PHARMACOLOGY

THE EFFECT OF ANESTHETICS ON THE BULBAR AND SPINAL VASOMOTOR FORMATIONS

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According to general opinion the suppression of vascular tone under the effect of anesthetics used in large doses is due to suppression of the bulbar vasomotor center. However, there are no direct experimental proofs of the effect of anesthetics on various components of the bulbar vasomotor center.

Using as a base the literature [1, 11-14, 17] and our own [3, 5] data on the morphological and functional organization of the bulbar vasomotor center, we decided to study in greater detail the effect of urethan and nembutal on its various components. As is known, in the formation of a vascular response participate spinal vasomotor centers to which pulses are sent from the suprasegmental vasomotor formations, therefore, we also investigated the effect of anesthetics on the level of the spinal cord.

EXPERIMENTAL METHOD

The experiments were carried out on 60 decerebrated (transection between the corpora quadrigemina) and spinal (transection at the level of the lower margin of the medulla oblongata) cats. There were 3 series of experiments in all. In the experiments we used the method of local stimulation of 2-3 points of the pons and medulla oblongata by means of isolated nichrome electrodes with a diameter of 30-50 μ [2]. In the spinal animals the lateral cornu of the 7th or 8th thoracic segment was stimulated by similar electrodes. In all experiments there was an histological check of the place of stimulation [7]. The shifts of arterial pressure (pressor and depressor effects) arising as a result of stimulation were recorded in the common carotid artery by the usual method. The magnitude of the vascular response was calculated in absolute figures, since it has been established that a ± 40 mm change of arterial pressure is not reflected in the absolute magnitude of the vascular response arising upon direct stimulation of the vasomotor center. The difference between the magnitude of the reaction before and after administering the anesthetic served as an index of the effect of the substance on the magnitude of the vascular response.

The investigated substances were injected intravenously in the following doses: urethan 25-3800 mg/kg, nembutal 1-45 mg/kg.

EXPERIMENTAL RESULTS

The study of the effect of anesthetics on the pressor and depressor vascular responses produced by point stimulation of the medulla oblongata elicited a definite relationship between the effect of the substance and the topography of the stimulated structure. The bulbar formations, upon stimulation of which pressor effects arose, were joined into 3 groups depending on the sensitivity to anesthetics: vestibular nuclei, medial and lateral reticular formations. The experiments demonstrated that pressor reactions from the vestibular nuclei begin to lessen already from small doses of anesthetics (urethan 50-100 mg/kg, nembutal 1-5 mg/kg), and complete depression was observed upon using non-anesthetic doses (urethan 600-700 mg/kg, nembutal 20 mg/kg). Pressor responses arising upon stimulation of the medial reticular nuclei (giant-cell, ventral, etc), were recorded under the effect of nembutal in doses of 25-35 mg/kg; urethan did not have such an evident depressing effect even in doses exceeding anesthetic (1800-2000 mg/kg). The pressor reactions from the reticular parvicellular nucleus belonging to the lateral reticular structures were quite

