Action tremor in Parkinson's disease

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SUMMARY Electromyographic activity of the biceps muscle was examined in 38 parkinsonian patients and 33 normal subjects during (i) rapidly alternating pronation-supination movements (RAM) of the forearm, and (ii) single pronation or supination movements in response to visual (light) or to kinesthetic signals (displacements of the hand). Biceps electromyography (EMG) displayed rhythmic activity over the supination phase of RAM in the majority of the parkinsonian patients, whereas continuous activity was evident in most normal subjects. Similar phenomena were observed when single movements were executed in response to visual or kinesthetic signals. Rhythmic activity could be triggered without any external displacements by voluntarily initiated supination of a previously quiescent limb even before actual movement of the limb occurred. Voluntary pronation (involving biceps inactivation) did not trigger any rhythmic biceps activity. The results are interpreted to support the hypothesis that parkinsonian patients have action tremor because voluntarily initiated activity leads to oscillations in an internal feedback circuit involving descending pathways from motor cortex to spinal cord, and ascending pathways from the spinal cord back to the motor cortex.

Central mechanisms are of major importance in the genesis of parkinsonian resting tremor. The pathology in this disorder is limited to the brain, and the tremor can be abolished by surgical lesions placed in the thalamus or the corticospinal pathways. However, various peripheral manipulations can modify parkinsonian tremor¹⁻⁴; limb displacement can both trigger tremor and abruptly change its phase.⁵ It has been suggested that parkinsonian tremors are due to oscillations within an unstable internal feedback loop involving ascending impulses from the spinal cord through thalamus to motor cortex, and back to spinal cord⁶. On the basis of this proposal, abrupt initiation of voluntary movement should generate an internal feedback signal similar to a sudden external kinesthetic stimulus. Voluntary movements should, therefore, be capable of triggering tremor. This would imply that the action tremor of parkinsonian may be similar, in its pathophysiology, to the more extensively studied resting tremor. Experiments were undertaken to test this hypothesis.

Subjects and Methods

Fast pronation and supination movements of the upper arm of 38 parkinsonian patients were studied (one postencephalitic and 37 idiopathic). Their age ranged from 38 to 72 years, median 61 years. Almost all the subjects were treated with levodopa, carbidopa and/or bromocriptine. The observations were compared to voluntary movements of 21 normal subjects with a median age of 70 years, range 52 to 80 years. In addition, studies were performed on 12 younger normal subjects, whose ages ranged from 20 to 45 years, median 23 years.

Fast pronation-supination movements were examined using two different paradigms: (i) the subject was instructed to make a single movement (either pronation or supination) as fast as he or she could in response to a signal, or (ii) the subject was asked to make a series of uninterrupted rapidly alternating movements (RAM) as quickly as possible.

The single movements were initiated in response to either light (visual stimulus) or displacement of the hand (kinesthetic stimulus). The differences between these two experiments was that the hand displacement was likely to trigger reflex activity superimposed on the subject's voluntary muscle

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activation, whereas this was not the case when the visual stimulus was used. The two types of stimuli were employed in an attempt to compare voluntary movement alone, with voluntary movement associated with a rapidly imposed passive displacement of the type known to disrupt and trigger tremor in parkinsonian patients.⁵

The subjects were studied in a seated posture. They grasped a handle that could be moved by pronation or by supination of the forearm (fig 1).

Fig 1 Subjects were studied seated. They grasped a handle that could be moved both by the subject and by a torque motor, in supination and pronation. Rigid physical stops limited the range of the movement to 45°. In front of the subjects were signal lights providing information on the movements to be made; either one of the two instruction lamps told the subjects whether they should pronate or supinate in response to a subsequent displacement of the handle (kinesthetic stimulus) or to a visual "go"-light (visual stimulus).

The handle grasped by the subject was coupled to the axle of a brushless DC torque motor (Aeroflex TQ-64) capable of sustaining steady state angular rotational forces, so that the subject was required to maintain muscular activity in order to keep the handle stationary. By regulating current through the motor, the experimenter could control the steady state activity of the biceps.

After establishing the correct handle position (fig 1) an alerting signal was given and then either of two instruction lamps was illuminated (one for pronation, the other for supination). The voluntary movement was subsequently made in response to a later "go"-signal (a light, or displacement of the handle). The perturbation stimuli were in either direction: turning the handle to inhibit (supinate)

biceps muscle, or to excite (pronate) the biceps muscle.

