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GROUP Ia SYNAPTIC INPUT TO FAST AND SLOW TWITCH MOTOR UNITS OF CAT TRICEPS SURAE

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SUMMARY

1 The characteristics of the group Ia synaptic input to triceps surae motoneurones have been examined in pentobarbitone-anaesthetized cats, using intracellular recording techniques. The mechanical properties of the muscle units innervated by the cells were determined and the motoneurone input resistance values were also measured.

2. A significant positive correlation was found between the maximum amplitudes of homonymous composite (electrically evoked) monosynaptic excitatory post-synaptic potentials (EPSPs) and the motoneurone input resistance values across the entire population of units sampled. The same correlation in the case of heteronymous EPSPs was also significant although somewhat less strong.

3. The distribution of the amplitudes of unitary miniature EPSPs (mEPSPs) of presumed group Ia origin, elicited by small static stretches of the homonymous muscles, were also studied. A significant positive correlation was found between the median amplitudes of the mEPSP distributions and the input resistance values in the motoneurones studied. Positive correlation was also observed between the amplitudes of the median mEPSPs and the maximum homonymous composite EPSPs in the cells for which both data points were available.

4. In each of these correlations, the synaptic potential amplitudes tended to be larger in the relatively high resistance type S (slow twitch muscle unit) motoneurones from both gastrocnemius and soleus motor pools, than in the lower resistance type F (fast twitch muscle unit) gastrocnemius cells.

5. Examination of the shape of the homonymous monosynaptic EPSP wave forms in different motoneurones showed that these tended to be significantly longer in duration in type S cells than in type F. This differ-

ence could not be entirely accounted for by the relatively small difference in mean time constant values found in types F and S cells.

6. The results suggest that the density of group Ia synaptic terminals tends to be higher on type S motoneurones than on the type F cells. Further, cells receiving a relatively high density of group Ia input apparently tend to have a greater proportion of this input distributed to distal membrane regions than is the case in motoneurones receiving a relatively low input density.

INTRODUCTION

In a previous paper (Burke, 1967*a*) evidence was presented for the notion that cat triceps surae motor units, defined as including the motoneurone plus the innervated fascicle of muscle fibres or muscle unit, can be divided into two groups, fast twitch (type F) and slow twitch (type S), on the basis of the mechanical response of the muscle unit. There were also significant differences in a number of motoneurone properties across the population of motor units studied, but it was not possible to make any clear-cut distinctions or groupings on the basis of these properties alone.

The patterns of motor unit properties dealt with in the above paper can be regarded as *intrinsic* to the units. In the present paper an attempt has been made to examine what may be regarded as an *extrinsic* characteristic of motor units, that is, the relative amount and organization of synaptic input to triceps surae units. This study has been limited to the monosynaptic group Ia input, both for technical simplicity and because this excitatory input to extensor cells is of considerable interest as it relates to motoneurone properties (see Eccles, Eccles & Lundberg, 1957*a*; Mendell & Henneman, 1967) and to motor unit firing patterns (see Denny-Brown, 1929; Granit, Henatsch & Steg, 1956; Granit, Phillips, Skoglund & Steg 1957; Henneman, Somjen & Carpenter, 1965*a*, *b*; Burke, 1968).

The present experiments were designed to study the inter-relation between the characteristics of group Ia afferent input to triceps surae motor units and (*a*) the apparent motoneurone size as measured by cell input resistance values (see Rall, 1959; Kernell, 1966; Burke, 1967*a*), as well as (*b*) the twitch type (type F or type S) of the units. The data were obtained for the most part from the same series of motor units studied in the previous report (Burke, 1967*a*). The results suggest several conclusions: (1) the density of group Ia synaptic contacts is apparently greater on the smaller high resistance type S motoneurones, which consequently tend to have larger monosynaptic EPSPs than are found in the lower resistance type F cells; (2) there is, however, no clear-cut point of distinction evident between types F and S cells in the apparent amount of group Ia input; and (3) examination of EPSP wave form dimensions

suggests that there is a tendency toward differences in the spatial distribution of group Ia endings on the receptive surfaces of type F and type S motoneurones, the latter tending to have a larger proportion of the input on distal dendritic membrane regions than the former. The interrelation of these factors with the dynamic reflex activity patterns of the motor units, studied in decerebrate preparations, will be examined in the next paper (Burke, 1968).

METHODS

The data to be reported in this paper were obtained largely from the series of experiments described fully in a previous report (Burke, 1967*a*). Briefly, cats anaesthetized with pentobarbitone were placed in a steel frame immobilizing the lumbosacral spine and the right hind limb. Both hind limbs were denervated except for the right medial gastrocnemius (MG) and lateral gastrocnemius-soleus (LG-Sol) nerves, which remained connected with the muscles and were placed on flexible stimulating electrodes. The tendons of the three heads of the triceps surae muscle (MG, LG and Sol) were separated from one another, cut and arranged for independent attachment to a myograph strain gauge. Muscle bellies and peripheral nerves in the right hind limb, as well as the exposed spinal cord, were covered with mineral oil pools maintained at 35–37° C. All dorsal and ventral roots remained intact. Most of the intracellular recordings were made with glass micro-electrodes filled with 2 M potassium citrate but in a few cases 3 M potassium chloride-filled pipettes were employed.

Records were made from which the motoneurone axonal conduction velocity was measured and the cell input resistance was determined by the spike-height method of Frank & Fuortes (1956). The mechanical properties of the muscle unit innervated by the motoneurone under study were recorded during intracellular stimulation of the cell with depolarizing current pulses passed through the micro-electrode. Intracellular data were included in the present report only if the motoneurone membrane potential exceeded -55 mV during recording. A number of additional experiments were performed using unanaesthetized decerebrate cats. Data from these animals are included in the membrane time constant section of the present report but not in the EPSP amplitude sections, for reasons which will be dealt with in the subsequent paper (Burke, 1968). Additional methods specific to obtaining data on the group Ia synaptic input to motoneurones are outlined below.

Maximum amplitude of homonymous and heteronymous monosynaptic ESPSs. Since both dorsal and ventral roots were intact in these preparations, the maximum homonymous EPSPs elicited by electrical stimulation of the MG or LG-Sol nerves could be studied only in situations in which antidromic invasion of the motoneurone under observation was not superimposed on the EPSP (see Eccles *et al.* 1957*a*). Three such situations are possible, as illustrated in Fig. 1. The threshold for the motoneurone axon may be higher than most or all of the group Ia axons in the muscle nerve (Fig. 1, A_1, A_2). This was the case with a number of type S gastrocnemius and soleus cells. The afferent spike potential recorded at the dorsal root entry zone then showed no increase as the stimulus intensity was raised above threshold for the motor axon. A second possibility is spontaneous blockade of antidromic invasion distal to the initial segment, resulting in an orthodromic EPSP superimposed on an antidromic M spike (Fig. 1, B_1; see Coombs, Curtis & Eccles, 1957). The amplitude of the EPSP was then measured from the extrapolated falling phase of the M spike (as in Fig. 1, C_2, dotted line). Finally, when antidromic invasion of the cell did interfere with EPSP measurement, it was necessary to block antidromic invasion with hyperpolarizing current pulses passed through the micro-electrode, as shown in Fig. 1, C_1 and C_2. No correction was made for EPSP amplitude changes due to the hyperpolarizing current, since such changes have been shown to be negligible (Coombs, Eccles & Fatt, 1955*a*; Nelson & Frank, 1967).

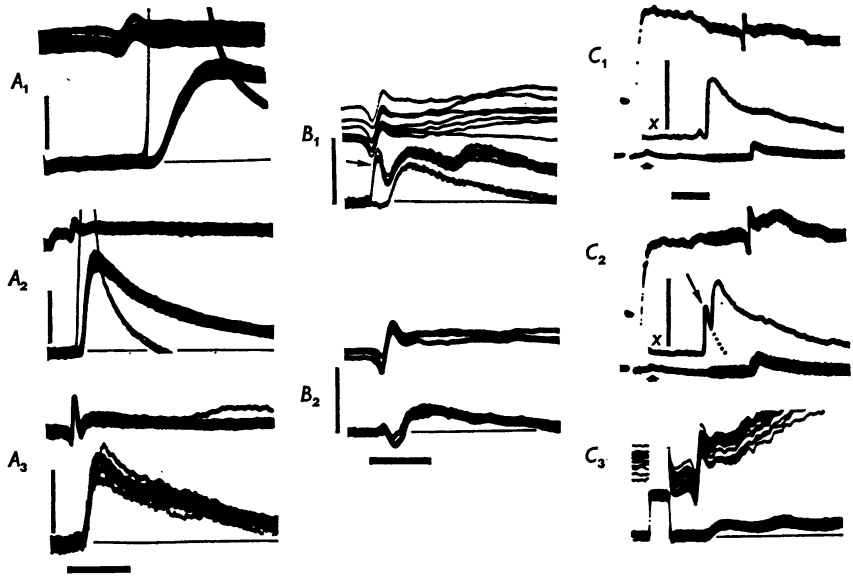

Fig. 1. Maximum homonymous and heteronymous monosynaptic EPSPs elicited by electrical stimulation of the MG or LG-Sol branches of the triceps surae nerve.

