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Motor units: how many, how large, what kind?

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Abstract

There are now at least nine methods for motor unit number estimation (MUNE) in living human muscles. All methods are based on the comparison of an average single motor unit potential (or twitch) with the response of the whole muscle. Such estimations have been performed for proximal and distal muscles of the arm and leg in healthy subjects and in patients with various neuromuscular disorders. In healthy subjects there is a loss of motor units which is most evident in distal muscles and after the age of 60 years. Substantial losses of motor units have been measured in patients with ALS, post-polio symptoms, and diabetic peripheral neuropathies. In contrast, normal MUNEs have been found in approximately half of patients with persisting obstetric brachial palsies. The sizes of motor units show considerable variations within the same muscle and also between muscles; very large units are usually present in severe partial denervation. Although many motor unit properties are largely governed by motoneurons, some exhibit less plasticity in humans than in other mammals.

Keywords: Motor units; Motoneurons; Muscle twitch; Muscle fiber types

1. Introduction

It was Sherrington [1] who, in 1929, introduced the term 'motor unit' to describe a single motor axon and the colony of muscle fibers which it innervated. Sherrington recognized that the strength of a voluntary or reflex contraction would depend on the numbers of participating motor units. In the same year Adrian and Bronk [2] described the coaxial needle electrodes which they had used, in combination with a capillary electrometer, to record the discharges of individual motor units during voluntary contractions of human muscles. Following this auspicious start, research on motor units proceeded only slowly and intermittently, until the experiments reported by Henneman and his colleagues in 1965. These workers were the first to dissect and stimulate single motor axons [3], and were able to show that the contractile properties of motor units differed considerably, even within the same muscle [4]. These important pioneering studies can be said to have ushered in the modern era of motor unit anatomy and physiology, an era which has seen its share of successes and surprises. The present review will examine selected aspects of this field and, for obvious reasons, will include contributions from our own laboratory.

2. Motor units: how many?

In animals the number of motor units in a muscle is easily found by counting the *large-diameter axons* which remain in the motor nerve after the muscle afferents have degenerated following dorsal rhizotomy (distal to the dorsal root ganglia). Alternately the muscle or motor nerve can be injected with a suitable tracer, such as horseradish peroxide; after allowing time for the tracer to be transported retrogradely in the motor axons, the number of labelled motoneurons can be counted in serial sections of spinal cord [5]. Such studies also show that the motoneurons for a particular muscle are arranged in an axial column and usually occupy more than one segment of spinal cord (see also Romanes [6]).

In humans the determination of motor

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units/motoneuron numbers is necessarily less precise, at least for the present, but there are nine electrophysiological methods which enable approximate values to be obtained rapidly and easily. All of these methods are based on the same principle, namely, the comparison of an average motor unit parameter with the corresponding parameter of the whole muscle. The parameter could be twitch or tetanic tension, but it is much more convenient to use electrical activity; in effect, the potentials of single motor units are compared with the maximum compound action potential (M-wave) of the same muscle.

2.1. Techniques for motor unit estimation

The first motor unit number estimations (MUNEs) were obtained by the method of incremental stimulation [7]. Using this method, electrical stimuli are applied to a peripheral nerve at an accessible point and recordings are made using an active electrode attached to the skin over the endplate region of the muscle. As the stimulus intensity is gradually raised from a subthreshold value, the muscle responses grow in discrete steps (Fig. 1) and it is assumed that each step reflects the excitation of an additional motor unit. After 10 or so increments have been obtained, the average peak-to-peak amplitude is calculated and is then divided into the peak-to-peak amplitude of the whole muscle response, obtained by maximal nerve stimulation; the answer is the approximate number of motor units in that muscle. Initial concerns about the adequacy of a small sample of motor units for such a calculation, and about the possibility of a sampling bias towards large motor units, have proved largely unfounded. There is, however, one major disadvantage of the manual incremental method, and this is the tendency for motor axons with similar thresholds to fire in different combinations as the stimuli are repeated. This phenomenon, 'alternation', results in the appearance of fictive motor unit responses and to an erroneously large MUNE. It is because of alternation that other methods have been devised for collecting the sample of motor unit potentials. There are now eight of these other collection methods and they include:

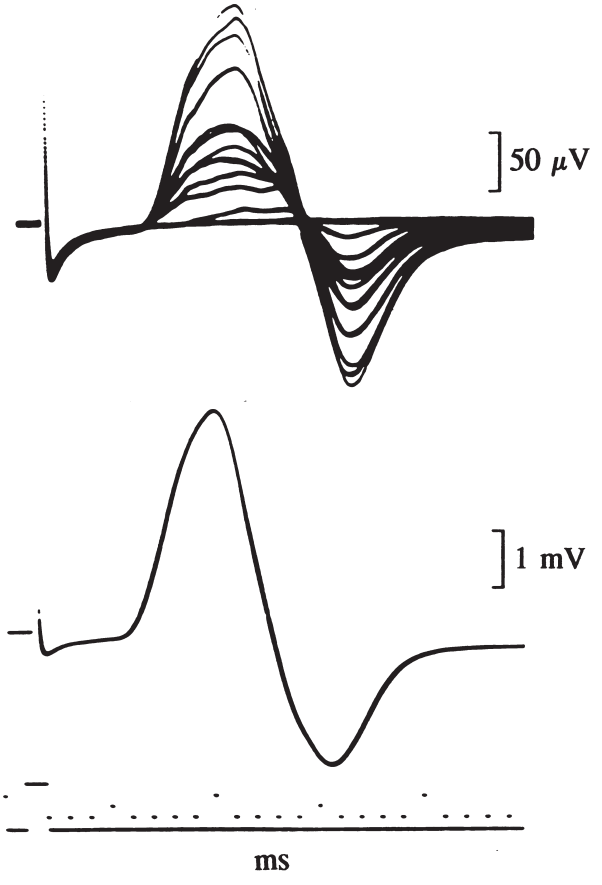

Fig. 1. Incremental motor unit number estimation (MUNE). At top are the responses of the thenar muscle group to stimulation of the median nerve. The stimulus intensity is gradually increased above threshold and each step in the response is assumed to result from the excitation of an additional motor unit. At bottom is the maximal M-wave of the same muscle (notice calibration).

