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Pharmaco-EEG-based assessment of interaction between ethanol and topiramate

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Abstract:
Topiramate, an anticonvulsant, has been reported to increase the number of abstinent days and decrease craving in alcohol-dependent individuals. However, maintaining abstinence during the therapy of addicts is a considerable problem. Therefore, it is important to assess the interactions of ethanol with the topiramate. In this study, we have decided to examine this interaction by using pharmaco-EEG method. The influence of topiramate on the effect of ethanol on EEG of rabbits (midbrain reticular formation, hippocampus, frontal cortex) was tested. Topiramate was administered (per os) at a single dose (2.5 and 100 mg/kg) or repeatedly at a dose of 25 mg/kg for 14 days. Ethanol was injected at a dose of 0.8 g/kg 120 min after topiramate treatment. Ethanol caused an increase in the slow frequencies (0.5–4 Hz) in the recording, as well as a marked decrease in the fastest frequencies (13–30 and 30–45 Hz). The above changes in the EEG spectrum composition are associated with a significant depressive effect of high ethanol doses on the central nervous system. Topiramate administered both at single and multiple doses affects EEG recordings from all the investigated structures. The drug administered at a single dose together with ethanol demonstrated marked synergism of action. Topiramate used at multiple doses enhanced the effect of ethanol on EEG recording from the frontal cortex and midbrain reticular formation. The drug reduced the sensitivity of the hippocampus to the effect of ethanol, which may be associated with the effectiveness of topiramate in the therapy of alcoholism in humans. The observed interaction is probably of pharmacodynamic character.

Key words:
pharmaco-EEG, ethanol, topiramate, rabbits