THE POSTSPIKE POSITIVITY OF UNMEDULLATED FIBERS OF DORSAL ROOT ORIGIN

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ABSTRACT

The positivity following the spike in the action potential of unmedullated nerve fibers of dorsal root origin (d.r.C) has been shown to be homologous with the first positive potential (P_1) of other varieties of nerve fibers. Thus it is only through the large size of the positivity that this group of nerve fibers is set apart from other groups. New findings accentuate and make more explicit the difference of d.r.C fiber behavior from that of the sympathetic unmedullated fibers.

Support of the conclusion is derived from re-examination of the A fibers as well as from observations on the d.r.C fibers.

Increase in size of the P_1 's in a tetanus of the d.r.C fibers can occur if the frequency is high enough; and it does not occur in an A fiber tetanus if the frequency is low enough. Frequency is also critical in the obtainment of increasing P_1 's in a tetanus of sympathetic C fibers.

Decrease in the size of the P_1 's in the course of a tetanus is attributable to development of the negative after-potential (N a-p). In rested d.r.C fibers the N a-p is latent. But it appears during a tetanus, develops in size, and after the tetanus leads to a long lasting and clearly defined second positive potential.

Absence of a supernormal period during the N a-p of the d.r.C fibers is accounted for.

An analysis is made of the apparent increase in size of the spike elevations during a tetanus, for the two subgroups of the C fibers.

The difference between the after-potentials of A fibers and of sympathetic C fibers is correlated with the shapes of the curves of cathodal electrotonus of these fibers.

When the physiology of the unmedullated fibers of dorsal root origin was first described, the fibers were classified as a subgroup (d.r.C) of the C fibers because of the unprecedented size of the positive deflections following the spikes. Some of the observations were so discordant with findings previously made on other fibers, that a way to an integral treatment of them was not apparent. It seemed to be unlikely that the behavior of one set of fibers would be completely divergent from that of all other fibers; therefore, the present experiments were undertaken. Not only was it found that additional informa-

tion was required about the d.r.C fibers, but also that gaps in the knowledge of the after-potentials of other fibers had to be filled in as well.

At the time of the earlier search for what there is in common among the several sorts of nerve fibers recording of the nerve action was routinely carried out with external leads. Now that the employment of internal-external leads for giant axons has come into vogue description of methods, terminology, and interpretations must be considered in relation to the method of leading. In all recording the changes in difference of potential between two electrodes are measured. The reference in this paper is exclusively to surface leading. Ideally considered, an active electrode is on the normal surface and a passive electrode is in position at some distance distally, sufficiently beyond a block effected without depolarization so as not to be affected by electrotonic spread from the potential change behind the block. What is theoretically recorded thereby, is the potential difference between a changing and an unchanging point, that is, the change in the membrane potential at the proximal lead as subjected to the operating circuits in the nerve. For practical purposes a carefully applied cocaine block furnishes a satisfactory working approximation to the theoretical ideal. There is, however, a residual difficulty: a false lead generated when the spike is creating a sink in the stretch between the two electrodes. It will be called the interlead artifact; and it will be left without further description as it enters into the interpretation of spike recording rather than of after-potential recording.

A diagram of the sort proposed in 1935 is still serviceable for outlining an hypothesis for intergrating the experimental findings later to be presented. The action potential is conceived as composed of two parts: a spike and an after-potential, only loosely related to each other as the after-potential can vary without concurrence of a spike change. In the absence of stress conditions the spike displays constancy of size and duration. On the other hand the after-potential is highly labile. It varies with the degree of nerve activity and within a range of nerve states which may be considered normal or close to normal. The after-potential starts with a negative after-potential (N a-p) and is continued by a positive after-potential. With changes in size and duration of the N a-p the ensuing positive potential undergoes related changes in the same parameters. For example, a large N a-p leads to a large positive after-potential. From the relationship comes the notion that the negativity and subsequent positivity reveal a temporal sequence in a single process. After activity the ultimate restoration of the initial membrane potential value is from the positive side.

Presumably the spike has an ending and the N a-p a start, neither of which can be defined with certainty. Also with indefinite start, another positivity has to be considered to account for the total configuration of the action potential. It cuts into the N a-p without having any apparent relation with it. Whatever linkage it may have would better be referred to the spike. Ambi-

guity is an inevitable result of trying to untangle parts, unknown in isolation and seen in algebraic sum in the action potential, from observations on how parts of the sum vary mutually. But this unsatisfactory methodology has to be faced as the only one at present available. Inasmuch as after a tetanus both positivities often become larger and more prominent, and since they are unrelated in origin and merge with each other in a way that cannot be interpreted as a continuous curve, the positive after-potential has since the earliest observations been described in two parts: first positive potential, P_1 , and second positive potential, P_2 . The designations are at least useful for pointing to the appearances in the action potential.

