Effect of fetal-hypoxemia on neurochemical profile of neonate guinea pigs during development

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INTRODUCTION

Guinea pigs are precocious in neurological development and recognized as a good model for such human pathology as juvenile diabetes, or pregnancy complications such as chronic fetal hypoxia. While most studies seeking to address guinea pig postnatal neurochemical changes have utilized *in vitro* biochemical analysis, ^{1}H MRS allows measuring metabolites non-invasively in defined regions of living tissues. Hypoxia is one of the pregnancy complications that lead to fetal neurodevelopmental brain damage. It has been shown that glutamate-mediated excitotoxicity may play an important role in neuronal damage [1]. In this study, ^{1}H MRS was employed to determine whether maternal hypoxia alters neurochemical levels in the brain of newborn guinea pig babies as an adaptive response to the reduced oxygenation before birth.

METHODS

Two groups of neonatal guinea pigs with maternal hypoxia and normoxia were studied. Pregnant guinea pigs were housed in either a Plexiglas chamber containing 10.5% oxygen for 8-22 days before delivery for the hypoxia group or in room air for normoxic controls. The MRS data were measured from the neonatal guinea pigs at three postnatal days (P0, P7, and P14) on a Varian 9.4 T MR system equipped with an 12-cm gradient coil (40 G/cm, 250 µs) and a shim coil (Magnex Sceintific, Abingdon, UK) with second-order shim strength up to 0.4 G/cm^2. The magnet was interfaced to a Varian INOVA console (Varian Inc., Palo Alto, CA).

During the experiments, the animals were anesthetized (air:oxygen = 1:1 with 1-2% isoflurane) and their core temperatures were maintained at 38˚C, which was verified using a rectal temperature probe. A quadrature surface RF coil consisting of two geometrically decoupled loops was placed on the animal head. First- and second-order shim currents were adjusted using FASTMAP [2]. Spectra were acquired from three brain regions: hippocampus, striatum, and cerebral cortex using ultra-short echo-time STEAM (TE = 2 ms, TR = 5 s, TM = 20 ms, ~18 µl) with VAPOR water suppression technique [3].

RESULTS AND DISCUSSION

Figure 1 shows the representative spectrum acquired from the hippocampus of guinea pig P0 with hypoxia. Metabolite concentrations between two groups were compared in the three brain regions (Fig. 2). In general, the trends of concentration variations for each metabolite in all three regions are very similar. For example, the concentrations of *myo*-inosital (Ins) and NAA increased over 2 weeks in all three regions of both normoxic and hypoxic guinea pigs. While the trends were similar, the metabolite levels on P0 were different between normoxic and hypoxic guinea pigs. For normoxic guinea pigs, concentrations of Ins and NAA in the striatum on P0 were 9.6 and 6.5 µmol/g, respectively, and those in the hypoxic brain were decreased by 11% (p=0.04) and 12% (p=0.006), respectively. The concentrations of glutamine (Gln) and glutamate (Glu) in the striatum were 3.96 and 7.72 µmol/g on P0 for normoxic guinea pigs, respectively, and those in the hypoxic brain were decreased by 15% (p=0.04) and 31% (p=0.005).

The results show the most significant neurochemical changes by maternal hypoxia occurred in the striatum although other regions also showed changes on P0. The decrease in Glu may be associated with delayed or damaged neuronal development due to hypoxia during gestation.

REFERENCES

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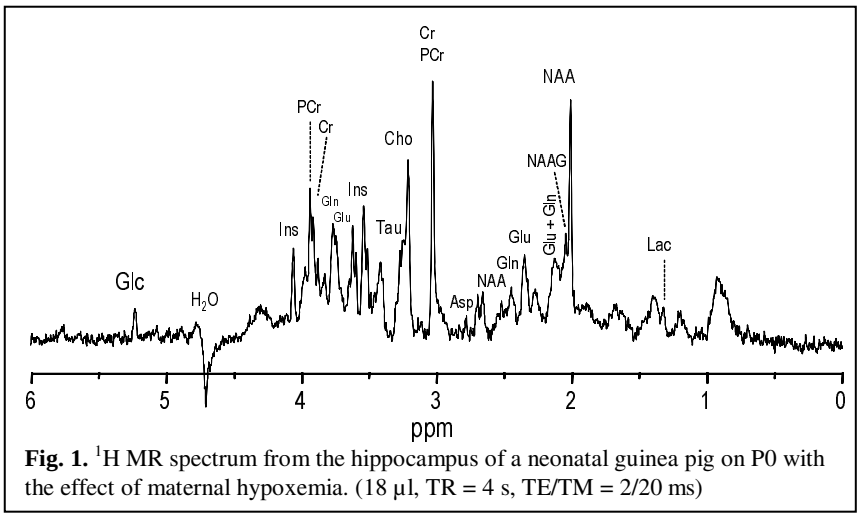

Fig. 1. ^{1}H MR spectrum from the hippocampus of a neonatal guinea pig on P0 with the effect of maternal hypoxemia. (18 µl, TR = 4 s, TE/TM = 2/20 ms)

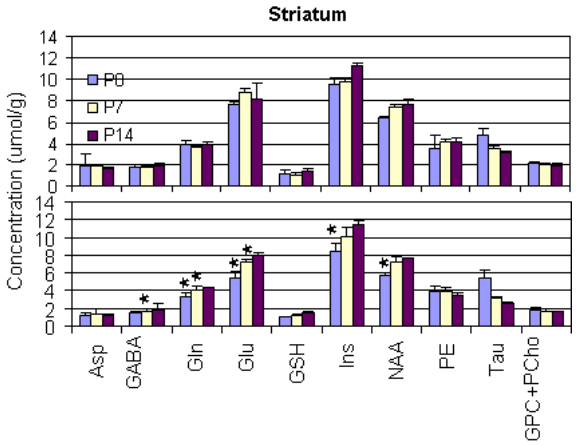

Fig. 2. Neurochemical changes in the striatum of the brain of normoxic (top) and hypoxic (bottom) guinea pigs. Error basr denote standard deviations, and * denote significance level p<0.05.