

# Pattern of recruiting human motor units in neuropathies and motor neurone disease

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**SYNOPSIS** The pattern of recruiting human motor units in the first dorsal interosseous muscle of the hand has been studied in 31 patients with ulnar neuropathies and motor neurone disease. Two years after surgical repair of an unilateral complete severance of the ulnar nerve, the twitch tensions increased to normal size. However, the normal orderly pattern of recruiting motor units of increasing size during increasing voluntary contractions was irretrievably lost. Among patients with pressure or entrapment neuropathies, the normal orderly pattern of recruiting motor units was always retained. Similarly, in patients with motor neurone disease (amyotrophic lateral sclerosis), the orderly pattern of recruitment was not disrupted.

After injury to the ulnar nerve there are a number of well-recognized histological and electrophysiological changes. If the nerve is completely severed, some reinnervation of the intrinsic muscles of the hand may occur without surgical intervention, particularly if the lesion is fairly distal along the course of the nerve. However, in most cases the nerve is explored surgically and the cut ends are rejoined by various suturing techniques. The regeneration of a peripheral nerve after repair results in the formation of an excess number of regenerating fibres formed by branching (Ramón y Cajal, 1928; Edds, 1953). These excess fibres may fail to make peripheral connections: motor branches that fail to reinnervate muscle fibres will atrophy and eventually disappear, whereas those that make peripheral connections will increase in size (Sanders and Young, 1946; Weiss and Edds, 1946; Aitken *et al.*, 1947). In addition, some motor fibres become connected with muscle fibres they did not formerly innervate (Esslen, 1960) and hence give rise to new motor units that are functionally as well as morphologically different from the motor units before injury.

We have recently developed a technique for

measuring the contractile properties of single motor units during isometric voluntary contractions while simultaneously recording the electrical activity using surface and needle electrodes (Stein *et al.*, 1972; Milner-Brown *et al.*, 1973a). Using this method, we made a detailed electrophysiological study of (a) five patients with a previous complete unilateral severance of the ulnar nerve; (b) 18 patients with pressure or entrapment neuropathies affecting the ulnar nerve; and (c) eight patients with motor neurone disease (amyotrophic lateral sclerosis). This paper deals mainly with the twitch tensions of the motor units in group (a) and the pattern of recruitment of motor units in all three groups. These three groups are interesting in that there is a loss of physical continuity of all motor fibres in group (a), while in groups (b) and (c) motor fibres are differentially affected, but a physically continuous pathway to the muscle is retained. The following paper deals with the contractile and electrical properties of motor units in groups (b) and (c).

## METHODS

The following contractile and electrical parameters of single motor units were systematically measured from the first dorsal interosseous muscle of both hands

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of all patients (the normal hands served as controls when the lesion was unilateral): (1) the 'threshold' level of voluntary force for recruiting a motor unit; (2) twitch tension; (3) contraction time; (4) half-relaxation time; (5) the peak-to-peak amplitude of the surface electromyogram (EMG); (6) the peak-to-peak duration of the surface EMG; and (7) the rectified and unrectified surface EMGs for synchronization studies. The methods used here have been previously described in detail (Milner-Brown *et al.*, 1973a), and so a less detailed description will be given below. The first two parameters will be introduced in this paper, and the other parameters considered in the following paper.

**EMG RECORDING** A bipolar needle electrode was inserted into the muscle and positioned so that the discharge of single motor units could be distinguished at a moderate level of voluntary contraction. The electrode consisted of two fine ( $75\ \mu\text{m}$ ) wires for differential recording fixed with epoxy in the barrel of a needle. Patients were provided with both visual and auditory feedback. The voluntary force was varied to recruit new motor units, but after recording all the motor units that could be distinguished at one electrode location, the position of the needle was

changed. Attempts were made in each session to record motor units which were recruited over a range of forces from very weak ones up to 1 kg or more. In addition to a needle inserted into the muscle, silver disc surface electrodes (with a diameter of 9 mm) were always placed  $3 \pm 0.5$  cm apart on the skin on opposite sides of the needle and electrode paste was used for good electrical contact. The three electrodes were then in a line parallel to the long axis of the muscle. A 5 ms electronic delay was introduced before recording the surface EMG so that its full time course could be observed when triggering from the needle EMG.

