September 21st, 2023 13:30 - 14:30

SHORT ORAL PRESENTATION SESSION 9 – BRAIN 2

ID 237. Establishment and characterization of a combined model of hyperoxia-mediated developmental brain and lung injury

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Background

About 1% of all newborns is born extremely preterm. Despite increasing survival rates, the risk for chronic diseases like bronchopulmonary dysplasia (BPD) and encephalopathy of prematurity (EoP) remain high. The extra–uterine foetus is very susceptible to oxygen exposure that is higher than in–utero, leading to developmental injuries especially in the immature brain and lung. Preterm infants suffering from BPD are at higher risk for poor neurodevelopmental outcome, however, the link between the respectively injured organs remains unclear. We established a combined model of

hyperoxia–mediated brain and lung injury in rats to analyse the lung–brain axis, allowing subsequent evaluation of the therapeutic potential of mesenchymal stem cells.

Methods

To establish a hyperoxia model suitable for assessment of both affected organs postnatal day 2 (p2) Wistar rats were exposed to 80% oxygen for 7 days. On P11 structural damage in the lungs was assessed with hematoxylin–eosin staining and immunohistochemistry (IHC) for pro–surfactant protein C (pSP–C) and in the brain with IHC for myelin basic protein. Changes in gene or protein expression for myelin–associated proteins in the brain and structural markers like alpha smooth muscle actin in the lung were investigated with qPCR and Western Blot. Cytokine expression and oxidative stress markers like superoxide dismutase were analysed with qPCR in both organs.

Results

Subacute analyses (P11) in the brain revealed a reduced expression of myelin associated proteins (CNPase, MBP, MAG) on cellular, gene and protein levels, indicating a pronounced white matter injury. Additionally, lung analyses indicated an impairment in lung development reflected by increased aSMA–levels and reduced gene expression for pSP–C and VEGFa.

Conclusion

Seven days of hyperoxia resulted in EoP– and BPD–like injury in the immature brain and lung. This combined model opens new opportunities to analyse therapeutic approaches like mesenchymal stem cells in neonatal lung and brain injury. Future analyses will focus on the effect of hyperoxic exposure on vascular architecture in

both organs using light sheet microscopy. Furthermore, motor–cognitive functions will be tested in 6 weeks– and 6 months–old rats.

None declared

ID 238. Evaluating the therapeutic potential of human mesenchymal stem cells in a double-hit model of encephalopathy of prematurity

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Background:

Premature born infants represent the largest patient cohort in pediatrics. While inflammation is one of the main risk factors for premature birth. Premature born infants are highly susceptible to different noxious like high oxygen concentrations (hyperoxia). As demonstrated previously, hyperoxia as well as inflammation induces perinatal brain injury affecting white and gray matter structures differently. Up to now, effective therapies are missing.

Mesenchymal stem cells (MSCs) appear promising because of their described neuro–regenerative effects.

Methods:

in vivo: At embryonic–day–20 pregnant Wistar–rat–dams received either a single injection of 100 µg/kg lipopolysaccharide or sodiumchloride intraperitoneal. Pups were kept under hyperoxia (80% O2) or normoxia (21% O2) at P3 for 48 h. At P11 the white and gray matter as well as neuroinflammatory responses were analyzed by different markers via immunhistochemistry (IHC) and western blotting (WB).

in vitro: To evaluate cell specific effects of MSC–treatment, primary oligodendrocyte precursor (pOLN) and hippocampal–neurons were used. Following hyperoxia at day 3 or 5 for 8 h, pOLN as well as embryonic–hippocampal–neurons were co–cultured in a non–contact system with naïve or hypoxic–pre–conditioned MSCs for 48 h. The degeneration, proliferation and differentiation capacity of the target cells were analyzed by immunocytochemistry (ICC).

Results:
in vivo: The differentiation capacity of oligodendrocytes, assessed by MBP and CC1, demonstrated marked alterations in the developing white matter. A combination of maternal inflammation and postnatal hyperoxia induced a significant reduction of MBP protein expression (IHC and WB), accompanied with decreased fiber length and intersections. Furthermore, the reduced brain volume in the double–hit condition was associated with a reduced expression of TBR–1 in deep cortical layers. Moreover, the combination of maternal inflammation and postnatal hyperoxia induced an activation of microglia assessed by co–staining of Iba1/CD68 via IHC.
in vitro: Hyperoxia–induced degeneration and reduced proliferation of pOLNs were ameliorated by co–culturing with naive as well as hypoxic–preconditioned MSCs. Preliminary data suggest that hyperoxia–triggered degeneration and disturbed differentiation of hippocampal–neurons is ameliorated by MSC–co–culture.