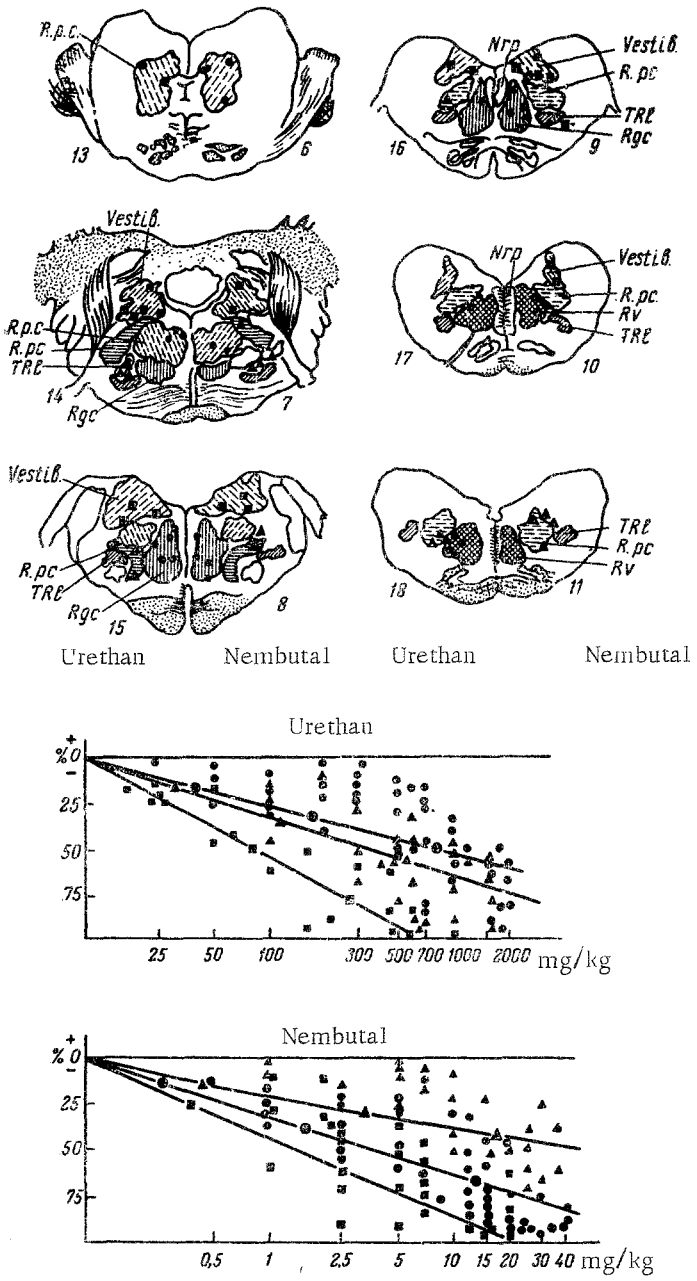

Fig. 1. Diagram of the localization of stimulation and direct.on of changes of pressor reactions in experiments with anesthetics. In the upper part of the figure are diagrams of the cat medulla oblongata. The figures on the left indicate the level of sections after Monnier [15], and on the right after Brodal [12]. The markings on the sections indicate localization of stimulation and their form reflects the type of change of the pressor responses: from the lateral reticular formations (triangles), from the medial reticular formations (circles), from the vestibular nuclei (squares). Rgc) Reticular giant-cell nucleus Rv) reticular ventral nucleus; Rpc) reticular caudal nucleus; pons; Nrp) reticular paramedian nucleus; R. pc) reticular parvicellular nucleus; Trl) lateral reticulospinal tract; Vestib) complex of vestibular nuclei (superior, descending, medial, lateral); X) complex of central structures of vagus nerve. In the lower part of the figure are graphs of the relationship between the dose and magnitude of the pressor reaction after injection of anesthetic. The initial magnitude of the pressor reaction before injection of the anesthetic was taken for the zero line. Along the axis of the ordinate is the degree of depression of the pressor reaction (in % of initial); along the axis of the abscissa (on a logarithmic scale) are doses of urethan or nembutal. The corresponding markings are results of individual observations.

Depression of Pressor Reactions Arising Upon Alternate Stimulation of Bulbar and Spinal Vasomotor Formations Under the Effect of Anesthetics (average data)

Localization of electrode	Urethan (500 mg/kg)	Nembutal (15 mg/kg)
	Degree of depression of reaction (in % of initial)	
Medial reticular nuclei	80	85
Lateral reticular nuclei	60	20
Vestibular nuclei	90	80
Lateral cornua (Th_7-Th_8) of spinal cord	50	35

resistant to anesthetics since they were not depressed at all upon injection of anesthetic doses of urethan and nembutal.

The data of all experiments with the use of urethan and nembutal are shown in Fig. 1.

The depressor reactions from the nuclei of the vagal complex, paramedian reticular nucleus and certain other formations were lowered by half only after the injection of anesthetic doses of urethan and nembutal.

Thus, the vascular reactions caused by stimulation of various components of the bulbar vasomotor center have dissimilar resistance to one and the same anesthetic. In turn the vascular responses from one and the same formation can be depressed differently by urethan and nembutal, as was shown previously [6].

As is known, from the medulla oblongata pass the descending reticulo-spinal, vestibulospinal, and other tracts along which propagation of the vasomotor impulses to the segmental vasomotor formations is apparently accomplished. According to the data in the literature the clumps of synaptic cells in the lateral cornua of the thoracic and a part of the lumbar segments are vascular centers of the spinal cord. Since a change in the magnitude of the vascular response can be caused by the effect of anesthetics at the spinal level, we considered it necessary to study the effect of urethan and nembutal on pressor vascular responses arising upon stimulation of the lateral cornu of the spinal cord. We previously described the method of these experiments in detail [4].

