Loss of tendon organ inhibition in Parkinson's disease

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Summary

Electrical stimulation via skin electrodes placed over human tendons results in a reflex inhibition of voluntary activity in the stimulated muscle, probably due to activation of Golgi tendon organ afferents. The characteristics of this response in the extensor digitorum communis (EDC) muscles of subjects with Parkinson's disease were compared with those in age-matched controls. The threshold of the inhibitory response was significantly increased in the patient population compared with controls (159±34 V for tremulous patients; 134±10 V for rigid patients, 90±5.5 V for age-matched controls and 70±16 V for all normals). The latency of the inhibitory wave was increased (onset latency was 68.01 ±5.5 ms in patients and 51.5±4.9 ms in controls). The duration of I was also increased in patients (60±20.8 ms) relative to controls (46±11.8 ms). This was associated with slow development of the inhibition with the result that maximal inhibition was delayed by ~20 ms. Other features of the patient response were its oscillatory character whereby the initial inhibitory and excitatory components were followed by further prominent peaks and troughs which gave the appearance of continuing response cycles. Such behaviour was not seen in normal records. Also electrical stimulation of the extensor muscle tendon produced concurrent records in the forearm flexor muscle, which resembled those from the stimulated muscle. This was in contrast to normal records which showed no response in the flexor. The possible contribution of a disorder of tendon organ reflexes to the rigidity and tremor of Parkinson's disease is discussed.

Keywords: Golgi tendon organ; Parkinson's disease; autogenic inhibition; tremor; muscle rigidity

Abbreviations: EDC = extensor digitorum communis muscle; FCR = flexor carpi radialis; FCU = flexor carpi ulnaris; FDP = flexor digitorum profundus; MVC = maximal voluntary contraction

Introduction

Electrical stimulation via skin electrodes placed over human tendons results in an autogenic reflex inhibition of voluntary activity in the stimulated muscle (Burne and Lippold, 1996). The rectified and averaged EMG response to this stimulus consists of two main components. The first, with a latency of onset of ~55 ms (in arm muscles) is an inhibitory phase lasting up to ~120 ms after the stimulus (the I wave). Following this, with a duration of ~60 ms is an excitatory phase (E wave) (Fig. 1A). These response components are seen against a background of weak, continuous voluntary contraction [15% of maximal voluntary contraction (MVC)].

The I component has been attributed to autogenic inhibition following Golgi tendon organ afferent stimulation (Burne and Lippold, 1996). The evidence for this was that the response could be clearly localized to the tendons of the following muscles: EDC, extensor pollicis brevis, extensor pollicis longus, tibialis anterior and abductor digiti minimi. Tendon stimulation produced autogenic inhibition without electrical (M response) or mechanical (muscle twitch) signs of direct muscle stimulation and without evidence of la fibre stimulation (H response). Control experiments showed that the response did not arise from skin afferents; the response was unaffected by anaesthesia of the skin under the electrodes or by the use of a subcutaneous stimulating electrode. Also, the response in hand muscles was not obtained by stimulation of the superficial branch of the radial nerve.

In this paper we describe the changes in the I and E components of the response to EDC muscle tendon
stimulation in patients with mild to moderate parkinsonism. A comparison is made with age-matched normals. In the patient population the response threshold was elevated and the latency of onset and latency of maximal autogenic inhibition were prolonged relative to age-matched controls. The response was completely absent in some patients with tremor. These findings suggest that changes in tendon organ reflexes may contribute to the tremor and rigidity in these patients.

Methods

Subjects

The subjects for this study were 11 patients from the neurological clinic at Westmead Hospital in Sydney; all had a clinical diagnosis of Parkinson's disease, over half of them had a resting tremor and most were on medication. Two subjects were tested on two occasions. The experimental conditions were similar on both occasions. These initial subjects were tested twice to confirm the reproducibility of the results. Thirteen age-matched controls were also investigated. The procedures were fully explained to the subjects beforehand and they gave their consent; they were free to discontinue the experiment at any time without giving a reason. Table 1 summarizes the patient's clinical details. The protocol was approved by the institutional ethics committee.

