Exp Brain Res (1987) 65: 352–360

Experimental Brain Research

Activity-related changes in electrical thresholds of pyramidal tract axons in the behaving monkey

A. Schmied* and E.E. Fetz

Regional Primate Research Center and Department of Physiology and Biophysics, University of Washington, Seattle, WA 98195, USA

Summary. In monkeys generating torques about the wrist we investigated changes in the excitability of pyramidal tract (PT) axons, measured as the probability of evoking antidromic responses in motor cortex with constant juxtathreshold stimuli delivered in the brain stem. When PT stimuli were delivered 2–20 ms after an orthodromic action potential in the PT neuron, the excitability of axons was elevated, with a characteristic post-spike time course. Excitability peaked at a post-spike delay of 7.0 ± 2.7 ms (n = 33). Axonal thresholds typically dropped to 80–90% of the unconditioned values (obtained for stimuli with no preceding spike). Controlling for such post-spike threshold changes by delivering stimuli at fixed post-spike delays, we found that excitability of many PT axons also fluctuated with the wrist responses, being slightly higher during flexion or extension. The phase of movement in which excitability increased had no consistent relation to the phase of movement in which the PTN fired. Task-related threshold changes were also seen in PTNs whose discharge was not modulated with the wrist response. Delivering a subthreshold conditioning stimulus also increased the excitability of most PT axons to a subsequent test stimulus. Such post-stimulus changes may be mediated by the effects of adjacent fibers activated by the conditioning stimuli. The post-spike and post-stimulus changes added in a nonlinear way. All three types of threshold change may be mediated by a common mechanism: changes in the ionic environment of the axon produced by activity of the axon itself or its neighbors. Such changes could enhance the effectiveness of corticospinal impulses: the post-spike excitability increase could enhance the invasion of corticospinal terminals, and the interaction between neighboring fibers could enhance synchronous arrival of impulses at common targets.

Key words: Pyramidal tract – Monkey – Axon – Threshold

Introduction

In monkeys performing alternating wrist movements, the threshold for evoking antidromic responses in pyramidal tract neurons (PTNs) was found to fluctuate systematically with alternating flexion and extension movements (Fetz and Cheney, unpublished observation): tested at random times, most pyramidal tract (PT) axons were slightly more excitable during the phase of movement in which the PTN discharged. Such changes in axonal thresholds could be related to two different phenomena reported previously. First, the axonal excitability of corticofugal neurons was shown to be transiently increased by peripheral stimulation in anesthetized cats (Dubner and Sessle 1971; Gugino et al. 1972; Mann et al. 1977; Rudomin et al. 1978; Mann and Follett 1982). This increase of excitability was thought to reflect an axonal depolarization, suggesting the possibility of presynaptic modulation of transmission in corticofugal pathways. Second, the electrical threshold of an axon changes after conduction of an action potential, as documented for frog sciatic fibers (Raymond 1979) and for callosal axons of anesthetized rabbits and monkeys (Swadlow et al. 1974, 1978). Following the refractory period is an increase of excitability lasting 10–50 ms (for review see Swadlow et al. 1980).

To investigate these two phenomena in awake, behaving primates, we studied the threshold for

* Present address: Laboratoire de Neurobiologie, Faculté des Sciences, Bat. 440, Université de Paris XI, F-91405 Orsay, France

Offprint requests to: E.E. Fetz (address see above)

