Background Excessive glutamate release followed by N-methyl-D-aspartate receptor (NMDAR) activation displays an important cascade in the pathophysiology of perinatal brain injury. We have previously shown that dextromethorphan, a low-affinity NMDAR antagonist, is neuroprotective in an animal model of neonatal excitotoxic brain injury. Of interest, dextromethorphan also shows agonistic properties at the sigma-1 receptor ($\sigma$1R). Sigma-1 agonists have given beneficial results in animal models of adult brain injury.

Aim of the study To evaluate the effect of the selective $\sigma$1R agonist 2-(4-morpholinethyl) 1-phenylcyclohexanecarboxylate (PRE-084) in neonatal excitotoxic brain injury.

Results A single intraperitoneal injection of 0.1 $\mu$g/g (low dose) or 10 $\mu$g/g (high dose) bodyweight (bw) PRE-084, given 1 h after the excitotoxic insult, significantly reduced lesion size in cortical gray matter 24 h and 120 h after the insult. Repetitive injections of 0.1 $\mu$g/g PRE-084 proved to be equally effective. PRE-084 treatment resulted in a decrease in cell death indicated by reduced TUNEL positivity and caspase-3 activation. PRE-084 reduced the number of isletin B4-positive, activated microglial cells. Quantitative real-time PCR analysis showed no effect on $\sigma$1R gene expression at 1, 4, 8, 12, 24 and 48 h after intracranial ibotenate injection compared to control animals always kept in room air.

Conclusion We demonstrate that systemic treatment with the selective $\sigma$1R agonist PRE-084 protects against NMDAR-mediated excitotoxic brain damage.

CIRCULATING PROGENITOR CELLS IN PRETERM NEONATES WITH CNS INJURY - A PRELIMINARY REPORT

Background and Aims The assumption that the circulating progenitor cells participate in a hematocytic way in the endogenous regeneration effort after damage of body tissues is controversial and the exact type of the cells involved remains unknown, especially when referring to damages of the Central Nervous System (CNS). We assume that preterm neonates who undergo CNS injury respond in a similar way, and we investigate the progenitor cell populations that might be related to the devastating event.

Methods 25 preterm newborns were enrolled (gestation age <32 weeks). 10 of them underwent severe perinatal stress with metabolic acidosis and developed CNS injury (IVH III or higher, PVL or infarct), whereas 15 of them were assumed as controls with no obvious CNS injury. Peripheral blood was collected at days 1, 3, 9, 18 and 45 after birth and analyzed using flow cytometry. Cell populations of interest were EPCs (Endothelial progenitor cells, CD34+/CD133+/CD184+), HSCs (Hematopoietic stem cells, CD34+/CD184+/CD45+) and VSELs (Very Small Embryonic-Like SCs, CD34+/CD184+/CD45+).

Results EPCs were significantly increased in the group with CNS injury at days 1.9 and 18 and VSELs were marginally increased at day 1 and significantly at day 9. HSCs showed no specific variation.

Conclusion Circulating progenitor cells seem to play a role in the endogenous regeneration effort. Enhancing this effort might prove to be a good therapeutic practice in the future, whereas delineation of the timeframe of this effort would be essential. Larger studies are needed, as well as correlation with chemoattractants and longterm outcome is necessary.

SEIZURE BURDEN AND NEUROBEHAVIORAL SCORES AFTER THERAPEUTIC HYPERTHERMIA IN THE NEWBORN PIGLET

Background Therapeutic hypothermia (TH) is standard of care in newborns with hypoxic-ischemic encephalopathy (HIE). Although the predictive value of amplitude-integrated EEG (aEEG) after HIE has been studied, the predictive value of aEEG during TH remains to be established.

Aim To study aEEG characteristics and timing of recovery of neurobehavior in a newborn piglet model of HIE following TH.

Methods Newborn piglets (N=14) were subjected to 30 min hypoxia-ischemia and survived to 72h. Animals were randomly assigned to hypothermia (N=6) or normothermia for 24h after hypoxia-ischemia (N=6). aEEG was continuously recorded until ~40h post-insult and at 48 and 72h post-insult. Background pattern aEEG and presence of seizures were analysed. Neurobehavior was scored from 40 until 72h post-insult.

Results In hypothemic piglets aEEG background pattern recovered to continuous low voltage (CLV) within 2h post-insult until 36h post-insult. Normothermic piglets recovered within 2h post-insult to continuous normal voltage (CNV) until 36h, where there was a decrease in background pattern to CLV aEEG recovered to CNV in both groups by 72h post-insult. Seizures were recorded in

Abstracts

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Objective A small fraction of children born very preterm have overt cerebral palsy but many of them display subtle deficits in motor coordination, balance, and attention-deficit/hyperactivity disorder-like behavior. In the immature brain, the sudden increase of oxygen tension after birth amounts to hyperoxia, and experimental hyperoxia causes wide-ranging cerebral changes in neonatal rodents.

Methods Newborn mice were exposed to 48 h of hyperoxia (80% O2) from P6 to P8, and motor activity in running wheels was tested starting at adolescent age P30. Thereafter, from P44 to P53, regular wheels were replaced by complex wheels with variable crossbar positions to assess motor coordination. To determine white matter diffusivity, MRI with diffusion tensor imaging was performed in the corpus callosum in mice after hyperoxia at ages P30 and P53 in comparison to control animals always kept in room air.

Results Mice after neonatal hyperoxia had significantly higher values for maximum velocity and mean velocity in regular wheels than did control animals (P<0.05). In contrast, the motor challenge of the complex running wheels caused a greater decrease of maximum velocity in mice previously exposed to hyperoxia than in controls (P<0.05). Lower fractional anisotropy and higher radial diffusivity were observed in the corpus callosum of P50 and P53 mice after neonatal hyperoxia compared to control mice.

Interpretation Newborn mice exposed to hyperoxia display hyperactivity, motor coordination deficits, and impaired white matter diffusivity at adolescent and young adult ages.