J. Physiol. (1962), **164**, *pp.* 238–251
With 6 text-figures
Printed in Great Britain

TRANSMISSION OF INFORMATION IN THE UNANAESTHETIZED CAT'S ISOLATED FOREBRAIN

By B. D. BURNS and G. K. SMITH*
From the Department of Physiology, McGill University, Montreal, Canada

(*Received* 2 *April* 1962)

The classical studies of Pavlov, the subsequent work of Lashley and the experiments of many other investigators have made it seem that any part of the mammalian brain can be functionally connected to any other. Despite evidence from the field of experimental psychology that such connexions are possible, physiologists have not managed to produce convincing electrical evidence that one part of the normal brain may control or modify the activity of neurones in remote areas.

Adrian (1936) was able to produce a relatively short-lasting facilitation in pathways through the cerebral cortex, a few millimetres in length. Such pathways could apparently be created in any area of cortex, but required for their production many exceptionally strong stimuli. More recently, Buser, Borenstein & Bruner (1959), using cats under chloralose anaesthesia, have demonstrated electrical responses to visual and auditory stimuli in parts of the cortex remote from the primary receiving areas. But this spread of cortical response, recorded with large surface electrodes, can only be demonstrated in the presence of chloralose.

At least three factors have contributed to the difficulties of demonstrating with electrical techniques that one part of the brain can control another. One such factor has undoubtedly been the continual or 'spontaneous' activity of brain cells. Averaging techniques, designed to eliminate from records the unwanted 'noise' caused by 'spontaneous activity', have revealed many local cortical responses that could not be demonstrated in the unanaesthetized brain by simpler methods (Dawson, 1947, 1954; Barlow, 1957; Clark, 1958; Brazier, 1961). In fact, the spread of cortical response described by Buser *et al.* (1959), required photographic averaging for its demonstration. Another difficulty has been the lack of detailed anatomical information; even where interconnexions between one part of the brain and another have been demonstrated there is no indication of their functional significance. Finally, the use of large recording electrodes

* Present address: Autonomics Division, National Physical Laboratory, Teddington, Middlesex, England.

has undoubtedly contributed to difficulties in this field. Such electrodes can only record the simultaneous activity of great numbers of neurones, and it seems possible that the important patterns of activity occurring in the unanaesthetized brain are too fine to be resolved by such techniques.

We therefore undertook a re-examination of this problem using micro-electrodes to record the times of discharge of individual cells. Thus, the experiments with single cortical neurones described below were designed to answer two questions:

(1) Can 'information' pass from any chosen point on the cerebral cortex to any other point?

(2) If so, in what ways can the activity of a localized group of cortical neurones modify the behaviour of a cell in some remote cortical district?

From the beginning of our work we used averaging techniques during the analysis of records. A recent description of the behaviour of cells in the cat's unanaesthetized visual cortex (Burns, Heron & Pritchard, 1962) demonstrates that the relation between retinal stimulus and response of individual neurones can only be stated in terms of probability. Thus we felt it likely that a local active part of the brain might do no more than alter the probability of discharge for cells in other remote regions. Moreover, when analysing our data we have ignored the known anatomical structure of the brain; our results are interpreted as though the brain were a large solid network of elements, with completely unknown connexions.

METHODS

Preparation. The isolated forebrain preparation was used for these experiments (Bremer, 1935). Cats were anaesthetized with ether and, after tracheal cannulation, the skull and dura were removed, thus exposing a large area of both cerebral hemispheres. A hole was made through the cortex into the lateral ventricle on one side to allow drainage of cerebrospinal fluid, and the mid-brain was transected at the level of the tentorium cerebelli with a blunt knife. While the animal was recovering from the anaesthetic the scalp was sutured to a ring above the head, and the well so formed was filled with warm mineral oil. Details of the procedure are given by Burns & Grafstein (1952). Throughout the experiment the temperature of the decerebrate preparations was kept at $37 \pm 0{\cdot}5°$ C by a heating pad thermostatically controlled from a thermistor, either in the rectum or buried among muscles of the axilla.

All the cats were reflexly active. To minimize movements which might interfere with extracellular recording from single cortical units some of the animals were treated with gallamine (40 mg) given intravenously, and respired artificially. Subsequent doses of 20 mg of gallamine were repeated every hour to maintain paralysis.

Recording. Recordings were made extracellularly from continually active cortical neurones in the lateral, suprasylvian, ectosylvian and sigmoid gyri. The micro-electrodes were glass micropipettes filled with 9/10 saturated NaCl solution. They had tip-diameters between 1 and 5 μ and d.c. resistances between 0·2 and 0·8 MΩ. The micropipettes were held in a 'weightless' micro-electrode holder, described by Burns & Robson (1960). The holder was mounted on an hydraulic micromanipulator (Li, Cullen & Jasper, 1956; Burns, 1961). A chlorided silver wire made contact with the salt solution of the electrodes and was con-

nected to a Grass P 5 amplifier with cathode followers at the input. The output was recorded on one channel of a two-channel Phillips magnetic tape recorder.

