EFFECT OF POLARIZATION OF CERTAIN SUBDIVISIONS OF THE BRAIN ON THE FORMATION OF APOMORPHINE VOMITING IN DOGS

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It has been shown experimentally that the formation of the vomiting act takes place as a result of the involvement of the structures of the reticular formation of the brain stem and also, possibly, of other parts of the subcortex and of the cortex [1, 2, 9-11, 17, 20-22]. However, neither the conditions favoring the onset or inhibition of this act nor the mutual influence of the various parts of the brain during the formation of vomiting has yet been explained. A highly effective method of studying the mechanism of nervous processes is that of polarization. Judging by a number of investigations [6, 7, 15], polarization of the brain causes changes in the excitability of the neurons of the reticular formation and in the conditions of their interconnected function. The method of polarization can therefore be used in addition to study the mechanism of formation of the vomiting act. The object of this investigation was to study the effect of polarization of the medulla and of other parts of the brain on the formation of apomorphine vomiting.

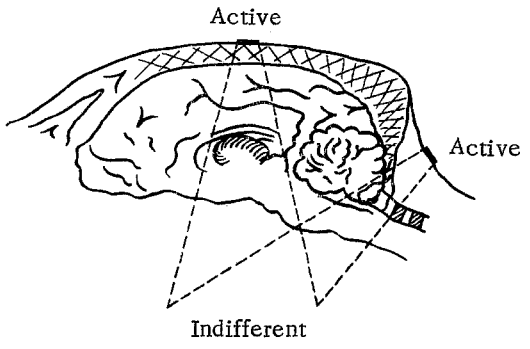
EXPERIMENTAL

Observations were made on dogs in chronic experimental conditions. The active electrode (1 cm^2) was placed either on the depilated skin on the dorsal surface of the animal's neck between the first cervical vertebra and the occipital bone, or on the cranial bones in the parietal region. The indifferent electrode (4 × 5 cm) was fixed to the skin of the neck (below the angle of the lower jaw). The areas of the brain falling within the polarization zone are indicated in the figure. The polarizing current, of ascending and descending direction and of a strength of 5-10 mA, was switched on at various time intervals (30-45 sec, 1 min 30 sec, 1 min 45 sec and 2 min) and maintained until 3 min 30 sec after injection of apomorphine.

Before and after the polarization experiment, the effect of subthreshold and threshold doses of apomorphine was tested in each animal. The threshold dose was taken to be the smallest dose of apomorphine which, when injected intravenously in 0.01% concentration, caused the animal to vomit. Our previous investigations [2, 3, 9] showed that if a single daily intravenous injection of apomorphine was given to dogs (and the experimental conditions were kept strictly constant), the threshold dose remained stable for a month. These findings are in agreement with those obtained by other authors [17, 20-22, etc.]. To provide additional, indirect evidence of the formation of the act of vomiting, the respiratory movements were recorded on a mechanograph. It has been found [8] that the intermittent increase in pressure inside the stomach and the change in the rate and depth of respiration during the formation of the vomiting act in dogs coincide in time. The experiment was performed once daily, 18-20 h after the animals were fed. Altogether two series of observations were made in 224 experiments with polarization of the brain and 650 control tests on seven dogs.

DISCUSSION OF RESULTS

The experimental results are summarized in the table. In all 79 experiments of series I, anodization of the medulla prevented the onset of vomiting, and often also the preliminary nausea after injection of threshold doses of



Scheme of polarization of the brain.

apomorphine. An increase in the strength of the current to 10 mA was accompanied by an increase in the inhibitory action of anodic polarization on the development of nausea and by the depression of vomiting. Total suppression of the vomiting effect of apomorphine was also observed in all 13 experiments conducted on the same animals when the active electrode was located more rostrally, in the parietal region.

In the experiments of series II the cathode was the active electrode. Cathodic polarization of the medulla, 30-45 sec after injection of threshold doses of apomorphine, prevented the onset of vomiting in 17 of 23 experiments (see the table). If the cathodic polarization of the brain began 60-90 sec after the injection of threshold doses of apomorphine, vomiting supervened in 32 of the 41 experiments. When the cathodic polarization of the medulla was started later, between 1 min 45 sec and 2 min after injection of threshold doses of apomorphine, vomiting developed in only 5 of the 24 experiments. Hence, phenomena developed which were opposite to those observed during cathode polarization of the medulla starting 60-90 sec after injection of apomorphine. In two dogs the inhibition of the vomiting act was inconstant. An increase in the strength of the current of 10 mA shortened the time and reduced the number of experiments in which vomiting took place, with polarization of the medulla in this particular direction.

In order to detect any possible potentiation of the vomiting action of apomorphine under the influence of cathodic polarization of the medulla, in the next group of experiments the same animals were given subthreshold doses of apomorphine instead of threshold doses. These experiments showed that the application of cathodic polarization by a current of strength 5 mA 60-90 sec after injection of subthreshold doses of apomorphine led to the onset of vomiting in 15 of 20 experiments.

