

New method for the estimation of the number of motor units in a muscle

2. Duchenne, limb-girdle and facioscapulohumeral, and myotonic muscular dystrophies

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SYNOPSIS The results of the application of a computerized method for the estimation of motor unit numbers in the human extensor digitorum brevis are presented. In patients with Duchenne and limb-girdle and facioscapulohumeral muscular dystrophies, motor unit numbers are within the normal range, but are significantly reduced in myotonic muscular dystrophy.

The concept of the muscular dystrophies as primary degenerative diseases of muscle has been increasingly challenged in recent years (Fenichel *et al.*, 1967; Gardner-Medwin *et al.*, 1967; Munsat *et al.*, 1972; Gallup and Dubowitz, 1973). Considerable support for the neurogenic hypothesis in muscular dystrophy has come from the results obtained using an electrophysiological technique for the estimation of the number of motor units in the human extensor digitorum brevis (EDB) muscle (McComas *et al.*, 1971b). Using this method a significant reduction in motor unit numbers has been claimed in Duchenne type (McComas *et al.*, 1971c), limb-girdle and facioscapulohumeral (Sica and McComas, 1971), and myotonic muscular dystrophy (McComas *et al.*, 1971a). We have recently presented a critique of the technique used by these authors and have proposed that the results so derived may be erroneously low in diseases where qualitative alteration in the configuration of motor unit potentials occurs, as, for example, in the myopathies (Ballantyne and Hansen, 1974). We have also described a computerized method for this estimation which has theoretical advantages over the earlier technique of McComas *et al.* (1971b). The usefulness of this method has been demonstrated in practice in a

group of patients with myasthenia gravis (Ballantyne and Hansen, 1974). The purpose of this paper is to present the results obtained by the application of this new method to patients with Duchenne type, limb-girdle and facioscapulohumeral, and myotonic muscular dystrophies.

METHODS

All values are expressed as mean \pm one standard deviation (SD). Mean values were compared using Student's *t* test.

SUBJECTS 1. *Controls* Fifty-one subjects, members and relatives of the staff of the Institute of Neurological Sciences were investigated. None had evidence of neurological disease. Fourteen of these subjects (age matched) were used as controls for the Duchenne dystrophy study, while the other 37 normal subjects formed a control group for the limb-girdle, facioscapulohumeral, and myotonic dystrophies.

2. *Duchenne type muscular dystrophy* Twelve boys aged 10 ± 2.9 years were studied. In all cases the primary diagnosis had been made previously on the basis of clinical history, family history, clinical examination, serum creatinine kinase, and muscle

