Further studies on the hypothesis of PARP-1 inhibition as a strategy for lessening the long-term effects produced by perinatal asphyxia: Effects of nicotinamide and theophylline on PARP-1 activity in brain and peripheral tissue

Allende-Castro, C.

Espina-Marchant, P.

Bustamante, D.

Rojas-Mancilla, E.

Neira, T.

Gutierrez-Hernandez, M. A.

Esmar, D.

Valdes, J. L.

Morales, P.

Gebicke-Haerter, P. J.

Herrera-Marschitz, M.

Oxygen interruption leads to death when reoxygenation is not promptly re-established. Re-oxygenation triggers a cascade of biochemical events for restoring function at the cost of improper homeostasis. The effects observed long after perinatal asphyxia (PA) have been explained by over-expression of sentinel proteins, such as poly(ADP-ribose) polymerase-1 (PARP-1), competing for NAD+ during re-oxygenation, leading to the idea that sentinel protein inhibition constitutes a therapeutic strategy. We studied the effects of nicotinamide and theophylline on PARP-1 activity assayed in brain and peripheral (heart) rat tissue 1-24 h after birth, as well as on changes in behaviour and monoamine neurotransmission in adult rats. PA was induced by immersing rat foetuses into a water bath for 0 or 21 min. After resuscitation, the pups were treated with nicotinamide (0.8 mmol/kg, i.p.), theophylline (0.14 mmol/kg, i.p.) or saline (0.9% NaCl) and nurtured by surrogate dams, pending behavioural and micr