THE RATE OF RECOVERY OF NERVES IN ASPHYXIA.

By SYBIL COOPER, Yarrow Student of Girton College, Cambridge.

(*From the Physiological Laboratory, Cambridge.*)

WORK on the behaviour of nerves in asphyxia was carried out by Verworn and his co-workers at the beginning of the present century; he argued that since nerve cells and other living substance were fatigued in absence of oxygen, there was good reason to suppose that nerves behaved in a similar way. Von Baeyer(1) found on exposing a stretch of frog's sciatic nerve to nitrogen or hydrogen and stimulating electrically either on the stretch or central to it, that the nerve ceased to be excitable in 3–5 hours; on replacing the asphyxiating gas by air, there was very rapid recovery in 3–10 minutes. Fillié(2) repeated these experiments, using oxygen free saline solution, and obtained the same results. He worked out the minimum value of oxygen necessary to maintain conduction and found this to be between ·1 and ·3 mg. oxygen per litre, or about ·03 p.c. by volume. Further work was carried out by Frö lich(3)(4), he postulated a region of decrement in the stretch of nerve asphyxiated, this was shown by a reduction of the propagation velocity of the impulse. He attempted to explain the mechanism whereby the nerve uses the oxygen and stated that asphyxia hindered the assimilation of oxygen and that the nerve contained a reserve store which it could only call upon if the pressure conditions were correct. Normally the oxygen maintained the excitability constant and delayed the appearance of asphyxia. He also studied the effect of the condition of the frog at the time of the experiment and stated that this affected the results both during and in the recovery after asphyxia.

At this time the excitability was expressed by the value for the threshold of the electrical stimulus on the asphyxiated stretch, and the conductivity was measured by the somewhat crude method of noticing if there was any muscular contraction on stimulating the nerve central to the asphyxiated part. Experiments showed that during asphyxia there was a gradual fall of excitability, and a sudden fall of conductivity just before the impulses failed to get through to the muscle. In order to obtain a more detailed account of the happenings in the nerve, Fröhlich(5) studied the change of refractory period. He sent in a series

of faradic stimuli at a known period and found at what period the muscle ceased to respond with a complete tetanus. He maintains that in asphyxia the value for the refractory period rises from the normal value of ·003″ to over ·1″ and from this he concludes that the nerve is unable to recover at the same rate as before. The only other record of a nerve having a very long refractory period is in the case of the application of yohimbine investigated by Tait and Gunn(6); they found an absolute refractory period rising to ·04 and a total period of 2·2 secs. It seems very probable in this case that the effect is specific in nature, and with such a long refractory period it is reasonable to suppose that the rate of recovery is also affected.

Lucas(7) studied the effect of alcohol on the rate of recovery of a nerve and incidentally elucidated several important facts concerning the behaviour of the nerve in narcosis. He showed clearly the distinction between the decrement in the nerve involving impaired conduction, and the recovery of the nerve after the impulse had passed. And with the help of some of Adrian's(8) work he makes it quite clear that the normal recovery of a nerve is expressed by the curve relating the interval for muscular summation to the strength of the second stimulus, the curve *AB* of Fig. 1. And that when the nerve is subjected to the action of a

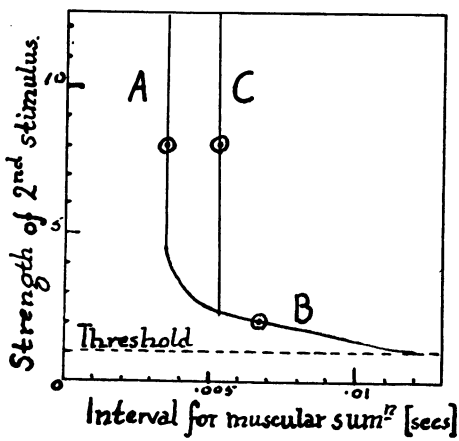

Fig. 1.