Stimulation. In the course of this work stimuli were applied either to the surface of the cortex or to the retina. The direct stimuli were delivered from Tektronix wave-form and pulse generators, through a transformer to paired platinum wires placed 1 mm apart on the cortical surface. For visual stimulation the pupil was dilated with 1% atropine and a contact-glass was placed on the cornea to prevent drying. Patterns, projected onto an opal-glass screen, were focused on the retina by a 10 D lens (Burns, Heron & Pritchard, 1962). In all experiments where visual stimuli were used, the animals were paralysed with gallamine to prevent movements of the eye relative to the screen. Each stimulus given to the animal was recorded on one channel of the magnetic tape.

Special equipment for analysis. In all these experiments stimuli were applied repeatedly, at a constant frequency, to the brain while records were taken of single neurones in the cortex. The records were analysed by dividing all the intervals between stimuli into a number of small, equal time segments. The number of action potentials falling into each segment was counted. This was done for a large number of stimuli and the total number of action potentials which occurred in corresponding time segments, following each stimulus, was obtained. This process is described in more detail under Results. This analysis was carried out during the experiments with a small electronic computer operating on a principle described by Smith & Burns (1960). The instrument consists essentially of a rotating switch which connects the action potential, for equal pre-set intervals of time, to each of ten digital counting registers in succession. Each stimulus initiates one cycle of the switch, so that at the end of a test the ten registers show counts equal to the total number of action potentials which occurred in each of ten time segments following the 'average' stimulus. The experimenter then reads off the post-stimulus histogram from the storage display (see also Gerstein & Kiang, 1960).

A second instrument was built to provide a larger number of segments and thus to allow a more detailed analysis. A signal driven by the action potential is printed on one track of an endless loop of magnetic tape and pulses indicating the moments of stimulation are printed on a second track. These data are then played back through a circuit which permits action potentials to be counted in a digital register only when they occur within a specified period following the stimulus pulse. Thus, during the play-back, one complete revolution of the loop of tape provides the total count for the first time segment of the post-stimulus histogram. The magnetic head which 'senses' the stimulus pulse is now moved along the tape by a distance representing the duration of one time segment and the data are replayed. The count printed at the end of this next revolution of the tape loop is the count for the second segment of the histogram. This process is repeated until the head has been moved through a distance representing an entire interstimulus interval, and the histogram is complete. By reducing the time following the stimulus pulse for which action potentials will be counted and by decreasing the stepwise increments of the mobile head with each revolution of the tape loop, the analysis may be made as fine as one likes. The instrument requires an amount of analysis time equal to the period of revolution of the tape multiplied by the number of histogram segments, and consequently is not suitable for use during the actual collection of the data. Records of the original action potentials were stored on magnetic tape and analysed at leisure after the experiment (Burns, Mandl & Smith, 1962).

RESULTS

The measurement of response

The isolated and unanaesthetized forebrain of an undisturbed animal exhibits electrical evidence of continual activity for many hours. This activity can be said to be 'spontaneous' in so far as no external stimuli are

intentionally provided, but one must remember that both first and second cranial nerves are intact; moreover, the decerebration cut cannot safely be regarded as histologically complete. Whatever its cause, continual activity can be recorded for at least 48 hr by a pair of electrodes placed anywhere upon the cerebral cortex of such a preparation. When a micropipette is pushed slowly through the cortical grey matter, many active neurones are encountered. We had the impression that, in a good preparation, every cortical unit discharged continuously. An unsuccessful surgical operation sometimes produced a brain to which the blood supply was visibly poor, or which was obviously oedematous; in these brains a roving microelectrode would often collide with a cell which provided no evidence of its presence until an injury discharge was evoked. (Another way of identifying inactive neurones with a micropipette is to explore the cortex while passing a continuous, tip-negative polarizing current (of some 0·3 μA) through the recording electrode.) We found that one common cause of inactivity among cortical units was the occurrence, during an operation, of a short period of cranial anaemia. Although no attempt was made to obtain a quantitative estimate of the fraction of all cortical neurones that were continually active, the results described below were all from preparations in which there were few, if any, inactive cortical units.

