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SINGLE-UNIT RECORDING FROM ANTIDROMICALLY ACTIVATED OPTIC RADIATION NEURONES

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Antidromic activation of cells in the central nervous system has proved to be a most useful method of studying the properties of neurones and the part these play in synaptic transmission (see e.g. Renshaw, 1941, 1946; Araki, Otani & Furukawa, 1953; Brock, Coombs & Eccles, 1953; Frank & Fuortes, 1955; Granit & Phillips, 1956; Phillips, 1956, 1959; Coombs, Curtis & Eccles, 1957*a*, *b*; Fatt, 1957; Fuortes, Frank & Becker, 1957; Martin & Branch, 1958; Bennett, Crain & Grundfest, 1959; Freygang & Frank, 1959; Machne, Fadiga & Brookhart, 1959). The method is also valuable in establishing the identity of various cells and in determining the extent of a tract, on the principle that an antidromic impulse will not cross a synapse (e.g. Woolsey & Chang, 1947). However, the existence of recurrent collaterals is a complicating factor here. We have stimulated the visual cortex in cats whilst recording extracellularly from units in the lateral geniculate nucleus (LGN) and optic radiation with both these objects in mind. The LGN projects to a large area of cortex and in these experiments no attempt was made to stimulate this entire area but only the most anterior part. Evidence will be produced to show that the majority of our records result from a true antidromic activation of the unit. This is a necessary step, because it has been suggested that the visual cortex sends an efferent supply to the LGN (e.g. Vastola, 1957; Widén & Marsan, 1960*a*, who also give a list of references to earlier work). Our results do, however, lend some support to this idea, because a few units could be activated only after rather long latencies. However, the results are most useful for the study of the process of impulse initiation in the cell body and in this respect support the theories advanced by Araki & Otani (1955), Coombs *et al.* (1957*a*, *b*) and Fuortes *et al.* (1957).

METHODS

The preparation is essentially as described in the earlier paper (Bishop, Burke & Davis, 1962*a*). In order to stimulate the visual cortex, bone and dura were removed over the anterior region of the striate area for a distance of about 1·5 cm (actually over that area

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which Doty (1958) found to yield the largest potentials to photic or optic-nerve stimulation). Into this part of the cortex was inserted a bank of stimulating electrodes arranged in six pairs along the length of the lateral gyrus. The distance between each pair and between each member of a pair was 2 mm. The stimulating electrodes were steel electrolytically pointed beading needles varnished almost to the tip (Grundfest, Sengstaken, Oettinger & Gurry, 1950), about 1 cm long, clamped in a small Perspex block with their tips level. The electrodes were inserted so that the tips lay 2–4 mm below the surface of the brain. The chamber through which the recording electrode was inserted (Bishop *et al.* 1962*a*) was enlarged so as to enclose the stimulating electrodes, the wires attached to the electrodes being brought through a small hole which was then sealed with dental impression compound. In all experiments the chamber was filled with liquid paraffin.

The stimulus, delivered via a pulse transformer, could be applied to any pair or combination of pairs of electrodes and consisted of a 50 μsec rectangular pulse. The stimulus artifact was roughly controlled by means of a 10 KΩ potentiometer placed across the secondary of the pulse transformer, the centre tapping of the potentiometer being taken to the indifferent lead on the cat and adjusted to give the least artifact.

In all experiments both optic nerves were prepared for stimulation. In all figures oscilloscope records are negative upwards.

RESULTS

In 11 experiments 46 units obtained in the LGN or optic radiation were activated by stimulation of the cortex. All except three of these units also responded to stimulation of one or other optic nerve. Many units activated from an optic nerve could not be discharged by cortical stimulation, presumably because they did not project to the anterior region of the striate cortex. On the other hand it was noticed that in a given track of the recording electrode several units might be obtained which were activated in this way; this occurred more frequently when the electrode was in the anterior part of the LGN. This suggests that there is some geographically arranged projection of the LGN on to the visual cortex, probably with the anterior part of the former projecting to the anterior part of the latter (cf. Minkowski, 1913; W. R. Haybow & C. Webb, unpublished).

Thirty-six units were identified as LGN cells by reason of the wave form of their response (type 'b') and by the various other criteria which we adopted (Bishop *et al.* 1962*a*). Examples of the responses from three LGN cells to optic nerve and visual cortex stimulation are shown in Fig. 1. In the examples shown the cortical stimulation produces a true 'antidromic' activation of the LGN cell, the response differing in a characteristic way from the response to orthodromic stimulation. However, before we could recognize this characteristic wave form as indicative of antidromic activation it was necessary to obtain direct evidence that this was the case.

Test for true antidromic activation

When the geniculate neurone has been activated orthodromically through the optic nerve, it will not be possible to produce a true antidromic response by cortical stimulation until the orthodromic spike has

reached the cortex and the post-synaptic axon has recovered sufficiently. Any attempt to produce an earlier response will result in a collision somewhere along the course of the post-synaptic axon. An impulse travelling from the cortex to the LGN through any axon other than the one carrying the original orthodromic spike does not suffer this restriction. Although such a cortico-geniculate impulse would have to activate the LGN neurone trans-synaptically it will always be possible to apply the shock to the cortex sufficiently early for the second geniculate response to occur immediately

