Electrical properties of motor units in Parkinsonism and a possible relationship with bradykinesia

H. S. MILNER-BROWN, M. A. FISHER, AND W. J. WEINER

From the Department of Neurological Sciences and Physiology, Rush-Presbyterian St Luke's Medical Center, Chicago, Illinois, USA

SUMMARY The electrical activity of single motor units was recorded from the first dorsal interosseous muscles of nine patients with Parkinson's disease. Six of these patients had a combination of the following abnormal motor unit properties: (1) a variable delay period of 20 seconds to 3 minutes between the initiation of voluntary effort and the recruitment of the first group of motor units; (2) after recruitment, some of the motor units stopped firing for durations of 10s, 40s, 75s . . . 3 min.; (3) some of the motor units fired at abnormally low frequencies of 2–3 per second. All these six patients had slowed finger movement, and five of the six were studied while off levodopa for two to seven days. One of these patients, reinvestigated after levodopa therapy had been restarted, demonstrated improvement in motor unit control. The three remaining patients who were studied while on uninterrupted levodopa therapy could make rapid finger movements, could recruit motor units without delay, and could fire recruited motor units continuously at normal frequencies of 6–14 per second. These results suggest that levodopa therapy is effective in Parkinson's disease at least partly because of its ability to correct abnormalities in the recruitment of motor units. Levodopa also corrects the abnormal motor unit firing pattern. The abnormal motor unit properties found in these patients could account for some aspects of bradykinesia.

The motor unit is the functional unit of the neuromuscular system. The initiation of voluntary activity involves the initial recruitment of relatively small motor units. The continuity of such activity requires the continuous firing of those units already recruited. It would seem reasonable that abnormalities in voluntary motor activity could be manifested as abnormalities in the firing of single motor units. Recent studies have, indeed, supported this view, and have provided considerable information about the electrical properties of motor units in both normal and abnormal states (Milner-Brown *et al.*, 1973a,b,c; Tanji and Kato, 1973a, b; Dietz *et al.*, 1974; Grimby *et al.*, 1974; Grimby and Hannerz, 1974, 1975; Milner-Brown *et al.*, 1974a, b; Freund *et al.*, 1975; Petajan and Jarcho, 1975).

With these considerations in mind, we have investigated the electrical characteristics of single

motor units in nine patients with Parkinsonism. We believe the data contribute to our understanding of the pathophysiology of the bradykinesia seen in this disorder.

Methods

The data were obtained using a TECA (TE4) EMG apparatus, an FM tape recorder (Hewlett Packard, 3964), and a signal discriminator. The DC force was measured with a force transducer (Grass FT.03). The patients were always comfortably seated with their arm resting on a board on top of a bed. The force transducer was virtually isometric, allowing only 1 mm movement. The output from the transducer amplifier (Grass 7P-122) was connected to a calibrated digital multimeter, so that the force exerted on the transducer could be read directly. As some of the patients had to resort to "trick movements", the force measured by the transducer at times included a significant contribution from other hand and even forearm muscles. As a result, the force transducer outputs did not

Address for correspondence and reprint requests: Dr M. A. Fisher, Department of Neurological Sciences, Rush-Presbyterian St Luke's Medical Center, 1753 West Congress Parkway, Chicago, Illinois 60612, USA.

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always measure the absolute force exerted by the first dorsal interosseous muscle, but may only have given an indication of the relative magnitude of the voluntary effort.

A bipolar needle electrode (DISA 13K80) was inserted into the first dorsal interosseous muscle and positioned so that the discharge of single motor units could be distinguished at a moderate level of voluntary contraction. The electrical activity was (1) amplified (input impedance 100 megohms), (2) filtered with a low frequency cut-off of 32 Hz and high frequency cut-off of 3.2 kHz, (3) fed through a delay line and trigger level, (4) fed into a discriminator which gave a pulse when the trigger motor unit discharged, (5) displayed on an oscilloscope, and (6) recorded on the FM tape recorder.