In the undisturbed brain the mean frequency of discharge of cortical neurones appears to remain constant indefinitely; we have often recorded the mean frequency of a unit for more than 1 hr without observing any significant change (see also Burns, Heron & Pritchard, 1962). This mean frequency of discharge may, however, be very different for neighbouring cells; we encountered frequencies anywhere between 1 and 30 discharges per second, but the most common frequency was around 10 c/s. The times of discharge of these cortical units appear to be completely random, in the sense that there is no visible or audible rhythm about their behaviour. Our purpose, in the experiments described below, was the detection of any modification of this continual and apparently random activity of neurones that might be produced by excitation of remote cortical areas.

It seemed reasonable to suppose that a periodically active group of cortical neurones might be capable of modifying the probability of discharge of units in relatively remote areas of the brain, without necessarily 'driving' such remote cells in any constant, cyclical fashion. For this reason, in our early experiments, which were recorded on film from a two-beam oscilloscope, we would stimulate an area of cortex with single shocks repeated at 1/sec, while recording the activity of a cortical cell some 15mm away. The resulting film provided a record of the times of discharge of the recorded unit on one trace, while the moments of stimulation were indicated on the other. The photographic record was analysed in the following

way: the time following each application of the stimulus was divided into a chosen number, n, of equal segments, and the number of action potentials falling within each segment was counted. This was done for a large number of stimuli and the results were combined in such a way that the total numbers of action potentials which occurred in the n corresponding time segments following each stimulus were obtained. The ordinate of the

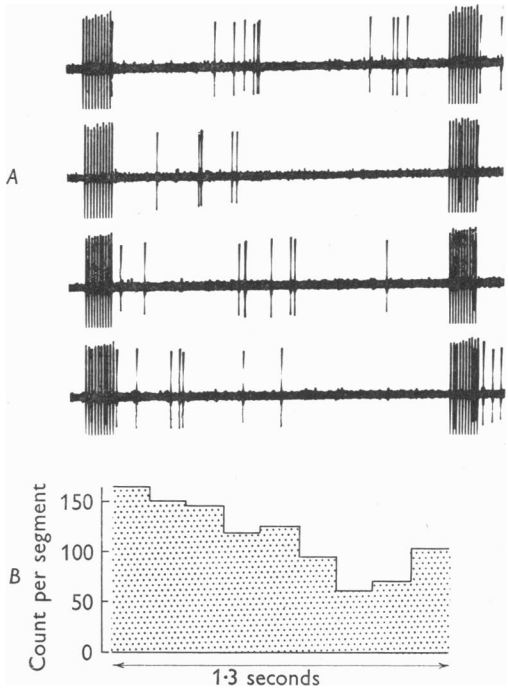

Fig. 1. Illustration of the method used to generate the 'post-stimulus probability histogram', described in the text. *A* shows randomly chosen samples from a record of action potentials generated by a cell in the median suprasylvian gyrus. The stimulus artifacts mark the times of application of bursts of 10 electrical pulses of 500 μsec duration to the cortical surface at a point 13 mm along the same gyrus from the recording point. The times of firing of the cell relative to stimulation were classified into nine equal segments following 138 presentations of the stimulus and generated the histogram shown in *B*.

histogram so obtained is obviously directly proportional to the *a posteriori* probability that the unit would fire within specified time limits after any of the stimuli provided. Figure 1 shows four samples of a record obtained from a cell in the median suprasylvian gyrus. 138 bursts, each of 10 stimuli, were applied to the cortex, one every 1·3 sec, at the times indicated by the stimulus artifacts. The post-stimulus histogram obtained from the

complete test is shown below the sample records. The histogram time scale is the same as that of the sample records.

This process of manual analysis from photographic film proved extremely laborious; 2–3 min of record necessitated about eight man hours of work. Therefore, directly we had assured ourselves of the usefulness of this approach, we began recording results on magnetic tape so that an identical analysis could be later performed by the small electronic computer described briefly in Methods above (Smith & Burns, 1960).

Clearly, the post-stimulus histogram for a cell that was completely uninfluenced by cortical stimulation would consist of a horizontal straight line, parallel to the abscissa, provided that the record analysed was of infinite length. In practice one cannot obtain very long records and the histogram for an uninfluenced cell must show deviations, which are the result of random sampling, from the ideal horizontal mean frequency line. When the excitability of a neurone is phasically modified by remote cortical stimulation, there must be significant deviations from the mean frequency line; the extent of these deviations provides one measure of the control of the unit by the periodic stimulus. Thus, one could use the net deviation from the mean as a measure of response. We have, in fact, made use of $\chi^2/\bar{x}$ to provide an objective assessment of response;

$$\chi^2/\bar{x} = \sum_0^n \frac{(x_k - \bar{x})^2}{\bar{x}^2},$$

where x_k = the height of individual histogram blocks;
$\bar{x}$ = the average height of the histogram, $(\Sigma x/n)$; and
n = the number of histogram blocks.

