

# Neurochemical profile in perinatal brain hypoxia-ischemia using advanced magnetic resonance spectroscopy

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## Introduction

In early preterm infants, periventricular leukomalacia represent the predominant form of brain injury: of those infants born weighting less than 1500 grams, 25-50% later exhibit developmental disabilities and up to 5-15% have a more major cerebral palsy. The 3-day old rat (P3) shares some similarities in terms of cerebral development with the very preterm infant.

## Objectives

The aim of the present study was to define the nature of acute and subsequent brain neurochemical profile alterations in a model of neonatal hypoxic-ischemic injury (HI) in the P3 rat pup using high-field MR imaging and spectroscopic techniques.

## Materials and methods

P3 Wistar pups underwent moderate (HI) injury under isoflurane anesthesia. After right carotid cauterization pups were exposed to hypoxia for 30 minutes at 6% O<sub>2</sub>. 24 hours (P4.n= 8) and 8 days after HI (P11.n= 8) <sup>1</sup>H-MRS was performed under continuous anaesthesia with temperature and respiratory monitoring using an actively shielded 9.4T/31cm bore system. MR images were used to position the volume of interest and to determinate the brain and the lesion volumes. <sup>1</sup>H-MRS spectra within the ipsilateral and contralateral cortical area were acquired. Metabolite concentrations in the cortex and hippocampus were analyzed with the LCModel.

Metabolites quantification results in a neurochemical profile of both the cortical lesion and the contralateral part. Significant difference of the brain volumes between HI and control groups were assessed by a Mann Whitney test. A Wilcoxon test was used to compare metabolite concentrations between ipsilateral and contralateral sides.

## Results

Under conventional imaging, HI injury appeared as a hypersignal in the ipsilateral cortex. The volume of the brain in the HI group compared to the control was not significantly different at P4 and P11. The lesion volume varied between the animals due to the variability of the model (lesion volume represents at P4 10% and at P11 5% of brain volume). At P4 the neurochemical profile of the ipsilateral cortex indicated significant decreases of several metabolites (Macromolecules, phosphocholine, creatine, inositol, N-acetyl aspartate, taurine, glutamate, glutamate/glutamine). At P11, only a few metabolites showed significant increase (Phosphocreatine, glutamate, taurine, glutamate/glutamine). The modifications of the metabolites at P4 reflect an acute energetic and functional slowing-down in the injured cortex. At P11, the variation of the metabolite concentrations need to be further investigated to define their role in this context.

## Conclusion

These results provide new in vivo insight into the neurochemical processes resulting from HI in the developing brain that can be used to monitor injury and the response to protective therapies.