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.

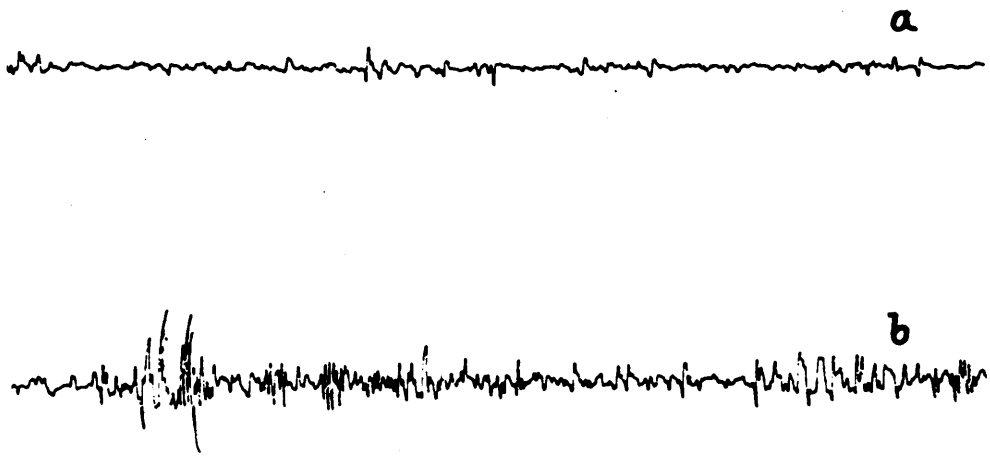

FIG. 1.

Cut No. 5. April 29, 1943. Cortex exposed and tracheal cannula installed under ether anesthesia. Four hours later—artificial respiration established under dihydro-β-erythroidine-hydrobromide. E.E.G. record (a) prior to local application of indole, (b) 7 minutes after local application of indole.

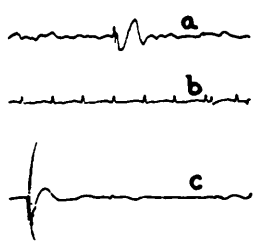

FIG. 2.

Dog. August 20, 1943. Under nembutal. Decerebration at level of superior colliculus. Synchronous records after intravenous injection of 25 mg of indole per kg. Whole dose in 2.5 cc propylene glycol. (a) E.E.G. from right hemisphere, (b) E.K.G. from both forelimbs, (c) E.M.G. from both hindlimbs.

cept those referable to the changes in circulation.[3-6]

With the larger doses of indole, the electrical record exhibited a late decline in both amplitude and frequency accompanied by a high O_2 tension.

Since indole has been shown to exert its convulsant action of the nervous system,[7] the experiments reported can be taken to indicate (1) that indole can act on many portions of the central nervous system, (2) that the thresholds of the various portions are all low and sufficiently nearly equal for other, uncontrolled, variables to determine which is the lowest, (3) that the characteristic motor seizure is certainly of subcortical and may, and in certain cases must, be of spinal origin.

[3] Ott, Isaac, and Ulman, Joseph F., *Therap. Gaz.*, 1907, **23**, 20.

[4] Danilewsky, B., *Pflüger's Arch.*, 1908, **125**, 361.

[5] Ets, Harold N., and Feinberg, I. M., *Proc. Pharm. Exp. Therap.*, 1939, 11.

[6] Ets, Harold N., and Feinberg, I. M., *Am. J. Physiol.*, 1942, **136**, 647.

[7] Yanai, Binici, *Tohoka J. Exp. Med.*, 1935, **25**, 385.