Oscillatory electromyographic responses to limb displacement in Parkinsonism

H TERÄVÄINEN

From the Laboratory of Neurophysiology, NIMH and Experimental Therapeutics Branch, NINCDS, Bethesda, Maryland, USA

SUMMARY Forty Parkinsonian patients and 26 normal subjects were instructed not to resist movements of a handle which they maintained in a specified position (1) during tonic activation of muscles against the force produced by a torque motor and (2) while no force was produced by the motor. Electromyographic responses to handle displacements were recorded in biceps muscle (pronating or supinating displacements) or in wrist extensor and flexor muscles (displacements which extended or flexed the wrist). Displacements involving changes of muscle length elicited (1) excitation and inhibition occurring at monosynaptic latency in muscles which were stretched and shortened, respectively; (2) a “silent period” following the initial excitation in the stretched muscle and excitation following the initial inhibition in the shortened muscle (shortening reaction); and (3) (in Parkinsonian patients) sustained oscillations at about 4 to 5 Hz (at rest) or about 6 to 8 Hz (during maintained posture). It was also observed that the initial muscle responses in both the stretched and shortened muscle could be reciprocal and biphasic, with the two peaks of excitation in the agonist occurring during reduced activity of antagonist muscles, and vice versa.

In a previous study¹ it was observed that Parkinsonian tremor could be initiated and reset by limb displacement, with the phase of the reset tremor depending on the direction of the displacement and on the phase of the tremor at which the displacement was delivered. In addition, it was noted that displacements which involved shortening of a given muscle could generate short-latency excitation of the shortened muscle even while the shortening was in progress. The purpose of the present study was to characterise this response, and to contrast the initial short-latency response to displacement with the later displacement-initiated tremor.

Patients and methods

Muscle responses to limb displacements were analysed in 13 experiments involving eight Parkinsonian patients with resting tremor (seven men 30 to 70 years of age, mean 58.8, and one 64 year

old woman) and in 32 recordings from 32 Parkinsonian patients with or without postural tremor. Their age varied from 38 and 72 years (mean 60.0), seven were women and 25 men. Responses were also obtained in 26 age matched normal volunteers 38 to 80 years of age (mean 62.2) and in seven patients with polyneuropathy, four females and three males 24 to 60 years of age (mean 48.3). Five had chronic relapsing polyneuropathy, one chronic demyelinating polyneuropathy and one Charcot-Marie-Tooth. All had prominent slowing of nerve conduction. They were included in the study mainly to introduce a loop delay in the peripheral circuitry responsible for the triggering of EMG responses.

The equipment has been described previously.¹ It allowed accurate detection of position simultaneously with EMG recordings (bipolar surface electrodes) of the activity at the muscles subjected to controlled stretch or shortening. These signals, together with codes providing information on timing and direction of perturbations, were recorded on magnetic tape for subsequent computer analysis.

Throughout a given test the subject was seated

Address for reprint requests: H Teräväinen, MD, PhD, National Institutes of Health, Building 10, Room 3D12, 9000 Rockville Pike, Maryland 20205 USA.

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with forearm fixed in a mould allowing flexion-extension movements of the hand but preventing the forearm movements. The hand was sandwiched between two closely fitting vertical bars connected to the axle of a brushless DC torque motor (Aeroflex TQ 64). Movement of the hand was measured by a potentiometer attached to the torque motor shaft. EMG activity was simultaneously recorded with bipolar surface electrodes over the wrist extensor and flexor muscles. Movement of the shaft, located below the wrist joint, accurately reflected the movements of the hand. The experimenter could also control the steady state activity of the muscles by regulating current through the DC motor. The strength (up to 4.9 Nm) and duration (between 20 and 300 ms) of the perturbations could be varied. All the experiments reported here were done using a steady state torque of 0.84 Nm and perturbations with a 3.4 Nm torque pulse of 50 ms in duration. A steady state torque of 1.7 Nm was employed in experiments involving long duration perturbations (300 ms). Thus, a force and not the distance was the controlled variable. In some experiments biceps EMG was recorded following stretch (pronation) or shortening (supination).

Results

Limb displacements could trigger tremor in some Parkinsonian patients when they were instructed to relax (fig 1) without any steady state load (resting tremor), but more easily when they resisted (fig 2) a unilateral steady state load (postural tremor). In normal subjects, oscillations were occasionally triggered by displacements when the subjects resisted unilateral steady state load prior to the perturbations.

