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THE INTERPRETATION OF POTENTIAL WAVES IN THE CORTEX.

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If two electrodes are placed on the surface of the brain a record of the potential difference between them shows repeated fluctuations which may be as large as a millivolt. Recent work on this subject dates from the string galvanometer investigations of Prawdicz-Neminsky [1913, 1925], and in the last five years a number of papers have been published from various laboratories. A review of the literature prior to 1932 has been given by Fischer [1932]. It has been shown that the potential waves are generated in the cortex, that they are modified by stimulation of sense organs and abolished by cutting off the oxygen supply to the brain; in fact there is no doubt that they are due to the activity of the cortical neurones. Recording them would seem to offer the most direct method of investigating cortical activity, but for the difficulty that they are certainly summated effects compounded out of the potential changes in many neurones. It is most unlikely that the change in each neurone is an exact copy, on a smaller scale, of the massed effect, and we cannot go much further until we know how the massed effect is built up.

The problem, then, is to decide what kind of changes to expect in the individual neurones. The potential waves recorded in the cortex are usually irregular and show wide variations in size and duration. Are the action potentials of the cortical cells as variable, or are they as uniform as the impulses in a nerve fibre? If the potential between two points on the brain increases for half a second and then decreases, are we to suppose that potential gradients have developed equally gradually in certain neurones, or that the effect is due to repeated brief outbursts which increase in number as more and more units are involved and as their activity rises? The question has been raised before by one of us [Adrian, 1931] in connection with the slow potential changes in the nerve ganglia

of insects. It was suggested that the depolarization of a nerve cell might be a much more gradual process than the explosive change which occurs in the nerve fibre. In the present work, however, we have found no evidence in favour of very slow changes in the individual neurones, and we have reached the conclusion that the cortical effect is mainly built up out of repeated brief pulsations, slower than the potential waves in a nerve fibre but of the same general character.

TECHNIQUE.

All our experiments have been made on animals under a general anæsthetic. The bearing of this on the results will be discussed later; for the present it is enough to say that the anæsthetized brain shows considerable electrical activity and that other workers have found no evidence of a radical change in the character of this activity when consciousness is lost. A few experiments were made on cats; the majority on rabbits under chloroform and ether, or urethane. Chloralose, dial or pernocton were used occasionally.

The brain was exposed by trephining the skull over the parietal region and enlarging the opening to about 2×2 cm. Bleeding from the bone was controlled by plasticine, the dura was opened and turned back, and the surface of the brain was repeatedly irrigated with warm Ringer. The head was held in a clamp but the body was not secured in any way. In some experiments respiration was recorded by a tambour connected to a branch from a tracheal cannula and the electrocardiogram by leads on the head and in the anus.

For leading from the surface of the cortex the electrodes were usually of the non-polarizable type in which a coil of silver wire coated with $AgCl_2$ dips into a glass tube containing Ringer's fluid. For many experiments we used tubes plugged at the lower end with china clay through which a worsted thread protruded to make contact with the cortex. For leading from very small areas with electrodes close together the tubes were drawn out to a point with an external diameter of 1 mm. or less and plugged with gelatin, the orifice of the tube resting lightly on the cortex.

The concentric needle system [Adrian and Bronk, 1929] gives the most restricted interpolar field, but we have found it troublesome to use on the brain. If the outer tube and inner wire are both of silver the area which can be coated with $AgCl_2$ is not large enough; the electrodes often develop a high resistance after they have been in contact with the brain for 10–20 min. If the tube and wire are not of the same metal, local circuits are often set up and may produce troublesome artefacts. Pointed gelatin electrodes are more reliable, though we have not tried to develop a concentric type.

For leading from the deeper layers of the cortex we have used both the pointed gelatin type and the concentric needle system (of silver), but many records have been made with a large indifferent electrode on the surface and an enamelled silver wire, bared at the tip and coated with $AgCl_2$. This could be thrust through the cortex with a minimum of damage.

The methods we have used for analysing the cortical waves have depended mainly on the comparison of simultaneous records from three

pairs of electrodes with three independent amplifying systems and three oscillographs. To begin with the amplifiers were of the usual type, one of the input leads being connected with the grid of the first valve and the other to earth. Thus one of each pair of leads was earthed, and as nothing was to be gained by using three distinct earthed electrodes we used a common one of large area on the cortex or in the mouth, with separate electrodes to the three grids. It was soon obvious that such an arrangement gave unsatisfactory results. The brain is a large mass of tissue in which all manner of potential changes are taking place; when the grid electrode rests on a point on its surface and the other is earthed and forms a diffuse lead from the whole mass, there is no reason to suppose that a change in their relative potentials is due to changes occurring at the point where the grid electrode is applied. The brain at this point may be inactive and the average potential of the rest of the brain (relative to the point) may have altered. With three pairs of electrodes, one of each pair going to a common earth, or with three grid electrodes and a single diffuse earthed lead the position is much the same—the simultaneous appearance of a potential wave at the three pairs does not necessarily imply simultaneous activity at the three regions to which they are applied. For this reason it is exceedingly difficult to draw any certain conclusions from the records. The difficulties which arise in this way are illustrated by a control experiment made on the frog with three concentric needle electrodes. The outer tube of each needle was earthed, the inner wires leading to the grids of the three amplifiers. With this arrangement if one needle system was on the heart and the other two on the liver, all three showed potential waves corresponding to the electrocardiogram. A single needle system on the liver showed only a minute disturbance, but connecting the outer tube with electrodes in other parts of the body caused its potential to fluctuate relative to that of the inner wire and so brought back the wave at each heart beat.

To overcome the difficulties introduced by the common earthed lead we adopted an amplifying system in which neither input lead was earthed. The system [Matthews, 1934] has been described elsewhere in detail, as it has some additional advantages over the usual form. Two input valves are used in a balanced circuit, the two electrodes lead to the two grids and the resulting changes in anode current are handed on through condensers to the later stages of the amplifier, which are of the usual condenser coupled type. With this arrangement the three pairs of electrodes are quite independent; a pair on the frog's liver shows only a very small deflection, although other pairs on the heart give simultaneous records

of the electrocardiogram (Fig. 1). Three Matthews' oscillographs were used to record the potential changes, which were photographed and could be viewed with the usual rotating mirror arrangement. A loud-speaker was not often used, as the cortical potentials often rise and subside too slowly to give clearly audible sounds. Our records of the cortical potentials are sometimes slightly distorted by the use of capacity-coupled amplifiers, but this has been controlled by the use of a battery-coupled amplifier (see p. 455) and the distortions are not of a kind which would affect the interpretation of the records.

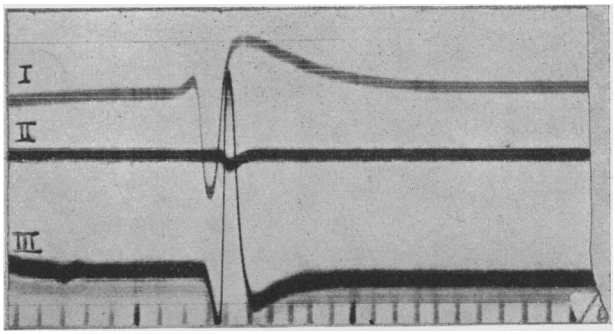

Fig. 1. Frog's electrocardiogram with balanced amplifiers. Three concentric needle electrodes, I and III on the heart, II on the liver. Sensitivity the same for all. Time marker gives 1/20 sec. With three earthed amplifiers the deflections from the liver are as large as those from the heart.

Results.

Characteristic potential changes from the cortex.

(*a*) *Rhythmic outbursts in deep anæsthesia.* In an animal which is lightly anæsthetized and still more in one which is not under a general anæsthetic [*vide* Fischer, 1932, 1933; Kornmüller, 1933; Tönnies, 1933] the potential changes in the cortex are irregular and may be difficult to predict. Under deep anæsthesia they become much more regular, and although there are variations from one rabbit to another we can make fairly certain of recording the same type of disturbance again and again over periods of several hours. We had not expected this result, though it is mentioned by Bartley and Bishop [1933]. It has been of great value, for it has enabled us to plan experiments knowing what kind of cortical response to expect.

Fig. 2 illustrates, in A, the type of record usually found in light urethane anæsthesia, and in B and C, the more regular type with deeper anæsthesia. In the latter a series of outbursts occur at intervals of 1–3 sec. Each consists of one or more large elevations rising and declining relatively slowly with a series of much smaller and briefer oscillations superimposed on them. The slow elevations represent potential changes of 0·5–1·0 millivolt. If the amplification is of the order needed to keep the whole of these waves on the record there is usually no sign of activity in the intervals between each outburst, but with higher amplification it is possible to detect oscillations of the brief type scattered through most of the quiet interval.

