

Influence of Electronarcosis on Secretory Activity of the Pituitary Gland.*

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Since 1938, electroshock therapy has been widely used in certain mental disorders, particularly in the involutional psychoses. More recently a related procedure, electronarcosis, has been studied in animals and in man with a view toward determining its suitability and therapeutic value in the treatment of schizophrenia.^{1,2} During the past several years investigations have been in progress in which various physiological effects of electronarcosis have been examined.²⁻⁴

Because of the position of the pituitary gland with respect to the path of the current and the possibility of either direct or indirect hypophyseal stimulation in consequence of the current application, it has seemed important to determine whether the pituitary secretory activity is influenced by electronarcosis. Guinea pigs and dogs have been used in the present investigation.

Methods. Electronarcosis was induced with 60 cycle sinusoidal current through electrodes placed over the temporal region according to the method previously described;¹ an initial current of high intensity (250 milliamperes for dogs, 50 milliamperes for guinea pigs) was applied for 30 seconds, after which the current was reduced to a level which just permitted a return of respiration (50 milliamperes for dogs, 7 milliamperes for guinea pigs). In

the experiments on dogs the electrodes were padded brass discs 2 cm in diameter, moistened with salt solution and held in position by bandaging. To assure contact, an electrode jelly was used. In the guinea pig experiments smaller electrodes (1 cm) were used.

On completion of the series of electronarcoses in guinea pigs the animals were sacrificed, and their thyroids, adrenals, and ovaries were removed, weighed and compared with those of animals kept and killed under the same conditions but without electronarcosis.

Blood was taken from dogs before and after a series of electronarcoses, and the concentration of thyrotropic hormone was determined by the method of Smelser⁵ using day-old Austra-white cockerels. The chicks were kept in an incubator in which a temperature of 33° C was maintained. Groups of about 10 chicks were used; a group of uninjected controls was kept in the same cage with each injected group.

Results. Symptoms of Electronarcosis.

Dogs: The symptoms which occur when electronarcosis is applied to dogs have been comprehensively and adequately presented.^{1,2}

Guinea pigs: Since electronarcosis in guinea pigs has not previously been described, the symptoms which they most uniformly show may briefly be considered. Immediately upon application of the high initial current, the animal falls over on one side, and almost at once develops a strong extensor spasm which usually is diminished to some extent after about 25 sec. Respiration is arrested during the entire 30 sec. application of high current, and does not return until about 15 sec. after the current has been reduced to the maintenance level. The high initial current pro-

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¹ van Harreveld, A., Plesset, M. S., and Wiersma, C. A. G., *Am. J. Physiol.*, 1942, **137**, 39.

² Frostig, J. P., van Harreveld, A., Reznick, S., Tyler, D. B., and Wiersma, C. A. G., *Arch. Neurol. Psychiat.*, 1944, **51**, 232.

³ van Harreveld, A., Tyler, D. B., and Wiersma, C. A. G., *Am. J. Physiol.*, 1943, **139**, 171.

⁴ Globus, J. H., van Harreveld, A., and Wiersma, C. A. G., *J. Neuropath. Exp. Neurol.*, 1943, **2**, 263.

⁵ Smelser, G. K., *Endocrinology*, 1938, **23**, 429.

⁶ Uotila, U. U., *Endocrinology*, 1939, **25**, 63.

duces regularly ejaculation in male guinea pigs, which does not occur in either dogs or man. Upon reducing the current to about 7 milliamperes most of the remaining extensor tone disappears, with the accompaniment, as a rule, of a few clonic twitches of the legs. Thereafter the animal becomes quiet, shows usually no response to severe pinching of the front feet, although in the hind feet the flexor reflex is frequently maintained at a low intensity. Pricking the skin over the body and head results in no response. Neither righting nor supporting reflexes are present. Considerable tone is found in nearly all guinea pigs, and frequently a more or less marked opisthotonic position is observed.

More like electronarcosis in man than in dogs, this quiet picture is gradually replaced in the course of the narcosis by an increasingly noticeable unrest or hyperkinesis on the part of the guinea pig. This can be suppressed to a greater or lesser extent by raising the current very slowly. However, in the guinea pig, secondary raises in the narcotizing current are often accompanied by a new convulsion, arrest of respiration, and frequently by death of the animal.

Recovery following discontinuation of the current passage is usually immediate. The animal generally shakes its head a few times and then hops away in an apparently normal manner.[‡] In a number of experiments recovery was somewhat delayed, the animal having only weak righting reflexes and little or no supporting tone for several minutes, after which recovery became complete.

Effect of Electronarcosis on the Thyroid Gland. Four guinea pigs were each given a series of 10 daily electronarcoses of 2 min. duration. At the end of the series the animals were killed and their thyroid glands removed,

‡ In 2 animals a complete motor paralysis of the hind legs developed following a series of electronarcoses. Postmortem examination disclosed, however, that this condition was due to a trauma of the spinal cord resulting from compression by the vertebrae during the strong extensor spasm which occurred during the initial stages of electronarcosis. Both of these accidents occurred when unusually high initial currents were used.

