neurogenesis pathway related genes (including Bdnf and Shh) on cerebellar and prefrontal cortical tissue.
Results Overall BDNF analysis showed no differences between term and preterm brains but levels were significantly different between day 5 and 26 in preterms only. SHH appeared to be lower in preterms compared to terms, but only significantly on Day 26.
Conclusions The reduced levels of SHH, specifically at day 26, suggest that SSH may be a useful biomarker for delayed brain development and indicate that the pig may provide a relevant model to study the premature brain.

PS-335 PRETERM AND TERM PIGLETS SHOW SIMILAR POSTNATAL ELECTROENCEPHALOGRAPHY (EEG)

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Background Electroencephalography (EEG) changes rapidly with maturation of the brain in preterm infants. Amplitude-integrated EEG (aEEG) becomes more continuous, bandwidth narrows, and frequencies switch towards faster rhythms, as the child grows older. In preterm infants with brain damage this maturation is typically delayed. We are in the process of developing a preterm piglet brain model. Here we present the results of the EEG as a measurement of brain development in 1–11-day-old preterm and term piglets.
Methods One hour of EEG was recorded in 31 preterm piglets aged 1, 2, 4 and 11 days and in 10 term piglets aged 2 and 11 days. All piglets were delivered by C-section at either 90% or 100% gestation. Upper and lower margins of the aEEG band were visually identified and bandwidth calculated as the difference between the two values. Spectral analysis of the raw EEG was used to determine the relative power in the delta-(0.5–3 Hz), theta-(4–7.5 Hz), alfa-(8–12.5 Hz), and beta-(13–30 Hz) bands. General linear models were used with term vs. preterm, and age as predictors.
Results All aEEGs were continuous. The overall means (SD) of upper and lower margin, and bandwidth were 7 mcV (1.7), 15 mcV (5.7), and 8 mcV (4.3). Upper-, lower margin, bandwidth, alpha, beta and delta bands were unaffected by the predictors whereas the theta band was negatively correlated to age.
Conclusions The preterm piglet EEG was continuous already 10 days prior to term. Thus, maturation of EEG was neither seen in preterm nor term piglets and EEG may not be useful for studying perinatal brain maturation.

PS-336 INFLUENCE OF N-ACETYLCYSTEINE AMIDE (NACA) ON THE INFLAMMASOME PATHWAY. A STUDY ON NEONATAL PIGS

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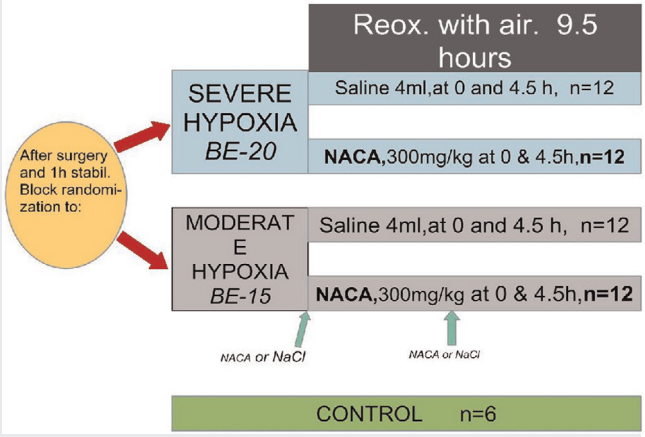
10.1136/archdischild-2014-307384.635

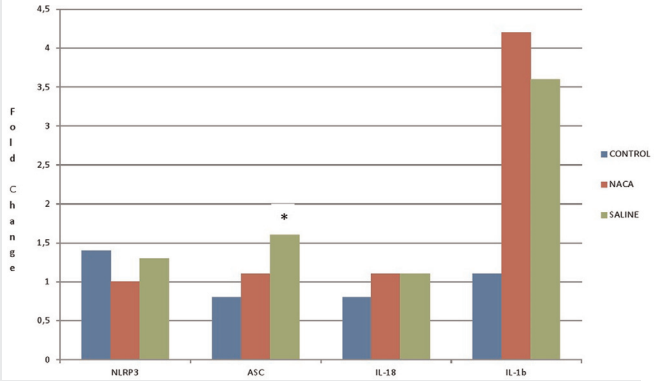
Abstract PS-336 Table 1 Study design: Fifty-four newborn piglets, age 12–36h, were included. Invasive blood pressure, EEG and ECG were measured continuously. One control group (n = 6) and 4 experimental groups (n = 12), exposed to global hypoxia, until BE was either -15 or -20 mmol/l (moderate/severe asphyxia with or without NACA) The pigs were observed for 9.5 h



Background and aims Severe perinatal hypoxia contributes to approximately 6% of spastic cerebral palsy (CP). Studies have indicated an association between elevation of IL-1beta after perinatal asphyxia and the development of CP. The NLRP3 Inflammasome complex may lead to release of the cytokines IL-1beta and IL-18 and cell death. Reactive oxygen species (ROS) have been proposed to be an upstream inducer of this complex and the anti-oxidant N-Acetylcysteine amide (NACA) may provide organ protection after hypoxia.
Objectives To map inflammasome activation in specific brain regions of the pig after neonatal hypoxia-reoxygenation and to investigate if the expression of different proteins in this pathway are modulated by NACA.
Methods
Study design (Table 1).

