Summary

Nerve agents belong to the most important group of highly toxic substances. The threat of their use is still actual in local conflicts or in terrorist attacks. Looking for the optimal measures of medical protection (antidotal therapy and prophylaxis) against them remains in the center of interest of both military and civilian sector.

Basic mechanism of action of nerve agents is their interference with cholinergic neurotransmission through the irreversible inhibition of acetylcholinesterase (AChE). We chose quantitative evaluation of AChE histochemistry as a method to assess changes in nerve tissue after untreated or treated intoxication by nerve agents, using computer image analysis. Description of these changes were the aims of this doctoral thesis.

The laboratory rats were intoxicated by LD_{50} or 1,2x LD_{50} of agent (Tabun, Soman, Sarin, VX or RVX). Prophylactic, respectively antidotal doses of drugs stated below were used as well. The cryostat sections of brains were treated by simultaneous histochemical detection of AChE by Karnovsky and Roots and alkaline phosphatase.

The results prove a decrease of enzyme activity in all studied CNS areas treated by mean lethal doses of nerve agents, more in case of G-agents. We establish good effect of obidoxime to reactivate AChE inhibited by tabun, less strong effect of HI-6 after tabun intoxication and good prophylactic effect of Huperzine A in case of soman exposure.

We demonstrate disputable effect of K048 on reactivation of AChE inhibited by tabun. Nor prophylactic effect of Huperzine A for RVX intoxication, nor increased penetration of oximes in circumventricular organs, nor selective effect of nerve agents to any respiratory center of oblongata was found.

AChE inhibition in brain nuclei and areas is uniform for no studied nerve agents.

We documented that our method is in good agreement with standardly used biochemical assessment of AChE activity. Furthermore, our method is eligible to judge the histochemical changes *in situ*.

This work was supported by the Charles University Grant Agency, No 82/2005 C.