narcotic the curve takes the form *CB* in which the vertical part *C* is an expression of the decrement in the nerve, and *B* is still part of the original recovery curve and expresses the rate of recovery. By taking a series of measurements of the least interval for muscular summation

during the passage of alcohol using a second stimulus of eight times the strength, *i.e.* determining a point on the steady part of the curve where the least interval does not decrease for an increase of the second stimulus, he is able to follow the onset and course of the decrement; the interval shows a gradual increase, whereas the "recovery time," the interval for muscular summation using a second stimulus of twice the threshold strength, remains steady until it is equalled by the least interval. From this, and other confirmatory experiments, he concludes that the conduction in a nerve and the rate of recovery are quite separate processes and that the latter is unaffected by narcosis. Since narcosis and asphyxia have been shown to have many similarities in their action on nerves, it seemed very possible that the unaltered rate of recovery would be found on asphyxiating a nerve with an inactive gas.

The experiments were carried out on the sciatic-gastrocnemius preparation of a frog, and an ebonite muscle nerve trough was used (Fig. 2).

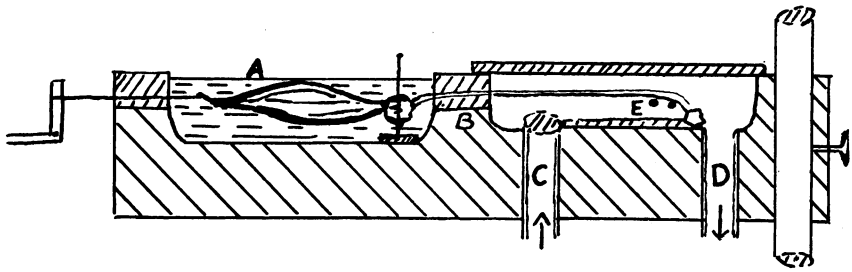

Fig. 2.

The muscle was placed in Ringer solution in the chamber *A* with its free end attached to a writing lever and the nerve passing back through a slot *B*, plugged with vaseline, into the nerve chamber where it passed over a pair of platinum electrodes *E* about 2·4 cms. from the slot. The nerve chamber had an inlet tube *C* and an exit tube *D* and it could be closed by a glass plate sealed on the top with vaseline. It was found advisable to have some blotting paper soaked in Ringer solution on the floor of the nerve chamber and also a small damp wad of cotton wool placed loosely in the opening of the inlet tube. At one time a second pair of electrodes were placed at about 4 mm. from the slot *B*, but these had to be abandoned as there was invariably current spread. The inlet tube could be connected with either a Mariotte bottle forcing damp air through the chamber or else with the source of hydrogen gas used for asphyxiating; the exit tube led to a wash bottle containing water, this served to prevent the entrance of air, and also on comparing the number of bubbles of gas

passing through a wash bottle just before entering the chamber with those issuing through this final bottle, it was possible to see whether the chamber had any appreciable leak. The hydrogen was obtained from a cylinder provided with a fine adjustment release cock so that the stream could be regulated. It passed through two absorption tubes containing alkaline pyrogallol and then through a wash bottle containing water; the resulting gas proved on analysis to contain about ·025 p.c. oxygen, an amount just lower than the one postulated by Fillié. The stimuli were break shocks from two coreless induction coils, the first coil was adjusted by moving the secondary coil relative to the primary, and the second had an adjustable resistance box in the primary circuit. The primaries of both circuits were opened by a spring contact breaker with two adjustable keys which could be set so that one was opened at a known time interval after the other.

When the preparation was set up, a slow current of air was allowed to flow until the threshold, the least interval for muscular summation and the recovery time were steady. This usually took about an hour an a half, and the values reached by that time were found in a control experiment to be maintained for five hours or more. Before turning on the hydrogen a recovery curve was plotted, for this is a good record of the state of the nerve. The air was then turned off and a current of hydrogen started; a stream of about 30 bubbles a minute was used. The nerves maintained their excitability and power of conduction in hydrogen for a period varying from three to five hours, agreeing in this detail with the results of von Baeyer and others. But during this time the least interval for muscular summation increased showing the onset of conduction with a decrement. Fig. 3 shows a typical set of results.