**TENSION RECORDING** Patients held a force transducer between their thumb and first finger while resting their arm comfortably on a table. The force transducer was rigidly clamped to a metal rod fixed in the centre of the table. Brackets were mounted on the frame of the transducer for the thumb and on the lever attached to the strain gauges to accommodate the lateral portion of the first finger, approximately midway between the base of the finger and the proximal interphalangeal joint. The transducer was virtually isometric, allowing only 1 mm movement, and was used with springs for recording forces up to

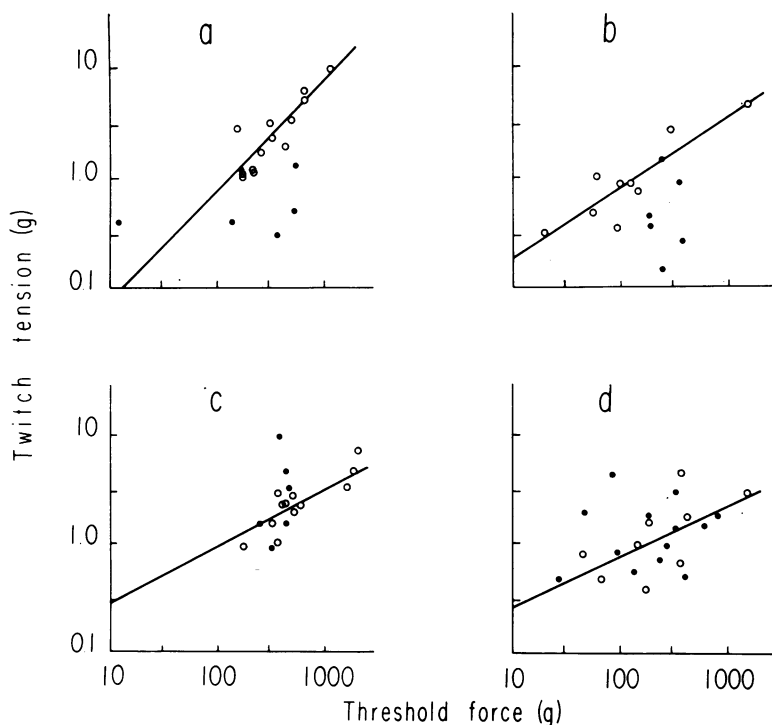


FIG. 1. *Twitch tensions produced by single motor units from four patients with previous complete severance of their ulnar nerves as a function of the threshold force at which the motor units were recruited. a, b: Early stage of regeneration. c, d: Advanced stage of regeneration. The computed best-fitting straight lines shown on these log-log plots are for the normal hands only. ○: Clinically normal hand; ●: affected hand.*

about 2 kg. During replay, impulses from single motor units were used to trigger a general purpose laboratory computer (LAB-8, Digital Equipment Corp.) and 500 sweeps were generally averaged. By averaging the force correlated in time to the impulses from a single motor unit, the twitch tension produced by that unit could be measured (Milner-Brown *et al.*, 1973a).

**STATISTICAL TREATMENT** Standard tests for statistical significance were used (Draper and Smith, 1967).

## RESULTS

**COMPLETELY SEVERED ULNER NERVES** *Twitch tensions and pattern of recruitment* The order of recruiting motor units can be examined by plotting the twitch tension generated by a motor unit against the 'threshold' force at which it becomes active during a voluntary contraction. Figure 1a and b are plots of twitch tension *vs* threshold force for two patients in an early stage of regeneration (~six months), while Fig. 1c and d are typical plots of patients at an advanced stage of regeneration (~two years after surgical repair) after complete lesions of the ulnar nerves by sharp objects. In Fig. 1a and b the mean slopes  $\pm$  SE of the mean of the best-fitting straight lines were  $1.005 \pm 0.164$  and  $0.63 \pm 0.11$

respectively, in the normal hands, with linear correlation coefficients of 0.864 and 0.88. These values show that there is an orderly recruitment of successively larger motor units during increasing voluntary contractions, as has been reported previously (Milner-Brown *et al.*, 1973b).

In the 'abnormal' hands, however, the slopes of the best-fitting straight lines were not significantly different from zero at the 5% level of confidence. The linear correlation coefficients of 0.3 and 0.15 respectively were also not significant (Draper and Smith, 1967). Thus, it appears that, besides the comparatively small size of the twitch tensions during the early stages of regeneration which might be expected, the pattern of recruitment of motor units during increasing voluntary contractions was random. The patient whose data are shown in Fig. 1b had regained about 50% of her strength in the abnormal hand, but was unable to use that hand in knitting; the randomness of her recruitment pattern could be partly responsible for this, as well as the possibility of anomalous reinnervation of the intrinsic hand muscles.