A. Type S MG motoneurone in which the maximum homonymous EPSP amplitude was attained with stimulus intensity below threshold for the motoneurone axon (A_1 A_2). Note lack of increase in the afferent spike at the dorsal root entry (upper trace in each frame) as stimulus was increased above threshold for the antidromic spike. Photographically superimposed records recorded on two different time bases. A_3 shows the maximum heteronymous EPSP (stimulus to LG-Sol nerve). Calibrations: 5 mV for A_1, A_2; 2·5 mV for A_3; time bar = 1 msec for A_1, 5 msec for A_2, A_3.

B. Maximum homonymous (B_1) and heteronymous (B_2) EPSPs in type F MG motoneurone in which spontaneous blockade of initial segment antidromic invasion occurred (note M spike in B_1, indicated with arrow). B_1 shows superimposed records taken with stimulus below (no M spike) and above (with M spike, arrow) the motoneurone axon threshold. Note late EPSP in the larger response. B_2 shows the heteronymous EPSP superimposed on antidromic field potential from invasion of neighbouring motoneurones. Calibrations: 5 mV and 2 msec.

C. Homonymous (C_1, C_2) and heteronymous (C_3) EPSPs in type F MG cell. C_1 shows the submaximal response to MG nerve stimulation during a hyperpolarizing current pulse (beginning at small arrow in the lower trace) passed through the micro-electrode; C_2 shows the maximum homonymous EPSP, superimposed on antidromic M spike (arrow) with full antidromic invasion blocked by the hyperpolarizing current. Estimated decay curve of M spike shown with dotted line. The top trace in each frame is the dorsal-root entry zone potential, lower trace is the intracellular potential on the same time base and low gain, and the middle trace (marked *X*) shows the EPSP on expanded gain and time scales. Calibration bars refer to the expanded traces and equal 5 mV and 2 msec. C_3 shows the maximum heteronymous EPSP. Calibration pulse = 5 mV and 1 msec.

Measurement of the maximum amplitude of heteronymous EPSPs (Fig. 1, A_3, B_2 and C_3) presented no problem other than the occasional distortion of the earliest phase of the PSP by the field potential generated by the antidromic invasion of neighbouring motoneurones, as in Fig. 1, B_2. It must be noted here that the LG and Sol nerves were stimulated together in these preparations (see Burke, 1967*a*, fig. 1), so that the 'homonymous EPSP' in LG or Sol cells actually represented a mixed EPSP with some heteronymous component, while the 'heteronymous' synaptic potential in the same LG or Sol cells represented only the MG input. As will be seen, the data points for the LG 'homonymous' and 'heteronymous' EPSPs did not distribute differently from those derived from MG cells in which the homonymous-heteronymous distinction was correct (e.g. see Fig. 6). The observations of Eccles and co-workers (Eccles *et al.* 1957*a*) indicate that group Ia input from LG to Sol motoneurones, and vice versa, tends to be smaller than that from MG to either group of cells. Therefore, the EPSP amplitude data from MG, LG, and Sol motoneurones have been treated as equivalent and the error introduced by this is probably negligible as regards the conclusions to be drawn from the present analysis.

Amplitude distributions of presumed group Ia unitary miniature EPSPs. Since the afferent pathways from triceps surae stretch receptors to the cord remained intact in these preparations, it was possible to record the unitary miniature EPSPs (mEPSPs) resolvable in synaptic activity produced by small stretches of one or another of the muscle heads in the homonymous motoneurones (see Kolmodin & Skoglund, 1958; Granit, Kellerth & Williams, 1964; Burke & Nelson, 1966). With moderately deep barbiturate anaesthesia as used here the 'spontaneous' synaptic activity impinging on these neurones (see Katz & Miledi, 1963; Hubbard, Stenhouse & Eccles, 1967) was reduced to a rather low level and the mEPSP activity elicited by small amounts of muscle stretch could be examined against a relatively quiet background (Fig. 2, upper record). There is evidence suggesting that the unitary mEPSPs which can be resolved in such stretch-elicited activity arise largely from impulses in single group Ia afferent fibres connecting with the neurone being recorded (Burke & Nelson, 1966; Burke, 1967*b*).

During the experiments the synaptic activity elicited by small stretches of the muscle head homonymous to the penetrated motoneurone was recorded on FM magnetic tape and, subsequently, selected portions were photographed on moving film with high gain and high film speed. Using records in which unitary mEPSPs could be resolved (see Fig. 2, lower records) and in which the noise level of the recording system was fairly small (peak to peak background noise not exceeding 80 μV), the amplitudes of 100 successive identifiable mEPSPs were measured. Potentials apparently caused by several superimposed mEPSPs were not included (Fig. 2, lower records, marked with questions) unless they could clearly be seen to be composed of two or three separable mEPSPs. The amplitude data thus obtained were plotted as histograms and the median amplitude as well as the upper and lower amplitude limits enclosing 90 % of the distributions were determined. Sample records and amplitude histograms from three representative units appear in Fig. 7.

Wave form characteristics of homonymous monosynaptic EPSPs. Evidence has been presented elsewhere which suggests that the group Ia monosynaptic EPSP evoked by electrical stimulation of a muscle nerve in the homonymous motoneurone is generated by synapses widely distributed over the receptive surface of the cell and that the shape of the EPSP wave form can give some idea of the relative proportion of juxta-somatic to more distal dendritic inputs contributing to the composite EPSP (Burke, 1967*b*; Rall, Burke, Smith, Nelson & Frank, 1967). The wave form measurements which have been most useful in comparing EPSP wave forms from different cells are (1) the EPSP time to peak, or the duration of the rising phase of the potential transient from the first point of inflexion to the point of maximum amplitude, and (2) the EPSP half-width, or the duration of the potential transient between points on the rising and falling phases which are at one half the peak amplitude (see Rall, 1967). In the present data analysis, measurement of these wave form dimensions was made only when the EPSP outline was not recognizably distorted by a late EPSP

apparently generated by ephaptic activation of the afferents by the muscle action potential (Fig. 1, B_1 and C_3; see Lloyd, 1942), or by a late group Ib IPSP (Eccles, Eccles & Lundberg, 1957*b*). In many cases these requirements necessitated measurement of EPSPs generated by somewhat submaximal afferent volleys. This is assumed to have introduced no systematic error since it has been demonstrated that the over-all outline of electrically-evoked EPSPs changes little over a rather wide range of variation in the afferent volley size (Coombs *et al.* 1955*a*).

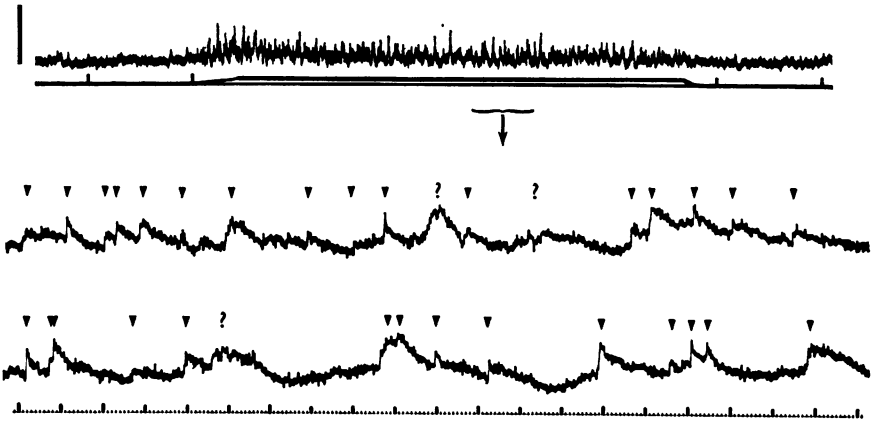

Fig. 2. *Top record:* Intracellular recording of synaptic activity elicited in a type F MG motoneurone during small (about 20 g) tonic stretch of the MG muscle (indicated by displacement of myograph record in lower beam). Calibration bar = 2 mV; time marks = 500 msec. *Bottom records:* Continuous film record of the portion of synaptic activity included in the bracket under the upper record, on greatly expanded time scale (time marks = 1 and 10 msec) and increased gain (upper calibration bar = 1 mV). Unitary mEPSPs identified as single events are marked with arrows; events of probably multiple mEPSP origin indicated by question marks.

