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A STUDY OF SOME ELECTROPHYSIOLOGICAL PROPERTIES OF HUMAN INTERCOSTAL MUSCLE

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It is of interest to compare the electrophysiological properties of normal human skeletal muscle with those of other mammalian species. In the present investigation the spontaneous subthreshold activity at the myoneural junction has been studied, and the membrane constants of the muscle fibres have been determined. As did Dillon, Fields, Gumas, Jenden & Taylor (1955); and Creese, Dillon, Marshall, Sabawala, Schneider, Taylor & Zinn (1957), we also found that human intercostal muscles proved to be excellent preparations for studies *in vitro*. It will be shown that the electrophysiological properties of these muscles are rather similar to those of other mammalian species, except that the frequency of the miniature end-plate potentials (m.e.p.p.) is considerably lower, and the membrane resistance higher.

METHODS

During thoracotomy operations on eight patients of both sexes and with no known muscle disease, specimens of external intercostal muscle were removed from the 5th, 6th, or 7th intercostal space in the mid-axillary line. The muscles were carefully dissected so that the specimens contained both origin and insertion, with continuous periosteum. Immediately upon removal the specimens were placed in continuously oxygenated Tyrode solution and taken to the laboratory for dissection and study. As described by Creese *et al.* (1957), longitudinal fusiform bundles of fibres, with their fibrous origin and insertion intact, could be dissected under a binocular microscope. The isolated bundles were about 15 mm long and 0·2–0·5 mm in diameter. They were mounted in a bath kept constantly at 37° C.

The composition of the bathing fluid was that used by Liley (1956) and it was oxygenated by bubbling 95 % O_2 + 5 % CO_2 through it immediately before its introduction into the muscle bath. The bath held about 30 ml. of solution, which was changed continuously at a rate of about 500 ml./hr.

The usual techniques were employed for intracellular recording with capillary glass micro-electrodes (Fatt & Katz, 1951). Electrodes of between 5 and 10 MΩ resistance were used, and the input time constant of the recording circuit was 20–50 μsec. M.e.p.p.s were photographed from an oscilloscope tube on single sweeps of 50 msec/cm. Usually at least twenty m.e.p.p.s were recorded from each fibre.

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Membrane constants were determined by the method of 'square-pulse analysis' (Hodgkin & Rushton, 1946; Fatt & Katz, 1951). The duration of the current pulse was 100–120 msec. The experimental procedure and methods of calculations were similar to those used by Boyd & Martin (1959) with the cat tenuissimus muscle.

RESULTS

It was possible to maintain the isolated muscle bundle in good condition for several hours with no significant decay of resting potentials, which ranged from 70 to 90 mV, with a mean of about 80 mV (Table 1). At the neuromuscular junction spontaneous subthreshold electrical activity was recorded (Fig. 1). These m.e.p.p.s were similar to those observed in frog muscle (Fatt & Katz, 1952), in rat diaphragm (Liley, 1956) and in cat tenuissimus muscle (Boyd & Martin, 1956). Their mean amplitude was about 0·7 mV, and they appeared to occur at random intervals. The

TABLE 1. The mean values and their S.E. for resting membrane potential, amplitude and frequency of m.e.p.p.s in four human intercostal muscles. For comparison similar values obtained from cat tenuissimus and rat diaphragm are shown. The numbers in brackets indicate the number of muscle fibres

Type of muscle	Resting membrane potential (mV)	Amplitude of m.e.p.p.s (mV)	Frequency of m.e.p.p.s (per sec)
Human intercostal	80·9 ± 1·00 (15)	0·74 ± 0·013 (26)	0·26 ± 0·065 (25)
Cat tenuissimus (Boyd & Martin, 1956)	75	0·54 ± 0·14 (54)	1·43 ± 0·88 (72)
Rat diaphragm (Liley, 1956)	73	0·6	1–2

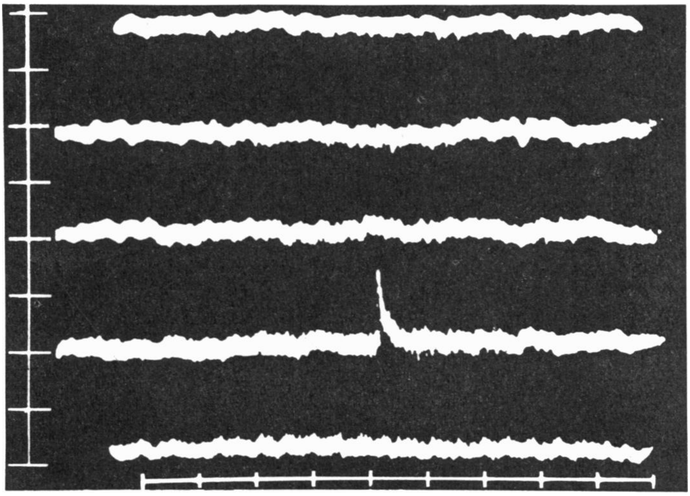

Fig. 1. A m.e.p.p. recorded on single successive sweeps. Human intercostal muscle; male aged 65. Time marker, 50 msec; voltage calibration, 0·5 mV.