1. Stimulating a motor nerve at different points and accepting only the responses of the one or two motor units with the lowest axonal thresholds (multiple point stimulation [8]).
2. Stimulating single motor axons with a needle electrode inserted in the endplate region of the muscles [9] (see also Garnett [10]).
3. Stimulating single motor axons with fine wire electrodes inserted into the motor nerve (Arasaki, personal communication; see also Thomas et al. [11]).
4. Treating F-waves as the responses of one, or very few, motor units [12].
5. Spike-triggered averaging of surface-recorded motor unit potentials, during relatively weak voluntary contractions [13].
6. Using computer algorithms to identify potentials of single motor units, recorded with surface electrodes, during voluntary contractions [14].
7. Applying Poisson analysis to muscle responses evoked by repetitive motor nerve stimulation at different intensities [15].
8. Our own attempt to improve MUNE has been based on the incremental stimulation method, but has used computer algorithms to control both the stimulus intensity and the collection of motor unit potentials [16]. Alternation is reduced by accepting only those responses which have been repeated twice within a limited time frame. At the end of the collection period, as many as 21 computer templates are available for analysis. The templates are ranked in order of increasing area (voltage × time) and each template is then subtracted from the next largest, so as to yield a putative motor unit potential (Fig. 2). Another algorithm compares each putative motor unit potential with every other potential in the sample. Any

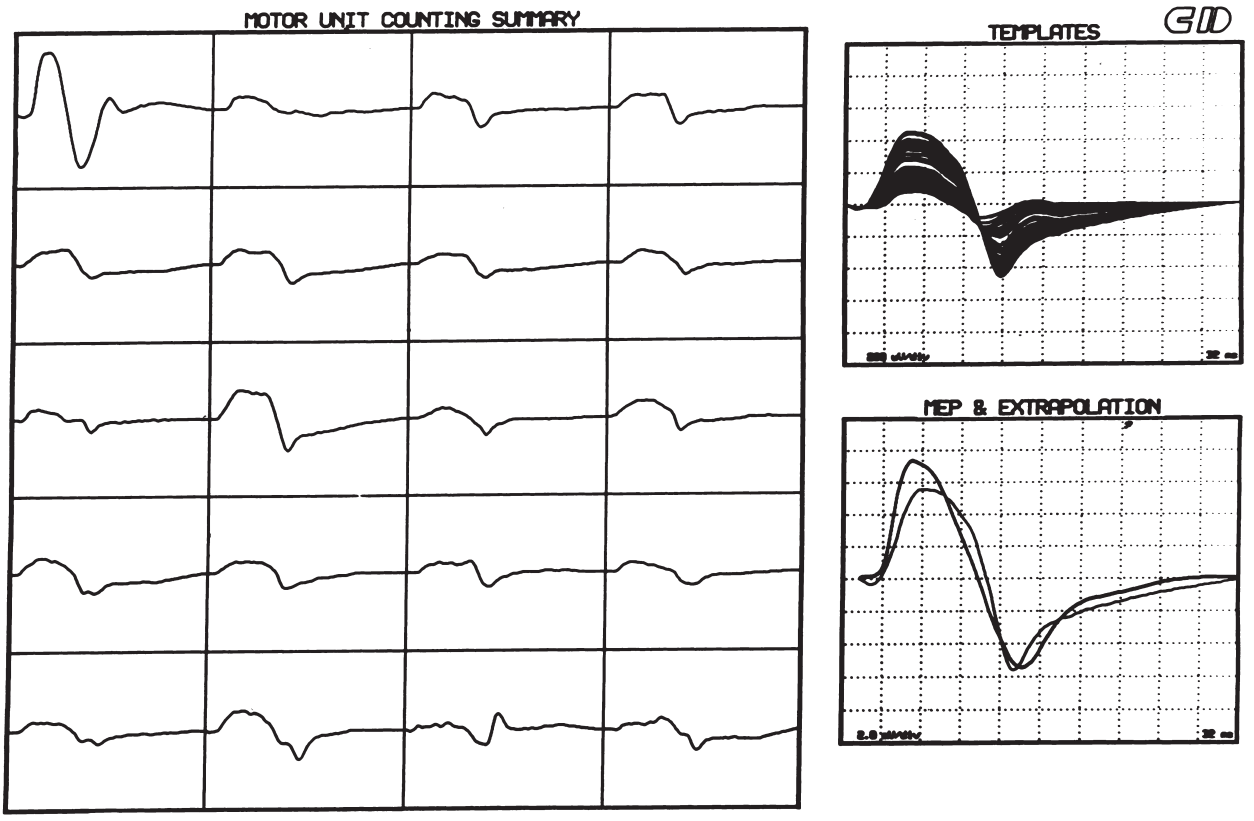

Fig. 2. Automated motor unit estimation of a normal medial vastus muscle. On the left are putative motor unit potentials obtained by subtracting each evoked response template (at top right) from the next largest in the series. At bottom right is a comparison of the wave-forms of the maximum muscle response and the sample of motor unit potentials.

close similarities are assumed to result from alternation and the duplications are removed from the analysis. A final algorithm tests the adequacy of the sample of motor unit potentials, by comparing the wave-forms of the largest template with that of the maximum M-wave.

It is not possible here to delve into the respective merits of the various methods. All of them provide valid ways of estimating motor unit numbers and, in the presence of control values, can be used with confidence in the clinical EMG laboratory to detect instances of denervation. The original manual incremental method, and some of the simpler alternatives, can be undertaken with almost any EMG machine. In contrast, a particular computer-based method will only be available from one manufacturer, at least for now. It is arguable as to whether or not there is a need to standardize MUNE, or whether the different methods should continue to coexist.

In our own laboratory we use the incremental method in both the original manual and automated forms. When both methods are applied to the same muscle, the automated estimate is nearly always lower than the manual one, due to the reduction in alternation.

2.2. MUNEs in normal subjects

Tables 1 and 2 list MUNEs for different muscles in the human arm and leg, obtained with the various advanced methods. The lists are by no means complete, but they contain at least one example of each method, and they also include ‘grand means’ for those muscles with MUNE results from more than one laboratory. We are indebted to our colleague, Dr. Victoria Galea, for the extensive values collected with the automated incremental method; it is these values which have formed the control ranges in the EMG clinics at McMaster University. In relation to the arm values, it should be noted that there are four muscles in the hypothenar group, and two and part of a third muscle in the median-innervated thenar group, so that a small muscle in the hand has, on average, 70–100 motor units. Larger limb muscles, such as the tibialis anterior and medial vastus, have more motor units, although fewer than the sizes of their muscle bellies might suggest. Indeed, the biceps, a conspicuously large muscle, may have only 100 or so motor units.

