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THE EFFECT OF A PRECEDING STIMULUS ON TEMPORAL FACILITATION AT CORTICOMOTONEURONAL SYNAPSES

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SUMMARY

1. Intracellular recordings were made of minimal corticomotoneuronal e.p.s.p.s in lumbar motoneurones of anaesthetized monkeys. For intervals of 2 msec and greater between paired cortical shocks, the average time course of facilitation of the second e.p.s.p. with respect to the first could be fitted closely by a negative exponential with a time constant of 10 msec.

2. In the same motoneurones, 'triplets' of corticomotoneuronal e.p.s.p.s were generated by delivering three identical stimuli to the motor cortex. Considering the triplet as a conditioning e.p.s.p. followed by a test pair, the facilitation of the third e.p.s.p. with respect to the second was measured for various combinations of test and conditioning intervals. In each case the amplitude of the third e.p.s.p. was also compared with that of the first (conditioning) e.p.s.p.

3. The effect of a brief conditioning interval was to reduce considerably the facilitation of the third e.p.s.p. with respect to the second at all test intervals from 2 to 50 msec. Combinations of brief conditioning intervals (e.g. 2 or 5 msec) and long test intervals (e.g. 20 or 50 msec) caused the third e.p.s.p. to be smaller than the second. As the conditioning interval lengthened, facilitation in the test pair increased towards the unconditioned values at all test intervals.

4. Facilitation of the third e.p.s.p. with respect to the first could be described approximately as the linear addition of two facilitation components, one due to the conditioning input and one due to the first stimulus of the test pair. Each component followed the same negative exponential time course as found for an isolated pair of e.p.s.p.s and each of the first two inputs contributed to the facilitation of the third e.p.s.p. as if the other of these two inputs had not occurred.

INTRODUCTION

For group I afferent synapses on motoneurones, temporal facilitation of synaptic action is not marked (Curtis & Eccles, 1960; Kuno, 1964; Phillips & Porter, 1964). Indeed, Iansek & Redman (1972) could find no convincing evidence for facilitation of unit group I e.p.s.p.s in cat spinal motoneurones. On the other hand, corticomotoneuronal synaptic action on spinal motoneurones exhibited a strong facilitatory effect of successive volleys during repetitive stimulation of the motor cortex of baboons (Landgren, Phillips & Porter, 1962*a*), even in the same individual motoneurones which showed no facilitation for group Ia synaptic input (Phillips & Porter, 1964). This facilitation appears to be similar in nature to that observed at the crustacean neuromuscular junction (Dudel & Kuffler, 1961) and at vertebrate neuromuscular junctions (del Castillo & Katz, 1954; Mallart & Martin, 1967; Katz & Miledi, 1968).

Although corticomotoneuronal excitatory synaptic potentials (e.p.s.p.s) can be produced in an apparently all-or-nothing manner and with amplitudes similar to those of unitary group Ia e.p.s.p.s (Porter & Hore, 1969) it is, nevertheless, likely that the corticomotoneuronal e.p.s.p.s are not unitary in the sense of deriving from activity in only one pyramidal tract fibre. Even at weak stimulus current intensities the focal surface anodal electrode is capable of exciting a population of pyramidal tract fibres (Landgren, Phillips & Porter, 1962*b*) one or more of which may possess synaptic terminations on the one motoneurone. However, the constancy of size of the compound action potentials descending in the pyramidal tract suggests that the number of synaptic inputs to the motoneurone remains relatively constant from one e.p.s.p. to the next.

On this basis it has been considered worthwhile to characterize the facilitation effect in a quantitative manner, and Porter (1970) has described corticomotoneuronal facilitation in monkeys as a function of the time interval between two identical cortical shocks. To be able to relate this facilitation description to the different effectiveness of various temporal patterns of impulses in depolarizing a motoneurone, it is first necessary to ask whether or not the same degree and time course of facilitation is applicable to any pair of consecutive volleys within a burst of activity descending in a corticomotoneuronal fibre. In the absence of any quantitative evidence to the contrary, this assumption was made during the development of a computer simulation of corticomotoneuronal excitatory synaptic action (Porter, Lewis & Muir, 1971; Porter & Muir, 1971). It was to test the assumption and to throw further light on the nature and implications of the facilitation phenomenon itself that the present experiments were performed. A part of the work reported here has been presented at a

meeting of the Australian Physiological and Pharmacological Society (Muir & Porter, 1972).