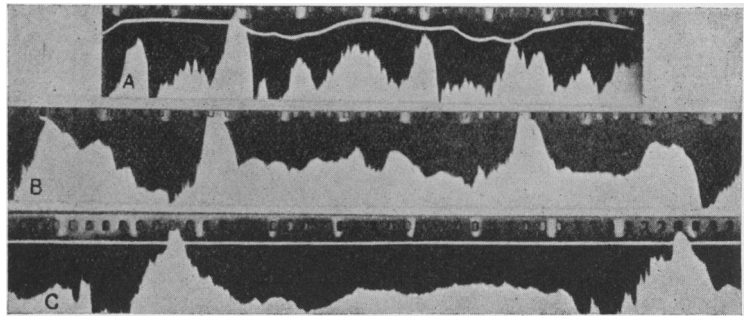

Fig. 2. Potential changes from cortex of rabbits under urethane anæsthesia. A, moderately light; B and C, deep. In deep anæsthesia the slow waves become more regular. The "brief" waves are just visible. Condenser-coupled amplifier, non-polarizable thread electrodes 1 cm. apart on cortex. White line in record A signals respiration. Time marker gives 1/4 sec. intervals.

Under urethane the outbursts seldom occur with complete regularity; more definite rhythms appear in rabbits under chloroform and ether. Those in Fig. 3 are typical of moderate degrees of anæsthesia (corneal reflex just abolished). The slow waves have a characteristic frequency of 3–4 per sec. with brief waves at 25–40 per sec. superimposed. Simultaneous records of the electrocardiogram and of respiration show that the cortical rhythm is quite independent, although these extraneous rhythms are often of the same order. In very deep anæsthesia (Fig. 4), the 3–4 per sec. rhythm gives way to a slower beat at intervals of 1–2 sec. The superimposed brief waves are on the whole more regular, and their frequency usually lies in the region of 25–30 per sec.

Both slow and brief waves are due to the activity of the cortex. It is true that when a large earthed electrode is used they persist after the

cortex under the grid electrode has been killed by freezing with solid CO_2, but this is due to the dead tissue acting as a lead from neighbouring

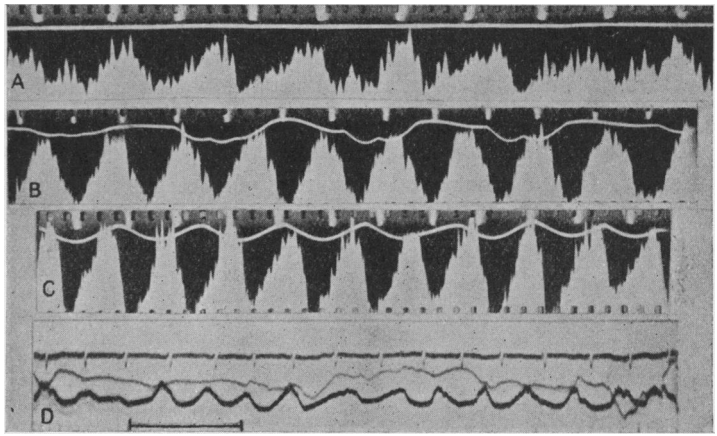

Fig. 3. Rhythmic waves from the rabbit's cortex in moderate C. and E. anæsthesia. Four different animals. Slow waves at 3–4 per sec. with brief waves superimposed. Respiration shown in B and C and electrocardiogram in D (upper line), not in phase with the slow waves. In D there are two records from different regions but the rhythm only appears in the lower. Time marker in A, B and C gives 1/4 sec. In D horizontal line = 1 sec.

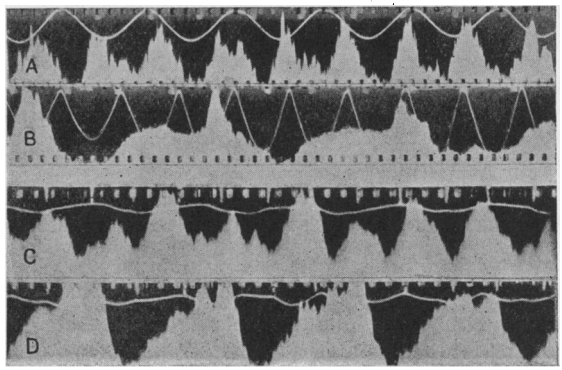

Fig. 4. Slower rhythm in deep C. and E. anæsthesia. A and B from one rabbit; A, moderate anæsthesia, waves 3·5 per sec.; B, deep, waves 1 per sec. C and D from another rabbit; C, moderate anæsthesia, waves 4 per sec.; D, deep, waves 1·3 per sec. Respiration not in phase.

regions, for with the balanced amplifier two electrodes on the killed area record little or nothing. Subcortical structures may possibly contribute to the effect under certain conditions, but we have no evidence as to this.

(*b*) *The injury response.* Another characteristic type of activity is that produced by injury to the cortex. It can be produced without fail, and it supplies important evidence as to the nature of the potential waves. If two electrodes rest at some distance apart on the cortex and a small cut is made in its surface near one of them, there is usually an outburst of brief potential waves in a regular series with a frequency somewhere between 90 and 35 per sec. A cut 1 mm. long and $\frac{1}{2}$ mm. deep is often enough, but a puncture with a fine wire to the same depth is usually without effect. On the other hand if a wire, a pointed gelatin electrode, or a concentric needle system is gradually pushed through the superficial layers of the cortex there is nearly always an outburst of the regular waves when the point has penetrated to a depth of 1·5–3 mm.

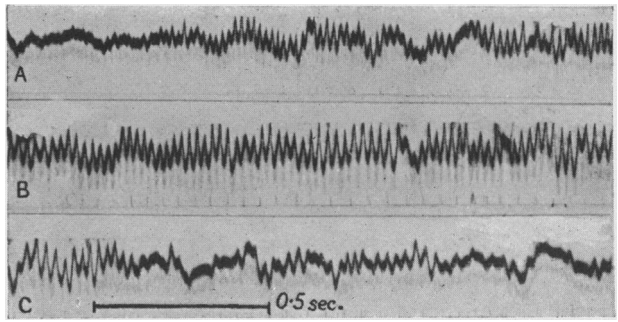

Fig. 5. Evolution of a typical "injury discharge." Rabbit under urethane. Puncture of cortex to 2–5 mm. depth by a fine silver wire forming the input electrode. A, beginning of discharge, frequency 64 per sec.; B, middle, frequency 44 per sec.; C, end, frequency about 40 per sec. during regular periods.

These injury discharges are clearly due to structures in the grey matter. In the rabbit's brain this has a thickness of about 2·5 mm., but the response of the white matter can be readily distinguished, for at a depth of about 3 mm. the response changes to a succession of small and very rapid oscillations like those given by a large nerve trunk pierced by a needle electrode. They are evidently due to impulse potentials in the axons, whereas the injury discharge is due to nerve cells and dendrites[1].

The response of the grey matter, whether to superficial or deep injury, shows a characteristic evolution as well as a characteristic frequency

[1] As there is no term which covers both the nerve cell and its dendrites but excludes the axon, we have spoken of the "cortical neurones" or "cortical nerve cells" as responsible for the potential waves. Some nervous constituent of the grey matter is responsible for them, cell bodies or dendrites or both.

range. The waves often begin a few seconds after the injury. They are small at first and can sometimes be seen as discrete, monophasic spikes with a duration of about 5–10σ. They become larger, and as they do so their outline broadens until the record becomes a sinusoidal oscillation. Usually the frequency reaches the maximum value (60–80 per sec.) at once and then falls gradually to a value in the region of 50 per sec. Occasionally the initial frequency is about 40–50 per sec. and the maximum is not reached for several seconds. The discharge may continue at about 50 per sec. for as long as half a minute, but eventually the frequency falls to 35–40 per sec., the waves begin to vary in size and the regularity ceases (Fig. 5). With more widespread damage the response usually appears after a shorter interval: the initial frequency may be as high as

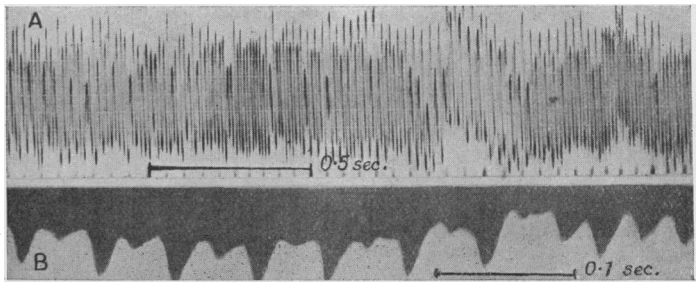

Fig. 6. A, beginning of injury discharge (rabbit, urethane). Waves alternately large and small, frequency 90 per sec. B, beginning of injury discharge (rabbit, urethane). Monophasic waves, frequency 40 per sec. (increased later).

100 per sec., and in the later stages occasional very large waves may occur, often diphasic. In many discharges there is a stage in which the successive waves are alternately large and small (Fig. 6), and sometimes the final break up of the rhythm is heralded by an alternating rhythm of this kind. Injury discharges have been recorded in twenty or more rabbits, and the frequency limits have shown no significant variation. The response to a superficial injury can be given a faster or slower rhythm by irrigating the surface of the cortex with hot or cold Ringer. The depth of anæsthesia has no obvious effect on the frequency, but in very deep C. and E. anæsthesia a greater injury may be necessary to produce the discharge. More severe injury seems to be needed in the cat than in the rabbit, though the discharge has the same frequency range and the same evolution (Fig. 7).

