IMMUNOPHILIN LIGANDS DECREASE RELEASE OF PRO-INFLAMMATORY CYTOKINES (IL-1β, TNF-α and IL-2) IN RAT ASTROCYTE CULTURES EXPOSED TO SIMULATED ISCHEMIA IN VITRO

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The aim of present study was to evaluate the effects of immunophilin ligands (cyclosporin A, FK506 and rapamycin) on the simulated ischemia-induced release of pro-inflammatory cytokines (IL-1β, TNF-α and IL-2) in rat primary astrocyte cell cultures. Astrocytes were exposed to cyclosporin A (CsA) (0.25, 0.5, 1, 10, 20 and 50 μM), FK506 (1, 10, 100, 1000 nM) and rapamycin (10, 100, 500 and 1000 nM). In vitro simulated ischemia significantly increased secretion of IL-1β, TNF-α and IL-2 by astrocyte cultures deprived of microglia (by shaking and incubating with L-leucine methyl ester). CsA (at concentrations of 10–50 μM), FK506 (at all used concentrations) and rapamycin (in dose-dependent manner) significantly attenuated IL-1β release after 24 h exposure to ischemic conditions. Immunophilin ligands at all used concentrations significantly decreased TNF-α levels in culture media after 24 h exposure to ischemia. Moreover, significant decrease in IL-2 secretion at 0.25, 0.5, 1 and 50 μM CsA and FK506 at concentrations of 100 and 1000 nM were observed.

The results suggest that immunophilin ligands may regulate glial activity during ischemia by affecting the release of pro-inflammatory cytokines.

**Key words:** astrocytes, ischemia, immunophilin ligands, cytokines, IL-1β, TNF-α, IL-2

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