CCXXXVIII. THE METABOLIC ACTIVITY OF THE CELLS OF THE TRIGEMINAL GANGLION.

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(Received October 26th, 1932.)

WE have so far but little information about the relative metabolic powers of the different parts of the central nervous system. Kinnersley and Peters [1930] have observed that the concentration of lactic acid differs in different parts of the brain of the avitaminous pigeon, though not in the different parts of that of the normal bird. Gavrilesco and Peters [1931] have found that different parts of the pigeon's brain take up oxygen at different rates. Some information is available [Holmes, 1930] about the metabolic activity of the different parts of the neurone. The white fibres in the central nervous system, and those which form the peripheral nerves, appear to differ very materially in their oxidative powers from what we may, for the moment, call the "cell complex," that is, the cell body, the dendrites, and the junctional or synaptic tissue. It was in the hope of analysing a little further the activity of this "cell complex" that the work here described was undertaken. In the brain and spinal cord itself, the cell is so closely associated with dendrites and, presumably, with synapses, that no mechanical separation is possible. In the posterior root ganglia, however, cells and fibres are found, but the dendrites and axons, which are both to all appearances ordinary medullated fibres, pass out of the ganglia without making contact with other neurones. These ganglia, therefore, afford material for the examination of the activity of the cell bodies, uncomplicated by that of non-medullated dendrites or synaptic tissue. On the other hand, to make use of this tissue for the study of the metabolism of nerve cells, and to draw deductions from the results as to the behaviour of nerve cells in general, involves the assumption that the cells are similar in metabolic behaviour to others in other parts of the central nervous system; and this assumption is not necessarily justified, for the cells are larger than, and differ in form from, most of the cells in the central nervous system. However, it must be remembered that the latter present an enormous variety of shapes and sizes, ranging from the large pyramidal Betz cells of the motor cortex and the rounded Purkinje cells of the cerebellum to the small pyramidal cells which are present in such large numbers in the grey matter as a whole.

The experiments present other difficulties. The most convenient tissue to use was found to be the trigeminal ganglia of sheep and oxen. These bodies

contain, besides nerve cells, considerable amounts of white fibres, and of connective tissue. It is difficult to assess accurately the exact proportion of cellular substance present. A glance at a fixed and stained section, however, shows that the cells occur in large masses, and that they are closely packed, and it seems unlikely that their metabolic activity could be seriously masked by the presence of the relatively inert white fibres and connective tissue. In the light of what follows, it is noteworthy that a brief inspection of a section of cerebral cortex stained, for instance, with methylene blue shows that even here the cell density is not very great. The cells are much smaller than those of the posterior root ganglia and are dotted about amid a mass, not in this case of white fibres, but of non-medullated processes. If, therefore, the trigeminal ganglion cells may be taken as typical nerve cells, we have a fair chance of examining their biochemical behaviour.

The experimental procedure was as follows. Sheep's heads (usually three), were obtained fresh from the slaughter house. The skulls were sawn open, and the brains removed, the Vth cranial nerve being cut through as near as possible to the brain. The trigeminal ganglia, which lie on either side of the cavernous sinus, surrounded by tough dura mater and bone, were exposed and removed by the use of saw, bone forceps, and scissors. The three divisions of the trigeminal nerve were cut through close to the ganglion. The six ganglia were chopped with scissors, and sampled. Portions of the cranial nerves, of white matter and of cerebral cortex were usually taken for comparison. The oxygen uptakes were measured in the usual way, in the Barcroft apparatus. The tissue was suspended in Ringer's solution buffered with 1/5 volume of $M/2$ sodium dihydrogen phosphate adjusted to p_H 7.6. On every occasion, the Barcroft cups were filled with oxygen. Whenever possible, 0.5 g. of tissue was placed in each apparatus.

The curves obtained were, on the whole, far less satisfactory than is usual when dealing with other parts of the central nervous system. This was due, probably (1) to the very low rate of oxygen consumption; (2) to the difficulty of sampling. The connective tissue, which binds together the elements of the ganglion is extremely tough. It is, in consequence, difficult to chop the organ satisfactorily, and the tissue tends to collect in lumps in the Barcroft cups. In spite of these difficulties, it is at once plain that the oxygen consumption of ganglion tissue is of a very low order, much the same, in fact, as that of the peripheral nerve of the same animal. Samples of cortex taken at the same time as the ganglion, showed the usual large uptake, and there is no reason to suppose that the ganglion cells had suffered more manipulative damage than did those of the cortex. Fig. 1 shows the oxygen uptakes of trigeminal ganglion, postganglionic cranial nerve (V), and cortex—sheep's tissue being used in each case.

In only one experiment was a much larger oxygen uptake than this recorded, this being a single experiment in which ox tissue was used, when the uptake after 150 minutes amounted to 421 mm.³ This was quite an excep-

tional observation, and even so, the oxygen consumed amounted to only about a quarter of that consumed by sheep's cortex.

Fig. 1.

Table I.

