



Effects of baclofen and L-AP4 in passive avoidance test in rats after hypoxia-induced amnesia

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Abstract:

Hypoxia-induced cognitive deficits are mainly due to disturbances of the balance between the GABAergic and glutamatergic systems. Acquisition, consolidation and retention impairment in passive avoidance test, hypolocomotion in the open field test, an anxiogenic-like effect in the elevated plus-maze test and hypothermia were observed in rats subjected to hypoxia. Drugs which reduce glutamate release may possess neuroprotective activity. Both, agonists of GABA_B (baclofen) and group III mGlu receptors (L-AP4) influence the release of glutamate.

We studied the behavioral effects of baclofen on hypoxia-induced amnesia and the role of L-AP4 in these processes. Baclofen impaired acquisition, produced an anxiogenic-like effect and lowered body temperature but reduced the hypoxia-induced deficit of acquisition and consolidation of conditioned avoidance, diminished the anxiogenic-like effect, and reduced the motor inhibition produced by hypoxia. L-AP4 improved the acquisition, consolidation and retrieval processes as well as the hypoxia-induced consolidation deficit in the passive avoidance test. Co-administration of baclofen with L-AP4 improved consolidation and enhanced the baclofen activity *vs.* the respective group without hypoxia. In a group of rats that had undergone hypoxia, joint administration of baclofen and L-AP4 improved retrieval as well as enhanced the effect of baclofen and L-AP4 *vs.* their respective group without hypoxia. The agonist of group III mGluRs did not change locomotor activity but diminished baclofen-induced motility in rats without hypoxia. L-AP4 given alone or with baclofen produced an anxiogenic-like effect in rats without hypoxia but produced an anxiolytic-like effect in those that had undergone hypoxia. L-AP4 did not influence the activity of baclofen in the elevated plus-maze test. L-AP4 given alone or with baclofen did not change body temperature.

It is concluded that baclofen and L-AP4 may cooperate in the consolidation process in rats without hypoxia and in retrieval of passive avoidance in animals that had undergone hypoxia. The observed interaction is probably the result of activation of the presynaptic receptors which influence glutamate and GABA release.

Key words:

hypoxia, baclofen, L-AP4, passive avoidance, open field, elevated plus-maze, rat