METHODS

With some minor differences, the methods used were essentially those described previously by Porter (1970). Anaesthesia was induced in cynomolgus monkeys (*Macacus fascicularis*) by an intramuscular dose of ketamine hydrochloride (Ketalar, Parke–Davis & Co., 10 mg/kg) and small maintenance doses (6–12 mg/kg) of pentobarbitone sodium (Sagatal, May & Baker, Ltd) were subsequently administered I.V. as required to maintain the animals in a lightly anaesthetized state.

A small craniotomy gave access to the 'leg' motor area for focal surface anodal stimulation and a lumbar laminectomy made possible exploration of the spinal cord with capillary micro-electrodes filled with 3 M-KCl. The muscles of the left hind limb were denervated and filaments of the medial and lateral popliteal nerves were prepared for electrical stimulation. Antidromic spikes enabled identification of impaled motoneurones as sending their axons into a branch of the popliteal nerve.

Only those identified motoneurones which had a stable resting membrane potential of 60 mV or greater and showed a smooth uncomplicated average e.p.s.p. in response to single weak cortical shocks were subjected to further analysis. The motor cortex was stimulated with single, paired and triple identical weak current pulses, each capable of generating only D waves in corticospinal fibres (Patton & Amassian, 1954). Intracellular responses in motoneurones were amplified, displayed and recorded by an electrometer (Model M4A, W-P Instruments, Inc.), oscilloscope (Tektronix RM565) and magnetic tape recorder (Ampex FR1300). At least 256 repetitions of each response pattern were recorded for subsequent averaging on a special purpose computer (Biomac 1000, Data Laboratories, Ltd.). Even with a repetition rate of nearly 2·5 sequences/sec, to obtain a complete set of data for any one cell required that a stable electrode penetration be maintained in that cell for more than 2 hr. Most motoneurone impalements showed less stability than this and it has therefore been necessary to pool average measurements from many cells in order to form a complete picture. Moreover, it was necessary to select a limited number of time intervals and to examine these in all the cells. Measurements were made of the responses to single cortical shocks, to paired shocks separated by 2, 5,10 20 and 50 msec and to all of these same pairs preceded by a conditioning shock 2, 5, 10, 20 or 50 msec before the pair. In the cells selected for analysis no significant changes occurred in the synaptic response to a given stimulus during the recording period.

The animal's body temperature and arterial blood pressure were monitored throughout the experiment. Rectal temperature was maintained between 36 and 38° C with a controlled electric blanket. The mean blood pressure was kept above 80 mm Hg by I.V. infusion of dextran to replace blood loss. Respiration was at all times spontaneous and, aside from the anaesthetic, no other drugs were administered.

RESULTS

Corticomotoneuronal e.p.s.p.s have been recorded from thirty-five cells whose axons descended in the medial or lateral popliteal nerve and thus innervated musculature of the lower hindlimbs of the monkeys. During subsequent computer averaging, records from two of these cells were found to suffer from excessive noise and the e.p.s.p. amplitude was unstable.

These were thus discarded, leaving thirty-three cells for analysis. Cortical stimulus amplitudes needed to produce minimal e.p.s.p.s free from the complications of I waves or interneuronal activity ranged from 0·2 to 1·0 mA in these cells when a pulse duration of 0·1 msec was used. The e.p.s.p.s themselves ranged in peak amplitude from 66 to 915 μV (mean = 277 μV) with 10–90% rise times in the range 0·44–2·5 msec (mean = 1·16 msec) and half-widths which ranged from 3·2 to 12·4 msec (mean = 6·8 msec).

