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Oxygen Consumption of Degenerated Optic Nerves.

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Michail and Benetato[1] found a 50 to 70% higher oxygen consumption in degenerated human optic nerves (from glaucomatous and atrophied eyes) than in optic nerves removed shortly after traumatization of the eye. Van Harreveld and Tyler[3] compared the metabolism of normal optic nerves of cats with that of eye nerves severed directly behind the eye 3 to 14 days before. A lower oxygen consumption of the operated nerves was found constantly. As the nerves examined by Michail and Benetato had probably been subject to degeneration much longer than the 2 weeks allowed for degeneration by van Harreveld and Tyler, the metabolism of optic nerves of cats, 6 months after transection was compared with that of the heterolateral normal eye nerves.

Methods. The optic nerve on one side was severed with aseptic precautions directly behind the eyeball. Six months later the oxygen consumption of the normal and degenerated nerves was determined in Warburg respirometers at 38°. The nerves were not minced but were left intact since previous experiments[3] had shown that the highest metabolism is found in undamaged nerves. The dura was removed with as little injury to the nerve as possible. The medium used was a glucose-Ringer, buffered with phosphates to a pH of 7.4. After the metabolism determination one part of each nerve was fixed and stained in osmic acid. The other part was fixed in Zenker's solution and later stained with hematoxyline eosin.

TABLE I.
Metabolism of Optic Nerves in Cubic Millimeters of O_2/Gram Wet Tissue/Hour.

No. of cat	Degenerated nerve	Normal nerve
1	460	590
2	530	480
3	430	510
4	510	470
5	340	510
6	320	470

Results. The results of the metabolism determination are shown in Table I. These figures give the oxygen consumption in mm^3 per gram of wet tissue during the hour between the 50th and 110th minute after the removal of the nerve from the animal. In 2 instances the degenerated nerve had a slightly higher, in 4 a lower metabolism than the normal nerve. The mean of the metabolism for the degenerated nerves was $430 \pm 20 mm^3$, for the normal nerve $510 \pm 10 mm^3$.

The degenerated nerves looked thinner and weighed less than the heterolateral normal optic nerves.

The osmic acid preparations of the normal side showed the fine nerve fibers with a thin myeline sheath typical for the optic nerve. In the degenerated nerve a few intact centrifugal fibers were found; the myeline of the degenerated fibers had, but for an occasional drop, disappeared. Few nuclei were found in the hematoxyline eosin preparations of the normal nerve. In the degenerated nerves there was, in all cases, a fair increase in the number of nuclei which were of two types, small well-stained nuclei (probably microglia), and larger, pale ones.

Discussion. An increase in metabolism in degenerated nerves would be conceivable on the basis of a relative (due to the resorption of axon material and myeline) and absolute increase of glia and connective tissue, assuming that these cellular elements have a

1 Michail, D., and Benetato, G., *C. R. Soc. Biol.*, Paris, 1936, **121**, 267.

2 Tobias, J. M., Clark, D. B., and Gerard, R. W., *Fed. Proceedings*, March, 1942, **1**, 85.

3 Van Harreveld, A., and Tyler, D. B., *Am. J. Physiol.*, 1942, **138**, 140.

higher metabolism than the axis cylinders, as is indicated for the glia by the work of Tobias, Clark and Gerard.[2] The above determinations do not bear out this expectation; the metabolism of the optic nerve in the cat, 3, 7 and 14 days[3] and 6 months after the beginning of degeneration is, if anything, lower than that of the normal nerve.

The degeneration in the optic nerves studied by Michail and Benetato was caused by pathological processes, and this may account for the higher metabolism found in their degenerated nerves. However, they minced their nerves, a process which reduces the oxygen uptake to a fraction of that of the undamaged nerve.[3] It is possible that mincing depresses the oxygen consumption of the normal nerve more than that of the degenerated one, which would lead to the erroneous conclusion that the degenerated optic nerve has a higher metabolism than the normal one.

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Site of Action of Indole in the Central Nervous System.

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Despite the amount of work that has been done since Herter[1] first studied convulsant properties of indole, several points seemed worth clarifying. To this end, experiments were undertaken with the surgical assistance of Dr. Edward Davis.

In the first place, indole directly applied to the cortex of dog or cat produces a localized discharge resembling in many ways that seen following local strychninization. This is apparent from Fig. 1. As with strychnine, the concentration required for local application to elicit these results is great.

On the other hand, rapid intravenous injections of 20 mg per kg into dogs, cats and rabbits bring on convulsions which differ from fits induced by cortical excitation in that the motions of various muscles are not synchronized, and in that the axial and axio-appendicular, not the appendicular, muscles are most involved. Yanai[2] has reported that seizures occur after decerebration, to which we can add that they are not significantly altered by decerebration.

After transection of the spinal cord, the seizures may be more pronounced and begin at lower concentrations of indole either below or above the transection. Frequently, following transection of the neuraxis at any level, both portions are involved independently. Fig. 2 exemplifies this in the decerebrate preparation. The top record is from the cortex, and the bottom is from the hind limbs. They show cortical electrical discharges unrelated to the twitches of the hind limbs.

Under full ether anaesthesia, several dogs and cats were prepared by inserting electrodes to follow the electrical activity and the oxygen tension of the cortex and by installing tracheal and arterial cannulae. Several hours were allowed for recovery from ether. They were then paralyzed with dihydro-β-erythroidine hydrobromide and given artificial respiration. Thereafter, 18 to 30 mg of indole per kg, dissolved in olive oil or in less than 1 cc of propylene glycol, was given intravenously. The ensuing alterations in circulation produced corresponding changes in the O_2 tension of the cerebral cortex. On a few occasions, a few sharp diphasic spikes appeared in the record of the cortical activity, but at no time was a typical cortical seizure recorded, nor any decreases in O_2 tension ex-

1 Herter, C. A., *N. Y. Med. J.*, 1898, **68**, 89.

2 Yanai, Binici, *Tohoku J. Exp. Med.*, 1935, **25**, 401.