Patients were provided with audiovisual feedback of the electrical signals, and were asked to maintain a continuous discharge of the single motor unit for about two minutes, and to increase the firing frequency of the same motor unit by increasing the force. At each recording session 10–20 motor units (MU) were recorded at different force levels.

The DC force, the MU potentials recorded with the needle, and the discriminator pulses were played back through a photosensitive chart recorder and the firing frequencies computed. Because direct photographs of the traces on photosensitive paper (Kodak Linograph 1895) proved unsatisfactory, all the figures presented in the results were retraced.

Nine patients with Parkinson's disease were investigated. Five of these were off medication (two to seven days) at the time of study. One patient was restudied when medication was resumed. The four other patients were investigated while on uninterrupted levodopa-carbidopa (Sinemet) therapy. All the patients were examined by one of the authors (MF) at the time of the study. The slowness of movement for the thumb and index finger was noted as the rapidity with which the patient could release the grip on the transducer (finger release-FR) and was rated simply as "fast" or "slow".

Results

A brief summary of neurological findings precedes the motor unit data for each of the nine patients investigated.

PATIENTS OFF MEDICATION

Case 1 FM

This man, aged 74 years, had a six year history of gait disorder characterised by rigidity and ab-

normal postural reflexes. Since 1974, he had shown progressive dementia and a CAT scan showed ventricular enlargement and cortical atrophy. Evaluation at the time of electrophysiological study revealed confusion with orientation only to person, frontal lobe release signs, moderate hypomimia, moderate to marked rigidity with cogwheeling at the elbows and knees, simian posture, and festinating gait. The FR was slow. Medication had been discontinued for seven days.

The 11 motor units recorded had the following properties. Six MUs fired at frequencies of 5–8 per second (low normal); three showed multiple pauses (duration 5–9s). Three MUs fired at abnormally low frequencies of 2–3 per second. Two MUs discharged in groups of 3–4 at 4 and 8 per second. No motor units could be recruited at low voluntary effort as determined by the transducer.

In addition, the patient was capable of maintaining a remarkably fixed level of force for 10 min. He could not adjust the level of force when instructed to do so.

These results are consistent with the previous report of Petajan and Jarcho (1975) who noted that "patients with Parkinson's disease are unable to adjust the firing rate of motor units that initiate contraction from zero to higher rates." Dietz *et al.* (1974) have also previously observed low firing rates of 3–5 per second as well as synchronisation of motor units in Parkinsonian tremor.

Case 2 JK

This patient, aged 69 years, had a 26 year history of insulin-dependent diabetes mellitus. Cramps had been prominent in the lower extremities for a year. There was distal sensory loss on examination, and electrodiagnostic findings were consistent with a peripheral neuropathy. In addition, there was a 21 year history of tremor, stiffness, and slowness of movement. Bilateral cryosurgery of the ventrolateral nucleus (right 1961, left 1962) had been performed. Examination showed resting tremor, moderate hypomimia, mild rigidity, and moderate to marked slowness of movement. The FR was slow. Medication was trihexyphenidyl (2 mg three times daily) and diphenhydramine (50 mg four hourly). Levodopa-carbidopa and amantadine had been discontinued two days earlier.

Of the eight motor units recorded, seven fired at 5–8 per second and one at 2 per second. Six of the MUs discharged in groups of 3–5 at 4–8 per second (synchronisation). This was in the same frequency range as the accelerometer tremor recordings (5–7 Hz). Figure 1 demonstrates this synchronisation of motor units at 6 per second. The patient could initiate, control, and sustain the firing

Fig. 1 Case 2. Synchronisation of motor units (3–6 MU at 6 per second), while patient maintained a force level of 300 g (top) and 600 g (bottom). Patient showed visible tremor at 5–7 per second (accelerometer recording).

of all motor units recorded; there were no motor unit pauses.