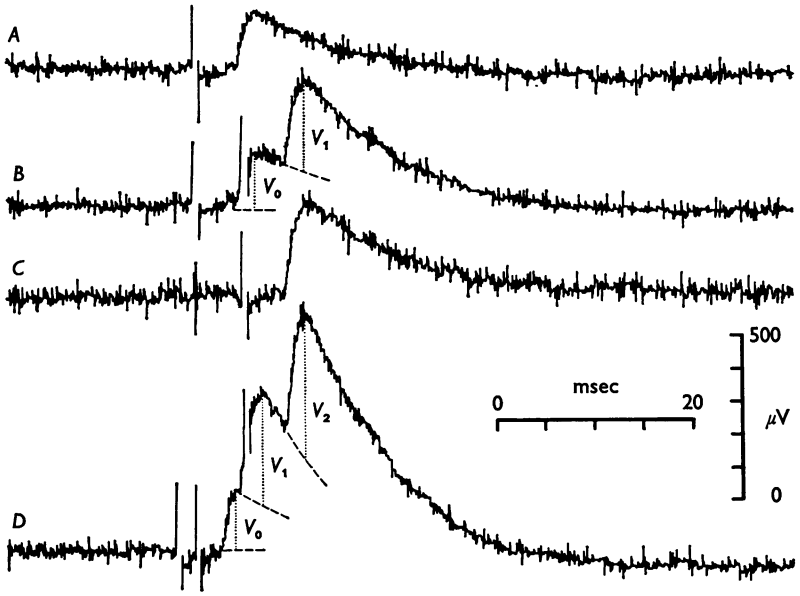

Fig. 1. Average corticomotoneuronal e.p.s.p.s produced in the one motoneurone by 256 repetitions of one, two or three identical cortical shocks. *A* indicates the average response to a single stimulus. *B* is the average response to a pair of stimuli spaced 5 msec apart. *C* is the result of subtracting trace *A* from trace *B* and indicates the time course of the second of the e.p.s.p.s in *B*. A comparison of trace *C* with trace *A* allows an assessment of the increase in amplitude of the second response in *B*. *D* shows the average response to three cortical stimuli with intervals of 2 and 5 msec. Large amplitude deflexions of stimulus artifacts have been omitted for clarity. The time and amplitude calibrations apply to all four traces. Dotted lines indicate the method of measuring e.p.s.p. amplitudes. Facilitation is defined by $f = (V_n - V_m)/V_m$, where $n > m$.

These, and all other measurements were obtained from computer averages of responses to 256 repetitions of the stimulus. In order to demonstrate that the repetition rate of about 2·4 sequences/sec had not altered the e.p.s.p. amplitudes or levels of facilitation, some recordings were repeated using longer cycle times (e.g. 0·5/sec) and no significant differences were found in the values obtained.

Examples of averaged e.p.s.p.s in a lateral popliteal motoneurone are shown in Fig. 1. Trace *A* shows a single unfacilitated corticomotoneuronal e.p.s.p., trace *B*, a pair of e.p.s.p.s resulting from two identical cortical stimuli spaced 5 msec apart and in trace *D* the same test pair has been preceded by a third e.p.s.p. 2 msec earlier. By subtracting record *A* from record *B* a plot, shown as trace *C*, is obtained of the facilitated e.p.s.p. alone; this can be seen to have a similar time course to the unfacilitated e.p.s.p. of trace *A* but a greater amplitude due to facilitation.

Facilitation has been measured quantitatively using a generalization of the definition described previously by Porter (1970), and was evaluated as the amplitude difference $(V_n - V_m)$ normalized with respect to the control amplitude (V_m), where commonly $n = m+1$. For an isolated pair of e.p.s.p.s, $f = (V_1 - V_0)/V_0$; for a pair preceded by an earlier e.p.s.p., $f = (V_2 - V_1)/V_1$.

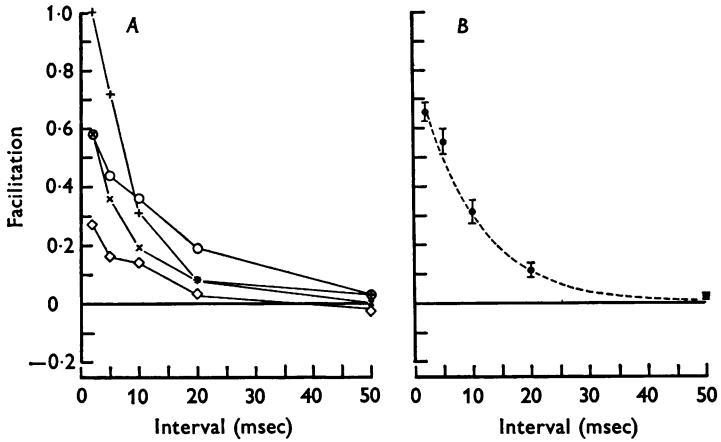

Fig. 2. Facilitation of the second e.p.s.p. of a pair with respect to the first, as a function of the time interval (i_T) between the two. *A* indicates the time course of facilitation of corticomotoneuronal e.p.s.p.s in four different motoneurones. *B* shows facilitation values obtained by averaging over twenty-four cells, with vertical bars indicating ± 1 S.E. of mean. The dashed line is the function $f = 0{\cdot}85 \exp(-i_T/10)$.