TABLE I.
Influence of Electronarcosis on the Thyroid Gland in Guinea Pigs.

No. of animals	No. of electronarcoses	Epithelial height (mean of 100 follicles in μ)
5	0	5.54
4	10 (2 min)	8.15
1	11 (10 ")	9.54
1	7 (10 ")	8.30

weighed and prepared for histological study.[§] The thyroids of the electronarcotized animals were found to be about 15% heavier than those of the controls. Histological examination showed a picture of moderate hypertrophy as evidenced by an increase in the height of the acinar epithelium from a mean of 5.5μ for the control animals to one of 8.1μ for those subjected to the series of electronarcoses. In a series of 10 min. electronarcoses on 2 animals it was found that the epithelial thickness was somewhat greater than that found in the series of 2 min. duration (Table I.) A marked withdrawal of the margin of the colloid and a conspicuous vacuolization of the colloid were also observed. The ovaries and adrenals of the electronarcotized guinea pigs were also from 25 to 30% heavier than those of the control animals.

In an earlier series of dog experiments in which electronarcosis was given for other purposes, the thyroids were removed and examined microhistometrically. Two of the dogs had been subjected to a prolonged series of electronarcoses prior to the acute experiment, 2 had had but a single previous electronarcosis, and the other 3 had not had any electronarcoses. No significant difference in the thickness of the thyroid epithelial cells existed between the control animals and those which had received a single previous electronarcosis. Those which had been subjected to a prolonged series of electronarcoses, however, showed a slight but significant thickening of the follicular cells.

Effect of Electronarcosis on the Concentration of Thyrotropic Hormone in Blood Serum.

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TABLE II.
Influence of a Series of Electronarcoses on Concentration of Thyrotropic Hormone in Dog Plasma as Indicated by Injecting Groups of 10 or More Chicks with the Plasma.

Dog	No. of electronarcoses	Chick thyroids			
		Weight in mg		Epithelial height in μ	
		Control	Injected	Control	Injected
1	Before	0	3.3	3.3	3.6
2		0	2.9	2.9	3.7
3		0	3.8	3.5	2.6
4		0	3.8	3.7	2.6
Mean before electronarcosis			3.3	3.4	3.1
1	After	7	3.2	5.0	3.6
2		5	2.3	3.6	3.3
3		7	2.4	3.1	3.0
4		7	2.4	2.9	3.0
Mean after electronarcoses			2.6	3.7	3.5
					4.6

Four dogs were subjected to electronarcosis once daily. In 3 of the animals 7 electronarcoses were given, in the other, 5. The duration of each treatment was 8 to 10 min. Just before the first, and 24 hours after the last treatment blood was collected from the dog. It was immediately centrifuged to separate the plasma from the cells. The plasma thus obtained was assayed for thyrotropic activity by injecting 0.2 ml of plasma into day-old cockerels daily for 4 days. The chicks were sacrificed on the 5th day and the thyroids removed. The weights of the chick thyroids and the microhistometric analyses of these glands from the post-electronarcotic sera have been tabulated in Table II, together with those of the uninjected control chicks.

The prenarcotic plasma of all 4 dogs showed no thyrotropic activity whatsoever. The mean weights of the thyroid glands of the injected chicks were the same as those of the uninjected controls, and the mean thickness of the acinar epithelium was the same in both groups. Following a series of electronarcoses, however, the dog serum produced a small but definite increase in gland weight and in epithelial height in the injected chicks.

Blood taken from one of the dogs (No. 2) one week after the last electronarcosis showed a reduced thyrotropic activity, and after 2 weeks no such activity was present.

The post-electronarcotic plasma of 3 of the 4 dogs also produced a moderate hypertrophy

of the testes of the chicks used for the thyrotropic hormone assay, indicating that not only the thyrotropic but other endocrinotropic factors may be found in the blood in greater concentrations following the passage of electronarcotizing currents.

Conclusions. Experimental evidence indicates that a series of electronarcoses in animals results in hypertrophy of the thyroid, adrenals, and gonads. Since in the blood of electronarcotized dogs an increase in thyrotropic substance is found, it is believed that the mechanism by which this thyroid hypertrophy is obtained is by way of an increased secretion of the pituitary hormones. It might be conceivable that the general cortical and subcortical stimulation which results from passage of current through the brain could produce a direct nervous stimulation of the respective endocrine organs. However, whereas direct stimulation of certain endocrine glands is possible,⁶ the response to such nervous stimulation is of a much smaller order than that resulting from activation of the organ by the specific hypophyseal "trophic" hormone. That direct stimulation of the thyroid is most likely not involved in the hypertrophic response to electronarcosis is shown by the increased thyrotropic activity imparted to dog serum by subjecting the dog to a series of electronarcoses. The increased endocrinotropic activity seems to be only temporary.