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 (σ1R). Sigma-1 agonists have been shown to beneficial results in animal models of adult brain injury.

Aim of the study
To evaluate the effect of the selective σ1R agonist 2-(4-morpholinyl) 1-phenylcyclohexanecarboxylic acid (PRE-084) in neonatal excitotoxic brain injury.

Results
A single intraperitoneal injection of 0.1 µg/g (low dose) or 10 µg/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. Repeat injections of 0.1 µg/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 84-positive, activated microglial cells. Quantitative real-time PCR analysis showed no effect on σ1R gene expression at 1, 4, 8, 12, 24 and 48 h after intracranial ibotenate injection compared to healthy controls. In vitro PRE-084 protected against glutamate-induced morphological and functional changes in primary hippocampal neurons.

Conclusion
We demonstrate that systemic treatment with the selective σ1R agonist PRE-084 protects against NMDAR-mediated excitotoxic brain damage.

Circulating progenitor cells in preterm neonates with CNS injury - a preliminary report

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 P50. 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 P30 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.

Seizure burden and neurobehavioral scores after therapeutic hypothermia in the newborn piglet

Objective
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=8) 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 hypothermic piglets aEEG background pattern recovered to continuous normal voltage (CNV) 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 neeeded, as well as correlation with chemoattractants and longterm outcome is necessary.

Hypermotor activity and disturbed motor coordination in adolescent mice after neonatal exposure to hyperoxia

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