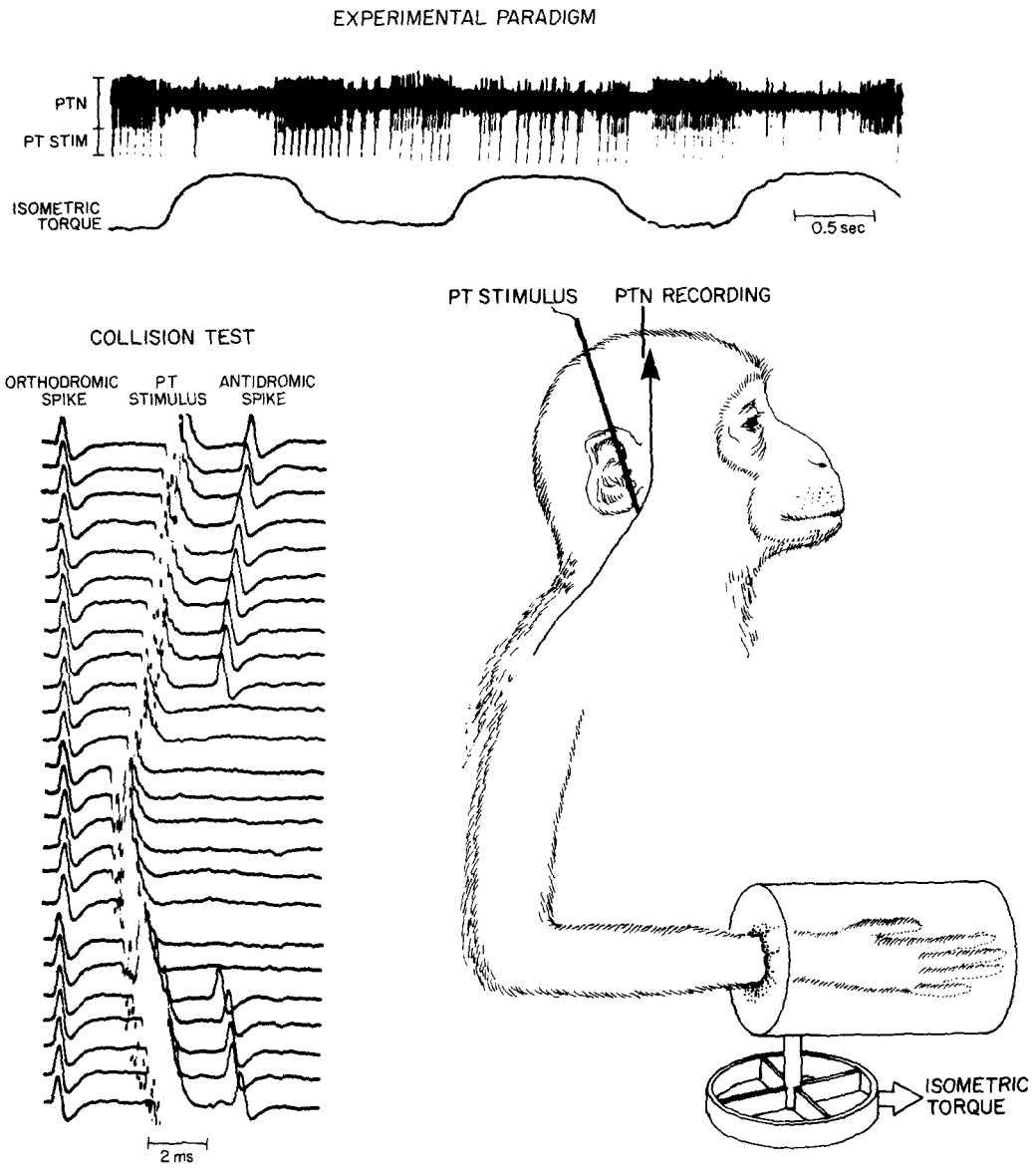

Fig. 1. Experimental paradigm: The monkeys performed isometric or auxotonic wrist responses with the arm and hand constrained by the manipulandum. Top record illustrates alternating ramp-and-hold torque trajectories. PT stimuli (large artifacts) were delivered after orthodromic spikes (small spikes). The response rasters at left illustrate secure antidromic spikes evoked by suprathreshold stimuli, and their elimination by collision for brief post-spike delays

evoking antidromic responses in single PTNs as a function of the delay after an orthodromic spike and as a function of motor activity. Our results indicate the existence of spike-related threshold changes as well as additional changes related to specific components of the behavioral task.

Material and methods

The electrical excitability of PT axons was tested in three rhesus macaques (*Macaca mulatta*) performing ramp-and-hold wrist responses (Fig. 1). The task involved generating flexion and extension torques, either isometrically or against an elastic load ("auxotonic" movements). Extracellular action potentials of PTNs were recorded in the hand area of precentral cortex with tungsten microelectrodes. Antidromic responses were evoked by 0.2-ms biphasic stimuli delivered by a constant-current stimulator (Nuclear Chicago). To minimize polarization, stimulus pulses were biphasic and were delivered at rates below 10/s. The concentric bipolar stimulating electrodes (tip separation 0.1 mm) were stereotaxically placed at the medullary level (2 mm lateral and 2 mm posterior to earbar zero). During implantation, electrode tips were optimally placed at the site having the lowest threshold for evoking finger movements with repetitive stimulation (0.5–1.3 mA in monkeys anesthetized with halothane). After activity-related threshold changes were documented in two monkeys, the post-