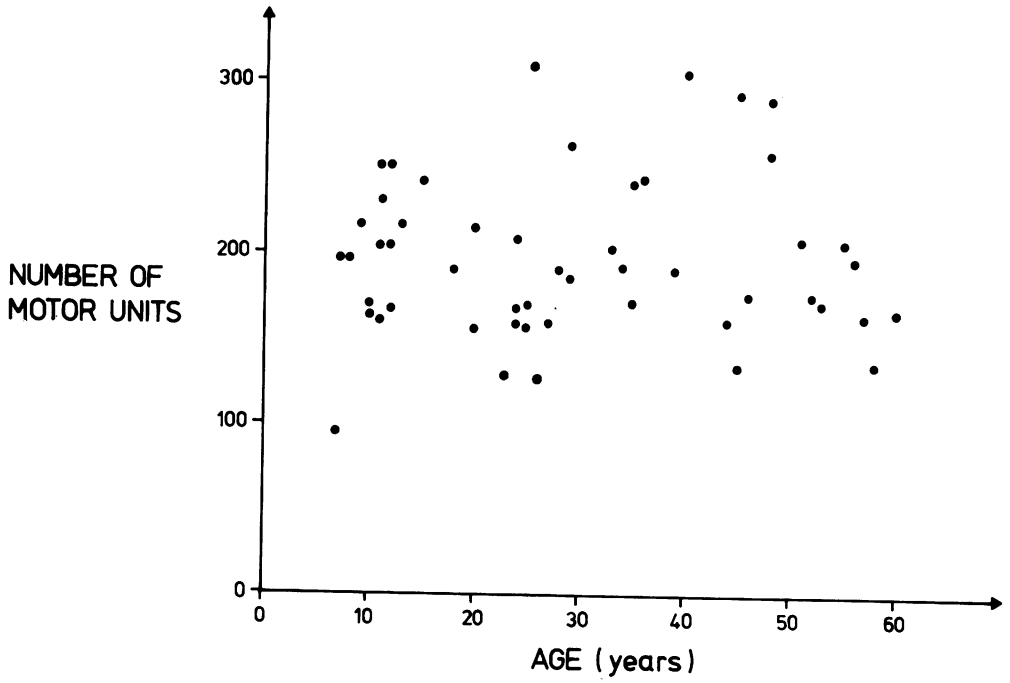


FIG. 1. *Motor unit numbers in EDB muscles: normal subjects.*

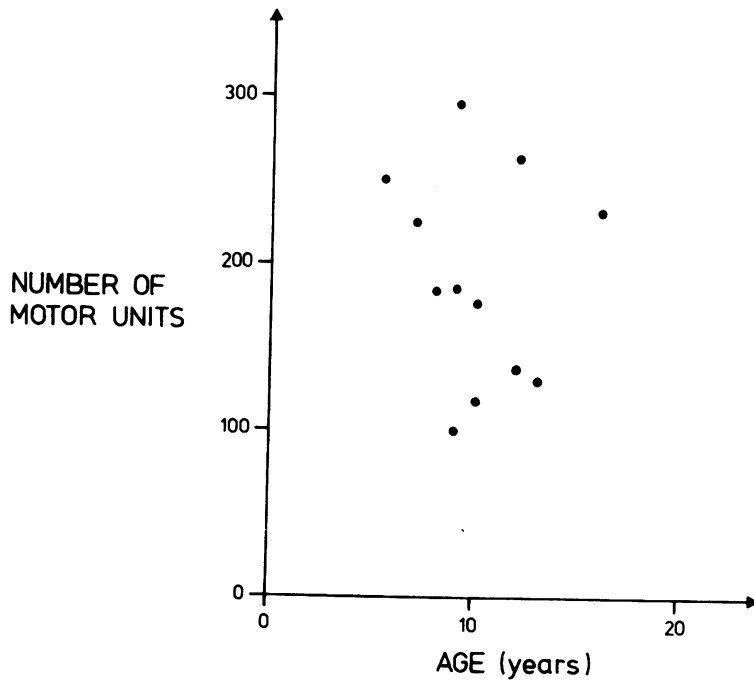


FIG. 2. *Motor unit numbers in EDB muscles: patients with Duchenne muscular dystrophy.*

biopsy. In four patients these investigations were supplemented by electromyography.

3. Limb-girdle and facioscapulohumeral muscular dystrophies Twelve patients aged 37 ± 17.4 years were studied of whom three had facioscapulohumeral muscular dystrophy. The mean duration of symptoms was 14 ± 8.2 years. The diagnosis was reached on the basis of clinical examination, muscle biopsy (seven patients), and electromyography (EMG) (12 patients). Serum enzyme studies, performed on all patients, were normal to slightly elevated. Only those patients in whom the EMG appearances were considered myopathic were included in the study.

4. Myotonic muscular dystrophy Twelve patients aged 45 ± 14.0 years were studied. The duration of the symptoms was 16 ± 12.2 years. In all patients the clinical and electromyographic features were characteristic of myotonic muscular dystrophy. In only one patient was a muscle biopsy performed and this was reported to show myopathic changes.

TECHNIQUES The placement and composition of the surface electrodes for stimulation and recording and the properties of the amplification and display systems have been previously described (McComas *et al.*, 1971b; Ballantyne and Hansen, 1974). For details of the computer handling of data for the identification of motor unit potentials and the estimation of motor unit numbers in the EDB muscle see Ballantyne and Hansen (1974).

ELECTROMYOGRAPHY Concentric bipolar needle electrodes (Medelec Ltd) were used to sample the extensor digitorum brevis (EDB), the tibialis anterior, the first dorsal interosseous, the biceps and deltoid muscles. The density of the interference pattern and the presence or absence of spontaneous activity at rest were assessed subjectively. Individual motor unit action potentials at minimal voluntary effort were evaluated in terms of duration, amplitude, and number of phases. The electromyographic appearances were interpreted by one of us (J.P.B.) as neurogenic or myopathic. In all patients and controls motor conduction velocities and distal motor latencies were measured. The values obtained will be presented in a further communication.