The characteristic evolution suggests that we are dealing with a synchronous pulsation in a number of units. Synchronous discharges

due to injury have been recorded in nerve [Adrian, 1930; Hoagland, 1933] and in muscle [Adrian and Gelfan, 1933], and in these structures, as in the cortex, the response consists of large regular oscillations which approach a sine curve but become small and less regular as soon as the frequency falls below a critical value. In the cortex it appears that the activity is at first confined to a few neurones and then gradually spreads to include more and more. This would account for the increase in size and the broader contour of the waves. Direct evidence of such a spread can often be obtained by recording simultaneously from two or three pairs of

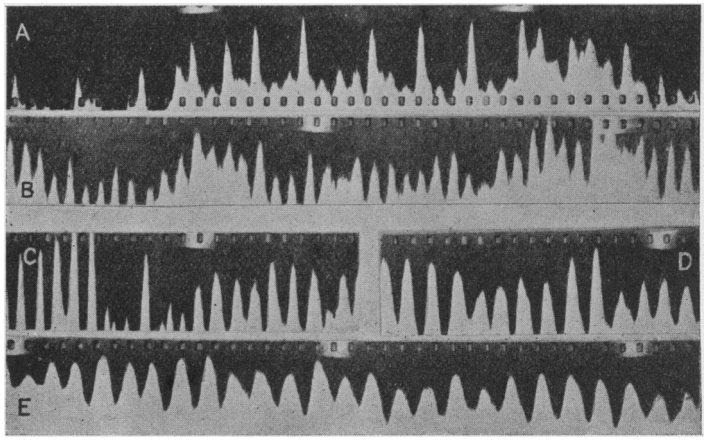

Fig. 7. Evolution of injury discharge in cat (C. and E. anæsthesia). Puncture of cortex by fine wire. A, large monophasic waves 30 per sec.; B, later, frequency 76 per sec.; C, later, frequency 72 per sec.; D, later, frequency 56 per sec.; E, later, frequency 48 per sec. Time marker gives 1/4 sec. intervals.

electrodes. Fig. 8 gives two examples of this. Further evidence of the synchronous pulsation comes from the fact that two electrodes placed very close together near the injured point often fail to show any sign of activity, whereas either of them in conjunction with a distant electrode shows large oscillations. Clearly no potential differences can be developed between two electrodes if both of them are on an area whose potential rises and falls synchronously at every point, but the oscillation will appear if one of the electrodes is removed to an inactive or less active region.

The units responsible for the injury discharge must have slower time relations than those of medullated nerve fibre. In a mammalian nerve trunk synchronous activity can occur over a frequency range of 600–120 per sec. In the cortex the range is about 100–35 per sec. Rhythms as high

as 200–300 per sec. have been observed occasionally with stimulation by a constant current, but 80–35 per sec. is the characteristic range. The form of the waves is another argument for slower time relations. The fully developed sinusoidal oscillation can only tell us that a number of units are pulsating together at a particular frequency, but there are often periods, sometimes at the beginning and sometimes towards the end of an outburst, when the waves are separated by distinct pauses (Figs. 6 B, 7 A).

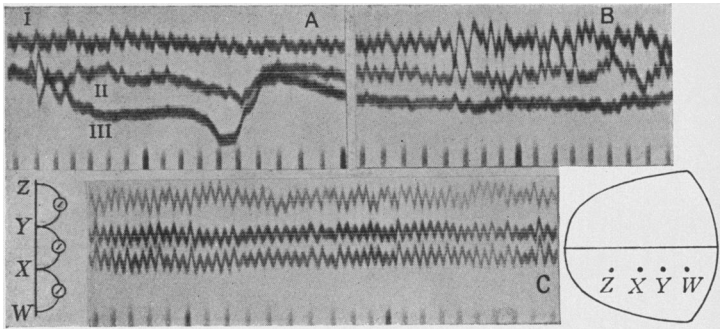

Fig. 8. Spread of injury discharge. Records from different points on the cortex (rabbit, urethane). A and B, successive stages in one experiment with four electrodes in line at intervals of 4, 3 and 3 mm. and three recording systems (cf. inset, full size). Injury at *Z* electrode: in A, record between *Z* and *Y* gives waves at 54 per sec. and that between *Y* and *X* gives half rhythm; in B, all three records give waves at about 45 per sec.; C, another injury giving waves at 50 per sec. between each pair of electrodes. Balanced amplifiers. Time marker gives 1/20 sec.

Since they still have a smooth contour and an over-all duration of about 5–10 σ it is unlikely that the response of each unit is much briefer than this.

The analysis of cortical potentials.

The nature of the injury response has been discussed at length because the waves which appear in it give a fair idea of the rapidity of the changes which can occur in excited nerve cells, and because they resemble very closely the brief oscillations which occur spontaneously. In the records of spontaneous activity already given (Figs. 2, 3, 4), the brief oscillations cannot be seen very clearly, but the size of the slow waves can be reduced by using smaller coupling condensers, and it is then possible to study the brief waves under higher amplification. Though they can always be observed if the amplification is great enough they are usually most prominent in moderately light C. and E. anæsthesia (Fig. 3 A). They are

certainly more variable than the waves of the injury discharge. Moderately regular waves at frequencies below 35 per sec. are often found, particularly in deep C. and E. anæsthesia, and there are occasional groups of frequencies as low as 10 per sec.; but regular oscillations at 35–50 per sec. are usually present in parts of the record, and it is often quite impossible to distinguish a regular train of spontaneous waves from the regular oscillation of an injury discharge (Fig. 9). It is true that no hard and fast line can be drawn between what we have called "brief" and "slow" waves, but there is no doubt that at the "brief" end of the scale the waves resemble those produced by injury to the cortex.

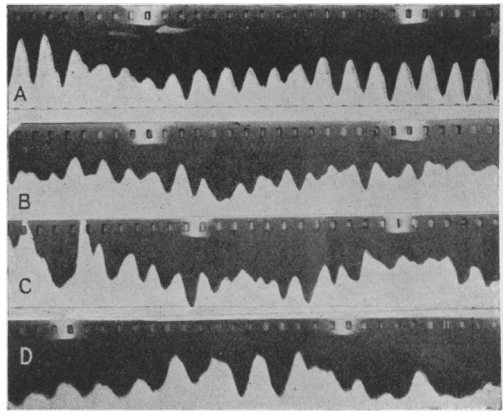

Fig. 9. Comparison of injury discharge and "brief waves" in spontaneous activity. Rabbit under C. and E. A, response to puncture of cortex: waves 48 per sec.; B, C and D, spontaneous activity in uninjured cortex with groups of brief waves; frequency between time signals, B 48 per sec., C 40 per sec. and D 36 per sec. (approximate). Time marker gives 1/4 sec.

Their likeness to the injury discharge shows that the brief waves represent the rapid pulsating activity of groups of nerve cells. Our problem, then, is to decide whether there is any other kind of activity. Are the slow waves merely summation effects compounded out of repeated brief pulsations in many neurones, or are some of the neurones capable of slow changes as well?

The fact that the brief waves in the injury discharge are initially monophasic has an important bearing on the question, for if the brief waves were invariably diphasic they could not summate to give a large, slow deflection. The waves which occur spontaneously are rarely separated by pauses distinct enough to show whether they are monophasic or

not, but at the beginning and sometimes at the end of an injury discharge there is no doubt of it. It might be argued that this is a natural consequence of injury, but the injury may be inflicted at some distance from the electrodes and the responses are still monophasic. Moreover, it would be natural to expect a monophasic potential change when a nerve cell becomes active, for one electrode may be regarded as leading from the point at which the activity originates and the other is a diffuse lead from

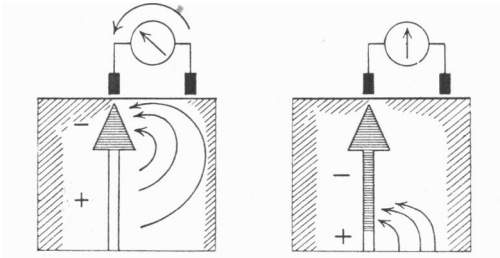

Fig. 10 A.

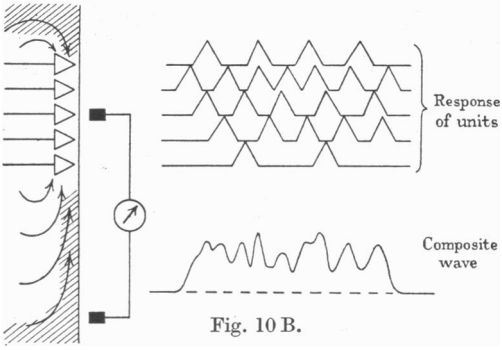

Fig. 10 B.

Fig. 10. A, potential gradients due to a wave of activity arising in a nerve cell and travelling down the axon, to show the production of monophasic waves: B, potential gradients due to repeated asynchronous activity in a group of nerve cells, to show the formation of the slow potential waves. For simplicity it is assumed that all the nerve cells will have the same effect on the recording system.

the whole of the axon (Fig. 10 A). Thus a series of rapid monophasic pulsations in a large number of neurones might give a composite potential wave in the way illustrated in Fig. 10 B. This would only occur if the pulsations were asynchronous, and it is noteworthy that in a synchronized injury discharge the slow waves disappear. This is perhaps the most direct evidence for the view that the slow waves are built up out of the same components as the injury discharge. The two types of activity are

mutually exclusive as they must be if one is due to asynchronous and the other to synchronous pulsations in the same neurones.