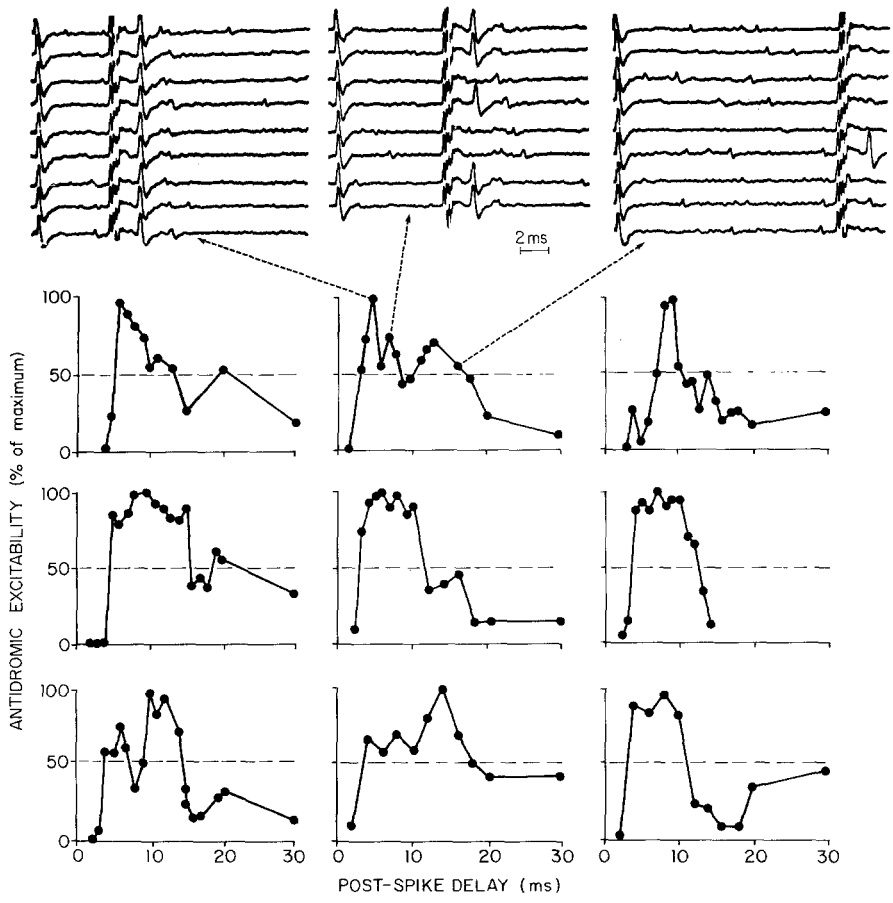

Fig. 2. Spike-related changes of excitability: the upper rasters illustrate the antidromic responses of one PTN to constant-intensity stimuli delivered at different post-spike delays (left: 5 ms; middle: 7 ms; right: 15 ms). The lower curves plot the time course of the post-spike excitability for nine PTNs as a percent of maximum excitability. For each post-spike delay the proportion of antidromic responses was calculated for a minimum of 100 PT stimuli at a constant intensity; for comparison, the curves were normalized to the maximum value for each unit

spike effects were systematically investigated and contrasted with task-related effects in a third. In this animal the electrode implant was guided by frontal X-rays and by recording afferent responses in the medial lemniscus, as well as by low-threshold finger movements evoked by electrical stimulation. In all animals, antidromic responses in motor cortex were identified by the collision test (for active cells) or by responses following 3 pulses at 400/s (for silent cells). Thresholds for antidromic responses ranged from 45 μA to 3 mA for all but three PTNs. Subsequent histologic reconstruction confirmed the proximity of electrode tips to the pyramids; in the third animal, the distal tip of the electrode was just below the pyramids, explaining the relatively high thresholds.

The electrical excitability of PT axons was quantified by the proportion of antidromic action potentials evoked by near-threshold stimuli ($n \geq 100$ stimuli). Suprathreshold stimuli invariably evoked antidromic spikes, confirming that antidromic invasion of the soma was secure (cf. Fig. 1, left); thus, failures to evoke a spike reflected fluctuations of *axonal* threshold rather than blocking of antidromic conduction at the soma. The proportion of peri-threshold pyramidal tract stimuli that evoked antidromic spikes was documented as a function of the stimulus delay after an orthodromic spike; any trials in which a second spontaneous action potential occurred during the post-spike interval were excluded. Although stimuli followed spontaneous action potentials, their rate was limited to a maximum of 10/s.

To document changes in axonal excitability specifically related to the behavioral task, we controlled for the post-spike effect by delivering stimuli at constant post-spike delays. The percentages of antidromic responses obtained during the static flexion hold vs. the extension hold were compiled separately with a gating circuit. Similarly, we compared the axonal responsiveness when the monkey was performing the wrist task and when he was inactive, during "time out" periods with the reinforcement schedule turned off.

To document changes in axonal excitability produced by activation of adjacent fibers, we also delivered pairs of juxta-threshold stimuli. The post-spike delay of the first stimulus and the delay of the second stimulus were systematically varied to compare post-spike and post-stimulus effects.

Results

1. Post-spike threshold changes

For the 29 PTNs tested, axonal excitability changed in a repeatable manner following an orthodromic spike, as illustrated in Fig. 2. The records at top show examples of the antidromic responses of one PTN evoked by a constant intensity stimulus triggered at three different delays after the orthodromic spikes. The same stimulus intensity (1.5 ma) evoked more antidromic responses when delivered 5 ms after an orthodromic spike (left) than for longer post-spike delays (7 and 15 ms are illustrated). The curves plot the time course of axonal excitability following an

Table 1. Relations between antidromic excitability changes (rows) and the PTNs' relation to an isometric wrist response (columns)

	Task-related firing		Task-unrelated firing		Total
Antidromic excitability	Extension E (n = 6)	Flexion F (n = 13)	Tonic (n = 10)	Silent (n = 4)	(n = 33)
Postspike changes	6/6	13/13	10/10	–	29/29
Task-related changes					
F > E	3/6	8/13	3/8	3/4	17/31
E > F	2/6	2/13	1/8		5/31
F ~ E	1/6	3/13	4/8	1/4	9/31
Inactive > active	2/4	1/8	1/6	2/3	6/21
Active > inactive	2/4	6/8	2/6	–	10/21
Inactive ~ active	–	1/8	3/6	1/3	5/21

orthodromic spike for nine representative PTNs; for each cell, the stimulus intensity was kept at a constant value appropriate to demonstrate changes in responsiveness as a function of post-spike delay. To facilitate comparison, the curves are normalized to a percent of maximum responsiveness. The 29 neurons tested with post-spike delays from 2 to 50 ms showed a similar increase of post-spike excitability. The highest probability for electrical excitation (i.e., the lowest threshold) occurred at an average delay of 7.0 ±2.7 (SD) ms after the orthodromic spike in the cortex (corresponding to about 6 ms after the orthodromic spike passed the stimulus site). During the post-spike supernormal period, the axonal threshold typically decreased to 80–90% of its unconditioned value (i.e., its value for long delays).

2. *Task-related threshold changes*

In addition to the post-spike threshold changes, most of the tested PTNs also exhibited excitability changes specifically related to the monkey's motor activity. Figure 3 illustrates two extension-related PTNs, which, during performance of an isometric ramp-and-hold task, showed greater excitability during static flexion. Both PTNs were more active with extension, so any cumulative post-spike effect should have produced greater excitability during extension. For the PTN on the top, the post-spike excitability is plotted separately for constant intensity stimuli delivered during static flexion and extension: the curves have a similar time course,but the axonal excitability was consistently higher during flexion than during extension for all post-spike latencies.

