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MEETING ABSTRACT

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Hypothermia prevents ischemic condition to release [^{3}H]dopamine from rat parietal cortex slices in a Ca^{2+}-independent manner

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Background: Stroke is the number two cause of death worldwide, and considering a further increase in the future in life expectancy, it may soon become the leading cause of death. In human brain during stroke an ischemic condition occurs. There is convincing evidence that a massive release of neurotransmitters occurs in the brain during ischemia. When glucose and oxygen were withdrawn (oxygen-glucose deprivation, OGD), the Ca^{2+}-independent release of various transmitters (noradrenalin/dopamine/glutamate) from *in vitro* slice preparations was increased and mediated via reverse operation of transporters. In addition, evidence showed that the excessive amount of released neurotransmitters and some of their metabolites are neurotoxic.

Methods: ***In vitro experiments:*** Using a superfusion microvolume chamber [1] we loaded the rat parietal cortex slices with [^{3}H]dopamine ([^{3}H]DA) in Krebs solution and measured the transmitter release at rest and in response to field stimulation (2 Hz). The fractional release of [^{3}H]DA was measured by liquid scintillation counting and the distributions of [^{3}H]DA and its metabolites was determined using HPLC. A thermoelectric device (Frigomix) was used to quickly change the temperature. ***In vivo experiments:*** "Stroke" was produced by transient occlusion of middle cerebral artery (TMCAO) in rats and after 24 hours they were decapitated. [^{3}H]DA release was measured from parietal cortex slices at various temperatures.

Results: (1) Removal of oxygen and glucose enhanced the resting and inhibited the stimulation-evoked release of radioactivity. We found that lowering the temperature (32°C and 27°C) reduced or prevented the release of [^{3}H]DA induced by ischemia (OGD) obtained at 37°C. Removal of Ca^{2+} from the Krebs solution and addition of 1mM EGTA failed to change the release of [^{3}H]DA evoked by OGD indicating that the release was external calcium-independent. (2) Lowering the temperature prevented or reduced the effect of OGD on DA release in parietal slices prepared from both control and operated sites of the brain taken from rats after *in vivo* TMCA occlusion.

Discussion: In our *in vitro* and *in vivo* model of ischemia we studied the effect of hypothermia on the release of [^{3}H]DA evoked by OGD from rat parietal cortex slice preparations. In summary, it seems likely that the application of hypothermic treatment in order to reduce the neurotoxic effect of an ischemic insult may have therapeutic importance. In the future, we are planning to test a device capable to quickly reduce the local temperature in animal experiments. Local hypothermia seems to be an alternative treatment for post-stroke patients or for those who suffer from spinal cord injury.

Reference

1. Vizi ES: **Different temperature dependence of carrier-mediated (cytoplasmic) and stimulus-evoked (exocytotic) release of transmitter: a simple method to separate the two types of release.** *Neurochem Int,* 1998; 33(4):359–366. doi:10.1016/S0197-0186(98)00040-0

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