In the experiments in which rapidly alternating movements (RAM) were studied, the subjects were instructed to move the handle back and forth as fast as they could for a period of twenty seconds. Steady state force was not generated by the DC-motor when testing RAM.

Electrical activity of the biceps muscle (EMG) was recorded from bipolar electrodes applied to the surface of the skin. The position of the handle was monitored by a potentiometer connected to the axle of the torque motor. Position and EMG were recorded on magnetic tape, together with code signals (providing information on instructions, direction of perturbation and direction of responses). Total range of movement was limited to 90 degrees by physical stops, that is, 45 degrees pronation or supination. The recordings were subsequently analysed by a PDP 12 "Digital" computer.

Resting tremor was evaluated here as clinically evident tremulous movement in a limb which was intended to be relaxed. Postural tremor was evaluated here as rhythmic movement in a limb sustained against gravity, or maintaining posture against force produced by the torque motor. The oscillating EMG activity revealed during movement was taken as an index of action tremor.

Results

RAPIDLY ALTERNATING MOVEMENTS (RAM)

As a group, parkinsonian patients differed from the normal subjects in the speed of RAM and the EMG activity associated with RAM. In general, slowing of RAM speed in individual patients correlated with the extent of clinical disability (Fig. 2), as also observed by Knutsson and Mårtensson.⁷

Fig 2 illustrates biceps EMG activity recorded during RAM in one normal subject and in three clinically dissimilar parkinsonian patients. In addition to the slower speed in parkinsonism, the figure reveals tremor, which was observed in the majority (26/36) of the patients. This contrasts with the pattern of biceps activation found in the normal subjects, whose muscles were continuously active during supination in most (32/33) cases (the one normal subject with oscillating biceps activity was 72 years of age with prominent physiological tremor). The frequency of the "action tremor" in parkinsonism was usually between 6 and 9 Hz, although higher frequencies (10 to 11 Hz) were observed in two patients. The presence or absence of action tremor during RAM was not related to resting or postural

tremor in the patients prior to the tests (table 1). Ten of the parkinsonian patients either did not have action tremor in biceps or they had such severe tremor before and during the tests that discrimination of oscillations triggered by voluntary movement

was not possible. Action tremor was detected in two out of four patients with drug induced dyskinesia, and in one predominantly bradykinetic patient (of postencephalitic aetiology) who had never exhibited tremor during clinical examination.

Fig 2 Reciprocal EMG activity of the biceps muscle during rapidly alternating voluntary pronation-supination movements for the upper arm is shown as raster display of rectified biceps EMG activity. Each of the rasters comprise 21 sweeps over a 2 second period. Each sweep consists of a horizontal row of dots. The density of the dots corresponds to amplitude of the EMG activity: the higher the EMG activity at a given moment the higher the dot density. The individual trials are aligned when the subjects are passing the midpoint (M) of their pronating movement. Large arrows point to small vertical lines which show completion of one repetitive movement cycle (pronation-supination-pronation). P and S indicate biceps activity leading to pronation and supination movements, respectively. "Control" is from a normal subject. "Dyskinetic" is from a parkinsonian patient who had mild choreoathetosis during the experiment due to excessive therapy. "Bradykinetic" is from a patient with severe bradykinesia and rigidity, but no clinical tremor. "Tremulous" is from a patient with severe resting tremor in addition to prominent bradykinesia and rigidity. The speed of repetitive movements was fastest in the control subject and the dyskinetic patient (6 to 7 repetitions within the 2 second period), and slowest (2 to 3 repetitions) in the two bradykinetic patients (this was not always the case). The biceps muscle was continuously active during the period of supination in the control subject; during similar movements in the parkinsonian patients, biceps activity was interrupted by alternating activation-inhibition periods (oscillations). This "tremor" was most clearly defined in the tremulous patient; three periods of biceps activity within one supination movement, whereas two periods of activity occurred in the other two patients.

Table 1 *EMG activity during RAM, related to clinical tremor. Numbers of patients.*

	No tremor	Resting tremor	Postural tremor	Both resting and postural tremor
Patients with EMG oscillations (N=26)	8	4*	6	8*
Patients without EMG oscillations (N=5)†	3†	1	0	1

*Includes four patients with unilateral clinical tremor, in whom oscillating biceps EMG activity was observed in both the tremulous and in the non-tremulous side.

