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Zinc/cPLA2 associated-mitophagy and CaMK II signaling contributed to the neuroprotective effects of chronic leptin treatment following neonatal seizures

The peptide hormone leptin is an important neuromodulator for brain energy homeostasis which has recently received considerable attention in neurodegenerative diseases. The aim of the present study was to evaluate whether chronic leptin treatment immediately after flurothyl-induced recurrent neonatal seizures would exert neuroprotective effects on neurobehavior, cognition and hippocampal mossy fiber sprouting, and whether this effects were achieved by the pathway of Zinc/cPLA2 associated-mitophagy and CaMK II signaling. 40 Sprague-Dawley rats (postnatal day six, P6) were randomly assigned to recurrent seizures group and control group. On P13, they were further randomly divided into the seizure group without leptin (RS), seizure plus leptin (RS+Leptin, 2 mg/kg/day, consecutive ten days), the control group without leptin (control), and the control plus leptin (leptin, 2 mg/kg/day, consecutive 10 days). Neurological behavioral parameters (negative geotaxis reaction reflex, righting reflex, cliff avoidance reflex, forelimb suspension reflex and open field test) were observed from P23 to P30. Morris water maze test was performed during P27-P32. Mossy fiber sprouting and protein levels in hippocampus were detected subsequently by Timm staining and western blot method, respectively. Flurothyl-induced seizures (RS group) significantly down-regulated mitophagy marker PINK/Drp1, pPLA2 and CaMK II alpha, meanwhile up-regulated zinc transporter ZnT1/ZIP7, lipid membrane injury-related cPLA2, autophagy marker beclin-1/bcl2, LC3II/LC3I, and its execution molecule cathepsin-E, which are in parallel with hippocampal aberrant mossy fiber sprouting and neurobehavioral and cognitive deficits. However, these changes were restored by chronic leptin treatment (RS+leptin group). The results imply that a zinc/lipid metabolism-associated mitophagy and CaMK II signaling is involved in the aberrant hippocampal mossy fiber sprouting and neurobehavioral deficits following neonatal seizures, which might be a potential target of leptin for the treatment of neonatal seizure-induced long-term brain damage.

Biography

Hong Ni is a Medicine Doctor, completed his PhD in Medicine. Currently, he is the Director in Department of Neurology at Children's Hospital of Soochow University and member of the Chinese Society of Microcirculation Council. His research focuses on "The children neurological rehabilitation, cerebral palsy and epilepsy".

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