The electrophysiologically derived MUNEs in Tables 1 and 2 are of the same order as the anatomical estimates of Feinstein et al. [20]. To obtain their values Feinstein

Table 1
MUNEs derived for muscles of the human arm, using improved techniques

Authors	Method[a]	Muscle(s)	MUNE (mean ± SD, *n*)
Galea[b]	AI	Thenar	230 ± 90 (90)
Doherty and Brown[8]	MPS	Thenar	288 ± 95 (37)
Felice[17]	MPS	Thenar	219 ± 81 (16)
Daube[15]	Poisson	Thenar	234 ± 95 (30)
Doherty et al.[12]	F-wave	Thenar	245 ± 105 (18)
Simmons et al.[18]	F-wave	Thenar	158 ± 58 (23)
Fang et al.[19]	I and STA	Thenar	243 ± 99 (5)
Stein and Yang[9]	STA	Thenar	122 ± 38 (10)
Stein and Yang[9]	IMS	Thenar	135 ± 27 (10)
Grand mean[c]		Thenar	208
Galea[b]	AI	Hypothenar	411 ± 174 (41)
Daube[15]	Poisson	Hypothenar	256 ± 115 (30)
Arasaki[b]	INS	Hypothenar	122 ± 40 (20)
Grand mean[c]		Hypothenar	263
Galea[b]	AI	Biceps	109 ± 43 (80)
Doherty et al.[21]	STA	Biceps–brachialis	357 ± 97 (24)

[a]AI, automated incremental; I, incremental; IMS, intramuscular stimulation; INS, intraneural stimulation; MPS, multiple point stimulation; STA, spike triggered averaging.
[b]Personal communication.
[c]'Grand means' calculated without regard to the number of observations in each study.

Table 2
MUNEs derived for muscles of the human leg by different methods

Authors	Method[a]	Muscle(s)	MUNE (mean ± SD, *n*)
Galea[b]	AI	EDB	143 ± 73 (86)
Arasaki[b]	INS	EDB	137 ± 48 (20)
Daube[15]	Poisson	EDB	158 ± 58 (30)
Barkhaus and Nandedkar[22]	IPI	EDB	189 ± 46 (24)
Slawnych et al.[23]	MUESA	EDB	87 ± 37 (23)
Grand mean[c]		EDB	143
Daube[15]	Poisson	Plantar	285 ± 187 (30)
McComas	AI	Plantar	381 ± 162 (26)
Grand mean[c]		Plantar	333
Galea[b]	AI	Tibialis anterior	256 ± 107 (22)
Galea[b]	AI	Vastus medialis	224 ± 112 (24)

[a]AI, automated incremental; INS, intraneural stimulation; IPI, incremental with phase interaction; MUESA, motor unit number based on stochastic activation.
[b]Personal communication.
[c]'Grand means' calculated without regard to the number of observations in each study.

and colleagues examined the motor nerves of a patient who had died from poliomyelitis and assumed that the only large axons remaining were sensory. They then subtracted the polio axon count from control nerve fiber counts in order to determine the proportion of large fibers that were motor. Most of their values are for a single muscle and give no indication of the normal range; further, myelinated fiber diameter histograms are not always bimodal, so that the distinction between 'large' and 'small' fibers can be arbitrary.

Are there any ways that the anatomical estimates for human muscles might be improved? We believe that there are. Rather than use a subtraction procedure, it would be better to count motor axons directly. This could be done in patients who had died in the presence of a purely sensory neuropathy, as in occasional cases of Guillain–Barré syndrome, or in suitably chosen ones of diabetic peripheral neuropathy. Cis-platinum, used in the treatment of ovarian carcinoma, is also known to induce a pure sensory neuropathy. Alternatively, it should eventually be possible to isolate an antibody against either sensory or motor axons, perhaps using plasma or CSF from a patient with a modality-selective form of Guillain–Barré syndrome. Such an antibody could then be used to identify motor or sensory axons in cross-sections of nerve prepared from non-neuropathic cadavers, such as victims of accidental death.

Although it would be satisfying to have anatomical confirmation of the electrophysiological MUNEs, there should be little hesitation in accepting the values in Tables 1 and 2, obtained by the improved methods, as reliable. One of the advantages of electrophysiological MUNE is that it is relatively easy to collect and pool the results from large numbers of muscles. This attribute effectively eliminates most motor unit sampling problems, leaving only those caused by systematic bias, as in the collection of potentials from the smaller motor units in techniques based on weak contractions [3].

2.3. Comparative aspects of MUNE

Before describing some of the applications of MUNE, there are several additional points that need to be made. First, in comparing the MUNEs of human subjects with those of smaller mammals, it is evident that the larger values in humans are proportionally much less than the increases in brain and spinal cord volumes, and in muscle size, between the species. In evolutionary terms, this suggests that there is little advantage in increasing the numbers of motoneurons beyond a certain value. A

further implication is that, in the relatively large human spinal cord, there must be greater numbers of interneurons per motoneuron than in lower animals.

A second point is that, in healthy humans, as in laboratory animals, there is an appreciable range of motor unit/motoneuron numbers for any given muscle. Also, it is our impression that there is some consistency in individual subjects, such that a person with a large MUNE for one muscle will have large values for other muscles. This correlation between motoneuron pools is likely to have a genetic basis and could involve differences between subjects in neuroblast proliferation in the embryonic neural tube, or differences in the degree of programmed cell death.

2.4. MUNEs in neuromuscular disorders

In the *clinical EMG laboratory*, we use the incremental stimulation method, in both the original and automated forms. Table 3 summarizes a two-year experience with the automated technique, and lists the clinical conditions to which the technique was applied. An overall denervation detection rate of 27% may seem low, but it reflects more the nature of the clinical referrals and the frequent desirability of *excluding* a neuropathic condition, than any limitation of MUNE. As yet, no comparisons have been made between automated incremental MUNE and the needle examination, in the ability to detect denervation. In an earlier study, however, manual incremental MUNE was shown to be clearly superior to the needle examination for distal muscles, even when automatic analysis of the needle recordings was performed [24].

