Background and aims  Acute kidney injury (AKI) is a common consequence of perinatal asphyxia (PA). Therapeutic hypothermia (TH) used for neuroprotection in hypoxic-ischaemicencephalopathy (HIE) may also ameliorate kidney injury. AKI can be associated with more severe PA, but association with worse neurological outcome remains to be proven. We aim to evaluate the incidence of AKI in neonates under TH and the association with HIE grades and outcome.

Methods  A total of 51 cooled infants were reviewed using a prospectively collected database. Modified AKIN criteria were used to classify AKI. We studied perinatal, resuscitation and clinical data during admission to the NICU. Outcome of interest was duration of NICU stay, predictable neurologic outcome and mortality.

Results  AKI was found in 17 of 51 neonates (33%). Based on the modified AKIN criteria, 13, 1, and 3 patients had stages I, II, and III, respectively. AKI was more frequent in HIE 2/3 than in the rare HIE 1 infants that were cooled (p < 0.03) and in those with worse base deficit at birth (p < 0.05). A significant association was found between vancomycin and gentamicin use and AKI (p < 0.01). Renal replacement therapy was needed in 2/3 of AKIN stage III infants. NICU stay, mortality and predicted adverse neurologic outcomes were not associated with AKI.

Conclusions  AKI was less frequent in our cohort than the one previously described in non-cooled newborns. More severely asphyxiated neonates were more likely to experience AKI, but AKI was not related to worse outcomes.

SCAVENGING OF EXTRACELLULAR HAEMOGLOBIN MODIFIES THE MONOCYTE-MACROPHAGE RECRUITMENT AND DIFFERENTIATION IN THE INTRAVENTRICULAR SPACE FOLLOWING IVH

Introduction  Severe cerebral intraventricular haemorrhage (IVH) in preterm infants continues to be a major clinical problem. To date, no available therapy prevents infants from neurologic sequel following IVH. Recruitment of monocytes-macrophages and periventricular infiltration is a key step in the inflammatory response leading to brain damage. The sequence of the recruitment and profiling of monocytes-macrophages following IVH is not well characterised. We have previously shown that extracellular haemoglobin induces chemotactic cytokines following IVH. Haptoglobin is a haemoglobin scavenger and could potentially protect the immature brain from the detrimental effects of haemoglobin.

Objective  To characterise the recruitment and differentiation of monocytes-macrophages in the intraventricular space following IVH and to investigate if haemoglobin scavenging with haptoglobin alters the recruitment and differentiation.

Methods  Using a preterm rabbit pup model of IVH we characterised the immune cell recruitment and differentiation in intraventricular cerebrospinal fluid (CSF) at 24 to 72 h following haemorrhage. Using flow cytometry, immunohistochemistry and mRNA and protein analysis we characterised the systemic and CSF infiltrating macrophages in animals with IVH, sham controls and animals treated with intraventricular injections of haptoglobin.

Results  Following IVH, there is an infiltration of M1 macrophages into the intraventricular CSF. Intraventricular introduction of the haemoglobin-scavenger haptoglobin modifies them into alternative M2 macrophages, expressing CD163. This causes a subsequent in vivo clearance of the accumulated haemoglobin.

Conclusion  Following IVH, intraventricular haptoglobin treatment modifies macrophage differentiation, initiating clearance of extracellular haemoglobin. Treatment of haptoglobin might be a feasible approach to protect the immature brain following IVH.

THE SIGMA-1 RECEPTOR AGONIST PRE-084 PROTECTS AGAINST GLUTAMATE INDUCED NEUROTOXICITY IN PRIMARY HIPPOCAMPAL NEURONS

Background  Prematurity is a major determinant of neonatal mortality and morbidity. The number of preterm birth is still on the rise. Recently we and others could demonstrate neuroprotective effects of sigma-1 receptor ligands in adult and newborn animal models of brain injury. Since sigma-1 receptor agonists are already undergoing clinical trials in adult neurological disease, they might be considered a promising therapeutic option also in preterm brain injury. We have previously shown that the selective sigma-1 receptor agonist PRE-084 (2-(4-morpholino-nethyl)-1-phenylcyclohexane-carboxylate) protects against neonatal excitotoxic brain injury in vivo. The aim of the present study was to investigate whether PRE-084 is able to prevent neurotoxicity following glutamate exposure in vitro.

Methods  Cultured primary hippocampal neurons (day in vitro 10) were pre-treated with PRE-084 before glutamate was applied. Subsequently cell death was quantified by means of PI/calcine – AM staining using live confocal microscopy. Neurons were randomly assigned to one of the following groups: i) control, ii) glutamate or iii) glutamate+PRE-084. PRE-084 was applied in two dosages (10 and 100 μM) prior to glutamate.

Results  The application of PRE-084 significantly reduced the percentage of dead cells (PRE-084 10 μM: 22.09 (20.50;28.84) and 100 μM: 25.87 (18.77;33.40)) compared to the untreated group (control 43.56 (39.86;46.02)).

Conclusion  Our data show that administration of PRE-084 protects against glutamate induced cell death in primary hippocampal neurons. PRE-084 shows considerable promise as a therapeutic strategy in preterm brain injury and might provide an adequate means of combating this major cause of neurological disability in infancy.

