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.

Aims:

- 1) to quantify the tissue UCB content (TUCB) spontaneously present in five brain regions of Gunn rats; and
- 2) to unravel the dynamics of TUCB entry and clearance after sulphadimethoxine treatment .

Methods: Cortex (Cx), superior collicula (SC), inferior collicula (IC), cerebellum (CLL) and the rest of the brain (RB) were collected 1, 6, 24, 48 and 72 hrs after injection of sulfadimethoxine (200 mg/Kg; IP) in 17 days-old jj animals and in not treated JJ, Jj and jj rats. TUCB was analyzed by the HPLC based method (Zelenska_2008).

Results: In untreated jj animals TUCB brain amounts was about 80 times higher than in Jj and JJ, and no regional differences were detected. After sulphadimethoxine administration TUCB picked differently in the regions analyzed: 1 hr in Cx and SC, 6 hrs in RB, 24 hrs in IC, 6 - 24 hrs in CLL. 72 hrs after injection, TUCB content was lower than in not treated littermates.

Conclusions: The differential entry and clearance across brain areas show regional difference in cellular mechanisms modulating tissue UCB concentration. The different kinetics might be involved in the tissue resistance/sensitivity to bilirubin toxicity of nervous system.

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AMPLITUDE INTEGRATED EEG AS A DIAGNOSTIC TOOL IN NEONATAL STROKE

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Background: The two-channel amplitude integrated EEG (aEEG) allows for continuous monitoring of cortical activity of each hemisphere separately.

Aim: We present three newborns with unilateral cerebral infarction, in whom the aEEG was an important diagnostic tool.

Methods: Infants were monitored routinely by two-channel aEEG, electrodes were positioned in C3-P3, C4-P4.

Case reports:

Patient 1: Term newborn boy, birth weight 3620 g, Apgar scores 9/10/10. Admission on day 1 for apnea. The aEEG showed an abnormal background pattern with ictal activity on the left. Cerebral ultrasound exhibited a slight difference in echogenicity between left and right parieto-occipital parenchyma, MRI showed left arteria cerebri media infarction.

Patient 2: Term newborn girl, birth weight 2750g, Apgar scores 8/10/10, admitted day 3 for jerks of the left arm. The aEEG showed an abnormal background pattern bilaterally and ictal activity on the right. Haemorrhagic infarction in the right fronto-temporal region was suspected by ultrasound examination and subsequently confirmed by MRI.

Patient 3: Preterm boy (32 weeks), birth weight 2350g, Apgar scores 7/7/10, uncomplicated postnatal period, normal ultrasound findings in the first week of life. The aEEG in the second week showed left-sided ictal activity. Left arteria cerebri media infarction was diagnosed by ultrasound and MRI.

Summary:

In all three cases, unilateral ictal activity was displayed in the two-channel aEEG (difficult to recognize in one-channel aEEG). Clinical signs of cerebral infarction may be unspecific and ultrasound changes might be detected only when high suspicion is raised by the aEEG findings.

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FEATURES OF CONDUCT AND TREATMENT OF RESISTANT EPILEPTIC ATTACKS IN CHILDREN OF EARLY AGE WITH A TUBEROUS SCLEROSIS

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Aim: optimization of early diagnostics and treatment of resistant epileptic attacks in children with a tuberous sclerosis.

Methods: during the last 7 years there were studied 9 children with a tuberous sclerosis in an age category to 3 years. On the basis of magnetic resonance tomography, for all nine children there were determined hamartomas from 3 to