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CHARACTERISTICS OF LATE VASOCONSTRICTOR A-RESPONSE IN CATS AFTER DECEREBRATION AT DIFFERENT LEVELS OF THE BRAIN STEM

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Single stimulation of A-fibers of the tibial nerve in cats decerebrated at the rostral border of the mesencephalon (mesencephalic animals) at various levels of the pons, including the region of the pontobulbar junction, and the most rostral levels of the medulla (pontine animals), or rather more caudally to this region (bulbar animals), evoked a late response in the renal nerve, consisting of excitatory and inhibitory components. In 53% of experiments on pontine animals, 42% of experiments on mesencephalic animals, but only 18% of experiments on bulbar animals the excitatory component of the response was small or even absent. The system generating the inhibitory component of the response was most active and most excitable in the pontine cats. However, features indicating relative potentiation of the inhibitory component of action of impulses in A-afferents on vasoconstrictor neurons in the pontine animals were not sufficiently constant to account for the switch from hypertensive reflexes to impulses from somatic A-afferents into hypotensive, taking place after disconnection of the structures of the pontobulbar junction and rostral levels of the medulla from the mesencephalon.

KEY WORDS: decerebration; somatosympathetic responses; blood pressure reflexes.

The A-afferent volley of spinal nerves can evoke discharges in sympathetic nerves which, depending on their latent period, are known as early, late, and very late A-responses [8,14,16,17]. The properties of the late A-response has been studied chiefly in experiments on anesthetized animals with an intact brain. Some workers [9,10] have also observed this response in cats after pre- or intercollicular decerebration, but the characteristics of the late A-response after transection of the brain stem at different levels has not been compared in detail.

The object of the present investigation was accordingly to study the reason why hypertensive reflexes to impulses in somatic A-afferents change into hypotensive when structures of the pontobulbar junction and rostral levels of the medulla are disconnected from the mesencephalon [1-3].

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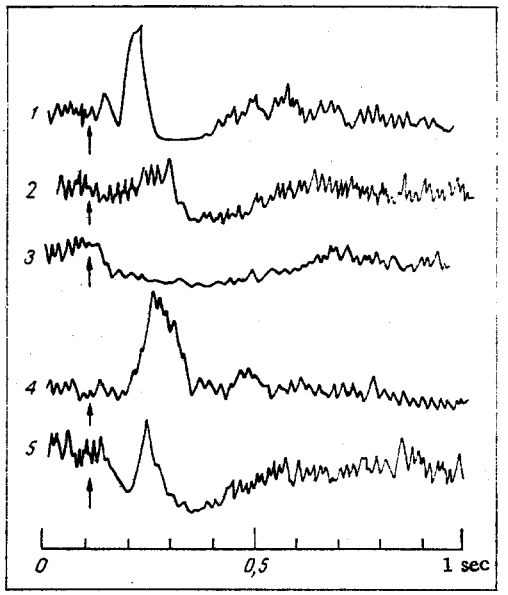

Fig. 1. Form of appearance of components of late A-response in decerebrate animals. Amplitude of stimuli 30 thresholds. Averaging of 20 realizations of responses to single (applied at intervals of 5 sec) stimuli in mesencephalic (1,4), bulbar (2), and pontine (3,5) animals. Arrows indicate times of application of stimuli.

EXPERIMENTAL METHOD

Cats were decerebrated under ether anesthesia by high-frequency electrocoagulation of the brain tissue [2-4]. In 12 cats the brain stem was divided in a plane passing through the mammillary bodies and just anteriorly to the corpora quadrigemina (mesencephalic animals); in 17 cats at different levels of the pons and also in the region of the pontobulbar junction and the most rostral levels of the medulla (this group was conventionally described as pontine animals); in 11 cats somewhat more caudally to this region (bulbar animals). The caudal boundary of division of the brain stem was identified in brain sections fixed in formalin.

After decerebration the ether anesthesia was stopped and, after an interval of 2-4 h, investigation of responses evoked in the renal nerve (representative of the vasoconstrictor system [5, 8, 9]) by volleys of impulses in A-afferents of the tibial nerve (TN) began. The nerve was divided at the metatarsal joint and stimulated electrically (pulses 0.1 msec in duration, 0.1-3.0 V in amplitude, or to excite A + C fibers of TN, duration 1.0 msec, amplitude 15 V), applied through an isolating transformer from an ÉSL-1 stimulator, controlled by an ESU-1 stimulator. An amplitude of 0.1 V, corresponding to the threshold of excitation of Aβ-fibers of TN, was taken as the unit of amplitude of the stimuli (1 threshold) [5, 8]. The left renal nerve, isolated extraperitoneally, was divided, flooded with warmed mineral oil, and connected through bipolar platinum electrodes to the input of a UBP-1-02 amplifier. The output of the amplifier was connected (through a bridge circuit, converting bipolar signals into monopolar) with an ATAS-201 instrument, carrying out coherent (to the stimulating pulses) accumulation of the signals followed by their averaging.

