ON THE MEASURE OF EXCITABILITY

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It was shown by Davis (1923) that the value of chronaxie depends on the nature of the stimulating electrodes. Rushton (1930, 1931) and Lapicque (1931) have confirmed the observation of Lucas (1906–07, 1907–08) that different time-intensity curves can be obtained on the same tissue. The fact that these different curves showed clearly that different measures of chronaxie were obtainable from the same tissue led Lapicque (1931) to adopt his empirical equation,

$$i = a \sqrt{\frac{t + \theta + \sqrt{(t - \theta)^2 + 0.16\,\theta^2}}{2\,t}}$$

as a criterion for the suitability of any particular time-intensity curve for use as an index of excitability. That is, time-intensity curves which conformed to this equation could be taken as indicative that the method being employed was the proper one for the determination of "true" chronaxie.

Rushton (1932) has recently shown, however, after allowing for possible instrumental errors and for possible inductance in his circuits that time-intensity curves for the frog's sciatic nerve using direct current and Lapicque's electrodes do not conform, even approximately, to Lapicque's equation. He therefore concludes that no use can be made of Lapicque's equation as a criterion.

The purpose of the present paper is to show that Rushton's data in common with that of Lapicque and others do conform to a particular equation but that the use of this fact probably lies in the establishing of experimental rather than theoretical criteria.

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The representation of time-intensity curves for various types of electrical stimuli by solutions of the differential equation,

$$\frac{dp}{dt} = KV - kp \tag{1}$$

where p is the local excitatory process, V the stimulating voltage, and K and k constants, was previously discussed (1932, a). Letting the threshold value of p be a function of the applied voltage of the form $h \pm \alpha V$ where h and α are constants the solution for direct currents is,

$$\log \frac{KV}{KV - k(h \pm \alpha V)} = kt \tag{2}$$

Putting V equal to the rheobase R, when t is great,

$$KR = k(h \pm \alpha R)$$

so that on substituting for kh in (2),

$$\log \frac{K}{K \mp k \alpha} \times \frac{V}{V - R} = kt \tag{3}$$

or,

$$\log \frac{V}{V - R} = kt + C \tag{4}$$

It is evident on inspection that C is negative when the threshold is $h + \alpha V$ and *vice versa*.

In Table I are given the results of applying this formula to Rushton's data. In each case he gave the greatest and least voltage observed. The mean value was used for calculating. It is given in the column *mean V*. He used four separate preparations but obtained two sets of data from each, one with increasing and the other with decreasing voltages. Each set of data was calculated separately as is shown by the table. The unit of time is the second and the constants are calculated to base 10 for convenience. The voltages marked with asterisks in each case were used to determine the constants. The choice of voltages for this purpose was made from graphs with $V/(V-R)$ on logarithmic scale against time on natural scale. Any two values giving a mean of the linear relation predicted by equation (4)

are suitable. For reasons previously given (1932, a) it is necessary to expect linearity only with voltages not very near the rheobase.

It will be seen from the table that the data conform to the equation as well as can be expected and that there are no systematic divergences. Again as with Lapicque's data (Blair, 1932, a) and as with those considered by Hill (1910) and Lucas (1910) the threshold depends on the voltage in most cases as C has appreciable magnitude except in set 4 in the second part of which it becomes zero. Sets 3 and 4 were taken near 0°C. The fact that C is small in these cases compared to sets 1 and 2 which were taken at room temperature may be significant although its magnitude appeared previously (1932, a) to be a function of electrodes as well.

In this regard it appeared desirable to investigate the data of Jinnaka and Azuma (1923) which were obtained with the pore electrodes of Pratt (1917). They claimed that their data disagreed with Hill's equation and they do. Examination of their papers led to the conclusion, however, that the method they used to calculate their currents was wrong and unfortunately sufficient data were not given to make a recalculation possible. It is assumed therefore that their results have no significance in their present form.

