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Effect of Striated Muscle Paralysis Induced with Erythroidine upon the Electroencephalogram (E. E. G.)

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In a series of previous studies, an analysis was made of the psychosomatic relations during the development of conditioned reflexes in curarized and erythroidinized mammals.[1-7] It was shown that there was a central as well as a peripheral effect, the electrical and extirpation data[1,2,3] indicating that the former consists of a depression of synaptic transmission in the cerebral cortex. A recent investigation by Feitelberg and Pick suggests that the cortical cell metabolism, as measured by the electroencephalogram, also suffers functional inactivity since the E. E. G. is completely abolished in the curarized frog.[8] The present study is concerned with a test of the same question in mammals.

The E. E. G. was recorded in a shielded room on an ink-writer activated by a single high-gain channel amplifier (approximate range was 1-40 cycles, sensitivity that of 0.4 mm/mv). Operative preliminaries, implanting of electrode (when pickup was desired in the normal before drug-injection), exposure of cortex, cannulation (in monkeys), all were performed under ether anesthesia. Breathing in the drugged animal was maintained by a Harvard respirator. The drug consisted of a 1% or 2% water-solution of dihydro *B* erythroidine hydrobromide.

Dosage for 10 dogs (intravenous injection) is presented in Table I. Incidental observations obtained from several other dogs, conforming with the data reported below, are excluded only because they lacked completeness. Two *Macacus rhesus* monkeys (1.0 and 1.5 kilos respectively), each subjected to a total dosage of 125 mg (intraperitoneal injection), were also studied. A great number of tests were made with visual and acoustic stimuli and in relation to the nature of the pickup from different cortical areas. In general, in an animal weighing from 2 to 4 kilos, complete recovery would not occur until 1 to 1½ hours after a single injection of 20 to 60 mg erythroidine, and a single dose of 100 mg

TABLE I.
Dosage of Erythroidine.

(I) Animal No.	(II) Wt in kilos	(III) Initial doses	(IV) Total dosage	(V) Duration in min
R-51	4.0	20, 70	290 (2)	140
R-52	9.0	10, 30	250 (2)	100
R-54	9.0	20, 20	140 (1)	132
R-55	7.0	50	350 (3)	68
R-56	2.0	10, 30, 60	100	32
R-57	2.0	60	160 (1)	40
R-58	4.0	60	60	84
R-59	2.0	10, 20, 10	100	95
R-60	3.2	5, 30	355 (3)	163
R-61	2.5	60, 80	240 (1)	52

Dosage is given in mg; in (III) the initial injections are given separately, in (IV) the total dosage is given and the number in parenthesis indicates the number of single injections each of 100 mg. Thus in dog R-51, the first two spaced doses were 20 mg and 70 mg respectively; later 2 subsequent injections of 100 mg each were made (total dosage 290 mg). The duration of the experiment (V) was counted from the time of the first injection until the animal was dispatched.

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would insure complete paralysis from 2 to 4 hours. As shown in Table I, the total dosage in many cases far exceeded the latter value. Greater reliance was obtained with functional criteria, and all stages were tested, from no observable change to complete striated muscle paralysis.

In general the E. E. G. in the drugged animal conformed to that recorded in the normal condition. There was some evidence that the magnitude of the pick-up in certain cases was reduced after the animal was erythroidinized, but the wave-form remained undisturbed. A series of supplementary doses, introduced subsequently, each one sufficient to produce complete muscular paralysis, likewise failed to disturb the E. E. G. On occasion, the E. E. G. was permanently distorted following the injection of a single massive dose (sufficient to produce complete paralysis for more than 4 to 6 hours). This effect was probably due to disturbed metabolism (reduction in the amount of available oxygen) since the blood pressure falls, temporarily, following the injection of even moderate dosage of the drug.[5,7] When artificial respiration was eliminated, the E. E. G. disappeared, to reappear undistorted, or permanently impaired, depending upon the length of the unrespirated interval. This effect, however, was not due to the direct action of the drug upon the cortex, but rather the indirect consequence of the lack of oxygen required to sustain normal cortical metabolism. Unlike the mammal, the curarized frog survives without tracheal insufflation due to the presence of the accessory skin respiratory mechanism. The disappearance of the E. E. G. in the curarized frog therefore, is more likely produced by the reduction in available oxygen rather than the *direct* effect of curare upon the cortex, as maintained by Feitelberg and Pick.[8]

Libet et al. have also reported the persistence of the cortical activity in curarized dogs subjected to metrazol.[9] No extended tests were made by these investigators with curare alone, and the metrazol disturbed the E. E. G. considerably. Their results, however, are in agreement with the present data in that the E. E. G. did not disappear following curarization, or, for that matter, after the metrazol took effect.

Summary. So long as proper artificial respiration is given, normal cortical activity, as measured by the E. E. G., persists undisturbed in both the dog and the monkey during complete striated muscular paralysis induced with erythroidine. The difference in results reported here with mammals and that previously reported by other workers in the frog (complete elimination of the E. E. G.) is interpreted to be due to a reduction in the available oxygen necessary for normal cortical metabolism in the latter organism.

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Some New Choline Esters with Cycloplegic and Mydriatic Action.*

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Choline derivatives such as acetylcholine and carbamylcholine (doryl) produce constriction of the pupil and contraction of the ciliary muscle. The halide salts of these compounds have little effect on the surface tension of water, *i.e.*, they are relatively surface-inactive; as surface activity has a profound influence on many biologic phenomena, it was believed choline derivatives which were surface-active might have an enhanced or even

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