Case 3 SS

This man, aged 75 years, had had gait difficulties and slowness of movement for two years. Neurological examination revealed moderate hypomimia, mild cogwheel rigidity at the elbows, and a festinating gait. The FR was slow. He had been off medication for six days.

The 10 motor units recorded from the first dorsal interosseous muscle fired at a normal frequency of 6–16 per second. Two MUs had multiple pauses (duration 4 s, 7 s, 25 s, 60 s, 75 s), even when the patient made an effort to maintain the force (Fig. 2). The patient had difficulty recruiting and

sustaining the firing of motor units at low force levels and, therefore, MUs were recorded at medium (500 g) and high force (1 kg) levels. Since motor units are recruited in an orderly pattern from small to large, this result would explain in part the delay in initiating movements (see Discussion).

Case 4 SF

This 61 year old patient had an 11 year history of tremor starting in the left upper extremity with subsequent slowness of movement. Dyskinesias and hallucinations were observed while on chronic levodopa-carbidopa combination. Examination revealed moderate bradykinesia—mild to moderate rigidity with cogwheeling at the knees, elbows, and

Fig. 2 Case 3. Firing patterns of a single motor unit recruited at 200 g. The motor unit fired at 7–11 per second, with multiple pauses lasting 5 s, 6 s, 7 s, 25 s, and 75 s; the figure shows a 25 s pause followed by a resumption of motor unit firing at 11 per second. In all figures, the top trace is the trigger pulse given by the discriminator when the MU being investigated fires; the second trace is the MU impulse recorded by the needle electrode, and the third is the force output from the calibrated transducer.

wrists, a stooped gait, and prominent resting tremor, left more than right. The FR was slow: he had been off medication for four days.

There was a delay of 30s to 2 min in the recruitment of motor units. Three to five MUs fired in groups at 4–6 per second (synchronisation). This was comparable to the accelerometer recorded tremor frequency of 5–6 Hz.

PATIENT OFF/ON MEDICATION

Case 5 RK

This 36 year old patient, had a 10 year history which began with a resting tremor of the right hand followed by increasing stiffness, bradykinesia, and a festinating gait. Examination off medication for five days revealed slow, limited movements with marked rigidity in all extremities and a slow FR. After levodopa-carbidopa (10/100 six a day) was reinstituted, muscle tone was normal, but prominent choreiform movements were present in all extremities. The FR was now fast.

This patient was investigated on two occasions. The first was five days after being off levodopa, and the second one week after resuming levodopa therapy.

In the first investigation, there was a variable delay period (20s to 3 min) between the initiation of voluntary effort and the recruitment of MUs (Fig. 3). Seventeen of the 20 MUs recorded had multiple pauses. These pauses ranged from 6s, up to 2 min. The motor unit firing frequencies of 6–12 per second were normal.

Fig. 3 Case 5 (off medication for seven days). "Delay" in motor unit recruitment. In this recording an effort was made to record a small motor unit at low threshold force. The patient was asked to exert a weak force; there was a 2 min delay between the initiation of voluntary effort and the recruitment of the motor unit (MU 8). Figure shows only a portion of the delay and firing period of the motor unit.

The second investigation was done two hours after taking levodopa-carbidopa when the patient was experiencing dyskinetic movements. Twelve of the 16 motor units recorded fired in a normal continuous pattern at 5–13 per second. However, the remaining four had multiple pauses of 15–25 s, 10 s, 20–25 s, and 30–80 s. This improvement in motor unit control after levodopa therapy was also observed by Petajan and Jarcho (1975).

PATIENTS ON MEDICATION

Case 6 TT

This patient, aged 64 years, had a 10 year history which began with resting tremor in the right upper extremity and progressed to bilateral tremor, stiffness, and slowness. Examination revealed mild hypomimia, moderate rigidity in all extremities with cogwheeling at the elbows and wrists, resting tremor most prominent in the right upper extremity, and simian posture and festinating gait. The FR was slow. Medication was levodopa-carbidopa (25/250 three times daily), amantadine (100 mg three times daily) Trihexyphenidyl (5 mg twice daily).

