J. Physiol. (1967), **191**, *pp.* 653–672
With 8 text-figures
Printed in Great Britain

RESPONSES OF THE PYRAMIDAL TRACT TO STIMULATION OF THE BABOON'S MOTOR CORTEX

BY D. KERNELL* AND WU CHIEN-PING†
From the University Laboratory of Physiology, Oxford

(*Received* 3 *April* 1967)

SUMMARY

1. The arm area of the baboon's precentral motor cortex was stimulated by brief surface-anodal pulses, and the discharge of the corticospinal tract (the 'pyramidal tract waves') was recorded by an electrode resting on the dorsolateral surface of the cervical spinal cord.

2. Some properties of the pyramidal tract waves were described, and they were also studied in relation to the firing of single cortico spinal fibres.

3. The results led to the conclusion that the later pyramidal tract waves (the 'I waves') were almost exclusively due to a semi-synchronous repetitive discharge of the same fast cortico spinal fibres as those responsible for the initial wave (the 'D wave').

4. Some problems concerning the origin and significance of the I waves were discussed.

INTRODUCTION

Electrical stimulation of the cerebral cortex has often been used as a tool for studying the functional connexions between the motor cortex and the spinal cord (cf. Phillips, 1966). The outcome of such experiments will, however, to some extent depend on the complex manner in which the cortex itself responds to the electrical stimulus, because a single brief pulse to the motor cortex may cause a prolonged discharge in the pyramidal tract (Adrian & Moruzzi, 1939; Patton & Amassian, 1954, 1960). In response to a strong cortical stimulus, an electrode placed in the medullary pyramid or in the lateral column of the spinal cord will record a rapid series of 'waves' (Patton & Amassian, 1954, 1960). Weak stimuli, especially surface-anodal ones (Hern, Landgren, Phillips & Porter, 1962; Phillips & Porter, 1964; Gorman, 1966), will elicit only the initial wave, the 'D wave' (Patton & Amassian, 1954). The D wave has a short and

* On leave of absence from the Nobel Institute for Neurophysiology, Karolinska Institutet, Stockholm 60, Sweden.

† Present address: Institute of Physiology, Academia Sinica, Shanghai, China.

stable latency, and it is due to the direct electrical activation of cortico-spinal neurones with fast conducting axons (Patton & Amassian, 1954, 1960; Hern, Landgren, Philips & Porter, 1962; Landgren, Phillips & Porter, 1962*a*; Phillips & Porter, 1964). The later waves, the 'I waves' (Patton & Amassian, 1954), are more distinct in the monkey than in the cat. The I waves are not obtained by stimulation of the subcortical white matter, and it has been concluded that they are due to an 'indirect' excitation of cortico spinal neurones via intracortical neuronal elements (Patton & Amassian, 1954, 1960).

The present study was originally undertaken because we wanted to use recordings of pyramidal tract waves for monitoring the pyramidal discharge in experiments concerning the effects of a cortical stimulus on forelimb motoneurones of the baboon. In such experiments it would be of interest to know, not only that the I wave discharge is elicited via intracortical synapses, but also whether the various I waves actually signal a synchronous repetitive discharge in fast cortico spinal fibres, such as those responsible for the D wave. The physiological function of these fast pyramidal fibres is most probably different from that of the slower components of the cortico spinal tract (Brookhart, 1952; Towe, Patton & Kennedy, 1963; Evarts, 1965, 1966; Hardin, 1965). In the monkey, the fast pyramidal fibres are known to have monosynaptic connexions with spinal motoneurones (Bernhard, Bohm & Petersén, 1953; Preston & Whitlock, 1960, 1961; Landgren *et al.* 1962*a*; Phillips & Porter, 1964).

There is evidence suggesting that the I waves may signal a repetitive discharge of fast cortico spinal fibres. Some published illustrations suggest that I waves elicited by stimulation of the monkey's precentral motor area travel along the spinal cord with the same fast conduction velocity as the D wave (Patton & Amassian, 1960, their Fig. 8; cf. also Bertrand, 1956). Single unit recordings from cat and, in a few cases, from monkey, have indicated that a strong cortical stimulus will tend to elicit a brief burst of repetitive firing in fast pyramidal fibres (Patton & Amassian, 1954, 1960; Berlin, 1964). No more specific study seems to have been done, however, concerning the role of fast fibres in the generation of the I waves.

In the present experiments, we have stimulated the arm area of the baboon's motor cortex with brief surface-anodal pulses, and have recorded the pyramidal tract waves with an electrode resting on the dorsolateral surface of the cervical spinal cord. We have also studied the discharge of single pyramidal fibres. The results establish that, at least under our experimental conditions, the I waves reflect almost exclusively a semi-synchronous repetitive discharge of fast pyramidal fibres. The Discussion deals with some problems relating to the origin and significance of the I waves.

METHODS

The experiments were performed on young baboons of either sex, weighing between 5·1 and 6·4 kg. The animals were anaesthetized by breathing 50–70 % nitrous oxide in oxygen, initially with 3 % chloroform added, and later on in combination with barbiturates (Hern, Landgren, Phillips & Porter, 1962). Pentobarbitone (20 mg/kg I.P.) was given at the onset of operation, and subsequently the anaesthesia was deepened as required by the intravenous injection of hexobarbitone. The arm area of the precentral motor cortex on the right side was exposed and covered with warm mineral oil. The cortex was stimulated unifocally via a silver ball electrode (ball diameter about 1 mm) resting lightly on the pia, the 'inert' electrode being sewn into the scalp. The stimulating pulses were surface-anodal and of rectangular shape with a duration of about 0·2 msec. The stimulating current was measured by recording the voltage drop across a 1000 Ω resistor in series with the brain. During an experiment, the silver ball electrode was generally kept at the cortical site at which, in the beginning of the experiment, the lowest threshold was found for eliciting a contraction of extensor digitorum communis of the left arm by a brief tetanic stimulation at a frequency exceeding 200/sec. This place was situated just anterior to the central fissure. In the experiments, cortical stimulus intensities up to 11–12 mA were used. With single brief pulses, such as those used in the present experiments, a weak contraction of extensor digitorum communis could sometimes be obtained at the highest stimulus intensities. It should be noted, however, that the strongest of the stimulus intensities employed were far above the strength needed for eliciting a movement with tetanic stimuli or with pulses of long duration.

The spinal cord was exposed between segments C 3 and Th 3, and was covered with warm Ringer solution or mineral oil. Pyramidal tract waves were recorded with a thin steel wire (insulated to the tip) resting lightly against the dorsolateral surface of the spinal cord (Phillips & Porter, 1964). The amplifier was a.c.-coupled (time constant 0·1 sec). Two leads from muscles surrounding the laminectomy were connected to the other input of the amplifier via a potentiometer. With these two leads in appropriate positions, the shock artifact from a cortical stimulus could be balanced by adjusting the potentiometer.

Single unit recordings from fibres in the lateral cortico spinal tract were obtained with conventional single-barrelled micro-electrodes filled with 3 M-KCl. The cathode follower output was connected to an a.c.-coupled amplifier (time constant 0·1 sec). In order to control cord pulsation, a saddle-shaped celluloid plate pressed lightly against the cord. The microelectrode was inserted through a hole in this plate (Hern, Landgren, Phillips & Porter, 1962).