The extension-related PTN on the bottom was tested with different stimulus intensities around threshold, also delivered at controlled post-spike delays. The proportion of antidromic responses evoked by each stimulus intensity is plotted separately for spike-triggered stimuli delivered at post-spike delays of 6 and 30 ms; the axonal threshold, defined as the stimulus intensity that would evoke 50% of responses, was lower during flexion for each delay. For 18 neurons, the relative magnitude of the threshold changes for flexion vs. extension, or for wrist activity vs. wrist inactivity, ranged from 4% to 20% (independently of the constant 10–20% decrease of threshold associated with the short post-spike intervals).

Table 1 summarizes the post-spike and the task-related changes of excitability observed for the 33 PTNs. In contrast to the consistent post-spike supraexcitability for each PTN, the task-related changes of excitability showed no systematic correlation with the cell's discharge properties. Nineteen PTNs showed task-related firing patterns, discharging at higher rates for wrist flexion (n = 13) or extension (n = 6); 11 of these 19 task-related neurons showed lower threshold during flexion; two of the flexion-related cells had lower threshold during extension and three extension-related cells had lower threshold during flexion. Twelve additional PTNs were unrelated to the task; they either discharged with a regular tonic frequency (n = 8) or were essentially silent (n = 4); six of these task-unrelated PTNs also had lower threshold during flexion, and five did not exhibit any movement-related changes of excitability. All these task-related changes of threshold were independent of the post-spike effect, which was controlled by delivering the stimuli at constant post-spike delays (Fig. 3). The greater number of flexion-related cells and flexion-related changes may be due to the fact that the flexion hold zone required greater torques than the extension zone. The table also contrasts excitability of axons when the monkey was performing the task ("active") and when the operant schedule was turned off and the monkey was inactive ("inactive"). A larger proportion of the cells showed greater net excitability during wrist responses (averaged over flexion and extension) than during rest.

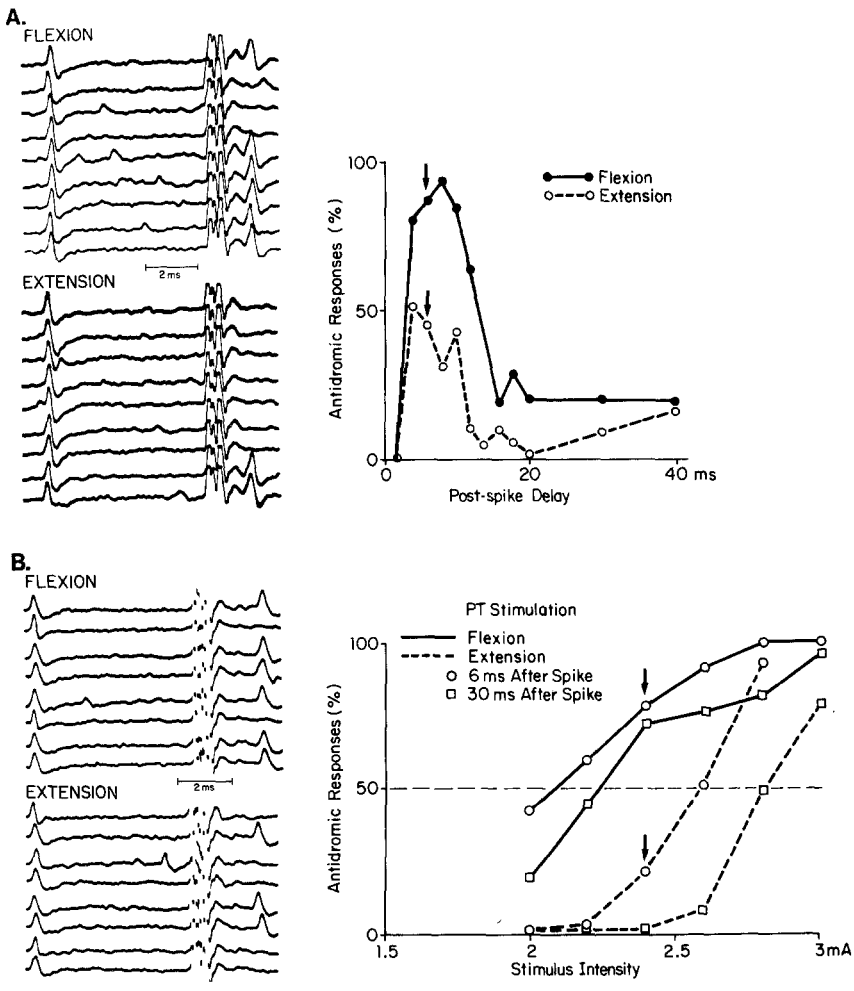

Fig. 3A, B. Task-related changes of excitability: The response rasters (left) illustrate the antidromic response of two PTNs evoked during static flexion and extension at a constant stimulus intensity and post-spike delay (indicated by arrows on graphs). Both units were more active during extension. For unit one (top) the post-spike excitability curves are plotted separately for stimuli delivered during the extension (circles) and flexion (black dots) phases. For all post-spike delays, the excitability was higher during flexion. For unit two (bottom) the response probability to different stimulus intensities was determined separately for flexion (continuous lines) and extension (dashed lines), with a post-spike delay of 6 ms (circles) and 30 ms (rectangles). For both delays the threshold (50% response intensity) is lower during flexion; this reflects a combination of task-related (20%) and spike-related (10%) changes