†Two of the patients were asymptomatic and one was dyskinetic.

‡In addition there were 5 patients on whom the observations were too variable to allow classification.

SINGLE MOVEMENTS

Examples of results in normal subjects are illustrated in fig 3. It was typical for the normal subjects to build up EMG activity rapidly in response to either visual or kinesthetic signals. There was no action tremor when normal subjects performed single movements.

The parkinsonian patients tended to display a more varied reaction time than the normal subjects. In seven out of 27 patients studied, initiation of supination in response to a visual signal resulted in oscillating biceps EMG activity (fig 4) well before completion of the movement. Of these seven, two

had no clinically evident tremor, one had intermittent low amplitude resting tremor, two intermittent low amplitude postural tremor, and two had clinically evident resting and postural tremor of moderate amplitude (table 2). All these seven patients also exhibited oscillations in RAM. Eight parkinsonian patients did not develop rhythmic activity during the single movement test. Of these, three did not have tremor (two were dyskinetic), four had intermittent low amplitude postural tremor, and one had clinical resting tremor. Observations on the remainder were inconclusive. In the

Table 2 *EMG activity during single movements, related to clinical tremor. Numbers of patients.*

	No tremor	Resting tremor	Postural tremor	Both resting and postural tremor
Patients with EMG oscillations (N=7)	2	1*	2*	2
Patients without EMG oscillations (N=8)‡	3†	1	4	0

*Tremor intermittent and of low amplitude.

†Two of the patients were dyskinetic.

‡In addition there were 6 patients on whom the observations were too variable to allow classification, and 6 patients in whom tremor continued during voluntary movement and prevented discrimination of possible EMG oscillations triggered by movement.

Fig 3 Rasters (bottom records) and averages (top records) of rectified biceps EMG from a series of separate supination movements in a normal volunteer. The subject was asked to make a supination (about 45°) and then turn the handle back into the starting position. EMG activity is aligned with respect both to the signal given to make the movement and to the detection of the end of the movement. Intense and uninterrupted voluntary EMG activity occurred (after a latency determined by individual's reaction time) in response to both the visual (light) and the kinesthetic signal (perturbation). A small peak of reflex activity in response to biceps stretch is seen prior to the voluntary activity (right). There is also a small peak of EMG activity after the end of the voluntary activity, due to the fact that the violent 45° supination was terminated by a physical stop. The rasters illustrate the consistency of the individual responses (each response forms one horizontal line in the raster display).

eight patients without rhythmic activity, oscillations were present during RAM bilaterally in two and unilaterally in four.

Fig 5 compares oscillations during voluntary biceps activity in a moderately parkinsonian patient when the supination was initiated in response to visual (right) or kinesthetic (left) signals. The results were markedly similar: in each case, rhythmic activity began in the biceps muscle after an identical delay and at the same frequency (about 6.3 Hz).

The observations described above were all

obtained from experiments in which the subjects were asked to supinate (or pronate) and to turn the handle back to its original position after completion of the movement. In fig 6, the patient was instructed to keep the arm supinated (or pronated) against a physical stop after completion of the movement. Oscillating biceps activity began prior to the detection of supination, and the 6.5 Hz rhythm continued after the movement had ceased. Pronation movements, which call for biceps inactivity, did not trigger action tremor.

Fig 4 EMG from a series of single supination movements in response to a visual signal (as in fig 3), in a slightly rigid parkinsonian patient with intermittent low amplitude resting tremor. Rasters (bottom) of biceps EMG activity (rectified) in individual trials and their averages (top) are aligned by the moment the visual signal was given ("go light"), and by the detected end of the supination movement ("end of movement"). Oscillating EMG activity occurred prior to the end of movement; this is best illustrated by the averaged response (right) aligned by the detection of the end of movement. The impaired discrimination of rhythmic activity in the left figure results from variations in the reaction time.

