Refractory period studies in a human neuromuscular preparation

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SUMMARY A subtraction technique has been employed to study refractoriness in the median nerve and thenar muscles in man. The absolutely refractory periods of the distal motor nerve branches and of the muscle fibres were found to be similar, the majority being within the 2.5–3.0 ms range; the values were distributed in a unimodal manner. The relatively refractory periods of the motor nerve terminals were about 5 ms. In some experiments it was possible to record non-propagated potentials at the endplate zones of the muscle fibres.

The concept of an inexcitable period after the discharge of an impulse was first described by Lucas (1909) in relation to frog sartorius muscle fibres and by Gotch (1910) during an investigation of frog sciatic nerve. A more extensive analysis of this phenomenon was subsequently made with the cathode ray oscilloscope by Gasser and Erlanger (1925); these authors described an ‘absolutely refractory period’ (ARP) after excitation during which a nerve or muscle fibre could not discharge an impulse to a second stimulus. Later it was shown that small, non-propagated, membrane depolarisations (‘local responses’) could take place during this time (Hodgkin, 1938). The absolutely refractory period was succeeded by a ‘relatively refractory period’ (RRP) in which the membrane displayed a rise in threshold but could be excited nevertheless, provided relatively strong stimulation was used. During the RRP there was also a slowing of impulse conduction which was most evident close to the stimulating electrode. This last phenomenon introduces a complication into any study of nerve or muscle excitability in which recordings are made at a distance from the stimulating electrodes. Because of the slowing of impulse conduction in the RRP the time separating the arrivals of two impulses at a distant point will be greater than the interval between the two initiating stimuli. Thus, while the ARP may be determined accurately in the region of membrane underneath the stimulating electrode, it is only possible to measure an ‘irresponsive period’ when recordings are made at a distance, this period being the shortest time observed between the arrivals of two impulses.

Although there have been numerous investigations of impulse conduction velocity in normal and pathological nerves, there have been comparatively few studies of refractoriness in human nerve and muscle. Among the latter studies, the investigation of peripheral nerve by Gilliatt and Willison (1963) was noteworthy in that the significance of impulse slowing during the RRP was emphasised; more recent studies of nerve have been undertaken by Lowitzsch and Hopf (1972) and by Tackmann and Lehmann (1974). In all of the studies cited above the main trunks of peripheral nerves were examined and consequently there is no information presently available as to the refractoriness of the distal ramifications of sensory and motor nerve fibres. This omission is an important one for in neuropathies of the axonal (‘dying-back’) type the pathological abnormalities are most marked in the nerve fibre extremities (Cavanagh, 1954).

In relation to the refractoriness of muscle fibres, Farmer et al. (1960) stimulated bundles of muscle fibres with intramuscular needle electrodes and recorded from single fibres with other needle electrodes at a distance. This technique has the advantage over indirect stimulation of muscle in that the contribution of slowed impulse conduc-

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tion in motor nerve fibres to the observed results is eliminated. Nevertheless, the detection of single muscle fibre responses may be a time-consuming procedure, and it is only practicable to examine a few of the tens of thousands of muscle fibres in any one muscle. There is also the influence of the stimulating electrodes to consider, for the threshold of a muscle fibre will be altered if the fibre has been damaged in any way by the needle.

For the various reasons presented above it was thought opportune to examine refractoriness in a human nerve–muscle preparation. The present paper includes the report of a method which enables the entire ARPs and RRPs of nerve and muscle fibres to be examined (see also Betts et al., 1976); it also describes the configuration and interpretation of the muscle potentials evoked by nerve stimulation during recovery from the RRPs of the nerve and muscle fibres. In a second paper (Delbecq et al., 1978) the effects of two physiological variables, aging and temperature, are described together with the results obtained in a small series of patients with neuropathies or myopathies.

**Subjects and methods**

Seven men and six women, aged 19 to 29 years and free of neurological disorders, served as control subjects; some were investigated on several occasions. The experiments were performed with the approval of the Medical Ethics Committee of McMaster University, and informed consent was obtained from the subjects.

**RECORDING AND STIMULATION SYSTEMS**

*Recording* Evoked action potentials were recorded from the median-innervated thenar muscles with a silver disc, 6 mm in diameter, attached to the skin overlying the endplate zones of the muscles. In each subject the best position for this ‘endplate electrode’ was found as the region yielding the largest and earliest response with an initially negative deflection. The reference electrode was a silver strip, 20 mm × 6 mm, fastened around the little finger; a longer strip attached around the wrist served as an earth (ground). All the electrodes were coated with a conducting cream. The arm under study was warmed with an infrared lamp and then covered with a blanket to maintain the skin temperature at 33–34°C.

