Hyperoximic Therapy of Hypoxic Neonatals Increases Cerebral Injury. DTI Study in Rats

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Introduction: Perinatal hypoxia has an adverse effect on the normal neurological development of infants. Recommended treatment is the inhalation of 100% oxygen, hyperoximia (1). We applied the P7 rat model to study perinatal ischemia and its treatment with hyperoximia using DTI.

Materials and Methods: Rat pups were divided into three groups: normal, HI (hypoxic injury), and HHI (HI treated with hyperoximia). At P7 the carotid artery of animals of the HI and HHI group was ligated. The animals were subsequently subjected to hypoxia. The rats of the HHI group were additionally treated with hyperoximia. The rats were scanned with a 7 Tesla horizontal bore scanner three weeks after injury. A 72mm i.d. volume coil was used for transmit, a 22 o.d. custom designed surface coil for receive. Animals were anesthetized during the scan with 2% isoflurane in an air/oxygen mixture. The respiration rate, surface body temperature, blood oxygen level, and heart rate were continuously monitored. The maps of the DTI metrics MD, axial diffusivity λl, radial diffusivity λt, and FA were generated using DtiStudio (Johns Hopkins University, Baltimore, MD). A more detailed description can be found elsewhere (2).

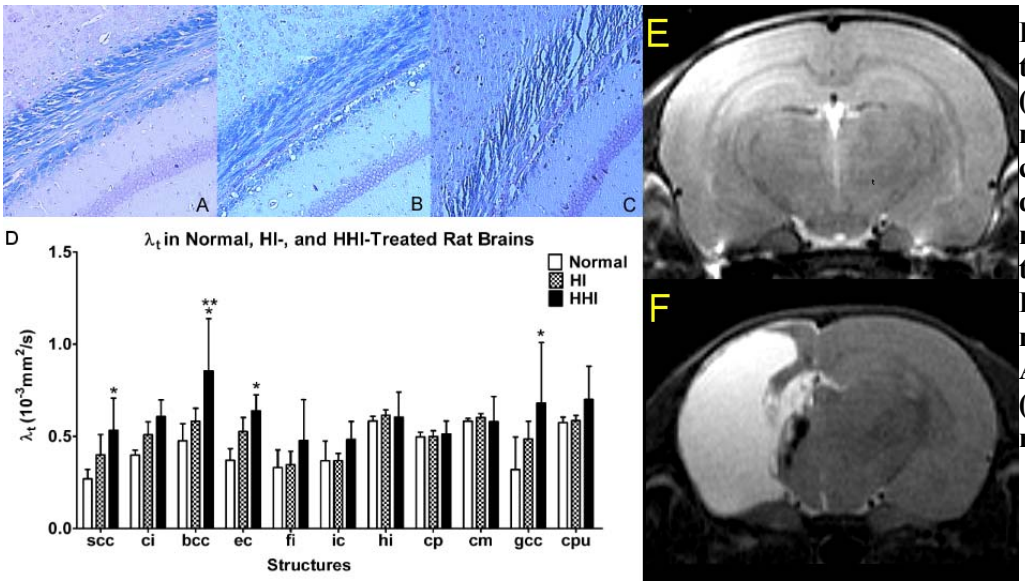

Figure 1: Histological sections of the contralateral external capsule (ec) stained for myelin: A; normal, B; HI, C; HHI. In contrast to A and B displays C disrupted cell architecture and missing tissue. In agreement are the average λt values of the ec in HHI significantly different from normal animals (Figure 1D). Axial T2 weighted MRI of a HI (E, histology in B) and of a HHI rat (F, histology in C).

Results: Figure 1 displays histological sections stained for myelin of the contralateral external capsule (ec): A; normal, B; hypoxia, C; hyperoximia. A and B do not show differences in cell structure and density. In contrast does C clearly show a disrupted cell architecture and missing tissue. In agreement is the average λt (Figure 1D) of the external capsule significantly different from the average normal ec, while the ec of hypoxic animals is not significantly different, neither from hyperoximic nor from normal animals. Figure 1E displays an axial T2 weighted MRI of a hypoxic (histology in B), Figure 1E of an hyperoximic rat (histology in C). Most significant differences of DTI metrics were found three weeks PI in the corpus callosum of hyperoximic rats.

Discussion: In summary, we found that hyperintense (edema) and hypointense lesions (hematoma) were larger in HHI than in HI (not shown). Histology showed disrupted cell architecture and loss of tissue more expressed in HHI than in HI. Generally, DTI-metrics of HHI were more frequently significantly different from normal rats than HI from normal rats. **Clinical Relevance**: In contrast to these findings does the '2005 International Guidelines on Cardiopulmonary Resuscitation and Emergency Cardiac Care' still recommend 100% oxygen as treatment for hypoxic neonatal infants (1). This recommendation needs to be reconsidered in the light of findings presented by us (3) and others.

References:

1. Resuscitation 67:293-303 (2005).
2. Bockhorst et al, JNR, 86 :1520-8 (2008).
3. Bockhorst et al, JNR, e-pub ahead (2009).