RESULTS

1. CONTROLS (Tables 1 and 2, Fig. 1) There was no significant change in motor unit numbers with age. Nor was there a significant difference in

TABLE 1

MEAN AGES AND MOTOR UNIT NUMBERS IN EDB MUSCLES: CONTROL SUBJECTS AND PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

	Number in group	Mean	SD	P
Age (yr)				
Controls	14	10.7	2.2	—
Duchenne dystrophy	12	10.0	2.9	NS
Motor unit numbers				
Controls	14	199	42	—
Duchenne dystrophy	12	191	62	NS

motor unit counts between the young control subjects (for the Duchenne muscular dystrophy) and the older control group. The control values were not influenced by the sex of the subject or whether the left or the right EDB muscle was studied.

2. DUCHENNE MUSCULAR DYSTROPHY In this group of patients motor unit numbers are within the range of control values (Table 1, Fig. 2). There is no relationship between the age of the patient and number of units counted.

3. LIMB-GIRDLE AND FACIOSCAPULOHUMERAL DYSTROPHIES Unit numbers in this group of patients were also within the normal range (Table 2, Fig.

TABLE 2

MEAN AGES AND MOTOR UNIT NUMBERS IN EDB MUSCLES: CONTROL SUBJECTS AND PATIENTS WITH LIMB-GIRDLE (LG), FACIOSCAPULOHUMERAL (FSH) AND MYOTONIC MUSCULAR DYSTROPHIES*

	Number in group	Mean	SD	P
Age (yr)				
Controls	37	35	14.2	—
LG and FSH dystrophy	12	37	17.4	—
Myotonic dystrophy	12	45	14.0	—
Duration (yr)				
LG and FSH dystrophy	12	14	8.2	—
Myotonic dystrophy	12	17	12.2	—
Motor unit numbers				
Controls	37	197	49	—
LG and FSH dystrophy	12	228	56	NS
Myotonic dystrophy	12	80	46	< 0.001

* The mean duration of symptoms is also given.

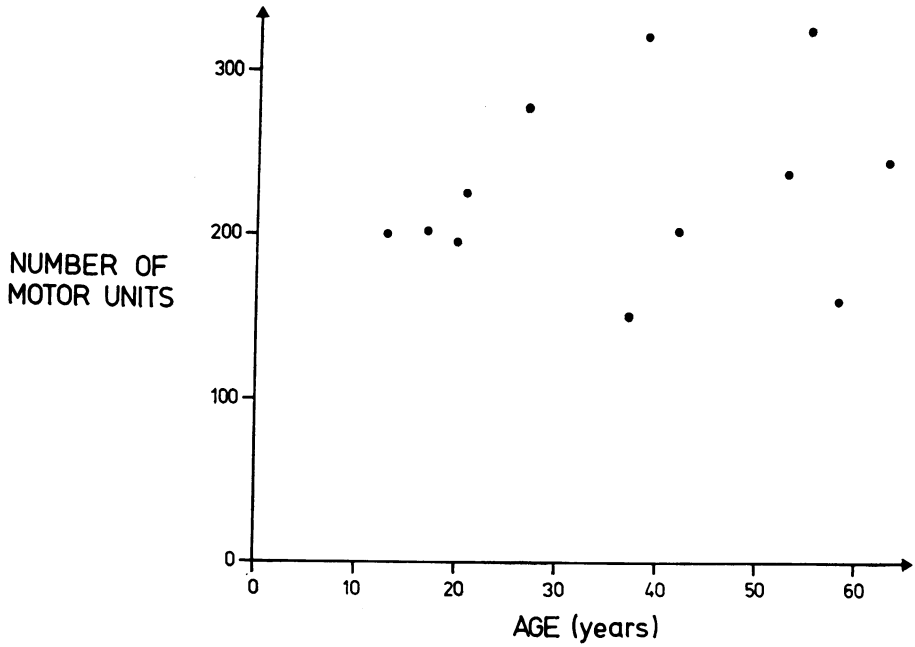


FIG. 3. Motor unit numbers in EDB muscles: patients with limb-girdle and facioscapulo-humeral muscular dystrophy.