It is clear that a weak response could be confused with random deviations from mean frequency, and any useful measure of response must leave one able to calculate the probability that a particular histogram could have been obtained by chance from an unresponsive cell. The statistical aspects of this problem are now under investigation and a preliminary report will be published in the near future. Fortunately, the responses that we are concerned with in the present communication are very clear-cut, and we believe that our conclusions are in no way dependent upon the choice of expressions for their measurement. Where values of $\chi^2/\bar{x}$ are given we have provided also the control value estimated from records obtained in the undisturbed brain and analysed with 'dummy' stimuli.

Responses to artificial stimulation of the cortex

In our first experiments we delivered single shocks to the cortical surface, repeated at regular intervals of approximately 1/sec. These stimuli were weak, in all cases less than the strength required to evoke a

maximal surface-negative response (Adrian, 1936; Burns, 1950, 1951; Chang, 1950). In Fig. 2*a* the post-stimulus histogram is shown for the effect of a single 0·5 msec stimulus upon a neurone 15 mm from the point of stimulation. The train of single stimuli provided appears to have produced a biphasic modification of probability of firing during the first three segments but, in fact, the value of $\chi^2/\bar{x}$ was slightly below that of the control. We soon found, however, that bursts of artificial stimuli offered a far more effective way of controlling the activity of remote cortical units.

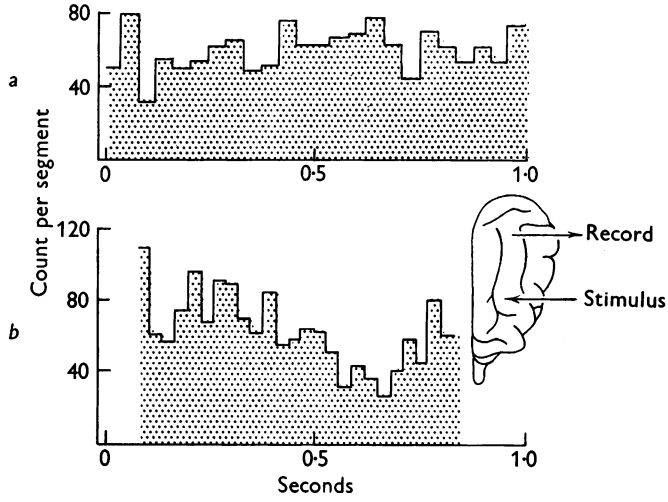

Fig. 2. Post-stimulus probability histograms comparing the effects of single and multiple artificial stimuli on the times of 'spontaneous' firing of a cortical neurone. In *a* single electrical shocks of 500 μsec duration were applied for 2 min at a frequency of 1/sec. From the histogram the cell appears to respond in a biphasic mode in the first three segments but when averaged over the whole interstimulus interval by the $\chi^2/\bar{x}$ test, this 'response' is insignificant compared with the control value. In *b* the same cell was recorded during 2 min of stimulation of the same point with bursts of 10 stimuli, 10 msec apart. The burst frequency was 1·25/sec. The response is more obvious and $\chi^2/\bar{x}$ has assumed a value just under twice the control value. Control, $\chi^2/\bar{x} = 0{\cdot}94$; *a*, $\chi^2/\bar{x} = 0{\cdot}86$; *b*, $\chi^2/\bar{x} = 1{\cdot}82$.

For comparison, Fig. 2*b* indicates the response of the same cell to bursts of 10 pulses at the same site and of the same strength and duration as in Fig. 2*a*. The 10 pulses were applied during the first 100 msec of the stimulus cycle of 1·25 bursts/sec. It will be seen that the burst stimulus is clearly more effective than single stimuli in altering the probability of firing of the observed unit. We therefore adopted this method of artificial stimulation as a routine for subsequent experiments. In general, we employed a burst of ten stimuli at 100/sec, repeated every 1–2 sec. The

results of tests similar to those of Figs. 1 and 2*b* indicate that stimulation of any cortical point can influence the behaviour of single neurones at any other cortical point upon the same hemisphere.

Experiments in which the stimulus is repeated once every 1–2 sec do not permit one to assess the duration of influence of a single stimulus upon the behaviour of remote cortical units. In order to obtain some estimate of the duration of the disturbance in the brain set up by 'single' stimuli we made some tests with stimuli repeated at low frequency. Figure 3 shows the post-stimulus histogram of a unit during remote cortical stimulation with bursts of 10 stimuli at 100/sec repeated once every 5 sec. Deviations from mean frequency are evident for at least 3·5 sec after stimulation.