Conclusion:
In this study, we newly established double–hit model and started to assess therapeutic effects of MSCs as a potential treatment option for neonatal brain injury.

None declared

ID 138. IGF-1 Supplementation Supports Motor Coordination and Affects Myelination in Preterm Piglets

Miss Line Christiansen[1], Miss Gemma Ventura[1], Miss Karoline Aasmul–Olsen[1], Miss Sandy Lindholm[1], Doctor Bo Holmqvist[2], Doctor Matthew Lycas[3], Doctor Yuki Mori[4], Doctor Jan Secher[5], Professor Douglas Burrin[6], Professor Thomas Thymann[1], Professor Per Sangild[1], Doctor Stanislava Pankratova[1]

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BACKGROUND: Preterm infants are born with low circulating insulin–like growth factor 1 (IGF–1) levels and high risk of impaired neurodevelopment. We previously showed that short–term IGF–1 supplementation (until 5–9 days after birth) promoted maturation of the immature brain in preterm pigs used as model for preterm infants (Christiansen et al., eNeuro, 2023). Here we examined the effects of postnatal IGF–1 supplementation for 19 days, on neurological development in a piglet model.

METHODS: For 19 days after preterm birth (90% gestation), pigs were supplemented with IGF–1 (2.25 mg/kg/day systemic IGF–1 in complex with IGFBP–3) to reach levels in term pigs. Neuromotor functional tests (in–cage activity, open field, balance beam test, gait analysis) and cognitive assessment (novel object recognition, operant conditioning) were conducted. Brains were collected for magnetic resonance (MRI) and immunohistochemical as well as qPCR analyses. Overall protein synthesis was measured for the cerebellum.

RESULTS: Compared with control pigs, IGF–1 pigs showed improved performance and stride length in the balance beam test. No effects were observed for other neuro–motoric or cognitive tests. The cerebellar protein synthesis rate was increased for IGF–1 pigs, without effects on regional brain weights except for reduced caudate nucleus weight. Expression of myelin–associated genes (MBP, MOG, MAG, OPALIN) was reduced in the caudate nucleus and cerebellum, together with reduced MBP protein expression in periventricular and cortical white matter regions. Oligodendrocyte proliferation and grey–white matter ratio (MRI) showed no differences. IGF–1 pigs showed reduced hilar synapse formation, but neuronal maturation and microglia density were unaffected. Reduced ratio of NKCC1:KCC2 gene expression in the caudate nucleus of IGF–1 piglets indicated enhanced maturation of the GABAergic system.

CONCLUSION: Three weeks of IGF–1 supplementation after preterm birth promoted postural control, possibly by enhancing GABAergic maturation in the caudate nucleus. The region–specific reductions in myelination by IGF–1 may reflect accelerated age–dependent changes or negative feed–back response to prolonged IGF–1 supplementation. No adverse outcomes were detected for neurofunctional tests or neuron and glial cell maturation. Supplemental IGF–1 may support brain development in preterm infants, but effects could be highly region–, age– and time–dependent. UCPH, represented by authors T.T, P.S, and S.P., and Oak Hill Bio have filed patent applications of rhIGF–1 use for preterm infants. The remaining authors report no conflict of interest.

ID 901. THE EFFECT OF REMOTE ISCHEMIC POSTCONDITIONING ON TUNEL STAINING AS A MARKER OF BRAIN INJURY IN A NEWBORN PIGLET MODEL OF MODERATE TO SEVERE HYPOXIA-ISCHEMIA

Doctor Lærke Hansen[1], Doctor Ted Andelius[1], Doctor Hannah Andersen[1], Medical student Mads Andersen[1], Doctor Mette Pedersen[1], Medical student Sofie Schaaning[1], Medical student Kasper Seiersen[1], Postdoctoral research associate Eridan Rocha-Ferreira[2], Professor Henrik Hagberg[2], Doctor Kasper Kyng[1], Professor Tine Henriksen[1]
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Background
Therapeutic hypothermia (TH) is currently standard treatment for hypoxic-ischemic encephalopathy (HIE). However, TH will only be neuroprotective in some individuals and additional treatment is therefore needed. Remote ischemic postconditioning (RIPC) may provide additional neuroprotection for newborns with HIE. TUNEL-staining is used to assess the extent of neuronal cell death in animal models of HIE. The aim of this study was to investigate the neuroprotective effects of RIPC combined with TH compared to TH alone in piglets using TUNEL staining from hippocampus as marker of brain injury.