frequency of discharge was, however, considerably lower than that reported from other species, the average being only 0·2/sec (Table 1). An increase in the osmotic pressure of the bathing fluid resulted in an immediate and marked increase of the frequency of the m.e.p.p.s (Fig. 2) (cf. Liley, 1956).

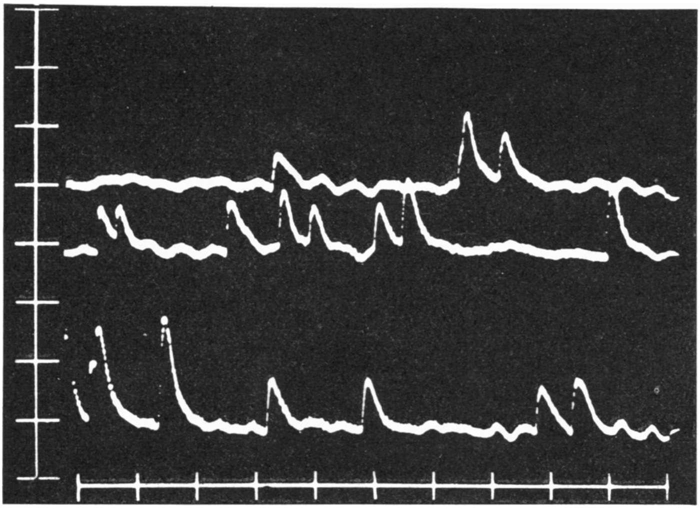

Fig. 2. Increased rate of m.e.p.p.s produced by hypertonic Tyrode solution. Human intercostal muscle; female aged 43. Time marker, 10 msec; voltage calibration, 0·5 mV.

The membrane constants were determined by inserting two microelectrodes into the fibre, at first as close together as possible, and then again at distances of about 0·5 and 1·0 mm between the electrodes. A rectangular hyperpolarizing current pulse was passed through one of the electrodes and the resultant change in membrane potential was recorded by the other. By applying the cable theory of Hodgkin & Rushton (1946) the potential change, V, produced by a steady current, I, through the membrane is given by the equation,

$$V = \tfrac{1}{2}I\,\sqrt{(r_m . r_i)}\,\exp\left[-x/\sqrt{(r_m/r_i)}\right],$$

where x is the electrode separation, r_m the transverse resistance of a unit length of fibre membrane, and r_i the internal longitudinal resistance per unit length of fibre. The term $\sqrt{(r_m . r_i)}$ is the space constant λ of the fibre.

When the ratio $V:I$ was plotted on a logarithmic scale against the electrode separation, almost straight lines (Fig. 3) were obtained. λ is the distance over which the electrotonic potential fell to $1/e$ of its value. $\tfrac{1}{2}\sqrt{(r_m . r_i)}$ was obtained from the point at which the lines intersected the vertical axis. From these two values r_m and r_i were calculated.

The specific resistivity of mammalian myoplasm, R_i, has been estimated as 125 Ω.cm by Boyd & Martin (1959), and this value was also used in our calculations. The fibre radius, ρ, was obtained from the relation