The facilitation produced by paired shocks

In most cells the magnitude of facilitation as a function of interstimulus time interval for isolated pairs of e.p.s.p.s showed a maximum at very brief intervals (2 msec) and fell steadily, in an exponential-like manner, as the interval lengthened, becoming negligible at about 50 msec. A slight peak at about 5 msec was evident in 36 % of the plots (see also Porter, 1970, Fig. 4). Although the curves relating facilitation to time interval showed essentially the same form in all cells examined, there were marked varia-

tions between cells in the peak amplitude of the facilitation curves and consequently in the scaling of the entire facilitation time course.

Frame *A* of Fig. 2 shows the graph of facilitation (f) against time interval (i_T) for each of four different cells while, in Fig. 2*B*, values obtained by averaging measurements from the twenty-four most stable cells have been plotted. The curve in Fig. 2*B* is an exponentially decaying function with a time constant of 10 msec ($f = 0{\cdot}85 \exp(-i_T/10)$ and illustrates the consistency of these results with the earlier findings of Porter (1970).

The facilitation produced by triplets of cortical stimuli

It is convenient to think of the corticomotoneuronal synaptic response to a group of three identical cortical stimuli (Fig. 1*D*) as being a test pair preceded by a conditioning input. Trace *D* of Fig. 1 was generated by a test pair of stimuli separated by 5 msec preceded by a conditioning stimulus which occurred just 2 msec before the first of the test pair; i.e. a conditioning interval of 2 msec was followed by a test interval of 5 msec. The lower plot in Fig. 3*A* shows the result, in the cell of Fig. 1, of holding the conditioning interval constant at 2 msec while varying the test interval over the range 2–50 msec as was done for the unconditioned pairs. Also plotted for comparative purposes is the facilitation time course for unconditioned pairs in the same cell (upper curve). The effect of the conditioning input was to reduce considerably the facilitation at all test intervals. Moreover, for test intervals of about 8–9 msec and greater, the conditioned facilitation was negative; i.e. the third e.p.s.p. was smaller than the second.

Frame *B* of Fig. 3 shows the average facilitation, from twenty cells, following a 2 msec conditioning interval. Again, for comparison, the average unconditioned facilitation values from Fig. 2*B* have been plotted on the same graph. Each of the average values has suffered a downward displacement as a result of the conditioning input, but the time course of facilitation has remained substantially unchanged.

By repeating the same series of test intervals in combination with each of a variety of conditioning intervals a family of similar curves was constructed. The curves obtained by averaging corresponding values, over the same twenty cells as for Fig. 3*B*, is displayed in Fig. 4*A*. As the conditioning interval (indicated to the right of each curve) lengthened from 2 up to 50 msec, the curves for conditioned facilitation tended towards the plot of unconditioned values (uppermost curve), such that near 50 msec the difference became almost negligible. The form of this tendency can be seen more easily in Fig. 4*B* where average facilitation has been graphed as a function of conditioning interval for each of the various test intervals (indicated to the right of each curve).

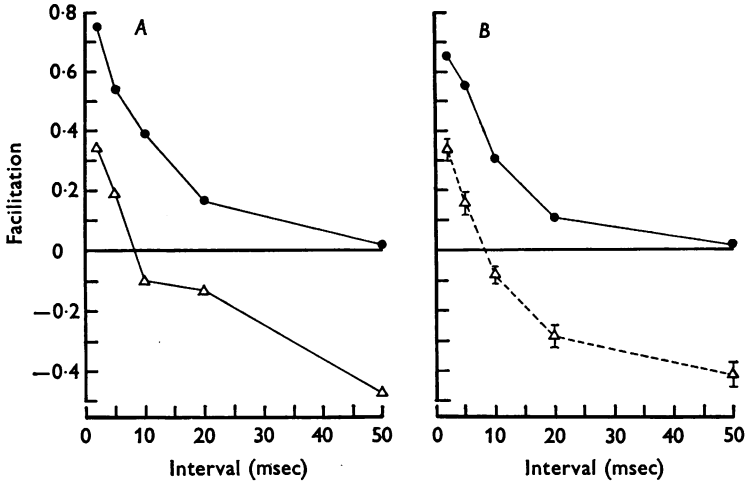

Fig. 3. *A*: the upper curve is the time course of facilitation calculated for pairs of corticomotoneuronal e.p.s.p.s separated by different intervals in the cell whose responses are illustrated in Fig. 1. The lower curve indicates the facilitation calculated for test pairs of e.p.s.p.s in the same cell when a conditioning stimulus preceded the test pair by 2 msec. *B*: the lower curve is the mean facilitation in twenty cells when the test pair followed in every case just 2 msec after a conditioning stimulus. Vertical bars indicate ± 1 S.E. of mean. Plotted on the same graph (upper curve) are the mean facilitation values for unconditioned pairs as shown in Fig. 2*B*.