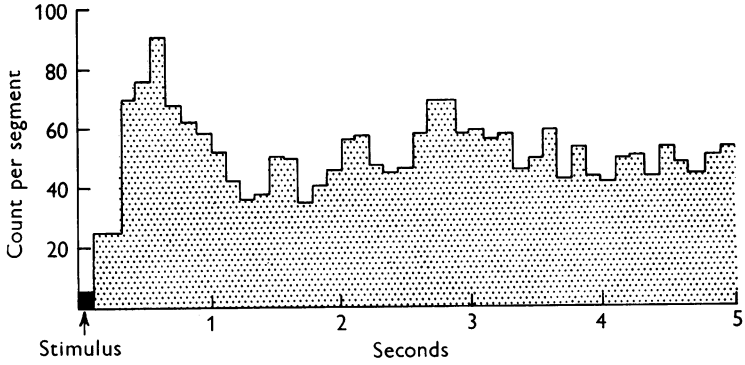

Fig. 3. Duration of influence of artificial stimulation on a cell 13 mm from the stimulated point, again in the median suprasylvian gyrus. The stimulus consisted of a group of 10 bipolar shocks of 0·5 msec duration presented in the first 100 msec of the 5 sec stimulus cycle. The histogram was the result of 3 min of stimulation. Control, $\chi^2/\bar{x} = 1{\cdot}05$; stimulation, $\chi^2/\bar{x} = 2{\cdot}49$.

Remote responses to visual stimuli

A demonstration that artificial local stimulation of the cerebral cortex can influence the behaviour of neurones in distant parts of the brain need not necessarily imply that 'physiological' excitation of the cortex will have the same effects. For this reason we did a number of experiments to test the effects of visual stimulation on cells outside the classical visual cortex. A small disk of light, projected on an opal glass screen in front of the cat's eye, was focused on the retina. This pattern was flashed on the screen for 100 msec, usually once every second (Burns, Heron & Pritchard, 1962). The post-stimulus histogram is shown in Fig. 4 for a cell in the median suprasylvian gyrus, well outside the primary visual receiving area. The effect of a similar stimulus on a cell in the ectosylvian gyrus (primary auditory receiving area) is shown in Fig. 5*b*. The shutter on the visual stimulator made a 'click' at the 'on' and 'off' of every stimulus. To ensure

that the response in Fig. 5*b* was not due to excitation of auditory fibres which might have escaped the decerebration knife, behaviour of the same cell was recorded when the visual stimulator was running but with its source of light turned off (Fig. 5*c*). For comparison, the response of a cell in the visual area to the same retinal stimulus is shown in Fig. 5*a*. Finally, Fig. 6 shows the influence exerted on a cell in the posterior sigmoid gyrus (sensory-motor area) to a similar visual stimulus.

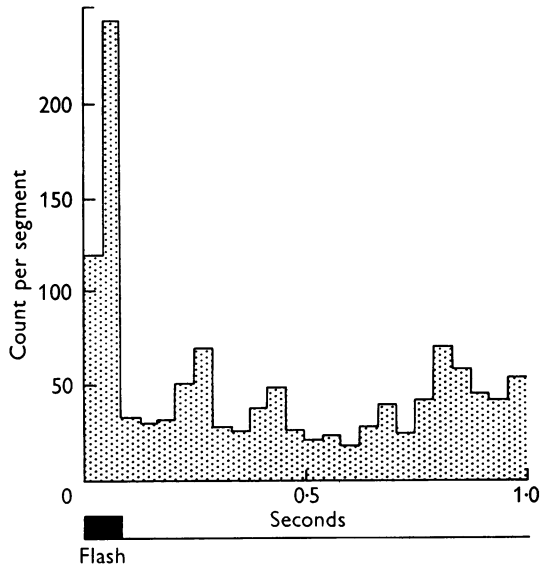

Fig. 4. 'Post-stimulus probability histogram' from a cell in the median suprasylvian gyrus of a cat during stimulation of the contralateral retina. A disk of light subtending 6·6° was flashed on the eye once per second for 100 msec. The histogram gives the cumulative results of 180 presentations of the stimulus. Control, $\chi^2/\bar{x} = 1{\cdot}05$; stimulation, $\chi^2/\bar{x} = 50{\cdot}10$.

DISCUSSION

The experiments described above were undertaken in the hope of ascertaining the extent and nature of the influence of a group of active cortical cells upon the behaviour of remote units in the cerebral cortex. The results suggest that subsequent to the discharge of any close-packed group of cortical cells there is a modification of the probability of firing of neurones in all areas of the cerebral cortex, however remote. We have not found any limits to the distances over which such influences can spread within the confines of the easily exposed surface of the hemispheres.