Systematic correlation of the parts of the action potential and of the polarization potentials with the membrane potential was a major contribution by Lorente de N6 (*a*). The membrane potential was conceived as built up of two principal fractions of which the first and largest was called the Q (quick) fraction. Alteration of this fraction produces the spike; and fast electrotonus is the expression of its modification by externally applied currents. Under well known conditions the membrane potential is augmented by addition to the Q fraction of a second fraction, variable in its amount and labile in its behavior: the L (labile) fraction. To variations in the magnitude of the latter are attributable the negative to positive after-potential sequence and slow electrotonus. In reaction to the decrease of L, during and immediately after a tetanus, L becomes transiently larger than in the resting state. Thus P_2 is formed. In order to explain P_1 there was invoked a reaction in a third fraction, M, a fraction originally set up to explain some details of behavior of the electrotonic potentials in frog nerve. Manifestations, in experiments on mammalian nerve, attributable to an M fraction involved producing a highly abnormal state of the nerve. As the author has personally derived no information indicating an intervening process no need will be left unsatisfied if P_1 be considered in direct sequence with the spike. Disregard of an intervening process does not imply a prejudice, one way or the other, about its existence. Room is left for reinsertion whenever findings may make the simplified view inadequate.

While much light is shed on the constitution of the action potential by the Lorente de N6 formulation, the latter has its own terminology; and terminology carries its theoretical implications with it. In order to keep the following presentation as close as possible to a descriptive level the older original designations will be continued because they carry with them a smaller load of theory. It would be desirable to have no load at all; but a residue of theory inevitably clings to the methodology imposed for the solution of the problem. We shall continue to speak of a spike process and an after-potential process. Their degree of independence has always been as great as that of the Q and L fractions; and the expressions are free from all the details of theory associated with the fractions.

A redrawing of the diagram representing the working hypothesis is given

in Fig. 1, *A*. While the purpose of the diagram is to present a scheme, variations of which will account for all the sorts of nerve fibers as particular cases, the drawing is adjusted in its temporal dimensions to the phrenic nerve of the cat, as observed at 38°C. Divergence between the effects of the spike and the after-potential processes appears early in nerve action. Tests made immediately after a spike bring out the difference. The phrenic nerve was selected for the tests on account of its single spike elevation and its well developed after-potential. A curve showing the ability of a nerve to produce a second spike, when a second strong shock is applied, is quite different from a curve out-

FIG. 1. *A*, a redrawing in the tempo of the phrenic nerve at 38°C. of an older hypothetical diagram depicting the action potential as determined by the interplay of two components. *B*, curves, over 10 msec., comparing the course of the relatively refractory period, measured with maximal spikes, and the course of the excitability, measured with threshold shocks. Phrenic nerve, composite from four experiments. Conditioning and testing shocks through separate electrodes. Ordinates, per cent of the control unconditioned response. The scale of the lower curve (refractory period) is on the left and is ten times as great as that for the excitability, on the right. The greater sensitivity of the excitability determinations necessitates a smaller scale in the interest of economy of space in reproduction.

lining the excitability determined by threshold shocks. In the determination of the former the spike process must be dominant, in the latter the after-potential process. The contrast between the two curves is illustrated in Fig. 1, *B*. In the course of the relatively refractory period the spike height rises rapidly for some 3 msec. then approaches full height more slowly. Before 10 msec. deviations from 100 per cent approach the experimental error; but there is usually a deficit in height measurable in a fraction of a per cent. Thereafter the curve tends to hug the 100 per cent line, though in many experiments there is a definable increase in the height of the spike during P₁, again measured in fractions of a per cent. Amplification of the spike permissible in spike height measurements is too low for a satisfactory demonstration of P₁. The excitability curve does not reach its maximum until about 3 msec. Although earlier the N a-p is much larger the recovery of the spike process must affect the readings. After the curve crosses the 100 per cent line the influence of the

N a-p is dominant in the dual determination of the curve. After the maximum the excitability falls with the N a-p and becomes subnormal during P_1 .