In Parkinsonian patients, the tremor oscillations varied in frequency, and were usually about 4 to 5 Hz in the case of resting tremor and about 6 to

Fig 1 Sustained oscillations in wrist position following 50 ms perturbations (P) which abruptly flexed the wrist into flexion. Two trials with oscillation frequencies of about 5.0 Hz and 4.5 Hz are shown. There was no steady-state load prior to the perturbation of right hand of a Parkinsonian patient.

Fig 2 Summated, rectified and low-pass filtered biceps EMG responses to ten displacements of 1 s in duration to pronation (stretch) beginning at P. The subject resisted steady state load requiring biceps activation prior to the perturbations as well as afterwards (postural tremor). Parkinsonian patient. Tremor frequency was 6.8 Hz.

8 Hz in postural tremor, as illustrated in figs 1 and 2. The cycle of activation of one muscle thus occurred at intervals of about 125 to 250 ms depending on the type of tremor. There was regular alternating activation of the antagonist and agonist muscles during sustained oscillations: the peak activity of antagonist muscle follows the peak activity of the agonist at an interval of half the tremor cycle (fig 3).

Fig 3 Summated, rectified and low-pass filtered EMG activity of wrist extensors and flexors during sustained oscillations (11 trials). The activity of extensor and flexor muscles alternated. Parkinsonian resting tremor, frequency 3.7 Hz.

Initial effects of perturbations

The latencies of reflex excitation of muscles depended on whether they were subjected to stretch or shortening. The sequence of events can best be illustrated with examples of responses in studies requiring muscle activation prior to the perturbations. In these tests, a steady state load was generated with the torque motor to turn the subject's hand into pronation, which had to be resisted (to keep the handle stationary) by activating the biceps muscle. Perturbations of 50 ms in duration which initially stretched biceps muscle resulted in reflex excitation sooner than displacements which

shortened the muscle. This is illustrated in fig 4 using the simplest possible example of a case in which biceps responses contained only one distinctive peak. Abrupt stretch by pronation of the forearm caused reflex excitation of the biceps muscle with a latency of about 20 ms and a peak of EMG activity at about 80 ms. On the other hand, perturbations which initially shortened the

Fig 4 Summated, rectified and low-pass filtered biceps responses to ten perturbations (P) to pronation direction (stretched) and ten perturbations (P) to supination direction (shortened). Stretch caused short latency excitation, whereas shortening caused initial inhibition followed by excitation. Thus, the phases of muscle activity depended on the direction of the displacement. On the other hand, the peaks of EMG responses to perturbations in opposite directions are separated by an interval of about 25 ms only. Records are from a Parkinsonian patient resisting a steady-state load requiring biceps activation prior to perturbations.

biceps by supinating the forearm, caused an initial inhibition of the EMG activity followed by excitation with a peak latency of about 105 ms (fig 4).

Individual muscle responses to stretch perturbations of the same force and duration varied in both patients and normal subjects. The amplitude and duration of the EMG responses depended, at least partially, on the degree of muscle activity prior to perturbations; this has previously been reported.^{2,3} When the duration of the muscle response to stretch exceeded about 125 ms, it frequently contained not one but two distinctive peaks. The peak latencies of these biphasic responses could be accurately determined in 15 of the Parkinsonian patients and in 14 normal subjects using cursor measurements of summated EMG responses. The mean latencies of the two peaks in Parkinsonian patients (36.8 ± 2.9 ms and 78.3 ± 8.7 ms, mean $\pm$ SD for biceps) were not significantly different from those of normal subjects (34.2 ± 5.4 ms, and 70.5 ± 3.4 ms).

Fig 5 illustrates the biphasic EMG responses of a Parkinsonian patient in whom resting tremor

Fig 5 Summated, rectified and low-pass filtered EMG responses of forearm flexors to 13 perturbations (beginning at P) of 50 ms in duration to extension (left hand) superimposed on summated responses in the wrist position (A). The two peaks of the initial biphasic EMG response were separated by an interval of 56 ms, and the frequency of oscillations triggered by the perturbation at P was 4.4 Hz. The EMG responses of both extensor and flexor muscles are superimposed in B. Both responses are biphasic and oscillate with inverse relation to each other; thus the first spike of extensor activation corresponds to the phase of reduced activity of the flexors in between the two peaks of excitation, and the reduction of EMG activity between the two peaks of extensor activity (separated by an interval of 60 ms) has a timing corresponding to the second peak of flexor activation. Variations in the individual trials of both flexor (C) and extensor (D) muscles are shown as raster displays of EMG activity. Parkinsonian patient, no steady state load.