If the slow waves are in fact due to a summation of the brief waves they should be much more in evidence when the distance between the electrodes is large. If the distance could be made so small that the main effect came from a single neurone we should expect to find nothing but a succession of the brief waves, and the summation effect would become larger and larger as there were more and more neurones to contribute to it. On the other hand, if single neurones can produce slow as well as brief changes of potential these should be still evident when a very small electrode system is used.

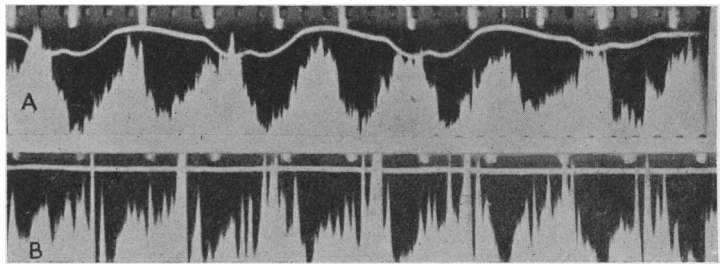

Fig. 11. Change in relative sizes of "slow" and "brief" waves with change in separation between electrodes, Rabbit under C. and E. A, input electrode on cortex, earthed electrode in cheek. B, concentric needle electrode system 1 mm. diam. on cortex. Recording system 10 times more sensitive. The brief waves are much larger, but the slow are if anything smaller than in A in spite of the increased sensitivity.

All our experiments agree in showing an increase in the size of the brief waves relative to the slow when a restricted electrode system is used. Thus Fig. 11 compares the rhythmic waves in C. and E. anæsthesia as recorded (*a*) with a diffuse earthed electrode and one lead from the cortex and (*b*) with a concentric needle system resting on the surface of the cortex. The amplification in (*b*) is greater than in (*a*), so that the reduction in the size of the slow waves is much greater than appears in the record. Again, Fig. 12 shows the typical urethane outbursts recorded with three pairs of pointed gelatin electrodes arranged as shown in Fig. 12 A. In the upper records the sensitivity is the same for all three pairs. There is no sign of the slow waves at the pair of electrodes which are only 1 mm. apart, though the brief waves are not very much smaller than at the more widely separated electrodes. In the lowest record the sensitivity has been greatly increased for the 1 mm. electrodes: the brief waves

are more prominent but the slow waves are still greater at the other electrodes.

A similar result is reached when we use electrodes at different distances from the surface of the cortex. Tönnies [1933] has already compared the effect of leading from the cortex, the dura and the unopened skull, and shown the greater prominence of brief waves in the cortical record. We have used the arrangement shown in Fig. 13. A pool of warm Ringer was formed on the surface of the cortex by building a wall of dental cement

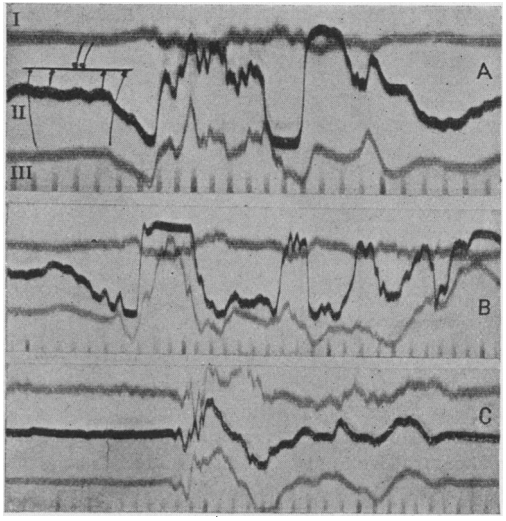

Fig. 12. Change in relative sizes of slow and brief waves with electrode separation. Rabbit under urethane. Balanced amplifiers. Electrodes arranged as shown in A; those to oscillograph I are 1 mm. apart, those to II 9 mm. and those to III 16 mm. In A and B all three oscillographs are equally sensitive. In C, No. 1 is made more sensitive (top record, 1 mm. between electrodes). Time marker gives 1/20 sec.

round the cut edges of the skull or by lifting up the scalp at each side. The electrodes were placed so that the points of one pair rested on the cortex with the others at various distances above it in the Ringer. The slow waves can be detected 6 mm. above the cortex, and in Fig. 13 B where the top pair of electrodes are 9 mm. apart and the bottom pair only 2 mm. there is no marked difference in their size, but in both records the brief waves appear only at the electrodes actually in contact with the cortex. Evidently the brief waves arise from structures very close to the surface electrodes, whereas the slow waves have a much wider or more distant origin. The diagram in Fig. 14 may make this clearer.

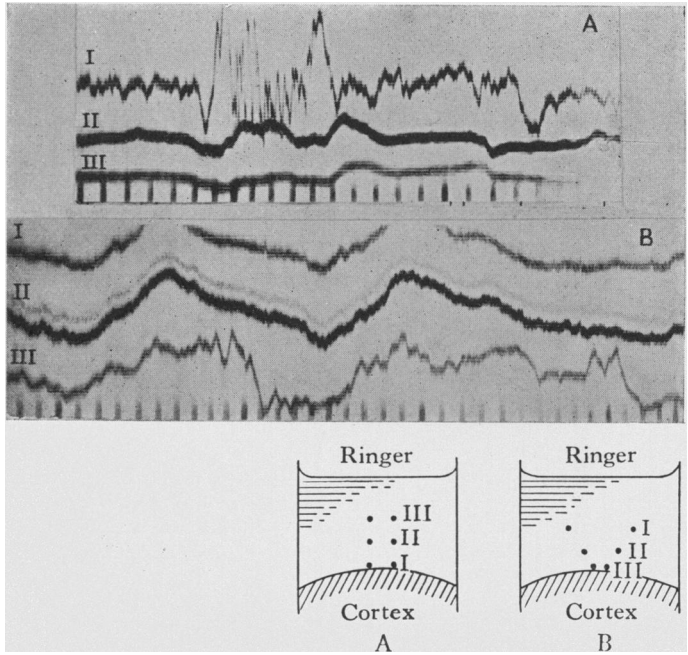

Fig. 13. Change in relative sizes of slow and brief waves with electrodes at different distances from surface of cortex. Pool of Ringer covering brain (rabbit, urethane). In A oscillograph I connected to electrodes 3 mm. apart on surface of cortex; II to electrodes 3 mm. apart and 3 mm. above surface; III ditto, 6 mm. above surface. I less sensitive —oscillographs adjusted to give approximately equal excursions.
In B, III is connected to surface electrodes 2 mm. apart; II to electrodes 4·5 mm. apart and 2 mm. above surface and I to electrodes 9 mm. apart and 5 mm. above surface. The very small oscillations in I and II are due to amplifier noise. Time marker gives 1/20 sec.

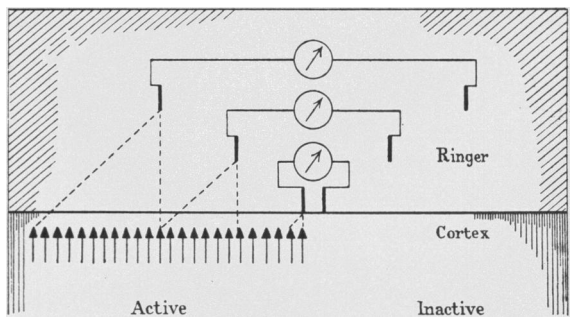

Fig. 14. Potential waves recorded by electrodes on the surface of the cortex and some distance above it (as in Fig. 13). The electrodes above the surface will record only the summated effect from a wide area. Those on the surface will be mainly affected by the neurones immediately under them.

Thus the composite nature of the slow waves is shown by our inability to localize their origin. They are greatest when a large mass of cortex intervenes between the two electrodes, but a detailed exploration of the mass, both in depth and on its surface, never reveals any region where the slowly developing potential gradients are greater than elsewhere. Their existence evidently depends on the activity of a large number of units, and the response of each unit bears no resemblance to them.

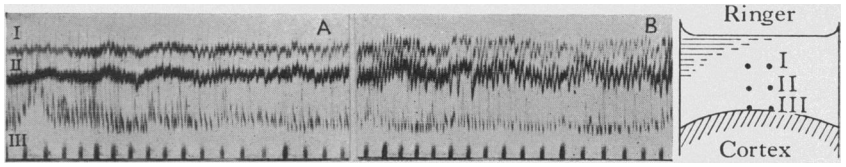

Fig. 15. Synchronized injury discharge from a large area appearing at electrodes 6 mm. above cortex. Rabbit, urethane. I, to electrodes 3 mm. apart and 6 mm. above surface (in Ringer); II, to electrodes 3 mm. apart and 3 mm. above surface; III, to electrodes 3 mm. apart and in contact with surface. In A the discharge is localized and has not much effect on the electrodes above the surface. In B it has spread and appears in all three recording systems. Time marker gives 1/20 sec.

Amplifier distortion.

As the foregoing experiments were all made with condenser-coupled amplifiers the slow waves will be distorted to some extent in the records. This does not affect the argument, but it is possible that the regions under the electrodes might sometimes change their potentials so slowly that nothing would appear in the record. To examine this possibility and generally to see how far our results are affected by amplifier distortion we have made some simultaneous records with a battery-coupled amplifier leading to one oscillograph and a condenser-coupled amplifier to another. With 1 mf. coupling condensers in the latter there is very little difference in the records, and in particular there is no indication of gradual (or sudden) shifting of the base line with the distortionless amplifier. Between the slow waves the potential returns to its original value just as it does with condenser coupling. Thus there is no evidence of very slow potential changes either in the cortex at large or, *a fortiori*, in the individual neurones.