Recordings were also made from the median nerve at the elbow using two chlorided silver discs, 10 mm in diameter, their centres being separated by 30 mm; these electrodes were embedded in a Plexiglass holder. The muscle and nerve action potentials were fed into pre-amplifiers with differential input impedances of 10 MΩ, using passbands of 2 Hz–3 kHz; the peak-to-peak noise levels, with the electrodes connected, were approximately 2 μV. The potentials were displayed on a storage oscilloscope with variable persistence (Hewlett-Packard (HP) type 141B), and were simultaneously entered into a signal averager (HP Signal Analyser type 5480B). The output from the averager was taken to a programmable calculator (HP Type 9810A) which, in turn, was connected to an X-Y plotter (HP Type 9862A).

*Stimulation* Stimuli were delivered to the median nerve at the wrist or at the elbow through silver disc electrodes similar to those used for recording from the nerve (see previous section). A Velcro strap was fastened around the limb and attached to the electrode holder; in order to prevent ischaemia of the extremity the undersurface of the strap was padded with foam rubber. Electric shocks, 50 μs in duration, were delivered from a stimulator (Devices Ltd type 3072), triggered by a digital timing instrument (Devices Ltd digitimer, type 32090). Each stimulus trial was separated from the next by at least five seconds. All stimuli were 10 to 20% above the maximal value; higher intensities caused some ulnar nerve axons to be excited and prevented analysis of the thenar responses.

**SUBTRACTION TECHNIQUE**

The response (R₁) of the muscle (or nerve) to a single supramaximal stimulus was stored in the first quarter of the memory in the signal analyser and was used as a reference. The responses to a pair of shocks comprising conditioning and test stimuli (responses R₂ and R₃, respectively) were

Fig. 1  *Method for extracting R₃ responses to testing stimuli from paired R₂, R₃ (conditioning-test) potentials; see text.*
then stored in the second quarter of the analyser memory. The programmable calculator read out the contents of the two memories and subtracted that of the first quarter from that of the second. Since the response to a conditioning shock \( R_3 \) was the same as that to a solitary stimulus \( R_1 \), the subtraction gave the response \( R_3 \) to the test stimulus alone (Fig. 1). A small error was introduced because the successive moments at which the amplified responses were sampled differed between the two averaging channels, in these experiments by 100 \( \mu \)s. A correction was made using the calculator such that the two successive points in one channel were averaged and then compared with the intervening point in the second channel. A residual error remained, its size being less than 1% for a 200 Hz signal and less than 5% for one of 500 Hz.

The results of the subtraction were plotted in analogue form on the X-Y plotter. In addition the maximum peak-to-peak amplitude of the \( R_3 \) response was computed, together with the response area (voltage\(X\)time).

**Results**

**CHARACTERISTICS OF RESPONSES**

Figure 2 demonstrates the ability of the subtraction technique to detect very small muscle responses to testing stimuli after brief conditioning-test stimulus intervals. In the left hand column are oscilloscope traces showing the combined \( R_2 \) and \( R_3 \) responses at varying conditioning-test \( S_2 S_3 \) stimulus intervals; in the right hand column the \( R_3 \) responses have been extracted leaving the \( R_3 \) potentials. It can be seen that the \( R_3 \) response was absent for an \( S_2 S_3 \) interval of 1.15 ms but was clearly present when the interval was 1.3 ms. At successively greater intervals the \( R_3 \) response became larger, growing rapidly for \( S_2 S_3 \) values between 1.3 and 3 ms and more slowly afterwards.

The pooled results for 20 experiments on 18 hands are displayed in Fig. 3; for each \( S_2 S_3 \) interval the \( R_3 \) response has been plotted as an amplitude (peak-to-peak) and as a trace area (voltage-time integral), both measurements being made by computer. The forms of both types of response curves are seen to be S-shaped, with the initial segments corresponding to non-propagated muscle responses (see below). The 'amplitude' curve differs from the 'area' curve in being significantly larger at \( S_2 S_3 \) intervals 3–100 ms, and it exceeds the control value at \( S_2 S_3 \) values of 10 to 200 ms. This overshoot of the amplitude response occurred during the phase of supernormality which follows the end of the RRP in a muscle fibre; during the supernormal phase the initiation and propagation of a further impulse (in \( R_3 \)) was

![Fig. 2](http://jnnp.bmj.com/)