Membrane time constant measurement. As pointed out elsewhere (Rall *et al.* 1967) comparison of EPSP wave form shapes recorded from different cells necessitates some knowledge of the passive membrane time constant (τ) values for the individual cells. For technical reasons (mainly electrode rectification and polarization) such measurements were not obtainable from each cell yielding EPSP shape data. However, in a subset of cells conditions were sufficiently good to permit determination of the time constant. In these cases, time constant values were derived from measurements of membrane voltage transients during relatively small, long duration pulses of constant current passed into the cells through the micro-electrodes via a bridge circuit. The instances selected for τ measurement were those in which the bridge balance remained stable at the initiation and at the end of the current pulse, without apparent rectification in the electrode (Fig. 3*B*). In many cases, the extracellular electrical behaviour of the electrodes was checked and this was usually excellent, but this was not used as a criterion for selection of the data to be included. In a few instances, double-barrelled micro-electrodes of 'theta' shape were employed (see Coombs, Eccles & Fatt, 1955*b*; Nelson & Frank, 1967) which were filled with 3 M potassium chloride.

Membrane time constant values were derived from the voltage transient records by the method of Rall (1960; see also Lux & Pollen, 1966). Photographically superimposed records of the charging transient were made (Fig. 3*A*) and the most closely fitting curve was

drawn by eye from enlarged tracings. The instantaneous slope (dV/dt) of the voltage transient was calculated at a number of points in time (t) along the curve and the natural logarithm of the quantity ($\sqrt{t}.dV/dt$) was plotted against t on linear co-ordinates (see Fig. 3, graph). The linear portion of this plot is dominated by the electrical properties of the cell membrane when the cell geometry is such that the dendritic to somatic conductance ratio (ρ) of the cell $\geqslant 2$; the reciprocal of the slope of the line then approximates to the membrane time constant value (see Rall, 1960 for complete discussion).

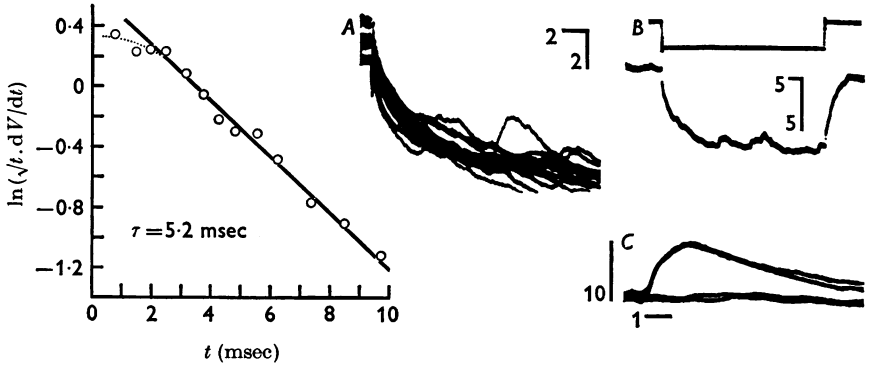

Fig. 3. Data from a Sol motoneurone obtained with single-barrel KCl-filled micro-electrode. The graph shows a plot of $\ln(\sqrt{t}.dV/dt)$ on the ordinate against time t on the abscissa, derived from measurement of the membrane voltage transient shown in *A*. The best linear fit to the points (by eye) is indicated by the line. A line segment covering 1·0 unit on the ordinate scale when projected on the abscissa time scale approximates to the passive membrane time constant, in this case 5·2 msec.

A. Photographically superimposed traces of the early phase of the membrane voltage curve during a hyperpolarizing current pulse, shown on a slower time base in *B*. A best-fit line drawn by eye through this curve was used to obtain the plot shown in the graph. Calibrations: 2 mV and 2 msec.

B. Membrane voltage transient (lower trace) produced by long current pulse (upper trace) of $4{\cdot}5 \times 10^{-9}$ A. Calibrations: 5 mV and 5 msec.

C. Homonymous (LG-Sol) EPSP in the same cell (time to peak = 1·9 msec; half-width = 6·6 msec). Calibrations 10 mV and 1 msec.

RESULTS

The graph in Fig. 4 shows the scatter of points relating the amplitude of the maximum homonymous monosynaptic EPSP to the cell input resistance in a series of forty-eight triceps surae motoneurones. Note that the input resistance values are plotted on a logarithmic scale. The data were obtained from twenty-seven type F (○) and thirteen type S (⊕) gastrocnemius cells and from eight soleus cells(●). Points from LG cells (six of the forty gastrocnemius units) showed the same scatter patterns as those from MG motoneurones. The correlation coefficient r = 0·555. The line best fitting the data by the method of least squares is shown and the

probability that the true slope of this line is zero is $P < 0{\cdot}01$ by the t test. Thus, the positive slope of the correlation is statistically significant with probability $P > 0{\cdot}99$.

The graph in Fig. 5 shows, using the same format, the relation found between the maximum amplitudes of the heteronymous EPSPs (as defined in the Methods section) and the cell input resistance values for the same

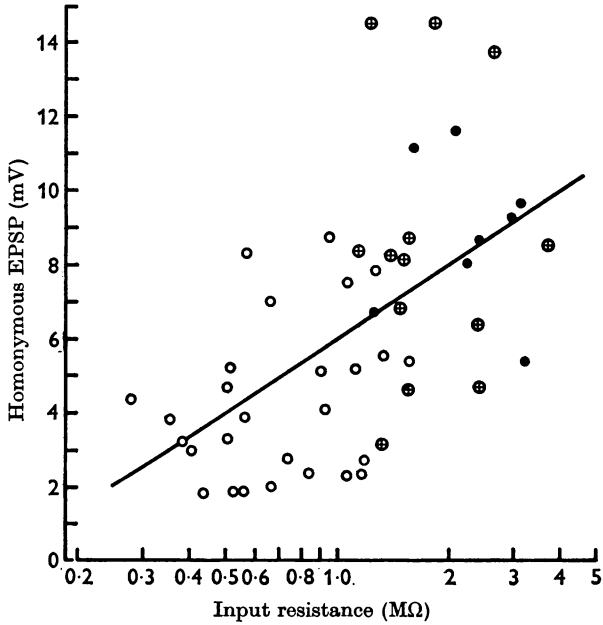

Fig. 4. Semilogarithmic plot of the maximum homonymous EPSP amplitude (ordinate; linear scale) against cell input resistance (abscissa; logarithmic scale) for the sample of motoneurones included in the present study. Data points from type F gastrocnemius cells indicated by ○; type S gastrocnemius cells by ⊕; Sol cells by ●. Regression line calculated by the method of least squares.

series of motoneurones. The line fitted to the data by the method of least squares is shown and the positive slope of the line is statistically significant with probability $P > 0{\cdot}99$. Here, the correlation coefficient $r = 0{\cdot}425$.

Several points can be noted here. A tendency for group Ia EPSP amplitudes to increase with increasing motoneurone input resistance was clearly present. There was in addition a rather large scatter of the data points which suggests that factors other than input resistance may also be important in determining EPSP amplitude. The nature of such factors will be taken up in later discussion. The scatter of points was quite sufficient to obscure the shape of the curves of these relationships and the selection of semi-logarithmic axes as used here was conditioned primarily by convenience in display of the data.