Areas contributing to brief and slow waves. (*a*) *The brief waves. Synchronous pulsation of neurones.* The existence of the slow waves implies an asynchronous pulsation in the different parts of the area which contributes to the potential gradient, for if all the neurones were pulsating synchronously we should record a rapid oscillation instead of a slow rise or fall. The widespread synchronous pulsation caused by injury does in fact appear as such at electrodes as much as 6 mm. above the surface of the cortex (Fig. 15), but this distance is enough to smooth out all trace of the brief waves in the normal spontaneous activity. On the other hand, it is

unlikely that the brief waves are due to single nerve cells, for the magnitude of the potentials (which may be as much as 100 microvolts) and the sinusoidal wave form both suggest a synchronous pulsation in a group of cells.

We have attempted to find out how large an area contributes to each of the brief waves, for this will give some idea of the magnitude of the group which is pulsating together. As might be expected, the results show a considerable variation. In Fig. 16, for instance, there is an occasional agreement in some of the brief waves recorded at two pairs of electrodes 3 mm. from one another, but in a good deal of the record there is no agreement at all. This shows that there is no likelihood of an electrical spread from one pair of electrodes to the other and makes the occasional agreement more significant.

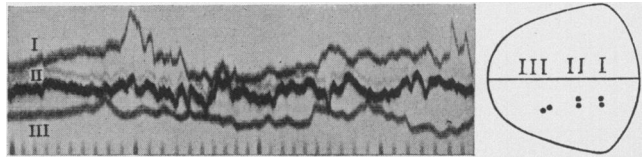

Fig. 16. Occasional agreement of brief waves at electrodes 3 mm. apart. Rabbit, C. and E. Pointed gelatin electrodes arranged in pairs, I, II and III (see diagram) with 1 mm. separation between the electrodes of each pair. I is 3 mm. from II and II is 4 mm. from III. In the first outburst the waves at I and II show some agreement, but there is very little in the later part of the record. No agreement at III. Time marker gives 1/20 sec.

From this and many similar records it appears that in the normal activity of the anæsthetized brain a synchronous pulsation does not cover an area of more than 3–4 mm. diam. and is often much more restricted. An area of 3 mm. diam. might be covered by the dendrites of a single nerve cell, but there is no reason to doubt that each brief wave is the product of a group rather than a unit. Synchronized action occurs, apart from gross injury, in different regions of the nervous system, *e.g.* in the motor centres of the cord, in the retina, the optic ganglion of *Dytiscus*, etc. It is most evident when there is an intense, uniform excitation of the whole region, and it might well occur in smaller areas if these were uniformly excited.

(*b*) *The slow waves. Rise and fall of activity in larger areas.* If the slow waves are due to summated brief waves from many neurones it follows that there must be a general agreement in the periods of rest and activity over considerable areas, although the neurones in them are not pulsating

in phase. The mere existence of a potential gradient shows, of course, that the activity is not uniform throughout the cortex. Indeed the size of the waves will be a measure of the gradient of activity along the line joining the electrodes, and by recording simultaneously at several points we can gain some idea of the distribution of activity from moment to moment.

It is found that the distribution is complex in light and moderate anæsthesia but simpler in deep anæsthesia; with light anæsthesia the waves at three pairs of electrodes 5 mm. or more apart show little or no

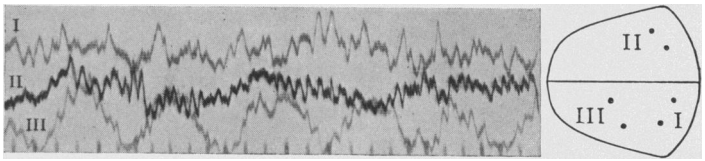

Fig. 17. Lack of agreement in activity at different points in moderate C. and E. anæsthesia. Thread electrodes, 4 mm. separation. Arranged as in diagram with 10 mm. between I and II and 5 mm. between II and III. Note continuous series of brief waves, and slow waves with regular 4 per sec. rhythm at electrodes III only. Time marker gives 1/20 sec.

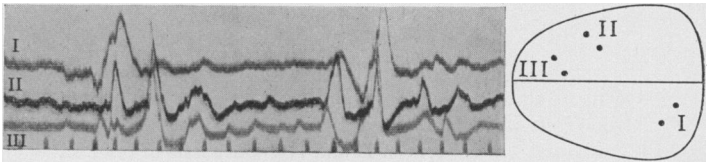

Fig. 18. Agreement of active periods in deep urethane anæsthesia (rabbit). Electrodes 3 mm separation arranged as in diagram. 15 mm. between I and II, 5 mm. between II and III. Time marker gives 1/10 sec.

correspondence (Fig. 17), but in deep anæsthesia they agree very closely. In the typical response under urethane the slow waves appear almost simultaneously at points 1 cm. or more apart (Fig. 18), and in deep C. and E. anæsthesia there is a regular cycle of rest and activity which is equally widespread (Fig. 19). This cycle has a period of 1–2 sec. and appears only when the anæsthesia is strong enough to threaten respiratory failure if its administration is prolonged. The regular waves at 3–4 per sec. which occur in lighter C. and E. anæsthesia are usually confined to one pair of electrodes, or appear with an independent rhythm at different points (Fig. 17).

Regular beating of this kind could scarcely occur except in a cortex undisturbed by external influences, and it is found that if sensory stimulation produces any effect at all that effect is to break up the rhythm. This is best seen in urethane anæsthesia light enough to allow a slight reflex contraction of the leg muscles when the foot is pinched. Illustrations of this are given in Fig. 20, and it will be seen that pinching the foot abolishes the slow rhythms and increases the prominence of the brief waves, which

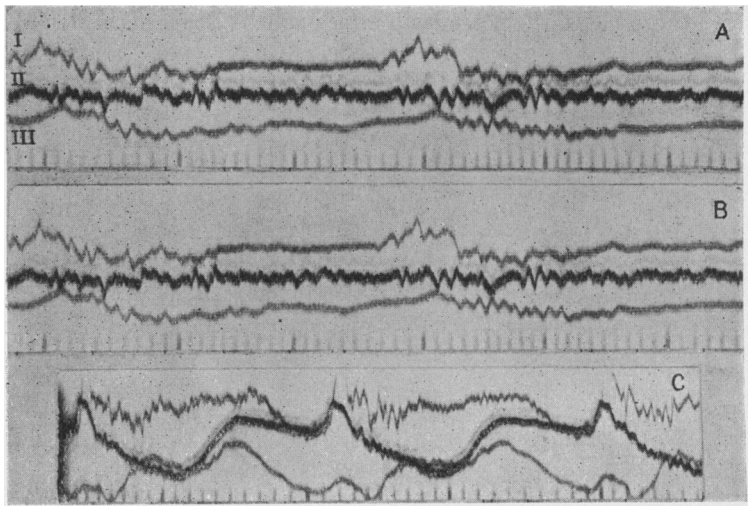

Fig. 19. Agreement of active periods in deep C. and E. anæsthesia (rabbit). A and B, pointed gelatin electrodes 1 mm. apart arranged in pairs as in Fig. 16 with 3 mm. between I and II and 4 mm. between II and III. Outbursts of brief waves at 1½ sec. intervals. C, another animal. Thread electrodes 4 mm. apart arranged in pairs as in Fig. 17. Outbursts at 1 sec. intervals. Note the presence of slow waves in C (electrodes 4 mm. apart) and their absence in A and B (electrodes 1 mm. apart). Time marker gives 1/20 sec.

now appear in a continuous outburst. In some records the slow waves have returned at a higher frequency towards the end of the stimulation.

It will be clear from Figs. 17–19 that in deep anæsthesia periodic waves of activity may sweep over the whole cortex (or rather over its dorsal surface), and that in lighter anæsthesia one or more regions may beat rhythmically at 3–4 per sec. Waves of the same kind occur in the cat as well as in the rabbit, though not with such uniformity. They are not in phase with respiration or the heart beat and are not appreciably altered by changing the blood-pressure or the composition of the air breathed by the animal. They may depend on subcortical mechanisms, but all that

can be said at the moment is that they show that the respiratory centre is not the only region of the brain which has a tendency to slow, rhythmic beating. The rhythmic movements of narcosis progression described by Graham Brown [1914] are probably due to beats of the same kind. Indeed, Graham Brown's suggestion of inherent rhythms modified by afferent control seems to be well illustrated by records such as those in Fig. 20.

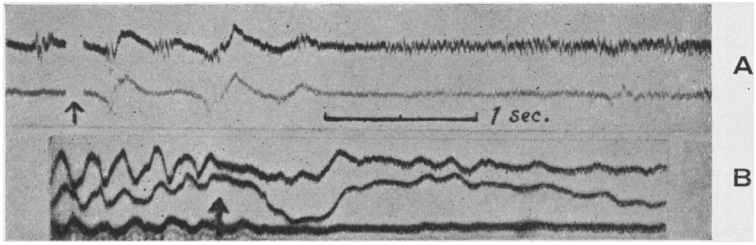

Fig. 20. Rhythmic outbursts cease on sensory stimulation in light anæsthesia. Both records are made with earthed amplifiers, not with the balanced type. The agreement in the waves may be due to the common earth leads. A, rabbit, urethane. Pinching foot at arrow. The slow waves give place to a continuous series of rapid oscillations. B, another animal. Pinching foot at arrow.