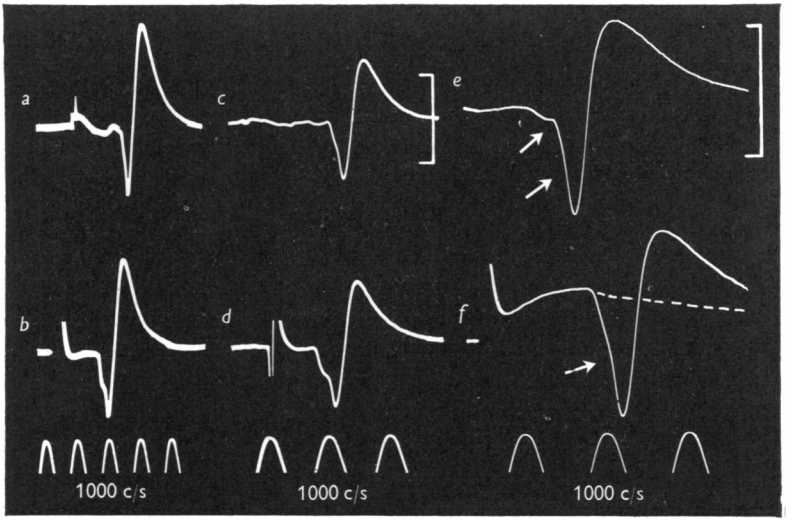

Fig. 1. Extracellular records of the orthodromic and antidromic responses, from the same LGN cell. *a, c, e*, orthodromic responses from three cells. *b, d, f*, antidromic responses from the same cells. The stimulus artifact in *f* was large, its time course during the response being indicated by the broken line. Voltage calibrations 5 mV: *c* for *a*, *b*, *c*, *d*; *e* for *e*, *f*.

after the cell has recovered from the orthodromic activation. The absolutely refractory period of the geniculate neurone is probably close to 0·5 msec, becoming supernormal at 1·6 msec (Bishop & Evans, 1956). Our single-unit studies (Table 1; cf. also Bishop, Burke & Davis, 1962*b*) have given similar values for the duration of refractoriness. When conditioning and testing shocks are applied to the presynaptic pathway some distance from the cell a major factor causing delay in the generation of a second geniculate spike is the slowed conduction in the recovering presynaptic pathway. This would obviously not occur in the case of the cortico-geniculate trans-synaptic activation mentioned above and the minimum orthodromic, 'antidromic' response–response interval in these circumstances will be less than 1·6 msec.

Measurements were made on two LGN cells whose responses to the two types of stimulation, orthodromic and antidromic, were regarded as characteristic. Typical single-shock responses from these neurones are illustrated in Fig. 1*a–d*. The minimum orthodromic, antidromic response–response interval was found to be 2·27 and 5·54 msec, respectively, for the two cells (Table 1). This indicates that the second response in each case must have been the result of true antidromic activation. The way in which the measurements were made is indicated in Fig. 2 (for further details see legend to Fig. 2).

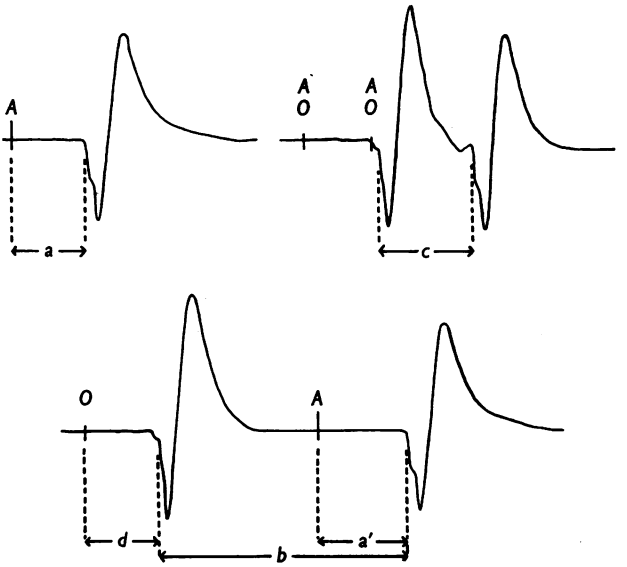

Fig. 2. Diagram to show the measurements that were made in testing for true antidromic activation. The short vertical lines on the tracings represent the stimulus artifacts. Measurements are to the foot of the A potential in each case. *A*, cortical stimulus. *O*, stimulus to optic nerve. *a* = antidromic shock-response interval. *a'* = antidromic shock-response interval following orthodromic activation. *b* = minimum orthodromic, antidromic response–response interval. *c* (unit 1) = minimum antidromic, antidromic response–response interval. *c* (unit 2) = minimum orthodromic, orthodromic response–response interval. *d* = orthodromic shock–response interval. Further details in text.

Further confirmation was provided by examination of the minimum orthodromic, antidromic response–response interval (*b*, Fig. 2) and the corresponding shock–response latency (*a'*) for the second response when cortical stimulation was increased from threshold (*T*) to five times threshold (5*T*). Altering the shock strength in this way will have a very different effect on these two intervals if the second response is truly anti-

dromic as opposed to trans-synaptic. If the response is trans-synaptic increasing the shock-strength will not alter the minimum response–response interval (equivalent to b) but will cause a small decrease in the shock–response latency of the second response (equivalent to a'). The latter change would be comparable to the small decrease in the value of a as seen in Table 1. With true antidromic activation, however, there will be a marked decrease in the response–response interval (b) because the second response will arise much earlier in the relatively refractory period of the post-synaptic axon, although this will be offset to some extent by the increased shock–response latency of the second response. This was found to be the case (unit 1, Table 1); the response–response interval decreased from 3·37 to 2·27 msec as the cortical shock was increased from T to $5T$ and the

TABLE 1. Test for true antidromic activation

	a	b	c	d	a'	$(b–a–a')$
Unit 1	0·89 (T)	3·37	< 1·04 (A)	1·13	0·92	1·56
Unit 1	0·85 ($5 \times T$)	2·27	< 1·04 (A)	1·25	1·00	0·42
Unit 2	1·64	5·54	1·70 (O)	1·70	1·94	1·96

The intervals a, b, c, d, and a' were measured as indicated in Fig. 2. The delay in the cortex was calculated = $(b–a–a')$. All times in msec. T = threshold stimulation. $5 \times T$ = 5 times threshold stimulation. A = interval determined by two antidromic stimuli. O = interval determined by two orthodromic stimuli.

shock–response latency of the second response increased from 0·92 to 1·00 msec. The latter increase is due entirely to a slower rate of conduction in the relatively refractory axon. When shocks of short duration are used as stimuli a second response can be set up at the stimulating cathode during the relatively refractory period as promptly as the normal process (Gasser & Erlanger, 1925). This explains why the difference between the antidromic shock–response latency during the relatively refractory state (a') on the one hand and the normal antidromic latency (a) on the other should be rather greater when the cortical stimuli in each case are five times threshold than it is when they are at threshold. At T the difference in the latencies ($a'–a$) was only 0·03 msec whereas at $5T$ the difference was 0·15 msec. The stronger stimulus excites the nerve much earlier in the relatively refractory period so that the latency increases because of slowed conduction. At threshold the stimulus, to be effective, has to be applied at the end of the relatively refractory period so that conduction now approximates to normal. In the case of unit 2 the increased latency was 0·3 msec but in this experiment the effect of alteration in the stimulus strength was not examined. The above considerations clearly indicate that the activation of the geniculate neurones by cortical stimulation was truly antidromic.