Movements of the animals were prevented by intravenous injection of succinylcholine (0.15 mg/kg·min continuously) or flaxedil (a single injection of 4 mg/kg, with addition of smaller doses as required). The volume of artificial ventilation of the lungs was determined from nomograms [11]. The rectal temperature was kept between 36 and 38°C by means of an electric heater. The pressure in the right femoral artery (contralateral to the stimulated TN) was measured by a mercury manometer. In all the experiments it lay between 110 and 160 mm Hg.

EXPERIMENTAL RESULTS

Like other investigators [12,13], we observed the appearance of an early A-response in the form of a short discharge with a latent period of not more than 50 msec in this nerve [5] and only extremely rarely in the postganglionic renal nerve. A late response (LR) was detected in all the decerebrate animals, although it could be absent in some of them during the first period of the experiment.

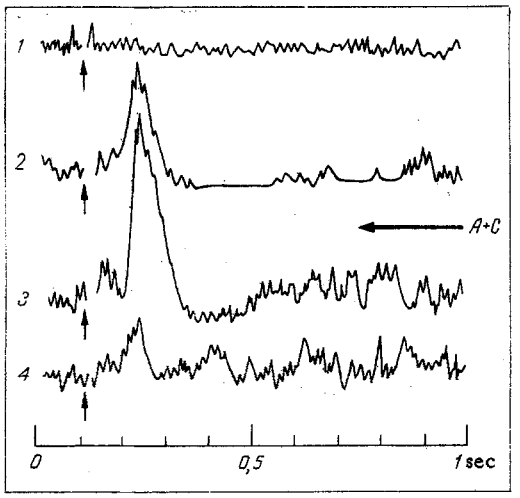

Fig. 2. Overcoming the state of "blockade" of late A-response (1) in mesencephalic cat during stimulation of TN with short volley of stimuli (2) and after repeated tetanic stimulation of A + C afferents of TN (3, 4). 1-3) Amplitude of stimuli 30 thresholds; 2,3) frequency 3 pulses/100 sec; 4) amplitude of stimuli 3 thresholds. Remainder of legend as in Fig. 1.

Most frequently, just as in anesthetized animals with an intact brain, the excitatory component of LR — a discharge with a latent period of the order of 100 msec — was followed by temporary interruption of tonic discharges — the inhibitory component of LR (Fig. 1: 1). In individual animals at certain periods of the experiment, the averaged excitatory component of LR was only a little stronger than the averaged tonic discharges (Fig. 1: 2), whereas at other times of the same experiment it was considerably greater. In some animals the excitatory component was persistently absent although the inhibitory component was well defined (Fig. 1: 3). Occasionally, when the excitatory component was clearly defined, the inhibitory component was absent (Fig. 1: 4). Finally, in some animals inhibition preceded the excitatory component and continued after its end (Fig. 1: 5). The existence of such pre-excitatory inhibition has also been described in anesthetized animals with an intact brain [15].

The variation in the shape of LR (Fig. 1), indicates that the appearance of its excitatory and inhibitory components can be regarded as the result of activation of two independent interneuronal pathways, each of which could in principle be the sole acting channel of transmission of impulses of somatic A-afferents to the vasoconstrictor neurons. To evaluate the state of the systems generating these components of LR after the different decerebrations, records of all 40 experiments obtained under the following identical conditions were compared: 1) stimulation of TN with a strength of 30 thresholds (sufficient to cause excitation of nearly all its group A afferents [5]), 2) number of averaged realizations 20, 3) period of repetition of single stimuli 5 sec, 4) recording in first stage of experiment, i.e., before stimulation of C-afferents of TN.

Comparison of these records gave the following results: First, an intensive excitatory component of LR, much stronger than the mean level of the tonic discharges (compare Fig. 1: 1 and 4-5) was observed most frequently in the bulbar animals (82% of experiments) and least frequently in the pontine animals (47% of experiments); in the mesencephalic animals an intensive excitatory component of LR occurred in 58% of experiments; second, most experiments in which the excitatory component of LR was absent (Fig. 1: 3) occurred in the group of pontine animals (24%), and rather fewer in the mesencephalic group (17%); among the bulbar animals there were no experiments in which the excitatory components of LR were absent. The occurrence of only a weak excitatory component of LR (Fig. 1: 2), or indeed its total absence, is evidence of an inhibited state of the system generating this component. Consequently, the system generating the excitatory component of LR in the mesencephalic animals was inhibited in 42%, in the pontine animals in 53%, but in the bulbar animals in only 18% of experiments.

The important result is that in the mesencephalic animals a state of "blockade" of the excitatory component of LR was usually accompanied by absence of its inhibitory component also (Fig. 2: 1), and this state could easily be overcome by stimulation of A-afferents of TN with a short high-frequency volley of stimuli

(Fig. 2: 2) or by preliminary stimulation of A + C afferents of TN (Fig. 2: 3), after which even weak single volleys of A-afferents caused a well-marked LR (Fig. 2: 4). By contrast with this, blockade of the excitatory component of LR in the pontine animals did not affect its inhibitory component (Fig. 1: 3) and neither an improvement in the conditions of temporal summation in the arc of LR nor an increase in the excitability of this arc by preliminary tetanic stimulation of the A + C afferents of TN [6] was able to cause the appearance of an excitatory component of LR. In half of the pontine animals persistent inhibition of the system generating the excitatory component of LR thus appeared.