In aging MUNE has shown a progressive loss of functioning motor units, which is most pronounced after the age of 60 years. Of the muscles studied, the EDB (extensor digitorum brevis) has the most prominent loss, and the brachial biceps shows the least change [25]. Fig. 3 shows the pooled values for the EDB muscle. Confirmation of a reduction in motor units after 60 years has come from anatomical counts of motoneurons in the lumbosacral cords of cadavers [27].

In *ALS*, MUNE is a valuable diagnostic tool, particularly since collateral reinnervation may delay decreases in strength and muscle mass. Fig. 4 summarizes the MUNEs in the thenar and EDB muscles of more than 100 patients, as determined at the time of the initial EMG examination. In both situations, the majority of subjects already showed sharp reductions in MUNE, even though denervation may not have been apparent clinically. Fig. 5 is taken from an earlier study [28] and illustrates the rapid, exponential rate of motor unit loss that usually occurs once a motoneuron pool becomes involved by the ALS process. On a more positive note, MUNE should become the method of choice for evaluating the responses of ALS patients to the newer experimental therapies [29,17]. The results in ALS stand in sharp contrast to those in *spinal muscular atrophy (SMA)*, for most adults with the latter condition show no progression in their loss of motor units [30]. We were able to argue that denervation must have been estab-

Table 3
Automated MUNE results in 225 consecutive patients examined in an EMG clinic over a two-year period

Disorder[a]	Abnormal MUNEs	Normal MUNEs	% Abnormal MUNEs
'None' (fatigability, cramps, unaffected relatives, etc.)	0	85	0
Neck symptoms	6	48	11
Low back pain, sciatica	21	30	41
Carpal tunnel syndrome	15	48	24
Other focal neuropathies	10	14	42
Generalized neuropathy	19	17	53
Brachial plexopathy	20	23	47
Motor vehicle accidents	2	26	7
Previous polio	7	8	47
ALS, SMA	23	11	68
Muscular dystrophy, myasthenia, collagen disease	2	15	12
CNS, other	2	15	12
Overall	127	340	27

[a]ALS, amyotrophic lateral sclerosis; CNS, central nervous system; SMA, spinal muscular atrophy.

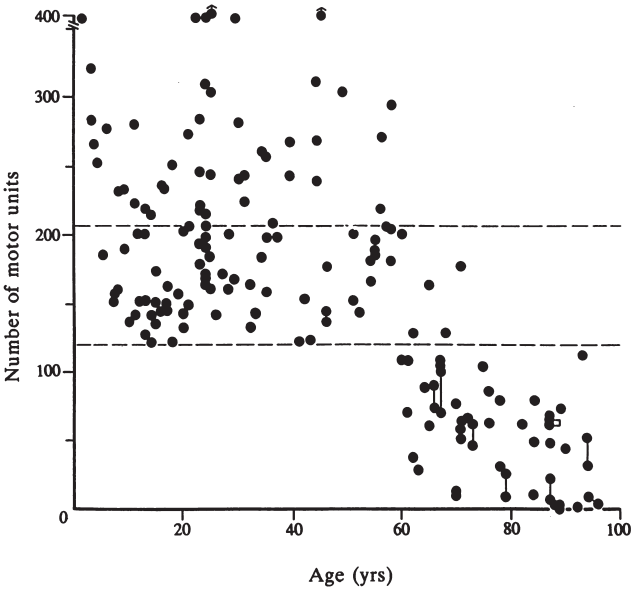

Fig. 3. Motor unit depletion with age. The values are for the EDB muscles of 207 healthy subjects aged between 7 months and 97 years. Linked values are for both feet of an individual. The upper and lower interrupted lines signify respectively the control mean (210 units) and the lower limit of the range for control subjects under 60 years (120) units. All values obtained by the original incremental technique. Reproduced from McComas [26] with permission.

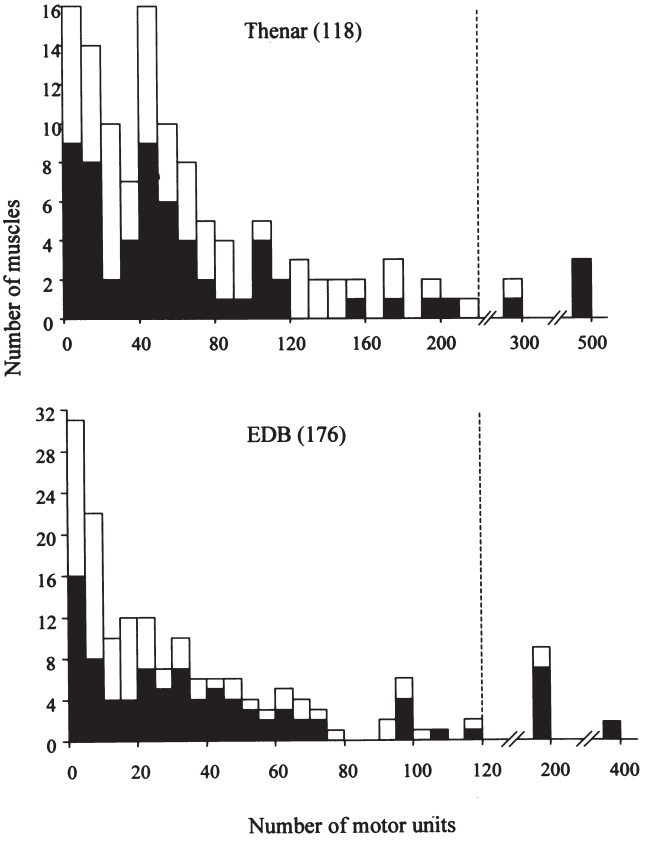

Fig. 4. Motor unit numbers, as estimated by the original incremental technique, in ALS patients. Filled and open columns show results for subjects below and above the age of 60 years respectively. The interrupted vertical lines show the lower limits of the control ranges.