3. Poststimulus threshold changes

The task-related changes raised the possibility that axonal threshold may be modified by impulses in neighboring fibers. To investigate the degree to which axonal excitability may be modulated by synchronous activity in adjacent fibers, these fibers were directly activated by a conditioning stimulus. Ten PTNs were studied using pairs of juxtathreshold stimulus pulses. Again, to control the post-spike effects, the pulse-pairs were delivered at constant post-spike delays. For trials in which the first stimulus evoked no response in the recorded PTN, the responsiveness to the second stimulus was used as an index of excitability changes which could result from the activation of adjacent fibers by the first. Such pulse-pair stimulation revealed an increase of responsiveness to the second pulse following a subthreshold conditioning pulse for seven of the ten PTNs tested.

Figure 4 illustrates the effect of the subthreshold conditioning pulse for two PTNs. The first pulse was delivered at a constant post-spike delay (either 5 or 20 ms) as indicated in the inset. The probability of response to the second stimulus is plotted as a function of the interstimulus interval. For the unit on the right (B) the time course of excitability reveals a maximum for interstimulus intervals in the range of 10–15 ms. This time course was the same, whether the stimulus pair was delivered at post-spike delays of 5 ms (top) or 20 ms (bottom). The response probability to the first stimulus of each set is also plotted as a control for non-stationary changes; responsiveness was essentially constant, but higher for the 5 ms post-spike delay.

The time course of post-stimulus excitability for the unit on the left (A) showed maximum excitability at a post-stimulus interval of 8 ms. Its time course was the same when tested during performance of wrist responses (top) and during spontaneous cell activity with the monkey at rest (bottom). For all the units tested, the peak of the post-stimulus excitability

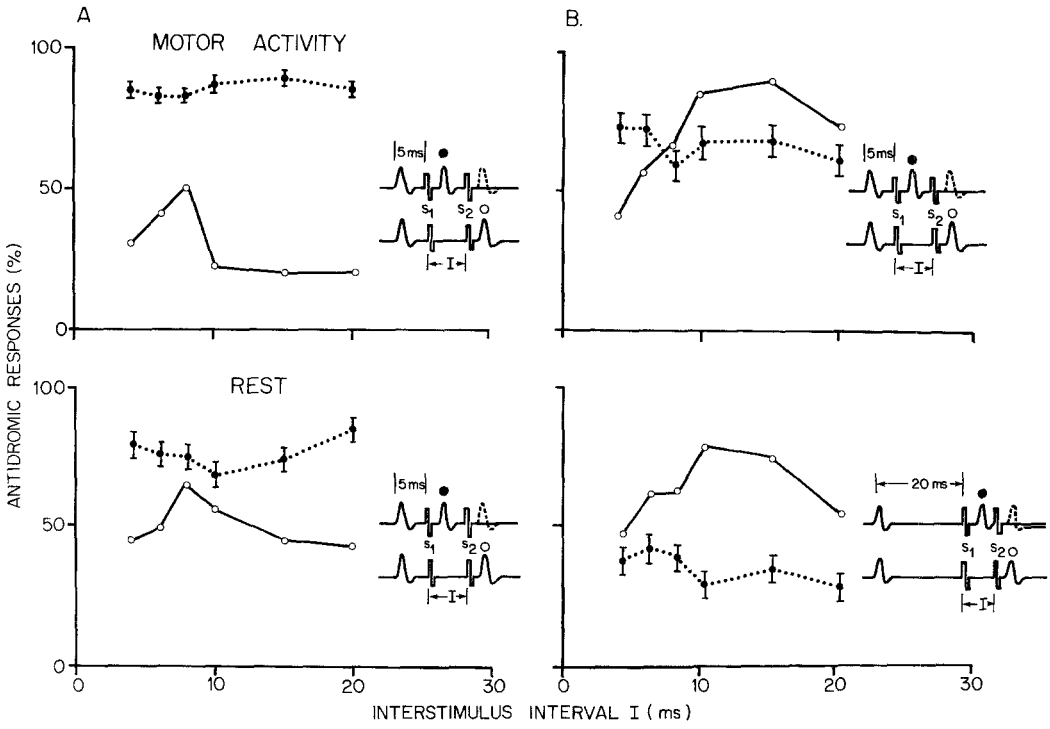

Fig. 4A, B. Stimulus-related changes in PT axon excitability: the effects of a subthreshold conditioning PT stimulus on the response to a test stimulus is plotted as function of interpulse interval for two PTNs (left and right). Insets illustrate the paradigm and the events plotted. The conditioning stimulus (S_1) was delivered after a fixed post-spike delay: 5 ms or 20 ms (bottom right). The response probability to the conditioning stimulus, shown as a control for each set (solid circles and dotted lines), is essentially constant. The response probability to the test stimulus (S_2) following subthreshold S_1 is plotted with open circles and solid lines. For the PTN at left (**A**), the post-stimulus excitability had the same time course, whether measured during wrist movements (left top) or with the monkey at rest (left bottom)

