

Induced seizures in mice activate expression of urokinase system genes

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Recent studies have shown that the urokinase system - urokinase (uPA) and its receptor (uPAR) - plays an important role in the processes underlying the formation and functioning of the nervous system [3], and may also be a component of the pathogenesis of certain pathological conditions. Consistently, in patients with incurable epilepsy a significant overexpression of uPAR in neurons of the frontal lobes was observed[1], and mice with knockout of the uPAR gene showed a tendency to develop epilepsy[2]. Further study of the role of the urokinase system in epilepsy may shed light on mechanisms of brain functioning in the norm and in pathology.

In this study, we examined the changes in relative expression of the plasminogen activator genes uPA, its receptor uPAR, the tissue plasminogen activator tPA, and the inhibitor PAI-1 in mice after injection of pentylenetetrazole (at a dose of 75 mg/kg), the inducer of generalized seizures. Using real-time polymerase chain reaction, we estimated the change in the level of mRNA expression and compared them with the control (mRNA level of corresponding genes in mice without induction of seizures). In the early period after induction of seizures (60 min) we observed a 3.0 ± 0.5 and 3.3 ± 1.5 -fold increase in uPAR expression in the anterior cortex and in the hippocampus, respectively ($p < 0.05$ here and after in comparison with control). In the hippocampus, uPAR expression remained elevated 6 and 24 hours after induction of seizures up to 3.8 ± 0.7 and 4.1 ± 1.1 times, respectively ($p < 0.05$), and decreased after 72 hours to control values. The level of tPA expression increased by 1.5 ± 0.1 times in the hippocampus 30 minutes after the induction of seizures, but within an hour it reduced to control level. 72 hours after the induction of seizures both in the anterior cortex and in the hippocampus, uPA expression increased by 4.0 ± 0.8 and 5.4 ± 0.8 times, respectively ($p < 0.01$), during the same period in the anterior cortex an 2.0 ± 0.2 -fold increase in PAI-1 expression was shown ($p < 0.05$). Despite the early activation of uPAR and tPA mRNA expression, these genes were not so-called immediate early genes, since in an experiment with the simultaneous injection of pentylenetetrazole and cycloheximide (90 mg/kg) to inhibit protein synthesis, an increase in the expression of these genes was observed only after the end of exposure to cycloheximide (3 hours).

Thus, observation of changes in the expression profile of the uPA, uPAR, tPA and PAI-1 genes in various regions of mice brain after induction of generalized seizures has shown that these proteins can play an important role in carrying out molecular response of neurons to this pathological condition by mechanisms that will be studied in future.

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Источники и литература

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