Transitional waves. (*a*) *Due to injury.* In the spontaneous activity of the anæsthetized brain there is no evidence of synchronous pulsation spreading over areas of more than 4 mm. diam. In the injury discharges much larger areas may be involved and there is often a progressive increase as the discharge proceeds. Thus the ease with which the pulsation of one neurone spreads to another can vary with the condition of the cortex. In certain conditions the spread takes place with abnormal ease, and a single pulsation may travel like a ripple over the surface of the brain, giving rise to a characteristic potential change.

This type of activity is often seen as a sequel to an intense injury discharge and it is invariably found with certain convulsant drugs. It leads to the production of very large potential waves, often with a smooth contour, representing a transition between the slow and the brief type.

The simplest case to take is that produced by injury. As a rule the rapid pulsation ceases by becoming irregular after the frequency has fallen below 35 per sec.; in some records, however, very large waves appear from time to time during the discharge and ultimately these become its most prominent feature. They may occur singly at intervals of

½ sec. or so, or in groups of three or four. Their potentials may be as great as 5 millivolts and they appear over a wide area. Examples of them are given in Fig. 21. The waves usually begin as simple monophasic spikes differing only in size from the other waves in the series (Fig. 21 C and D), but ultimately they may become di- or triphasic, or may present multiple crests and troughs as in Fig. 21 B. This change in appearance seems to be

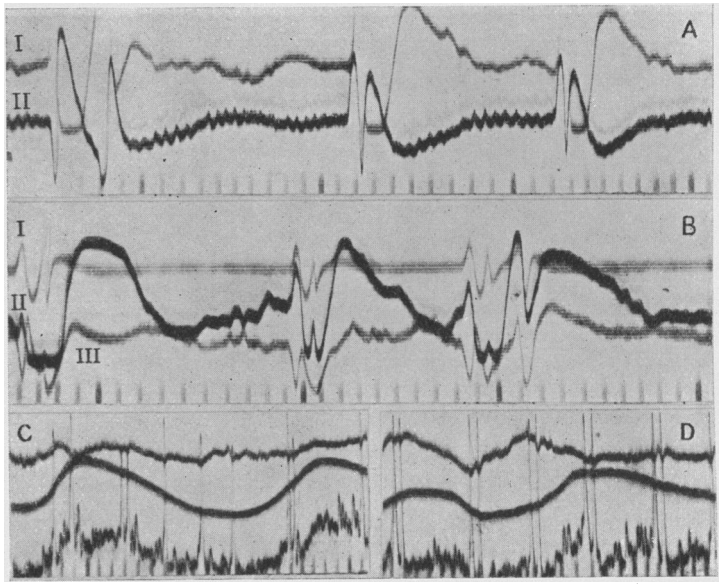

Fig. 21. "Transitional" waves due to injury. A, rabbit, urethane. Earthed amplifiers. Later stage of injury discharge with three large waves and small oscillations at 40 per sec. B, rabbit, urethane. Balanced amplifiers. Electrodes arranged as in Fig. 12. I 1 mm. apart, II 9 mm. and III 16 mm. Sequel to prolonged injury discharge. Note absence of slow waves at I. C and D, rabbit, urethane. Earthed amplifiers. Lowest record shows development of large transitional waves (monophasic) occurring singly at first and then in couples. Time marker gives 1/20 sec.

due to the waves or groups of waves spreading at a finite rate through the cortex so that the region of maximum negativity lies now under one electrode and now under the other. But the conduction takes place without the waves losing their individuality and an almost identical pattern of activity may appear at points 10 mm. or more apart.

The development of these large waves out of the brief pulsations of the injury discharge shows how a broader contour and a diphasic form may result from a pulsation which spreads over the cortex instead of being

confined to a small area. In the discharges produced by convulsant drugs we find the same kind of conducted pulsation and can sometimes follow the change from the transitional type into the usual complex of slow and brief waves.

(*b*) *Convulsant drugs, thujone.* Strychnine produces widespread synchronous activity in the nervous system and might therefore be expected to give a cortical discharge made up of widespread pulsations. Fischer [1933 *a*], Bartley [1933] and others have recorded the cortical response, and their records show a succession of waves of very large potential repeated as rapidly as 25 per sec., or occurring singly or in groups at lower frequencies. At the higher frequencies they have the simple contour of the waves in an injury discharge and at lower frequencies they resemble the large "transitional" injury waves shown above. Fischer has used other convulsant drugs, picrotoxin, caffeine, etc., with the same results. In our own experiments with convulsants we have generally used thujone, the active principle of wormwood oil. In the unanæsthetized animal thujone produces convulsions which are said to resemble those of epilepsy. In an animal deeply anæsthetized with urethane there is usually no motor effect, but there is an obvious counterpart of the convulsion in the potential record from the cortex.

We have used an emulsion of thujone in olive oil and gum arabic solution injected into the femoral vein. A dose of 0·5 c.c. of a 1 in 10 emulsion is enough to produce the typical cortical discharge in a rabbit under urethane. As a rule the first sign of the effect is that the slow urethane waves disappear: then after an interval of apparent inactivity there is a more rapid series of slow waves, each with a small group of brief waves superimposed. Very soon, instead of a group of brief waves on a slow deflection, we find a sudden large oscillation, wider and more complex in form than that of the usual brief waves, but no longer clearly divisible into fast and slow components. A series of records showing the evolution of a thujone discharge is given in Fig. 22. To avoid confusion only one oscillograph tracing is shown in the figure, although three simultaneous tracings were made from different points. It will be seen that the discharge works up into a series of large diphasic waves of simple contour; the wave form changes from time to time and ultimately the discharge stops suddenly and completely.

In this particular record the frequency of the large waves is never greater than 10 per sec., but it may reach 20 per sec. or more with larger doses, and the large beats are sometimes preceded or followed by smaller 50 per sec. oscillations.

The factors underlying the wave form and the changes it undergoes can be studied by simultaneous recording at different points. At the height of the discharge the whole surface of the cortex pulsates with the same rhythm though occasionally a beat is missed at one pair of elec-

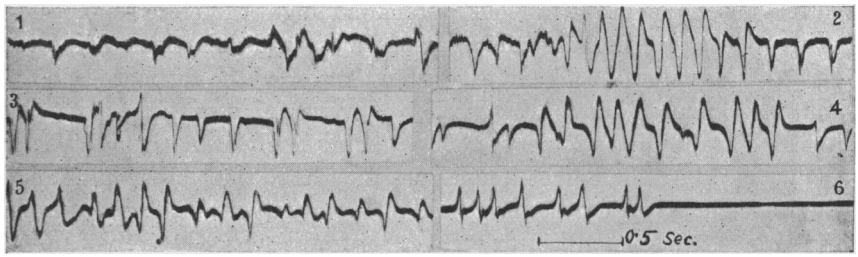

Fig. 22. Evolution of discharge due to thujone in a rabbit under urethane. Portions of a continuous record, intervals of 2–3 sec. between successive strips. Pointed gelatin electrodes 1 mm. apart on surface of cortex. Three simultaneous records were made from different points but the tracings of oscillographs I and III have been painted over to show II more clearly. The largest deflections represent potential changes of about 5 mv.

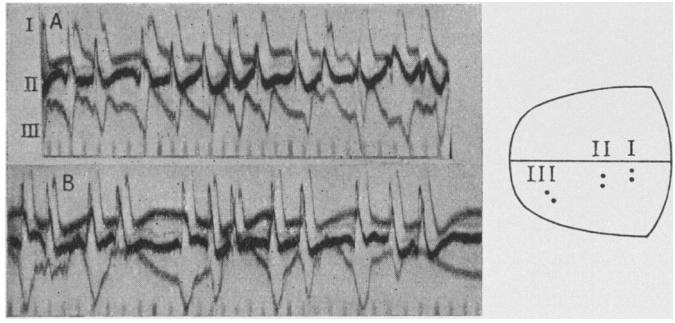

Fig. 23. Record of thujone discharge from three points on the cortex, showing agreement of waves. A, near the beginning of the discharge, waves 10 per sec. One wave is missed at III (8 mm. from II), but otherwise there is complete agreement. B, later; I and II still agree, but more waves are missed at III. Gelatin electrodes 1 mm. apart, 4 mm. between I and II, 8 mm. between II and III. Time marker gives 1/20 sec.

trodes (Fig. 23). More information can be gained, not from three pairs of electrodes a long distance from one another, but from four electrodes in line (*W*, *X*, *Y*, *Z*, Fig. 24) with the three recording systems between adjacent electrodes. With such an arrangement we can map out the potential distribution along the line and see how it changes from moment

to moment. Two characteristic records from the same discharge are given in Fig. 24. In Fig. 24 A the waves have a broad contour, they are diphasic and the maximum negativity of *W* relative to *X* occurs about 0·025 sec.