Electrical recording

The stimulation and recording was carried out as described in Burne and Lippold (1996). The extensor muscle studied was EDC and the flexors were flexor digitorum profundus (FDP), flexor carpi ulnaris (FCU) and flexor carpi radialis (FCR).

Electrical stimulation

Stimuli were constant voltage pulses, 50 μs in duration and up to 350 V in amplitude. Paired pulses of these dimensions were used to elicit responses in some patients. No attempt was made to achieve maximum responses. The protocol consisted of stimulation at five different voltages so that the stimulus/response relationship could be studied in each patient. Thresholds were calculated by extrapolation of this curve to zero. The subjective threshold for sensation in the skin under the electrodes was also determined for each patient.

Background contraction

As in the accompanying paper (Burne and Lippold, 1996), patients were requested to maintain a constant background contraction. This was monitored by a voltmeter that displayed the integrated, smoothed EMG from EDC to the subject.

Table 1 Basic clinical data of the 11 patients

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Duration of symptom (years)</th>
<th>Medication</th>
<th>Tremor (left/right)</th>
<th>Rigidity (left/right)</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>59</td>
<td>F</td>
<td>5</td>
<td>Br+Si</td>
<td>2/0</td>
<td>0/2</td>
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<tr>
<td>2</td>
<td>63</td>
<td>F</td>
<td>3</td>
<td>Br</td>
<td>0/2</td>
<td>0/0</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>M</td>
<td>5</td>
<td>Si</td>
<td>2/1</td>
<td>1/1</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>M</td>
<td>5</td>
<td>Ni</td>
<td>2/2</td>
<td>1/1</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>M</td>
<td>14</td>
<td>Si</td>
<td>0/1</td>
<td>1/2</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>F</td>
<td>7</td>
<td>Ma</td>
<td>2/0</td>
<td>1/0</td>
</tr>
<tr>
<td>7</td>
<td>52</td>
<td>F</td>
<td>6</td>
<td>Ma</td>
<td>0/0</td>
<td>1/3</td>
</tr>
<tr>
<td>8</td>
<td>61</td>
<td>M</td>
<td>4</td>
<td>Si</td>
<td>0/0</td>
<td>1/3</td>
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<td>9</td>
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<td>M</td>
<td>10</td>
<td>Ma</td>
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<td>0/0</td>
</tr>
<tr>
<td>10</td>
<td>51</td>
<td>M</td>
<td>9</td>
<td>Si</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>11</td>
<td>56</td>
<td>M</td>
<td>9</td>
<td>Si</td>
<td>1/0</td>
<td>2/1</td>
</tr>
</tbody>
</table>

Description of subjects in experimental series. Tremor and rigidity are indicated by a five-point scale at clinical examination on the day of testing. Rigidity was determined subjectively as the resistance to passive manipulation of the limb at rest. Si = Sinemet; Br = Bromocriptine; Ma = Madopar.
Measurement of the I and E waves
The amplitude of the I wave was measured as the ratio of the minimum averaged EMG voltage (between 50 and 100 ms after the stimulus) to the mean background EMG level and expressed as percentage inhibition. Latencies were measured to the onset of the I wave and to the minimum average voltage. The difference between these values was a measure of the sharpness of onset. If the inhibition was complete then a plateau resulted, in which case the latency was measured to the beginning of the plateau. The latency and amplitude of the E wave were also measured. However, since the I wave was followed immediately by E, the latency of E may have been influenced by the duration of I.

Statistics
The latency, threshold and amplitude values were pooled and tested for significant differences between the experimental groups, using unpaired, single-tailed t-tests. All the error values shown in the text are standard deviations.

Results
Response to Golgi tendon organ stimulation
Typical responses to tendon stimulation are illustrated in Fig. 1; an averaged response from a normal elderly subject in part A and one from a patient with moderate rigidity and tremor is shown in part B. The significant differences are described below.