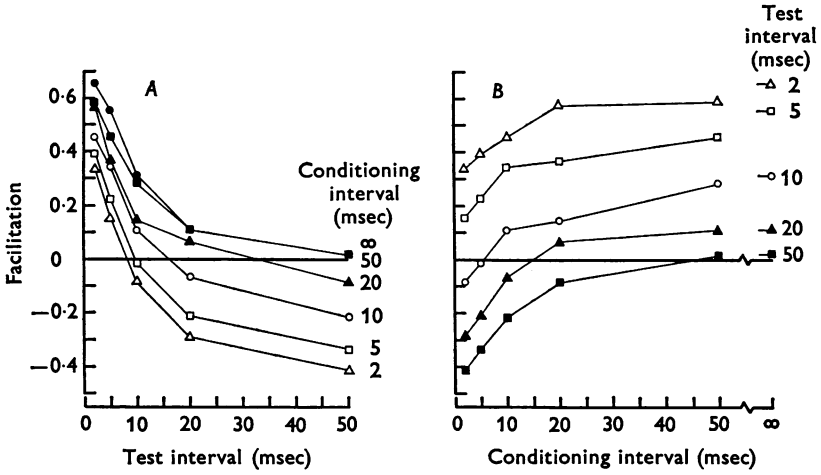

Fig. 4. Mean facilitation for conditioned pairs of e.p.s.p.s is plotted as a function of test interval (frame *A*) for various conditioning intervals (indicated to the right of each curve) and as a function of conditioning interval (frame *B*) for various test intervals (indicated to the right). Also plotted are the average values of facilitation for unconditioned pairs (indicated by ∞).

Even though the effect of the conditioning input was to reduce the facilitation in the test pair, this facilitation still remained significantly positive for brief test intervals (2 or 5 msec) with all conditioning intervals used, and for medium test intervals (10 or 20 msec) following long conditioning intervals (20 or 50 msec). Only for combinations of medium to long test intervals with brief conditioning intervals was the third e.p.s.p. smaller than the second.

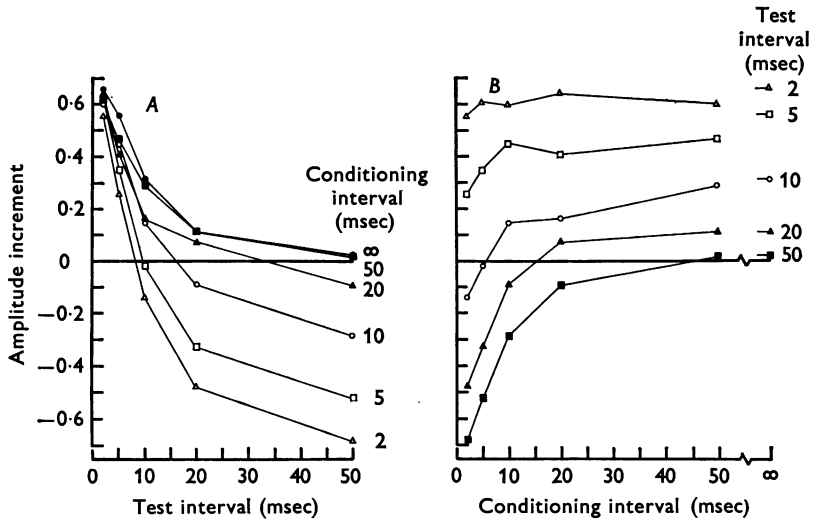

Fig. 5. The format of the Figure is the same as that of Fig. 4 except that a different quantity is plotted on the ordinate. Here the ordinate is the mean increment in amplitude between the first and second e.p.s.p.s of conditioned or unconditioned pairs. In every case the amplitude increment has been normalized with respect to the amplitude of the control (unfacilitated) e.p.s.p.; direct comparison of vertical differences between curves is therefore possible.