Rectal temperature was kept between 37 and 39° C.

RESULTS

The pyramidal tract waves. The records of Fig. 1 are from two different baboons (*A* and *B* respectively), and they were obtained with an electrode resting on the dorsolateral surface of the cervical spinal cord (Phillips & Porter, 1964). The potentials result from a brief stimulus delivered to the precentral motor cortex contralateral to the side of recording. Weak stimuli are seen to elicit only a brief single 'wave' which has an initial positive and a more prominent negative phase (Fig. 1). The latency to the onset of the negative-going phase is only about 1·3 msec (Fig. 1). There is no doubt that this initial wave corresponds to the 'D wave' of previous workers (Patton & Amassian, 1954, 1960; Hern, Landgren, Phillips & Porter, 1962;

Phillips & Porter, 1964), i.e. that it reflects the activity of rapidly conducting fibres belonging to directly stimulated pyramidal units (see Introduction). The sharp onset of the negative-going phase of the D wave corresponds approximately to the earliest arrival of pyramidal impulses

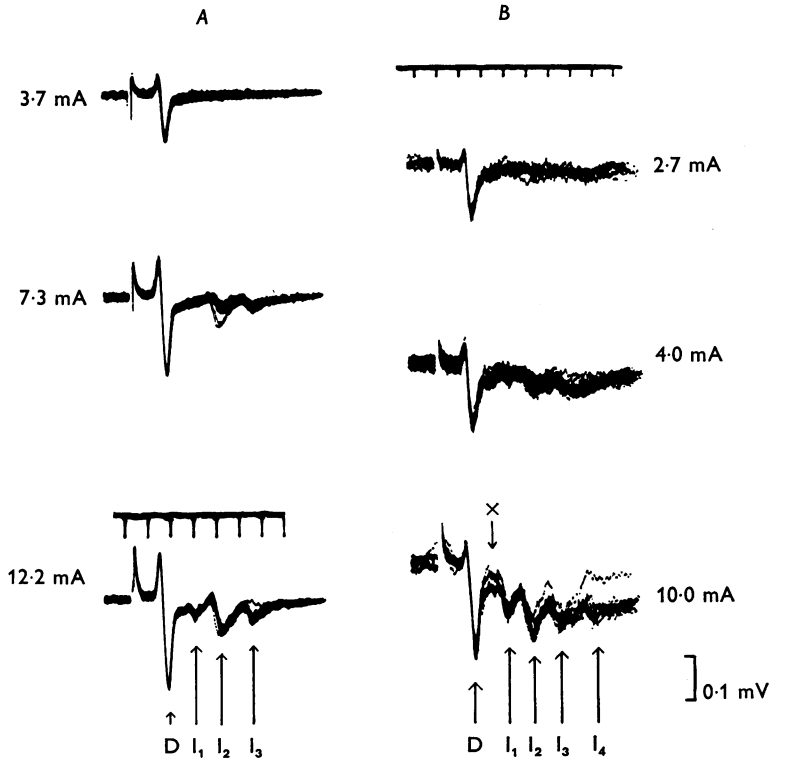

Fig. 1. *A*. Pyramidal tract waves elicited by brief, surface-anodal cortical stimuli at the indicated intensities (mA). The records were obtained with an electrode resting on the dorsolateral surface of the spinal cord at C 4–5. Single stimuli were repeated once a second, and each record consists of about ten superimposed traces. Negativity is downwards. Time: msec. *B*. As in *A*, but from another animal. Same voltage calibration for *A* and *B*. Arrows in *A* and *B* point to the negative peaks of the indicated pyramidal tract waves. Concerning arrow marked ' × ', see text.

at the spinal site of recording (Hern, Landgren, Phillips & Porter, 1962; Landgren *et al.* 1962*a*; cf. also Fig. 6). At higher stimulus strengths the D wave attains a greater amplitude, and it is then succeeded by a series of rapidly recurring, smaller, and predominantly negative-going waves (Fig. 1). The whole sequence is finished some 6·5–8·5 msec after the onset of stimulation, and the intervals between the various waves is of the order of 1–2 msec (Figs. 1 and 2). Experiments with micro-electrodes showed that the D wave as well as all the late waves were best recorded from a site

laterally in the spinal cord where single unit recordings from fast cortico-spinal fibres were obtained. It was also checked that no late waves could be made to succeed the D wave by stimulation of the subcortical white matter after removal of the cortex by suction. Taken together, these data strongly indicate that the waves succeeding the D wave (Fig. 1) correspond to the 'I waves' of previous workers, i.e. that they represent activity of indirectly activated cortco-spinal fibres without any significant contamination from other spinal elements (see Introduction). That this interpretation is correct will be further demonstrated later on in this paper.

In the present study, the cortical stimulation was unifocal and surface-anodal, and the D wave could therefore generally be obtained alone at low current strengths (Fig. 1) (Hern, Landgren, Phillips & Porter, 1962; Phillips & Porter, 1964; Gorman, 1966). As the stimulus strength was increased, the amplitude of the D wave continued to grow until it attained a maximal size at a stimulus intensity which could be as low as 5 mA or as high as 9–10 mA (cf. Phillips & Porter, 1964). I waves began to appear at a current strength between about 2 and 6 mA, and at their first appearance the D wave had usually reached between 40 and 80 % of its maximal size.

With strong cortical stimuli (e.g. 10 mA), the D wave was always succeeded by at least three I waves (Fig. 1*A*, 12·2 mA). In many cases a fourth I wave would follow (Fig. 1*B*, 10·0 mA), and in a few cases a small fifth I wave was seen. In Fig. 2, the latency of the pyramidal tract waves is plotted against cortical stimulus intensity. The values were obtained from the same experiment as that partly shown in Fig. 1*B*. Over the whole range of stimulus strengths, the latency of the various I waves is seen to shorten only by between 0·2 and 0·5 msec (Fig. 2). This was actually about the largest change in latency observed during the present experiments. In some cases, the latency of the I waves hardly changed at all with stimulus intensity. The latency of the D wave could shorten some tenth of a msec with stronger stimuli. The latency of the I waves was usually fairly constant for long periods of time during an experiment. Some change of latency could occur, however, and it was then more marked for the later I waves than for the initial ones.

The various I waves were numbered according to their latency at strong cortical stimuli, and below they will be referred to as the I_1, I_2, I_3 and I_4 waves respectively (Figs. 1 and 2). In Fig. 1*B* at 10·0 mA a small 'notch' is seen between the D wave and the I_1 wave (arrow marked '×'). Such a notch was clearly visible only in some experiments, it was always very small and brief, and it could always readily be distinguished from the I_1 wave.

The intervals between the various I waves were generally not exactly equal (Figs. 1 and 2). Thus, for instance, the interval between the I_2 and I_3

waves was generally somewhat longer than the interval between the I_1 and I_2 waves (Figs. 1 and 2). The latter interval was usually of the order of 1 msec, and the I_1 wave generally started about 1·5 msec after the onset of the negative-going phase of the D wave. There was usually no clear difference between the end of one I wave and the onset of the succeeding one (Fig. 1).