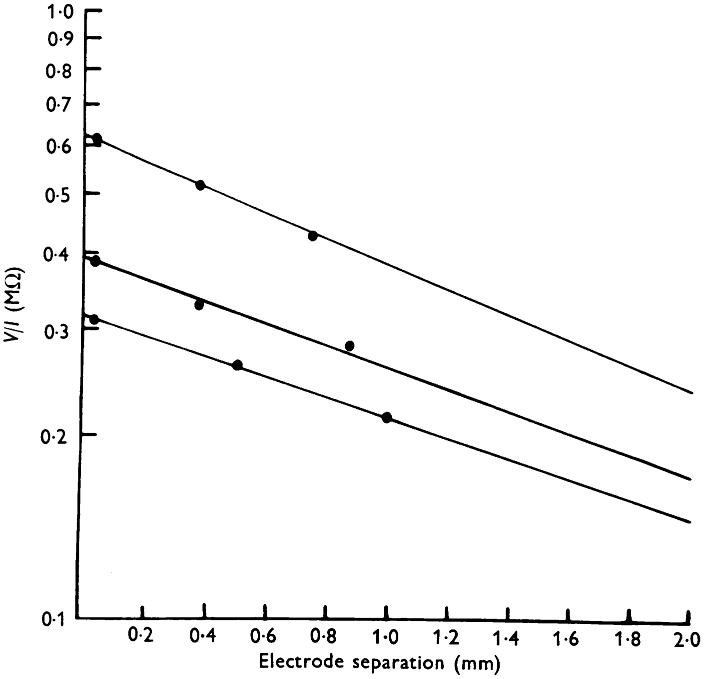

Fig. 3. Spatial decay of electrotonic potentials in three fibres. Ordinate, amplitude of electrotonic potential, when a steady state is recorded, divided by amplitude of current pulse; logarithmic scale. Abscissa, separation between current and voltage-recording electrodes.

TABLE 2. Data derived from two human intercostal muscles in which curves were obtained similar to those in Fig. 3. *RP* = resting membrane potential at the beginning and end of each experiment

	Fibre	$\frac{1}{2}\sqrt{(r_m \cdot r_i)}$ (Ω)	$\lambda = \sqrt{(r_m/r_i)}$ (mm)	τ_m (msec)	ρ (μ)	R_m (Ω cm²)	C_m (μF/cm²)	*RP* (mV)
Female, 30 years	1	6×10^5	1·75	20·5	24	3200	6·4	84–82
	2	$3{\cdot}9 \times 10^5$	2·10	20·5	33	3420	6·0	85–71
	3	$3{\cdot}9 \times 10^5$	2·44	20·5	35	4200	4·9	88–78
Male, 38 years	1	$6{\cdot}4 \times 10^5$	2·35	18·0	27	5100	3·5	86–72
	2	$6{\cdot}1 \times 10^5$	2·27	15·5	27	4700	3·3	90–80
	3	$3{\cdot}1 \times 10^5$	2·65	14·0	41	4200	3·3	86–81
	4	$4{\cdot}3 \times 10^5$	2·15	23·0	32	3700	6·2	83–70
Mean			2·24	18·9	31	4070	4·8	
Cat's tenuissimus (Boyd & Martin, 1959)								
Mean			1·10	4·9	22	1430	3·5	

$\rho = \sqrt{(R_i/\pi r_i)}$ and the transverse resistance of a unit area of membrane, R_m, by $R_m = 2\pi\rho r_m$. The time constant of the membrane, τ_m, was measured from the time taken for the potential to rise to 83 % of its maximum steady value, at about zero electrode separation. The membrane capacitance per unit area, C_m, was then derived from $C_m = \tau_m/R_m$.

The results of such calculations for seven fibres are shown in Table 2, along with the corresponding values for the cat tenuissimus muscle, for comparison. It is evident that the membrane resistance of the human intercostal muscle is considerably higher than that of the cat tenuissimus muscle. The calculated values for the fibre diameters agree with the value of about 60μ obtained by direct measurements from histological transverse sections by Creese *et al.* (1957).

DISCUSSION

The isolated human intercostal muscle has proved to be a stable preparation which is well suited for studies with intracellular electrodes. It can be obtained during thoracotomy procedures or by biopsy. Thus it seems appropriate to use that muscle in studies of the alterations in the electrophysiologic behaviour of human skeletal muscle in disease of muscle and lower motor neurone.

The low frequency of m.e.p.p.s in the human as compared with other species is difficult to explain. It is possibly related to the fact that all our specimens were obtained from adult patients, i.e. from mammals of a much greater age than that of any laboratory animal. Or it may be that a low 'miniature' frequency is a unique property of the intercostal muscle, as opposed to other skeletal muscles. The transverse resistance of the fibre membrane is about 4000 Ω.cm^2, which is higher than that of the cat tenuissimus muscle, but about the same as that observed by Fatt & Katz (1951) for frog muscle.

SUMMARY

1. By the use of intracellular electrodes the spontaneous miniature end-plate potentials and the membrane constants of the muscle fibre have been studied in the isolated human intercostal muscle.

2. The mean resting membrane potential was about 80 mV. The average frequency of miniature end-plate potentials was about 0·2/sec, and their mean amplitude, 0·7 mV.

3. The transverse resistance of the fibre membrane was about 4000 Ω.cm^2 and the membrane capacitance varied between 3 and 6μF/cm^2.

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