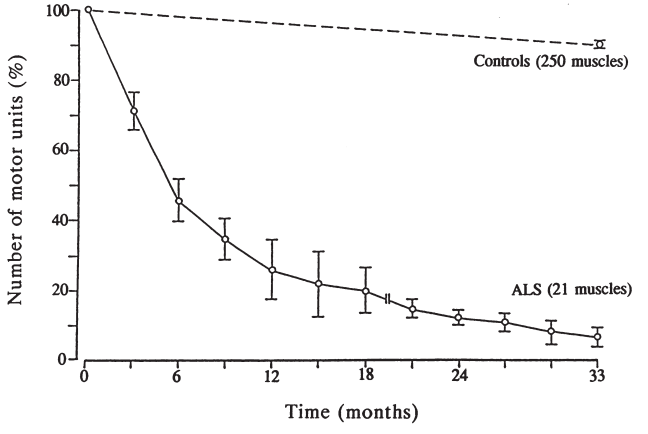

Fig. 5. Exponential loss of motor units in ALS patients. Results pooled for 21 muscles of the arm and leg, and normalized. Reproduced from Dantes and McComas [28] with permission.

lished before birth, a conclusion consistent with subsequent molecular biology studies showing absence of a factor inhibiting programmed motoneuron death in the human embryo [31].

More recently we have completed a study of MUNE in *post-polio* patients [32] and the results are given in Fig. 6. As in ALS, the majority of MUNEs fall below the normal range and motor unit loss can often be demonstrated in limbs not thought to have been affected in the acute viral infection. By examining some of the subjects two years later, it was possible to show that the rate of motor unit loss was considerably higher than that in normal aging, and that this was the likely basis for the postpolio syndrome.

Another clinical illustration of MUNE is in the diagnosis and assessment of *peripheral neuropathy*. Fig. 7 shows MUNEs for the intrinsic muscles of the hand in diabetic patients referred to the EMG clinic. Once again, many of the values are abnormally low but, in keeping with the clinical findings, there is a relatively greater reduction in conducting sensory nerve fibers.

Normal MUNEs can also be extremely informative, not only in the diagnosis of individual patients but also in research studies. For example, approximately half of patients with persisting obstetric brachial palsy have normal MUNEs in their biceps muscles (Fig. 8). This surprising result has given rise to the concept of a developmental apraxia as the main factor underlying the clinical problem [33].

Finally, there is the issue of reversibility of motor unit loss. While this is to be expected in Guillain–Barré neuropathy, or in the peripheral neuropathy that follows vincristine therapy for malignancy, reversibility may be seen in more unexpected circumstances. It is, for example, a regular feature in patients treated for severe hyperthyroidism [34] and has occasionally been observed in renal failure and in trauma to the brachial plexus. We have suggested that some of these surprising results may be due to the presence of neuromuscular junctions that are temporary incapable of transmitting (the silent synapse phenomenon [35]).

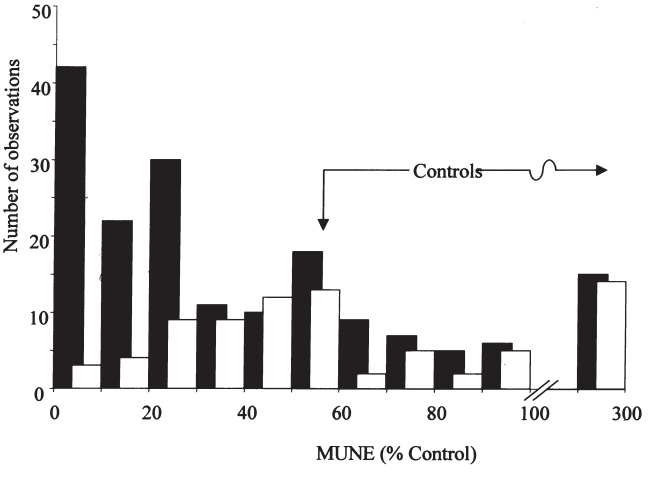

Fig. 6. Numbers of motor units in postpolio patients. Results pooled for 76 muscles of the arm and leg, and normalized. Filled and open columns show values for limbs known to have been affected, and limbs thought not to have been affected, respectively. Reproduced from McComas et al. [32] with permission.

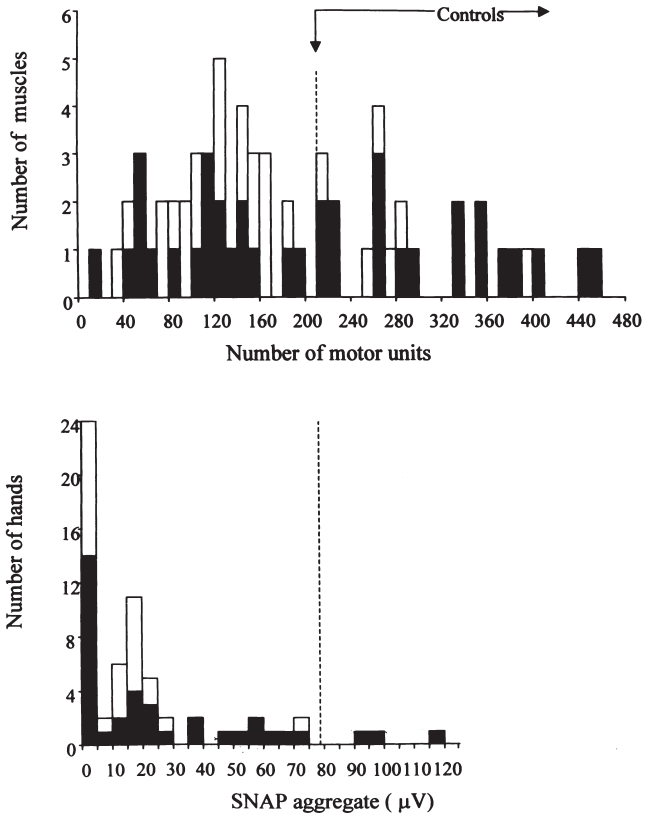

Fig. 7. Top: MUNEs in thenar and hypothenar muscles of 63 subjects with diabetes mellitus. Bottom: The aggregate of the sensory nerve action potentials recorded orthodromically from each digit of the same hands. The filled and open columns show the results for subjects below and above the age of 60 years respectively. Vertical interrupted lines denote lower limits of control ranges. Note that the sensory nerve fibers are more severely affected than the motor ones.