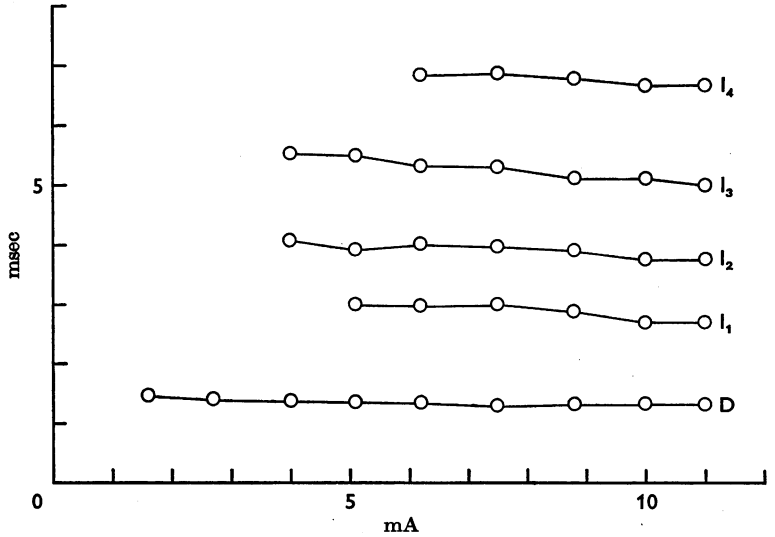

Fig. 2. Diagram showing the latency of the indicated pyramidal tract waves (ordinate) at different intensities of cortical stimulation (abscissa). Latencies were measured from the onset of the cortical stimulus to the onset of the negative-going phase of the respective waves. The values were obtained from the same experiment as that partly shown in Fig. 1*B*.

The I_1 wave was not the first I wave to appear as stimulus intensity was increased and it regularly had a higher stimulus threshold than the I_2 and I_3 waves. Thus, in Fig. 1*A* the I_2 and I_3 waves are obtained with about the same latency at 7·3 and 12·2 mA respectively, but the I_1 wave is clearly seen only at the latter stimulus intensity. In Fig. 1*B* at 4·0 mA, the I_2 and I_3 waves are clearly visible, whereas the I_1 wave was obtained only in some of the superimposed traces. The appearance of the I_1 wave at higher stimulus intensities was clearly not due simply to a gradual shortening of the latency of already existing I waves (Figs. 1 and 2). The I_2 and I_3 waves often had about the same stimulus threshold. In many cases the I_2 wave had a lower stimulus threshold than any of the other I waves (Figs. 4 and 5*A*).

Within the present range of stimulus intensities (up to about 12 mA), the I waves did not always attain a maximal size, but they generally grew

only slowly with stimulus strength above some 7–10 mA. At the stimulus strength at which it just started to appear, the size of an I wave could be markedly unstable (e.g. Figs. 4 and 5) but was fairly stable at higher stimulus intensities (Fig. 1).

During the present experiments, the arm area of the motor cortex was stimulated, and a large number of the activated pyramidal fibres would therefore be expected to leave the cortico spinal tract within the cervical enlargement. As expected, the D wave as well as the I waves generally showed a gradual but marked decrease in size as the recording electrode was moved towards the thoracic segments of the spinal cord. It was also generally found that, with the electrode in a more caudal position, the pyramidal tract waves would all be delayed by about the same amount of time. In two animals, the actual conduction velocity of the D wave and the three initial I waves was estimated by measuring their change in latency as the recording electrode was moved in small steps along the cervical spinal cord. Both these experiments gave results such as those shown in Fig. 3, i.e. the conduction velocity of the three initial I waves

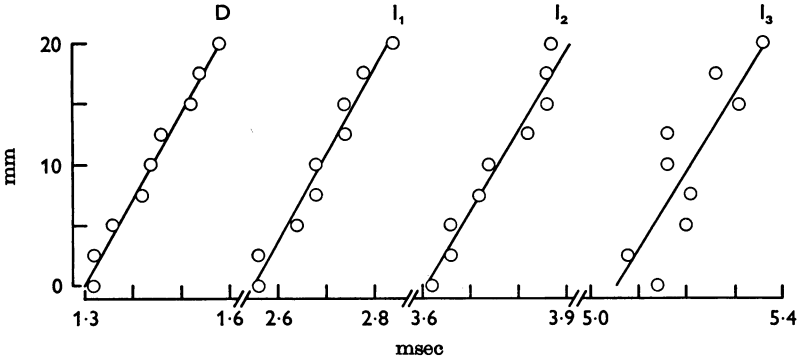

Fig. 3. Diagram showing the speed of conduction of the D wave and the three initial I waves along the cervical spinal cord. The cortex was stimulated at 12·2 mA. The recording electrode was placed on the dorsolateral surface of the spinal cord at C4–5 (zero on ordinate), and at successively more caudal sites (ordinate). Latencies were measured as in Fig. 2 (abscissa). Regression lines were calculated by the method of least squares. The slope of the respective lines is for the D wave 70 m/sec, for the I_1 wave 71 m/sec, for the I_2 wave 67 m/sec, and for the I_3 wave 64 m/sec.

(64–71 m/sec in Fig. 3) was about the same as that of the D wave (70 m/sec in Fig. 3). The conduction velocity of the D wave was similar to that obtained by previous workers on the monkey (Bernhard *et al.* 1953; Patton & Amassian, 1954; Phillips & Porter, 1964).

The results of Fig. 3 indicate that the I waves are predominantly caused by the discharge of pyramidal fibres with the same fast conduction velocity

as those responsible for the D wave. The results do not show, however, whether the fibres fired during the D wave actually produce I waves by a repetitive discharge. The discharge of single pyramidal fibres was therefore studied in relation to the pyramidal tract waves.

Single units. In the search for single pyramidal fibres, the micro-electrode was directed into the lateral part of the cervical spinal cord while the contralateral cortex was stimulated once a second at 10 mA or more. Single units, responding with all-or-nothing spikes to this cortical stimulus, were found in the region where the pyramidal tract waves recorded by the micro-electrode were most prominent. The action potentials were positive-going, their amplitude ranged from about 1 mV up to more than 20 mV,

