Perinatal asphyxia as the leading cause of death and brain injury of newborns: prognosis and neuroprotection of long-term outcomes

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Abstract

Interruption of oxygen availability and re-oxygenation at birth implies a severe metabolic insult, affecting the development of the central nervous system (CNS), increasing its vulnerability to challenges occurring at adult stages. It has been reported that perinatal asphyxia produces regionally specific neuronal decrease and neurite atrophy in basal ganglia, and hippocampus. In hippocampus, a concomitant increase of neurogenesis and neurite hypertrophy has also been observed. The potential neuroprotection of nicotinamide, a non-selective inhibitor of poly (ADP-ribose) polymerase (PARP-1), has been investigated, finding functional and morphological improvements when administered 24h after the insult (0.8 mmol/kg, i.p., 24, 48 and 72 h after birth.). The main effect of nicotinamide has been seen in neostriatum, preventing an asphyxia-induced decrease of the number of nNOS cells, and nNOS- and dopamine-like neurite atrophy. The present results support the idea that nicotinamide can prevent the effects elicited by a sustained energy-failure condition, as occurring during perinatal asphyxia, enlightening the enzyme PARP-1 as a novel target for neuronal protection. The support by FONDECYT, ICBM-Enlace, DAAD-CONICYT Programme-2007 grants is acknowledged.

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