3. Motor units: how large?

The sizes of motor units, that is, the numbers of muscle fibers supplied by single motor axons, were first estimated by dividing the total number of muscle fibers in the muscle by the number of motor axons. These simple calculations were sufficient to show that the human external ocular muscles and the platysma had very much smaller motor units than the limb muscles [20]. In the arms and legs there was a correlation between the respective sizes of the muscles and motor units, such that the muscles with greatest bulk had the largest motor units. However, following the first recordings of single motor unit contractions in the cat hindlimb, by Henneman and colleagues in 1965 [4], it was apparent that, even within the same muscle, there is considerable variation in the sizes of the motor units. These variations were subsequently confirmed by the technique of glycogen depletion, whereby those fibers exhausted of their glycogen by repetitive stimulation of a single motoneuron or motor axon, can be identified and counted in the muscle belly [36,37]. In the cat hindlimb the motor unit sizes range from less than 50 to more than 1000 fibers, as determined by glycogen depletion [38], with the 'slow' motor units (type I units) being the smallest [39,40]. Why the slow units should be the smallest is not known. One possibility is that, since these units are the most active, the amount of impulse activity may limit the numbers of neuromuscular junctions that can be retained during the phase of synapse elimination in the embryo. The same sort of process appears to be at work during muscle reinnervation since, in cat triceps surae, Gordon and Stein [41] have found that there is a phase of remodelling which restores the relationship between motoneuron size, motor unit size and twitch contraction time.

Other than studying limbs, or parts of limbs, that were about to be amputated, there is no prospect of obtaining comparable data in man. The best that can be done is to determine the relative sizes of the motor units, by comparing their twitch or tetanic tensions. Such comparisons assume that there are no differences in the cross-sectional areas of the fibers, between different units, or in their specific tensions (i.e., tensions per cross-sectional areas). Neither assumption may be valid in animal muscles [42], but in human muscles at least the diameters of the different muscle fiber types appear very similar (e.g., Brooke and Engel [43].)

Table 4 sets out the ranges of twitch tensions for muscles of the human arm and leg, most of which were values obtained during weak voluntary contractions by the spike-triggered averaging technique. This technique would be expected to yield reduced tensions, because of partial fusion of the motor unit contractions, and it is therefore curious that the values obtained are so similar to those derived from motor axon stimulation [11]. Table 4 shows that there is as much as a 100-fold range of motor unit tensions in the various muscles (see also Table 12.4 in McComas [26]).

It might be anticipated that the largest motor units would be incapable of any further increase, but investigation of partially denervated muscle shows that this is not so. Fig. 9 displays the relative sizes of human motor units, measured as the peak-to-peak amplitudes of their surface-recorded action potentials, in the hypothenar muscles of ALS patients with different degrees of denervation. The relationship between motor unit size and motor unit number (MUNE) is seen to have a hyperbolic form. This relationship implies that surviving motor units will continue to enlarge, by axonal sprouting, in proportion to the numbers of denervated muscle fibers present. The effectiveness of axonal sprouting in maintaining contractile force was demonstrated in the human EDB many years ago [53].

It has long been suspected that such enlargement, because of the increased demands on cellular metabolism, might prematurely age the motoneuron, and there are experimental results in animals to support this possi-

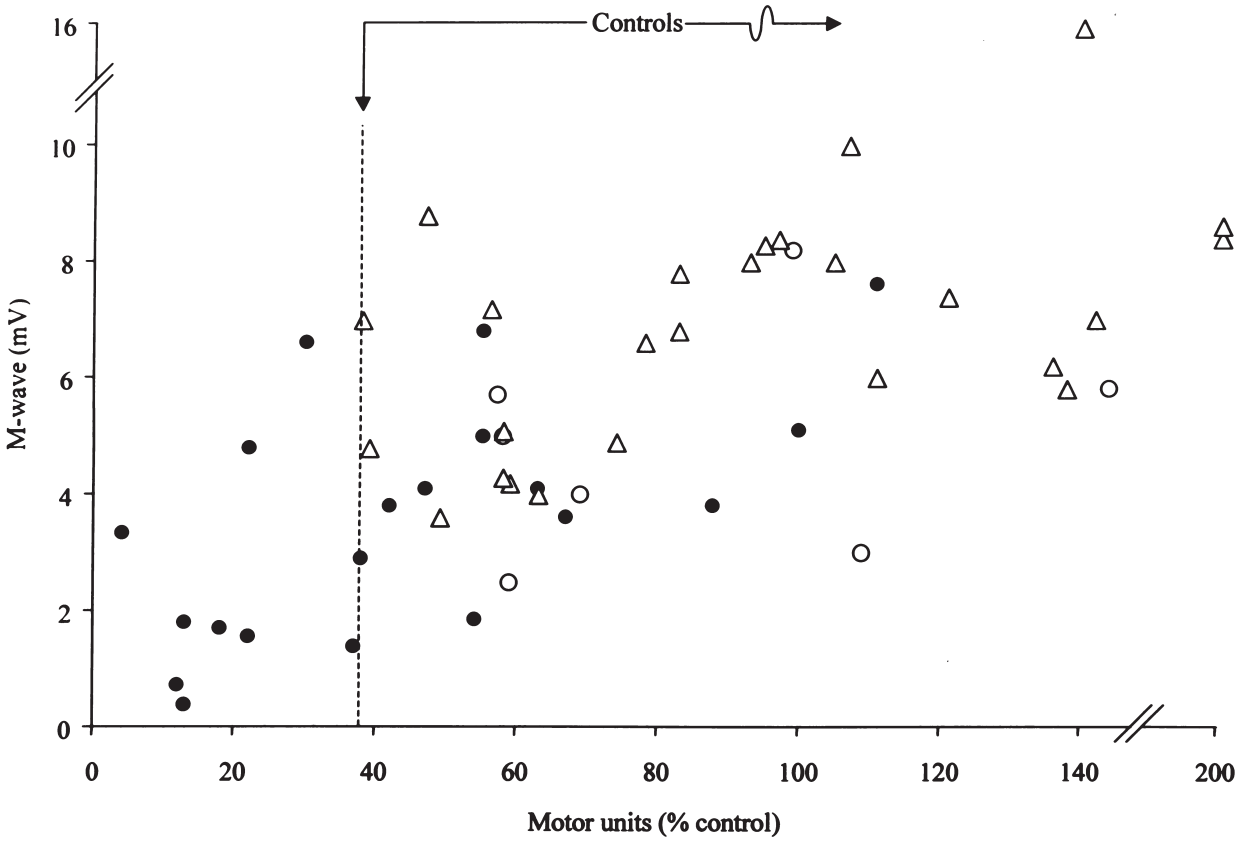

Fig. 8. MUNEs and maximum M-wave responses in brachial biceps muscles of subjects with persisting obstetric brachial palsy. Filled and open circles show values for affected and non-affected arms respectively, while triangles represent results for age-matched controls. Note that more than half of the biceps muscles in the affected arms have values above the lower limit of the control range (interrupted vertical line).