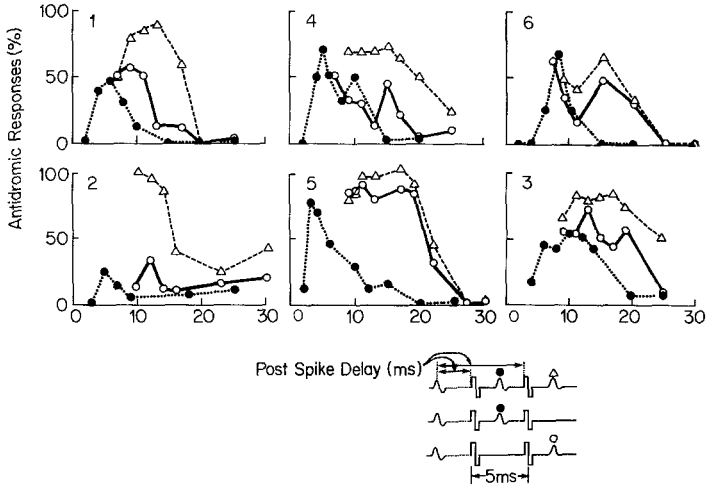

Fig. 5. Combination of post-spike and post-stimulus excitability changes tested with pairs of stimuli (inset). The responsiveness to the stimulus is plotted as a function of post-spike delay for both the first pulse, which had no intervening stimulus (solid dots), and the second pulse, which was preceded by 5 ms by a conditioning pulse of the same intensity (open symbols). Responses to the second pulse are plotted separately for trials in which the conditioning pulse evoked an action potential (open triangles) and in which it was subthreshold (open circles). Results indicate a non-linear summation of post-spike and post-stimulus effects. Numbers identify the cells tested

occurred at a mean latency of 8.6 ± 4.0 ms (n = 12 determinations under different behavioral conditions for five PTNs).

The combination of post-spike and post-stimulus effects enhanced the excitability above that of either alone, as illustrated for six PTNs in Fig. 5. In these experiments, the pulse-pair interval was constant (5 ms) and the pair was delivered at different post-spike delays (see inset). Each graph plots the responsiveness to stimuli of constant intensity as a function of post-spike delay. Responses to the first stimulus, plotted with solid dots, show the pure post-spike excitability and illustrate the supra-normal period for each cell. Responses to the second stimulus, plotted

with open symbols, show responses at the same post-spike delay when an additional conditioning pulse was delivered 5 ms prior to the test pulse. Two curves plot separately this responsiveness when the conditioning pulse evoked an action potential (open triangles) and when it did not (open circles). In general, the post-spike excitability was increased by a subthreshold conditioning pulse (the open circles tend to be higher than the closed circles); excitability was even greater when the conditioning pulse evoked an action potential (the open triangles are higher than the open circles). However, these effects do not summate linearly; if summation were linear, the separation between the curves would be constant. In fact, the post-stimulus effect is a decreasing function of the post-spike delay. Possible explanations for this behavior are discussed below.

Discussion

Our results show that the electrical excitability of PTN axons in the behaving monkey may change as a function of three different factors: the occurrence of an action potential, the delivery of a subthreshold conditioning stimulus and the performance of motor activity. Several possible mechanisms for the observed threshold changes can be considered.

The excitability changes were probably not produced simply by displacement of the stimulating electrode, for several reasons. This mechanism could not explain the post-spike or post-stimulus changes, which had a short-latency time course. To test for electrode movement, X-rays of the anaesthetized monkey were taken at extreme flexion and extension positions of the head; these X-rays confirmed that electrode tip was not displaced in the brain stem for head-body angles which greatly exceeded normal head positions. Moreover, during excitability testing the head position was securely fixed in such a way as to preclude any neck movements.

The possibility of a cortical modulation of antidromic invasion of the PTN soma must also be considered, especially for the pulse-pair test. Previously reported changes in somatic antidromic invasion have required repetitive PT stimulation; security of antidromic invasion was not affected by single PT stimuli (Stephanis and Jasper 1964). Moreover, in the present study, a slight increase of the PT stimulus intensity assured 100% of antidromic responses for all PTNs tested. Thus, the excitability changes reflect changes in axonal threshold rather than security of somatic invasion.

A common physiological mechanism can be proposed to explain the threshold under all three sets of conditions: the post-spike, the post-stimulus and the task-related changes of threshold may all depend on transient changes in ionic concentrations (possibly K^+) around the tested axons.

1. Post-spike increase of excitability

A post-spike supernormal period was observed for the 29 tested neurons; these PTNs had antidromic latencies ranging from 0.4 to 3 ms. The time course and amplitude of the post-spike increase of excitability were in agreement with those previously reported for myelinated and unmyelinated fibers, both central and peripheral (for rev. see Swadlow et al. 1980). K^+ accumulation around the axon following each action potential has been proposed to explain the post-spike excitability increase (Somjen 1979; Sykova 1983; Nicholson 1983). An increase of extracellular K^+ can depolarize the axonal membrane and reduce the threshold, as recently demonstrated for cerebellar parallel fibers (Kocsis et al. 1983). In the present study, post-spike delays longer than 30 ms were not practical because of the increasing likelihood of intervening spontaneous spikes; this precluded investigation of the more subtle post-spike decrease of excitability (i.e., subnormal period) which often follows the supernormal period (Chung et al. 1970; Swadlow et al. 1980).

The functional consequence of the post-spike increase of excitability may be particularly important for conduction of action potentials into terminal arborizations, where the safety factor for spike invasion may be low (Chung et al. 1970; Swadlow et al. 1980). If the post-spike supernormal period that we observed at the medullary level also exists at spinal terminals, and if invasion of terminal arborizations is not always complete, the second of two consecutive spikes could invade more terminals and generate a larger postsynaptic potential. This might explain the facilitation of corticomotoneuronal EPSPs produced by two consecutive cortical stimuli separated by brief intervals (Phillips and Porter 1964; Porter 1970; Muir and Porter 1973). The time course of the facilitation of corticomotoneuronal EPSPs is comparable to the time course of the post-spike supraexcitability of PTNs in the current study (Fig. 2).