The correlation between the amplitudes of the homonymous and heteronymous monosynaptic EPSPs found in the present series of units is shown in Fig. 6. The line again denotes the least square fit to the data, displayed in this case on linear co-ordinates. With one exception, the heteronymous EPSPs were smaller than the homonymous in each cell measured (Eccles *et al.* 1957*a*) and there was a significant positive correlation between the

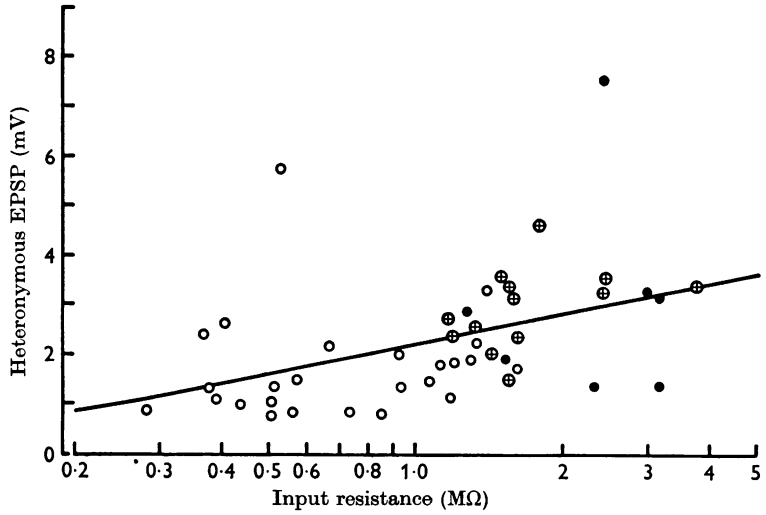

Fig. 5. Semilogarithmic plot, as in Fig. 4, of maximum heteronymous EPSP amplitudes against the cell input resistance values. Symbols used are the same as in Fig. 4.

two synaptic potential amplitudes ($r = 0{\cdot}468$ and $P > 0{\cdot}99$; these symbols are used here and subsequently with the same connotation as in Fig. 4). There was no apparent qualitative distinction between the ratio of homonymous to heteronymous EPSP amplitudes in type F and type S motoneurones. The graph also shows that the few points obtained from LG units (marked with arrows) were for the most part distributed within the same scatter pattern as those from MG cells.

Amplitude distributions of unitary miniature EPSP. The details of the methods used to obtain the amplitude distributions of unitary miniature EPSPs of presumed group Ia origin have already been dealt with (see Methods). The top part of Fig. 7 displays short sections of intracellular records of mEPSP activity during homonymous muscle stretch in three different cells, recorded at equal gain and on the same time base. Below these are shown the mEPSP amplitude histograms derived from the same cells by measuring 100 successive indentifiable unitary mEPSPs in similar records (the histogram ordinates thus represent the percentage as well as the number of mEPSPs found in each amplitude class). The

amplitude class width selected was 0·1 mV, except for mEPSPs between 0·09 and 0·1 mV, which are indicated in histograms *A* and *B* by a half-bar. In no case were mEPSPs of less than 0·09 mV amplitude identifiable with assurance. The record and distribution designated *A* were obtained from

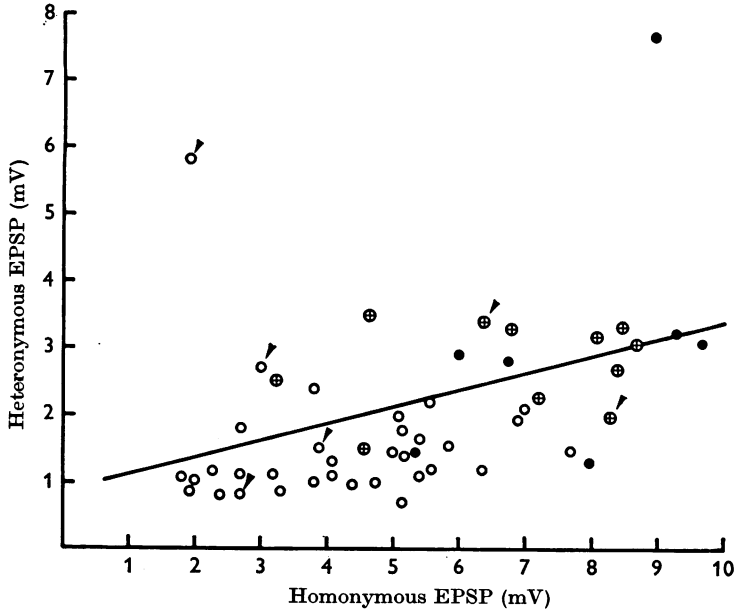

Fig. 6. Graph of the relation between the maximum amplitudes of homonymous (abscissa) and heteronymous (ordinate) EPSPs in the experimental sample of cells. Symbols as before. Data points from LG cells are indicated with arrows.

a type F MG motoneurone with a measured input resistance of 0·63 MΩ; those labelled *B* came from a type S MG unit with input resistance of 1·34 MΩ, and those designated *C* from a Sol cell with input resistance of 3·0 MΩ. The differences among these cells with regard to mEPSP amplitude which are evident in the histograms are also apparent when comparing the intracellular recordings by eye. The shape of the mEPSP amplitude distributions found here, apparently unimodal and skewed to the right, was the same in all of the cells measured (see also Fig. 8). The degree of skew to the right was, in general, greater in the distributions with larger median values.

In the interpretation of data such as shown in Fig. 7, it will be assumed that the mEPSP amplitude distribution found in a particular cell under the given experimental conditions represents a reasonable sample of the synaptic potentials generated in that cell by activity in the group Ia afferent fibres impinging upon it. There are several lines of evidence to support this notion. In certain instances unitary mEPSPs have been demonstrated to occur in predictable rhythmic sequences, as would be expected if they were generated by impulse

activity in single group Ia afferent fibres (Burke & Nelson, 1966; Burke, 1967*b*). Even when such rhythmic sequences of EPSPs were not apparent, the overall pattern of stretch-elicited mEPSPs was that expected from a population of primary muscle spindle afferents, showing marked activation at the onset of stretch, a subsequent plateau response with relatively little accommodation during tonic stretch and prompt cessation on release of the stretch (see Fig. 2), and also complete cessation during an active muscle twitch (Burke & Nelson, 1966). It has been noted in these and in earlier experiments that mEPSPs elicited by progressively greater muscle stretches apparently do not change in average amplitude.

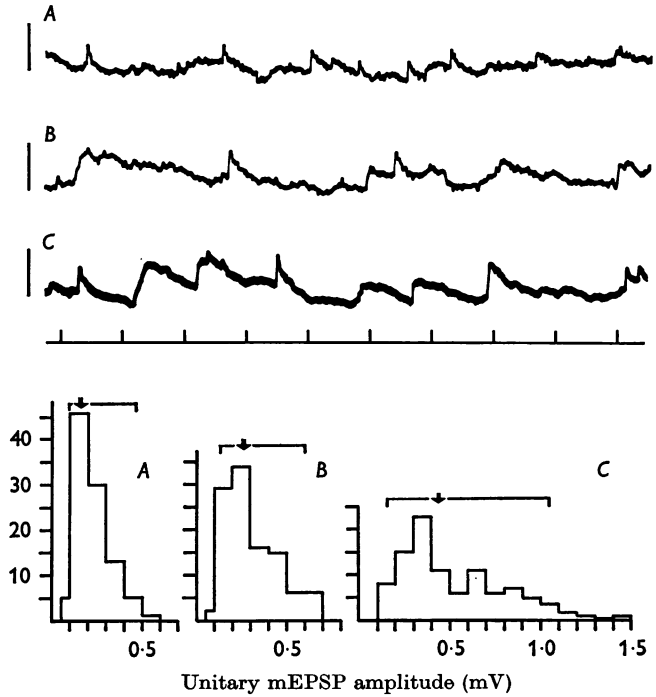

Fig. 7. *Top records:* Short segments of intracellular records of stretch-elicited mEPSP activity in a type F MG cell (*A*), a type of S MG cell (*B*) and a Sol cell (*C*). Calibrations: 1 mV for each record; time marks are 10 msec.

Bottom histograms: Histograms of the amplitude distributions of 100 successive identifiable unitary mEPSPs measured from longer segments of records as shown above for each of the cells. Ordinates: number of mEPSPs in each amplitude class; abscissae: mEPSP amplitude in mV; class amplitude is 0·1 mV. The arrows above each distribution indicate the median values; the brackets enclose 90 % of the distributions (from 5 to 95 %).