Table 4
Ranges of motor unit twitch tensions for human arm and leg muscles, obtained with various methods

Muscle	Force range (mN)	Method[a]	Authors
Abductor pollicis brevis	2–163	STA	Thomas et al. [44]
Thenar	3–34	INS	Thomas et al. [11]
First dorsal interosseous	1–122	STA	Milner-Brown et al. [45]
First dorsal interosseous	2–294	STA	Stephens and Usherwood [46]
First dorsal interosseous	2–423	IMS	Young and Mayer [47]
First dorsal interosseous	3–215	STA	Thomas et al. [48]
First dorsal interosseous	1–100	STA	Dengler et al. [49]
Flexor carpi radialis	0.2–98	STA	Calancie and Bawa [50]
Extensor digitorum communis	5–49	STA	Monster and Chan [51]
Extensor hallucis brevis	20–140	SS	Sica and McComas [52]
Medial gastrocnemius	15–2000	IMS	Garnett et al. [10]

[a]IMS, intramuscular stimulation; INS, intraneural stimulation; SS, surface stimulation; STA, spike-triggered averaging.

bility [54]. Such an effect might, for example, be responsible for the postpolio syndrome. It is perhaps relevant that Dengler and colleagues [55] have recorded abnormally small twitch tensions from some motor units in ALS. These reduced responses could indicate motoneurons failing from either the ALS process or from metabolic exhaustion or, indeed, from both. As yet we do not know the nature of the stimulus, delivered by the denervated muscle fibers, which causes neighboring axons to sprout; the possibility that sprouting is due to the absence of a repressive factor seems equally plausible [56].

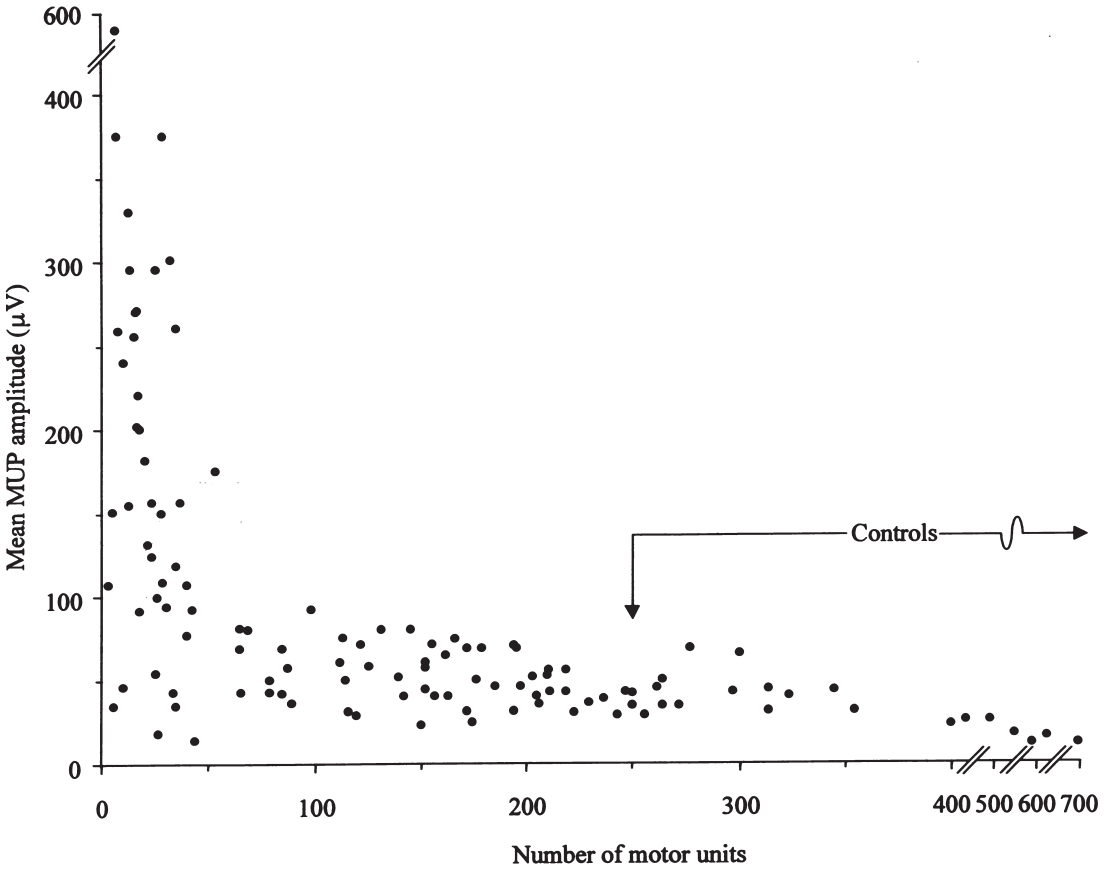

Fig. 9. Relative sizes of motor units, measured as mean motor unit potential amplitudes, in 116 hypothenar muscles of ALS patients. Each value represents a single muscle. Note the hyperbolic form of the curve. See text.

4. Motor units: what kind?

The fact that there are types of motor units which differ from each other in their contractile, histochemical and immunochemical properties, as well as in their sizes and fatigability, has already been referred to. The definitive animal studies in this field were started by Henneman in 1965 [3] and then developed by others, notably Burke (see Burke [42] for review) and Stuart (see Stephens and Stuart [57]). A more recent view is that, although certain motor unit characteristics tend to occur together, there is a continuum of properties rather than sharply isolated groups. This seems to be especially true for human muscles, since the very first study of single unit twitches, in the EDB muscle [52], failed to show the inverse correlation between twitch tension and duration expected from animal experiments. Lack of an association was also reported by other workers [45,51,47], although both Stephens and Usherwood [46] and Andreassen and Arendt-Nielsen [58] have reported results similar to those in animals. All studies have, however, confirmed an approximately three-fold range in contraction times among human motor units (Fig. 10, top) and it is variations in the proportions of units with short and long contraction times which is responsible for the different appearances of the twitches among human muscles (Fig. 10, bottom).