The state of the system generating the inhibitory component of LR was assessed by the presence, completeness, and duration of inhibition of tonic discharges. In 33% of mesencephalic animals the inhibitory component was absent (see Figs. 1: 4 and 2: 1), whereas in the bulbar and pontine animals the same phenomenon was found extremely rarely — in only one animal from each group. Among the bulbar and mesencephalic animals, the number of experiments in which inhibition of the tonic discharges was complete was small, but among the pontine animals the number of these experiments was considerable, namely 59%. The duration of inhibition in mesencephalic cats did not exceed 0.27 sec and in bulbar cats 0.36 sec, but in five pontine animals it was appreciably greater than 0.5 sec, and even reached 1-1.5 sec, i.e., values considered to be normal for anesthetized animals with an intact brain [14,17]. Consequently, a tendency toward the appearance of a more marked inhibitory component of LR was characteristic of the pontine decerebrations: Inhibition was often complete, and sometimes it was very prolonged.

The threshold for detection of the inhibitory component of LR in all the decerebrate animals was either a little below the threshold of detection of its excitatory component (this was particularly characteristic of the pontine animals — in 86% of experiments), or it coincided with the latter (in 40% of experiments in mesencephalic and 60% of experiments in bulbar animals). No appreciable differences could be found in the threshold of appearance of the excitatory component of LR that could be linked with the levels of decerebration. It can therefore be suggested that the persistent inhibition of the excitatory component of LR in 53% of pontine cats was due, not to a decrease in the excitability of the corresponding interneuron system, but to a decrease in the number of preganglionic vasoconstrictor neurons capable of responding with a discharge to an A-afferent volley. The possibility of such a change in different states of the CNS will be clear, in principle, from Fig. 2.

The suprabulbar structures responsible for controlling excitability of spinal LR arcs [5, 7, 8] are evidently capable of changing the efficiency of signal transmission along interneuronal pathways with excitatory and inhibitory action on neurons of the spinal common path — preganglionic neurons — or even causing complete blockage of one or other of these pathways. In this connection it is interesting that it was in some of the pontine cats that only an inhibitory component of LR could appear (Fig. 1: 3), and its duration could be particularly long. It seems likely that these phenomena reflect enhanced activity of the spinal pathway for transmission of the inhibitory component of LR [7, 8, 18] and that inhibition of the excitatory component of LR in pontine cats is the result of the enhanced effect of this inhibitory pathway on preganglionic neurons.

Although several features pointing to relative enhancement of the inhibitory component of the action of impulses in A-afferents of TN could be found in the LR of the pontine cats, they were not sufficiently constant to explain why it is in these animals that even strong tetanic stimulation of A-afferents lowers the arterial blood pressure [1, 3]. The decisive factor for this effect is inhibition of the very late A-response in the pontine animals, which may lead to predominance of the inhibitory action of impulses along A-afferents on the system of vasoconstrictor neurons and, correspondingly, to the appearance of depressor reflexes instead of pressor.

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FORMATION OF COMPLEXES OF EPILEPTIC ACTIVITY IN THE CEREBRAL CORTEX UNDER THE INFLUENCE OF A DETERMINANT FOCUS INDUCED BY ACETYLCHOLINE

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Foci of enhanced excitability, with independent discharge patterns, were created by means of weak solutions of strychnine and penicillin in cats. The creation of a hyperactive focus by means of acetylcholine (ACh) and neostigmine led initially to an increase in the amplitude and frequency of the paroxysmal discharges in the nearest foci of activity, and later in foci remote from the hyperactive focus. Qualitative changes subsequently developed in the pattern of activity of the strychnine and penicillin foci (with the appearance of ACh-activity in them) and a single functional complex of foci with the same discharge pattern as the ACh-focus was formed. The latter thus plays the role of determinant structure. Inhibition of the activity of the determinant focus was followed by disappearance of ACh-activity in the other foci, restoration of original (penicillin or strychnine) activity in them, and destruction of the epileptic complex.

KEY WORDS: determinant focus; epileptic complex; neocortex; strychnine; penicillin; acetylcholine.

Previous investigations showed [3-6] that a focus of powerful excitation created in the orbital or temporal region of the cerebral cortex can play the role of a determinant structure [1,2], i.e., one which determines the character of activity of other separate foci of paroxysmal activity, strengthens excitation in them, unites them into a single functional complex, and determines the behavior of the complex as a whole. Such a complex could be destroyed by inhibiting the action of the determinant focus, whereas disconnection of the other foci forming the complex had no significant effect on its behavior. In the investigations cited above a focus created by means of strychnine and penicillin, which disturbed various types of inhibition [7-11], possessed determinant properties.

In the present investigation acetylcholine (ACh) was used to create the determinant focus.

The use of ACh is interesting from several points of view. It is known to cause direct depolarization of neurons [12,13]; the mechanisms of formation and the functional structure of the focus of activity arising under the influence of ACh differ from those produced by the action of strychnine and penicillin; the character of activity in an ACh-focus is also different in principle. The question arose whether such a focus could play

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