We have recorded the response of cortical neurones to the excitation of remote cortical districts in terms of the post-stimulus histogram (Gerstein & Kiang, 1960; Burns, Heron & Pritchard, 1962), thereby displaying the

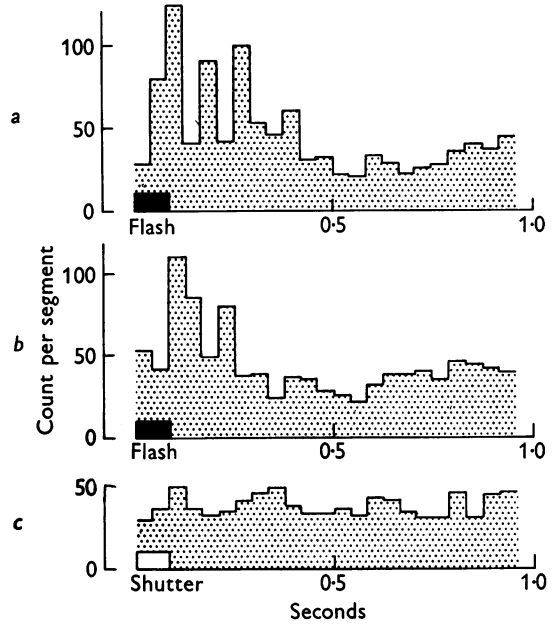

Fig. 5. *a*. 'Post-stimulus probability histogram' of effect on a cell in the lateral gyrus (primary visual receiving area) of 120 presentations of a stimulus similar to that given in Fig. 5. Control, $\chi^2/\bar{x} = 0{\cdot}31$; stimulation, $\chi^2/\bar{x} = 7{\cdot}44$.

b. Effect of the same stimulus as in *a* on a neurone in the ectosylvian gyrus (primary auditory receiving area) in the same cat. Control, $\chi^2/\bar{x} = 1{\cdot}65$; stimulation, $\chi^2/\bar{x} = 5{\cdot}01$.

c. Same cell as in *b*. The stimulus parameters were unchanged except that the light source on the visual stimulator was extinguished. $\chi^2/\bar{x} = 1{\cdot}13$.

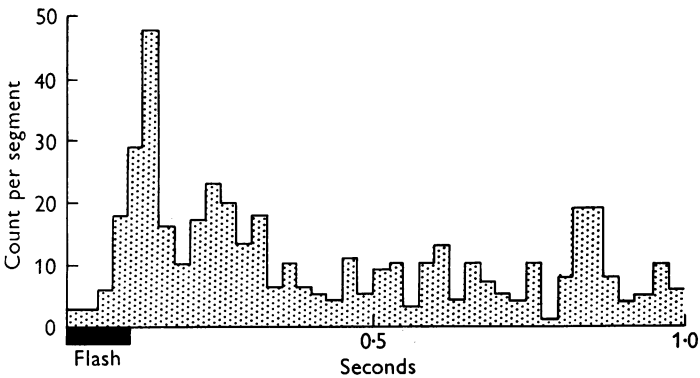

Fig. 6. 'Post-stimulus probability histogram' taken from a neurone in the posterior sigmoid gyrus (sensory-motor area). The stimulus was a large rectangle of light, flashed once per second for 100 msec on the contralateral retina. The histogram is the result of 120 stimuli. Control, $\chi^2/\bar{x} = 4{\cdot}01$; stimulation, $\chi^2/\bar{x} = 23{\cdot}20$.

relative *a posteriori* probabilities that these neurones would fire at various times after the average stimulus was applied. Any single objective measure of the response in these circumstances must depend largely upon estimates of the deviation of the post-stimulus histogram from the horizontal straight line which would indicate no influence of the stimulus upon the unit recorded. There are many possible ways of making such an estimate, all of which seem equally legitimate in the present state of physiological knowledge; we arbitrarily chose a measure $\chi^2/\bar{x}$ (specified under Results, p. 243) which used the sum of squares of deviations from the mean discharge frequency normalized for sample size.

The post-stimulus histogram only gives information about the average behaviour of the cell following a number of stimuli (usually 100 or more). The distribution of action potentials following any one of these stimuli may not resemble the histogram at all (Fig. 1). The histogram therefore gives only the *probabilities* of firing after stimulation, and hence the influence of a stimulus upon the behaviour of remote neurones must be stated in terms of the probability of their discharge. The changes in probability of discharge that we have observed presumably indicate a variation of excitability imposed by the stimulus, which is added to the rapidly fluctuating excitability caused by whatever mechanisms are responsible for 'spontaneous' or continual activity in the unstimulated brain. It is therefore possible that the influence of stimulation upon excitability remains relatively constant over periods of a minute or two and that the variation of behaviour of a neurone following consecutive stimuli is wholly referable to other sources of excitation.