Methods
Thirty-eight piglets were anaesthetized, subjected to a standardized global HI insult, and randomized to RIPC+TH (n = 13) or TH (n = 13). A no treatment group (NT) (n = 8), and a sham group (n=4) was included to provide proof of concept. RIPC was performed 1 hour after HI by occluding blood flow to both hind limbs for five minutes followed by five minutes of reperfusion in four cycles. RIPC was repeated after 12,

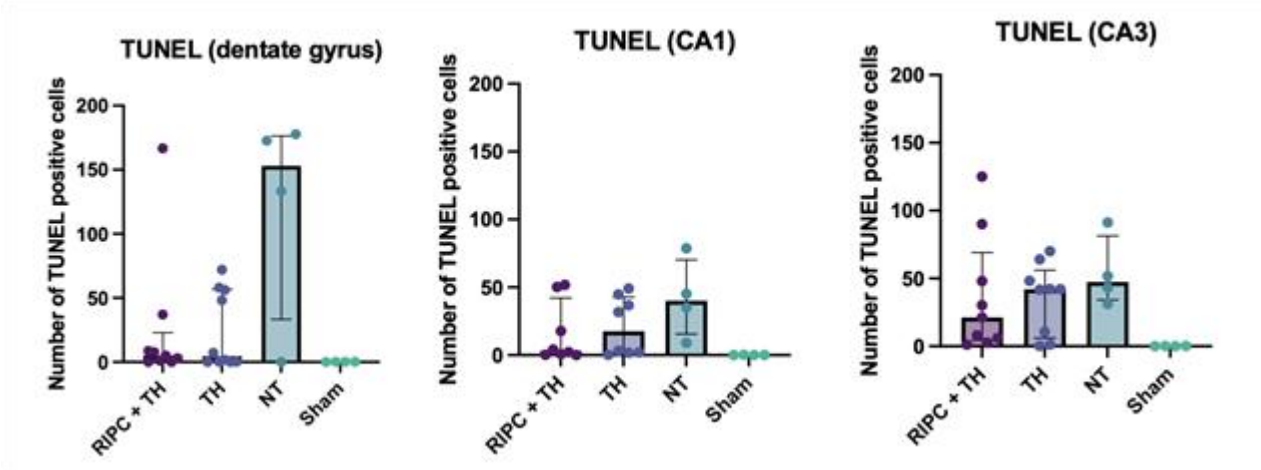
and 24 hours. The piglets were euthanized after 44 hours, and the brains were removed for histological analysis.

Results

Baseline– and insult characteristics were similar between groups. Three piglets died in each of the two treatment groups and four in the NT group. We found no difference between the two treatment groups in number of TUNEL positive cells in any of the three regions of hippocampus. We observed fewer TUNEL positive cells in the two treatment groups compared to the non–treated group in the dentate gyrus. The same pattern was observed in the two other regions but without statistical significance (Fig.1).

Conclusion

In these preliminary analyses RIPC showed no added neuroprotective effect in combination with TH following HI in newborn piglets when measured by the number of TUNEL positive cells. Histology from additional brain regions including the periventricular white matter, thalamus, and putamen as well as other markers of brain injury will be presented at the conference.



Number of TUNEL positive cells obtained in three different regions of hippocampus. Scatter plots with superimposed median with interquartile range. Mann–Whitney test showed no statistical difference between RIPC+TH and TH.

Number of TUNEL positive cells obtained in three different regions of hippocampus. Scatter plots with superimposed median with interquartile range. Mann–Whitney test showed no statistical difference between RIPC+TH and TH.

None declared

ID 912. Uncovering Early Predictors of Cerebral Palsy through the Application of Machine Learning

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Background. Cerebral palsy (CP) is a neurological disorder with profound implications for child development and well-being. Early identification of children at risk for developing CP may lead to improved outcomes. This study aimed to identify early predictors of CP using a machine learning (ML) approach.

Methods. Two population-based databases, the National Perinatal Information System (NPIS) and the Slovenian Registry of Cerebral Palsy (SRCP), were merged using birth date, birth weight, gender, and birth multiplicity as matching criteria. Three hundred eighty-two unique CP cases were identified. Controls were selected at a control-to-case ratio of 3:1, with matching gestational age and birth multiplicity. Various ML algorithms were evaluated using ROC, sensitivity, and specificity values, to identify the best model for predicting CP.