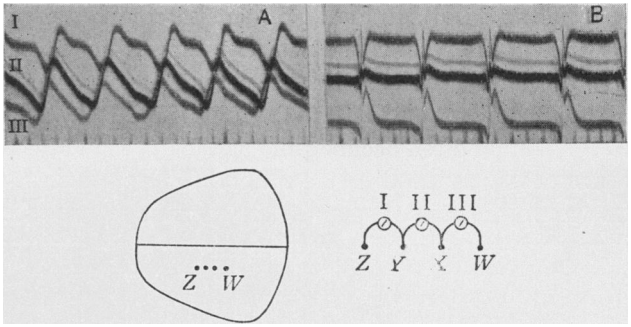

Fig. 24. Thujone waves recorded at four electrodes in line, 1 mm. apart. Two strips from a continuous record. Rabbit, urethane (deep). 0·5 c.c. of 1 in 10 thujone emulsion into femoral vein. Electrodes etc. arranged as in diagram, at *W*, *X*, *Y*, *Z*. Negativity of *W* relative to *X*, *X* to *Y* and *Y* to *Z* gives a downward deflection. In A the wave is simple and travels slowly from *W* to *Z*, in B it is complex and travels much more rapidly, see analysis in Fig. 27. Time marker gives 1/20 sec.

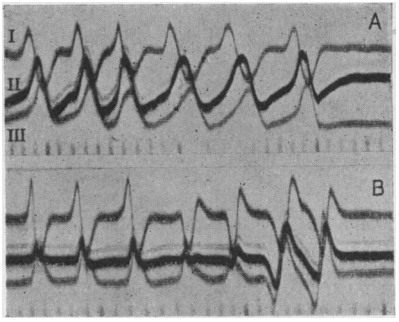

Fig. 25. Thujone waves with four electrodes in line 1 mm. apart, showing progressive changes in rate and direction. Electrodes arranged as in Fig. 24. In A the wave starts from *Z*, and successive waves spread more and more slowly until the discharge ceases. In B the wave starts from *Z* at the beginning of the record and has come to start from *W* by the end of it. Time marker gives 1/20 sec.

before that between *X* and *Y*, and 0·05 sec. before the maximum between *Y* and *Z*. In Fig. 24 B the waves are sharper and more complex and they occur almost together in each recording system. It follows that in the upper record a single pulse of activity begins at *W* and spreads relatively slowly to *Z*, whereas in the lower there are several pulses and the rate of

spread is very much more rapid. In Fig. 24 the wave form remains very nearly constant throughout the record, but there is often a gradual change from moment to moment. Thus in Fig. 25 A as the frequency of the beat declines the activity spreads more and more slowly along the line (starting in this case from the Z end). In Fig. 25 B there is a complete reversal during the seven waves in the record: the activity starts from the Z end in the first beat, in the middle of the series it appears first in the region XY and by the end it has come to spread down the line from W to Z. The change in velocity and direction often occurs quite suddenly, as in Fig. 26 A, where a single beat starts from the W end, and Fig. 26 B, where there are several abrupt changes in the rate of spread. The rhythm may be disturbed by these changes, but it is never disturbed enough to suggest that an entirely

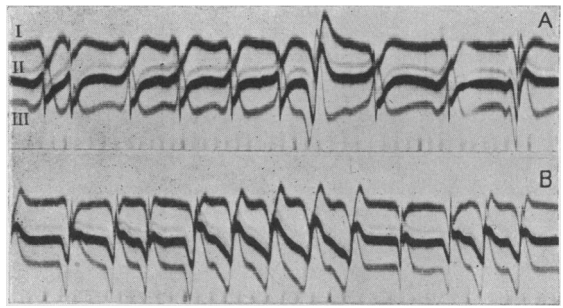

Fig. 26. Sudden changes in direction and rate of spread. Electrodes arranged as in Fig. 24. In A a single beat starts from Z. In B the rate of spread changes abruptly from time to time. Time marker gives 1/20 sec.

independent source of activity has taken charge. The potential gradients between the four electrodes at different moments are represented, for a few typical beats, in Fig. 27. They show that the beat sometimes involves a double pulsation in part of its course and that it travels at a variable rate, sometimes in one direction and sometimes in another. The change in rate may well be due simply to the change in the direction of the wave, for if it travels in a direction parallel to the line joining the electrodes the rate of conduction will appear much slower than if the direction is nearly at right angles. The rate in Fig. 24 A is of the order of 10 cm. per sec., but the uncertainty as to the direction of travel makes it impossible to say how far this applies to all the beats.

The sudden or gradual shifts in direction are not surprising if we assume that the cortex behaves under thujone like a mass of cells as closely linked as are the muscle fibres of the heart. Spontaneous beats

may arise now from one point and now from another, or the origin may shift progressively without affecting the rhythm. Similar changes often take place in the spontaneous beats produced in skeletal muscle fibre bathed in NaCl solution. A record illustrating this is given in Fig. 28, and it will be seen that the origin of the beat shifts gradually during the discharge so that the action potentials come to be reversed in phase, as in the

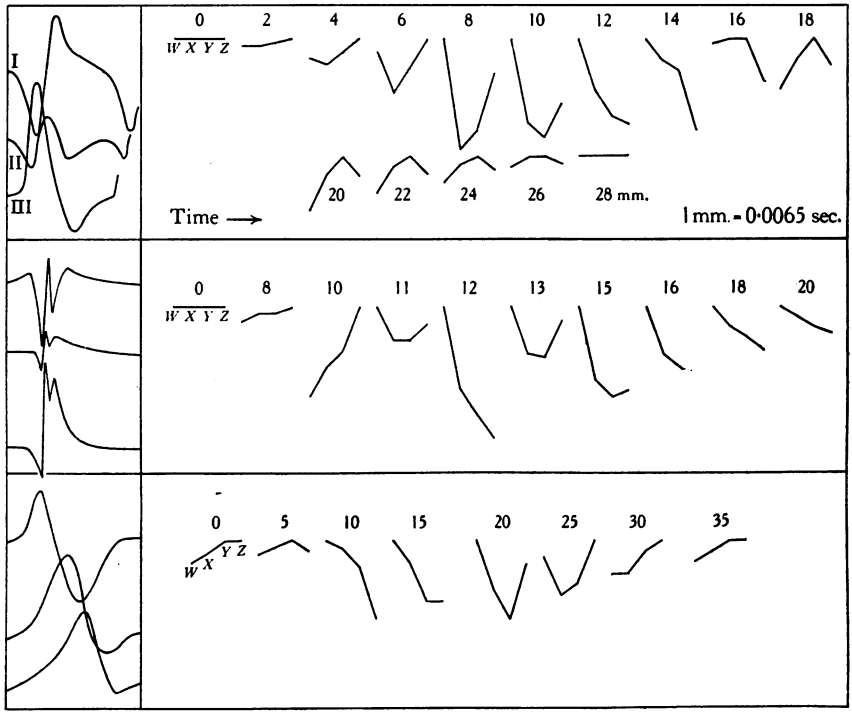

Fig. 27. Relative potentials at the four electrodes, *W*, *X*, *Y* and *Z*, at different periods during the passage of a wave. Tracings of the oscillograph record are given on the left. The potential distribution is given at various intervals after the beginning of the wave.

cortical record in Fig. 25 B. It is possible that the cortical beats arise as the result of impulses coming from subcortical structures, though there is evidence to show that in certain forms of experimental epilepsy the fit spreads by conduction in the cortex. There is no reason to suppose, however, that the thujone waves will always spread uniformly. Some areas may be more fatigued than others, and these may form occasional islands of inactivity round which one wave must travel though the next may find them responsive again.

As the effect of the drug wears off there is a gradual return to the usual complex of brief and slow waves typical of urethane—as though the syncytium were breaking up again into smaller and smaller groups.

For the present argument the chief interest of the thujone discharge is that it gives no evidence of distinct brief and slow components in the cortical response. The diphasic form of the waves is obviously due, as in a nerve or muscle fibre, to the passage of the active region from one electrode to the next, and the monophasic potentials in each neurone may well be quite as brief as they are in the typical injury discharge.

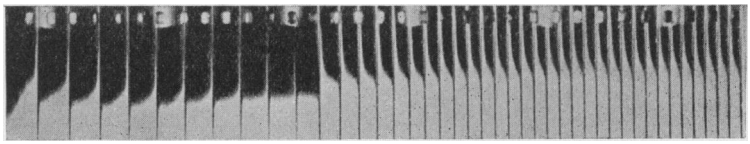

Fig. 28. Record of action potentials in a muscle fibre of the frog's sartorius immersed in NaCl solution, showing progressive shift in the origin of the waves (compare with Fig. 25 B). Muscle in bath divided by a slot, leads taken from the fluid on either side. There is a gradual reversal of the waves as the origin shifts from one side of the slot to the other. Maximum frequency 44 per sec. Time marker gives 1/4 sec. Battery-coupled amplifier.

Discussion.

The main outcome of these experiments has been to satisfy us that the potential waves in the cortex are all built up out of relatively brief pulsations in the individual neurones, that the slow potential changes are summation effects and have no counterpart in the response of the units. We set out with a bias towards the opposite conclusion and for a time our results seemed to support it. The turning point came when we began to use the balanced amplifier system for independent recording from several points. This gave conclusive evidence that the slow waves needed large areas for their development and showed how the earlier results were vitiated by the use of diffuse earthed leads.