It is difficult to interpret a more quantitative comparison of conditioned with unconditioned values in Fig. 4 since the amplitude increments for conditioned pairs ($V_2 - V_1$) have been normalized with respect to an e.p.s.p. (V_1) which is itself facilitated by the conditioning input. A direct comparison becomes possible if these amplitude increments are instead normalized with respect to the amplitude of the unfacilitated e.p.s.p. (V_0). Fig. 5 shows the result of multiplying each of the conditioned facilitation values by the appropriate ratio, V_1/V_0, such that all amplitude increments for both conditioned and unconditioned pairs, have been normalized with respect to V_0.

Average amplitude increment for conditioned pairs is plotted against test interval in frame *A* of Fig. 5 for each conditioning interval (indicated

to the right of each curve). Vertical distance between any point on these curves and the unconditioned facilitation plot (uppermost curve) indicates the amount by which the amplitude increment was reduced when a stimulus preceded the test pair by the indicated conditioning interval. The reduction of amplitude increment was small for brief test intervals (2 msec) but for long test intervals, particularly with brief conditioning intervals, there was a marked amplitude decrement between the second and third e.p.s.p.s of a triplet. These features and the relationship between amplitude increment and conditioning interval can be seen in Fig. 5*B* where each curve is for a particular value of test interval (indicated to the right).

A test interval of 2 msec produced an amplitude increment which was 60 % of the unfacilitated e.p.s.p. amplitude almost independently of any preceding conditioning input. At other test intervals the amplitude increment suffered a reduction which was greatest when the conditioning interval was much briefer than the test interval. The 50 msec curve in Fig. 5*B* is very nearly a mirror image of the facilitation plot exhibited by an unconditioned pair of responses (Fig. 2*B*), indicating that for this test interval the amplitude decrement between the second and third e.p.s.p.s was equal to the amplitude increment between the first and second e.p.s.p.s. The same conclusion can be reached by examination of the corresponding curve in Fig. 6*B* where it can be seen that the amplitude of an e.p.s.p. following a 50 msec interval was always at or very near the control (unfacilitated) level, regardless of conditioning interval.

To enable comparison of the amplitudes of the third e.p.s.p. and a control, rather than increments between successive responses, the facilitation of the third e.p.s.p. with respect to the first ($f_{3,1} = (V_2 - V_0)/V_0$) has been graphed in Fig. 6. The close approximation of the curve for 50 msec conditioning interval to the unconditioned facilitation time course (Fig. 2*B*) is consistent with the statement that a 50 msec conditioning interval has little or no effect on the test pair. Since none of the points on these plots is significantly negative, or even significantly below the corresponding values of unconditioned facilitation, it is thought that while the conditioning input may produce influences ranging from 'no effect' to a substantial facilitation reduction (Fig. 4), it does not cause subsequent e.p.s.p.s to be smaller than the control (unfacilitated) response.

Indeed the gross form of the family of curves in Fig. 6*B* suggested that the increased size of the third e.p.s.p. compared with the first may result from the sum of two facilitation components, one due to the first stimulus of the test pair (with time interval i_T) and the other due to the conditioning input (with interval $i_T + i_C$). Perhaps even the same relationship

found for unconditioned pairs ($f = 0{\cdot}85\exp(-i_T/10)$) would apply for each of these two influences. Accordingly a family of curves from the function:

$$f_{3,1} = 0{\cdot}85\exp(-i_T/10) + 0{\cdot}85\exp(-(i_T+i_C)/10)$$

was drawn, together with the data points from Fig. 6*B*. Fig. 7 illustrates the degree of correspondence between this simple mathematical model and the experimentally measured data.

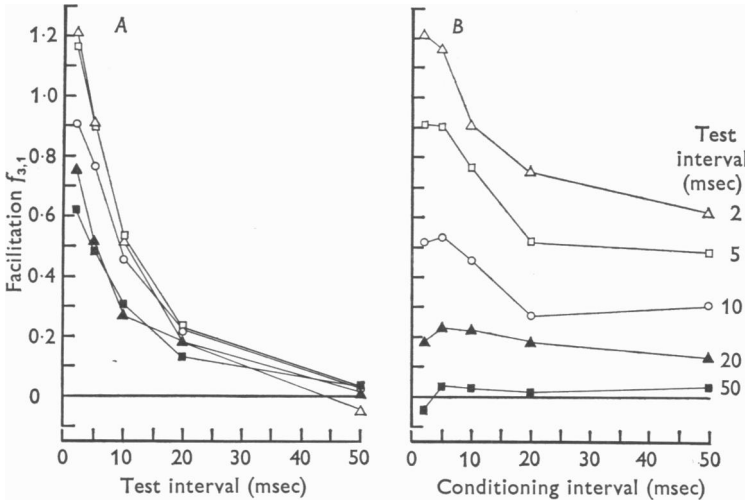

Fig. 6. The format of this figure is the same as Figs. 4 and 5. But the ordinate here is the average facilitation of the third e.p.s.p. of a triplet with respect to the first (unfacilitated) e.p.s.p., defined by $f_{3,1} = (V_2 - V_0)/V_0$. The symbols in frame *A* correspond with the same conditioning intervals with which they were associated in Figs. 4*A* and 5*A*.