Fig 5 EMG from a series of single supination movements (as in fig 3) of a moderately bradykinetic and rigid parkinsonian patient with intermittent low amplitude tremor. The responses are aligned by the instant the signals were given (top) and by the detection of the end of the supination movement (bottom). As previously, averaged and rectified EMG responses are shown above the raster display of individual movements. The reaction time was shorter and more constant with kinesthetic ("perturbation") than with visual ("light") signal. In both, the biceps EMG activity began to decrease 50–60 msec after the beginning of activity, and a second peak of activity occurred before the movement was terminated by the physical stop.

Fig 6 EMG from a series of single supination and pronation movements of a slightly rigid but not bradykinetic patient who had a relatively constant low amplitude postural tremor without any resting tremor. The subject was requested to keep his hand in the supinated position against a physical stop, after the completion of the supination. The EMG activity is aligned by the moment the visual signal was given ("signal light") the detection of the beginning of the movement ("beginning of movement") and the detection of the end of the movement ("end of movement"). Initiation of supination resulted in activation of the biceps muscle, followed by a period of relative quiescence and, subsequently, by another peak of activity. The first response began to decrease after some 60 msec, giving a frequency of oscillation in the region of 6.5 Hz. The oscillation started before any movement could be detected, and continued after the movement was terminated. Pronation movements in response to visual go-signal are also shown aligned by the detection of the end of movement; biceps activity was not triggered by pronation.

Discussion

The pathophysiology of parkinsonism is difficult to study because patients exhibit a broad spectrum of symptoms, the relative severity of which varies not only between different individuals but also within the same patient at different times. Numerous psychological factors, or changes in motor activity, can alter the symptomatology from moment to moment. Well known clinical examples are suppression of resting tremor by will or by voluntary movement, enhancement of tremor by excitement, and increase in the rigidity of a limb by contraction of muscles in the contralateral extremity. In the present series of patients, rhythmic biceps activity was observed in some but not in all subjects, more often during RAM than single supinations. The presence of

resting or postural tremor was not a prerequisite for EMG oscillations to occur during voluntary movements. Oscillations were triggered by motor activation, they were not seen when muscles moved as antagonists.

A triphasic pattern of agonist and antagonist activation has been reported to occur in association with fast step movements.⁸⁻¹¹ This triphasic pattern consists of agonist activation, followed by a period during which the agonist is inactive and antagonists are active and, subsequently, another peak of agonist activity. The initial stage of the triphasic response seems identical to the early EMG oscillations observed in our results with voluntarily activated muscles. In the preprogrammed step movements the antagonists provide a braking force to decelerate the movement⁹ whereas no such

activity was required in our experiments, in which the antagonist was silent throughout (fig 6).

The present analysis was undertaken to determine whether parkinsonian patients trigger tremor when they initiate brief, abrupt voluntary movement, and the results provide evidence that they do. This phenomenon has been seen previously. Hallett *et al*¹¹ studied both smooth and fast elbow flexion (step) movements in parkinsonian patients with and without tremor, using conventional EMG recording techniques. They observed that in fast flexion movements, "a single beat of tremor occasionally occurred before the pattern which moved the limb". Our conclusion is that initiation of rhythmic muscle activity by both voluntary muscle activation and passive kinesthetic disturbances of maintained position,⁵ favours the hypothesis that parkinsonian tremors are due to oscillation of signals within an internal feedback loop between the spinal segments and the motor cortex.

Lance *et al*¹² were among the first to apply modern electrophysiological techniques to the study of parkinsonian action tremor. Their observations led to separation of resting and action tremors as distinct physiological entities because firstly synchronous activation of agonist and antagonist muscles was found during action tremor, while reciprocal inhibition was evident in resting tremor, and secondly a higher frequency spectrum was seen in action tremor without any harmonic relationship to that of resting tremor. Other workers have found that the pattern of EMG activity in parkinsonian tremors is variable; it can be either synchronous or reciprocal in both action and resting tremor.¹³⁻¹⁶ The frequency of action tremor is faster at smaller displacements¹⁷ and it increases as the amplitude falls with augmented strength of voluntary contraction.³ "It would appear that the tremor amplitude is related to effort. . . . and tremor rate is related to contraction power".¹⁴

We suggest, on the basis of observations reported here and observations previously made,⁵ that resting and action tremor in parkinsonism share similar pathophysiological properties. In spite of their clinical dissimilarity both may involve oscillations within internal feedback loop between the motor cortex and the spinal cord. They may possibly, but not necessarily, even employ the same circuits in the central nervous system.

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