Date	Tissue	Uptake after 150 mins. (mm. ³ /g.)
1. iii. 32	Trigeminal ganglion (sheep)	132
8. iii. 32	"	140
"	"	98
15. iii. 32	"	170
"	"	128
22. iii. 32	"	236
29. iii. 32	"	178
	Average	154
8. iii. 32	Nerve (sheep)	86
15. iii. 32	"	118
"	"	128
29. iii. 32	"	114
	Average	112

Table I shows figures observed for total oxygen consumption both of ganglia and of cranial nerves. The values recorded for the uptake of the ganglia varied so much from experiment to experiment, even when the tissue was taken from the same mass of chopped ganglion, that it is impossible to say with certainty whether the oxygen consumption is or is not increased by the addition of lactate. That no large increase (such as may be observed with cortex) takes place is certain, but the experiments throw no light on the question as to whether or not a slight increase occurs. With succinate, on the

other hand, there is a very large increase. For instance, after 150 minutes, the oxygen uptake of sheep's trigeminal ganglion in Ringer and succinate ($M/20$) was 790 mm.³ per g. Quastel and Wheatley [1932] have shown that both grey and white matter readily change succinate to *l*-malate. The increase was therefore not necessarily due to the activity of the cells.

Since the oxidative powers of the nerve cells in question are evidently not of a high order, it was surprising to find that they readily gave a strong "Nadi" reaction. This is easily observed by freezing and cutting sections of the fresh ganglia, placing them in the "Nadi" reagent for a short time and then examining them under the low power of the microscope. The cells will be seen to be stained a deep blue colour, while the other tissue elements are nearly colourless. They, too, eventually become blue, but the colour is less intense than in the case of the cells and develops much more slowly. Incidentally, it was noticed that cooling to temperatures obtained with an ordinary acetone spray very much reduced the power of cortical tissue to consume oxygen.

The glycolytic power of the ganglion cells was also examined. A sample (0.7 g.) of tissue was placed in each of the two cups of a large Barcroft apparatus. One cup contained plain Ringer, the other Ringer containing 0.5 % glucose. The apparatus was filled with oxygen-free nitrogen and shaken for 3 hours in a thermostat at 37°. For purposes of comparison, samples of white matter and of cerebral cortex were treated in exactly the same way. The tissue, at the end of the experiment, was treated with trichloroacetic acid, made up to volume, filtered, and lactic acid estimated as usual. (Calcium hydroxide-copper sulphate precipitation: lactic acid estimated according to Friedemann, Cotonio and Shaffer [1927]).

The results are given in Table II. It will be seen that, in every case, less lactic acid is formed by the ganglia even than by white matter; cortex shows its usual (and marked) glycolytic power.

Table II. *Mg. of lactic acid formed per g. of tissue, after shaking for 3 hours anaerobically, with and without glucose.*

Ganglion			White matter			Cortex		
Glucose absent	Glucose present	Formed from glucose	Glucose absent	Glucose present	Formed from glucose	Glucose absent	Glucose present	Formed from glucose
1.60	2.21	0.61	1.30	3.15	1.85	1.46	8.64	7.17
1.02	2.04	1.02	0.66	2.89	2.23	1.00	13.4	12.40
1.47	3.58	2.11	1.20	4.42	3.22	1.02	10.44	9.42
		1.24			2.43			9.66

These results show that mammalian sensory ganglia have feeble powers of oxidation and of glycolysis, when compared with the cerebral cortex. It has already been pointed out that the experiments on oxygen consumption are not without technical difficulties. Nevertheless, I venture tentatively to put

forward the hypothesis that, so far at least as oxidation and glycolysis are concerned, the chief seat of metabolic activity in the neurone is neither the medullated axon nor the cell body, but the dendritic and synaptic structures (supposing the latter to have a real and separate existence) which form such a large proportion of the bulk of the grey matter of the central nervous system.

It is of interest that Bethe [quoted by Evans, 1930], has found that the reflex mechanism of the tentacle of *Carcinus menas* continues to function, even after all the cell bodies have been cut away from the ganglion upon which the reflex depends, while Steinach [see Evans, 1930] has found that the posterior root ganglia of the rabbit continued to conduct impulses even after all the cells were dead and degenerated as a result of the cutting off of their blood supply. These findings, as Evans points out, suggest that the cell body is not essential for the conduction of impulses through the neurone, provided, of course, as in these cases, its destruction does not involve any actual interruption of continuity. But if the function of the neurone, as a unit, depends on its metabolic processes, these (or at any rate those of them which are important for function) must occur at some situation other than the cell body itself. We can eliminate, from previous studies, the medullated axon, and all that remains are the dendrites and synapses.

SUMMARY.

The trigeminal ganglia of sheep show very poor powers of oxidation, although the cells contain indophenol oxidase. Their power of forming lactic acid from glucose is less than that of the white matter of the central nervous system. It is suggested that oxidation and glycolysis in brain occurs in the dendrites and synaptic structures, rather than in the cell bodies.

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