Fig. 2 \( R_3 \) responses to testing stimuli \( (S_2) \) delivered at different times after conditioning \( (S_2) \) shocks; stimulus intervals \((1.15–8.0 \, \text{ms})\) given at right. At left are corresponding oscilloscope traces showing the paired \( R_2 R_3 \) (conditioning-test) potentials.
fibres were not of fibres participating the 'terminal interval was increased in contrast to nerve the median R3 responses resulted in the contraction resulting from the R2 potential also contributed to the enlargement of the R3 potential. Because of the complication introduced by the supernormal period the 'area' curve provides a better indication of the number of fibres participating in a response. It was of interest that, even at the relatively long S2 S3 interval of 200 ms, the R3 response had not fully recovered to the control size, being approximately 5% diminished.

Figure 3 also shows the mean latencies of the R3 responses after S3 stimuli; these correspond to the 'terminal motor latencies' as measured in clinical electromyography. At short S2 S3 intervals the R3 responses were delayed, being 4.36 ms for a stimulus interval of 1.1 ms. As the S2 S3 interval was increased the latency of R3 shortened, reaching the control value of 2.80 ms at a stimulus interval of approximately 7 ms.

The final curve in Fig. 3 is the amplitude of the median nerve compound action potential when recorded at the elbow. It can be seen that, in contrast to the muscle fibres, some nerve fibres were capable of responding to a testing stimulus given 0.5 to 0.6 ms after a conditioning shock; the response had regained virtually the full control amplitude at a stimulus interval of 1.4 ms.

EFFECT OF STIMULUS POSITION
In six experiments paired stimuli were applied to the median nerve at the elbow, and the muscle responses were compared with those obtained after stimulation at the wrist with similar shock intervals (see above). It was found that the minimum S2 S3 interval for which an R3 response could just be detected was always less if the stimuli were applied to the elbow rather than at the wrist. An example of this difference is given in Fig. 4, in which it can be seen that the minimum interval was 0.8 ms for paired stimulation at the elbow and 1.1 ms for that at the wrist. The results differ in another respect in that the curve for 'elbow' stimulation arises abruptly from the abscissa whereas the initial segment of the curve for 'wrist' stimulation develops slowly, giving the graph an S-shape. When the individual records in Fig. 5 are examined it can be seen that the earliest R3 responses after elbow stimulation were diphasic (negative-positive), while those after wrist stimulation were monophasically negative (compare the results for 0.8 and 1.10 ms stimulus intervals).

![Figure 3](image_url)

Fig. 3  R3 responses at different conditioning-test stimulus intervals (abscissa). Values shown are of peak-to-peak amplitude (○), potential area (●), terminal motor latency (□), and median nerve action potentials at elbow (■, n). Points represent means of 20 experiments ±1 SD.
further difference between the two sets of results was that, in relation to the respective control latencies, the R₃ responses for small S₂ S₃ intervals were delayed to a greater extent when the stimuli were applied to the elbow than to the wrist.

At this point it can be stated that the two differences noted above depend on the slowing of impulse conduction in the RRP and on the additional length of nerve available for conduction between the wrist and elbow. Thus, until the RRP is terminated, the testing nerve volley (evoked by S₃) will lag further and further behind the conditioning volley (evoked by S₂), provided nerve is still available for impulse propagation. The consequences of slowed impulse conduction are dealt with in more detail in the Discussion.

In a further subject several attempts were made to obtain a set of recovery curves of ulnar-innervated thenar muscles after paired stimuli applied to the motor point of the adductor pollicis muscle. These attempts were mostly unsuccessful because the S₃ stimulus artefact could never be eliminated completely from the R₃ response. In the best of these experiments a minimum S₂ S₃ interval of 1.3 ms was obtained; the terminal latency of a control response was 1.5 ms and the distance between the stimulating cathode and the endplate electrode was 10 mm.

**Initial Muscle Responses**

As already observed, when the paired shocks were delivered to the median nerve at the elbow the earliest R₃ responses had a diphasic (negative-positive) appearance as in Fig. 5. The interpretation of such potentials was that the initial negativity represented the development of an impulse from an endplate potential while the succeeding positivity indicated propagation of the impulse, the area membrane under the stigmatic electrode now acting as a ‘source’ of current for a receding ‘sink’.