In the diagram (Fig. 1, *A*) the spike ending is drawn with the curve of recovery of the spike height in view. The spike is conceived as falling rapidly enough to permit a maximum in the excitability curve at 3 msec., then to proceed along a gradual course into P_1 . Owing to absence of information about the earliest portion of the N a-p, the graph of the latter starts at a time when the N a-p has become overt in action potential records. The negativity is drawn with a duration sufficient to permit on occasion the appearance of N a-p after P_1 , as in Figs. 3 and 6. In order to represent the P_2 into which the N a-p passes the scale had to be exaggerated, as P_2 , though readily visualized after tetanization, is too small to be visible in records of single responses of A fibers.

Allocation of the postspike positivity of the d.r.C action potential to the appropriate position among the manifestations in the action potentials of other sorts of nerve fibers depends upon an analysis of the changes taking place in the course of tetani. As both of the positive components of the action potential must represent membrane hyperpolarization, the possibility of translating the terminology describing the parts of the action potential into terms of reference to the membrane potential was considered, then abandoned. If the positive after-potentials were to be described as hyperpolarizations, in the interest of economy in description one should be able to describe the spike as a depolarization. According to the findings from external-internal leads in giant axons, often confirmed since the original descriptions of Hodgkin and Huxley and of Curtis and Cole, during the passage of the spike the membrane is more than depolarized. Its potential is reversed.

A summary of the terminology used in the descriptions in this paper is as follows. Zero potential, seen in the records at the position of the starting base line, is defined as the level yielded by the electrodes when in contact with well rested nerve. During activity an upward deflection denotes a change to negativity at the active electrode, and a downward deflection a positivity. Differentiation of the parts of the positive after-potential will be continued with the letters P_1 and P_2 . P_2 as a sequela of the negative after-potential has its counterpart in Lorente de Nó's L fraction description. P_1 is treated as though continuous with the spike. The author agrees with Lorente de Nó that it is not a fluctuation taking place in the L fraction. At the end of this paper what in the d.r.C fibers was non-committally designated as the postspike positivity (Gasser, 1950) will be identified with what had been called P_1 in other fibers. With some propriety all the P_1 's could be called postspike positivities. In that way they could be contrasted with P_2 's, as post N a-p positivities.

Methods.—The nerve chamber was surrounded by a temperature-controlled outer chamber, and equipped for a continuous flow of preheated and prehumidified oxygen

containing 5 per cent of CO_2 , and with a trough for liquid paraffin-pre-equilibrated with the same gas mixture. After the assembly had reached the desired temperature the nerve was placed on the electrodes and a tiny ball of cotton containing cocaine placed on the distal lead. The nerve was kept in the gas until monophasicity, tested on the A fibers, was proved to be satisfactory. Usually one-half hour was required for this stage. Then, without opening the chamber, the oil bath was elevated until the nerve was submerged in the oil. Recording was not started until the temperature had been in a steady state long enough for assurance that no change would take place during a series of experiments. Amplification was always d.c. and differential.

FIG. 2. Upper, cat peroneal nerve. A fiber tetanus, 2.1 sec. at 400 per sec. c.d. (conduction distance) 12 mm. l.d. (distance between leading electrodes) 23 mm. 37.8°C .

Lower, cat saphenous nerve. C fiber tetanus, 2.5 sec. at 10 per sec. c.d. 30 mm. l.d. 25 mm. 37.5°C .

The stimulating cathode was grounded and the shocks were square waves of known duration and voltage. For C fibers the duration was usually 0.5 msec. and the strength 15 to 20 volts.

For the study of after-potentials, particularly those of C fibers, the nerves must be in first class condition. And for attainment of that end the method is not ideal. Considerable time is lost in establishing the conditions necessary for experimentation. One condition is an unchanging obliteration of a lead from the distal electrode. For its production cocaine is still the preferred agent and cocaine action is slow. But all of its action time is not a net loss. Transfer of the nerve from the body to the nerve chamber, no matter how rapid, produces a change for which restoration in the gas mixture is required. The minute ball of cotton is used to offset the solubility of cocaine in oil. The ball is held in a loop on the distal electrode to prevent spreading of the cocaine, and its size and the distance between the leads are adjusted to obviate

undesirable effects. In the final steps of preparation the distal lead is moved slightly distally (without opening of the nerve chamber) to insure that the block is proximal to the lead and that there can be no electrotonic spread for the blocked impulses. Other conditions imposed are prevention of drying and a steady base line. These necessitate the oil bath. After all the conditions are fulfilled the nerve usually remains in first class shape for an hour or more. With experience the beginning of deterioration can be detected as small changes in the behavior of the after-potentials. When they appear the preparation is discarded.

Results.—Solution of the specific problem demands a survey of the action potential as a whole. If the hypothesis be entertained that the d.r.C post-spike positivity is a representation of P_1 , one would expect to find a P_2 from which P_1 could be differentiated. And if there is a P_2 , where is the antecedent negative after-potential?