Latencies
Three of the 11 patients did not produce Golgi tendon organ responses in EDC, even following paired pulses at voltages up to 350 V. The remaining patients gave a total of 65 responses to Golgi tendon organ afferent stimulation, at raised thresholds. All controls had clearly defined Golgi tendon organ responses. The onset latency of the I component was delayed in patients (68.6±5.5 ms) compared with controls (51.5±4.9 ms). The distribution of latencies is given in Fig. 2. The duration of I was also increased in patients (60±20.8 ms) relative to controls (46±11.8 ms). This was secondary to an increased latency to the peak of I (95±11.3 ms in the patients and 76±7.8 ms in normals). Thus, as well as being delayed in onset, the inhibition reached maximum ~20 ms later in the patients.

In patients, I was followed by a large E1 component and often well-marked E2 and E3 waves. The frequency of waves E2, E3, etc. was that of the tremor when present. However, the E1 latency was always less than the inter-burst tremor period; the E1–E2 period was usually slightly less. These data are summarized in Tables 2 and 3 with statistical confirmation.

Of the 11 patients studied, seven complained of tremor, two had rigidity without tremor and two were more atypical in that they had akinesia without marked tremor or rigidity. It was of interest to know if the amplitudes and latencies of the various components were different in tremorous and non-tremorous groups. Table 3 shows this comparison; there was no significant difference between patients with tremor and those without it in terms of the latency and amplitude of the I wave.

Threshold for eliciting the tendon response
Table 3 shows a comparison of the stimulus threshold voltages for the I wave. It can be seen that there is a highly significant difference in this respect, between parkinsonians and normals (159±34 V for tremulous patients; 134±10 V for rigid patients, 90±5.5 V for age-matched controls; 70±16 V for all normals).

In two of the tremor patients, I responses were absent at all stimulus strengths to 350 V. In these patients, as well as two others, the less affected arm was also tested. In all four cases, the thresholds on the normal side were well below that found on the affected side, but still elevated above control values.

Sensory thresholds were determined too, from subjective detection of the stimulus in the skin. These were not significantly different between groups, even though they were approximately half the voltage required to just elicit an I response in normals.

Events in associated musculature
The rectified averaged response to Golgi tendon organ afferent stimulation was simultaneously recorded in flexor muscles whilst the extensor tendons were stimulated. These muscles were FDP, FCU and FCR.

Simultaneous recordings from extensors and flexors in patients showed, in contrast to those in normal subjects, a
Table 2 Comparison of latency measurements in patients and normals

<table>
<thead>
<tr>
<th></th>
<th>Latency (ms)</th>
<th>SD</th>
<th>n</th>
<th>d.f.</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of the I wave</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>68.6</td>
<td>5.5</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normals</td>
<td>51.5</td>
<td>4.9</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum of the I wave</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>95</td>
<td>11.3</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normals</td>
<td>76</td>
<td>7.8</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak of the E1 wave</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>153</td>
<td>23</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normals</td>
<td>124</td>
<td>11</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients = all Parkinson’s disease patients. Normals = whole group of controls in I wave (first inhibitory component) measurements and matched controls in E1 (first excitatory wave) comparisons.

d.f. = 75; \( t = 13.1 \) \( P < 0.0001 \)

d.f. = 91; \( t = 29.7 \) \( P < 0.0001 \)

d.f. = 20; \( t = 5.0 \) \( P < 0.0005 \)

Table 3 Comparison of latencies, amplitudes and threshold for the I wave in rigid patients, tremulous patients, age matched controls and unselected controls