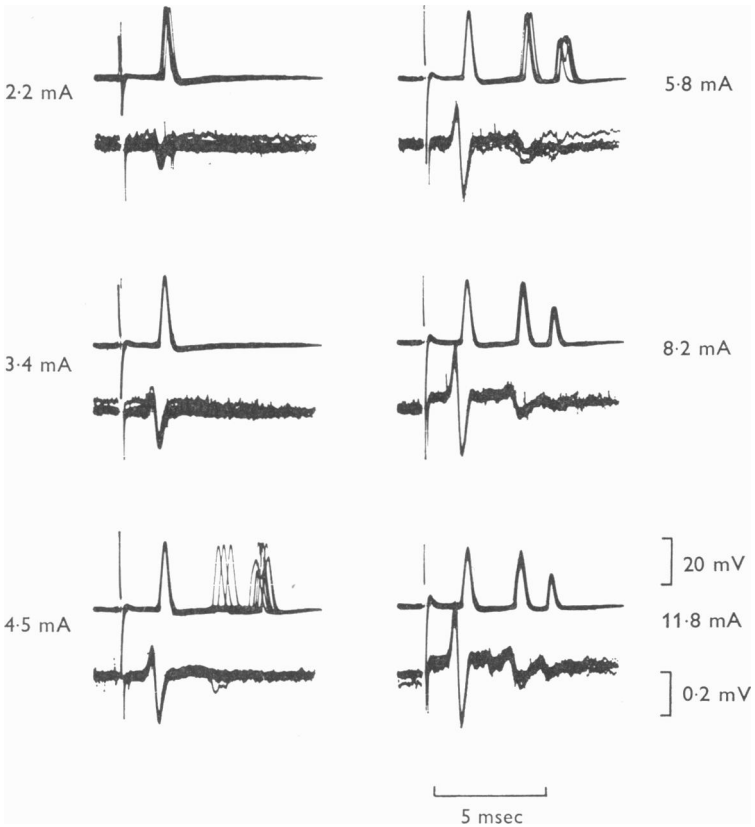

Fig. 4. Spikes of a single pyramidal fibre (upper traces) and pyramidal tract waves (lower traces) elicited by brief cortical stimuli at the indicated intensities (mA). The pyramidal tract waves were recorded from the cord surface at C 5–6, close to the insertion of the micro-electrode used for the single unit recording. Single cortical stimuli were repeated once a second, and each record consists of about ten superimposed traces. Negativity is downwards. Voltage calibrations: 20 mV for the single unit, 0·2 mV for the pyramidal tract waves.

and their duration was about 0·5–0·7 msec (Figs. 4 and 5, upper traces). In all the experiments, the discharge of the single unit and the pyramidal tract waves (Figs. 4 and 5, lower traces) were recorded simultaneously, the latter being obtained with an electrode resting on the cord surface about 1 mm medial to the insertion of the micro-electrode.

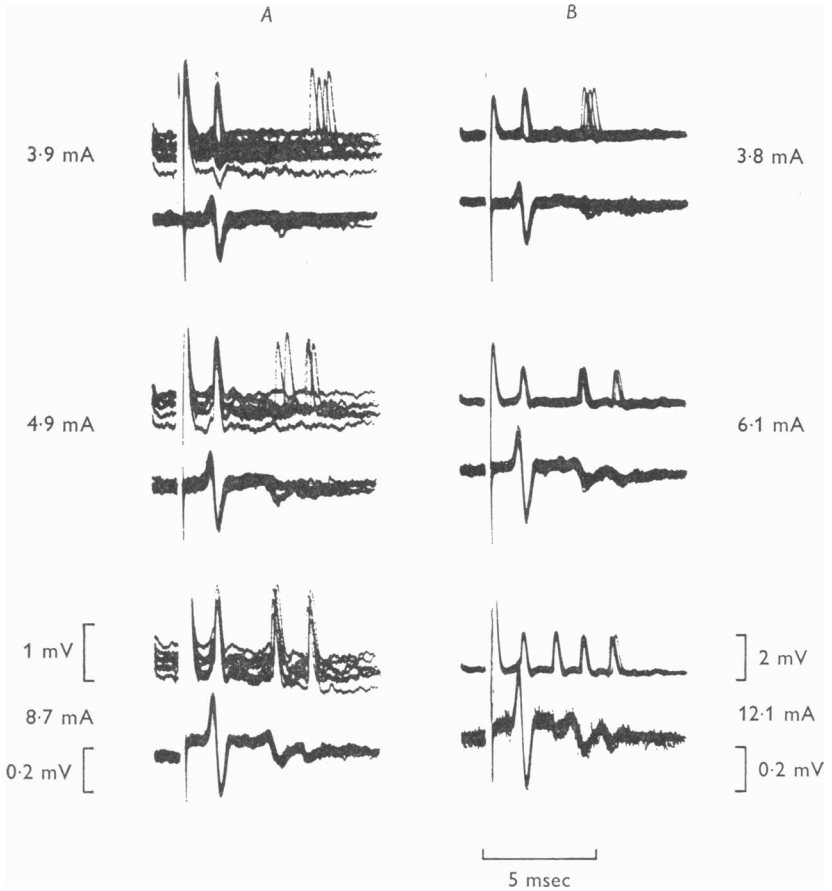

Fig. 5. Records obtained as in Fig. 4 for two other pyramidal fibres (*A* and *B* respectively). Voltage calibrations: 1 mV for single unit in *A*, 2 mV for single unit in *B*, 0·2 mV for pyramidal tract waves in *A* and *B* respectively. Same time calibration for *A* and *B*.

Records were obtained from 52 units responding to single cortical pulses. As is demonstrated in Fig. 6, an early spike with a minimal latency close to that of the D wave could be elicited from most of these units (cf. Landgren *et al.* 1962*a*). For forty-four of the units, the latency of the initial spike differed from that of the negative-going phase of the D wave by 0·4 msec or less (Fig. 6; cf. also Figs. 4 and 5). The earliest spike of these

'fast' units must have been directly elicited by the cortical stimulus, because its minimal latency is too close to that of the D wave to allow for an intercalated synapse. The fast units may safely be regarded as fast pyramidal fibres, and the earliest spike of such a unit will below be referred to as the 'D spike'. As would be expected, the D spike followed a

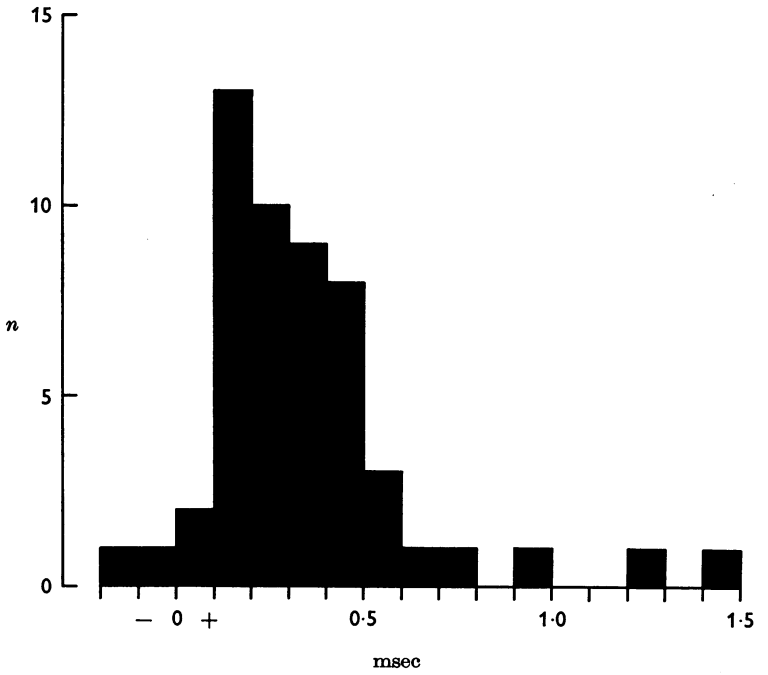

Fig. 6. Diagram showing the latency of the initial spike for 52 single units studied as in Figs. 4 and 5. The latency of the initial spike was measured from the onset of the negative-going phase of the simultaneously recorded D wave, and the values of the diagram were obtained with cortical stimuli stronger than 10·5 mA.

tetanic stimulus at 500/sec or more whenever tested (tried in thirty out of the forty-four fast units).

The analysis below will largely be confined to the forty-four pyramidal units. This division of the material was done because the main aim was to study the discharge of pyramidal fibres responsible for the D wave. For units with a relative latency of 0·6 msec or more (Fig. 6), the earliest spike did not start until after the end of the simultaneously recorded D wave. The three units with a relative latency of 0·5 msec (Fig. 6) represent a transitional group; their earliest spikes started just before the end of the D wave.