As an introduction to a comparison, records of two tetani are placed together in Fig. 2: one of peroneal A fibers, and one of saphenous C fibers. The peroneal tetanus is selected¹ because it shows clearly the two post-tetanic positivities. Immediately after the tetanus there is a sharply defined P_1 . It is succeeded by the N a-p, augmented by the tetanus; and the latter in turn leads to the start of P_2 . In common with the peroneal tetanus the saphenous d.r.C tetanus shows a positive notch at the end; and the latter is sharply succeeded by a long second positivity.

Effect of Frequency on the Increase of P_1 in A fibers.—From the d.r.C record of Fig. 2 it is apparent that the postspike positivity was decreasing in the course of the tetanus. P_1 , originally defined for A fibers, was described as increasing during a tetanus. Re-examination of the subject brought out the importance of the repetition frequency on the mode of behavior. In the low frequency tetanus, 17 per sec., depicted in Fig. 3 for the A fibers in a saphenous nerve, P_1 progressively decreased. Any tendency of P_1 to increase was overpowered by a growing N a-p, which revealed itself in a negative hump after the end of the tetanus.

When the responses are caused to occur in faster sequence, the size of the P_1 positivity at the end of a train is effectively increased (Fig. 4). In order to show how frequency affects the growth of P_1 it is necessary to obtain records of tetani at the intervening durations. In the graph of Fig. 5 each dot shows the depth of P_1 when the tetanus was terminated at that point. The graph

¹The selection here and in other records is to illustrate a point. Owing to the variability of after-potentials, post-tetanic after-potentials, produced by changes in two processes with different origin, can manifest considerable variation in configuration, even in experiments with the same intended specifications. All the variations can be considered to be within the range of normal, and are interpretable in terms of the degree to which the components of a single set of basic factors enter into the picture obtained.

shows, in addition to the dependence of the maximum attained at the frequency, that the growth takes place rapidly at the beginning of the tetanus. In longer tetani the level may rise again in the algebraic summing with the growing N a-p.

FIG. 3

FIG. 4

FIG. 5

FIG. 3. Cat saphenous nerve. A fiber tetanus, 0.5 sec. at 17 per sec. c.d. 16 mm. l.d. 23 mm. 37.5°C.

FIG. 4. Cat phrenic nerve, A fibers. Single response and tetani, 0.1 sec. at indicated frequencies. The spikes maintained a constant height in the tetani at 100 and 200 per sec.; reduced 3.9 per cent at end of tetanus at 300 per sec. c.d. 11 mm. l.d. 27 mm. 38°C.

FIG. 5. Cat phrenic nerve, A fibers. Effect of frequency on the growth of P_1 during a 0.1 sec. tetanus. Ordinates, P_1 sizes in arbitrary units. Tetani terminated at the times marked by the dots yielded the sizes. The spikes maintained a constant height in the tetani at 40 and 100 per sec.; reduced respectively 3.2 and 4.9 per cent at the ends of the 200 and 300 per sec. tetani. c.d. 9 mm. l.d. 22 mm. 38.1°C.

Growth of P_1 is shown in another way in Fig. 6. Records were made of single responses, and of trains of 2, 3, and more. Prints were made on film, the base lines scratched in, the prints superimposed on these base lines, and prints made on paper through the pile. The lines reaching the tops of the records were made by the N a-p's. Cutting into the N a-p's by the increasing P_1 's causes the times at which the N a-p lines cross the base line to shorten.

At 200 per sec., in spite of the fact the third response started 10 msec. later than the first response, the time of the third P_1 maximum is not measurably later than the first; and the first three N a-p's cross above the base line. These apparently increasing slopes of the N a-p's do not reveal the department of the negative after-potential process. For there is clear evidence that the N a-p

FIG. 6. Cat saphenous nerve, A fibers. Figure made from registered prints on film (see text). Upper, superimposed records of one, two, three, and eight responses at 100 per sec. Lower, superimposed records of one, two, three, and seventeen responses at 200 per sec. Spikes maintained constant height. c.d. 12 mm. l.d. 29 mm. 37.4°C.

is progressively getting larger, as after the 0.08 sec. tetanus a clear negativity appears after the terminal P_1 .