Time course of facilitated e.p.s.p.

In eight cells which showed particularly stable control e.p.s.p. amplitudes it has been possible to perform the subtraction as illustrated in trace *C* of Fig. 1, and obtain a clean, reliable representation of the complete wave form of the facilitated e.p.s.p., assuming of course that the two e.p.s.p.s summed linearly to produce the measured response at the motoneurone soma. This assumption is probably valid if the residual depolarization at the post-synaptic site is small when the second e.p.s.p. is initiated and if the transmitter-induced conductance change is brief compared with the inter-stimulus intervals used. The rise time and half-width were measured for each of fifteen facilitated e.p.s.p.s and these were compared with the shape indices for the corresponding control responses.

Changes in rise time ranged from -21 to $+19\%$ with six of the fifteen responses showing less than 5% difference. There appeared to be no con-

sistent tendency one way or the other and when averaged over all eight cells the mean difference was $-0{\cdot}8\,\%$, a value lower than the estimated measurement inaccuracies. There was also no systematic variation in rise time with inter-stimulus interval or the time course of the control e.p.s.p.

On the other hand the half-widths, although also exhibiting both positive and negative changes, did show a tendency to increase when the e.p.s.p. was facilitated. Changes in half-width ranged from -6 to $+76\,\%$ with responses in two cells showing no detectable change. The mean half-width for facilitated e.p.s.p.s was $13\,\%$ greater than that for control responses. There were no significant correlations between changes in half-widths and either inter-stimulus interval or the time course of the control e.p.s.p.

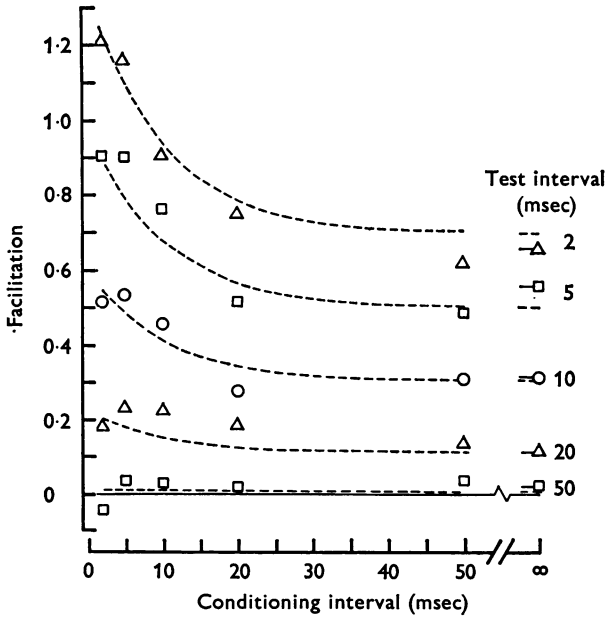

Fig. 7. The mean values of $f_{3,1}$ which were plotted as a function of conditioning interval (i_C) for each test interval (i_T) in Fig. 6*B* are plotted here in the same manner. Also included to the right are the average values of unconditioned facilitation (symbols preceded by short continuous line). The dashed lines are graphs of the function

$$f = 0{\cdot}85\exp(-i_T/10) + 0{\cdot}85\exp(-(i_T+i_C)/10)$$

for each of the test intervals used. The figure illustrates the degree of correspondence between the experimental data and this mathematical model.

DISCUSSION

Although these experiments did not set out specifically to test for the presence of temporal facilitation or depression at inter-spike intervals beyond 50 msec, they produced indirect evidence that any such effects, if present at all, are of minimal magnitude. However, for brief intervals (2–5 msec) facilitation may cause the second e.p.s.p. of a pair of corticomotoneuronal synaptic responses to be even twice the amplitude of its predecessor. But this facilitation decays with increasing interval in an approximately exponential manner with a time constant of about 10 msec.