In the experiments of Fig. 6, the latency to the onset of the negative-going phase of the D wave was about 1·4 msec. As has been shown before

(Landgren *et al.* 1962*a*), the onset of the negative-going phase of the D wave corresponds approximately to the earliest arrival of pyramidal impulses at the site of recording (Fig. 6). If a latency of 1·4 msec corresponds to a conduction velocity of about 65 m/sec (Fig. 3; Phillips & Porter, 1964), then units with an initial latency of 1·8 msec would have a conduction velocity of around 50 m/sec. Thus, the forty-four fast units of Fig. 6 would have a conduction velocity of the order of 50–70 m/sec. According to a similar calculation, the eight slower units of Fig. 6 would conduct at between 30 and 50 m/sec.

The records of Fig. 4 show the discharge of a fast pyramidal fibre to various strengths of cortical stimulation. Weak stimuli elicit only the D spike (2·2 and 3·4 mA). At 4·5 mA the D wave is sometimes succeeded by an I wave (I_2), and the D spike is now also succeeded by one or, in some instances, two later action potentials, both with a somewhat variable latency. At stronger stimuli (8·2 and 11·8 mA) the variability in latency is virtually absent, and the two late spikes are regularly elicited. A doubling of stimulus intensity (from 5·8 to 11·8 mA) shortens the latency of the two late spikes only by a few tenths of a msec, and it did not lead to the production of any further action potentials. At 11·8 mA it is clearly seen that the latency of the two late spikes corresponds closely to the latency of the I_2 and I_3 waves respectively (Fig. 4).

At 4·5 and 5·8 mA (Fig. 4) the third spike is, as it were, 'fractured', and at 8·2 and 11·8 mA the third spike has a smaller size than the two preceding ones. During the present experiments, signs of such a change in spike configuration were seen only in ten out of fifty-two single units, and in these cases it always developed progressively during the recording. In several of the units, the change was apparent only as a notch on the rising phase of the spike. It is highly unlikely that the large spikes in these ten cases represented the summed activity of two single units. For instance, for the case of Fig. 4 this would imply that two such units would also fire with a perfect synchrony when the latency was variable (4·5 mA). Besides, the large size of the positive-going spikes of Fig. 4 suggest that they are intracellularly recorded, i.e. they should also for this reason reflect the activity of only one single fibre. A progressive change in the spike configuration, such as that seen in Fig. 4, is most probably developing because the fibre has been damaged by the micro-electrode somewhere close to the site of recording (cf. Hern, Phillips & Porter, 1962).

Figure 5*A* shows records from another fast pyramidal fibre, which arrives at a final firing pattern similar to that seen in Fig. 4, i.e. the three spikes have latencies similar to those of the D wave, the I_2 wave and the I_3 wave respectively. The fibre of Fig. 5*B* could discharge spikes corresponding to all the three initial I waves (12·1 mA). It is of interest to note that the I_1 wave as well as the spike with the corresponding latency occur only at the highest stimulus intensity (Fig. 5*B*). The latency of the I_2 and I_3 spikes respectively is about the same before and after the appearance of the I_1 spike (Fig. 5*B*).

The diagram of Fig. 7 demonstrates that almost all the fast pyramidal units would respond by a rapid repetitive discharge to a strong cortical stimulus (cf. Figs. 4 and 5). In constructing the diagram, only spikes

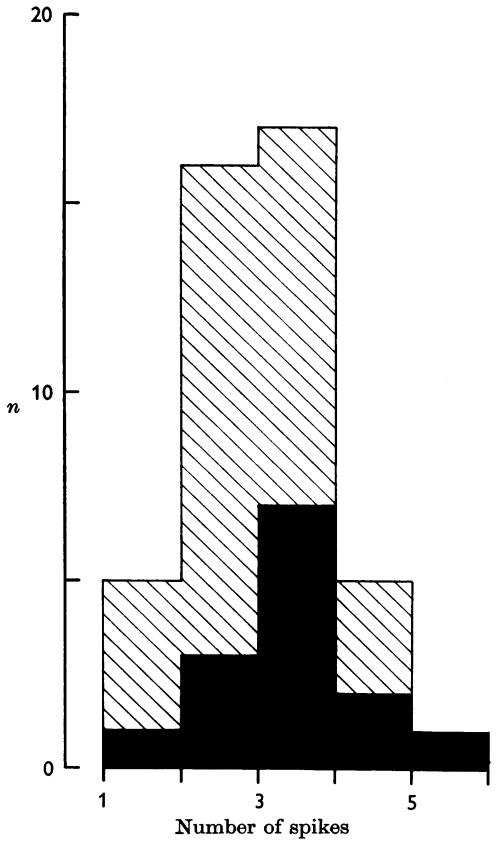

Fig. 7. Diagram showing the maximal number of spikes elicited in fast pyramidal units with cortical stimuli at an intensity exceeding 10·5 mA. Spikes included in the diagram occurred within 8·5 msec following the onset of cortical stimulation. The initial spike (the 'D spike') was included in the count. The 44 fast units of this diagram all had an initial spike latency which differed from that of the D wave by 0·4 msec or less (cf. Fig. 6). *Black areas*: values obtained from units whose cortical stimulus threshold for the D spike was less than 3·0 mA.

occurring during the initial 8·5 msec. following the stimulus were included, i.e. spikes occurring during a period of time approximately covering the four initial I waves. As was demonstrated by Figs. 4 and 5, the spikes succeeding the D spike in such discharges (the 'I spikes') all tended to occur at given preferred latencies. The latency of an I spike was generally remarkably stable at stimulus intensities well above its threshold (Figs. 4

and 5), and even at threshold it would often vary only by some tenth of a msec. During the present experiments, the cortex was regularly stimulated once a second, and in some cases an I spike with a given latency would be elicited only by approximately every second stimulus even at the

