EFFECT OF WEAK SOLUTIONS OF ALDEHYDES ON CHANGES IN THE RAT EEG

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Previous investigations have shown that the safe periods of cerebral ischemia can be essentially prolonged by the use of weak solutions of aldehydes as protectors [4-6]. The protective action of aldehydes is considered to be based on inhibition of the biochemical and physiological responses. There have been many investigations of the biochemical anti-ischemic mechanisms of action of aldehydes, notably formaldehyde [2, 3, 7, 8], but little information has been obtained about physiological reactions taking place when aldehydes interact with nerve tissue. Moreover, we do not know which of these reactions may promote a favorable course of the ischemic and, in particular, the postischemic process. The aim of the present investigation was to study physiological responses of the CNS to small doses of weak solutions of aldehydes and mixtures of aldehydes.

EXPERIMENTAL METHOD

Experiments were carried out on 50 mature noninbred male rats weighing 240-280 g. Gold plated electrodes 0.4 mm in diameter were implanted into the rats' brain. The electrodes were located epidurally, bilaterally, in the medial and lateral regions of the frontoparietal cortex, according to the atlas of Paxinos and Watson [15], and were fixed by self-hardening plastics. The reference electrode was secured in the nasal bones. To apply the test solutions the right axillary artery was catheterized. Isotonic solutions of formaldehyde for glutaraldehyde, in concentrations of 0.2 and 0.02%, respectively, were injected in a dose of 0.1 or 0.2 ml/100 g body weight. A mixture of these same aldehydes in the proportion of 1:1 was used in a volume of 0.2 ml/100 g body weight. These doses of aldehydes were those which prolonged the safe period of total cerebral ischemia. As the control, the same volume of physiological saline was injected. Superficial anesthesia with hexobarbital and ether was used for the experiments. Anesthesia was induced with 1% hexobarbital solution in a dose of 0.5 ml/100 g body weight. To maintain a constant level of anesthesia, ether was inhaled. The EEG was recorded on a "San'ei" electroencephalograph (Japan). Regions of the EEG 10 sec in duration immediately before injection of the solutions and 1, 3, 5, 20, and 25 min after their injection were analyzed. In some cases, for a more detailed analysis the EEG was processed during the interval from the 5th to the 20th minute and at the 30th minute. An "Elektronika BK-0010" personal computer carried out this processing by the method of spectral analysis. The significance of differences was calculated by Cochran's test for a level of significance of $p \leq 0.05$.

EXPERIMENTAL RESULTS

Injection of physiological saline (seven experiments) caused an increase in amplitude of the EEG 20-30 sec after infusion on average by 16.3-0.7%. This change in amplitude was observed in both hemispheres in both the motor and the sensory zone of the cortex. The
increase in amplitude was not accompanied by any changes in the spectral composition of the EEG. The amplitude usually returned to its initial level by the 5th minute of the experiment.

When formaldehyde alone was injected (14 experiments) the spectral composition of the EEG likewise remained virtually constant throughout the period of observation. However, formaldehyde did not activate the EEG, but inhibited it. For instance, when 0.1 ml of formaldehyde/100 g body weight was injected, the amplitude of the EEG was reduced on average by 21.6 ± 1.3%. This decrease occurred 20-30 sec after infusion, but lasted for 1.5-2 min. By the end of the 3rd minute, the normal amplitude of the EEG was restored (Fig. 1).

Doubling the dose of formaldehyde enhanced the effect. At the 1st minute the amplitude was reduced on average by 29.4 ± 1.9%, significantly more than the decrease in amplitude of the EEG in response to the smaller dose. The EEG likewise returned to normal at the 3rd minute. By contrast with the previous series, inhibition of the EEG was repeated, starting on average at the 5th minute of observation, and it continued for about 8 min. In this case the decrease in amplitude was 8.2 ± 1.2%. By the 14th minute of the experiment the initial amplitude of the EEG was fully restored (Fig. 1).

The action of glutaraldehyde (11 experiments) caused a similar effect of a temporary reduction in the amplitude of the EEG, whereas its spectral composition remained virtually constant. In this case the first phase of inhibition was reduced but, on the other hand, the depth and duration of the second phase were increased (Fig. 2). An increase in the dose of glutaraldehyde led to a more marked action on the second phase of inhibition of the EEG (Fig. 2).

The action of a mixture of the two aldehydes (18 experiments) was similar in character in general with their action separately. At the 1st minute the amplitude of the EEG was profoundly inhibited on average by 42.2 ± 4.1%. The initial level was restored and the second phase of inhibition developed at the usual times (Fig. 2). This phase was characterized by considerable depth (to 62.7 ± 4.6%) and duration, which was about 18 min. The EEG was restored completely to normal after 25-27 min. In this case also, it is important to note, the spectral composition of the EEG was virtually unchanged throughout the experiment.

Early inhibition of the EEG following injection of weak solutions of aldehydes could be due to their action on vascular reflexogenic zones. Evidence in support of the reflex origin of the first phase of inhibition is given by its rapid onset and the similar times of its course in all series of experiments, although other mechanisms of "rapid" response cannot be ruled out.

We know that aldehydes become involved in metabolism very rapidly [2, 14]. Of the many reactions in which compounds of this class may take part, attention is drawn in particular to their ability to bind with monoaminergic mediators [2, 9, 10-13]. A mechanism of inhibition of the EEG linked, for example, with competitive blocking of membrane receptors by products of interaction of aldehydes and mediators may therefore be suggested. Moreover, it has been shown [1] that condensation products of aldehydes with catecholamines