<table>
<thead>
<tr>
<th></th>
<th>Tremulous patients</th>
<th>Rigid patients</th>
<th>Age-matched controls</th>
<th>All controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency to I(_{\text{max}}) (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>99±2.2</td>
<td>95±2.9</td>
<td>77±1.2</td>
<td>76±1.1</td>
</tr>
<tr>
<td>n</td>
<td>41</td>
<td>15</td>
<td>51</td>
<td>69</td>
</tr>
<tr>
<td>Amplitude of I (mV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>0.16±0.01</td>
<td>0.13±0.02</td>
<td>0.16±0.009</td>
<td>0.16±0.01</td>
</tr>
<tr>
<td>n</td>
<td>40</td>
<td>15</td>
<td>50</td>
<td>69</td>
</tr>
<tr>
<td>Stimulus threshold for I (V)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SE (V)</td>
<td>159±34</td>
<td>134±10</td>
<td>90±5.5</td>
<td>70±16</td>
</tr>
<tr>
<td>n</td>
<td>8</td>
<td>4</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

I\(_{\text{max}}\) is the lowest mean voltage during the I wave. The amplitude of I is the difference between the mean background voltage and I\(_{\text{max}}\).

The presence of a response in the flexor musculature of patients following extensor tendon stimulation was possibly due to a persisting co-contraction in these muscles while the hand was held in posture. Since the flexors of normals were electrically silent in posture, a response was never seen in their muscles. A flexor response could be obtained in normals if background muscle activity was maintained by preferential flexor activation or co-contraction. This response was of a different form to the extensor response though, in that an inhibitory component was not evident and the E component tended to be out of phase with that of the extensor. A single excitatory peak occurred at 150–175 ms after the extensor stimulus.

The similarity of extensor and flexor responses, such as those shown in Fig. 3, might suggest that the latter response arose from volume conduction of the extensor response to the flexor electrodes. However, in our experiments no significant volume conduction to the flexor electrodes occurred since the trace from relaxed normal flexor muscles was always flat following extensor shocks of up to 250 V (0.05 ms).

Oscillatory behaviour of the Golgi tendon organ response

A prominent feature of the response to tendon stimulation in the patient group was its oscillatory character. In normal subjects the oscillations were rapidly damped and returned to noise levels within one or two cycles after the stimulus. The patient responses, in contrast, tended to display a series of prominent peaks following the stimulus (Fig. 3C). This stimulus-induced oscillatory behaviour was seen in all but two of the limbs examined.

The EDC extensor and its antagonist (FCR) both showed this feature and it was present in both the more and less affected limbs. It was not dependent on tremor since most patient records had some oscillatory tendency, including those without a history of tremor as well as those who complained of tremor but had no sign of it during their test.

The Golgi tendon organ stimulus and entrainment of tremor

The appearance of tremor waves (E1, E2, E3, etc.) in the averaged records of tremulous patients indicated that the Golgi...
Golgi tendon organ inhibition and parkinsonism

Fig. 3 Simultaneous records from (A) extensor (EDC) and (B) flexor (FCR) muscles in a patient following extensor tendon stimulation. In contrast to normals, a background discharge often occurred in the flexors of patients during contraction of EDC at 15% of MVC. This apparently enabled the flexor response to be obtained. Note the broad similarity of the two responses. (C) A prominent feature of the response to tendon stimulation in the patient group was its oscillatory character. In normal subjects the oscillations decayed sharply and returned to noise levels within one or two cycles after the stimulus. In the patient responses, prominent and prolonged oscillations were frequently seen. This oscillatory behaviour was not dependent on the presence of tremor at the time of stimulation. It was occasionally present in records from patients without a history of tremor as well as those who complained of tremor but had no sign of it during their test.

tendon organ stimulus was effective in entraining their tremor. Accentuated E1–En waves were seen in all subjects with tremor. In addition, it was observed in subjects with intermittent tremor that the Golgi tendon organ stimulus was effective in initiating a sustained tremor, which could then be seen as a series of action potential bursts in the raw EMG (see Fig. 4 for photographic record). It is noteworthy that these effects occurred in the absence of a muscle twitch or apparent limb movement, which would accompany nerve or muscle stimulation. It should be noted also that the timing and amplitude of the Golgi tendon organ response was altered by the presence of tremor. These effects are described below.