The results after nerve stimulation at the wrist were usually different in that the earliest R₃ responses were monophasically negative, as in Fig. 5 for an S₂ S₃ interval of 1.10 ms. These potentials could be shown not to propagate from the endplate since no evoked activity could be detected in simultaneous recordings made from a distant region of the muscle (Fig. 6, upper). These observations served to identify the negative poten-
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Latencies of responses

As described earlier the impulse initiated in a motor nerve axon by stimulus S₂ is followed by an ARP and then by an RRP. If stimulus S₁ is delivered to the nerve during the RRP, the evoked action potential initiated will travel along an axon with a reduced conduction velocity. Because of this slowing, the interval separating the arrivals at the motor nerve terminals of the impulses evoked by S₂ and S₃ respectively will be greater than the S₂ S₃ inter-stimulus period. There are no techniques available at present for reliably detecting action potentials in human motor nerve terminals in vivo and the best that can be achieved is to record the onset of the postsynaptic responses from the muscle fibres instead. With reference to Fig. 9, it can be seen that this time (T') is equal to the sum of the S₂ S₃ stimulus interval and the terminal latency of the R₃ response, less the terminal latency of the R₂ response—that is, T' = T(S₂ S₃) + T(R₂) - T(R₃). As long as the testing nerve impulse spends some part of its journey in the RRP, T(R₃) will exceed T(R₂) and T' will consequently be longer than S₂ S₃. Once S₃ falls outside the RRP T(R₃) will be the same as T(R₃) and hence T' will equal T(S₂ S₃).

In the 12 experiments in which the first R₃

**Fig. 5 R₃ responses at different conditioning-test stimulus intervals (numbers at right). The upper and lower traces in each pair of records correspond to stimulation at the wrist and elbow respectively. Same subject as in Fig. 4.**
response was an endplate potential, the mean value for $T'$ was $2.24 \pm 0.24$ ms. After an additional delay of 0.1–0.2 ms the monophasic endplate potentials had successfully initiated action potentials in the muscle fibres. The subsequent recovery of the full muscle action potential as a function of $T'$ is shown in Fig 7 (curve a); in this figure the mean response areas of the 20 experiments have been pooled. For comparison the figure also shows the recovery curve in terms of the $S_2 S_3$ interval (curve b), as previously plotted in Fig. 3. As would be expected from the preceding discussion the initial segment of curve a is shifted to the right of that of curve b; subsequently the two graphs fuse. Curve c in Fig. 7 displays the growth of the muscle response as a function of the time to the negative peak of the potential. In practice this measurement was easier to make than that of terminal motor latency, as used for curve a. The 'time-to-peak' measurement has a further value in that it provides information concerning the majority of muscle fibres; in contrast, the estimation of terminal latency is determined from only a small proportion of fibres, namely those generating the earliest detectable responses. In Fig. 7 it can be seen that the initial sections of curves a and c differ from b not only in being displaced to the right but in being very much steeper. Thus, as the $S_2 S_3$ interval is lengthened there is a great increase in muscle response with almost no accompanying change in $T'$. This situation arises because the decrease in terminal latency almost matches the increase in $S_2 S_3$ interval; the possible significance of this behaviour is considered later (see Discussion).

The steepness of the recovery curve is reflected in Fig. 8 in which successive increments in response area have been shown as functions of $T'$. Using measurements of terminal latency, the largest increments occur within the 2.40–2.80 ms epochs; when measurements of latency-to-peak are used instead, the unimodality of the results is more striking still, 75% of recovery taking place between 3.0 and 3.2 ms.

**Discussion**

The events in time and space which follow the initiation of an impulse in a motor axon can be displayed diagrammatically, as in Fig. 9. In this figure the abscissa represents the distance between the site of stimulation of a motor axon and the endplate zone of a muscle fibre within the motor unit. The two ordinates represent time after a conditioning stimulus ($S_2$ being delivered at zero time). The lowest curve represents the passage of the impulse evoked by $S_2$ from the stimulating electrode to the muscle fibre. For most of its journey from the wrist the velocity of the impulse is constant, and it is not until the boundary of the muscle has been reached that appreciable slowing occurs. Thus, when the stimulating electrodes were applied in the palm over the motor point of
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Fig. 7  $R_3$ response areas (voltage\times time) plotted as functions of intervals between stimuli (b), onsets of $R_2$ and $R_3$ responses (a), and negative peaks of $R_2$ and $R_3$ responses (c); see text.

