

Poly(ADP-ribose) polymerase in brain aging and neurodegeneration

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Nuclear DNA bound enzyme poly(ADP-ribose) polymerase (PARP-1; EC 2.4.2.30) is a key enzyme in DNA excision repair and plays an important role in regulation of transcription factors and gene expression. Its overactivation leads to β NAD⁺ and ATP depletion and to cell death. Our last studies indicated age related alteration of PARP-1 activity in hippocampus, cerebral cortex and cerebellum. In aged rats (24 months old) PARP activity was enhanced in all investigated brain parts comparing to adult animals (4 months old). The enhancement of PARP activity in old hippocampus is in contrast with our previous observations when the opposite effect was observed. The explanation for these discrepancies could be a different environmental conditions in which the animals were kept. In additional *in vivo* studies we observed that PARP-1 activity was significantly stimulated in hippocampus but not in brain cortex after transient forebrain ischemia. PARP inhibitor 3-aminobenzamide (3-AB) protects neurons in CA1 layer of hippocampus against edema and death after short (3 min) ischemic insult. Moreover, the effect of 3-AB on intracellular organelles alteration was investigated. The electron microscopic examination indicated pronounced protective effect of 3-AB on the swelling of astrocytes and neurons 1 day after 3 min of ischemic insult. 3-AB decreased evoked by ischemia swelling of mitochondria. The significant ameliorating effect of 3-AB was also observed at 7th day of reperfusion. Our results indicate that PARP inhibitors may have an protective effect on intracellular organelles alterations evoked by short ischemic insult.