The graph in Fig. 8 summarizes the amplitude distribution data for the entire sample of motoneurones studied. The distributions are plotted vertically against the amplitude scale; the round symbol denotes the median value of each distribution and identifies the twitch type of the unit (symbol key as used earlier), and the vertical lines show the 90% inclusion limits in each case. The position of each plotted distribution

with reference to the abscissa indicates the input resistance value measured for each of the cells. This scale is again logarithmic. The dashed horizontal line at about 0·07 mV indicates the average peak-to-peak noise level present in these recordings. The amplitudes of both the median and the largest mEPSPs observed in these cells were positively correlated with the cell input resistance values while the lower amplitude limits of the distributions tended to remain somewhat more constant, near the limit for recognition of the unitary mEPSPs.

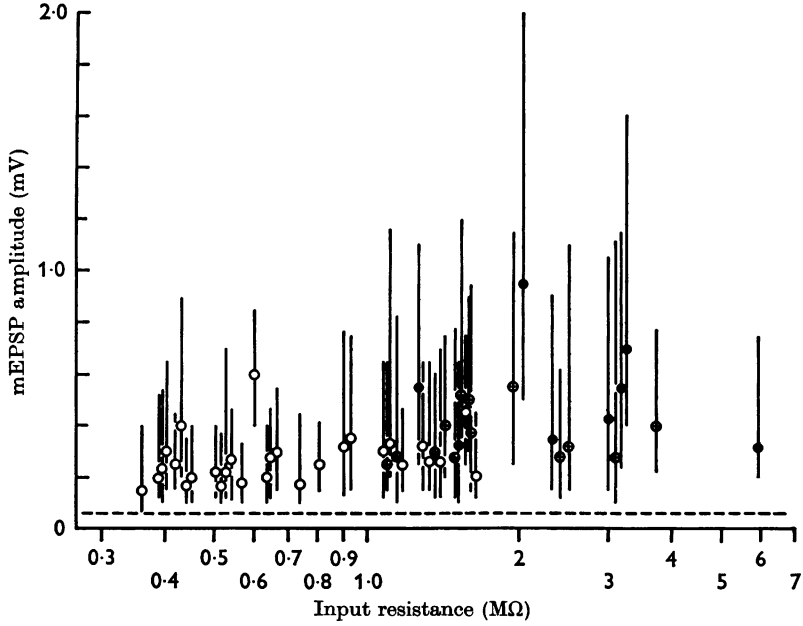

Fig. 8. Semilogarithmic plot of the median values (round symbols) and 90% inclusion limits (vertical bars) for the mEPSP amplitude distributions in the experimental sample (amplitude on linear ordinate scale), plotted against the cell input resistance values (abscissa, logarithmic scale). Average peak-to-peak noise level of the recording system (about 0·07 mV) indicated by the horizontal dashed line. Symbols identify the motor unit twitch types as before.

The correlation between the median mEPSP amplitudes and input resistance values is more clearly apparent in Fig. 9, in which the amplitude scale (ordinate) is somewhat expanded and the 90% limits are not shown. The symbol key is as before and the line denotes the least-square fit to the data ($r = 0{\cdot}479$; the positive slope is significant with probability $P > 0{\cdot}99$). Thus, as was the case with composite EPSPs (Figs. 4 and 5), there was a significant correlation between the amplitudes of mEPSPs and cell input resistance values over the entire population of motoneurones studied.

Since the mEPSPs studied in these motor units were assumed to represent a reasonable sample of the group Ia component potentials making up the electrically evoked composite EPSPs, it was of interest to compare the average amplitude of the components (the median mEPSP amplitude) with the maximum amplitude of the composite homonymous EPSPs for those cells in which both data points were obtained. The graph

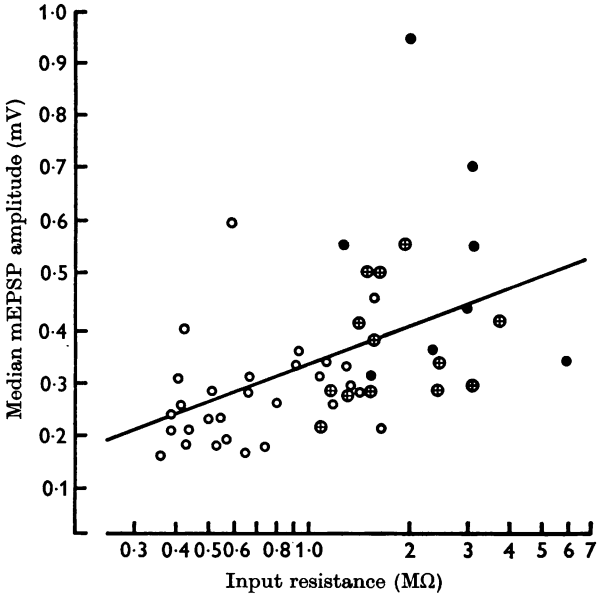

Fig. 9. Semilogarithmic plot similar to Fig. 8, including only the median mEPSP amplitudes plotted against cell input resistance values. Regression line calculated by the method of least squares.

in Fig. 10 shows this correlation, which was reasonably good ($r = 0{\cdot}631$; $P > 0{\cdot}99$), indicating that the larger amplitude composite EPSPs in both type F and type S neurones were composed of, on the average, larger component mEPSPs. The slope of the least-square fit line suggests that, again on the average, some 15–20 component mEPSPs (at least) would be required to make up composite EPSPs with the observed distribution of amplitudes.

Wave form shape of monosynaptic EPSPs. The shape of a composite monosynaptic EPSP transient can be taken to represent an average of the shapes of the individual unitary mEPSP components which sum more or less synchronously following a peripheral muscle nerve volley. The temporal dimensions of the composite EPSP can thus give some indication of the relative proportion of fast-rising, short duration, juxtasomatic mEPSPs to more slowly-rising, longer-duration, dendritic unitary com-

ponents making up the composite potential (Burke, 1967*b*; Rall *et al.* 1967; see also Fadiga & Brookhart, 1960; Rall, 1964). As mentioned in the section on methods the EPSP shape indices which have been found useful are: (1) the EPSP time to peak, and (2) the duration of the EPSP at one-half amplitude, or half-width. When making comparisons within a population of motoneurones with roughly equal membrane time constants, it

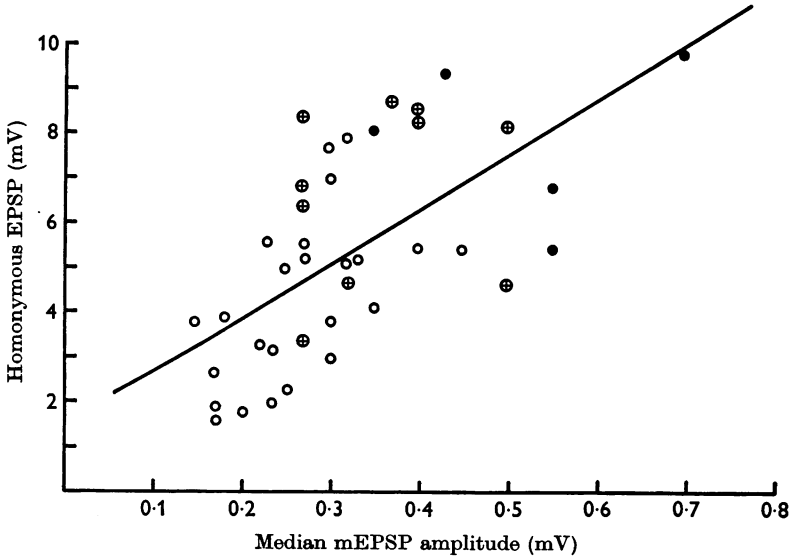

Fig. 10. Linear plot of the relation between the unitary mEPSP median amplitudes (abscissa) and the amplitudes of homonymous EPSPs (ordinate). Symbols as before; regression line calculated by method of least squares.

can be inferred that composite monosynaptic EPSPs with shape indices of relatively short duration arise from inputs distributed predominantly to membrane regions relatively near the cell soma, while those potentials with longer shape indices appear to be generated with a larger fraction of the input on more distal dendritic regions. The relative nature of this distinction must be emphasized, since comparison of the wave form measurements of the shortest duration mEPSPs with those of composite EPSPs indicates that the group I a input to α motoneurones must be widely distributed over the receptive surface in almost all cases (see Burke, 1967*b*).