It was previously shown (1932, a) and can be readily seen from equation (4) that chronaxie is given by,

$$\tau = \frac{1}{k} \left(\log 2 \pm C\right)$$

and is therefore a function of C as well as of k. The question arises as to what extent the different chronaxies on the same tissue obtained by different methods are conditioned by changes in k and to what extent by changes in C. The importance of this is obvious since chronaxie can only have meaning as a function of variables which are, in turn, functions of those properties of the tissue which govern the rate of excitation. k itself is of course a direct measure of excitability according to the conception of Keith Lucas (1910) in the sense that it measures the rate of decay of the excitatory process. The quantity $\log \theta$ derived from Hill's formula and used by Keith Lucas is in fact numerically equal to k but opposite in sign. There are practical advantages, however, in the use of chronaxie if the experimental condi-

TABLE I

Time	1a			1b		
	Volts	Mean V	Calc. V	Volts	Mean V	Calc. V
sec.						
∞	14–13.4	13.7	13.7	13.4–13	13.2	13.2
0.000175	31–30	30.5	33.0	30–29	29.5	30.6
0.00011	47–45	46.0*	46.0	45–43	44.0	43.3
0.00007	65–62	63.5	64.6	63–60	61.5*	61.5
0.000032	115–110	112.5*	112.5	115–110	112.5*	112.5
0.000012	>140		194			213.2
	$k = 1232; C = 0.0171$			$k = 1332; C = 0.0116$		

Time	2a			2b		
∞	5.0–4.8	4.9	4.9	5.2–4.8	5.0	5.0
0.000295	11.2–10.6	10.9	10.4	11.7–11.2	11.45	10.1
0.000175	14.5–14.0	14.25	15.2	15.0–14.5	14.75*	14.75
0.000106	23–22	22.5*	22.5	22–21	21.5	21.9
0.00007	32–30	31.0	31.2	31–29	30	30.6
0.000035	55–50	52.5*	52.5	55–50	52.5*	52.5
	$k = 901; C = 0.0110$			$k = 974; C = 0.0093$		

Time	3a			3b		
∞	5.4–5.0	5.2	5.2	6.0–5.6	5.8	5.8
0.00098	13.5–13.0	13.25	13.6	14.0–13.5	13.75	13.6
0.00050	23–22	22.5	23.4	23.5–22.5	23.0	23.2
0.00031	36–34	35.0*	35.0	36–34	35.0*	35.0
0.000195	53–50	51.5	51.6	55–52	53.5	52.6
0.00012	83–78	80.5	77.4	83–79	81.0	80.1
0.00008	107–102	104.5*	104.5	115–110	112.5*	112.5
0.000065	>132		123.4	132		134.7
	$k = 207; C = 0.0055$			$k = 243; C = 0.0034$		

Time	4a			4b		
∞	10.5–10	10.25	10.25	10.5–10	10.25	10.25
0.00082	19–18	18.5	18.6	19–18	18.5	18.5
0.00050	27–26	26.5*	26.5	28–27	27.5	26.4
0.00031	40–38	39.0	38.9	40–38	39.0*	39
0.000195	62–59	60.5	58.4	60–57	58.5	58.6
0.00012	92–88	90*	90	94–90	92.0*	92.0
0.00008	>130		130.8	>130		138.3
	$k = 421; C = 0.0017$			$k = 427; C = 0.0001 = 0$		

* The mean voltages marked with asterisks were used to calculate k and C, and these constants were used in equation (4) to obtain the calculated voltages (Calc. V).

tions can be controlled as it requires only one measurement in addition to the rheobase while the evaluation of k requires at least two. The situation is not promising, however, as can be seen from the following examples. The largest C with Rushton's data is 0.0171. In this case chronaxie is proportional to $\log 2 - C$; i.e., to 0.284 while it should be proportional to $\log 2 = 0.301$. This is not a great divergence but of the data given in Lapicque's book which were previously considered (1932, a) C was frequently about 0.06 which would make chronaxie proportional to 0.24. In one case C was 0.128 making it proportional to 0.173 while in Lapicque's later work (1931) the C's were sometimes even greater than 0.15 which would make chronaxie at least 100 per cent in error as a measure of excitability on a common basis. Since C can be either positive or negative as was previously shown (1932, a) it is quite evident that chronaxies varying by more than 100 per cent may be obtained on the same tissue in the same state of excitability by virtue of variations of C with different conditions.

Whether or not the variations of chronaxie with interelectrode distances are due to variations of C or k or both cannot be decided with available data. Nor does the extensive work of Rushton (1927) on the variation of threshold with the separation of the electrodes throw any light on the matter. The experimental problem is to obtain time-intensity curves as functions of the interelectrode distances, and of the types of electrodes.