Results. CP cases with birth defects (n=44) were excluded from the analysis. A final number of 338 CP cases was included in the study. Multiple prenatal and neonatal

factors were included as predictors. The average ROC values of different machine learning algorithms ranged from 0.50 to 0.80, with a mean sensitivity below 0.50 and mean specificity above 0.90.

Conclusion. In our cohort, early prenatal and neonatal factors were not found to be sensitive indicators of whether a child will develop CP. However, this might be due to the highly heterogeneous sample of CP and the low presence of severe clinical problems in our sample. Therefore, validation in larger cohorts is needed. In addition, an extended set of crucial variables is needed to distinguish between CP cases and controls. As a next step, we plan to evaluate the added value of genetics and magnetic resonance imaging data to improve the prediction models. These findings could have significant implications for identifying and managing children at risk for CP, potentially improving outcomes in this population.

None declared.

ID 419. Gender and Inflammation in Neonatal Encephalopathy

Doctor Lynne Kelly[1,2], Dr Aoife Branagan[1,2], Prof Catherine Greene[4], Dr Afif El-Khuffash[5], Prof Martin White[7], Dr Jan Miletin[7], Dr Claudine Vavasseur[3], Prof Eleanor Molloy[1,2,6,7,8]

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Background

Neonatal encephalopathy (NE) is a devastating condition of the term newborn infant which can result in adverse neurodevelopmental outcomes, cerebral palsy or even death.

There is a well-recognised difference in incidence and outcome of NE according to gender with a pronounced male disadvantage. Females have a lower incidence of developmental delay and learning difficulties in comparison with males.

The aim of this work was to delineate the immune responses between male and female infants with NE.

Methods

Peripheral blood from infants with NE were treated with either, endotoxin (LPS; 10ng/ml), Estradiol (E2; 10^8nM) or E2+LPS combined for 1hr at 37°C.

The NLRP3 inflammasome components, NLRP3, IL1β and ASC and the X-linked genes BTK, IRAK and IKKγ were analysed between genders via RT-PCR. Multi-spot

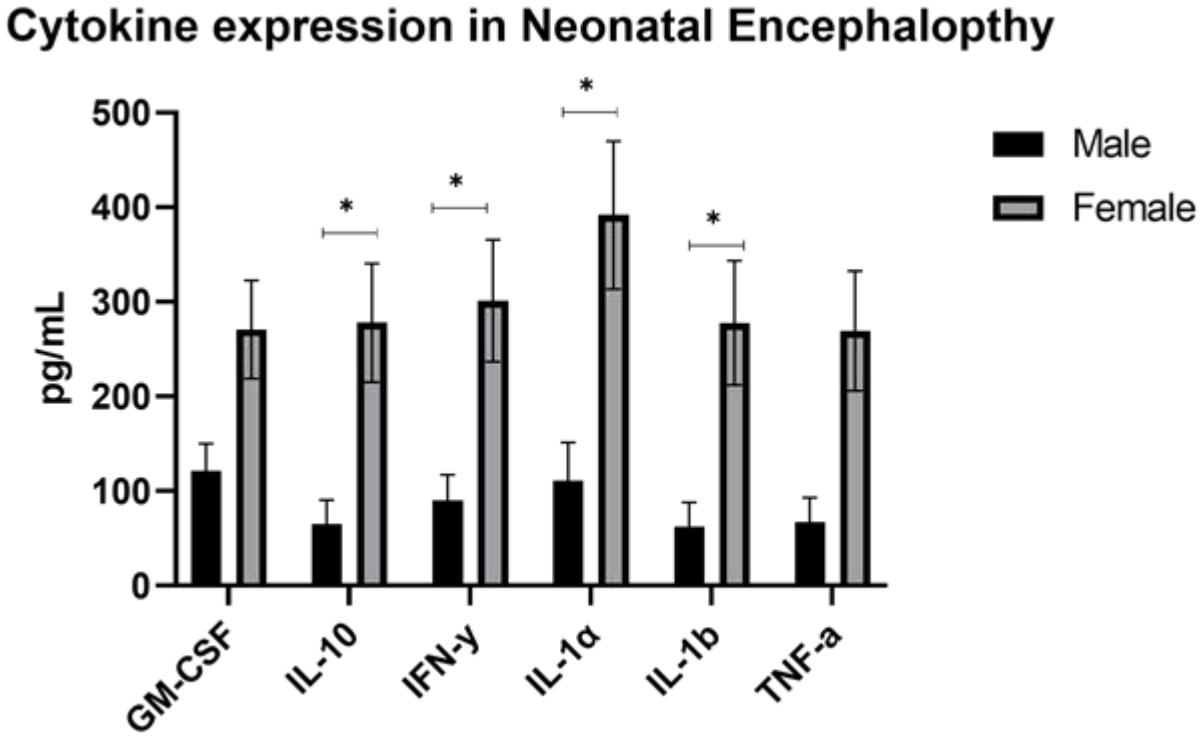
ELISA analyses of serum cytokines were gender stratified and flow cytometry was performed to assess activation of neutrophils and recognition of LPS.
Statistical analysis was carried out using Graphpad Prism V9.4.