The experiments carried out on spinal cats demonstrated that for a 25% depression of the pressor effects arising upon stimulation of the segmental vasomotor formations, urethan in doses of 200-300 mg/kg must be injected. An increase in the dose of the substance led to a further decrease of the pressor response, however complete depression did not occur even after the injection of urethan in doses of 2500-3500 mg/kg, i.e., in doses appreciably exceeding the anesthetic. Nembutal in equivalent doses more strongly depresses vascular responses from the segmental formations. Thus, in doses of 5-10 mg/kg this substance lowered the pressor responses by 25-35%. Upon an increase in the dose of nembutal we observed in most experiments a further depression of the vasomotor effects. The results of all experiments are summed up in the graph (Fig. 2).

In the III series of experiments upon decerebrated cats we studied the effect of urethan and nembutal on vascular reactions arising with alternate stimulation of the bulbar and spinal vasomotor formations in the same animal. In this case we selected a stimulation force which would cause similar pressor reactions. This made it possible to compare the sensitivity to anesthetics of the reactions arising upon stimulation of the vasomotor formations at a different level. It was established in the experiments that urethan and nembutal in the same dose mainly depressed the pressor effects from most structures of the medulla oblongata (see table).

Thus, the pressor reactions from the reticular giant-cell nucleus (Fig. 3a, 1) and descending vestibular nucleus (a, 2) were almost completely depressed by nembutal in a dose of 10 mg/kg (b, 1,2), whereas the pressor reaction arising upon stimulation of the lateral cornu of the 7th thoracic segment of the spinal cord remained unchanged (a and b, 3).

Our data do not agree with the widespread point of view that the bulbar centers are less sensitive to the effect of anesthetic than the segmental formation of the spinal cord. However, it is necessary to note that among the bulbar structures we also encountered those more resistant to anesthetics, for example the parvicellular reticular nucleus, superior olivary nucleus, intercalated nucleus, ambiguous nucleus, etc.

The obtained data cannot be explained by the effect of anesthetic on the peripheral links of vascular regulation, since we previously demonstrated that urethan and nembutal scarcely changed vascular responses upon stimulation of the preganglionic segment of the splanchnic nerve [4].

Taking into account the extensive connections of individual reticular neurons [12, 16] we can assume that in the formation of vascular responses with point stimulation can participate functional units which do not enter into a given stimulated structure. Therefore, the dissimilar degree of depression of vasomotor reactions under the effect of

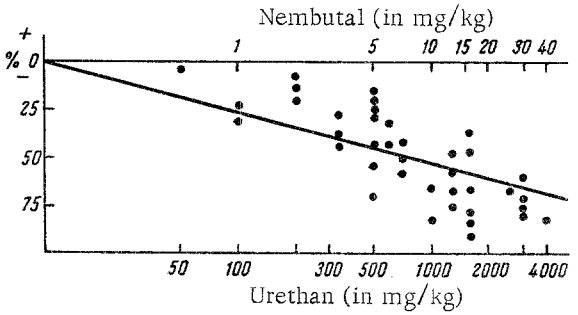

Fig. 2. Relationship between dose of anesthetic and degree of depression of pressor responses arising upon stimulation of spinal formations. Along axis of ordinate is the drop in response (in % of initial level); along axis of abscissa are doses (in a logarithmic scale) of urethan (bottom) and nembutal (top). The dots are results of individual observations.

urethan and nembutal, which we observed in the experiments, is apparently explained not only by the peculiarities of the morphological structure of the stimulated structures themselves, but also by the different sensitivity of their connections with other elements of the brain stem and spinal cord. Testifying in behalf of this assumption are the investigations carried out recently at the cellular level [8-10, 18] in which it was demonstrated that within the brain stem and spinal cord are appreciable individual fluctuations in the sensitivity of neurons to urethan and nembutal.