Further, this problem is of great importance in that it will show the dependence, if any, of k on the positions of the electrodes for it appears quite improbable that the whole burden of the variations of chronaxie with the method of its derivation can be laid upon C alone. It was shown in discussing Lapicque's recent work that values of k varying from units to hundreds were obtainable on the same tissue. There seem to be but two possible explanations: the classical one on the basis of the tissue having different excitabilities and one on the basis of k being a function of the mode of stimulation as well as of the properties of the tissue. In the latter event it would appear quite hopeless to expect ever to measure the excitability proper for even though a method could be found to give consistent results there would be no way of determining from the time-intensity curves themselves whether a real or pseudoexcitability was being measured. The only feature of

the problem which indicates that a real measure of excitability is possible is the fact that a standard technique such as Lapicque's has led to results which classify different tissues into the proper general order. In addition, which is more important, it has led to correlations between chronaxie and such other phenomena considered functions of excitability as the velocity of propagation of the impulse.

It is scarcely possible to avoid adopting the view that the ultimate meaning of excitability can only be in terms of some type of measurement. The requirements of the measure are just that it should be consistent with any other measure which may be a criterion of the same thing. The solution of the problem then from the present point of view depends on whether there can be found by experiment conditions applicable to all tissues which will give consistent and comparable values of k. If this is found possible it will then be sufficient to define the excitability as k or as some function of k providing the results so obtained appear to properly measure the attributes included under the term excitability.

The fact that it seems possible at present that k may have many different values for the same excitability provides a real difficulty but does not, however, deprive it of its value as a criterion providing that some limiting conditions can be reached in a way analogously, for example, to that by which the rheobase approaches constancy as the interpolar length is increased. A further difficulty may appear, however, in establishing the same condition for different tissues so that the k of one will be comparable with that of another.

The Meaning of k

Since the elimination of C will probably not be possible except under very particular conditions and since as a consequence it may be necessary to use k rather than chronaxie as a measure of excitability it will be of interest to consider the meaning of k in reference to equations (1) and (4).

By equation (1) as was previously indicated, k is the rate of return to normal per unit of state of excitation.

From equation (4) it is evident that k is the slope of the graphic representation of a time-intensity curve when log $(V/V - R)$ is plotted against time as abscissa. Such a representation would provide a con-

venient picture of comparative excitabilities for, if any sets of curves from different tissues were appropriately shifted so as to pass through the origin, the ordinates for any particular value of the time would be proportional to the respective k's of the corresponding tissues.

Putting $V = nR$ where n is a number, *i.e.* expressing intensity in rheobases instead of volts or amperes, equation (4) becomes,

$$\log \frac{n}{n - 1} = kt$$

Differentiating,

$$\frac{dn}{dt} = n\,(1 - n)\,k \tag{5}$$

In particular when $n = 2$, *i.e.* when $t =$ chronaxie, k is numerically equal to $\frac{1}{2}$ the tangent to the time-intensity curve. No practical use of these relations is probable but they show that the shape of the time-intensity curve on a scale of rheobases is a function of k alone. In other words, equation (5) is a formal proof that k and k only is a factor which expresses the variations of excitabilities as measured by the time-intensity relations.

The extent to which the other constants K and α may be evaluated requires consideration in regard to experimental investigations of C. Taking the case when C is positive in (4), *i.e.* when $\log K/(K \pm k\,\alpha)$ is negative in (3), *i.e.* when $C = \log (K + k\alpha)/K$ it is evident that from experimental data there are derivable the relations,

$$\frac{K + k\,\alpha}{K} = C' \text{ where } \log C' = C.$$

This gives on division by K

$$\frac{k\,\alpha}{K} = C' - 1$$

so that since k may be determined separately the ratio $\alpha : K$ is obtainable. From the rheobase conditions $KR = kh \pm \alpha R$ and the ratio $\alpha : K$ the ratio $h : K$ can be calculated and these ratios can be studied as functions of experimental conditions.

The discussion thus far has been based on the assumption that equation (4) is the proper representation of the time-intensity curve, but in view of the possibility that some other equation may be found to represent the data equally well the question arises as to whether chronaxie, since by definition it is quite independent of the shape of the curve, would not be a better measure of excitability than k. The answer to this is that the whole concept of comparative excitabilities in terms of chronaxies is derived from the assumption that all the time-intensity curves when expressed in the proper units give identical equations. Lapicque (1926, p. 225, footnote) gives the following argument. Let τ_1, τ_2 respectively be the time constants for two excitabilities. Then if i represents the currents and a_1 and a_2 the respective rheobases,

$$\frac{i}{a_1} = f\left(\frac{t}{\tau_1}\right) \quad \text{and} \quad \frac{i}{a_2} = f\left(\frac{t}{\tau_2}\right)$$

i.e., the currents in rheobases are functions of the time in terms of τ. If by experiment the times t_1 and t_2 are determined for the condition

$$\frac{i}{a_1} = \frac{i}{a_2}$$

which is the condition for determining chronaxies,

$$f\left(\frac{t_1}{\tau_1}\right) = f\left(\frac{t_2}{\tau_2}\right) \quad \text{or} \quad \frac{t_1}{\tau_1} = \frac{t_2}{\tau_2} \tag{6}$$

i.e., the time constants are proportional to the times required to excite. The validity of this argument depends entirely on the assumption that the two functions concerned are precisely the same. Certainly there does not exist as yet any such set of functions which represent the data adequately. There is therefore no justification at present for the use of chronaxie.