Six single motor units were recorded from the first dorsal interosseous muscle. Three of the MUs recruited at threshold tension levels of 500 g, 600 g, and 800 g fired continuously at frequencies of 8, 10, and 5–9 per second respectively. The three other MUs showed the following abnormal properties: MU 1 was recruited at a threshold force level of 200 g. The unit fired continuously at 8 per second for 26 s then stopped firing, even when the patient tried to maintain the force level at 200 g. The duration of non-firing was 40 s, after which a new motor unit was recruited at a different force level; MU 7 was recruited at a threshold force of 550 g, fired at a rate of 5 per second for 22 s, then stopped firing for 100s, after which a new motor unit was recruited; MU 9 recruited at a threshold force of 700 g with a firing frequency of 7 per second. This motor unit fired continuously for a maximum duration of only 25 s; between the brief periods of firing there were six pauses of 13s, 16 s, 40 s, 16 s, 25 s, and 70 s (Fig. 4).

Fig. 4 Case 6. MU 9 recruited at about 700–800 g. This motor unit fired intermittently at 7 per second, with six pauses of 13 s, 16 s, 40 s, 25 s, 16 s, and 70 s. The Figure shows two motor unit pauses of 16 s and 70 s durations. Only 5 s of the 70 s pause is shown.

Case 7 AD

A 59 year old patient had an eight year history of rigidity, gait disorder, slowness of movement, and mild resting tremor. Examination revealed mild to moderate hypomimia, resting tremor, and rigidity, a simian posture and a festinating gait.

Case 8 JJ

This man, aged 61 years, had a 17 year history which began with difficulty in fine movements of the left hand. Right cryothalamotomy was performed in July 1965. Since then he has experienced slowly progressive "rigidity", and difficulty with gait. At the time of the examination there was moderate hypomimia but no rigidity, bradykinesia, or gait abnormality. The FR was fast. Medication was bromocriptine (45 mg four times daily), and levodopa-carbidopa (25/250; 2 four times daily).

Patients 7 and 8 were investigated two to three hours after medication. Motor units could be recruited without delay. Recruited MUs fired continuously at normal frequencies of 6–14 per second.

Case 9 MS

This patient, aged 77 years, had an eight year history of gait difficulty and slowness of movement. Examination showed moderate hypomimia and rigidity as well as a festinating gait. The FR was fast. Medication was levodopa-carbidopa (25/250; $\frac{1}{2}$ tablet thrice daily), amantadine (100 gm four times daily), and trihexyphenidyl (2 mg four times daily).

The patient was investigated two hours after medication. He had no problem starting or stopping voluntary contraction in the first dorsal interosseous muscle. All of the 12 motor units recorded fired continuously in a normal frequency of 8–14 per second. Figure 5 is a typical MU recording from this patient.

Discussion

The electrical properties of motor units have been recorded from the first dorsal interosseous muscle in a series of patients with Parkinson's disease. We believe that the results amplify our understanding of the pathophysiology of bradykinesia, in particular that aspect which involves the delay in the initiation of voluntary activity and the pro-

longation of the transit time in the execution of movement.

The six patients investigated who showed slowness of the relevant finger movement had a combination of the following abnormal motor unit properties: (1) there was difficulty in the recruitment of motor units at low threshold force levels, and as a result there was usually a variable delay period of 20 s to 3 min between the initiation of voluntary effort and the recruitment of the first few motor units; (2) after recruitment some of the motor units stopped firing (motor unit pauses of 10 s, 40 s, 75 s, 3 min). These pauses occurred while the patients made an effort to maintain voluntary force; (3) some of the motor units fired at abnormally low frequencies of 2–3 per second.