After the orthodromic spike has reached the cortex there is a delay

before the antidromic impulse can be initiated. This interval can be calculated from the results, being given by the expression b–a–a'. For unit 1 this delay was 1·56 msec for threshold stimulation and 0·42 msec for supraliminal ($5 \times T$) stimulation. To a first approximation these values could be regarded respectively as the relatively and absolutely refractory periods of the nerve. Assuming a conduction distance to the cell of 15 mm, the conduction velocity would have been about 17·7 m/sec. For a fibre of this conduction velocity these calculations of the refractory period are rather low but this is to be expected from the method, which differs from the classical procedure in that the test impulse travels in the opposite direction to the conditioning impulse and can therefore be initiated at a shorter interval at a point remote from the cathode. In the case of unit 2, evidently a neurone of smaller diameter (a = 1·64 msec), the delay in the cortex was 1·96 msec.

Extracellular wave form of antidromically activated cell

The antidromic response has a positive/negative wave form with a prominent step on the downstroke of the positive phase. The response may fractionate at this level to reveal a smaller, sometimes positive, sometimes positive/negative, response (Fig. 3). Since our interpretation of the two

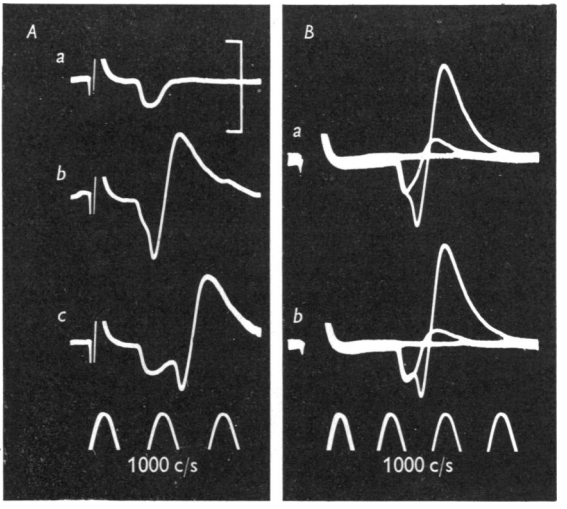

Fig. 3. Fractionation of antidromic wave form to reveal A potential. *A*, responses obtained with constant strength of stimulus to cortex. *a*, monophasic A potential only; *b*, A+B potential. *c*, B potential arises late. *B*, similar effects in another unit, but A potential diphasic. *a*, *b*, three superimposed records in each case to a constant stimulus of threshold strength (note blank sweeps). The full response has a large negative phase in both *A* and *B*. Voltage calibration 5 mV applies to all records.

components of the antidromic response is the same as that of Phillips (1959) for the antidromic responses of Betz cells, we shall henceforth refer to the smaller response as the A component and the additional response as the B component, using the terminology of Fuortes *et al.* (1957) concerning the intracellular record from antidromically activated motoneurones. We shall likewise refer to the A and B components of the orthodromic response and discuss them more fully in the next paper (Bishop *et al.* 1962*b*).

Comparison of orthodromic and antidromic responses

In thirty LGN cells comparison of the orthodromic and antidromic responses shows that they differ in several respects:

(i) There is never more than one step on the downstroke of the positive phase of the antidromic response, whereas in the orthodromic response there may be two steps (Fig. 1, arrows; see also Figs. 1, 2 in Bishop *et al.* 1962*b*).

(ii) The A–B step on the orthodromic response although it corresponds in amplitude to the A–B step on the antidromic response, is much less prominent (Fig. 1).

(iii) As already mentioned, the antidromic response often fractionates at the level of the A–B step to give a smaller response (the A component). This fractionation may occur at any supraliminal strength of stimulus and is therefore a failure not in the axon but in or near the cell body itself. Normally, a fractionation of the orthodromic response at this level occurs only rarely, although it can be brought about in various ways (see Bishop *et al.* 1962*b*).

(iv) Figure 3 also illustrates another point of difference between orthodromic and antidromic responses. The B component of the antidromic response (a positive/negative wave form which behaves in an all-or-nothing manner) commences at a varying interval after the A component and this variation in delay is also unrelated to the level of stimulation. In the orthodromic response there is also a variation in latency but it occurs not at the A–B step but at an earlier step on the positive phase. Furthermore, it is marked only at threshold stimulation, the latency decreasing with stronger stimuli (cf. Bishop *et al.* 1962*a*). The greatest shortening of the latency of the A response in any unit with increase in stimulus strength from threshold was 0·17 msec, the mean decrease being about 0·10 msec. The maximum variation in latency of the B response in any unit was 0·55 msec and this delay occurs mainly near the cell. For example, the variation in latency of the B response *relative* to the A response is of the same order. Brock *et al.* (1953) reported A–B delays of 0·05–0·40 msec (in different cells).

(v) The amplitude of the antidromic response is usually slightly less than

that of the orthodromic response and the duration slightly more. These differences in amplitude and duration are probably due to the slightly longer delay in generation of the B response in the antidromic activation of the cell.

Although a detailed examination of the responses of radiation axons to orthodromic and antidromic stimulation has not been made, no differences in wave form have been noted. Presumably one might expect a deteriorating axon to give a slightly different response depending on the direction from which the impulse approached (cf. Tasaki, 1952).