was triggered by 50 ms perturbations. Biphasic response occurred in wrist flexor muscles in response to abruptly extending the wrist. The EMG responses have a latency of 36 ms and peaks at 88 and 144 ms from the beginning of the perturbation (fig 5A). Responses of the wrist extensor muscles were simultaneously recorded (fig 5B). Biphasic excitation of the initially shortened extensor muscles occurred later: peak responses took place 126 ms and 186 ms after the beginning of the perturbation. These simultaneous recordings

of agonist and antagonist muscles also illustrate that the excitation-inhibition cycle within the initial EMG responses alternated in the antagonist and agonist muscles (fig 5B). Thus, the latencies of the peak excitation of the antagonist and agonist wrist muscles for displacements in *one direction* are, to a close approximation, similar to the differences of peak excitation of the biceps muscle in response to stretch and shortening (fig 4). These results also show that the period between the peaks of the initial oscillatory process initiated by the displacement is less than the period between the peaks of the later sustained tremor (fig 3), which could also be initiated by a displacement.

There remained the problem of distinguishing between a "shortening reaction" and a stretch reflex elicited secondarily by the handle rebound. These alternatives were examined by obtaining simultaneous recordings of wrist extensor and flexor muscle EMG activity in response to perturbations under the following conditions: accurate measurements of muscle excitation in relation to the duration of the position displacement, and by using long duration perturbations (300 ms) in normal man resisting steady state load. In addition, patients with neuropathy were studied to introduce a peripheral delay into the oscillating circuitry.

Response latencies

The 50-ms ramp perturbations caused wrist displacement usually lasting about 80 ms, possibly due to inertia of the moving masses of the subject's arm, the hand, the handle, the shaft, and the torque motor. This is illustrated in fig 5A, where the wrist position began to turn back to flexion ("rebound") 81 ms after the beginning of extensor perturbation. The rebound occurred at about the same time or somewhat later than the latency to the beginning of excitation of the shortened extensor muscles (fig 5B). If the extensor excitation were due to stretch of the extensors secondary to the position rebound, the increase in the EMG activity would have been expected to start about 35 ms later, which was the measured latency of the stretch reflex in this patient. This would indicate that central nervous system (CNS) determined the antagonist excitation. Similar results were obtained from other subjects, but inconsistently.

Long duration perturbations in normal subjects

When the extensor muscles were activated by resisting a steady state load prior to the perturbations, stretch of the extensors caused an increase in the extensor EMG activity with a short

Fig 6 Simultaneous recordings of wrist position (A) and EMG responses of forearm extensor muscles to 15 perturbations (beginning at P) into flexion (B) and extension (C) directions. Prior to the perturbations (300 ms in duration) the subject had to activate the extensor muscles to resist a steady state torque. The magnitude of the displacement to flexion was considerably smaller than that to extension, presumably because the perturbations were either resisted or assisted by the force produced by the active extensor muscles. The subject's responses to perturbations in both directions were strong enough to cause position rebound beginning either at 100 ms (flexion) or at 125 ms (extension) after beginning of the perturbations. The initial response of the extensor muscle to stretch was short latency excitation (B) and inhibition to its unloading (C). Two successive bursts of EMG activity in response to stretch (B) were seen; the first occurred at the time when the muscle was lengthening (note the differences in the time scale in position and EMG recordings) and the second spike when the muscle was shortening. Two bursts of extensor activity were also seen in response to perturbations causing initially shortening of the extensors (C). Both occurred after the position rebound at the time the extensors were lengthening.

latency and peak excitation at 70 ms. This response was strong enough to overcome the force produced by the torque motor and resulted in position rebound 100 ms after the beginning of the perturbations. However, at the time the extensor muscles

were *shortening*, another burst of excitation of the extensors occurred with a latency to the peak response of about 220 ms (fig 6B). Displacements in the opposite direction rebounded in this experiment after 125 ms, the difference in the rebound being due to the steady state level of flexion torque requiring extensor activation and flexor inactivation prior to the perturbations. Extensor perturbations thus suddenly assisted the force produced by the active extensor muscles and stretched inactive flexors. After initial inhibition, between 40 and 125 ms following the beginning of extensor perturbations, two peaks of excitation of extensor muscles occurred separated by an interval of about 125 ms (fig 6C). Thus, initial perturbations triggered oscillatory muscle responses when the muscles were lengthening and shortening. A powerful stimulus was needed to demonstrate this phenomenon in normal subjects. Only stretch of a rather active muscle initiated repeated oscillations. Stretch of its inactive antagonist was not a sufficiently strong stimulus to cause excitation of the previously active muscle during the period of initial shortening.