Five of these six patients were off levodopa for two to seven days. The one patient studied after resumption of levodopa therapy showed definite improvement in his motor unit control associated with a decrease in bradykinesia.

The three patients on uninterrupted levodopa therapy had very little slowness of finger movement. The majority of their motor units could be recruited without delay. After recruitment these motor units fired in a normal continuous pattern at normal frequencies.

The biochemical lesion in Parkinson's disease is primarily a striatal dopamine deficiency secondary to degeneration of the nigrostriatal pathway. Levodopa or levodopa-carbidopa therapy has become the most efficacious treatment for relief of symptoms of Parkinsonism including bradykinesia (Cotzias *et al.*, 1967; Klawans and Garvin, 1969; Markham *et al.*, 1974; Sweet and McDowell, 1975; Weiner and Bergen, 1977). It is, therefore, of interest that three of the four patients examined while on uninterrupted levodopa therapy could recruit motor units without delay and could modulate the firing of these motor units. The one patient studied both on and off therapy demonstrated normalisation of motor unit firing after levodopa was restarted.

There is physiological evidence that both the striatum and the ventral lateral (VL) nucleus of the thalamus are involved in the initiation and modulation of voluntary movement (Evarts, 1971; Hongell *et al.*, 1973; DeLong, 1973, 1974). The VL nucleus projects to the motor cortex. Direct con-

Fig. 5 Case 9. Normal continuous firing of motor units at 12 per second. Patient had no problem initiating or terminating voluntary contraction in the first dorsal interosseous muscle. All of the 12 motor units recorded had a similar firing pattern.

trol of spinal motoneurons by the motor cortex via the pyramidal tract has been established (Lawrence and Kuypers, 1968; Phillips, 1969; Clough *et al.*, 1971; Kuypers, 1973). Recently, the motor cortex of awake patients undergoing neurosurgery for various neurological disorders (epilepsy, gliomas) was stimulated electrically (Milner-Brown *et al.*, 1975). The parameters of the electrical stimulus were chosen to excite as selectively as possible the direct cortico-motoneuronal projection (Phillips and Porter, 1962, 1964; Phillips, 1969). Results of these studies demonstrated that the latency (20–25 ms) of the motor units recorded from thenar muscles after cortical stimulation, was suggestive of monosynaptic excitation of the spinal motoneurons. Using the amplitude of the surface EMG to gauge the size of the motor units that were first recruited after cortical stimulation it was determined that these units were comparable to the motor units first recruited during voluntary contraction (Milner-Brown *et al.*, 1973,a,b,c; Milner-Brown and Stein, 1975). Increasing cortical stimulus currents recruited motor units with large surface EMG amplitudes in an orderly pattern comparable to that observed during increasing voluntary contraction (Milner-Brown and Brown, unpublished). These results suggest that the direct corticomotoneuronal projection of the pyramidal system is involved in the recruitment of the first group of motor units during voluntary activity.

Based on the above evidence, we postulate that the recruitment of the first motor units during the initiation of voluntary activity involves the transmission of impulses through the nigrostriatal pathway, the ventrolateral thalamus, the motor cortex, and down through the direct cortico-motoneuronal projection of the pyramidal system to the spinal motoneurons. After the first motor units have been recruited, the continuation of a voluntary activity, such as squeezing an object or flexing a muscle, requires the continuous firing of motor units, the recruitment of increasing number of motor units, and the ability to increase the firing frequencies of motor units already recruited. However, if the majority of motor units are recruited with a delay, fire sometimes at abnormally low frequencies and with multiple pauses, these abnormalities together could account for some aspects of the abnormal motor behaviour observed in the bradykinesia of Parkinsonism.

Since lesions of the substantia nigra (Parkinson's disease) result in prolonged delays in the initiation of voluntary activity (bradykinesia) and in the motor unit recruitment abnormalities described above, one may speculate that the nigrostriatal

system may be a dominant neuronal system in the initiation of voluntary motor activity.

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