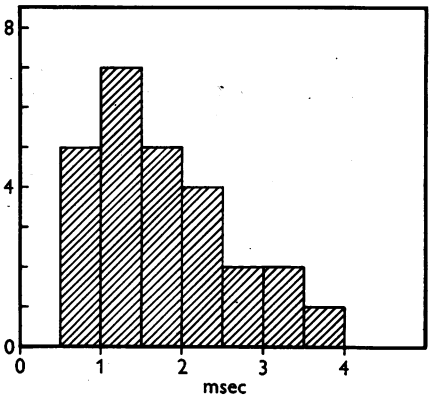

Fig. 4. Histogram of the latencies of twenty-six LGN cells to supraliminal antidromic stimulation in the visual cortex. The latencies are divided into groups of 0·5 msec width.

Latencies

The latencies to supraliminal antidromic stimulation for twenty-six cells are grouped in the histogram of Fig. 4. The latencies range from 0·54 to 3·80 msec, in all cases the values being the mean of several (usually six) responses. Only two of these units did not have a prominent A–B step on the positive phase. Their latencies were 1·39 and 3·19 msec respectively, which would allow time for transmission through a synapse. The histogram does not include three units which fired only after a long and variable latency (more than 10 msec). None of the responses with a very long latency had the characteristic wave form. However, two units of short latency (1·54 and 3·80 msec) also fired much later. If we assume a conduction distance of 15 mm, the range of latencies corresponds to a range of conduction velocities from 4·0 to 27·8 m/sec.

A and B potentials

In twelve of twenty-four units (50 %) exhibiting a prominent A–B inflexion the A component appeared occasionally to single cortical stimuli.

In four other units (16·7 %) an A component was revealed only during stimulation repeated at short intervals. Eight units were not adequately tested. The antidromic response always fractionates to give an A response during short trains of stimuli at a frequency of 250–500/sec. The actual pattern of behaviour varies in different units (Fig. 5). Usually there is a failure of the B component within one or two stimuli after which the B potential usually reappears. Occasionally the B response does not reappear (Fig. 5*c*). During a short train of impulses in which the B component is present the A–B step becomes progressively more prominent

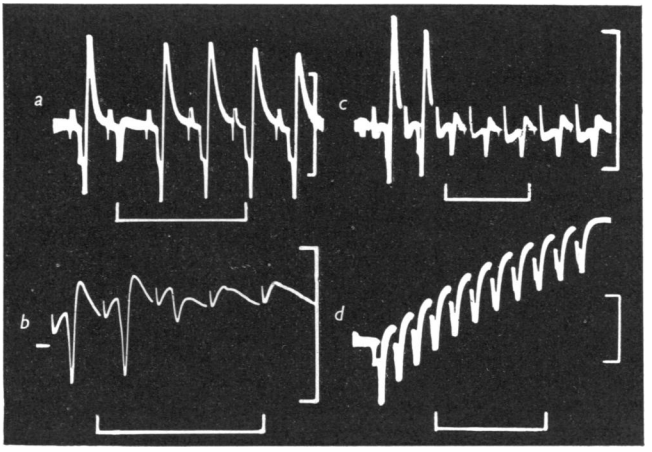

Fig. 5. Effect of repetitive stimulation (250–500/sec) on the antidromic response. *a*, LGN cell, second response an A potential only. Note increasing prominence of A–B step in third and sixth responses. *b*, LGN cell. Elevation of base line is due to summation of stimulus artifacts, as also in *d*. An A potential, alone in third response, fails in fourth and fifth responses. *c*, LGN cell. Full response only to first and second stimuli. A potentials to subsequent stimuli continued indefinitely. *d*, post-synaptic axon. No failure to response but note increasing prominence of notch on downstroke. Voltage calibrations, *a*, *c*, 5 mV; *b*, *d*, 10 mV. Time marks 10 msec.

ending in failure of the B response (Fig. 5*a*, *c*). Figure 5*b* shows an uncommon occurrence, the disappearance of the A potential. The small positive wave in the fourth response may represent the multineurone potential. Alternatively, it might be due to the response of the myelinated part of the nerve (cf. Brock *et al.* 1953). However, it is not present in the fifth response. A failure of the A potential is so unusual that we have not been able to study this behaviour in any greater detail. Figure 5*d* shows, by way of comparison, the response of a radiation axon to antidromic stimulation at high frequency; the response is unchanged apart from the development of a notch on the downstroke (cf. Bishop *et al.* 1962*a*).

Of the sixteen units which gave an A potential to antidromic stimulation, 5 had an A potential which was diphasic (positive/negative). The ratio of the amplitudes of the negative and positive phases was 0·50, 0·55, 0·20, 0·57 and 0·32 (mean 0·43), respectively. In all five cases the B potential had a large negative phase. The ratio of the amplitudes of the negative phases of the A and B potentials was 0·15, 0·13, 0·18, 0·16 and 0·16 (mean 0·16), respectively. In the other eleven units the A potential was monophasic. In five of these the B potential had lost all or most of its negative phase implying that the electrode had damaged the membrane (Bishop *et al.* 1962*a*); hence in these five cases it is possible that at some stage the A potential may also have been diphasic.

Refractory period of A and B potentials

Figure 6 illustrates the fractionation of the antidromic response brought about by two antidromic stimuli at various short intervals. In Fig. 7 the amplitudes of the two components are graphed against the interval between the commencement of the two responses (see arrows in Fig. 6) for the entire series partially illustrated in Fig. 6. The A potential first appears at a response interval of about 1 msec but this refractory period would probably be significantly reduced if slowed conduction of the test impulse down the relatively refractory optic radiation axon could be avoided (cf. Bishop & Evans, 1956). The B potential appears at about 1·5 msec. This experiment shows that the A and B components may grow in amplitude during the period of relative refractoriness. The variation in amplitude of the A potential occurs over a very short range of intervals (< 1 msec) and gradations of the B response can be obtained only over a still shorter range (Fig. 7).