Latencies of initial responses in patients with neuropathy

Fig 7 illustrates responses of wrist extensor and flexor muscles to flexor perturbations in a patient with neuropathy. Oscillations in the wrist position after 50 ms perturbations occurred as in the normal subject with a rebound at about 85 ms. The loop delay introduced into the oscillatory circuitry was considerable in this subject: the muscle excitation in response to stretch began some 30 ms after the position rebound with a latency of about 115 ms, that is, the latency was about four times longer than in the normal subject. Because the latency of the stretch reflex was 115 ms, the expected excitation of the antagonist muscle, if due to the stretch secondary to the rebound, would be expected to occur at the earliest some 115 ms after the beginning of the rebound or about 115 ms after the burst of EMG activity of the stretched agonist muscle. However, the latencies of EMG responses of the flexor and extensor muscles were separated by only 28 to 40 ms. In fig 7, simultaneous responses of the wrist flexor and extensor muscles to extending perturbations of the wrist are shown. The flexor muscles were excited 28 ms before the excitation of the extensors. These results indicate that the *initial* stretch triggered CNS responses and resulted in phase dependent activation of both the stretched and shortened muscles.

Fig 7 Summated, rectified and low-pass filtered responses of forearm extensor and flexor muscles to perturbations into flexion direction in a patient with chronic relapsing polyneuropathy. Position recording and EMG activity of the flexor muscles are superimposed in the upper part of the figure. In the lower part simultaneous flexor and extensor muscle responses to the same perturbations are shown. Note that i the latencies of responses are about four times longer (115 ms) than in normal man (for example, fig 6) or in Parkinsonian patients (fig 4) due to the slow conduction velocities of the peripheral nerves, and ii that excitation of the extensor and flexor muscles are separated by only 28 ms, despite the marked difference in response latencies. This difference at about 28 ms is about the same as in the Parkinsonian patient illustrated in fig 4. If the excitation of the shortened flexor muscle would have been secondarily due to position rebound, the response would be expected to occur at the earliest some 115 ms and not about 30 ms after the rebound, as was the case in this subject. These results also illustrate that muscles can produce considerable force to resist sudden displacements (position rebound occurred before reflex activation of the muscles) due to length-force relationship and elastic properties. The subject had absent tendon reflexes, mild interosseus atrophy, decreased motor nerve conduction velocity (24 ms in upper extremities), distally diminished skin sensitivity to touch and pain, normal position sense, and absent sensory nerve potentials.

Discussion

Stretch of muscle causes several distinctive bursts of EMG activity. The first burst⁴ has a response latency approximately corresponding to the latency of the tendon jerk, and is presumably mediated by monosynaptic Ia afferents to spinal motoneurons. The second burst of EMG activity has a latency which is long enough to allow supra-

spinal pathways to play a role in its occurrence. It is reported to be smaller or absent in patients and experimental animals with lesions in the posterior column, in the motor cortex internal capsule or both.⁵⁻⁹ These observations indicate that the long latency responses are mediated through the motor cortex as originally suggested by Hammond¹⁰ and Phillips.¹¹ On the other hand, Ghez and Shinoda¹² recorded, in decerebrate and spinal cats, similar bursts of EMG activity whose peaks of excitation corresponded to those of short and long latency responses reported by Tatton and Lee.⁴ This last finding suggests that intraspinal oscillations may play a role in long latency responses. It is, therefore, difficult to evaluate the relative quantitative roles of spinal and supraspinal circuits to the long latency components of the stretch reflex. Lesions of the CNS at different levels may well result in variations both in the subliminal drive to lower motoneurons and CNS modulation of spindle sensitivity, both of which will undoubtedly modify responses of motoneurons to Ia activation. This point is illustrated, for example, by the need of a steady state load prior to the stretch to reveal or increase the long latency components (see Results), as has been well documented previously,^{2 3 13-15} and by differences in responses depending whether the muscle was used as antagonist or agonist at the time of stretch.¹⁶

