„Influence of farmacological activation and inactivation of ventral tegmental area on hippocampal EEG rhythm in freely moving rats"

mgr Łukasz Braszka

Hippocampal theta rhythm are slow, regular oscillations of the hippocampal electric activity observed in the rat's brain at the frequency between 3 and 12 Hz. There are two types of this rhythm: type I is visible during the locomotion and exploration, type II episodes can be observed during the REM sleep phase, learning, experiencing the novelty and behavioural fear response called freezing. One of the structures that modulates theta rhythm generation is ventral tegmental area (VTA). It is also an important dopaminergic source for limbic structures. VTA activity is regulated mainly by three neurotransmitter systems: dopaminergic, GABA-ergic and glutaminergic. In these study, the model of freely moving, aversively conditioned rat was used to compare the dopaminergic and GABA-ergic theta regulating mechanisms described for the model of urethanized rat.

Wistar rat males (n=45), divided into 7 groups were used in these experiments. The animals were implanted with the cannulas to the VTA and bipolar electrodes to the hippocampi. The EEG and rats' behaviour were recorded during the pharmacological VTA activity manipulations of the whole structure (microinjections of amphetamine or procaine) or its' GABA-ergic component ($GABA_A$: muscimol, bicuculine, $GABA_B$: saclofen, baclofen). In contrast to the urethanized rat model, where typically only type II theta is recorded, freely moving aversively conditioned rat model allowed to record the electrical activity for both the type I (locomotion) and type II (freezing response) theta rhythm, as well as behavioural data. The percent of EEG power change and escape latency were measured and compared before and after the pharmacological activation or inactivation of VTA.

I have observed that the whole structure inactivation (procaine) led to the maximal power decrease for the 3-6 Hz and 9-12 Hz bands during the behavioural freezing. These results are in accordance with the data gathered from the recordings on the urethanized rats for the type II theta but also provide new information for the higher theta rhythm band. The post-infusion latency was significantly longer in the 20 minutes. The indirect dopaminergic neurons activation (amphetamine) did not cause the significant changes in the EEG power or latency. Activating $GABA_A$ receptors with the muscimol infusions caused EEG power decrease for the hippocampal type II theta rhythm (3-6 Hz). The escape latency increased and I have observed the effect during the whole experimental sessions. Bicuculine inactivation decreased slightly the power in 0-3 Hz band right after the infusion, which correlated with similarly small, but still significant increase in escape latency. $GABA_B$ – activating phaclophen infusions caused the power decrease in type II theta rhythm band. The escape latency increased, and reached 60 s (interpreted as no escape) as the fastest among all the test groups. The phaclophen infusions ($GABA_B$ inhibitor) similarly to baclofen, caused delta band EEG power decrease but contrary to $GABA_A$ receptor inhibitor there was no significant difference in the escape latency.

These results indicate that decreasing VTA dopaminergic neuron activity also decreases the power of the hippocampal theta rhythm, especially its' lower band (3-6 Hz). Effects were the strongest when the whole structure's activity was blocked, then after the activation of ionotropic $GABA_A$ receptors, and lastly after activation of metabotropic $GABA_B$

receptors. I have also observed an increase of escape latency during the dopaminergic neurons activity decrease. The convergence of the results between the whole structure inactivation and GABA-ergic inhibition leads to the conclusion that GABA-ergic system might play a significant role in the dopaminergic hippocampal theta rhythm regulation.