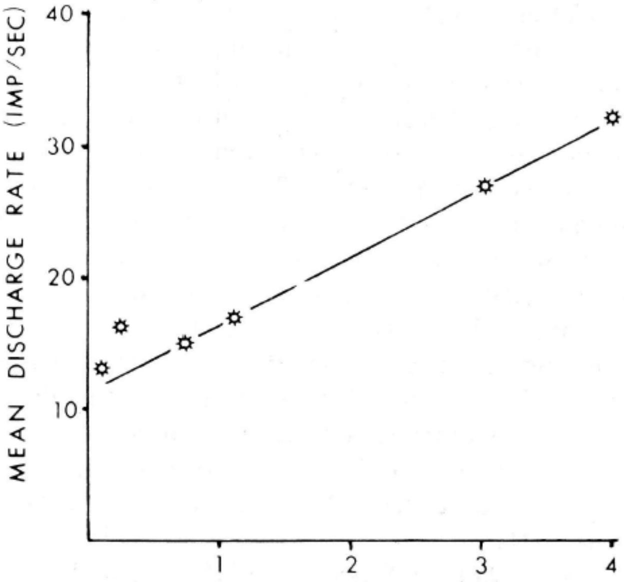

FIG. 10. Excitability of gamma efferent is well correlated with the concentration of volatile anesthetic in the inhaled air. A vaporizer was used in setting the concentration of halothane in the mixture with O_2 and N_2O (Murthy, unpublished observation).

gamma activity (Diete-Spiff *et al.*, 1962; Andrew, 1966; Pascoe, 1965). This is illustrated in Fig. 10, where the level of spontaneous activity in a gamma efferent is observed to be well correlated with the level of anesthesia. This feature affords the experimenter with an opportunity to obtain different levels of fusimotor activity with the use of a vaporizer to control the level of halothane anesthesia.

Diete-Spiff and Pascoe (1959) observed excitatory effects on gamma motoneurones by ether and urethane, but inhibitory effects by chloralose, thiopental, hexobarbitone and acetylpromazine. Most of these effects must be due to activation or depression of the various reticular nuclei. Under light barbiturate anesthesia a steady spontaneous discharge of fusimotor neurones has been observed by a number of investigators (Proske and Lewis, 1972; Lewis, 1973; Gilman, 1976; Gildenberg and Murthy, 1977). A majority of these spontaneously active gamma efferents (under barbiturate anesthesia) seems to be the static fusimotor type (Lewis, 1973; Gladden and McWilliam, 1977b). Gildenberg and Murthy (1977) were able to observe a population of slowly discharging gamma efferents that were more depressed by barbiturate anesthesia than others with faster mean rates.

7. Fusimotor Effects Observed in the Human

Fusimotor effects in conscious and normal human volunteers and in patients with motor abnormalities have recently begun to be demonstrated in greater detail by the technique of microelectrode recordings in peripheral nerve fascicles of activity originating from muscle spindle endings. The technique was introduced by Hagbarth and Vallbo (1967, 1968) and was subsequently used extensively in investigations on normal subjects and on patients with CNS lesions conducted in Hagbarth's and in Struppler's laboratories (Vallbo *et al.*, 1978). The results from their observations will be reviewed here. Earlier investigations on fusimotor function in the human have used more indirect techniques. These have involved studies of tendon reflexes (knee and ankle jerks) and H-reflexes for phasic responses and the studies of stretch and vibration reflexes for tonic effects. In addition, a number of studies have attempted to evaluate the effects of a "gamma block" on the motor performance by injecting local anesthetics to block preferentially the conduction in gamma efferents. Such techniques and others have been described in a number of papers presented at recent symposia (Desmedt, 1973, 1977).

In comparison to the data from animal experiments, the results from human experiments are obviously of great importance due to the variety of voluntary movements that the human is capable of executing and the variety of supraspinal excitations that can be achieved to modulate the spinal motor apparatus. In spite of the restraints and constraints imposed on the repertoire of movements that may be performed by the human subjects during a microelectrode recording from peripheral nerve fascicles, a number of interesting features of fusimotor excitations to the human muscle spindles have been observed (Burke, 1978). The differences in observed effects have contributed to conflicting points of view. The following pages will be devoted to an analysis of such issues and to determine the answers.

7.1. RESTING FUSIMOTOR TONE AND THE SENSITIVITY OF HUMAN MUSCLE SPINDLES

As mentioned earlier in Section 4 of this review, spontaneous fusimotor activity is a commonly observed feature of many animal preparations. Hagbarth (1974) points out that though there may be a resting fusimotor activity in the conscious man, it will be an insignificant amount as observed from a lack of effect on muscle spindle discharge on application of a lidocaine block of the muscle nerve (Wallin *et al.*, 1973). In passive, relaxed human muscles, the muscle spindle endings possess a low rate of spontaneous activity (less than 20 imp $\sec^{-1}$) and display poor position sensitivity (Vallbo, 1974a). Under these conditions, a peripheral fusimotor block with lidocaine (Burke *et al.*, 1976b) produces very little effect on the resting background discharge rate of the muscle spindles (Fig. 11). Burke and Eklund (1977) arrived at a similar conclusion from observations of muscle spindle discharge in