The graph in Fig. 11 shows a plot of the shape indices for homonymous composite EPSPs found in the present series of motoneurones, with time to peak on the abscissa and half-width on the ordinate. The motor unit twitch type is in each case indicated by the symbol, as in earlier graphs. It is evident that short duration composite EPSPs were found in many more type F cells than in type S, although there is a good deal of overlap

between the twitch type groupings. With the assumption of equal time constants in both types of units (which will be examined below), this suggests that there may have been a difference in the relative distribution of synaptic input locations according to the twitch type of the units in question. A corollary of this observation is that the unitary mEPSPs found in type S cells should have shown a similar tendency toward longer

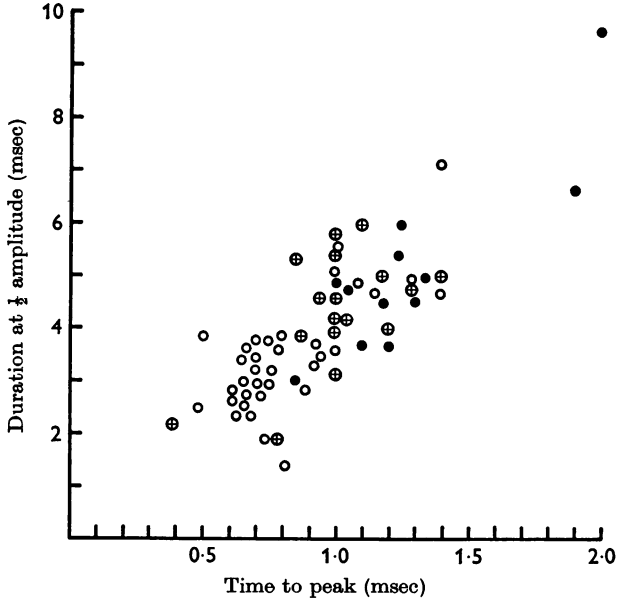

Fig. 11. Linear plot of homonymous EPSP shape indices found in the experimental sample of cells, with EPSP time to peak on the abscissa and duration at ½ amplitude (or half-width) on the ordinate.

shape indices. Unfortunately, reliable measurements in a reasonable sampling of mEPSPs proved to be impossible because of the low signal-to-noise ratio, which interferes with accurate shape discrimination much more than with amplitude measurements. However, a representative qualitative comparison can be seen in the intracellular records in Fig. 7 (top rows), in which a greater proportion of long duration mEPSPs can be resolved in the records from type S motoneurones (records *B* and *C*) than in that from the type F cell (record *A*).

The homonymous EPSP shape indices were positively correlated with the maximum amplitude of the potentials. This is illustrated in the three-dimensional plot in Fig. 12, in which the EPSP shape indices are plotted on the horizontal plane (origin at the left-hand corner) and the synaptic potential amplitudes in the vertical dimension. The symbol key is again as used before and the heavy diagonal line through the points indicates

the central trend of the data by the method of least square estimation for three variables, using amplitude as the dependent variable (see Croxton, 1953). The heavy vertical lines at either end of the estimated line indicate the locus of the estimated line on the shape index (horizontal) plane. The three-variable correlation coefficient $r = 0{\cdot}629$, and the slope of the

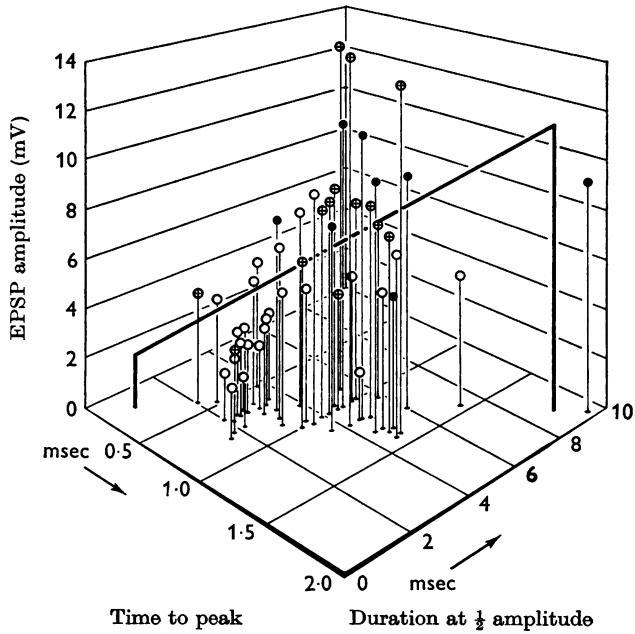

Fig. 12. Three-dimensional linear plot of the homonymous EPSP shape indices (horizontal plane, origin at the left-hand corner) against the maximum amplitude of the potentials (vertical dimension). Symbols as before. The three-variable least square regression line is indicated by the heavy line through the data points (see text).

estimated line with reference to the amplitude dimension is significantly different from zero with probability $P > 0{\cdot}99$, by the F test (Croxton, 1953). The plot shows that EPSPs with longer shape indices tended to be of larger amplitude than those with short duration shape indices, within both the type F and type S groups of motoneurones as well as across the entire population of units.

Relation of EPSP shape characteristics to membrane time constant. As noted above, interpretation of the EPSP shape index plots in terms of the spatial distribution of synaptic input sites requires information about the membrane time constants of the motoneurones being compared (see Rall, 1967; Rall *et al.* 1967). Time constant (τ) values were obtained for thirteen type F gastrocnemius and fourteen type S (eight gastrocnemius and six

soleus) motoneurones. The methods used and time constant calculations have been discussed and illustrated in the section on methods (see Fig. 3).

The graph in Fig. 13 shows the distribution of τ values, plotted against cell input resistance (spike height method). There is no correlation apparent between τ and input resistance values ($r = 0{\cdot}236$) but although the distributions of τ values in type F and in type S cells overlap, they are not

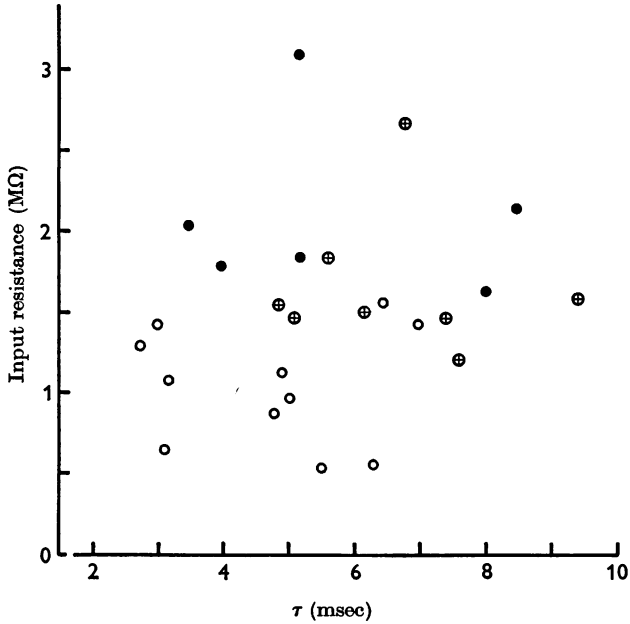

Fig. 13. Linear plot of the relation between measured membrane time constant (τ) values on the abscissa and cell input resistance values on the ordinate. See text.

co-extensive. The mean τ value for the type F group of cells was 4·8 msec ± 1·5 msec S.D. and that for the type S motoneurones was 6·2 msec ± 1·7 msec S.D. These mean values are significantly different (probability that the means are actually the same: $P = 0{\cdot}025$ by the t test). This observation raises the question whether or not the differential clustering of shape index values for EPSPs in types F and S cells (Fig. 11) may be entirely explained on the basis of a systematic difference in the τ values for the two groups of motoneurones.

