and new treatment modalities. Seven day old rat hypoxia-ischemia model can be used to evaluate the effect of different agents. The complex role of nitric oxide and its antagonists in neonatal hypoxic ischemia has been widely known. However effects of L-arginine, an NO precursor, on apoptotic cell death in neonatal hypoxia-ischemia animal models have not been studied before. The aim of this study is to investigate the effects of the pre and post treatment of L-arginine on apoptotic cell death in hypoxia-ischemia neonatal rat model. Seven-day-old rats were administered L-arginine intraperitoneally before and after hypoxic ischemia inflicted through right carotid artery ligation and the exposed to 8 % oxygen. Apoptotic cell death was shown by Tunnel method after three-day recovery. Right hippocampal and striatal apoptotic cell death percentage in L-arginine post-treated group were significantly lower than those of vehicle groups, but no change was found in cortex. L-arginine pre-treatment was found to have no effect on apoptotic cell death in the three brain regions.

As a result, nitric oxide may play an important dual role in apoptotic cell death in neonatal hypoxic-ischemic brain injury. Pre-treatment of L-arginine, an NO precursor has not been proven to reduce apoptotic cell death, while early treatment after hypoxic ischemia has antiapoptotic effect on neurons in neonatal rat model.

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CELL DEATH AND AUTOPHAGY AFTER SEVERE HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN HUMAN NEONATES

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Perinatal asphyxia remains one of the challenging conditions in neonatology, with high prevalence, high mortality and neurological morbidity and no pharmacological neuroprotective strategy. Three main types of neuronal cell death have been described: apoptosis, necrosis and more recently, autophagic cell death, which is a physiological process of degradation, but excessive autophagy may be involved in cell death. Recent studies from

others as well as from our own group showed that inhibition of autophagy is neuroprotective in neonatal models of cerebral ischemia in animals. We showed in a model of perinatal asphyxia in rats an increased neuronal autophagic flux linked to cell death. Following our observations in animals, our objectives for the present study were:

- 1) to describe all the cell death features encountered in brain tissue samples from severely asphyxiated human neonates
- 2) to determine the presence of autophagy histologically and using immunohistochemistry
- 3) to determine the distribution and regional pattern of the different cell death types.

8 newborns at term who died in the Division of Neonatology from 2004-2008 were selected retrospectively and anonymously on the criteria: asphyctic event, Sarnat III, death and accorded autopsy. In histological sections from the frontal cortex, hippocampus, basal ganglia and thalamus, necrosis, apoptosis, but also autophagy were present, with a distinct distribution pattern. The different markers of autophagosomes, lysosomes and apoptosis were tested by immunohistochemistry, showing an increase of autophagic flux in areas affected by asphyxia. These observations lead to a new understanding in the mechanisms of neuronal cell death following perinatal asphyxia.

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DIFFERENTIAL REGIONAL DYNAMICS OF UNCONJUGATED BILIRUBIN ENTRY AND CLEARANCE IN THE BRAIN OF GUNN RATS

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Background: “Kernicterus” historically describes the unconjugated bilirubin (UCB) accumulation in selective brain regions, leading to neurological damage in hyperbilirubinemic newborn babies and in Crigler-Najjar type I patients. Hyperbilirubinemic (jj) Gunn rats develop neurological deficits that parallels the human pathology and a similar pattern of regional brain UCB distribution under displacing agents treatment.