2. Post-stimulus effect

Increases of excitability produced by a subthreshold conditioning stimulus pulse have been previously observed in cerebellar parallel fibers (Merrill et al.

1978; Kocsis et al. 1983) and in the spinal cord (Wall 1958; Merrill et al. 1978) in anaesthetized cats. These observations were explained as being mediated by the post-spike effects of the neighboring fibers activated by the conditioning pulse. Similarly, in the present study, with a controlled post-spike delay, we found that a subthreshold conditioning stimulus increased the probability of a response to a second pulse of the same intensity; the responsiveness to the second pulse peaked in the range from 4 to 20 ms after the conditioning pulse. Such a long-latency rebound of excitability after the conditioning pulse is hard to explain purely by local passive membrane changes (Blair and Erlanger 1936); it seems more likely due to ionic changes produced by activation of adjacent fibers by the first pulse. As directly shown for cerebellar parallel fibers, the external K^+ concentration around an axon can be modified either intrinsically, following its own firing, or extrinsically, following the activation of neighboring axons (Kocsis et al. 1983). Consequently, both extrinsic and intrinsic post-spike ionic modifications are capable of altering the electrical excitability of an axon.

Compared with the intrinsic supernormal period following an action potential, the rebound of excitability following a subthreshold conditioning pulse was weak, in agreement with previous observations (Kocsis et al. 1983). Moreover, it appeared to depend on the post-spike delay: the pulse-pair effect was more apparent less than 20 ms after an orthodromic spike. In fact, the pulse-pair effect seemed to be more effective during the period of higher K^+ conductance which follows each spike. A similar dependence of K^+ effect on the post-spike delay has been described in invertebrates (Baylor and Nicholls 1969). In vertebrate CNS artificial increases of external K^+ (exceeding 3 mM) can reduce axonal excitability (Kocsis et al. 1983); however, actual measurements of external K^+ changes induced by neuronal firing in the cerebellum, mesencephalic reticular formation and the spinal cord do not attain these extreme values, possibly because of ionic regulatory mechanisms (Sykova 1983).

One functional consequence of the increase of axonal excitability following activity of neighboring axons could be an enhanced synchronization of adjacent fibers discharging in close association. An action potential propagating along one fiber would leave an ionic trail tending to accelerate conduction in adjacent fibers. This ionic mechanism could bring action potentials sufficiently close for direct electrical interaction between neighboring fibers (Clark and Plonsey 1970; Markin 1970). Such interactions could explain the synchronous arrival of corticospinal volleys evoked by a cortical stimulus and reflected in the fact that CM-EPSPs increase with negligible change in latency as more CM cells are activated (Phillips and Porter 1964). Similarly, the antidromic action potentials in neighboring PTNs evoked by axonal stimulation show a clear tendency to arrive simultaneously (Canedo and Towe 1985). The synchronous activation of multiple fibers by an electric stimulus probably exaggerates this interaction over that occurring under normal conditions. Nonetheless, the efficacy of this interaction during normal activity is suggested by the task-related changes. For neighboring PTNs with similar targets, the enhanced synchrony of arrival of impulses in their terminals would enhance the effectiveness of their temporal summation.

3. Task-related changes of excitability

When tested with a controlled post-spike delay, the excitability of PTN axons was also found to depend on motor behavior. These changes had no apparent relation to any task-related modulation of the cells' firing rates. Even some silent cells showed task-related threshold changes. Such changes of threshold specifically related to motor activity could reflect various neuronal mechanisms extrinsic to the PTN itself.

These task-related changes of excitability could be compared with threshold changes previously observed in anaesthetized cats following stimulation of peripheral receptors (Dubner and Sessle 1971; Gugino et al. 1972; Mann et al. 1977; Rudomin et al. 1978; Mann and Follet 1982). The increase of excitability following a conditioning peripheral stimulus in corticofugal axons has been suggested to reflect terminal depolarization associated with presynaptic inhibition. This would require the presence of depolarized terminals within electronic conduction distance of the stimulation site, such as corticomesencephalic and corticobulbar collaterals. However, the changes of excitability observed in corticofugal axons after peripheral stimulation were not restricted to specific locations but were often present in the same axon, from the internal capsule to the spinal cord (Mann and Follet 1982). Moreover, the changes of excitability were generally associated with orthodromic activation of corticofugal axons (Gugino et al. 1972; Mann and Follet 1982). Thus, the increases of excitability observed in those studies could also reflect the intrinsic post-spike supernormal period associated with the firing of the recorded PTN, as well as the extrinsic effects of activity in adjacent PTNs.

In the present study, the post-spike effect was controlled by delivering test stimuli at constant post-

spike delays. Thus, the task-related changes of excitability we observed were independent of the axonal supernormal period and could have resulted from extrinsic effects associated with the firing of adjacent fibers during the motor activity. The net influence of adjacent fiber activity on PTN excitability should depend on the number of neighboring axons firing together and producing ionic changes around the recorded PTN. If the neighboring axons are not differentially active during movements, no consistent extrinsic ionic change would be expected around the PTN axon; indeed, one-fourth of the recorded PTNs showed no task-related changes of excitability. The fact that the task-related changes in excitability were often different from the task-related firing patterns of the tested PTN would suggest that neighboring fibers may fire independently.

