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MEETING ABSTRACTS

IN SEARCHING FOR THE MECHANISM OF BUTYRYLCHOLINESTERASE ACTIVATORS

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It is known that cholinesterases show homotropic pseudocooperative effects: their activity at millimolar substrate concentrations is higher than expected by simple saturation kinetics and they are strongly inhibited at the submolar concentrations. However, we have reported that the anionic site directed inhibitors tetramethylammonium and tetraethylamonium too, increase the activity of human butyrylcholinesterase. At that time, the same phenomenon could not be shown for the horse counterpart. Here, it was searched for other putative activators among often used compounds in cholinesterase research. Indeed, imidazole significantly increase the activity of human enzyme, but also its atypical form and the horse enzyme. On the other hand, 2-PAM shows a certain degree of activation with both human enzymes, but inhibits the horse BChE in a classical competitive manner. To avoid substrate activation, the experiments were performed at around 50 micromolar starting substrate concentrations and were followed by its completion in the presence of different modulator(s) concentrations. Subsequently, the effect of 2-PAM on the phosphorylation by DFP was studied, since the bottom of the active site does not differ in these three enzymes. It seems that the distinctive action of activating agents on the wild type, the atypical human and horse BChE is a consequence of differences in the dynamics of the acylation loop at the active site entrance, rather then the composition of the enzyme's peripheral anionic site.

Keywords: reaction mechanism; butyrylcholinesterase activation; kinetics