Postnatal Brain Maturation in Rabbits Studied by Combined NIRS and MRI

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Introduction The neonatal rabbit's brain shows prolonged post natal development both structural and physiologic[1]. Directly after birth cerebral blood flow (CBF) is low, and by day 17 oxidative metabolism and capillary density are positively correlated reflecting the maturing of the microvascular anatomy and establishment of steady state vascular autoregulation[2]. In our study we have used non-invasive near-infrared frequency-domain optical spectrometry (NIRS) and magnetic resonance imaging (MRI) to follow changes in post natal cerebral hemodynamics and anatomy respectively.

Methods Normal group (n=8) : Optical measurements were performed in 8 animals (same litter) every 2-3 days from day 3 up to day 60. Hypoxia ischemia, HI group (n=7; 5 HI, 2 ligation control): 7 rabbits (same litter) were subjected to right common carotid artery ligation (post natal day 9, P9) Subsequently 5 of these animals were exposed to 10% hypoxia and the extent of brain cellular depolarization (ADC) was determined using dynamic diffusion weighted imaging[3]. T_2 weighted and diffusion tensor images were also acquired. Animals were recovered for 12 hours and optical measurements of the brain taken at intervals up to P76. NIRS measurements were performed (on awake animals) with a frequency-domain tissue spectrometer (Model No. 96208, ISS, Inc., Champaign, IL)[4]. The amplitude (ac) and phase (ph) data from four source-detector distances (ranging from 0.5 to 1.0 cm) were analyzed using the frequency-domain multi-distance method[5] to calculate absorption and reduced scattering coefficients at two wavelengths (690 and 830 nm). From these coefficients the absolute values of oxy-hemoglobin concentration ($[HbO_2]$), deoxy-hemoglobin concentration ([HbR]), total hemoglobin concentration (HbT), and hemoglobin saturation (StO_2) were calculated.

Results ADC decreased within the entire cortex (on average 50 % of baseline) during HI and returned to baseline post HI. There was no significant change in cortical (gray matter) fractional anisotropy values (0.21±0.05) for HI and ligation control animals. Cortical thickness (all HI and 2 normals) measured from T_2 weighted images, increased on average from 1.49 mm at P9-10 to 2.36 mm at P43. Light penetration into brain tissue was on average 3.0 mm, i.e., optical measurements were chiefly from cortical layers and the mean scattering coefficients remained unchanged in all animals throughout. StO_2 increased in all animals (40% at P9 to 70 % at P43) and there was no difference between normal, HI controls and HI brains (figure 1). HbT (figure 2) peaked between P15-17 (0.07 µm).

Discussion StO2 measured optically reflects blood oxygenation concentration found in the microvasculature, chiefly in the capillaries and increased steadily up to P76. This increase in StO2 is in agreement with the reported increase in blood flow during the first two months of life. HbT reflects blood volume which peaked at P17 as expected since the capillary density increases up to P17 when the microvasculature matures. After this period, tissue volume and vasculature both increase, resulting in constant blood volume. Our optical measurements support literature studies[2] which showed capillary maturation and coupling with metabolism at about P17. There was no difference, compared to normals, in hemoglobin saturation or total hemoglobin concentration in brain tissue that suffered transient ischemia. This may be due to the mechanism of tissue loss in this HI model. This data suggest that transient HI may not result in permanent changes in tissue oxygenation and blood volume.

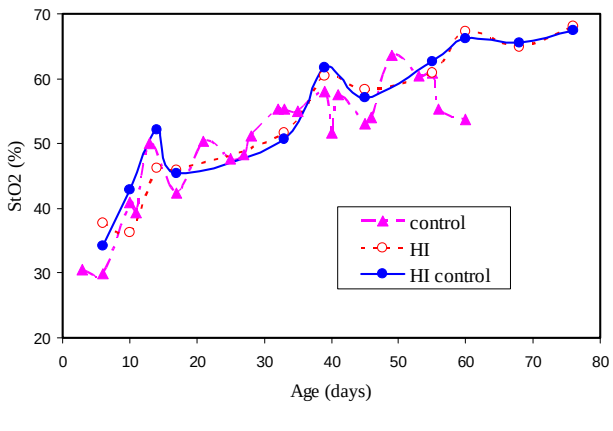

Figure 1: Oxygen concentration increases steadily with age.

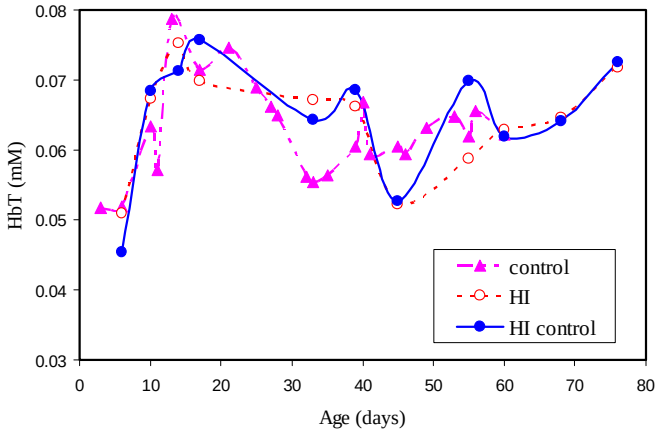

Figure 2: HbT increases rapidly (=50%) up to P17.

References

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