Influence of afobazol on neuromediator amino acids level in rat brain caused by global ischemia

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OBJECTIVE

Afobazol (5-etoxy-2-[2-(morpholino)ethylthio]benzimidazole dihydrochloride) is a selective anxiolytic drug designed in Institute of Pharmacology RAMS. In recent studies we found out that afobazol among with its anxiolytic effect possess neuroprotective properties. It is common knowledge that the depth of ischemic brain damage depends on drift of balance between excitatory and inhibitory amino acids down to excitation. The concern of our study was to determine the tardive effects of Afobazol on neuromediator amino acids in model of global ischemia.

METHODS

Global ischemia was formed in white male randomly-bred rats weighing 260-300 g. using model by M.L. Smith (1984). Afobazol was intraperitoneally administrated (10 mg/kg) 30 minutes after reperfusion. Rats were anesthetized with chloral hydrate (325 mg/kg, i.p.) with natural breathing. Reperfusion performed 10 minutes after ischemia. 24 hours after reperfusion rats were decapitated, brains were quickly removed. We extracted hypothalamus, frontal cortex, striatum, hippocampus and nucleus accumbens. Structures homogenisation was performed in 0,1 M HClO4 with the addition of homoserine as internal standard in a concentration of 1 nM. Derivatization time was 21 minutes in the presence of 20 μl 0,1 M borate buffer and 10 μl ortho-phthalaldehyde. Amino acids were separated on a Hypersil BDS C18 column using 2 mM phosphate buffer containing 3% acetonitrile as mobile phase (pH 3.6).

As an internal standard for monoamines used 3,4-dihydroxybenzaldehyde (DBBA) in a concentration of 0,5 mM. Monoamines (NA, DA, 5-HT) and their metabolites (DOPAC, HVA, 5-HIAA) were separated on a Zorbax SB C18 column using as mobile phase 0,1 M citrate-phosphate buffer containing 0,3 mM sodium octansulphonate, 0,1 mM EDTA and 8% acetonitrile (pH 3.0).

In the group (ANOVA; Fisher LSD) as compared with control group (intact animals) No significant differences compared to the control group (false-operated group of animals).

RESULTS

The concentration of amino acids in the striatum of random-bred rats. Relative values of random-bred rats. Relative values

The content of amino acids in the hippocampus of random-bred rats. Relative values

The most notable changes in neurotransmitter pattern were observed in striatum. We detected significant increase of glutamate level up to 65% and decrease of GABA level down to 67% in comparison to intact rats. In afobazol treated animals level of glutamate was 27% lower and level of GABA 32% higher than observed in ischemic animals. Concentrations of glutamate and GABA observed in afobazol treated animals were of no significant difference compared to the control group. Taurin level was 50% and 114% higher in ischemic and afobazol administrated animals respectively than observed in intact rats.

We can assume that afobazol prossessing membrane stabilizing effect, prevents the uncontrolled release of neurotransmitters and depletion of neurotransmitter systems. Afobazol restore disrupted balance in striatum between excitatory and inhibitory amino acids caused by global ischemia and activate taurin-dependant neuroprotection.

CONCLUSION

There is no potential conflict of interest

Influence of afobazol on neurotransmitter monoamines in the hypothalamus of random-bred rats with global ischemia

Influence of afobazol on the concentration of neurotransmitter monoamines in the NAC of random-bred rats with global ischemia

There is no potential conflict of interest