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NEUROPROTECTIVE EFFECTS OF CABERGOLINE ON ISCHEMIA-INDUCED CELL DEATH: IN VITRO STUDIES

Francioli E.[a], Miglio G[a]., Varsaldi F.[a], Papini M.G.[b], Battaglia A.[b], Canonico P.L.[a], Lombardi G.[a]

[a]DISCAFF Department, University of "Piemonte Orientale", Novara, Italy
[b]Medical Department, Pharmacia Italia S.p.a., Milano, Italy

Cabergoline, a long-lasting selective dopamine D2 receptor agonist, is able to protect SH-SY5Y neuroblastoma human cell lines from oxidative stress (1). Since free radicals are generated during and after ischemia, we studied if cabergoline has neuroprotective effects also in an *in vitro* model of cerebral ischemia. SH-SY5Y cells were exposed to 5 hr oxygen-glucose deprivation (OGD) at 37°C, and then re-oxygenated for 20 hr. After this time the ischemia-induced cell injuries were studied in parallel as necrosis and apoptosis. The necrosis was evaluated by measuring the amount of lactate dehydrogenase (LDH) released from necrotic cells into the culture medium. Cell viability was determined by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) and by intravital fluorescein diacetate-propidium iodide staining (FDA/PI). The typical chromatin abnormalities of apoptosis were analyzed by fluorescence microscopy with the nuclear dye Hoechst 33258, and the cellular responses to ischemic insult were examined by Western blot analyses of anti-apoptotic Bcl-2 protein expression. 5 hr OGD caused a 40$\pm$5% of cell necrotic death, which was significantly ($P \leq 0.01$) prevented by cabergoline, added into the culture medium during OGD and/or re-oxygenation period, in a concentration-dependent manner (EC_{50}: 1.8 µM). Microscopic analysis of cultures stained with FDA/PI confirmed these results. The appearance of cell apoptotic nuclei was revealed by the nuclear dye immediately after OGD, and the number of these nuclei decreased over 20 hr of re-oxygenation. Cabergoline (10 µM), added during and/or immediately after OGD, did not change the number of apoptotic nuclei. Moreover, Bcl-2 protein level was changed in neither buffer- nor cabergoline (10 µM)-treated OGD samples after 20 hr of re-oxygenation.
Our results suggest that cabergoline has neuroprotective effects against OGD-induced cell death by reducing necrotic ischemic injuries.

1) Lombardi G., Varsaldi F., Miglio G., Papini M.G., Battaglia A., Canonico P.L. (2002) Eur. J. Pharmacol. 457: 95-98.