The upper curve shows the alteration of the threshold as the percentage of the normal value, the curve remains steady or rises slowly during the early stages of asphyxia, then there is often a sharp rise just before the excitability fails completely. The lowest curve shows the course of the least interval for muscular summation, this too remains steady for some time, then on the rise of the threshold it also begins to increase in value as the decrement becomes more pronounced. This rise may occur before or after the rise of the threshold, the experiments showed no majority one way or the other. The sharp final rise usually took about an hour, at the end of this time the nerve was no longer excitable and the least interval had risen to a mean value of about ·012 sec. a value comparable with the length of the total refractory period and in no-wise suggesting the value of ·1 sec. put forward by Fröhlich as the limit

reached. The middle curve shows the recovery time of the nerve, the values found remained approximately the same throughout the course

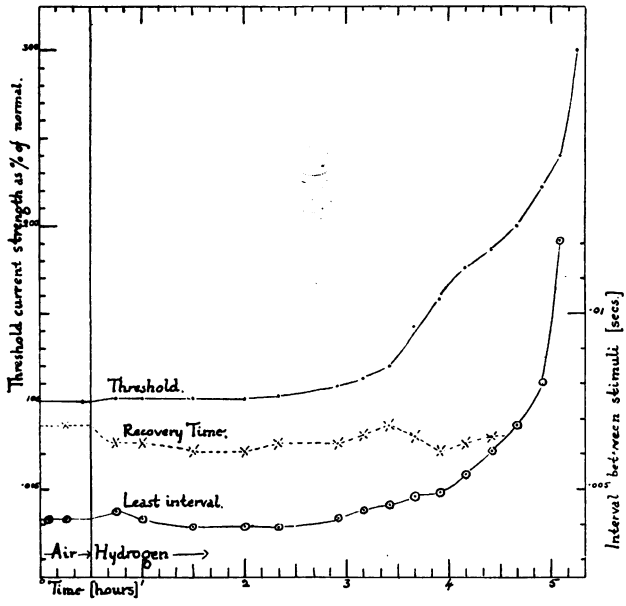

Fig. 3.

of the experiment until the value for the least interval equalled them. Sometimes the recovery time showed slight fluctuations in value when the least interval was beginning to rise, but these were never very great and can possibly be explained by the experimental difficulty of obtaining an accurate value for the threshold; when the latter is increasing rapidly the strength of the second stimulus might be less than twice the threshold and the value for the recovery time would be slightly too large.

Expt.	Asphyxia time	Limits of recovery time	% rise	Limits of least int.	% rise
1	5h 0m	·0066 to ·0079	120	·0035 to ·0121	340
2	3 0	·0078 ·0088	113	·004 ·0132	330
3	4 50	·0061 ·0065	106	·0039 ·0122	287
4	3 0	·0073	100	·0049 ·0121	226
5	3 50	·007 ·008	114	·0035 ·014	400

In the table the percentage rise of the recovery time shows an average value of 110 whereas the least interval for muscular summation rises to about 320 p.c. of its resting value, these figures are in no-wise comparable with each other and one may conclude that the recovery time is unaltered.

After the asphyxia it is of interest to note that the nerve did not

recover completely when the current of air had been on for some minutes. The least interval recovered slightly in air, then it often began to rise again, a more complete recovery could only be obtained by placing the nerve in Ringer solution for a few minutes. Fig. 4 shows this very well,