Independence of P_1 from the N a-p is supported by the reverse correlate, the dependence on the size of P_1 of the time at which the N a-p ceases to appear as negative. When responses are obtained in pairs at various intervals, readings can be made of the sizes of the first and second P_1 's in relation to the times at which the two N a-p's reach the base line. Graphs of the two sets of readings have a similar form (Fig. 7). The second P_1 becomes larger than the first one, even when it starts in the period in which the recovery of respon-

siveness is incomplete,—which incidentally calls attention to the close relationship between P_1 and the spike. P_1 reaches a maximum at an interval of 2 msec., then gradually decreases as the intervals are made longer. As P_1 decreases, the N a-p times concomitantly lengthen.

Positive After-Potentials in Sympathetic C Fibers.—A difference from A fiber behavior enters into that of sympathetic C (s.C) fibers during a tetanus. The positive after-potentials are dominated by the P_2 's following large N a-p's, in such a way that P_1 is obscured and its duration is not susceptible to accurate measurement. In the tetanus of the hypogastric nerve at 5 per sec. shown in Fig. 8, P_2 positivity is increasing; and there is no visible P_1 . Many

FIG. 7. Cat saphenous nerve, A fibers. Correlation between the size of P_1 and the time at which the N a-p crosses the base line. Readings obtained from single responses and second responses at the intervals indicated on the abscissae. Dotted line, P_1 sizes registered in arbitrary units on ordinate at left. Open circles, N a-p times on ordinate at right. At interval 0.5 msec., second spike 52 per cent of the first; at 1 msec., 86 per cent; at 2 msec., 100 per cent. c.d. 14 mm. l.d. 30 mm. 37.8°C.

of the special features of a hypogastric tetanus can be seen in Fig. 9, in which the crests of the spikes are visible. The increasing length of the heavy white lines at the base of the spikes shows the increase of the N a-p's. On the last response there is a notably high ratio of the N a-p to the total spike height; and following the tetanus there is a large P_2 , at the beginning of which a P_1 notch has appeared.

An accounting for the special features of a tetanus of s.C fibers can be derived from the composition of the membrane potential. From experiments on the superior cervical ganglion of the turtle Laporte and Lorente de Nó deduced the existence of a large L fraction in the composition of the C fiber membrane potential. In order to bring out the difference between A and s.C fibers, experiments were made for comparison of the ratios of the slow electrotonus with the fast electrotonus in subrheobasic cathodal polarizations. As the ratio is known to vary with the distance from the cathode, corresponding distances must be selected. For instance, the comparisons could be made at the characteristic lengths for the fast electrotonus. But, as the latter were found diffi-

cult to determine with accuracy, and since the differential was well illustrated with the proximal lead in contact with the cathode, contact leads were employed. The splanchnic nerve of the bullfrog is a good example of a nerve with a predominance of C fibers. When its polarization curve is compared with one from the sciatic nerve of *R. pipiens*, there is no mistaking of the fact that its component of slow electrotonus is much larger in relation to the

FIG. 8

FIG. 9

FIG. 8. Cat hypogastric nerve. After-potentials in a sequence of five responses at 5 per sec. The small notch in the early part of the first response is caused by an inter-lead artifact. c.d. 10 mm. l.d. 8 mm. 37.5°C.

FIG. 9. Cat hypogastric nerve. 8.5 sec. tetanus at 10 per sec. c.d. 9 mm. l.d. 6 mm. 37.8°C.

fast electrotonus then it is in the sciatic nerve (Fig. 10). For the hypogastric nerve of the cat, in spite of its content of B fibers, the same relationship is apparent when its polarization curve is compared with one of the saphenous nerve (Fig. 10).

It is consistent with the relatively large slow electrotonus that the negative after-potential and the ensuing positivity should be large. Conversely, it may be inferred that with the relatively smaller fast electrotonus, P_1 in some way coupled with it would be proportionally less prominent. Though less prominent, P_1 behaves as in other nerves. It is augmented most by responses at short intervals. In Fig. 11 it can be seen how its size following a single response is increased when two responses occur at an interval of 10 msec. After nine

responses at 10 msec. intervals it is still larger; but at this tetanus duration the negative after-potential has already become so large that it introduces a convexity into the post-tetanic positivity clearly marking the start of a P_2 .

It would be instructive to have an electrotonus curve for d.r.C fibers. But no nerve is known from which it can be obtained. It must be different from that of the s.C fibers, as can be deduced from the behavior of the d.r.C fibers, which will now be presented.