In two other experiments this gradation in the B potential could not be obtained. It behaved in an all-or-nothing fashion at a critical response interval; in these two units this interval was about 1·5 and 4·0 msec, respectively. In each case the B component had a longer refractory period than the A component. At the shortest intervals (e.g. Fig. 6*d*) the A–B step is very prominent and the B component is always diphasic.

These experiments were intended to illustrate the fractionation of the response at short intervals rather than to give representative data on refractory periods, for which a much larger series would be needed.

DISCUSSION

We have produced evidence that records from two of the units in this study were true antidromic responses. It was necessary to obtain this evidence because of the possibility that cells in the LGN could be activated

from the cortex via either corticifugal fibres (cf. Widén & Marsan, 1960*a*) or recurrent collaterals (O'Leary, 1940; cf. Eccles, Fatt & Koketsu, 1954). The evidence completely excludes the first possibility and excludes the second possibility *except* in the case in which the unit in question is an interneurone projecting on to the radiation cell from which it receives back a recurrent collateral. However, the number of recurrent collaterals in the

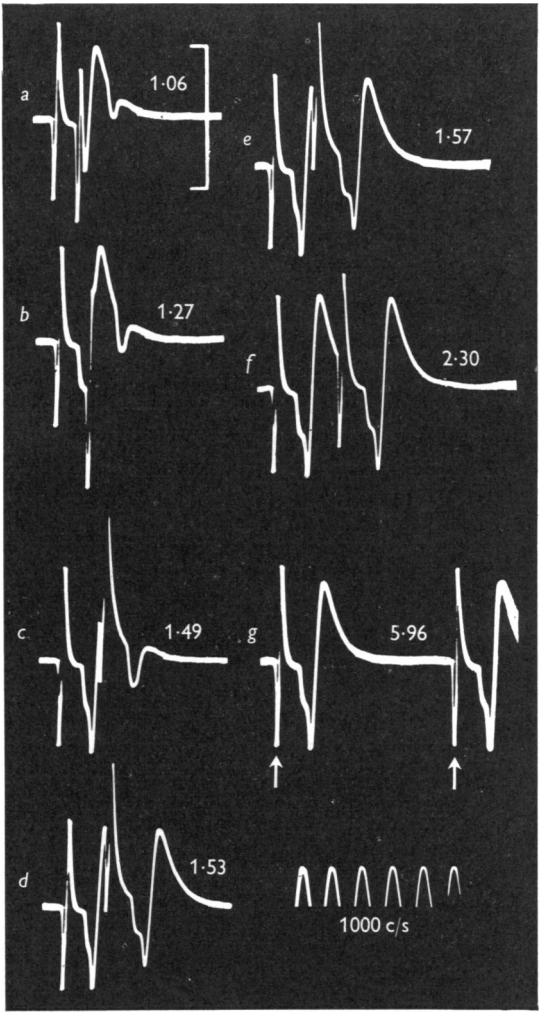

Fig. 6. Effect of two antidromic stimuli at short intervals. Each response is preceded by a large positive/negative stimulus artifact. The figures indicate the interval in msec between the commencements of the two responses. A potentials alone result from the second stimulus in *a*, *b*, *c*. In *d*, *e*, *f*, the A–B step of the second response is more prominent than usual and the amplitude of the response is smaller. Voltage calibration 10 mV.

LGN is probably very small (O'Leary, 1940) and could account for very few of our results.

The two units which were tested by the method described (Fig. 2) responded with a wave form which was characteristically different depending on whether activation was from optic nerve or visual cortex. Similar differences were found between most of the cells which responded to both routes of stimulation. This may be regarded as additional evidence that the responses to cortical stimulation were true antidromic responses because it would be expected on anatomical grounds that a majority of cells must respond in this way. Hence we consider that the criteria we have adopted for true antidromic activation of a cell are entirely reliable.

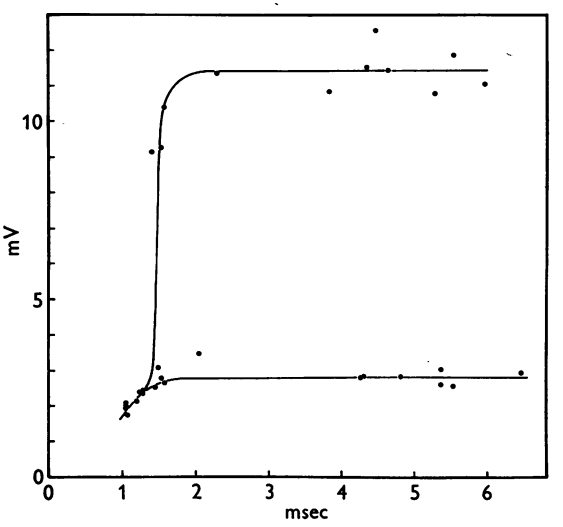

Fig. 7. Graph of amplitude of second of two antidromic responses (mV) against interval between the commencement of the two responses (msec) from a series of records partly illustrated in Fig. 6. The upper curve is drawn through points taken from records containing a B component; the lower curve is drawn through points which have an A component only (i.e. all points below 5 mV). Note that, characteristically, even at long intervals the second stimulus occasionally elicits only an A potential. In all the records used for the graph the first stimulus produced a full response. At intervals less than about 1 msec no response to the second stimulus could be detected. Gradation of amplitude of response is obtained only over very short intervals.

In short these are, that the response should exhibit a prominent A–B step, that there should be very little variation in latency of the A potential (about 0·1 msec) and that fractionation to give an A potential should be readily obtained, if not spontaneously, then at least by a short train of stimuli at 250–500/sec.

Only two out of twenty-six units lacked a prominent step on the positive phase. In these two units the orthodromic and the 'antidromic' latencies of these units were 1·39 and 3·19 msec, respectively. It is not improbable that these units were activated orthodromically by corticifugal fibres from the cortex; in one or both of these units the pathway may well have been monosynaptic. Evidence for the existence of corticifugal fibres running to the LGN has been brought forward by Widén & Marsan (1960*a*), who also give a list of references to the literature in this field. Units with antidromic latencies longer than 10 msec were not studied systematically. None of these responses had the characteristic antidromic wave form and it may safely be assumed that the units concerned were being activated orthodromically. Considerable interest attaches to the existence of what are presumably longer routes from cortex to LGN, but at the moment we have no information concerning these pathways.