Lapicque's condition does not, however, have to be fulfilled except for making chronaxie valid. It is sufficient for the existence of a time constant which can be used to measure excitability that the conditions of equation (5) should be fulfilled. These conditions are not so restricting as those of Lapicque for chronaxie. With equation (4), for example, as has already been pointed out from experimental con-

siderations the chronaxie condition (Equation 6) requires the identity of the constants C which is unnecessary when use is being made of k. If, however, the constancy of C can be attained experimentally the argument leading to equation (6) shows that the use of chronaxie as a measure of excitability will give just as consistent a scale as k if the relative ease of its determination makes it preferable for ordinary use.

It may clarify the problem to discuss the conditions with reference to equation (4). According to equation (4) all time-intensity curves can be put in the form,

$$\log \frac{n}{n-1} = T + C \tag{7}$$

where n is the voltage in rheobases and T the time in units of $1/k$, *i.e.* in the natural tissue units, and C is as usual. The meaning of this is that all time-intensity curves will be congruent on these scales except for the variable displacement C. In particular if $\log n/(n-1)$ is plotted against T the basic curve is a straight line through the origin whose slope is unity and the plot of any time-intensity data on the same scale will be parallel to this and at a distance C from it.

Lapicque's condition which is obeyed only when C in equation (7) is the same for all tissues requires in general that,

$$f(n) = T$$

where T is measured in chronaxies. If such a function is ever discovered all time-intensity curves on these scales will be congruent without displacements.

The situation may be summed up as follows: chronaxie is no longer valid as a measure of excitability from the point of view of equation (4) since it is a function of the quantity C which depends on experimental conditions as well as on the time constant k. The existing data neither provide a means of determining the factors involved in the variations of C nor indicate how successfully they can be controlled so that the solution of the problem requires a thorough experimental investigation of the time-intensity relations. The data so obtained will also be useful in determining whether k itself is a function of the experimental method as well as of the properties of the tissue. If it is a function of the method the only hope of obtaining a quantitative scale

of excitabilities is in the determination of standard limiting experimental conditions applicable to all tissues. The criteria for these conditions will for the present probably have to depend on the determination of situations where the experimental variables no longer change or change only very slowly with alterations of the conditions. Eventually they should enable consistent correlations to be established between different phenomena included under the concept of excitability in order to inspire confidence in their validity. Any conclusions drawn from chronaxie measurements, except perhaps those obtained by the same method, must be looked upon with considerable suspicion at present for whether or not equation (4) is the true time-intensity relation it shows that a neglect of the possible effect of boundary conditions is dangerous when drawing conclusions from the time-intensity curve about the properties of the tissue from which it is obtained. Whether or not equation (4) is the true representation it can be used equally well as a basis for research, for since it fits the existing data within the experimental error for all values of durations and voltages its constants must be simply related to those of the true representations except in the unlikely event that the existing data are not representative.

SUMMARY

Recent time-intensity data by Rushton (1932) on the sciatic nerve of the frog are shown to provide additional support to the writer's suggestion (1932, *a*) that integrals of the equation

$$\frac{dp}{dt} = KV - kp$$

where V is the applied voltage, p is the local excitatory process and K and k are constants adequately represent the just effective direct current stimuli when the threshold value of p is made a linear function of the voltage of the form $h \pm \alpha V$ where h and α are constants.

The measurement of excitability is discussed and it is shown that the criteria for "true" measurements are not likely to be found by the agreement of the data with canonical time-intensity functions as suggested by Lapicque (1931) but rather in the establishing of standard experimental conditions. These conditions may permit the use of

chronaxie as a measure of excitability, but it seems more likely that the constant k of the above equation will have to be adopted. There is sufficient evidence to cast considerable doubt on the validity of any conclusions drawn from the existing measurements of chronaxie although those derived through a particular technique may be valid. The problem requires a thorough experimental investigation in terms of integrals of the above equation.

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