It has now been demonstrated that each of two preceding synaptic actions will contribute a component of facilitation to a test e.p.s.p. (presumably at the same synapses) as if each had occurred without the other. Quite possibly the same principle would apply for three or more preceding corticomotoneuronal volleys, providing of course that all these occurred within about 50 msec of the test response. Mallart & Martin (1967) found a similar linear summation of temporal facilitation during their studies on the frog neuromuscular junction.

It is tempting now to postulate this principle of additive facilitation as a rule for the prediction of e.p.s.p. amplitudes generated by any particular impulses within a train of corticomotoneuronal spikes. A possible corollary which is also supported by these experimental results is that once a period of 50 msec or more passes without the occurrence of a synaptic input, the next e.p.s.p. will have an amplitude very nearly equal to the control value. Furthermore, there will be no effect from preceding activity on either the amplitudes of successive responses or the levels of facilitation generated by these responses. However, it remains possible that long-term effects of tetanic stimulation of corticomotoneuronal fibres, or the effects of long bursts of natural activity in these fibres, could produce changes which have not been revealed here. Both of the postulated rules need further definitive experimental study.

The existence of additive facilitation reinforces the suggestion of Porter (1970) that the facilitation phenomenon may play an important role in the initiation of motoneuronal discharges by natural pyramidal tract activity. Pyramidal cells of conscious monkeys often show spike frequencies in excess of 60/sec within bursts of activity associated with limb movements (Evarts, 1968; Porter, Lewis & Horne, 1971). At these discharge frequencies, each e.p.s.p. beyond the first few of the train will be facilitated by the combined effect of at least two and possibily four or more preceding impulses.

Summation of facilitation will increase the significance of temporal patterning within the pyramidal cell bursts (Porter & Muir, 1971). The

motoneurone will show a greater response to sequences of short intervals within descending corticomotoneuronal activity, and the precise time at which critical depolarization and initiation of an action potential (and hence muscle unit contraction) occurs will be very dependent on the temporal arrangement of impulses within bursts of short intervals (Porter, 1972).

The validity of the assumptions underlying the comparison of facilitated and unfacilitated e.p.s.p. wave forms has not been demonstrated. Conductance transients at group I a synapses on motoneurones have been measured experimentally (Smith, Wuerker & Frank, 1967) and estimated by the matching of theoretical results with practical observations (Rall, 1967; Jack, Miller & Porter, 1967; c.f. Curtis & Eccles, 1959; Eccles, 1961) but there is little consistency between results from these different methods. The duration of the conductance changes at corticomotoneuronal synapses is not known. The fact that some of the facilitated e.p.s.p.s showed time course shape indices insignificantly different from those of the control e.p.s.p. suggests that the transmitter action may have the same duration in both cases. The discrepancies observed in the remaining e.p.s.p. comparisons may be caused by distortions resulting from residual conductance changes, or other membrane non-linearities.

On the other hand, the e.p.s.p. shape differences may be due to factors more closely related to the facilitation mechanism itself. For instance, it is possible that even if the number of pyramidal fibres activated remains constant the second of a pair of action potentials in these fibres might invade more synaptic knobs than the first and thereby produce a facilitated e.p.s.p. If the distribution of excited synaptic terminals over the soma-dendritic surface also changed, this could account for the observed changes in e.p.s.p. wave form. If, as is thought to be the case for the amphibian neuromuscular junction, facilitation is mediated by an increase in transmitter release from the same synaptic terminals (Dudel & Kuffler, 1961) then large differences in the duration of transmitter action would be implied by the wide time course variations observed in some of the e.p.s.p. comparisons. It is unlikely that the duration of transmitter action would increase by an amount sufficient to explain the large increases in half-width sometimes observed (Jack & Redman, 1971).

Also there was great variation in the time course differences exhibited by the second of a pair of corticomotoneuronal e.p.s.p.s. It remains possible, for example, that in some cases later components were added to, or subtracted from, the second e.p.s.p. by interneuronal discharge generated at a spinal level by a pair of corticomotoneuronal volleys. However, there was no consistent correlation between the time course of facilitation observed and those cells which did or did not show changes in the shape indices of

the facilitated e.p.s.p. Hence the contribution of later events, either excitatory or inhibitory, to the e.p.s.p. facilitation described here cannot have been a major factor.

The whole question of corticomotoneuronal synaptic facilitation will need to be re-examined when techniques can be developed to permit reliable excitation of one and only one pyramidal tract fibre. Until such time, the mechanism of this facilitation may be difficult to elucidate, and its role in the contribution of the pyramidal tract to motor control may be a more fruitful field of investigation.

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