The histogram of latencies to antidromic activation is similar to the larger series of Widén & Marsan (1960*a*) who found a peak latency at about 1 msec. However, Li, Ortiz-Galvin, Chou & Howard (1960), stimulating the LGN, found that the minimum latency of any cortical cell response was 2 msec; this suggests that some of their cells were activated only after transmission through more than one synapse. Vastola (1957) and Widén & Marsan (1960*b*) regard 0·5 msec as a 'normal' latency for conduction from LGN to cortex and the latter authors state that in exceptional cases latencies of up to 1·75 msec may be obtained; our results indicate that true latencies, not involving any synapse, may extend to 3·80 msec and probably to longer times in view of the small number of cells in our sample. This consideration weakens the claim of Widén & Marsan (1960*a*) that the effects of facilitation and inhibition which they obtained on LGN units by cortical stimulation were due mainly to orthodromic conditioning, i.e. via corticifugal fibres. The proportion of corticifugal fibres may not be as great as Widén & Marsan (1960*a*) suppose. It must be remembered also that Widén & Marsan obtained best results from stimulation of part of visual area II.

The responses of LGN cells to antidromic activation are very similar to those of other neurones. The most detailed examination of the extracellular response of a cell has been made by Fatt (1957) who plotted the field due to a single active motoneurone (cf. also Nelson, Frank & Rall, 1960). His records differ from ours and from most other workers in that the responses are mainly negative-going potentials. There are two possible reasons for this. The first is that most of Fatt's records were obtained from positions not very close to the cell; it was possible for him to record in this way because he was activating only one, or at most only a few, motoneurones. The response of the cell could therefore be picked up over a

much greater distance than if other cells in the vicinity were active. However, if the electrode is not close to the cell such responses are usually of low amplitude (not more than about 1 mV) and are mainly negative-going (cf. some of the records in the preceding paper, e.g. Figs. 12, 13, Bishop *et al.* 1962*a*). Only in the immediate vicinity of the cell, possibly only when the electrode is actually touching the cell, can one obtain 'giant' potentials (Bishop *et al.* 1962*a*). A second reason may be that the electrodes used by Fatt were relatively coarse (tip diameter 2–4 μ); such electrodes cannot detect gradients of potential occurring over very short distances, e.g. over the surface of the cell body (cf. Bishop *et al.* 1962*a*). A coarse electrode sees the cell body as a point, its net potential being negative during activity. Positivities are recorded only when there is a potential gradient extending over a considerable distance, probably more than 100 μ, e.g. from soma to axon or along the dendrites. In Fatt's records the cellular components are both negative, the second component occasionally failing. These components appear to correspond to the A and B components of the intracellular records (Fuortes *et al.* 1957).

Our records are very similar to those of Phillips (1959) who used electrodes capable of recording intracellularly. Phillips was able to fractionate the extracellular response by repetitive stimulation. From a comparison of the intracellular and extracellular responses, he concluded that the two components corresponded to the A and B components of Fuortes *et al.* (1957). The same conclusion has been reached by Freygang & Frank (1959) regarding the extracellular responses of spinal alpha motoneurones, by Eccles, Eccles, Iggo & Lundberg (1960) regarding gamma motoneurones and by Kandel, Spencer & Brinley (1961) regarding hippocampal neurones.

Whereas we have not been able to make satisfactory comparisons between intracellular and extracellular responses in LGN cells, there are good reasons for believing that in the responses of these cells also the two components correspond to the A and B components. Thus in favour of this point of view we have (i) the close similarity between our antidromic records and those of Phillips; (ii) the occasional failure of the second component; (iii) the absence of failure of the second component in orthodromic activation; (iv) the progressive increase of the interval between the two components during a train of high-frequency impulses, leading to failure of the second component; (v) the shorter refractory period of the first component relative to that of the second component; (vi) the longer interval between first and second component of the antidromic response relative to the corresponding interval in the orthodromic response. In all these respects the two components behave analogously to the A and B components of the intracellular record (Fuortes *et al.* 1957).

Accepting the two components as corresponding to the A and B components of Fuortes *et al.* (1957) or the IS and SD spikes respectively of Coombs *et al.* (1957*a*, *b*), we have noted some points of difference between LGN cells, Betz cells and spinal motoneurones in respect of the behaviour of these two components to antidromic stimulation. Thus many spinal motoneurones respond with only an A (IS) potential when activated antidromically, others giving this response occasionally, whilst the A potential is regularly obtained by applying two or more stimuli at brief intervals (Brock *et al.* 1953). In only one out of twenty-four LGN cells did the full response fail to appear; in this case an A potential only was obtained, although it was shown with orthodromic stimuli that the full response was nevertheless possible. However, twelve out of twenty-four cells responded occasionally with only an A potential in response to single antidromic stimuli. In all cells that were tested with double or repeated stimuli (seven), an A potential response was regularly obtained. In the Betz cell an occasional A potential response to a single stimulus is apparently never obtained and in only seven out of fifty-seven cells tested with two stimuli at brief intervals did the second response consist of an A potential (Phillips, 1959). Presumably with repetitive stimulation (Phillips, 1959) the proportion was higher.

It is evident that there is a gradation of properties here from Betz cells through LGN cells to spinal motoneurones, ease of invasion of the cell by an antidromic impulse decreasing in that order. It would appear that frog dorsal-root ganglion cells (Svaetichin 1958) and frog sympathetic ganglion cells (Svaetichin, 1958; Nishi & Koketsu, 1960) are intermediate between LGN cells and Betz cells in this respect. Frog spinal and sympathetic ganglion cells are without dendrites so that the presence or absence of dendrites cannot be a critical factor in the invasion of the cell. Although a prepotential similar to the A potential appears in the extracellular records of cerebellar Purkinje cell responses it is not certain that the two are identical, one difficulty being the spontaneous occurrence of the prepotential (Granit & Phillips, 1956). The difficulty of invasion of the cell is explained by the lowered safety factor at the initial segment/soma junction due to the large expansion of membrane at this point (Brock *et al.* 1953) and by the fact that the soma-dendritic membrane has a higher threshold than that of the initial segment (Coombs *et al.* 1957*a*, *b*). Differences between various types of cells could be due to differences in one or other of these two factors.

