REVIEW

APOPTOSIS IN THE CENTRAL NERVOUS SYSTEM: MECHANISMS AND PROTECTIVE STRATEGIES

Małgorzata Kajta#

Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Smetana 12, PL 31-343 Kraków, Poland


Naturally occurring neuronal cell death, which is essential for normal development, tissue homeostasis and as a defence against pathogens, is generally considered to be apoptotic. Apoptosis, called also a programme cell death, though the meanings of these terms are not identical, is a common phenomenon induced either by specific insults mediated through so-called “death receptors” (external pathway) or by non-specific insults leading to reduction of mitochondrial potential (internal pathway). At the molecular level, apoptosis is regulated by the activation of the caspase cascade, which depends either upon the participation of mitochondria and the activation of procaspase-9 or on the interaction of a death receptor with its ligand and subsequent activation of procaspase-8. Considering various mechanisms of programmed cell death, either during neural development or neurodegeneration, finding the most suitable and effective protective strategy needs evaluation of risk-to-benefit ratio. Unlike malignant tissues, neuronal cells have to be protected, but only if the protection does not disturb natural cell elimination. Defining molecular mechanisms is, therefore, the necessary step preceding the adaptation of new protective and then, possibly, therapeutic strategies. At present, the most promising are discoveries related to caspases, JNK, and GSK-3β and their crucial role in stress-dependent and spontaneous apoptosis. Inhibitors of caspases and JNKs succeed in defending cells against kainate-, β-amyloid- or MPTP-induced neuronal cell death. Among protective agents those, which easily cross the blood-brain barrier and exert profound neuroprotective action without side effects, seem to be the most important.

Key words: caspases, calpains, JNKs, GSK-3β, neural development, neurodegeneration, estrogens

# correspondence: e-mail: kajta@if-pn.krakow.pl

1 The topic of paper was presented as a monograph lecture delivered at the Institute of Pharmacology, Polish Academy of Science, Kraków, Poland