CHANGES IN THE EEG AND AUTONOMIC RESPONSES IN POISONING BY ORGANIC TIN COMPOUNDS

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Poisoning of rabbits with dichlorodibutyl tin (DCDBT) and tetraethyl tin (TET) caused marked and persistent desynchronization of the EEG and weakening of responses of the heart (ECG) and respiration to stimulation of the upper respiratory tract by ammonia.

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In the comparatively few investigations of the toxicology of organotin compounds the neurotropic character of their action has been reported [2, 5, 6]. However, the general question of the character and mechanisms of functional and structural disturbances of the nervous system arising during poisoning by organotin compounds has received little study. In particular, no attempt has been made to study the state of the autonomic nervous system. Similarly no investigations have been made of the EEG during poisoning by organotin compounds.

In the present investigation we studied certain responses of the heart and respiratory center and the EEG in rabbits in acute poisoning with tetraethyl tin (TET) and dichlorodibutyl tin (DCDBT).

EXPERIMENTAL METHOD

To record the EEG potentials, unipolar constantan wire electrodes were inserted 6-8 days before the experiments began into the skull of rabbits over the frontal and occipital regions of the cortex. The EEG was recorded twice before poisoning began (the day before and the day of administration of the compounds) and daily after poisoning until the animals died. Responses of the heart and respiration to standard stimulation of the sensory endings of the upper respiratory tract with ammonia vapor (the trigeminovagal reflex [1]) were recorded in a similar manner. This test was carried out three times at intervals of 4-5 min in each experiment.

The EEG was recorded in one standard lead and the respiratory excursions of the chest were recorded by means of a piezoelectric detector. The animals were poisoned by a single injection of the compound into the esophagus through a flexible tube. The dose of TET was 25 mg/kg and of DCDBT 100 mg/kg. All the indices were recorded on a Japanese "San-Ai" multichannel encephalograph.

EXPERIMENTAL RESULTS

All the animals receiving TET or DCDBT developed a basically similar picture of poisoning: loss of appetite, adynamia, salivation, untidiness, loss of weight. From time to time muscular spasms were observed. In two cases, while the animals' general condition appeared satisfactory, suddenly they developed convulsions and died from respiratory arrest. All the animals died between 3 and 7 days after poisoning. No special pattern of severity of poisoning over this period could be observed. Likewise no regular changes took place in the reactions of the heart and respiratory center to stimulation of the receptors of the respiratory passages by ammonia. Both the intensity and duration of the responses varied within relatively narrow limits, and analysis of the results revealed only a slight tendency for the responses to ammonia stimulation to weaken. In no case was significant strengthening of the responses observed.

Changes in the EEG were more regular. In all experiments immediately after poisoning the frequency spectrum showed a marked shift into the region of fast waves and at the same time the amplitude

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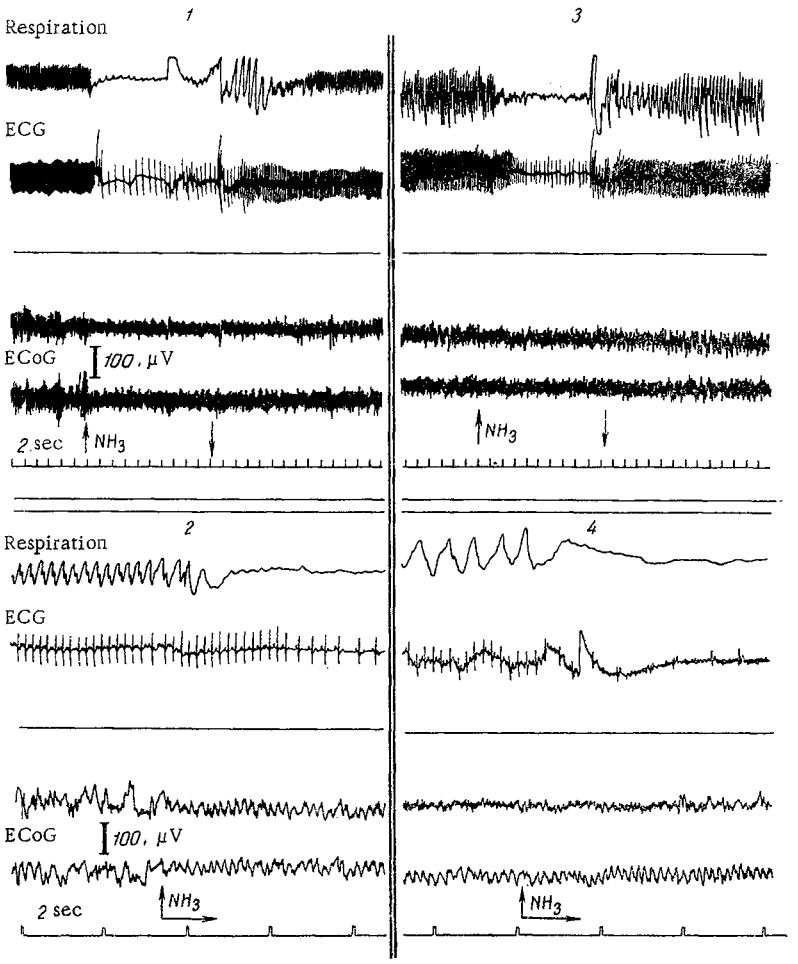

Fig. 1. Changes in ECG, respiration, and ECoG in response to inhalation of ammonia before (1, 2) and after TET poisoning (3, 4).

of the waves fell significantly, i.e., marked and persistent activation (desynchronization) of the EEG took place. Corresponding changes were observed in the reaction of the electrocorticogram (ECoG) to stimulation of receptors of the trigeminal nerve by ammonia. Whereas before poisoning this response was very clearly defined and took the form of activation of the EEG, during development of poisoning, against the background of increasing and persistent desynchronization, the electrical responses rapidly weakened and ultimately disappeared completely (Fig. 1).

It can be concluded from these results that the investigated organotin compounds do not stimulate reflex responses incorporating cholinergic components and in the mechanism of their action on the body they do not resemble cholinomimetic and anticholinesterase substances. They likewise do not increase the general tone of the central parasympathetic nuclei participating in the regulation of cardiac activity. This is confirmed by the fact that bradycardia was not observed in any experiment, in contrast to the findings of Tauberger and Klimmer [6].

It can thus be concluded that individual manifestations which could be regarded a priori as components of a single syndrome of pathological excitation of cholinergic structures in fact cannot be linked together on this basis and have different mechanisms.

So far as the effect of TET and DCDBT on cerebral cortical function is concerned, the ECoG shows that it consists of persistent and diffuse excitation. Our results cannot answer the question whether the persistent and generalized activation is connected with the direct action of the preparations on central nervous structures or whether it is based on modification of afferent impulses from the periphery. However, we never once found evidence of action "relaxing" and "paralyzing" the centers as some workers

have reported [3, 4]. Possibly the phase of "relaxation" or "inhibition" of the central nervous system described by these workers [3, 4] during the action of organotin compounds is nonspecific in origin.

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