The graded amplitude of A and B components when elicited at critical intervals after a full response is similar to the gradation of the A (IS, NM) and B (SD) spikes in the motoneurone elicited in a similar way (Brock *et al.* 1953; Frank & Fuortes, 1955). These gradations may be ascribed to

inactivation of the sodium-carrier mechanism and increased potassium permeability occurring during a period of relative refractoriness. The number of LGN cells studied in this way is too few to justify a detailed comparison with other cells. However, it appears that the refractory period of both A and B components (tested by two antidromic stimuli) is less than in the case of spinal motoneurones (A, 1·23–1·45 msec (four cells), B, 2·5–50 msec (ten cells), Brock *et al.* (1953); cf. also Frank & Fuortes (1955)) and more than in Betz cells in which the critical stimulus interval for both A and B spikes may be as brief as 0·5 msec (Phillips, 1959). This behaviour is probably closely related to the ease with which the soma may be invaded by an antidromic impulse.

The antidromic response of the LGN cell also appears to differ from that of the Betz cell in its time course. The published records of Phillips (1959) indicate that the total duration of the Betz cell response is no more than 1 msec, whereas the duration of the LGN cell response is never less than 1·5 msec and is usually 2–5 msec. On closer examination the difference appears to lie mainly in the negative phase, the positive phase of the LGN response being only slightly larger than that of the Betz cell (both 0·25–0·50 msec). In general the negative phase of the LGN response is up to 5 or more times as long as the positive phase, whereas in Betz cells it appears to be of about the same duration. In this respect, Purkinje cells (Granit & Phillips, 1956) and crustacean stretch receptor cells (Edwards & Ottoson, 1958) resemble LGN cells, whereas mammalian spinal motoneurones (Freygang & Frank, 1959) and frog dorsal-root ganglion cells (Svaetichin, 1958) resemble Betz cells. These differences may be fortuitous because not every response falls neatly into one or other group. They may arise because of the differing lines of approach of the electrode to the cell or they may reflect real differences in the way in which the impulse invades the cell. One suggestion is that the long negative phase may reflect a failure of the impulse to invade the dendrites. Propagation along the dendrites would be expected to decrease the duration of the negative phase and possibly give a terminal positive phase.

An interesting feature of the A potential is that on several occasions it was diphasic, the second (negative) phase being up to 57 % of the first (positive) phase. A diphasic A potential occurs only if the B potential is also diphasic. Discussion of this point will be reserved until the following paper (Bishop *et al.* 1962*b*).

A description has been given of the differences in wave form between antidromic and orthodromic responses. These differences resemble those found by other authors (see e.g. Araki *et al.* 1953; Coombs *et al.* 1957*a*, *b*) between orthodromic and antidromic intracellular responses of spinal motoneurones. These differences will be discussed in more detail in the

following paper (Bishop *et al.* 1962*b*) but it should be mentioned here that it is a relatively easy matter to recognize a true antidromic response in the LGN simply from an examination of the wave form. This may be true for many other cells also. As yet the only other report dealing with a comparison between orthodromic and antidromic extracellular responses is that of Kandel *et al.* (1961) who describe the more prominent A–B step on the antidromic response.

SUMMARY

1. Extracellularly recorded antidromic responses from optic radiation axons and cells of the lateral geniculate nucleus (LGN) have been described. A method is given of checking that the response is a true antidromic response.

2. The antidromic response of the LGN cell resembles the orthodromic response in having a positive/negative wave form with an inflexion on the positive wave (the A–B step). The two responses differ in several respects:

(i) there is often a second inflexion on the positive phase of the orthodromic response, absent in the antidromic response.

(ii) the A–B step on the orthodromic response is less prominent than on the antidromic response.

(iii) the antidromic response commonly fractionates at the A–B step to give an A potential; this occurs only rarely in the orthodromic response.

(iv) a variation in latency or response occurs in both antidromic and orthodromic responses but in a characteristically different way in each.

(v) the amplitude of the antidromic response is usually slightly less than that of the orthodromic response.

3. The A potential obtained by fractionation of the antidromic wave form is considered to be the response of the initial segment of the axon and may be a monophasic positive wave or a diphasic positive/negative wave. The B potential is a positive/negative wave which follows the A potential and is believed to represent the invasion of the soma-dendritic membrane.

4. LGN cells have been antidromically activated with latencies as long as 3·8 msec, corresponding to conduction velocities of down to 4·0 m/sec. However, the modal values are 1 msec and about 15 m/sec, respectively.

5. A comparison is made between the antidromic responses of various types of cells.

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REFERENCES

ARAKI, T. & OTANI, T. (1955). Response of single motoneurons to direct stimulation in toad's spinal cord. *J. Neurophysiol.* **18**, 472–485.

ARAKI, T., OTANI, T. & FURUKAWA, T. (1953). The electrical activities of single motoneurones in toad's spinal cord, recorded with intracellular electrodes. *Jap. J. Physiol.* **3**, 254–267.

BENNETT, M. V. L., CRAIN, S. M. & GRUNDFEST, H. (1959). Electrophysiology of supramedullary neurons in *Spheroides maculatus*. I. Orthodromic and antidromic responses. *J. gen. Physiol.* **43**, 159–188.

BISHOP, P. O., BURKE, W. & DAVIS, R. (1962*a*). The identification of single units in central visual pathways. *J. Physiol.* **162**, 409–431.

BISHOP, P. O., BURKE, W. & DAVIS, R. (1962*b*). The interpretation of the extracellular response of single lateral geniculate cells. *J. Physiol.* **162**, 451–472.

BISHOP, P. O. & EVANS, W. A.(1956). The refractory period of the sensory synapses of the lateral geniculate nucleus. *J. Physiol.* **134**, 538–557.