In addition to the lack of correlation between motor unit size and twitch duration, human muscles appear to differ from animal muscles in another respect, and this is in relation to plasticity of the contractile process. Thus, following the classic cross-innervation experiments of Buller et al. [60], it has been accepted that the motoneuron determines the muscle fiber characteristics within the motor unit (though not necessarily in the embryo; see Butler et al. [61]). And indeed, inasmuch as fiber type grouping is a feature of partially denervated muscle, the influence of the motoneuron must be present for human muscle fibers too. Yet, whereas animal muscles are readily modified by changes in motoneuron or muscle fiber impulse activity, the same may not be true for all human muscles. For example, animal muscles can be converted from slow-twitch to fast-twitch by disuse [62], with preferential atrophy of type I fibers and some conversion of type I fibers to type II. In the human quadriceps muscle, however, disuse following fractures is associated with marked atrophy of both type I and type II fibers, rather than of type I fibers alone [63], and similar findings have been obtained for the triceps muscles of immobilized arms [64]. Recently we have studied another model of

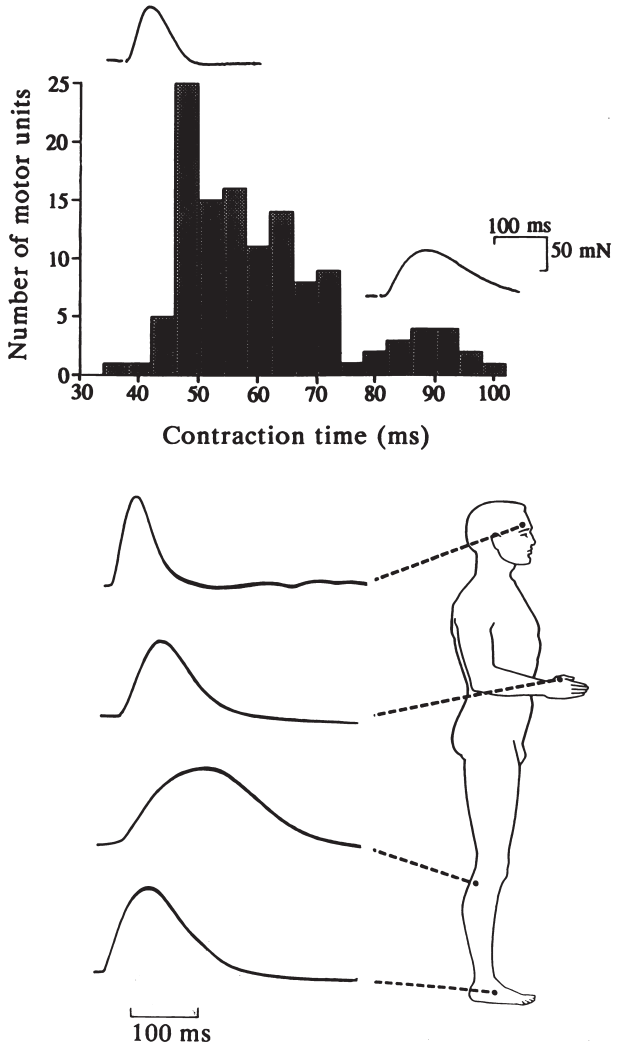

Fig. 10. Top: Contraction times of 122 motor units in extensor hallucis brevis muscles of healthy subjects. Examples of 'fast' and 'slow' motor unit twitches are included. Adapted from Sica and McComas[52] with permission. Bottom: Twitches of entire human muscles, recorded with a piezo-electric device pressed into the muscle bellies. Note that the facial muscles have the briefest twitches, and the calf muscles the longest. Reproduced from McComas and Thomas[59] with permission.

disuse, the neglected arms of children with persisting obstetric brachial palsy. Rather than the twitches being briefer, as would be anticipated from animal experiments, we have found them to be of similar durations to those in the normal arms or even longer [65] (see also Stefanova-Uzunova et al. [66]), as in Fig. 11, bottom. Perhaps the most striking absence of twitch plasticity occurs in those patients who have been treated for irreversible facial palsy with muscle grafts and cross-innervation from the normal side of the face. We have now seen two patients who have undergone this procedure and in both the grafted gracilis muscles have twitches which are visibly slower than those of the normal muscles on the other side of the face (Fig. 11, top; see Hawrylyshyn et al. [67]).

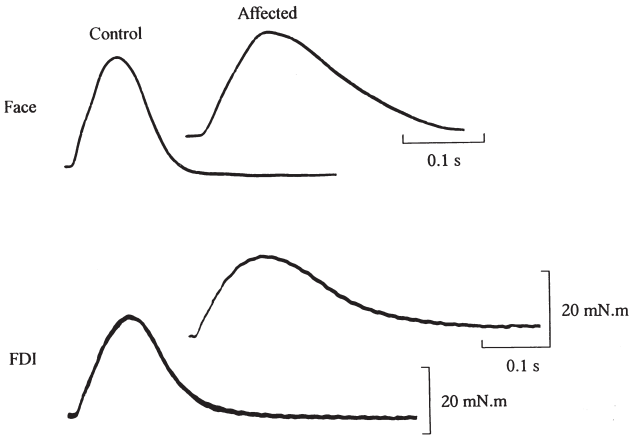

Fig. 11. Prolongation of the twitch in (top) a gracilis muscle grafted into the face, and (bottom) a first dorsal interosseous muscle in a disused arm. In each pair of twitches, that for the affected side is shown on the right, and that for the 'control' side on the left. See text.

Why should human muscles be so much more resistant than animal muscles to changes in impulse activity? Is it because the adult human muscle fibers are so much older than those of adult cats and rats? The possibility that human fibers are more responsive to trophic messages from the motoneuron, than to the patterns and amounts of impulse activity, seems unlikely; thus, similar trophic messages would have been received by muscles on both sides of the face in the patients with nerve and muscle grafts (cf. Fig. 11, top).

5. Conclusions

Motor unit number estimation, and the ability to record twitches of single motor units, have increased our knowledge of human muscle in a number of important respects. Nevertheless significant questions remain to be answered and care should be exercised before the results of animal experiments are applied to the human situation.

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