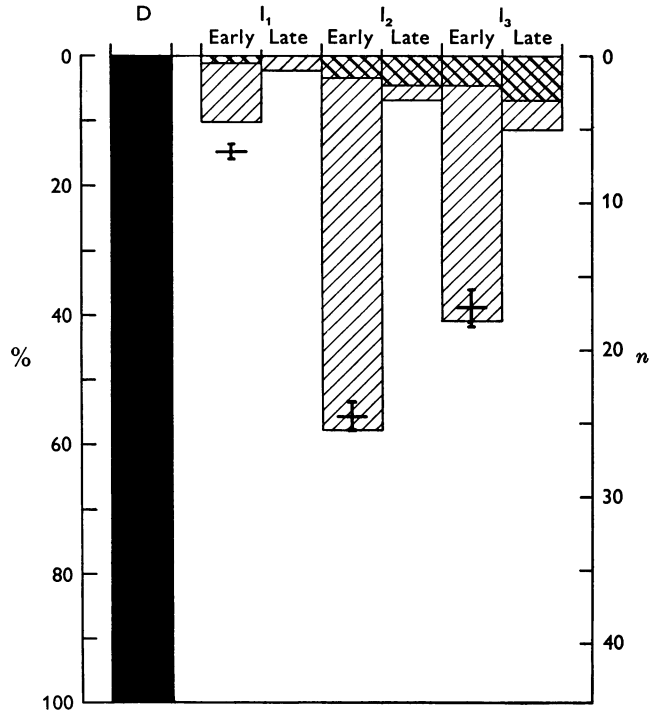

Fig. 8. Diagram showing for 44 fast pyramidal units (see Fig. 7) the number of spikes arriving during the former and latter half ('early' and 'late') respectively of simultaneously recorded I waves (see Fig. 4). The beginning of an I wave was taken as the onset of its negative-going phase, and the duration of an I wave was taken as the time from its beginning to the beginning of the succeeding I wave. For 8 out of the 28 units discharging during the I_3 wave, no I_4 wave was clearly seen. The duration of the I_3 wave was then measured till the end of its negative-going phase. The latter durations varied over the same range and had about the same average value as those obtained when an I_4 wave was visible. All values in the diagram were obtained with cortical stimuli at 10·5 mA or more. All 44 units fired an initial spike coinciding with the D wave. *Right-hand scale*: number of units. *Left-hand scale*: percent of total number of units. *Cross-hatched areas*: spikes occurring at a particular latency only about every second trial (stimulation repeated once a second). These spikes are counted as half a unit each. *Horizontal bars*: the mean surface area of the negative-going phase of the respective I waves, expressed as a percentage of the corresponding surface area of simultaneously recorded D waves. *Vertical bars*: standard error of the respective means. The measurements of I waves were done in thirty-nine of the forty-four experiments relating to single units.

highest stimulus intensities. In several of these cases, an I spike would alternate between two preferred latencies, corresponding to two different I waves.

For the units of Figs. 4 and 5, the preferred latencies of the I spikes were obviously related to those of the I waves. The diagram of Fig. 8 demonstrates that this was generally the case for fast pyramidal fibres. The histogram shows, for the forty-four fast pyramidal units, the number of I spikes arriving during the former and the latter half ('early' and 'late') respectively of the three initial I waves. The histogram was assembled from discharges elicited at a cortical stimulus intensity exceeding 10·5 mA, and I spikes which were elicited only by about every second stimulus (see above) have been counted as half a unit each (Fig. 8, cross-hatched areas). The histogram is plotted upside down in order to facilitate comparisons with illustrated records of pyramidal tract waves. It is seen that I spikes may occur during the early as well as during the late half of any I wave. It is also seen, however, that the vast majority of I spikes occur during the early half of each I wave (Fig. 8). Thus, the repetitive firing set up in fast pyramidal fibres by a strong cortical stimulus occurs in a series of semi-synchronous bursts with a timing corresponding to the I waves.

The units of Fig. 8 were all fast, i.e. they would all discharge an early spike coinciding with the D wave. The diagram of Fig. 8 thus gives an approximate estimate of the extent to which fibres responsible for the D wave discharge during each of the three most common I waves at strong cortical stimuli. As is seen (Fig. 8), nearly 60 % of these fast fibres fired during the early half of the I_2 wave, whereas only about 10 % of the fibres discharged during the I_1 wave.

In thirty-nine out of the forty-four experiments (Fig. 8), the stimulus artifact was small enough to permit an approximate measurement of the surface area of the negative-going phase of the D wave and the three initial I waves respectively at the same strong stimulus intensity as that used for the single units of Fig. 8. In each case, the surface area of the respective I waves was expressed as a percentage of the surface area of the D wave from the same record. The horizontal bars in Fig. 8 give the average of the relative surface area of the three respective I waves, and vertical bars give the standard error of the respective means. These mean values would serve as a rough estimate of the extent to which fibres responsible for the D wave would have to discharge at times corresponding to the three initial I waves in order to produce the latter. These values, obtained from measurements of pyramidal tract waves (horizontal bars), are seen to fit well with the percentage of fast pyramidal fibres actually found to discharge during the respective I waves (Fig. 8). Thus, it may be concluded that the repetitive discharge of fast pyramidal fibres was almost completely

responsible for at least the three initial I waves. This was apparently the case also for the I_4 wave. The latter wave was not obtained in all the experiments, and it was often too small and vague to measure its duration accurately. Therefore, it has not been included in Fig. 8. However, eleven out of the forty-four fast pyramidal units would give a spike with a preferred latency corresponding to that of the I_4 wave.

The discharge properties of fast pyramidal fibres, such as those shown in Figs. 7 and 8, were not found to be related in any obvious manner to the latency or cortical stimulus threshold of the D spike of the respective units. Possibly, there might have been a slight tendency for units with a low threshold for direct stimulation to deliver a larger number of spikes during the I wave. Black areas in Fig. 7 show the maximal number of spikes elicited in fast fibres with a threshold for the D spike of less than 3 mA.

The stimulus threshold for the D spike was between 1·6 and 8·2 mA, and at the D spike threshold the simultaneously recorded D wave had attained between about 5 and 95% of its maximal size. Fast pyramidal units would, of course, be expected to be recruited for as long as the size of the D wave increases with stimulus intensity. The stimulus threshold for an I spike could be a little lower than that for the I wave with the corresponding latency (Fig. 4, 4·5 mA). This is not surprising, because most probably a substantial number of simultaneously discharging I spikes would be required to give rise to a clearly visible I wave in recordings from the cord surface. In many cases, the threshold for an I spike was about the same as that for the corresponding I wave. In several cases, the threshold for an I spike could be much higher than that for the corresponding I wave. It was noted above that I waves did not always attain a maximal size within the present range of stimulus intensities (p. 658).

In the present experiments, thirty-nine fast pyramidal fibres would discharge repetitively during the initial 8·5 msec following the cortical stimulus (Fig. 7). For one third of these fibres (13 units) the threshold for the D spike was less than 3 mA, and in all these cases the D spike appeared at a lower stimulus intensity than any of the later I spikes (Fig. 4). This is consistent with the well-known fact that, especially with surface-anodal stimuli, the I waves start to appear at a higher stimulus strength than the D wave (Fig. 1; Hern, Landgren, Phillips & Porter, 1962; Phillips & Porter, 1964; Gorman, 1966). Previous workers have shown that a weak surface-anodal pulse will selectively activate the D spike of a unit when the latter is stimulated by an electrode placed close to the 'best point' on the cortex, i.e. at the site when the unit can be activated by a minimal amount of stimulating current (Phillips, 1956; Hern, Landgren, Phillips & Porter, 1962; Phillips & Porter, 1962). It has also been shown that

the 'direct' threshold of a unit is markedly increased as the stimulating electrode is moved only a few mm away from the best point (Landgren, Phillips & Porter, 1962*b*; Phillips & Porter, 1962).

Two thirds of the thirty-nine repetitive fibres of Fig. 7 (26 units) had a direct threshold of 3 mA or more. For 11 of these units, the threshold for the D spike was about the same as that for one or several of the succeeding I spikes (Fig. 5*A*, 3·9 mA), and in 2 of the units, the threshold for the D spike was actually lower than that for one or several of the I spikes. Thus, as has been previously noted (Phillips, 1956; Hern, Landgren, Phillips & Porter, 1962), a surface-anodal pulse may apparently be used for a selective activation of the D spike of a pyramidal fibre only for units whose direct stimulus threshold is low, i.e. presumably for the units which are closest to the site of the cortical stimulating electrode (Landgren *et al.* 1962*b*; Phillips & Porter, 1962).