BROCK, L. G., COOMBS, J. S. & ECCLES, J. C. (1953). Intracellular recording from antidromically activated motoneurones. *J. Physiol.* **122**, 429–461.

COOMBS, J. S., CURTIS, D. R. & ECCLES, J. C. (1957*a*). The interpretation of spike potentials of motoneurones. *J. Physiol.* **139**, 198–231.

COOMBS, J. S., CURTIS, D. R. & ECCLES, J. C. (1957*b*). The generation of impulses in motoneurones. *J. Physiol.* **139**, 232–249.

DOTY, R. W. (1958). Potentials evoked in cat cerebral cortex by diffuse and by punctiform photic stimuli. *J. Neurophysiol.* **21**, 437–464.

ECCLES, J. C., ECCLES, R. M., IGGO, A. & LUNDBERG, A. (1960). Electrophysiological studies on gamma motoneurones. *Acta physiol. scand.* **50**, 32–40.

ECCLES, J. C., FATT, P. & KOKETSU, K. (1954). Cholinergic and inhibitory synapses in a pathway from motor-axon collaterals to motoneurones. *J. Physiol.* **126**, 524–562.

EDWARDS, C. & OTTOSON, D. (1958). The site of impulse initiation in a nerve cell of a crustacean stretch receptor. *J. Physiol.* **143**, 138–148.

FATT, P. (1957). Electric potentials occurring around a neurone during its antidromic activation. *J. Neurophysiol.* **20**, 27–60.

FRANK, K. & FUORTES, M. G. F. (1955). Potentials recorded from the spinal cord with microelectrodes. *J. Physiol.* **130**, 625–654.

FREYGANG, W. H., Jr. & FRANK, K. (1959). Extracellular potentials from single spinal motoneurons. *J. gen. Physiol.* **42**, 749–760.

FUORTES, M. G. F., FRANK, K. & BECKER, M. C. (1957). Steps in the production of motoneuron spikes. *J. gen. Physiol.* **40**, 735–752.

GASSER, H. S. & ERLANGER, J. (1925). The nature of conduction of an impulse in the relatively refractory period. *Amer. J. Physiol.* **73**, 613–635.

GRANIT, R. & PHILLIPS, C. G. (1956). Excitatory and inhibitory processes acting upon individual Purkinje cells of the cerebellum in cats. *J. Physiol.* **133**, 520–547.

GRUNDFEST, H., SENGSTAKEN, R. W., OETTINGER, W. H. & GURRY, R. W. (1950). Stainless steel microneedle electrodes made by electrolytic pointing. *Rev. sci. Instrum.* **21**, 360–361.

KANDEL, E. R., SPENCER, W. A. & BRINLEY, F. J., Jr. (1961). Electrophysiology of hippocampal neurons. I. Sequential invasion and synaptic organization. *J. Neurophysiol.* **24**, 225–242.

LI, C.-L., ORTIZ-GALVIN, A., CHOU, S. N. & HOWARD, S. Y. (1960). Cortical intracellular potentials in response to stimulation of lateral geniculate body. *J. Neurophysiol.* **23**, 592–601.

MACHNE, X., FADIGA, E. & BROOKHART, J. M. (1959) Antidromic and synaptic activation of frog motor neurons. *J. Neurophysiol.* **22**, 483–503.

MARTIN, A. R. & BRANCH, C. L. (1958). Spontaneous activity of Betz cells in cats with midbrain lesions. *J. Neurophysiol.* **21**, 368–379.

MINKOWSKI, M. (1913). Experimentelle Untersuchungen über die Beziehungen der Grosshirnrinde und der Netzhaut zu den primären optischen Zentren, besonders zum Corpus geniculatum externum. *Arb. hirnanat. Inst. Zurich*, **7**, 255–363.

NELSON, P. G., FRANK, K. & RALL, W. (1960). Single spinal motoneuron extracellular potential fields. *Fed. Proc.* **19**, 303.

NISHI, S. & KOKETSU, K. (1960). Electrical properties and activities of single sympathetic neurons in frogs. *J. cell. comp. Physiol.* **55**, 15–30.

O'LEARY, J. L. (1940). A structural analysis of the lateral geniculate nucleus of the cat. *J. comp. Neurol.* **73**, 405–430.

PHILLIPS, C. G. (1956). Intracellular records from Betz cells in the cat. *Quart. J. exp. Physiol.* **41**, 70–84.

PHILLIPS, C. G. (1959). Actions of antidromic pyramidal volleys on single Betz cells in the cat. *Quart. J. exp. Physiol.* **44**, 1–25.

RENSHAW, B. (1941). Influence of discharge of motoneurons upon excitation of neighbouring motoneurons. *J. Neurophysiol.* **4**, 167–183.

RENSHAW, B. (1946). Central effects of centripetal impulses in axons of spinal ventral roots. *J. Neurophysiol.* **9**, 191–204.

SVAETICHIN, G. (1958). Component analysis of action potentials from single neurons. *Exp. Cell Res.*, Suppl. 5, 234–261.

TASAKI, I. (1952). Properties of myelinated fibers in frog sciatic nerve and in spinal cord as examined with microelectrodes. *Jap. J. Physiol.* **3**, 73–94.

VASTOLA, E. F. (1957). Antidromic action potentials in lateral geniculate body. *J. Neurophysiol.* **20**, 167–185.

WIDÉN, L. & MARSAN, C. A. (1960*a*). Effects of corticipetal and corticifugal impulses upon single elements of the dorsolateral geniculate nucleus. *Exp. Neurol.* **2**, 468–502.

WIDÉN, L. & MARSAN, C. A. (1960*b*). Unitary analysis of the response elicited in the visual cortex of the cat. *Arch. ital. Biol.* **98**, 248–274.

WOOLSEY, C. N. & CHANG, H.-T. (1947). Activation of the cerebral cortex by antidromic volleys in the pyramidal tract. *Res. Publ. Ass. nerv. ment. Dis.* **27**, 146–161.