Fig. 8  Increases in $R_3$ potential as functions of intervals between onsets (filled columns) and peaks (open columns) of $R_2$ and $R_3$ responses. Same data as in Fig 7.
the thenar muscles the evoked response had a latency of approximately 1.5 ms, the distance to the endplate recording electrode being about 10 mm; the mean terminal latency after stimulation at the wrist was 2.8 ms, and the corresponding conduction distance was about 80 mm. These results correspond to impulse conduction velocities of 54 m/s from the wrist to the motor point and of 8 m/s from motor point to endplate, allowing 0.2 ms for the release and diffusion of transmitter from the motor nerve terminal (Hubbard and Schmidt, 1963). The value for impulse conduction velocity beyond the motor point is a gross estimate which does not take into account the progressive slowing which would occur each time an axon divided into thinner branches; nor would it allow for the extra distances incurred by an axon pursuing a tortuous rather than a direct path towards a muscle fibre. It is of interest that similar terminal motor latencies (1.2–1.5 ms) were obtained after the stimulation of a variety of other muscles at their motor points with the recording electrodes being placed over the endplate zones at distances of approximately 10 mm; these muscles included the abductor digiti minimi, extensor digitorum brevis, and biceps brachii. Returning to Fig. 9, the time \( a \) denotes the ARP of the motor axon under the stimulating cathode after the initial impulse. In these experiments this value was determined by recording the compound action potential of the nerve at the elbow; the value for the first axons to recover was 0.5–0.6 ms. Inspection of Fig. 3 shows that the ARPs were over in about 95% of fibres by 1.1 ms. The RRPs of the motor axons at the point of stimulation could have been determined by measuring the minimal \( S_2 \) \( S_3 \) interval at which the compound action potential had regained its control latency. These measurements were omitted in the present study but the related experiments of Lowitzsch and Hopf (1972) yielded a mean value of 3.08 ms for the RRP on the basis of latency; the corresponding ARP of 0.51 ms was similar to the present one.

Suppose now that the testing stimulus, \( S_3 \), is given at the moment the ARP finishes (at time \( a \) in Fig. 9). The ensuing impulse is slowed as it travels in the RRP and Fig. 9 shows that, to begin with, it becomes increasingly separated from the ARP as it recedes from the stimulation site. In the present experiment, however, such an impulse still failed to evoke a muscle response if it was initiated in the early part of the RRP (up to 1 ms). The simplest explanation would be that the neuromuscular junctions were activated while the muscle fibres were still in their own ARPs after response \( R_2 \). It is known from the early experiments of Kuffler (1942) that synaptic transmission will not add any extra depolarisation during the spike component of a muscle fibre action potential, and hence the effect of a second nerve impulse arriving at that moment will be undetected. However, if the second nerve impulse is slightly delayed so as to arrive just after the spike component of a muscle fibre, the latter can respond to synaptic transmission with a local potential. Using the extracellular recording technique of the present experiments, these local potentials presented as monophasic negative deflections and, upon occasions, had the characteristic sharply rising appearance of endplate potentials (see Fig. 6, lower). The fraction of the ARP during which only local potentials could be detected was approximately 0.1–0.2 ms (no in Fig. 9). Nerve impulses arriving later than this evoked diphasic potentials; these responses signified that impulses had been initiated in the muscle fibres and that the RRPs of the fibres had begun. This type of behaviour, namely a local response followed by a propagated potential at a slightly greater conditioning-test interval, was encountered in 12 of the 20 experiments. In the remaining eight experiments it appeared that the element with the longest refractoriness may not have been the muscle fibre but the fine nerve
twigs. In these experiments the initial response recorded from the muscle to the testing (S₃) stimulus was a diphasic potential, signifying that the muscle fibres had already emerged from their ARPs by the time that the testing nerve volley had reached the axon terminals. In these preparations one might envisage that a slightly earlier impulse travelling in the RRP of the motor nerve fibre might be suppressed by an abrupt increase in ARP, presumably at a site where fine nerve twigs are formed from the parent axon. Even in the 12 preparations in which the initial R₃ responses at some of the neuromuscular junctions were local potentials, it appeared that at the remaining junctions the axons had the longest refractory periods. Thus, the extreme steepness of curves a and c in Fig. 7 indicates that, as the S₂ S₃ interval is lengthened, increasingly large numbers of muscle fibres can respond, even though hardly any extra time has been gained between the arrivals of the conditioning and testing nerve volleys at excitable neuromuscular junctions. Such a situation could have arisen if, at most junctions, the muscle fibres were ready to fire again before their axon twigs had recovered from their ARPs. The enlargement of the response would then reflect increasing numbers of conducting axons, each exciting previously primed muscle fibres.