So far, the investigation has been concerned only with the discharge of fast pyramidal fibres within 8·5 msec after the onset of stimulation. For 35 of the fast units records of the discharge were also taken on slower sweeps, covering about 50 msec following the cortical stimulation. Five of these cells were found to discharge at times later than 8·5 msec, i.e. at times later than that corresponding to the four initial I waves. These later discharges were generally relatively irregular, and their impulse frequency was slower than that of the fast initial discharge. No obvious signs of preferred latencies were seen during the late discharges. The impulse frequency as well as the duration of the late discharge would increase with the strength of the cortical stimulation. The maximal duration of these discharges (counted from the onset of the cortical stimulus) ranged from about 15 to 40 msec, different in different units.

The analysis above has concerned units whose D spike latency differed from that of the D wave only by 0·4 msec or less. It should be mentioned that all except one of the eight slower units of Fig. 6 would discharge repetitively during the initial 8·5 msec in a manner approximately similar to that described for fast units. These slower units were also probably pyramidal fibres, because they were intermingled with the fast units in the spinal cord, and their initial spikes would follow tetani at 500/sec or more whenever tested (tried in five of the eight cases). The direct threshold for these units was between 2·5 and 8·2 mA.

None of the I spikes of fast pyramidal units had an onset earlier than that of the I_1 wave (Fig. 8). This would indicate that the little notch which could sometimes be seen between the D wave and the I_1 wave (Fig. 1*B*, arrow marked '×') was produced by directly excited corticospinal units with a slower conduction velocity than that of the fast fibres responsible for the D wave.

DISCUSSION

The results have shown that, at least under the present experimental circumstances, the I waves predominantly reflect the repetitive discharge of fast cortico-spinal fibres such as those responsible for the D wave (Figs. 3 and 8). Thus, only a relatively small proportion of all the pyramidal fibres contributed significantly to the I waves. The D wave must have been produced by fibres with a conduction velocity of the order of 50–70 m/sec (p. 673), and the diameter of these fibres would then be expected to be between around 8 and 12 μ (Hursh, 1939). The large majority of pyramidal fibres are much smaller, and this is presumably the case also when considering only the fibres emerging from the precentral motor area (e.g. Lassek, 1941, 1942, 1943).

There was no evidence indicating that slow pyramidal fibres were directly or indirectly activated to any great extent by the cortical stimulus. It should be pointed out, however, that such negative findings might not be very reliable. Most of the single units responding to the cortical stimulus had indeed a short initial spike latency, i.e. the material consisted mainly of fast pyramidal fibres (Fig. 6, cf. also Landgren *et al.* 1962*a*). Slow units are, however, likely to be underrepresented in such samples, because micro-electrode recordings are presumably more easily obtained from large fibres than from the small ones. In the extracellular records of pyramidal tract waves, the activity of a large fibre would be expected to give rise to a more prominent potential deflexion than that caused by a small fibre (e.g. Blair & Erlanger, 1933). Thus, during the present experiments, a number of slow pyramidal fibres might well have been discharging without giving rise to any significant potential deflexions in recordings from the cord surface. Furthermore, even if fast and slow units were activated simultaneously from the cortex, their impulses would naturally arrive at different times at the spinal cord. Distinct 'waves', such as the I waves, would obviously be expected to be produced predominantly by a group of fibres with similar conduction velocities. It may be concluded that the I waves give information concerning the discharge of the very fastest pyramidal fibres, but they do not necessarily tell much concerning the discharge of the more numerous smaller fibres of the corticospinal tract.

Although exceptions might possibly occur, it appears likely that the I waves studied in cat and monkey by previous investigators have also been predominantly produced by the discharge of fast cortico spinal fibres (see Introduction). In some experiments, the I waves have been used for monitoring the output of the motor cortex in studies relating to intracortical mechanisms (e.g. Wall, Rémond & Dobson, 1953). For the interpretation of such experiments it might be of some interest to consider that

the I waves are likely to represent only the activity of the fastest group of pyramidal fibres. The function of fast pyramidal fibres is most probably different from that of the slow ones, and there could well be important differences between the intracortical synaptic connexions of fast and slow corticospinal units (Brookhart, 1952; Towe *et al.* 1963; Evarts, 1965, 1966; Hardin, 1965).

The latency of the I waves and that of the corresponding spikes of single units did not vary much with stimulus strength; each cell tended to fire at certain preferred latencies (Figs. 1–5 and 8). The I waves are thus clearly not the result of a repetitive discharge set up by an asynchronous synaptic impact (cf. Creutzfeldt, Lux & Nacimiento, 1964). The excitatory post-synaptic potentials (EPSPs), which are presumably triggering the spikes of the I wave discharge, should be markedly synchronous and sharp-peaked to give such a rapid discharge with well defined latencies.

It is of some interest to note that the I_1 wave had a higher stimulus threshold than two waves with a longer latency, the I_2 and I_3 waves (Figs. 1, 4 and 5). This finding would suggest that the I wave discharge was not kept going exclusively by a stereotyped repetition of facilitatory actions generated by axon collaterals of the discharging cortico spinal neurones. A similar conclusion was reached also by previous workers, who failed to elicit an I wave discharge by antidromic stimulation of the cortico spinal tract (Patton & Amassian, 1954, 1960, Landau, Bishop & Clare, 1965). The intervals between the three initial I waves were of the order of 1–2 msec (Fig. 2). If a cortical stimulus elicited 'triggering' EPSPs corresponding to all the three initial I waves, then the intervals between these EPSPs would almost certainly be too brief to allow one of them to decline completely before the succeeding one appeared. Thus, the I_2 and I_3 EPSPs, but not the I_1 EPSP, would be superimposed on and added to the declining phase of a preceding EPSP. Spikes corresponding to the I_2 and I_3 waves could therefore occur at a lower stimulus strength than those of the I_1 wave even if the three respective EPSPs were of a similar size. The difference in threshold between the initial I spike and the succeeding ones would, of course, be even more marked if the 'triggering' EPSPs were superimposed on a more slowly rising, asynchronous excitation produced by the cortical stimulus.

A crude and unphysiological stimulus, such as a strong electrical pulse delivered to the cortical surface, is likely to activate a confusing multitude of intracortical neuronal systems. It is not very surprising that such a stimulus may elicit a repetitive discharge in most of the fast cortico-spinal cells (Fig. 7; cf. Patton & Amassian, 1954, 1960; Berlin, 1964). The onset of the cortical activity responsible for the I wave discharge would evidently tend to be synchronized by the strong electrical stimulus.

It is, however, of some interest that also I spikes later than those of the wave are elicited with such a high degree of synchrony for a whole population of cortico-spinal cells (Fig. 8). It has been suggested that the regular recurrence of the I waves is due to a 'periodic bombardment of Betz cells through chains of neurons with fixed temporal characteristics' (Patton & Amassian, 1960). The 'periodic bombardment' of the cortico spinal cells could also be due to, for instance, a synchronous oscillatory activity started by the electrical stimulus in a population of intracortical neurones provided with a recurrent facilitation of some sort. Several other alternative explanations are also possible. Further experimental knowledge concerning the mechanisms responsible for triggering the I wave discharge could be of interest with respect to the organization of the motor cortex.