Although the time relations found in the injury discharge have been surprisingly constant in all our experiments we can scarcely conclude that the response of all the cortical neurones is a series of brief waves of identical duration. The constant form of the action potential in a nerve trunk seemed to indicate uniformity in the constituent fibres until Gasser and Erlanger [1927] showed how widely the units might differ. There may be as great or greater differences in the units of the cortex, though, as in nerve, the major part of the electric effect is probably due to a more or

less homogeneous group. Again, we cannot be sure that the pulsations of a given cortical unit do not vary from moment to moment, *e.g.* with fatigue. All that can be said is that the response is probably a simple monophasic spike which occupies not much more than 0·1 sec. and not much less than 0·01 sec. We cannot say that the responses do not vary in size, but all the variations we have found could be explained as due to changes in the number of units in action, and it can often be shown that an exceptionally large wave is in fact the product of a greater number of neurones.

Thus the cortical waves seem to be built up out of relatively simple components, rhythmic pulsations in the nerve cells varying in frequency like the impulses in a nerve fibre but not necessarily varying in any other way. The complexity of the cortical response is due to the complexity of the structure which gives rise to it, not to a more variable type of activity in the units. This means that we must abandon the hope that the slow potential changes in the cortex might be an index of slow change of polarization in the nerve cells and so an index of the rise and fall of the excitatory state which preludes activity. Slow changes may occur, indeed the work of Gasser and Graham [1933] on the after-potentials in the spinal cord and of Eccles [1934] on the cervical sympathetic ganglia makes it probable that they do occur—but in the cortex they must be so much smaller than the "spike" potentials that in the normal spontaneous activity they cannot be detected.

This leads at once to the further question as to the origin of slow potential changes in other parts of the nervous system. The slow respiratory waves in the brain stem of the goldfish [Adrian and Buytendijk, 1931], in the thoracic and optic ganglia of *Dytiscus* [Adrian, 1932] and in the retina have all been considered as evidence favouring the idea of slow potential changes in individual nerve cells. Their smooth contour was the main reason for supposing that they were not summation effects, but the smooth contour of many of the slow waves in the cortex makes it very doubtful if the argument can be sustained. The fact that the potential wave of the nerve cell is much less abrupt than that of the axon is probably a sufficient explanation even for the slow changes in insect ganglia.

Effects of anæsthesia.

It must be admitted that all our observations on the cortex in animals have been made under general anæsthesia. There was no lack of electrical activity, but in the unanæsthetized brain it might turn out to be an

activity of an entirely different order. As regards the individual neurones, however, there is no evidence to suggest any radical difference. Fischer, Kornmüller and Tönnies have worked on animals immobilized by curare, and their records have shown the same mixture of slow and brief waves, and Bartley and Bishop [1933] state that the only definite change as anæsthesia develops is a slight reduction in the magnitude of the potential waves. With light as opposed to deep anæsthesia we have found a more continuous and more irregular succession of waves with a more complete lack of correspondence in the waves at different points. In this condition the cortex may be accessible in a slight degree to afferent impulses, for stimulation may change the nature of the response for a time (*vide* Fig. 20). It is probable, then, that in the lightly anæsthetized and still more in the unanæsthetized brain afferent impulses will always break up any tendency to uniform activity. With deeper anæsthesia there is less to interfere with the spontaneous activity of the nerve cells, and we find more regular waves and greater uniformity in different regions.

With C. and E. there is a gradual diminution in the size of the waves as the anæsthesia deepens, but the final disappearance of activity occurs abruptly within a few seconds of the failure of respiration (either before or after) and coincides with the blanching of the cortex. It seems to be due not so much to the direct action of the anæsthetic on the cortex as to the sudden fall of blood-pressure. As soon as the circulation is restored (by artificial respiration and massage of the chest) the potential waves reappear, often as large rhythmical outbursts with intervals of complete rest, returning later to the more usual type of response. Failure of the oxygen supply is thus the most important factor in the failure of the electrical activity. The dependence on oxygen supply can also be shown by giving a few breaths of nitrogen or by compressing the vertebral arteries (the carotids having been ligatured previously).

It is remarkable to find so much electrical activity in the anæsthetized cortex and still more to find that it is not so much a random activity of independent units as a series of disturbances spreading over large areas. With thujone, for instance, the whole cortex may pulsate with the same rhythm, and waves seem to be conducted freely in all directions: this may occur in an animal in urethane anæsthesia deep enough to prevent any movement during the thujone discharge and to prevent any sensory stimulation from reaching the cortex and modifying its response. All this supports the suggestion made by Bartley and Bishop [1933] that the chief effect of the anæsthetic is on the afferent and efferent pathways

rather than on the cortex itself, but more evidence is needed before any certain conclusion can be reached. It is at least clear that the same physical laws will govern the potential distribution in the unanæsthetized brain, so that there will be the same opportunity for summation effects from large areas.

To sum up—our evidence points to the conclusion that the electrical activity of the cortex is due to events of the same character as those taking place in active nerve or muscle fibre, *i.e.* to successions of brief action potentials repeated rhythmically with a frequency which can vary within wide limits. Arguing from nerve and muscle fibre we may expect that there is little or no gradation in the electrical response of each unit apart from the change in frequency. The evidence on this point is scanty, and all that can be said is that an increase in the size of the brief waves is usually found to involve an increase in the area contributing to the wave. But this, in itself, is an important distinction between the behaviour of the cortical units and those of a nerve trunk. In the latter the units, if undamaged, are completely independent. In the cortex they pulsate in groups small or large. With intense excitation rapid synchronous pulsations may extend over an area of 5 mm. or more diameter, and from time to time a single beat may travel through the entire cortex. In fact with a focus of intense excitation (*e.g.* from injury) or under the action of a convulsant drug the mass of cortical neurones behaves more like the linked fibres of the heart muscle than the independent fibres of a skeletal muscle or a nerve. In the unanæsthetized brain the constant arrival of afferent impulses at different points must break up the tendency to synchronous action. It must be remembered, however, that we are dealing throughout with brains which are very small compared to that of man, and that the largest areas of synchronous action which we have found would occupy only a very small fraction of the human cortex.

Summary.

1. Potential changes recorded from the cortex of the anæsthetized rabbit are roughly divisible into large slow waves and smaller brief waves superimposed on the large. We have tried to find out what kind of electrical activity takes place in the individual neurones of the cortex to give rise to these waves.

2. In the light anæsthesia the waves occur irregularly, but in deeper anæsthesia there is much greater regularity, the slow waves occurring at intervals of 1–2 sec. in deep C. and E. or urethane and at 3–4 per sec. in

moderate C. and E. anæsthesia. In lighter anæsthesia sensory stimulation often abolishes the rhythmic beat and substitutes a continuous train of brief waves.

3. Injury to the cortex produces a characteristic discharge of brief waves in a rapid sinusoidal oscillation. The frequency falls gradually from a maximum of 100–60 per sec. to a minimum of 40–35 per sec. Below this the discharge becomes irregular. By recording simultaneously with three pairs of electrodes it can be shown that the potential changes in the injury discharge often occur over an area 5 mm. or more in diameter. They are probably due to synchronous pulsation in a large number of cortical units.

4. The injury discharge shows that the cortical neurones may develop a pulsating activity, like that of a nerve or muscle fibre. The brief waves in the response of the uninjured cortex are due to an activity of the same kind. The problem is to decide whether the slow waves represent a different kind of activity, or whether they are merely due to a summation of the brief waves.

5. If the slow waves are summation effects they should be present when the electrodes are widely separated, but absent or very small when they are close together. It is found that they are only present when the electrodes are arranged so that large areas can contribute to the potential changes. With restricted electrodes only the brief waves appear. It is concluded that the response of the individual neurone is a brief pulsation and not a slow change.

6. In the anæsthetized, but uninjured, brain the neurones tend to pulsate in small groups covering an area not more than 3–4 mm. diam. Periodic waves of activity may spread over the whole cortex in deep anæsthesia, but the neurones which take part in it still react in small groups which pulsate out of phase with one another.

7. After severe injury or under the action of a convulsant drug (thujone) a pulsation may spread widely through the cortex. The potential waves are then of "transitional" type and are no longer divisible into slow and brief components. An analysis of the waves in the thujone discharge shows that the pulsations often change their direction of travel. The cortex behaves as a freely conducting mass with beats starting now from one focus and now from another. Each beat probably represents a single brief pulsation, or rapid series of pulsations, in the individual neurones.

8. The effects of anæsthetics are discussed. It is suggested that their main effect is on the afferent and efferent pathways rather than on the

cortical neurones themselves, and that these are not likely to show any different type of electrical activity in the unanæsthetized brain.

9. It is concluded that the activity of the cortical neurones consists of a series of brief pulsations which can vary in frequency but probably not in size. Their time relations are not as rapid as those of the action potential in a nerve fibre. Except with intense excitation the frequency of the discharge does not rise much higher than 50 per sec.

It has not been possible to detect very slow changes of potential apart from summation effects. Gradual changes of polarization may occur, but the electrical effects must be much smaller than those due to the brief action potentials. Many of the slow potential changes in other preparations of the central nervous system may be due, like the slow waves in the cortex, to a summation of the brief responses of individual neurones.

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