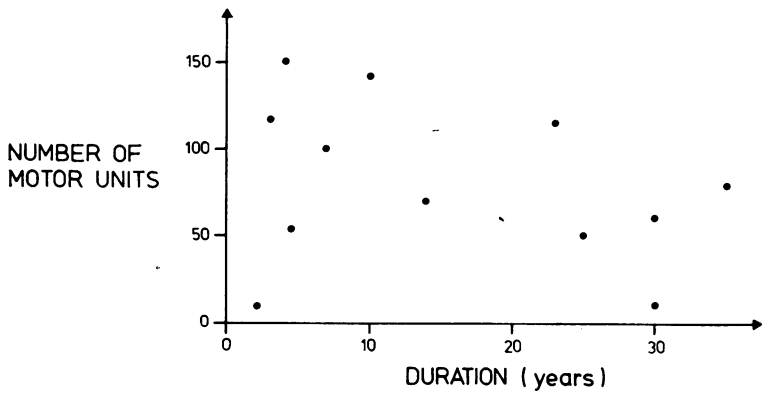
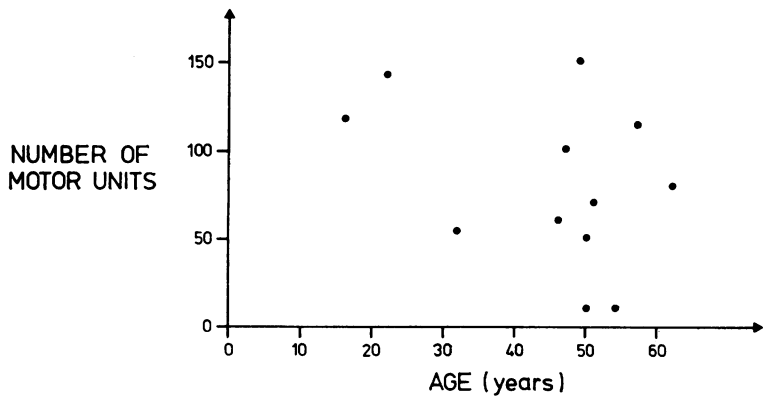


FIG. 4. Motor unit numbers in EDB muscles: patients with myotonic dystrophy; plotted against age (upper graph) and duration of symptoms (lower graph).

3). There was no significant difference from the control group. There was no correlation between the number of units counted and the duration of the symptoms or the age of the patient.

4. MYOTONIC MUSCULAR DYSTROPHY In this group of patients there was a significant reduction in the number of motor units in the EDB muscle (Table 2, Fig. 4). There was no significant correlation between unit numbers and the clinical duration of symptoms or the age of the patient.

DISCUSSION

In our group of control subjects we have found that the number of motor units in the EDB muscle did not change with age between 5 and 65 years. The results were uninfluenced in either the control or, where appropriate, the dystrophic patients by sex or whether the right or left EDB muscle was studied. Duchenne muscular dystrophy has emerged in recent years relatively intact as the classical example of a primary degenerative myopathy. Evidence from electromyography (Kugelberg, 1947; Buchthal *et al.*, 1960; Lenman and Ritchie, 1970), histopathology (Adams, 1969), and serum enzymes (Pennington, 1969) has consistently supported the myopathic nature of the condition. Electrophysiological evidence for a neurogenic influence in the aetiology of Duchenne muscular dystrophy has come from the claim by McComas *et al.* (1971c) that there is a reduction in the number of motor units in the EDB muscle in these patients. Their method has not been accepted without reservations (Engel and Warmolts, 1973; Scarpalezos and Panayiotopoulos, 1973a, b) and we have presented a critique of the method which indicates that erroneously low values would be obtained when motor unit potential configurations are qualitatively altered from normal (Ballantyne and Hansen, 1974). The normal values for motor unit numbers which we have obtained in this group of patients using the computerized method of estimation confirms the theoretical objections to the amplitude method of McComas *et al.* (1971b). Certainly reports in the literature from other disciplines would support our present observations. Pearson (1963) reported that the population of anterior horn cells and peripheral axons is preserved in human

muscular dystrophies and Jerusalem *et al.* (1974) were unable to detect morphological changes in the motor endplates or intramuscular nerve fibres in patients with Duchenne muscular dystrophy. In murine muscular dystrophy also, anterior horn cells are present in normal numbers (Papapetropoulos and Bradley, 1972). The development of a full interference pattern on electromyography during voluntary effort in these patients is interpreted as due to the activity of a full complement of motor units albeit of reduced dimensions (Richardson and Barwick, 1969). The association between mental deficiency and Duchenne muscular dystrophy (Dubowitz, 1965; Rosman and Kakulas, 1966; Kayser-Gatchalian, 1973) may indicate a genetic cross linkage but is not of itself evidence of a neurogenic influence in this condition. Our results do not necessarily invalidate the neurogenic hypothesis but if a neuropathic influence is present it does not progress to the stage where motor units are lost.