As was noted in the Introduction, there is in the monkey a monosynaptic connexion between fast cortico spinal fibres and spinal motoneurones (Bernhard *et al.* 1953; Preston & Whitlock, 1960, 1961; Landgren *et al.* 1962*a*). It has also been shown that a strong cortical stimulus will give rise to prolonged synaptic effects in spinal motoneurones (Bernhard *et al.* 1953; Preston & Whitlock, 1960, 1961; Phillips & Porter, 1964). The present experiments have shown that a strong cortical stimulus will produce a semi-synchronous repetitive discharge in most of the fast cortico spinal fibres (Figs. 7 and 8), and it has also been demonstrated that this discharge (i.e. the I waves) is easy to monitor with an electrode resting on the surface of the spinal cord (cf. Phillips & Porter, 1964). Cortically elicited, prolonged synaptic effects in spinal motoneurones could obviously to a great extent be due to a prolonged discharge of fast pyramidal fibres. In the light of the present findings, this question will be investigated in a succeeding paper (Kernell & Wu, 1967).

We wish to thank Professor C. G. Phillips for valuable discussions and comments and for the hospitality of his laboratory, and Mr C. H. Carr for technical assistance. D.K. is grateful to 'Harald och Greta Jeanssons Stiftelse', Sweden, for a personal grant.

REFERENCES

ADRIAN, E. D. & MORUZZI, G. (1939). Impulses in the pyramidal tract. *J. Physiol.* **97**, 153–199.

BERLIN, L. (1964). Effects of seizures on single pyramidal tract neurones. *Archs Neurol., Chicago* **10**, 271–282.

BERNHARD, C. G., BOHM, E. & PETERSÉN, I. (1953). Investigations on the organization of the corticospinal system in monkeys. *Acta physiol. scand.* **29**, suppl. 106, 79–105.

BERTRAND, G. (1956). Spinal efferent pathways from the supplementary motor area. *Brain*, **79**, 461–473.

BLAIR, E. A. & ERLANGER, J. (1933). A comparison of the characteristics of axons through their individual electrical responses. *Am. J. Physiol.* **106**, 524–564.

BROOKHART, J. M. (1952). A study of cortico-spinal activation of motor neurons. *Res. Publs. Ass. Res. nerv. ment. Dis.* **30**, 157–173.

CREUTZFELDT, O. D., LUX, H. D. & NACIMIENTO, A. C. (1964). Intracelluläre Reizung corticaler Nervenzellen. *Pflügers Arch. ges. Physiol.* **281**, 129–151.

EVARTS, E. V. (1965). Relation of discharge frequency to conduction velocity in pyramidal tract neurons. *J. Neurophysiol.* **28**, 216–228.

EVARTS, E. V. (1966). Pyramidal tract activity associated with conditioned hand movement in the monkey. *J. Neurophysiol.* **29**, 1011–1027.

GORMAN, A. L. F. (1966). Differential patterns of activation of the pyramidal system elicited by surface anodal and cathodal cortical stimulation. *J. Neurophysiol.* **29**, 547–564.

HARDIN, W. B. JR. (1965). Spontaneous activity in the pyramidal tract of chronic cats and monkeys. *Archs Neurol. Chicago* **13**, 501–512.

HERN, J. E. C., LANDGREN, S., PHILLIPS, C. G. & PORTER, R. (1962). Selective excitation of corticofugal neurones by surface-anodal stimulation of the baboon's motor cortex. *J. Physiol.* **161**, 73–90.

HERN, J. E. C., PHILLIPS, C. G. & PORTER, R. (1962). Electrical thresholds of unimpaled corticospinal cells in the cat. *Q. Jl exp. Physiol.* **47**, 134–140.

HURSH, J. B. (1939). Conduction velocity and diameter of nerve fibers. *Am. J. Physiol.* **127**, 131–139.

KERNELL, D. & WU CHIEN-PING (1967). Post-synaptic effects of cortical stimulation on forelimb motoneurones in the baboon. *J. Physiol.* **191**, 673–690.

LANDAU, W. M., BISHOP, G. H. & CLARE, M. H. (1965). Site of excitation in stimulation of the motor cortex. *J. Neurophysiol.* **28**, 1206–1222.

LANDGREN, S., PHILLIPS, C. G. & PORTER, R. (1962*a*). Minimal synaptic actions of pyramidal impulses on some alpha motoneurones of the baboon's hand and forearm. *J. Physiol.* **161**, 91–111.

LANDGREN, S., PHILLIPS, C. G. & PORTER, R. (1962*b*). Cortical fields of origin of the monosynaptic pyramidal pathways to some alpha motoneurones of the baboon's hand and forearm. *J. Physiol.* **161**, 112–125.

LASSEK, A. M. (1941). The pyramidal tract of the monkey. A Betz cell count and pyramidal tract enumeration. *J. comp. Neurol.* **74**, 193–202.

LASSEK, A. M. (1942). The pyramidal tract. The effect of pre- and post-central cortical lesions on the fiber components of the pyramids in monkey. *J. nerv. ment. Dis.* **95**, 721–729.

LASSEK, A. M. (1943). The pyramidal tract. A study of the large motor cells of area 4 and the fiber components of the pyramid in the spider monkey (*Ataleus ater*). *J. comp. Neurol.* **79**, 407–413.

PATTON, H. D. & AMASSIAN, V. E. (1954). Single- and multiple-unit analysis of cortical stage of pyramidal tract activation. *J. Neurophysiol.* **17**, 345–363.

PATTON, H. D. & AMASSIAN, V. E. (1960). The pyramidal tract: its excitation and functions In *Handbook of Physiology—Neurophysiology II*, ed. FIELD, J., pp. 837–861. Washington: American Physiological Society.

PHILLIPS, C. G. (1956). Cortical motor threshold and the thresholds and distribution of excited Betz cells in the cat. *Q. Jl exp. Physiol.* **41**, 70–84.

PHILLIPS, C. G. (1966). Changing concepts of the precentral motor area. In *Brain and Conscious Experience*, ed. ECCLES, J. C., pp. 389–410. New York: Spinger-Verlag.

PHILLIPS, C. G. & PORTER, R. (1962). Unifocal and bifocal stimulation of the motor cortex. *J. Physiol.* **162**, 532–538.

PHILLIPS, C. G. & PORTER, R. (1964). The pyramidal projection to motoneurones of some muscle groups of the baboon's forelimb. In *Prog. brain Res.* **12**, 222–242. Amsterdam: Elsevier.

PRESTON, J. B. & WHITLOCK, D. G. (1960). Precentral facilitation and inhibition of spinal motoneurones. *J. Neurophysiol.* **23**, 154–170.

PRESTON, J. B. & WHITLOCK, D. G. (1961). Intracellular potentials recorded from motoneurones following precentral gyrus stimulation in primate. *J. Neurophysiol.* **24**, 91–100.

TOWE, A. L., PATTON, H. D. & KENNEDY, T. T. (1963). Properties of the pyramidal system in the cat. *Expl Neurol.* **8**, 220–238.

WALL, P. D., RÉMOND, A. G. & DOBSON, R. L. (1953). Studies on the mechanism of the action of visual afferents on motor cortex excitability. *Electroenceph. clin. Neurophysiol.* **5**, 385–393.