This factor may indeed explain part of the observed EPSP shape indices difference but two lines of evidence suggest that τ values were not the whole explanation. In the neuronal model system described by Rall (1964, 1967; see also Rall *et al.* 1967), synaptic potentials resulting from specified combinations of input parameters can be measured in dimension-

less units, t/τ. On millisecond time scales, as in Fig. 11, the shape index values for an EPSP resulting from a given set of input parameters would thus be linearly dependent on the τ value of the cell in question. Given that all other factors were equal, the scatter of EPSP shape index points from type F cells in Fig. 11 would overlap the main scatter of points from type S cells if the time constant of each type F cell were increased by about

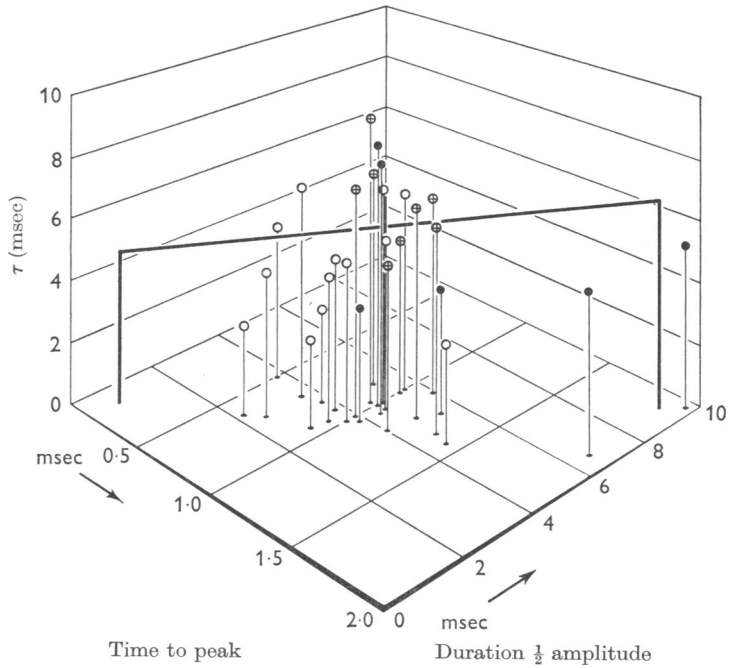

Fig. 14. Linear three-dimensional plot of the relation between homonymous EPSP shape indices (horizontal plane, origin at left-hand corner as in Fig. 12), and the membrane time constant in the same cells (vertical dimension). Three variable least-square regression line indicated by the heavy line as in Fig. 12. See text.

50%. The difference in mean τ values between types F and S cells was only about 25%. A more direct test of the question was possible, however, since the homonymous EPSP shape indices were measured in most of the cells used for time constant measurements. The three-dimensional graph in Fig. 14 illustrates the relation found between EPSP shape indices (horizontal plane, origin at the left-hand corner) and the measured τ values, shown in the vertical dimension. As in Fig. 12, the heavy line through the data points denotes the least-square fit to the data, regarding τ as the dependent variable. The correlation coefficient $r = 0{\cdot}316$ and the slope of the estimated line is not significantly different from zero (probability that the slope is zero: $P > 0{\cdot}1$, by the F test). If the EPSP shape

indices were determined largely or entirely by the τ values of the cells in which the potentials were generated, a stronger correlation would certainly be expected even in this relatively small sample of units.

Rhythmically-occurring unitary mEPSPs. In a previous study (Burke & Nelson, 1966), it was shown that in 10–15% of extensor motoneurones it is possible to demonstrate rhythmically-occurring relatively large amplitude mEPSPs of group Ia origin. It was not known then whether or not post-synaptic factors such as cell input resistance were crucial to this phenomenon, or alternatively, whether such large unitary mEPSPs resulted primarily from purely presynaptic factors such as the number of synaptic boutons from a particular afferent fibre terminating on a particular cell. In the present series of triceps surae motoneurones, instances of such rhythmically-occurring mEPSPs of large amplitude have been seen in both types F and S cells, apparently irrespective of input resistance. This then suggests that such large mEPSPs result more importantly from presynaptic factors than from the nature and size of the post-synaptic neurone.

DISCUSSION

The notion that there is a relation between motoneurone size, cell input resistance and the amplitude of synaptic potentials in the cells has been widely accepted (see Granit *et al.* 1956, 1957; Eccles *et al.* 1957*a*; Henneman *et al.* 1965*a*, *b*; Kernell, 1966; Mendell & Henneman, 1967). Katz & Thesleff (1957) have indeed shown a direct relation between the input resistance of frog muscle fibres and the amplitude of miniature end-plate potentials in the fibres. The present results have confirmed the observations of Eccles and co-workers (Eccles *et al.* 1957*a*) that there is a significant tendency towards larger monosynaptic EPSPs in the relatively small, high resistance soleus motoneurones than are found in most gastrocnemius cells; but in addition, the data shown in Figs. 4, 8 and 9 suggest that even within the spectrum of gastrocnemius motoneurones there is a more-or-less continuous relation between input resistance and EPSP amplitude, both for composite electrically-evoked EPSPs and for unitary miniature EPSPs generated by single group Ia afferents. The scattering of data points in such correlations further suggests that other factors, such as the organization of the synaptic input to particular cells, may also play an important part in the determination of EPSP amplitude. The factor of synaptic organization is also implied by the relation found between EPSP amplitude and wave form (Fig. 12). Before discussing the results in greater detail, it will be useful to consider a conceptual frame of reference which may permit some specification of which synaptic organizational factors are most important in producing the observed results.

Theoretical considerations. Considering a spherical neurone without dendrites, the cell input resistance (R_n) measured from the current–voltage curve obtained with an intracellular electrode obeys the simple relationship

$$R_n = \frac{R_m}{A_n},$$

where R_m is the specific membrane resistivity in Ω-cm^2 and A_n is the cell surface area in cm^2. If this hypothetical neurone receives a given density, D, of synaptic terminals per unit surface area, each generating the same average amount of synaptic current, ΔI_s, then the total synaptic current in the cell during simultaneous activation of all the synapses would be

$$I = \Delta I_s . D . A_n .$$

Neglecting membrane capacity for simplicity, the voltage, V, recorded intracellularly during such synchronous synaptic activation would be

$$V = R_n . I = R_m . \Delta I_s . D .$$

Thus, in this simple case when the synaptic density, (D), membrane resistivity (R_m) and the current produced by a single synapse (ΔI_s) remain constant in neurones of varying size, the amplitude of the synaptic potentials in these cells, resulting from synchronous activation of all the synapses, remains constant and *independent* of cell size and cell input resistance.

This simplified treatment of synapses as constant current sources, bypassing their true nature as variable conductances, is reasonable when the number and the density of synapses are low relative to the total cell surface area. This ensures that the voltage perturbation produced by synaptic activity represents a small fraction of the EPSP equilibrium potential (see Martin, 1955) and reduces the mutual interaction of the perturbations to negligible levels (see Rall, 1964; Burke, 1967*b*). This assumption seems plausible with regard to the group Ia input to motoneurones (Gelfan & Rapisarda, 1964). The present treatment also ignores the time-varying character of the synaptic current transients. This simplifying notion seems reasonable if one only wishes to compare the relative peak amplitudes of voltage transients in cells of varying resistance, where the cell membrane time constants and the time course of the synaptic current transients can be assumed to remain more-or-less constant over the sample of cells studied.

The situation is more complex when neurones with dendritic trees are considered. However, by making the additional assumption that the synaptic inputs to the cells are distributed *uniformly* over the entire receptive surface, the case becomes in several important respects similar

to that of the spherical neurone. With uniformly distributed input, each region of the cell interior is depolarized to the same extent during a synaptic potential transient and no electrotonic currents flow in the cell interior (see Rall, 1967). Thus, with this condition and given that R_m, ΔI_s and the density of synapses, D, are the same in each case, the amplitude of a synaptic potential recorded at any point inside a neurone with complex geometry would be the same as that recorded in a spherical cell with the same total membrane area. Given these constant initial conditions, synaptic potential amplitude would be again independent of cell size even in neurones with complex geometry. Of course, in such neurones the values of R_n measured with an intrasomatic electrode would no longer reflect the total membrane area but would be conditioned to a large extent by the dendritic to somatic conductance ratio, ρ (Rall, 1959). However, this would in no way affect the synaptic potential invariance in neurones of different size.

The assumptions. It is necessary now to examine the extent to which the above assumptions are applicable to spinal cord α motoneurones. The notion that the specific membrane resistivity, R_m, is more or less constant in motoneurones of different size may not be strictly correct. Despite the lack of clear correlation between input resistance and measured τ values (Fig. 13), the difference in mean time constants in type F and type S cells suggests that there may be a relatively small difference in R_m in the two types of motoneurones, since $\tau = R_m.C_m$ (where C_m is the specific membrane capacitance and is assumed to be constant). However, the available data indicate that any systematic increase in R_m in smaller motoneurones must be relatively slight and could not account by itself for the observed correlations of synaptic potential amplitude with input resistance.