Although we have been able to demonstrate the average response of a neurone to about 100 remote cortical stimuli given at 1/sec, it proved quite impossible to detect the influence of any single stimulus with extracellular micro-electrodes. This observation implies that during any one second a single neurone does not provide the rest of the brain with sufficient information to identify the presence and nature of a stimulus. The experiments reported above have been most concerned with cortical nerve cells outside the primary receiving areas; but the same apparent indeterminacy exists for the response to retinal excitation of single units within the visual area (Burns, Heron & Pritchard, 1962). It is clear, on the other hand, that the normal brain does not have to wait for 100 identical stimuli before any decision is possible about the site and nature of stimulation. The fact that reaction time is about $\frac{1}{4}$ sec implies that even a complex set of external stimuli can be identified in less than 250 msec. However, our results show that the behaviour of very many (possibly all) cortical neurones is modified by local cortical excitation. Thus, while the information passed on by one neurone in 1 sec is insufficient to describe the source

of excitation, the information received from several hundred neurones might well justify a specific output from the nervous system after 250 msec. Interpreted in this way, our results suggest that sensory inputs to the brain set up a spatial and temporal pattern of activity which probably involves most of the cells in the cerebral cortex. It would appear that differentiation of the effects of a stimulus from the 'noise' of continual or 'spontaneous' activity is only made possible by the simultaneous, weak responses of many neurones. This picture of brain activity stresses the physiological importance of redundant behaviour of cerebral neurones. Moreover, it makes more intelligible the somewhat surprising observation that many cortical cells in a close-packed column respond in a similar way to each somatic or visual stimulus (Mountcastle, 1957; Powell & Mountcastle, 1959; Hubel & Wiesel, 1962).

The concept that a small modification in the behaviour of many thousands of cerebral neurones is necessary to the identification of every stimulus implies that the outputs from these same nerve cells must converge somewhere in the brain upon a set of 'detector' cells. It suggests that persistent attempts might ultimately reveal a neurone which would respond only to presentation in the visual field of a three-legged white mouse, running from left to right across a black background! With some 10^{10} cortical neurones to explore there seems no reason yet to doubt such a possibility. But it is important in the context of this argument to remember that the nervous system only gives a response to a very small fraction of all the stimuli it receives. In this connexion it is interesting that we consistently observed more clear-cut responses from cortical neurones to physiological excitation of the retina with patterned light than we did to artificial direct excitation of the cortex. Direct cortical stimulation must excite together neurones which have never before fired synchronously; whereas the adult cat's brain must have received many previous stimuli similar to the white disk that we exposed in the visual field.

No attempt was made to establish the route taken by the spread of excitation that has been demonstrated. Unfortunately, the magnitude of unit responses to remote stimulation was found to vary from minute to minute. This unpredictable variability of the response prevented any quantitative comparison of the responses of a single unit to stimuli given at different sites. Nevertheless, the prolonged and variable nature of the response to the average single stimulus suggests a complex and inconstant pathway for the spread of excitation.

We have produced evidence that excitation of a group of cortical cells, apparently anywhere on the brain's surface, can modify the behaviour of cortical neurones at any other accessible point in the cerebral cortex. We

cannot yet state whether the activity of *all* cortical neurones is modified by such remote excitation. Of the 100 or so neurones that have been examined by the procedures described above, the majority showed a clear response to remote stimulation. There were, however, some among those examined which showed doubtful responses; that is to say, the post-stimulus histograms for such cells did not exhibit dramatic deviations from the horizontal straight lines representing their mean frequency of discharge. Thus, it soon became clear that some statistical test of significance would be useful in these circumstances. Unfortunately, it has been shown (Martin & Branch, 1958; Smith & Burns, 1959) that in neither stimulated nor unstimulated brains, do the firing patterns of cortical neurones conform to any simple laws, e.g. Poisson or Binomial processes. Hence it has not been possible to use conventional statistical methods to deal with this problem. The statistical structure of action-potential trains is now being investigated and a preliminary report will appear in the near future.

SUMMARY

1. The responses of single cortical neurones to remote artificial and physiological excitation of the cerebral cortex have been examined with extracellular micropipettes in the cat's neurologically isolated and unanaesthetized forebrain.

2. In the unstimulated brain the majority of (probably all) cortical neurones exhibit continual or 'spontaneous' activity. Although the exact moments of firing are unpredictable, the mean frequency of discharge per minute remains constant for long periods of time.

3. The behaviour of cortical neurones was not detectably modified by a single artificial stimulus given to some remote part of the cerebral cortex.

4. Responses of single neurones to artificial stimulation at 1/sec of remote areas of cerebral cortex were assessed from the post-stimulus histogram, in which the probability of discharge at various times after the average stimulus is displayed.

5. Expressed in this way, a response could be demonstrated from neurones all over the readily accessible cerebral cortex to the local excitation of apparently any close-packed group of cortical cells.