In Fig. 1c and d after two years of regeneration, the twitch tensions were approximately the same as the normal hand. However, the slopes of

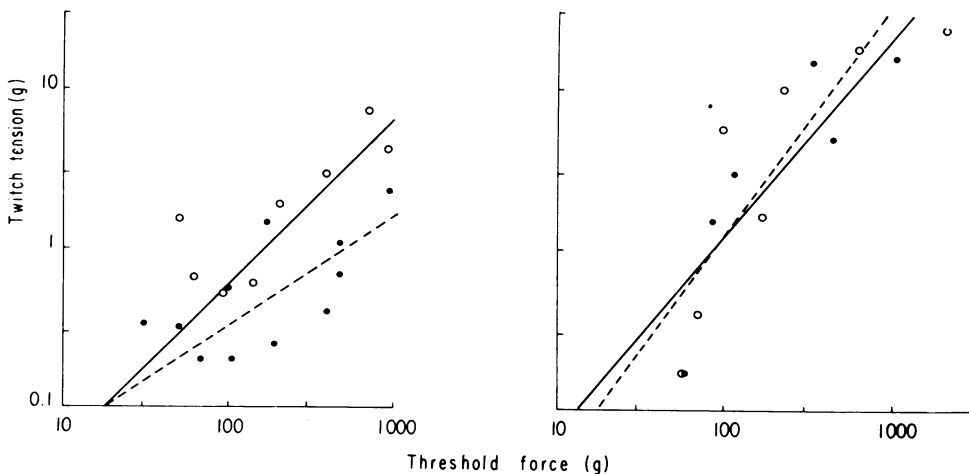


FIG. 2. Twitch tensions produced by single motor units, as a function of the threshold force at which the motor units were recruited from two patients with ulnar neuropathies. The computed best-fitting straight lines (— normal; --- affected) on these log-log plots had slopes significantly different from zero at the 5% level of confidence in both the normal and affected hands. ○: Clinically normal hand; ●: affected hand.

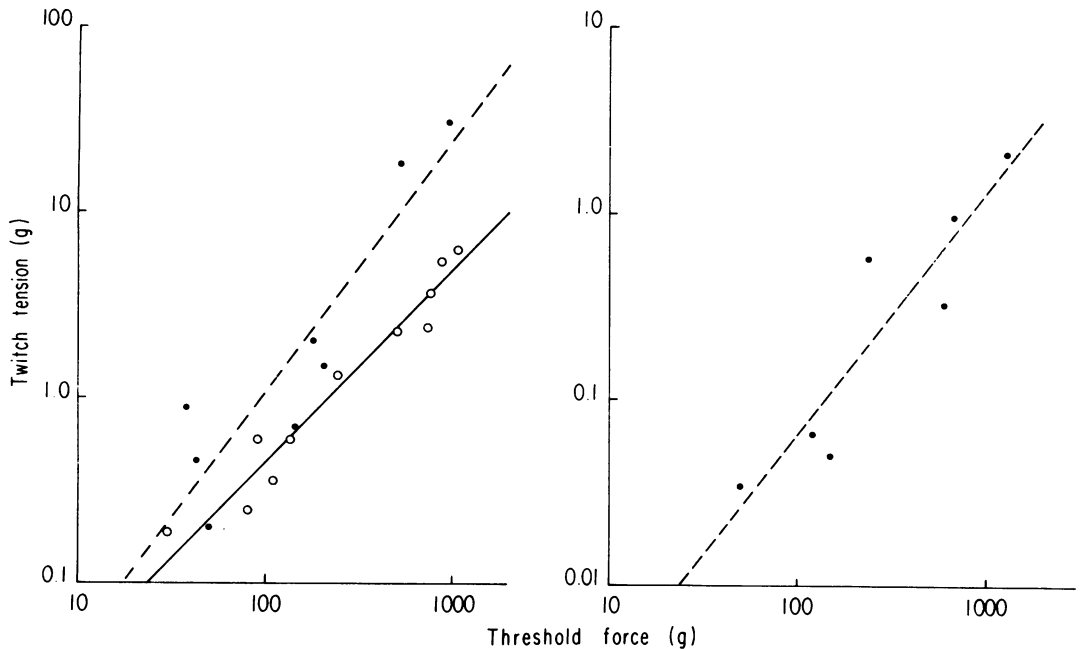


FIG. 3. *Twitch tensions produced by single motor units as a function of the threshold force at which the motor units were recruited from two patients with motor neurone disease. The computed best-fitting straight lines (— normal; --- affected) on these log-log plots had slopes significantly different from zero at the 1% level of confidence in both the normal and affected hands. ○: Clinically normal hand; ●: affected hand.*

the best-fitting straight lines were still not significantly different from zero and the linear correlation coefficients of 0.44 and 0.16 respectively were not significant. This clearly illustrates the fact that, while the twitch tensions of motor units after regeneration can return to normal size, the normal orderly pattern of recruitment of motor units during increasing voluntary contraction was irretrievably lost.