The assumption that the average synaptic current produced by single group I a endings (ΔI_s) is more or less constant irrespective of post-synaptic factors appears likely by analogy with the neuromuscular junction (Katz & Thesleff, 1957) and receives some support from the observations of Kuno (1964) which suggest that single group I a terminal boutons may release on the average only one quantum of transmitter substance per afferent impulse.

There is no direct support for the assumption that the group I a synaptic terminals on cat motoneurones are distributed uniformly over the cell receptive surface. However, anatomical work has resulted in the description of terminals degenerating after dorsal root section on both the somata (Szentagothai, 1958) and dendrites (Bodian, 1966; Sterling & Kuypers, 1967) of motoneurones. Physiological studies (Burke, 1967*b*, Rall *et al.* 1967) have provided indirect evidence that group I a synapses are widely distributed over the cell receptive surface in α motoneurones and it seems

not unreasonable that such distribution may approach the condition of uniformity sufficiently that the model system outlined above may be at least approximately applicable. The evidence with regard to departures from the condition of uniformity of distribution, as well as the question of the density of synapses, will be dealt with below.

Interpretation of the results. The results of the present experiments demonstrate significant positive correlations between the amplitudes of both composite monosynaptic EPSPs and unitary mEPSPs of group Ia origin with the input resistance values of α motoneurones. To the extent that the above conceptual model fits these motoneurones, the observations suggest that the average density of group Ia synaptic terminals tends to be greater on the relatively small, high resistance cells (mostly type S) than on the larger cells with low input resistance (mostly type F). The trend toward higher group Ia density on smaller cells seems more marked with the homonymous muscle afferent input than with the heteronymous, on the basis of the relative slopes of Fig. 4 versus Fig. 5.

It must be emphasized that this conclusion regarding the apparent density of synaptic inputs from a particular source implies nothing about the *total* density of synaptic endings on a particular cell, nor do the results permit any unambiguous estimate of the absolute number of group Ia synapses on particular motoneurones. The observed trend toward an increase in homonymous EPSP amplitude in smaller cells may have resulted from activity in a decreasing absolute number of terminals; the density of contacts per unit surface seems to be the critical factor.

The relation between the maximum homonymous EPSP and median mEPSP amplitudes shown in Fig. 10 has some bearing on the question of the number of afferent fibres impinging on motoneurones of differing sizes. To the extent that the measured median mEPSP amplitudes do represent an accurate assessment of the average group Ia mEPSP amplitudes in the cells, the slope of this correlation suggests that, on the average, between fifteen and twenty group Ia afferent fibres impinge on triceps surae motoneurones, with somewhat fewer fibres projecting to the small soleus and type S gastrocnemius cells than to the larger type F gastrocnemius cells.

The above conclusions refer to the average trends of the observed correlations denoted by the least-square fits to the data points, which in all of the correlations show a great deal of scatter. Such scatter may of course result from errors in measurement and from the comparison of data pooled from a number of different experiments. With these reservations in mind, however, one can still point to the considerable vertical scatter (that is, for a given input resistance value) such as in Fig. 4 as perhaps representing an equally considerable variation in the amount of group Ia

input to different motoneurones of roughly the same size and the same twitch type.

One assumption made in connexion with the hypothetical model proposed above remains to be discussed, which is that the synaptic input under consideration is distributed uniformly over the motoneurone receptive membrane. A systematic difference in input spatial distribution could lead to different EPSP amplitudes irrespective of cell input resistance or number and density of synaptic contacts, by virtue of the greater electrotonic attenuation of synaptic potentials generated on distal dendrites at considerable distance from the cell soma (see Rall, 1964). Thus, the positive correlation between input resistance and EPSP amplitudes could be explained without postulating an increasing density of synaptic contacts on smaller cells if a large proportion of the input were dendritic in the large, low resistance cells and/or conversely, a large fraction of the input were juxta-somatic in the small cells. However, the differences in EPSP shape indices shown in Fig. 11 suggests that the spatial distribution of the group Ia input to large and small motoneurones is just the opposite, to the extent that a somewhat greater dendritic predominance is apparently present in the input to small motoneurones than is the rule in the larger cells. Thus, the positive EPSP amplitude-input resistance correlation would appear to imply a somewhat greater increase in synaptic density on the small cells than would be required given a perfectly uniform spatial distribution of the input.

It should be noted that the suggested asymmetry in input spatial distribution in large and small motoneurones is not a point of qualitative distinction between the type F and type S cells, since there is a good deal of overlap in the shape index distribution shown in Fig. 11. The correlation of shape indices with EPSP amplitudes illustrated in Fig. 12 further suggests that the group Ia input to cells with a relatively low density of such terminations, whether type F or type S, distributes predominantly to membrane regions relatively close to the cell somata while cells receiving a higher density of contacts, thus having larger EPSPs, apparently have the input more widely distributed to both proximal and distal dendritic regions, again irrespective of twitch type.

Recent anatomical results are consistent with a predominantly dendritic location for the group Ia synaptic terminals on α motoneurones (Bodian, 1966; Sterling & Kuypers, 1967). There is, however, no anatomical data on possible variations in the density and predominant locus of this input in relation to post-synaptic cell size. Gelfan & Rapisarda (1964) have presented convincing evidence that the *total* synaptic density on spinal cord ventral horn cells is more or less the same over the entire cell surface, including very distal dendritic regions. They concluded that there was no

relation between cell size and total synaptic density in ventral horn cells, although in their fig. 2 it appears that the highest synaptic densities were found on the ventral horn cells with smallest cross-sectional area. If such tighter synaptic packing were actually the rule on smaller motoneurones, it might contribute both to larger PSPs from a variety of sources and also to some increase in the effective membrane resistance per unit area, which in turn might be related to the small increase in mean τ values found in the type S cells.

Gelfan & Rapisarda (1964) estimated that the average total number of group Ia synaptic contacts on α motoneurones is between 20 and 30 boutons per cell. The relation observed in the present results between median mEPSP amplitudes and the homonymous composite EPSP amplitudes (Fig. 10) suggests that motoneurones may receive synaptic contacts from some 15–20 afferent fibres. Physiological evidence also at hand suggests that a group Ia afferent may have from 3 (Kuno, 1964) to as many as 20 or more (Burke & Nelson, 1966) synaptic contacts with a given motoneurone. Thus, the average total number of group Ia terminals on motoneurones may be 3–5 times the previous estimates (see also Sterling & Kuypers, 1967). This number, however, still represents only a small proportion of the total number of synapses on α motoneurones.

General conclusions. The present results provide direct evidence for a positive correlation between motoneurone size (judged by input resistance) and group Ia EPSP amplitude, not only when comparing motoneurones of the 'fast' muscle gastrocnemius pool with the 'slow' soleus cells (see Eccles *et al.* 1957*a*), but also *within* the population of motoneurones innervating the gastrocnemius heads. This population of gastrocnemius motor units is not homogeneous and a quite definite pattern of variation in unit intrinsic properties exists within it (Burke, 1967*a*, see also Wuerker, McPhedran, & Henneman, 1965; Henneman & Olson, 1965). The majority of gastrocnemius units (the type F) possess apparently large, low resistance motoneurones innervating fast twitch muscle units with relatively large tension outputs, and the gross twitch and tetanus properties of these fast muscles appear to be dominated by this fraction. However, there is also present a less numerous but by no means insignificant complement of motor units (the type S) characterized by smaller higher resistance motoneurones innervating slow twitch muscle units with small tension output, which resemble soleus motor units not only in intrinsic properties but also in the pattern of group Ia synaptic input (see especially Figs. 4, 11 and 12). It may well be that these type S gastrocnemius motor units resemble soleus units in dynamic activity patterns as well, forming a fraction of the gastrocnemius motor unit pool which is easily excited to tonic activity, thus underlying the tonic or postural

reflex tension adjustments which the gastrocnemius, like the soleus, exhibits under a variety of conditions (see Creed, Denny-Brown, Eccles, Liddell & Sherrington, 1932). The type F units, then, may subserve primarily the phasic, large tension output requirements of the muscle.The question of the reflex excitability and firing patterns exhibited by identified type F and type S gastrocnemius units and the correlation of these patterns with the characteristics of the group Ia synaptic input to the units will be dealt with in the subsequent paper (Burke, 1968).

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