The hypothesis that discharge of neighboring fibers may affect axonal excitability is favored by the fact that the pulse-pair test revealed an increase of responsiveness following the conditioning subthreshold pulse in all but one case in which a task-related change was observed. Both increases could be mediated by activity in adjacent fibers.

The extrinsic post-spike effects suggested by the pulse-pair results and by the task-related changes of excitability could depend on various local factors affecting the ionic changes, such as fiber packing, presence of myelin, and buffering action of glial cells. The interactions of neighboring fibers would be particularly effective for those PT fibers that fire simultaneously; their correlated activities in a restricted microenvironment could produce ionic changes tending to enhance synchronous conduction of impulses and their synaptic efficacy at common targets.

In conclusion, we propose that the post-spike, the post-stimulus and the task-related changes of excitability observed in the behaving monkey might reflect a common mechanism: extracellular ionic changes (possibly K^+) produced either by the discharge of the recorded PTN or its neighboring axons.

Acknowledgements. This study was supported by NIH grants RR00166 and NS12542 and a grant from the Phillippe Foundation. We thank Randolph Gaylord for help with the experiments and Kate Schmitt and Nancy Goldfogel for editorial assistance.

References

Adrian ED (1920) The recovery process of excitable tissues. Part 1. J Physiol (Lond) 54: 1–34

Baylor DA, Nicholls JG (1969) Changes in extracellular potassium concentration produced by neuronal activity in the central nervous system of the leech. J Physiol (Lond) 203: 555–569

Blair E, Erlanger J (1936) On the process of excitation by brief shocks in axons. Am J Physiol 114: 309–316

Canedo A, Towe AL (1985) Superposition of antidromic responses in pyramidal tract cell clusters. Exp Neurol 89: 645–658

Chung SH, Raymond SA, Lettvin J (1970) Multiple meaning of single visual units. Brain Behav Evol 3: 72–101

Clark JW, Plonsey R (1970) A mathematical study of nerve fiber interaction. Biophys J 10: 937–957

Dubner R, Sessle BJ (1971) Presynaptic excitability changes in primary afferent and corticofugal fibers projecting to trigeminal brain stem nuclei. Exp Neurol 30: 223–228

Gugino L, Stoney SD Jr, Morse RW (1972) Presynaptic facilitation and inhibition of pyramidal tract fibers terminals. Fed Proc 31: 385

Kocsis JD, Malenka RC, Waxman SG (1983) Effects of extracellular potassium concentration on the excitability of the parallel fibers of the rat cerebellum. J Physiol (Lond) 334: 225–244

Mann MD, Follett KA (1982) Excitability changes along pyramidal tract axons after sensory stimulation. Exp Neurol 78: 685–702

Mann MD, Holt WS, Towe AL (1977) Afferent modulation of the excitability of pyramidal tract fibres. Exp Neurol 55: 414–435

Markin VS (1970) Electrical interaction of parallel non-myelinated nerve fibers. I. Change in excitability of the adjacent fibre. Biofisika 15: 120–128

Merill EG, Wall PD, Yaksh TL (1978) Properties of two unmyelinated fibre tracts of the central nervous system: lateral Lissauer tract and parallel fibres of the cerebellum. J Physiol (Lond) 284: 127–145

Muir RB, Porter R (1973) The effect of a preceding stimulus on temporal facilitation at corticomotoneuronal synapses. J Physiol (Lond) 228: 749–763

Nicholson C (1983) Regulation of the ion microenvironment and neuronal excitability. In: Jasper HM, van Gelder NM (eds) Basic mechanisms of neuronal hyperexcitability. Liss, New York, pp 185–216

Phillips CG, Porter R (1964) The pyramidal projection to motoneurones of some muscle groups of the baboon's forelimb. Progr Brain Res 12: 222–242

Porter R (1970) Early facilitation of corticomotoneuronal synapses. J Physiol (Lond) 207: 733–745

Raymond SA (1979) Effects of nerve impulses on threshold of frog sciatic nerve fibers. J Physiol (Lond)290: 273–303

Rudomin P, Jankowska E, Madrid J (1978) Presynaptic depolarization of corticospinal and rubrospinal terminal arborization produced by volleys to cutaneous nerves. Soc Neurosci Abstr 4: 571

Somjen GG (1979) Extracellular potassium in the mammalian central nervous system. Ann Rev Physiol 41: 159–177

Stefanis C, Jasper H (1964) Recurrent collateral inhibition in pyramidal tract neurons. J Neurophysiol 27: 855–877

Swadlow HA (1974) Properties of antidromically activated callosal neurons and neurons responsive to callosal input in rabbit binocular cortex. Exp Neurol 43: 429–444

Swadlow HA, Kocsis JD, Waxman SG (1980) Modulation of impulse conduction along the axonal tree. Ann Rev Biophys Bioeng 9: 143–179

Swadlow HA, Rosene DL, Waxman SG (1978) Characteristics of interhemispheric impulse conduction between prelunate gyri of the rhesus monkey. Exp Brain Res 32: 439–443

Sykova E (1983) Extracellular K^+ accumulation in the central nervous system. Progr Biophys Molec Biol 42: 135–189

Wall PD (1958) Excitability changes on afferent fiber terminations and their relation to slow potentials. J Physiol (Lond) 142: 1–21

Received March 11, 1986 / Accepted August 6, 1986