#### PRESSURE OR ENTRAPMENT ULNAR NEUROPATHIES

##### *Twitch tension and pattern of recruitment*

Among the unilateral ulnar neuropathy patients, there was a tendency for the twitch tensions to be smaller in the affected hand but the normal orderly pattern of recruitment was still apparent in most patients. Figure 2 shows two typical plots of twitch tension *vs* threshold force for two patients with ulnar neuropathies. In Fig. 2a the patient had recently developed an ulnar neuropathy associated with a partial block of conduction at the elbow, and recordings were

made eight months after anterior transposition of the nerve. The slopes of the best-fitting straight lines were  $1.05 \pm 0.29$  (normal),  $0.7 \pm 0.15$  (affected), the linear correlation coefficient in each case being 0.8. In Fig. 2b the patient had a 10 year history of ulnar neuropathy of uncertain aetiology. The twitch tensions were approximately equal in both hands and the slopes of the best-fitting straight lines were  $1.242 \pm 0.308$  (normal),  $1.423 \pm 0.316$  (affected): the linear correlation coefficients were 0.84 (normal), 0.86 (affected). These results indicate that the orderly pattern of recruitment of motor units is preserved.

**MOTOR NEURONE DISEASE** All of the patients in an advanced stage of this disease had few motor units so plots of twitch tension *vs* threshold force could not be obtained. Figure 3 shows two cases in which enough units were recorded. In Fig. 3a the patient was unilaterally affected and the slopes of the best-fitting straight lines were  $1.02 \pm 0.07$  (normal),  $1.357 \pm 0.161$  (affected):

the linear correlation coefficients were 0.97 and 0.94 respectively. The patient whose data are plotted in Fig. 3b was paralysed in the right hand; units were recorded only from his weak left hand (power=3 on a 5-point scale). The slope of the best-fitting straight line was  $1.287 \pm 0.21$ , with a linear correlation coefficient of 0.92. Thus, even though there is a general decrease in the number of motor units, the remaining motor units are recruited in an orderly fashion.

#### DISCUSSION

This study presents new quantitative data on the nature of regeneration in human motor units. Given a reasonable period of time after surgical repair of a completely severed ulnar nerve, the twitch tensions of single motor units returned to normal. Any remaining deficit in strength should be due to a reduction in the total number of motor units, due to the inability of some motor axons to reach the muscle and reinnervate muscle fibres. This prediction could be tested using recently developed methods for estimating the number of motor units in a muscle (McComas *et al.*, 1971).

We were intrigued to find that the normal orderly pattern of recruiting larger and larger motor units during increasing voluntary contraction (Milner-Brown *et al.*, 1973b) was irretrievably lost after complete severance of a nerve. It is not at all obvious why this orderly pattern appears during normal development but does not reappear after severance and regeneration of the nerve. Perhaps during development larger  $\alpha$ -motoneurons begin to sprout axons somewhat earlier and so reach more uninnervated muscle fibres than do the smaller  $\alpha$ -motoneurons. An analogous situation would be the earlier myelination of larger axons. After severance of the nerve, all  $\alpha$ -motoneurons would have an equal start and hence the pattern of innervation would be random. This hypothesis is clearly testable in animal experiments.

In pressure or entrapment neuropathies in which the ulnar nerve is not severed there is

always a physically continuous path between nerve and muscle fibres, and the normal orderly pattern for recruiting motor units was still evident. When the nerve trunk is not severed and axons are blocked without much disorganization of the myelin channels, regrowing sprouts may follow the pre-existing route across the point of injury and down to the muscle again after surgical decompression of the nerve. This explanation could account for the orderly pattern of recruitment found in partially recovered patients, who had only one or two functional units before surgery. Similar results on the pattern of recruitment from motor neurone disease patients support the suggestion that a maintained physical continuity between nerve and muscle is a necessary condition for the preservation of the orderly recruitment of motor units during voluntary contraction.

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