In the next group of experiments the active electrode was placed in the parietal region and the following parts of the brain were subjected to cathodic polarization: the sensorimotor cortex, the thalamus and other suprabulbar formations. Vomiting took place after injection of threshold doses of apomorphine in only 2 of 24 such experiments (see table). An increase in the strength of the current of 10 mA did not alter the trend of the reaction. Although threshold doses of apomorphine were injected, vomiting did not take place. Hence, during cathodic polarization of the middle portions of the brain, in contrast to polarization of the medulla, inhibition of the vomiting action of apomorphine, rather than its potentiation, was observed.

Electrophysiological investigations have shown that in galvanization experiments the parts of the brain to undergo polarization are mainly those whose axons and cells lie in the line of the polarizing current, and are located closer to the active electrode. The figure shows that when the active electrode is in the parietal position, the polarized areas are principally the sensorimotor area of the cortex (P_2C_1 – area praecoronalis prima), the thalamus and part of the diencephalon. These parts of the brain are known to be associated with autonomic functions [5, 13, 14, 18, 19].

When the active electrode was placed in the occipital position, mainly the structures of the reticular formation were polarized. It has been shown [17, 20-22] that these formations play an active part in the formation of vomiting. Apomorphine, when injected into the blood stream, initially activates the trigger zone, and possibly other chemoreceptor zones [1]. Excitation is transmitted from these zones to the cells of the lateral reticular formation of the medulla, the site of the vomiting coordinating center.

Cathodization of the medulla causes depolarization of the neurons of the reticular formation and thereby facilitates the onset of vomiting. This action is manifested, however, only for a definite range of intervals between the injection of apomorphine and the onset of polarization, namely between 45 sec and 1 min 45 sec after the injection of apomorphine.

This demonstrates that the process of development of the vomiting act after injection of apomorphine is characterized by definite time relationships. If the polarization properties of the neurons of the reticular formation of the medulla are changed too soon or too late, the harmonious functioning of the neurons coordinating the interconnected action of the various centers concerned in the act of vomiting is disturbed.

TABLE 1. Effect of Polarization of the Brain on the Formation of Apomorphine Vomiting (pooled results of 234 experiments on 7 dogs)

Direction of polarization	Time of onset of polarization after injection of apomorphine	Area of brain polarized: medulla; dose of apomorphine: threshold; effect against background of polarization by a current with a strength of: 5–10 mA; −	Area of brain polarized: medulla; dose of apomorphine: threshold; 5–10 mA; +	Area of brain polarized: medulla; dose of apomorphine: subthreshold; 5 mA; −	Area of brain polarized: medulla; dose of apomorphine: subthreshold; 5 mA; +	Area of brain polarized: cortex and subcortical structures; dose of apomorphine: threshold; 5–10 mA; −	Area of brain polarized: cortex and subcortical structures; dose of apomorphine: threshold; 5–10 mA; +
Anode	30—45 sec	24	0	—	—	5	0
	1—1½ min	36	0	—	—	7	0
	2 sec	19	0	—	—	1	0
Cathode	30—45 sec	17	6	—	—	6	1
	1—1½ min	9	32	5	15	14	1
	1 min. 45 sec — 2 min	19	5	—	—	2	0

Conventional signs: −) absence of vomiting after injection of apomorphine; +) appearance of vomiting; numbers) number of experiments.

Depolarization of the neurons of the reticular formation (cathodization) after the injection of apomorphine probably leads to an increase in the excitability of the neurons of the lateral reticular formation, facilitating the reception of impulses from the chemoreceptor zones of the vomiting center and the excitation of the centers taking part in vomiting. In these conditions vomiting ensues after what hitherto were subthreshold doses of apomorphine. Conversely, anodization of the medulla causes hyperpolarization of these structures and lowers the excitability of the neurons of the reticular formation, and these results are reflected in the suppression of vomiting after threshold, and even superthreshold, doses of apomorphine.

Investigation of the bioelectrical reactions of single reticular neurons [6] has shown that hyperpolarization leads to inhibition or slowing of the activity of these neurons and, consequently, to a lowering of the excitation of the individual centers. This phenomenon may be regarded as inhibition of "anelectrotonic type" [4].

Irrespective of the direction of the polarization current, polarization of the middle portions of the brain—the sensorimotor cortex, the thalamus and the other suprabulbar portions of the brain—inhibited vomiting in nearly every case when the same strength of current and the same time relationships were used. This may probably be explained by assuming that the parts of the brain lying in the zone of polarization are not directly related to the formation of the vomiting act, i.e., they are not included in the concept of the "vomiting center," although they are functionally connected with the bulbar structures. This view is supported by work [17] which has shown that the injection of apomorphine into the lateral ventricles of the brain does not give rise to vomiting until the drug enters the fourth ventricle and reaches the chemoreceptor trigger zone. Evidently the depression of apomorphine vomiting during polarization of the suprabulbar structures may have the character of reciprocal inhibition, through the cortico-thalamo-, and hypothalamo-reticular connections, rather than being the result of local changes.

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