Effect of reinforcement
In subjects with intermittent tremor, it was possible to make tremor appear in a non-trembling limb by various methods of reinforcement. These included waving of the contralateral arm, serial tapping of the fingers of the contralateral hand, reciting of serial sevens and Jendrassi’s manoeuvre.

Fig. 4 Generation of 5 Hz tremor in a patient by Golgi tendon organ stimulation. The four records show nonconsecutive traces from the same patient session. Top trace: raw EMG from EDC; bursts of EMG were synchronous with the extensor movement of the wrist/middle finger joint. Bottom trace: timing of the electrical stimulus to the EDC tendon. In all these records a sustained tremor was initiated by the Golgi tendon organ afferent stimulus. Time bar = 500 ms; voltage bar = 300 μV. The tendon of EDC was stimulated by a 250 V, 50 μs pulse. No bursts of EMG occurred before the stimulus and there was no tremor of the wrist joint. Following the stimulus, the EMG was broken up into bursts occurring at ~200 ms intervals and a 5 Hz tremor was present. Note that the first action potential burst in each of the records, occurred ~175 ms after the stimulus. This approximates the latency of E1 in averaged records.

Reinforcement was associated with significant changes in the I and E responses, concomitant with the onset of tremor. The effect generally lasted for at least 2 min following the reinforcement. The major changes were a decrease in the size of the inhibition (I wave) and a prolongation of the I and E1 latencies. It is worth noting that tremor occurred in the patient illustrated in Fig. 4 only if a reinforcement technique was used.

Discussion
Loss of tendon organ inhibition and the implications for parkinsonian tremor and rigidity
We have found that the threshold of the inhibitory response, obtained in the rectified and averaged EMG following muscle tendon stimulation, is significantly elevated in parkinsonism (>80%). Also, onset and peak latencies were prolonged. Maximal inhibition was delayed by >20% when compared with age-matched normals.

If we assume that electrical stimulation activated the Ib afferents rather than their Golgi tendon organ endings, i.e. that the receptors were not involved, then the abnormality
must then be associated with a loss of Golgi tendon organ afferent fibres or defects in the spinal reflex centre, including its descending control system. The evidence of delayed conduction and raised threshold may be consistent with loss of large diameter (Ib) afferents; however, this is unlikely since Ib H wave and stretch reflex responses are intact in Parkinson’s disease. We are thus left with the possibility of central demodulation of the reflex. Both corticospinal (Lundberg et al., 1962; Illert et al., 1976) and rubrospinal (Hongo et al., 1969, 1972) fibres converge with Ib muscle afferents on spinal interneurons and activation of these pathways produces enhancement of Ib inhibition (see also review by Jami, 1992). As would be expected, decerebration results in depression of Golgi tendon organ reflexes (Eccles and Lundberg, 1959; Holmqvist and Lundberg, 1959; Engberg et al., 1968).

In Parkinson’s disease, activity in the motor cortex is ‘clamped’ down by the basal ganglia and this results in poverty of voluntary movement (akinesia). This could also result in withdrawal of descending facilitation via cortex of Ib interneurons, thus damping the Golgi tendon organ reflex activity. We describe below a possible link between loss of Golgi tendon organ reflexes and the rigidity and tremor of Parkinson’s disease.

The rigidity of Parkinson’s disease is appreciated clinically as increased resistance to passive rotation of a rigid limb. Previous attempts to attribute this to enhanced stretch reflex activity have been unconvincing. Tendon reflexes are not enhanced and the short latency M1 component of the stretch reflex is not increased, though there have been some reports of increased longer latency responses (Lee and Tatton, 1978; Beradelli et al., 1983). Other authors have reported enhanced resistance to sinusoidal muscle stretches in Parkinson’s disease (Teraväinen et al., 1989). The interpretation of changes in stretch reflex responses is complicated by the tendency for a background discharge to persist in flexor and/or extensor muscles at rest. Stretch reflex changes must therefore be interpreted against this abnormal background discharge and may well be secondary to it.