THE NEUROPEPTIDE SECRETONEURIN IS PROTECTIVE IN ESTABLISHED IN VITRO MODELS OF NEONATAL BRAIN INJURY

Background  Prematurity is a major determinant of neonatal mortality and morbidity. The number of preterm birth is still on the rise. Recently we and others could demonstrate neuroprotective effects of sigma-1 receptor ligands in adult and newborn animal models of brain injury. Since sigma-1 receptor agonists are already undergoing clinical trials in adult neurological disease, they might be considered a promising therapeutic option also in preterm brain injury. We have previously shown that the selective sigma-1 receptor agonist PRE-084 (2-(4-morpholino-nethyl)-1-phenylcyclohexane-carboxylate) protects against neonatal excitotoxic brain injury in vivo. The aim of the present study was to investigate whether PRE-084 is able to prevent neurotoxicity following glutamate exposure in vitro.

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Conclusion  Our data show that administration of PRE-084 protects against glutamate induced cell death in primary hippocampal neurons. PRE-084 shows considerable promise as a therapeutic strategy in preterm brain injury and might provide an adequate means of combating this major cause of neurological disability in infancy.
Background Hypoxic-ischaemic encephalopathy leads to neurologic impairment or even death. Secretoneurin (SN), a neuropeptide with angiogenic and anti-apoptotic properties, provided strong neuroprotection in an adult animal model of cerebral ischaemia.

Aim To evaluate the effect of SN in established in vitro and in vivo models of neonatal hypoxic-ischaemic brain injury.

Methods Seven day old mice underwent unilateral common carotid artery ligation, followed by exposure to hypoxia (8% oxygen). Thereafter, mouse pups were randomly injected intraperitoneally with SN (0.25 mg/g body weight) or vehicle. As endpoint we determined the histological injury score and the number of caspase-3 positive cells 24 h after the insult. Primary cultured hippocampal neurons were treated with oxygen glucose deprivation (OGD) on day 10. Neurons were assigned to the following groups: i) control ii) OGD iii) OGD+SN (1, 10 or 50 μg/ml). As primary outcome parameter, cell death was evaluated via real time live confocal imaging using calcein-AM and propidium iodide (PI).

Results SN displayed a non-significant trend to lower mean values of histological injury score compared to control (n = 11–12, p > 0.05) and significantly reduced the number of cells stained positively for activated caspase-3 (n = 6, p < 0.05). In vitro SN application on hippocampal neurons (OGD+SN) significantly reduced the number of dead cells assessed by the PI/calcein ratio compared with the untreated OGD group (n = 8, p < 0.05).

Conclusion We provide first evidence that SN is neuroprotective in established in vitro and in vivo models of neonatal hypoxic-ischaemic brain injury and might therefore be considered a promising therapeutic option.

Poster abstracts

PO-0398 INvolvement of the corpus callosum after perinatal asphyxia demonstrated using diffusion weighted MRI is related to neurodevelopmental outcome
T Alderliesten, Y Khall, C Koopman-Esseboom, MNL Benders, IC van Haastert, LS de Vries, F Gijnvendaal. Department of Neonatology, Wilhelmina Children’s Hospital University Medical Center Utrecht, Utrecht, Netherlands

Abstract PO-0398 Table 1

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<tr>
<td>Corpus callosum anterior</td>
<td>1094 ± 131</td>
<td>1033 ± 286</td>
<td>899 ± 233</td>
</tr>
<tr>
<td>Corpus callosum posterior</td>
<td>1064 ± 130</td>
<td>921 ± 265</td>
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Development at 18 months by age appropriate psychometric evaluations to see whether tests used at younger ages could predict worst outcomes at older ages in relation to some neonatal factors.

Method Along with neurologic examinations, 33 infants were prospectively evaluated at 3, 6, 12, 18, 24 months of corrected age with Bayley Scales of Infant Development – II (BSID-II), at 3, 5 years by age appropriate psychometric evaluations to see whether tests used at younger ages could predict worst outcomes at older ages in relation to some neonatal factors.

Results 72% of children had no (IQ >85), 24.3% had mild (IQ 74–84), 3% had major (IQ <70, blindness) impairments. 24.2% had special education, 15.2% ADHD, 6.1% autism, 9.1% learning/language, 6.1% anxiety disorders. The probability of neurodevelopmental test and IQ scores of VLBW infants <1000 gr being lower than healthy children at same age was 10.5 times higher (OR 4.7, 95%, CI 0.92–24.5) at 8 years of age. Oxygen treatment >30 days adversely affected the scores up to 18th month (OR 2.1%, 95%, CI 0.44–9.8). Babies having low scores of the 18th month-cognitive and motor sub-test of BSID-II had 16 times higher probability of having low WISC-R total IQ scores at 8 years. (p < 0.05). 19 children with sepsis at 8 years had lower performance and total IQ scores (p < 0.05).

Conclusion Prolonged oxygen therapy and having and sepsis are significant factors affecting later IQ of VLBW infants. Lower BSID-II scores at 18th month may predict future lower total IQ scores. Longitudinal follow up and early intervention is of paramount importance.

PO-0399 Neuroprotective Effect of Pentoxifylline in Rat Pups with Hypoxic-Ischaemic Encephalopathy
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Abstract PO-0399 Table 1

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