6. Responses were greater when the direct, artificial, cortical stimulus consisted of a burst of 10 stimuli at 100/sec repeated once every second, than when single shocks were delivered at 1/sec.

7. Excitation of the visual cortex by flashing a focused 6° white disk upon the animal's retina produced responses from neurones in all parts of the accessible cerebral cortex, remote from the primary visual area.

The authors wish to express their thanks to the United Cerebral Palsy Association and the Canadian National Research Council for their generous financial support of this work; to Dr A. M. Uttley and Dr D. R. Smith of the National Physical Laboratory of England for valuable advice and suggestions; to Mr A. Binder for his help in the preparation of animals and to Mr G. Mandl for assistance and advice in the design of electronic equipment.

REFERENCES

ADRIAN, E. D. (1936). The spread of activity in the cerebral cortex. *J. Pysiol.* **88**, 127–161.

BARLOW, J. S. (1957). An electronic method for detecting evoked responses of the brain and reproducing their average waveforms. *E.E.G. Clin. Neurophysiol.* **9**, 340–343.

BRAZIER, M. A. B. (1961). Recordings from large electrodes. *Methods in Medical Research*, Vol. 9, Section IV, pp. 405–432. Chicago: Year Book Medical Publishers.

BREMER, F. (1935). Cerveau 'isolé' et physiologie du sommeil. *C.R. Soc. Biol., Paris*, **118**, 1241–1244.

BURNS, B. D. (1950). Some properties of the cat's isolated cerebral cortex. *J. Physiol.* **111**, 50–68.

BURNS, B. D. (1951). Some properties of isolated cerebral cortex in the unanaesthetized cat. *J. Physiol.* **112**, 156–175.

BURNS, B. D. (1961). Use of extracellular microelectrodes. *Methods in Medical Research*, Vol. 9, Section IV, pp. 354–380. Chicago: Year Book Medical Publishers.

BURNS, B. D. & GRAFSTEIN, B. (1952). The function and structure of some neurones in the cat's isolated cerebral cortex. *J. Physiol.* **118**, 412–433.

BURNS, B. D., HERON, W. & PRITCHARD, R. (1962). Physiological excitation of the visual cortex. *J. Neurophysiol.* **25**, 165–181.

BURNS, B. D., MANDL, G. & SMITH, G. K. (1962). An auto- and cross-correlator for digital information. *Electron. Engng*, (in the Press).

BURNS, B. D. & ROBSON, J. G. (1960). 'Weightless' microelectrodes for recording extracellular unit action potentials from the central nervous system. *Nature, Lond.*, **186**, 246–247.

BUSER, P., BORENSTEIN, P. & BRUNER, J. (1959). Étude des systémes 'associatifs' visuels et auditifs chez le chat anesthésiè au chloralose. *Electroenceph. clin. Neurophysiol.* **11**, 305–324.

CHANG, H. (1950). Dendrite potential of cortical neurones produced by direct electrical stimulation of the cerebral cortex. *J. Neurophysiol.* **14**, 1–21.

CLARK, W. A. JR. (1958). Average response computer (ARC-1) *Quarterly progress report research laboratory of electronics*, M.I.T.

DAWSON, G. D. (1947). Cerebral responses to electrical stimulation of peripheral nerve in man. *J. Neurol. Neurosurg. Psychiatry*, **10**, 137–140.

DAWSON, G. D. (1954). A summation technique for the detection of small evoked potentials. *Electroenceph. clin. Neurophysiol.* **6**, 65–84.

GERSTEIN, G. L. & KIANG, N. Y.-S. (1960). An approach to the quantitative analysis of electrophysiological data from single neurones. *Biophys. J.* **1**, 15–28.

HUBEL, D. H. & WIESEL, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol.* **160**, 106–154.

LI, CHOH-LUH, CULLEN, C. & JASPER, H. H. (1956). Laminar microelectrode studies of specific somatosensory cortical potentials. *J. Neurophysiol.* **19**, 111–130.

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

MOUNTCASTLE, V. B. (1957). Modality and topographic properties of single neurones of cat's somatic sensory cortex. *J. Neurophysiol.* **20**, 408–434.

POWELL, T. P. S. & MOUNTCASTLE, V. B. (1959). Some aspects of the functional organization of the cortex of the postcentral gyrus of the monkey: a correlation of findings obtained in a single unit analysis with cytoarchitecture. *Johns Hopk. Hosp. Bull.* **105**, 133–162.

SMITH G. K. & BURNS, B. D. (1959). Probability analysis of unit activity in the cerebral cortex. *Proc. Can. Fed. Biol. Soc.* **2**.

SMITH, G. K. & BURNS, B. D. (1960). A biological interval analyser. *Nature, Lond.*, **187**, 512–513.