The loss of Golgi tendon organ inhibitory feedback may be expected to disturb both the tonic and dynamic actions of the reflex, thereby contributing to both rigidity and tremor. The tonic actions of the reflex could provide a force-operated servo appropriate to regulation of resting muscle stiffness, i.e. force change per unit length. The importance of a servo system for muscle stiffness regulation has been argued (see Houk, 1979). In this context, Parkinsonian rigidity may be seen as a resetting of the stiffness control servo due to reduced inhibitory feedback from the force transducers, i.e. from the tendon organs, leading to increased resting levels of co-contraction and apparent joint stiffness. The concept of stiffness regulation introduces the need for a parallel rather than a reciprocal input to antagonist muscle groups and therefore the need for a parallel control system. Our observation that Golgi tendon organ afferent stimulation frequently produced very similar responses in extensor and flexor muscles provides quite good evidence that the reflex does possess these connections.

The tremor of parkinsonism could result from a disturbance to the dynamic actions of the Golgi tendon organ reflex. If we propose that Golgi tendon organ inhibition can play an important role in stabilizing the joints by damping natural oscillations at the tremor frequency, the dampening effect will be critically dependent on the timing of the inhibition relative to the resonant or natural oscillatory frequency of the joint. Figure 1 illustrates that the normal Golgi tendon organ wave is phase advanced by at least 20 ms relative to the tremor oscillation seen in patients. It thus acts to damp down joint oscillation at this frequency. With increasing delay of the reflex, as seen in the patients, the damping effects of the Golgi tendon organ reflex will diminish and its own resonant frequency will come to match that of the tremor. The joint will then be underdamped and the Golgi tendon organ reflex could sustain the tremor oscillation rather than reduce it.

**Antagonist muscle action**

As described above, in most patients the responses of antagonist muscles to Golgi tendon organ stimulation appeared very similar in phase and waveform to those in extensors, differing only in amplitude (Fig. 3). The implied parallel connections of the Golgi tendon organ reflex onto antagonist muscle pairs may also be helpful in interpretation of the bursting patterns seen in ongoing tremor. The in-phase action of an oscillating Golgi tendon organ reflex on opposing muscles would be expected to produce synchronous bursts of EMG activity. Such patterns are commonly described in clinical observations of small amplitude parkinsonian tremor as well as in other forms such as essential tremor. The tremor patients studied here were mildly affected by the disease and their tremor was relatively small.

Essential tremor patients may exhibit both synchronous and alternating (180° phase difference) bursting patterns in the two (antagonist) EMGs within a single observation period (Elble, 1986). This alternating form of tremor, which is common in advanced parkinsonism, tends to be associated with large amplitudes, with antagonist muscles no doubt contributing to force generation. Under conditions where a joint oscillation is large enough to drive the reflexes of antagonist muscles, these reflexes may be expected to interact to produce a ‘flip-flop’ oscillation (Burne, 1987) when the outputs from each muscle are 180° out of phase. In one patient in the present study, Golgi tendon organ stimulation did produce such a pattern.

We have observed that Golgi tendon organ stimulation may initiate sustained reflex oscillations in muscles predisposed to parkinsonian tremor, but not initially exhibiting it. These oscillations are associated with periodic EMG bursts that are indistinguishable from tremor in the same patient. This is further evidence that the oscillator which produces the tremor is of reflex origin and cannot lie wholly within the brain.
Conclusion
We report reduction of Golgi tendon organ reflex activity in Parkinson's disease and suggest that it results from reduced supraspinal facilitation. A potential relationship between this and production of rigidity and tremor is described. The work was prompted by the need for a method that would provide early diagnosis of Parkinson's disease. The responses from patients and normal subjects could be differentiated on the basis of onset latency, threshold and form. When combined, these features enabled 100% discrimination between the two populations studied. Further, significant changes were apparent in the asymptomatic limbs of those patients tested. These observations suggest that tendon stimulation could be of value in early diagnosis and as an objective marker of the disease. Longitudinal studies on larger groups of patients would be required to confirm this.

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