microstructure that relate to inferior IQ in VLBW young adults. Lower birth weight and perinatal problems seem to have permanent negative effects on white matter integrity.

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P75^{NTR} IS UPREGULATED AFTER NMDAR - MEDIATED EXCITOTOXIC BRAIN INJURY IN NEWBORN MICE

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Background and aims: Perinatal brain injury, leading to lifelong neurological handicaps, depicts a major problem in preterm infants. It has been shown that activation of P75 neurotrophin receptor (P75^{NTR}) plays a role in hypoxic-ischaemic and inflammation-mediated brain injury in adults. The role of P75^{NTR} in the pathogenesis of perinatal brain injury is unknown. We hypothesized that activation of the NMDA (N-methyl-D-aspartate) receptor in the immature brain induces an upregulation of P75^{NTR} and knock out of P75^{NTR} decreases brain injury.

Methods: We subjected 5-day-old P75^{NTR} knock out (KO) and wild type (WT) mice to excitotoxic brain injury by a single intracranial ibotenate (glutamate analogon) injection. P75^{NTR} expression was analysed at 4, 8 and 24 hours after brain injury by immunohistochemical staining for p75^{NTR} positive cells. Furthermore the number of activated caspase-3 positive cells was evaluated 24 hours after brain injury in P75^{NTR} KO and WT animals.

Results: In the WT cohort excitotoxicity significantly increased the number of P75^{NTR} positive cells in white (WM) and grey matter (GM) at 4 hours (GM $p< 0,01$; WM $p< 0,01$) and in WM also at 8 ($p< 0,01$) and 24 ($p< 0,05$) hours after injury. The number of caspase-3 positive cells was significantly decreased in WM in KO compared to WT animals ($p< 0.05$) 24 hours after injury.

Conclusion: We show the potential role of P75^{NTR} in a neonatal animal model of perinatal brain injury. Studies analysing detailed interactions of P75^{NTR} in developmental brain injury are ongoing.

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MOLECULAR CHANGES AFTER WHOLE BODY COOLING ON PIGLETS WITH INDUCED TRANSIENT HYPOXIC-ISCHEMIA IN THE DEVELOPING BRAIN

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Objective: To study the effect of whole body cooling and/or xenon treatment on molecular changes induced by transient hypoxic-ischemia (HI) in the developing brain.

Methods: Experiments were performed under UK Home Office licence in accordance with UK guidelines. Newborn Large-White piglets were anesthetized and subjected to controlled transient HI. Piglets remained anesthetized and randomised to: (i) no treatment (ii) whole body cooling to a rectal temperature of 33.5 ±0.5 °C after HI; (iii) xenon or (iv) cooling + xenon treatment. (v) naïve group subjected only to anaesthesia. Piglets were subjected to intensive care and monitoring. After euthenasia brains were perfused with 4% formalin and processed for in situ hybridization and immunohistochemistry. To characterize possible effects HI and treatments on the transcriptional activity of key neuronal and glial genes, we used in situ hybridization with probes designed to detect mRNA encoding HSP70, MAP2 and GFAP.

Results: HI caused GFAP mRNA levels to increase in cortex cerebri, but not in striatum. None of the treatments could counter act the increase in cortex. HSP70 mRNA was increased by HI in cortex and striatum. Treatments enhanced cortical increases, while slightly counteracting striatal. MAP2 mRNA decreased in cortex by HI. Protective effects were noted by both xenon and hypothermia, although not additive. Striatal levels were lower then cortical, although the general pattern was similar to cortex. Understanding of the molecular mechanisms of hypothermic and other neuroprotective agents will assist in determining optimal combination(s) of neuroprotective agents for protection of the challenged newborn brain.