ELISA was used to measure IL-1b protein in cerebral cortex and Realtime PCR for mRNA expression of NLRP3, ASC, IL-1b and Il18 in cortex, cerebellum, hippocampus and striatum.
Results After severe hypoxia the protein expression of IL-1b in cerebral cortex was reduced for the NACA treated pigs vs. saline, $p < 0.05$.

Abstract PS-336 Table 2 Fold change for NLRP3, ASC, IL-18 and IL-1b measured in cerebral cortex. Significant difference in Fold Change of ASC (*), $p < 0.05$. All values are Median values



When comparing all the pigs treated with NACA vs. saline after hypoxia Fold Change of ASC in cortex was significantly reduced, p (Table 2).

In hippocampus, cortex and Striatum Fold Change of IL-1b was elevated in all the hypoxia groups compared with the control group, p

Conclusion NACA reduces the protein expression of Il-1beta and mRNA-expression of ASC in cortex after hypoxia. This may indicate that NACA has some neuroprotective abilities after perinatal asphyxia.

Upcoming analyses of histopathology and injury markers will elucidate possible neuroprotective effects of NACA treatment following birth asphyxia.

PS-337 WITHDRAWN

PS-338 CONCURRENT ALLOPURINOL AND HYPOTHERMIA TREATMENT IN A TERM NONHUMAN RAT MODEL OF HYPOXIC ISCHAEMIC ENCEPHALOPATHY

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Background and aims Hypoxic-ischaemic encephalopathy (HIE) has been associated with long-term disabilities. Hypothermia is effective but does not provide complete neuroprotection, adjunctive therapies are necessary. Allopurinol has been proved as a good neuroprotector, but it has never been tested associated with hypothermia. The aim of the present study was to examine therapeutically effectiveness of dual therapy (hypothermia + allopurinol) versus hypothermia, in a neonatal rat model of HIE.

Methods 120 Wistar pups at postnatal day 10 were used and divided into 5 groups: Sham-Operated, Hypoxic-ischaemic (HI) aggression, HI aggression + Allopurinol, HI aggression + Hypothermia, HI aggression + Hypothermia + Allopurinol.

At 25 day of life, spatial memory was assessed via water maze test. Finally, rats were anaesthetised and sacrified. In order to assess possible alterations in the hippocampal synaptic network, 3 specific synaptic proteins (PSD95, SNAP25, synaptophysin) were tested by Western Blot.

Results There were differences in the learning outcomes among hypoxic, hypoxic + allopurinol, hypothermia, hypothermia + allopurinol and sham operated ($p < 0,05$). The worst group was the hypoxic one.

Synaptophysin and SNAP25 levels were higher in controls and treatment groups compared with hypoxic untreated animals. However, the highest level of PSD95 corresponded to the hypoxic group.

Conclusions Hypothermia and allopurinol seem to improve learning in HIE pups.

Increased levels of presynaptic proteins in the treatment groups suggest that hypothermia and allopurinol improve synaptic plasticity compared with untreated group.

PSD95 was also described in the literature as a suppressor of dendritic arbour development, so this could explain our results in the hypoxic group.

PS-339 THERAPEUTIC HYPOTHERMIA IN THE ASPHYCTIC NEWBORN: IMMUNOHISTOCHEMICAL COMPARISON OF THREE COOLING TARGET TEMPERATURES IN THE PIGLET BRAIN

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Background and aims Therapeutic hypothermia has now become standard of care for neonatal hypoxic-ischaemic brain injury, as it reduces death and neurological sequelae without neurodevelopmental disabilities. There are however around 40% of infants who, despite treatment, have an adverse neurodevelopmental outcome. We aimed to assess brain regional cell death and microglial activation with cooling to 35°C, 33.5°C, and 30°C after hypoxia-ischemia (HI) in the piglet asphyxia model.

Methods Following HI and resuscitation, 28 newborn piglets were randomised to: (i) normothermia (38.5°C throughout), or whole-body cooling 2–26 h post-insult to (ii) 35°C, (iii) 33.5°C, or (iv) 30°C (all groups $n = 7$). At 48 h after HI, regional neuropathological analysis was performed to assess delayed cell death (quantitative analyses of both TUNEL-positive cells and cleaved caspase 3 immunoreactivity) and microglial activation (Iba-1 staining).

Results Compared with normothermia, cooling to 33.5°C showed a strong reduction in delayed cell death in periventricular white matter, hippocampus, caudate, putamen, thalamus and midtemporal cortex, a beneficial effect also extended to other cortical areas when analysing microglial activation. Cooling to 35°C was also beneficial, but in fewer regions than at 33.5°C. On the contrary, cooling to 30°C neither reduced delayed cell death nor maintained the microglial ramification index, showing a global neuropathological pattern similar to that observed in the normothermic group.

Conclusions In our piglet perinatal asphyxia model, the optimum therapeutic hypothermia temperature is 33.5°C, thus suggesting that the extent of neuroprotection might not proportionately increase with temperature decreases.

PS-340 AGE-RELATED CHANGES AND EFFECTS OF MILD HYPOTHERMIA ON CAROTID ARTERY REACTIVITY IN NEWBORN RATS

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Introduction Therapeutic hypothermia has become a standard neuroprotective treatment in term newborn infants following perinatal asphyxia. Hypothermia-induced changes in the reactivity of the vessels supplying the brain might play a role in its therapeutic or side effects. We investigated the putative age-related changes and the effect of clinically relevant cooling (33°C) on the reactivity of the newborn rat carotid artery.