Can d.r.C Postspike Positivity Be Interpreted as P_1 ?—From the foregoing

FIG. 10. Electrotonus curves. Subrheobasic cathodal polarizations, recorded with proximal lead in contact with the cathode. 5 per cent CO_2 . Upper records, A fibers; lower records, C fibers. Frog A, *R. pipiens*, 25°C. Bullfrog splanchnic, 23.5°C. Cat saphenous, 37.3°C. Cat hypogastric, 37.8°C.

survey it follows that the rate of growth of P_1 during a tetanus depends upon the frequency. The P_1 of A fibers may not get larger during a low frequency tetanus, so the usually found decrease in size of the d.r.C postspike positivities does not rule out a P_1 interpretation if frequencies can be found at which the positivity increases. Therefore d.r.C tetani were performed at high frequencies. Since d.r.C responses are always recorded on the A after-potentials as a base line, special measures had to be taken in behalf of the base line. As the size of the positivity can only be determined at the end of a tetanus, for each frequency a single response was recorded and tetani with two, three, or more components. To obtain the base lines corresponding A tetani were recorded after reducing the shocks to strengths subliminal for C fibers. Superimposition of film prints of the d.r.C records and their base lines then permitted measurements. Some examples from the series are shown in Fig. 12. A broader survey

is provided in Table I. It is clear that there is an increase of the postspike positivities at the higher frequencies, and that on a second response the positivity is the more increased the shorter the interval. Conformity with P_1 behavior is thereby identified. The increase may be continued into later responses. However, at some stage a decrease will begin. A maximum at 75 per sec. is to be noted at the third response; at 20 per sec. where there is no increase on the second response, there is actually a decrease on the third. Twenty per second is still a high frequency for d.r.C fibers; and the original

FIG. 11. Cat hypogastric nerve. Tetani at 100 per sec. From tetani with an increasing number of components three have been selected for illustration. Upper, with film prints, as in Fig. 6, two responses have been superimposed on a single response. Amplification too large for spikes to be seen. Early small notches, interlead artifacts. Lower, tetanus with nine components. c.d. 10 mm. l.d. 8 mm. 37.6°C.

impression that the postspike positivity decreases during a tetanus is accounted for.

Two factors contribute to reduction of postspike positivity. Spikes evoked when the hyperpolarization is already high are unable to produce much additional positive reaction. This state is seen in early tetani at high frequency; and its discussion will be referred forward to a consideration of the apparent spike height. The other, of an entirely different origin, is best seen in longer tetani at lower frequencies. Although there is no apparent N a-p in single responses of rested nerve, one potentially may be present and augment in size during a tetanus. This hypothesis will now be examined.

Fig. 13 shows specimens from tetani at several frequencies and durations, recorded at speeds permitting the changes taking place to be visualized. What happens as the P_1 level rises, is that it is filled in from the beginning of the

complex by something producing negativity, so that at the end of the tetanus the more slowly conducted elevations may start above the level of the main component. If this negativity be considered to be a N a-p, the absence of

FIG. 12. Cat saphenous nerve, d.r.C fibers. Film prints of C fibers on corresponding A fiber base lines (see text). Print 1 shows a single response. The other responses are in pairs, except print 3 which records four responses. The intervals between the responses are marked on the records. 38.1°C.

TABLE I
Saphenous C Post-Spike Positivities in Tetani

Frequency per sec.	Per cent increase over a single response at the end of tetani with the number of components listed					
	2	3	4	5	6	7
300	21	38				
200	16	21	25			
100	15	16				
75	12	17	13	12	9	2
50	8		9		5	
20	0	-4				

supernormality must be explained. It can be, on the basis that in spite of the change the fibers are still in a hyperpolarized state. When the nerve is conditioned by such brutal tetani as presented in the 1950 paper, tests made

in the post-tetanic period are made on depolarized nerve; but there another factor has entered.

In 1927 Levin described in fatigued (or depolarized) nerve a "retention of action current." This postspike negativity should not be confused with the negative after-potential. Retention is caused by a terminal slow restoration of the spike potential. The N a-p is produced by a decrease in the labile component of the membrane potential with the result that the threshold is higher, as determined in the control on rested nerve with a high membrane potential,

FIG. 13. Cat saphenous nerves, d.r.C fibers. 1, 20 sec. tetanus at 5 per sec. Samples at start, at 10 sec., and at end. c.d. 30 mm. l.d. 28 mm. 37.2°C. 2, 10 sec. tetanus at 8 per sec. Samples at start, at 2 sec., at 6 sec., and at end. c.d. 30 mm. l.d. 24 mm. 37.2°C. 3, 10 sec. tetanus at 10 per sec. Samples at start, at 5 sec., and at end. c.d. 30 mm. l.d. 24 mm. 37.7°C. The position of the base line is in constant relationship to the time line in 1 and 2. In 3, a reference line has been inscribed.

than it is when tested during the decrease of the membrane potential occasioned by the N a-p. Long lasting negativity after a tetanus means failure of restoration of the spike potential. In this state thresholds are high and the conduction times of the spikes are increased (Lorente de N6 (*b*)). When a control threshold is determined in such a state, it would be expected that added negativity following a conditioning spike would raise the threshold still more, rather than decrease it. The spikes are delayed during the prolonged negativity following a severe d.r.C tetanus. Therefore, the nerve is not in a condition in which demonstration of supernormality would be anticipated.

