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Effect of the pyridoindole SMe1EC2 and compounds affecting A_1 and A_{2A} adenosine receptors in rat hippocampus under ischemia *in vitro*

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Abstract:
The effect of the newly synthesized pyridoindole antioxidant SMe1EC2 (1 μmol/l) and drugs activating or inhibiting adenosine receptors was tested under ischemia. Synaptic transmission was recorded extracellularly before and under 6-min ischemia and 20-min reoxygenation in rat hippocampal slices *in vitro*. In untreated slices, ischemia elicited failure of synaptic transmission and excitability expressed by a population spike decay ($t_{0.5}$ = 1.7 ± 0.1 min) and poor recovery of synaptic transmission at the end of reoxygenation, expressed as percentage of PoS amplitude of that at zero minute of ischemia (9.9 ± 3.6%). The compound SMe1EC2 increased recovery of PoS amplitude in reoxygenation (31.2 ± 7.0% of that at the beginning of ischemia) and decreased the number of irreversibly damaged slices in reoxygenation (64%) compared to untreated slices (80%). Co-administration of SMe1EC2 + SCH-58261 (1 μmol/l, A_{2A} adenosine receptor antagonist) resulted in delayed synaptic transmission decay during 6-min ischemia ($t_{0.5}$ = 2.3 ± 0.1 min), increased PoS amplitude recovery during reoxygenation (37.7 ± 12.4% of that at zero minute of ischemia), and in a decreased number of slices with damaged synaptic transmission at the end of reoxygenation (54%), all data compared to untreated controls. Co-administration of pyridoindole with CGS 21680 (1 μmol/l, A_{2A} adenosine receptor agonist) or with DPCPX (100 nmol/l, A_1 adenosine receptor antagonist) eliminated the described effect. Further studies are required to elucidate the putative influence of manipulation with adenosine receptors on the neuroprotective effect of SMe1EC2 under ischemia.

Key words:
ischemia, hippocampus, synaptic transmission, adenosine, pyridoindoles