SUMMARY

Vascular response to local stimulation of various components of the bulbar vasomotor center and of the lateral spinal cord horns (Th_7-Th_8) were recorded in decerebrated and spinal cats. Histological control was carried out in all the experiments. Depression of the vascular responses by

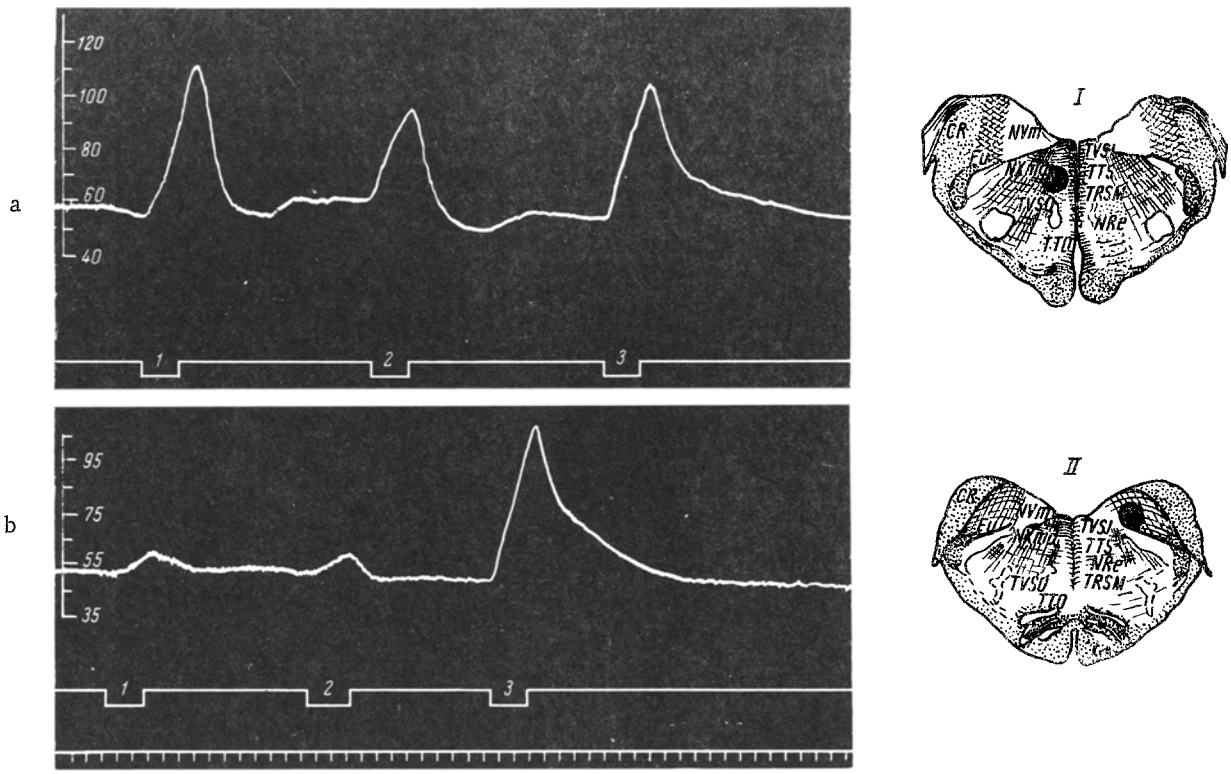

Fig. 3. Effect of nembutal on pressor reactions caused by local stimulation of various bulbar formations (I, II) and of the lateral cornu of the 7th thoracic segment of the spinal cord. a) In the norm; b) 10 min after injection of nembutal in a dose of 10 mg/kg. The figures on the stimulation marker designate the numeral of the electrodes in conformity with their localization. Localization of stimulation: 1) giant-cell reticular nucleus; 2) descending vestibular nucleus; 3) lateral cornu (Th_7) of spinal cord. Significance of curve (from top down): frontal sections of the cat medulla oblongata from Monnier's atlas [15]; recording of arterial pressure; stimulation marker; time marker (5 sec).

urethane (25-3,800 mg/kg) and nembutal (1-45 mg/kg) differed depending on the localization of stimulation (medial and lateral reticular nuclei, vestibular and vagus nuclei). The same agent exhibited a different effect on the vascular reactions caused by stimulation of various bulbar vasomotor center components.

In comparing the efficacy of the depressive effect produced by the anesthetics at the bulbar and the spinal level in experiments on the same animal it appeared that the minimal doses of urethane and nembutal primarily depressed the pressor effects from the bulbar vasomotor structures.

The data obtained may evidently be explained by the peculiarities of morphological structure of the vasomotor formations and their tracts, as well as by a different sensitivity of the reticular neurones to urethane and nembutal.

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