The original reservations against calling the d.r.C postspike positivity a P_1 have now been removed; and that designation will henceforth be applied.

Scrutiny of Fig. 13 shows that, although the curve determined by the bottoms of the P_1 's is rising, the curve of the points at which the main C elevations start from the A after-potentials is falling. An accounting for the latter course must be derived from the C-fibers, as the A fibers have nothing to do

FIG. 14

FIG. 15

FIG. 14. Cat saphenous nerve, d.r.C fibers. A single response and the fourth response of a 40 per sec. tetanus are mounted on the same base line. c.d. 30 mm. l.d. 21 mm. 38.1°C.

FIG. 15. Cat saphenous nerve, d.r.C fibers. Tetanus at 50 per sec. Three film prints have been superimposed on the starting base line, a single response and tetani with two and four responses. Above the second response can be seen its position in a three response tetanus. c.d. 30 mm. 38.1°C.

with it. The positivity of the line at the end of the tetanus (especially of tetanus 3) indicates that P_2 is developing. The level of start of the second C response is determined by the frequency. From then on further fall in the position of the starting points may well mean that after each increment of negative after-potential there follows an increment of P_2 . In the converse view,

when P_2 gets large, the N a-p's get large,—a rule which generally holds for other fibers. A similar situation is seen even more strikingly in the tetanus of Fig. 17, with the added feature that at the end of the tetanus the negative potentials are beginning to overbalance the P_2 accumulation and the starts of the C's begin to rise. Fig. 17 shows the beginning of the P_2 period. At the end of the record the P_2 value was 40 microvolts. Two minutes after the tetanus the after-potential was still positive, although there was a very slight drift in the direction of negativity.

The duration of the positivity following a tetanus, as in other fibers, depends upon the frequency and duration of the tetanus. Beyond the fact that it lasts a

FIG. 16. Cat hypogastric nerve. Antecedent tetanus of the nerve supplying Fig. 9. Same duration and frequency, but recorded at a faster film speed. The start and end of the tetanus have been mounted on their common base line. The tops of the first two spikes have been retouched.

long time, its duration cannot be given. D. C. stability to a few microvolts over a 10 min. period would be necessary, a stability which our technique cannot meet, probably on account of small changes at the lead beyond the cocaine block, as the drift is more that of the amplifier. It is impractical to repeat tetani at less than 15 min. intervals. Other than about its duration some statements about the post-tetanic after-potential can be made. The positivity is not described by a simple decremental curve. There is regularly a discontinuity caused by the terminal P_1 as in Figs. 2 and 17. Another feature is that even when the tetanus is driven to post-tetanic negativity subsequent positivity follows, and restoration of the membrane potential is ultimately from the positive side.

The Apparent Height of the Spikes During a Tetanus.—The term “apparent” is used because the reference is not to unit spikes, but to a dispersed system. Temporal dispersion increases with the conduction distance. At a given distance it is more marked for fibers of different and low velocities than it is for fibers with the same velocity differential and high velocities. A long conduction distance must be selected for clearance of the A fibers by the C fibers.

Two unrelated features of d.r.C fiber activity make for increase of the recorded spike elevations. One has already been mentioned: that spikes evoked when P_1 hyperpolarization is already high are unable to produce much additional P_1 . That feature will now be illustrated by two experiments on different nerves. Fig. 14 compares a single response with the fourth response in a tetanus at 40 per sec. Although the fourth response starts far below the base line, the maximal positivity reached is no greater than that of the single response which starts above the base line. In Fig. 15, showing superimposed a single response

FIG. 17. Cat saphenous nerve. 20 sec. C fiber tetanus at 7 per sec. Upper, samples at start, at 4 sec., at 14 sec., and at end. The base line is in constant relationship to the time line. Lower, end of the tetanus with start of the after-potential. The level of the starting base line has been inscribed. c.d. 30 mm. 37.4°C.

and tetani with two and four responses at 50 per sec., it can be seen that as the spike starts descend the P_1 maxima (below the starts) decrease. On the first responses the P_1 reactions are so large that even within the compass of the main elevation the later units are recorded on a level positive to the earlier ones, as shown in greater detail in Fig. 16 of the 1950 paper. Subsequent elevations are recorded at more positive levels. As the P_1 reactions become less on responses after the first one, they have less effect. The spikes thus seem to become higher for the simple reason that they cease to be recorded on a very rapidly descending base line. The relative positions of the elevations marked x in Fig. 14 are to be noted.