The main object of the present experiments was to study initial EMG responses of agonist and antagonist muscles to stretch and shortening in Parkinsonism. This was done while the patients resisted a steady load and were instructed not to react to sudden perturbations of short duration (50 ms). These perturbations caused a short-lasting displacement in the maintained position after which the hand resumed its original position without any voluntary effort. A large body of data is available on muscle responses to stretch and shortening in normal subjects and in patients with various diseases. This cannot, however, be directly compared with the present results because of the different experimental conditions employed. Much of the previous work has been performed to study the effects of stretch or release during the course of voluntary tracking movement,^{2 5 6 8 9 13-18} a paradigm requiring the subjects to respond to perturbations of long duration (500 ms) by making a movement or by letting the arm be moved,^{15 19} or to study the effects of repetitive linear or sinusoidal movements.^{20 21} Furthermore, much of the previous work was done under conditions in which the decreased load on the muscle allowed it to shorten more or less by its own stiffness, whereas

a strong shortening displacement was employed in the present experiments. In addition, there were differences in the muscles studied. While the present observations are valid with regard to large arm muscles the observations may not be extended to more distal smaller muscles, which may behave differently.²² Nevertheless, the presence of a biphasic muscle response to stretch previously observed was confirmed in the present study. It was also found that displacements caused excitation of the shortened muscles in both patients and normal subjects resisting a steady load, in the accord with earlier observations.^{15 20} The initial effects of displacements followed the current concepts²³ of agonist and antagonist innervation; stretch caused muscle activation (for example, figs 4 and 6B) and shortening caused inhibition, provided the muscle was active prior to the unloading (figs 4 and 6C). However, this pairing of reflexes (unloading and stretch) in agonist and antagonist muscles occurred only during the *initial* phases of the first EMG responses, with short latencies comparable to those of the tendon reflex. Evidence based on measurements of *later* phases of the first EMG responses in relation to the movement in normal subjects, Parkinsonian patients, and patients with neuropathy, indicated that: i oscillating EMG responses are triggered by the displacements, ii the peak excitation of the shortened muscle can follow the peak excitation of the stretched muscle with a delay of only about 30 ms irrespective of several fold differences in the peripheral nerve conduction velocity, iii the phase of oscillations in the antagonist and the agonist muscles is dependent on the direction of the *initial* displacement, iv muscle responses may not be related to changes in the muscle length (paradoxical excitation or shortening reaction).

Excitation in the passively shortened muscle ("paradoxical contraction") was first described in patients with "certain central nervous system diseases".²⁴ In patients with Parkinsonism and other extrapyramidal diseases it was subsequently observed to show two parts: an initial phasic (or dynamic) and a later static (or tonic) component.^{25 26} Early studies indicated that injection of procaine into the stretched muscle abolished or diminished the activation of both the stretched and shortened muscle.^{25 27} This has not been confirmed in more recent work,²⁰ where the static shortening reaction was abolished but the phasic component remained after the stretch reflex of the infiltrated muscle had disappeared. The observations thus differ on whether or not the phasic shortening reaction, primarily under consideration

in the present study, depends on the intact fusimotor innervation of the stretched muscle. The finding that the phasic stretch and shortening reactions could be demonstrated in subjects with severe peripheral sensory neuropathy and absent tendon reflexes supports the view that intact Ia afferents are not solely responsible for the triggering of the muscle responses to large external displacements. Other afferent inputs may be involved in reinforcing the segmental reflexes.^{17 28} The peripheral afferent mechanisms responsible for triggering the phasic responses in subjects with neuropathies remain obscure, particularly in the setting of current ignorance of possible compensatory changes in the CNS related to altered afferent input.

Other examples of muscle activation during shortening are i bursts of EMG activity following the silent period of the unloading reflex,²⁹ ii antagonist activation during shortening in fast voluntary step movements,³⁰⁻³³ and iii tonic increase in the activity of the shortened muscle.³⁴ The functional significance of these different shortening reactions may well be varied. The antagonist activation in step movements has been thought to be determined by central programming and to provide a braking force to decelerate the movement.^{31 33 35} Later work has shown that the antagonist response can be abolished if the movement is halted, indicating that peripheral feedback is also of importance.¹⁸ The phasic activity following the silent period of the unloading reflex and that of the shortening reaction of passive displacements may serve to adjust the shortened muscles to their new length or to increase the stiffness³⁶ around the displaced joint (preventing overshoot during rebound and oscillations).

That the short latency reflexes (both unloading and stretch) in response to *large external displacements* (as used in the present work) were reinforced by other sources of excitatory input to spinal motoneurons is fully compatible with the idea that segmental reflexes are primarily involved in the regulation of *small disturbances*.³⁷ Several studies have shown that compensation for large load is not achieved by segmental mechanisms alone.^{38 39} If the prolongation of the short latency muscle responses to large displacements is a result of long-loop CNS activity reinforcing segmental reflexes, the *modulation* of the response to result in biphasic activity in both agonist and antagonist muscles remains to be considered. Possible mechanisms include segmental spinal circuitry, long-loop intraspinal, spino-bulbo spinal and previously mentioned transcortical loops.

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