In contrast with the Duchenne type the clinical syndromes of limb-girdle and facioscapulohumeral dystrophies conceal a variable histopathology and neurophysiology. Gardner-Medwin *et al.* (1967) found that 15 patients whose clinical appearance suggested muscular dystrophy were examples of benign spinal-muscular atrophy. Hudgson (1973) reports that these cases had been diagnosed clinically as limb-girdle dystrophy. Neurogenic changes in biopsy material have been reported in two patients with clinical features of facioscapulohumeral dystrophy (Fenichel *et al.*, 1967), while Munsat *et al.* (1972) found that four such patients had biopsy appearances characteristic of polymyositis. The electromyographic findings in these patients are of interest. None of the cases reported by Gardner-Medwin *et al.* (1967) had EMG signs of myopathy, while two of the four cases investigated by Munsat *et al.* (1972) had the electromyographic features of polymyositis, one was normal and another showed no diagnostic abnormality. Fenichel *et al.* (1967) did not observe a myopathic EMG pattern in their cases. It appears therefore that the non-dystrophic forms of the limb-girdle and facioscapulohumeral syndromes can be identified on EMG examination. In our group of patients the diagnosis was based on clinical, EMG, and, in

in many cases, biopsy appearances. No patient was included in the series who did not have a 'myopathic' EMG. It is probable that our patients are a more homogeneous pathological group than those we have cited from the literature. In none of our patients was a diagnosis of spinal muscular atrophy or polymyositis seriously entertained. On the other hand, our series is comparable with that of Sica and McComas (1971). In only one of their 11 patients, in the EDB muscle, did they find EMG signs of a neurogenic type but all patients had a myopathic pattern on examination of the vastus lateralis. All of the muscle biopsies from their patients were reported to show myopathic changes. Our patients do differ from their series as the mean age of our group is lower and the average duration of symptoms is shorter. This is unlikely to be of significance as we found no evidence that numbers of units were related to the duration of symptoms. The normal motor unit counts we have obtained in this condition again support the theoretical objections to McComas's method (Ballantyne and Hansen, 1974). In the light of our results we propose that there is an identifiable pathological entity within the clinically diagnosed group of limb-girdle and facioscapulohumeral dystrophies which is distinct from polymyositis and the spinal muscular atrophies and in which motor unit numbers in the EDB muscle are within the normal range.

A different picture emerges in the patients with myotonic dystrophy. There is a significant reduction in the number of motor units in the EDB muscle in these patients and our results are, in general, comparable with those reported by McComas *et al.* (1971a). That this is unlikely to be related to traumatic denervation in the anterior tibial nerve at the ankle in a disabled patient is supported by the normal unit counts obtained in patients with Duchenne dystrophy who were generally more disabled, often with inversion deformities of the ankles. There is convincing evidence in the literature implicating a neurogenic process in myotonic dystrophy. Electromyography frequently demonstrates spontaneous activity resembling fibrillation (Lenman and Ritchie, 1970). Abnormalities of the intramuscular nerve endings have been reported (MacDermot, 1961; Allen *et al.*, 1969). The predominant type 1 muscle atrophy in this condition

(Engel and Warmolts, 1973) supports a neurogenic influence. Frank denervation atrophy in moderately to severely affected patients was noted by Engel and Brooke (1966). Kito *et al.* (1973) found demyelination and loss of axons in sural nerve biopsies. The occurrence of mental retardation in myotonic muscular dystrophy is well known (Walton and Gardner-Medwin, 1969) but is no more significant in this context than the similar observation in Duchenne dystrophy. However, Rosman and Rebeiz (1967) found a correlation between the degree of the mental deficiency, the extent of cerebral dysgenesis and the severity of the histopathological changes in skeletal muscle. Lastly, we have found that the motor nerve conduction velocities are significantly slowed and distal motor latencies prolonged in the lateral popliteal nerve in patients with myotonic muscular dystrophy. These observations will be discussed in a later paper. The reduction in motor unit numbers in the EDB muscle in these patients is therefore not unexpected, confirms earlier reports (McComas *et al.*, 1971a), and provides further evidence for a neurogenic aetiology in this disease.

In two of the three groups of patients with muscular dystrophy investigated in this study we have been unable to confirm the original observations of McComas *et al.* (1971c) and Sica and McComas (1971). We have found no evidence of a loss of motor units in the EDB muscle of patients with Duchenne muscular dystrophy or the limb-girdle and facioscapulohumeral varieties but have found a significant reduction in those patients with myotonic muscular dystrophy. It has not been our aim in this paper to discuss in detail the merits of the case for the neurogenic hypothesis in the muscular dystrophies. We will, however, present further observations on the pathophysiology of these diseases from conduction velocity studies and from the analysis of individual evoked motor unit potentials obtained by an extension of the technique used in this investigation.

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