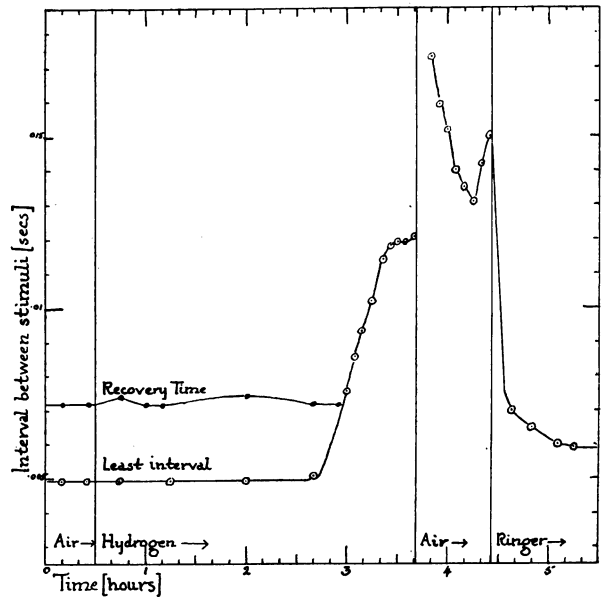

Fig. 4.

though the high value of the least interval in air was not universal. These observations agree with some work put forward by Gottschalk(9) in 1920. He states that oxygen alone or oxygen free salt solution alone is not sufficient for full recovery, but a combination of both is needed. One can assume that during or as a consequence of activity, a nerve uses oxygen and accumulates metabolites; on continued stimulation in dry air the latter of these effects may impair excitability and conductivity; in deoxygenated Ringer solution the use of oxygen is hindered. In oxygenated Ringer the behaviour of the nerve is unimpaired owing to an adequate supply of oxygen and a surrounding fluid medium to wash away the metabolites as they are formed, this assumption agrees with Fillié's work. But in hydrogen the nerve is deprived of oxygen and (unless the nerve is kept very moist) of the fluid necessary for the diffusion of the metabolites; thus both these factors must be supplied for complete recovery. Thörner's(10) results also agree with this, for he shows that if a nerve is put in an asphyxiating gas and not stimulated then its

conductivity is maintained for a longer time than if it is stimulated frequently.

The conclusions reached are that the actual transmission of the impulse is independent of oxygen. A process can be conceived analogous to the process in muscle about which far more is known both chemically and physically. The nerve conducts the impulse and develops an absolute and relative refractory period during its recovery process in a fashion comparable with the contraction and relaxation of a muscle; these are independent of oxygen, but in both cases products are formed which require oxygen for their complete removal. If a muscle is subjected to an atmosphere of an indifferent gas, Fletcher(11) has shown that the deficient oxidation of the metabolic products within the muscle causes fatigue and finally rigor mortis. These products have since been identified and in a single twitch the chemical changes and the heat accompanying the recovery in oxygen have been worked out. Similarly in a nerve metabolites accumulate in the absence of oxygen and these in time cause a decrement in conduction and finally death. The substance produced may be carbon dioxide as stated by Tashiro(12), there may be more than one substance; whatever it is, it gradually accumulates if there is no oxygen. In the early period of the passage of hydrogen, the nerve shows no decrement, this is probably due to the time taken to wash out all the oxygen for, as Fillié has shown, a very minute quantity is sufficient to maintain conduction; also the presence of reserve oxygen has not been actually disproved. But as this oxygen, whatever may be its source, is cleared away, the metabolites gain ground; it is important that the nerve should fulfil its function as long as possible, and this is secured by the recovery time being maintained unchanged.

Summary.

Fröhlich has inferred from his experiments that if a nerve is asphyxiated, then its refractory period is lengthened to ·1 sec., and its rate of recovery is greatly prolonged. The present experiments show that in an atmosphere of hydrogen a frog's sciatic nerve conducts with a decrement, as shown by the lengthening of the least interval for muscular summation. But the least interval never exceeds ·015 sec., the time of the total refractory period in a normal nerve, and when there is a considerable decrement, the recovery time remains unaltered, showing that the refractory period is not prolonged.

These results confirm the view that the nerve does not require oxygen for the actual transmission of the impulse or the recovery of excitability

and conductivity; but it needs it to oxidise the break down products formed during the passage of the impulse, so that the next impulse may find an adequate local supply of energy for its transmission.

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