The other feature of nerve activity in the production of enhancement of recorded spike elevations is the N a-p. Observations on this point began when

d.c. recording became routine. In 1938 Gasser published a record showing in A fibers, in its proper membrane potential relationship with a pretetanic control test, a test with a large N a-p set up during a post-tetanic P_2 . In the same year Grundfest and Gasser made a similar observation on the hypogastric C fibers of the cat; and in addition demonstrated that concomitantly there was an increase in height of the recorded spikes. In 1949 Lloyd found augmented spikes during the P_2 of tetanized dorsal root A fibers of the cat. We have recently looked for augmented spikes after a tetanus of the cat phrenic nerve. They are often present, but the increase is small. Measurements must be made with an accuracy permitting detection of a 1 per cent increase or less. Recently Richie and Straub, from experiments on the cervical sympathetic nerve of rabbits, have emphasized the importance of the augmented N a-p in the production of increased height of the spike complex. And in their summary they state that there is no evidence of any large increase in the absolute size of the spike potential of individual nerve fibers.

When the striking difference between the post-tetanic augmentations of the spike in A and C fibers is considered at the same time as the difference between the electrotonic potential curves, that the N a-p may be instrumental is strongly suggested. Whenever there is a P_2 hyperpolarization a spike is accompanied by an increased N a-p. Theoretically there should be some augmentation of the uncondensed spike complex. To the spike proper there should be added whatever there is of underlying N a-p. Although the author does not accept the assumption that the N a-p starts at a maximum there must be some N a-p under the spike. And the more there is the greater the addition.

Along with the increasing N a-p's in Fig. 9, previously mentioned, there is a continuous growth of the spike heights. Indeed, Fig. 9 shows in another way the same phenomenon illustrated by Richie and Straub in their Fig. 12. In order to bring out more details, the beginning and end of the previous tetanus of the nerve yielding Fig. 9, in which a tetanus of the same duration and frequency was recorded at a higher film speed, are reproduced in Fig. 16. From Figs. 9 and 16 it is clear that the spike crests are continuously descending. Additions to the recorded height are from a level positive to the starting base line. In measuring the height of the spike complex one has to keep in mind that it is made up of two parts: the spike proper and the underlying N a-p. On the last response of the tetanus in Fig. 16 the N a-p is greatly increased over the one on the first response. Compared with the first spike the last spike, measured from its start, is increased. It is not so, measured from one-half the N a-p height; and it is decreased if measured from the point at which the N a-p becomes overt. The trace is so conventionally that of a spike in summation with the increased N a-p, regularly present in a P_2 hyperpolarization, that there is no indication pointing to an increase of the spike itself.

Fig. 17, showing the effect of the N a-p on the spike heights of d.r.C fibers

during a tetanus, beginning with the 4 sec. segment has a notable resemblance to the s.C tetanus shown in Fig. 9. During the first 4 sec. the increasing N a-p's reduce the P_1 deflections. After 4 sec. they appear in a position negative to the start of the response precisely in the same manner in which they do in the s.C fibers. If the line of the starts of the spikes be followed it will be seen that they descend up to 14 sec. due to the incrementing P_2 . In the last 6 sec. the potentiality for addition of P_2 has passed its limit and the starts rise slightly. If retention has already begun it is too small to prevent a positive after-potential. Throughout the tetanus the spike complexes progressively increase in height. At the end the main elevation was 2.3 times the height at the start. The other elevations also increased in height (not resolvable in the small dimensions of the figure), and the late ones were carried up on the N a-p in the usual way.

DISCUSSION

All the new information about the positive phase of the after-potential of the several sorts of nerve fibers, derived in the interest of interpreting the potential cycle of d.r.C fibers, supports the long held view that the positive after-potential is in two parts. The descriptions are presented in terms of membrane potential changes at a time when there is great interest among neurophysiologists in the ionic movements taking place during nerve activity. No contribution is made to this subject, beyond a clarification of the problem to be solved. It is actually two problems. The origins and behaviors of the two positive potentials, P_1 and P_2 , are so different, that probably the ionic movements involved are not the same. At least, in the light of present information, in reasoning about a given ionic movement, to which positive potential it applies is an indicated consideration.

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