THE SIGNALLING PATHWAYS TRIGGERED BY PULSED ELECTROMAGNETIC FIELDS IN THE RELIEF OF HYPOXIA-INDUCED NEURONAL CELL DEATH

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Introduction: Low-energy low-frequency pulsed electromagnetic fields (PEMFs) mediate numerous protective effects, regulating physiological systems by delivering an inductive signal coupled to the treatment site, thus inducing anti-inflammatory and pro-regenerative effects in mammals. However, the mechanism responsible of their neuroprotection has not been clearly elucidated.

Materials and methods: Nerve growth factor (NGF)-differentiated pheochromocytoma PC12cells have been injured with 1% hypoxia. Then cell vitality, in the absence and in the presence of PEMF for different time of incubation, was evaluated through ATPlite assay. The protective pathways activated by PEMFs to relief neuronal cell death, were characterized by using selective inhibitors of adenylyl cyclase (AC), phospholipase C (PLC), protein kinase C epsilon (PKC-e) and delta (PKC-d), p38, ERK1/2, JNK1/2mitogen activated protein kinases (MAPK), Akt and Caspase-3by using ATPlite assay. Finally, the regulation by PEMFs of prosurvival HSP70, CREB, BDNF and Bcl-2apoptotic family proteins through p38MAPK was investigated through AlphaLISA and ELISA kits.

Results: The results obtained in this study show a protective effect of PEMFs able to decrease neuronal cell death induced by hypoxia by regulating p38, HSP70, CREB, BDNF and Bcl-2family proteins. Specifically, we found a fast activation (30 min) of p38kinase cascade, which then recruits HSP70 survival chaperone molecule, producing a significant enhancement of CREB phosphorylation (24h). In this cascade, later (48h), BDNF and the antiapoptotic pathway regulated by the Bcl-2family of proteins are enrolled by PEMFs to increase neuronal survival.

Discussion and conclusion: These data elucidate and characterize the signalling pathways activated by PEMFs to produce neuroprotection from hypoxic cell death. As a consequence this study paves the way to the use of PEMFs as a new neuroprotective approach to treat cerebral ischemia.