From Fig. 7 it is possible to derive values for the ARP of the nerve-muscle preparation in two ways. First, by using terminal latency measurements, more than half of the nerve-muscle fibres appeared to have ARPs in the 2.2–2.8 ms range. However, these values depend on activity in the fastest conducting nerve fibres only and, for this reason, measurements were also made of the latencies to the negative peaks of the evoked muscle responses. These measurements give a better indication of the behaviour of the nerve-muscle fibre populations as a whole; their drawback is that the rate of rise of the test muscle response (R₃) will be decreased during the RRP since not all the sodium conductance channels in the muscle fibre membrane are available for activation. Thus the ARP of 3.0–3.2 ms, derived for 75% of fibres in this way, should be regarded as an upper limit. On the basis of the above reasoning a better estimate for the ARP would be 2.5–3.0 ms in the majority of fibres. These values are significantly smaller than the mean ARP of 3.6 ms found by Farmer et al. (1960) using direct stimulation of muscle fibres. The same authors obtained a lower limit of 2.2 ms in the population of muscle fibres studied; in the present investigation the shortest response interval (T') observed for a propagated response was 2.0 ms. The present examination differs from that of Farmer et al. (1960) in finding no evidence of a bimodal distribution of ARPs among the muscle fibres. This anomaly might well depend on differences of technique but there is the added possibility that, in terms of excitability, the intrinsic muscles of the hand contain a more homogeneous population of fibres than the larger muscles of the limbs, as studied by Farmer and colleagues.

Unfortunately, the present study does not enable an upper limit to be determined for the muscle fibre ARP because of the problem introduced by diminution of the action potential during the RRP. Thus, beyond the steep part of the muscle recovery curve (Fig. 7) it is not possible to distinguish between the excitation of additional muscle fibres and the further enlargement of action potentials in fibres already recruited. On the basis of the amplitudes of the compound muscle action potentials, it would appear that the majority of the muscle fibres pass from the RRP into the supernormal period when the S₂ S₃ interval is about 10 ms; deducting 2.7 ms for the mean ARP, the RRP would be approximately 7.3 ms. The supernormal period was greatest at approximately 50 ms and was still present at 100 ms. Similar estimates of supernormality have been made on the basis of impulse conduction velocities in single fibres by Stålberg (1966). In contrast Farmer et al. (1960) estimated that the supernormal period occupied only 6–10 ms post-stimulus on the basis of conduction velocity, or 5–30 ms on the basis of threshold for excitation.

So far as the motor nerve fibres are concerned, the determination of the ARP and RRP at the point of stimulation has already been described (see above). For that segment of nerve between the stimulating electrode and the endplate the analysis is complicated in some of the experiments by the refractoriness of the muscle fibres. This complication did not arise in the 12 experiments in which the initial muscle fibre response was a local potential, for clearly the ARPs of the most excitable nerve fibres cannot have been greater than the corresponding value for T' (2.25 ms). For the remaining fibres, however, reasons have already been presented for supposing that the ARPs of the terminal motor axons were either equal to, or rather greater than, those of the corresponding muscle fibres. The majority of nerve fibres would, therefore, be expected to have ARPs of less than 3.0 ms (see above).

The RRRPs of the most excitable terminal motor axons can be estimated by finding the least S₂ S₃ interval for which the latency of the R₃ response is equal to that of the control (R₂) response. With
reference to Fig. 9, an impulse starting at (time) \( d \) will depolarise the muscle fibre at \( p \); the terminal motor latency (\( dp \)) will be slightly prolonged, however, since the nerve impulse will have travelled the last part of its journey within the RRP and will have been slowed accordingly. In contrast a nerve impulse initiated at \( e \) will just avoid entering the RRP of the distal ramifications of the motor axons and will depolarise the muscle fibre at \( q \); the corresponding terminal motor latency (\( eq \)) will be equal to the control value (\( m \)). From Fig. 7 it was found that the RRP of the most excitable motor axon terminals, determined in this way, lasted approximately 5 ms from the end of the ARP. This result is double the value of 2.5 ms found for the motor axons in the forearm by Gilliatt and Willison (1963); the difference would be expected because it is known that small nerve fibres, such as those formed by repeated divisions and subdivisions of the parent motor axon, have long refractory periods, together with low conduction velocities and high thresholds for excitation (Blair and Erlanger, 1933).

Apart from the measurements of refractoriness in terminal motor axons and muscle fibres, the present study has enabled for the first time the endplate potentials of human muscle to be recorded in situ. It remains to be seen whether these new types of measurement will be of value in the investigation of nerve and muscle diseases.

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