Results

33 infants with NE were recruited (20 male and 13 female).
IL–1β levels are lower in females with significant differences in the males upon LPS stimulation ($p=0.0002$) versus baseline and E2 attenuates this effect significantly ($p=0.03$). ASC expression differed between male and female infants significantly in response to LPS ($p=0.043$).Both males and females have increased NLRP3 following LPS stimulation and estradiol reduces this expression.
X–linked genes were not significantly different, although IKKγ expression differed with E2+LPS stimulation ($p=0.011$) and there were no differences in neutrophil CD11b or TLR4 expression between sexes.
Multiple linear regression showed significant gender differences in the levels of IL–10 ($p<0.03$), IFNγ ($p<0.03$), IL–1α ($p<0.008$) and IL–1β ($p<0.03$) with females having overall higher levels of expression.

Conclusion

Inflammasome components IL–1β and ASC showed significant gender differences.
Stimulation with the female hormone Estradiol reduced LPS responsiveness in IL–1β.
Downstream protein expression also differed significantly between genders with female NE infants having a more robust inflammatory profile.
Understanding why males have higher rates of adverse outcomes is key to designing therapeutic interventions to improve the health of this cohort. Further mechanistic investigations are necessary to better understand these gender differences.



Cytokine profile of male and female infants with NE at baseline

Cytokine profile of male and female infants with NE at baseline

None declared

ID 1000. Implementation of a Preterm Neuroprotection Care Bundle

Doctor Alison Mintoft[1], Doctor Monika Janagill[1], Doctor Danielle Furnell[1], Doctor Alina Petric[1], Doctor Emma Pearson[1], Doctor Sehar Khushi[1], Ms Sarah Hines[1], Doctor Jessica Ellis[2], Doctor Madeleine Barnett[1], Doctor Leigh Dyet[1], Doctor Audrienne Sammut[1]

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Background

Intraventricular haemorrhage (IVH) is a frequent complication of prematurity, with those born most prematurely at highest risk. Although trends in survival of those born prematurely have improved, the risk of developing IVH and neurodevelopmental impairment (NDI) remains high (Marlow et al 2014 and Bolisetty et al)). Isolated low grade IVH is independently associated with NDI (Rees et al 2022 and Uccella et al 2023) and IVH associated complications including surgical intervention for post–haemorrhagic ventricular dilatation (PHVD) are highly associated with severe NDI. Evidence based neuroprotective care bundles have been shown to reduce the incidence of IVH (de Bijl–Marcus et al and Benlamri et al). Our aim was to implement an evidence–based preterm neuroprotection care bundle to reduce the incidence of IVH in infants born <30 weeks gestation in a tertiary NICU.

Methods

We implemented a neuroprotection bundle consisting of interventions targeting antenatal optimisation (complete steroid course, magnesium sulphate) stabilisation (deferred cord clamping), and the first 72 hours of life (minimal handling, midline

head position, and standardisation of initial hemodynamic and respiratory management) in March 2021. The bundle of care was implemented alongside an education programme, regular data benchmarking and preterm care champions. Anonymised patient data were collected from Sept 2019–December 2022 from electronic patient records. Cranial Ultrasounds were reviewed by two clinicians and graded according to the Papille classification. Mann Whitney U tests were used to assess differences between pre and post intervention groups for continuous variables. Chi Squared tests were used to assess differences in dichotomous variables.

Results

There were no significant differences in characteristics between the pre intervention and post intervention cohorts (Table 1). Our intervention was shown to reduce the rate of IVH in infants (40% vs 23%, p value = 0.004).

Conclusion

We have demonstrated that implementation of a preterm neuroprotection care bundle reduced the incidence of IVH in our tertiary neonatal unit.

	Pre-intervention (107)	Post-Intervention (128)	P Value
Male Sex (%)	63 (59)	66 (52)	0.262
Gestational Age	27.14 (22.57-29.86)	27.43 (22.86-29.86)	0.568
Weight (g)	840 (446-1744)	859 (447-1661)	0.444
5 min APGAR	8 (1-10)	8 (2-10)	0.582
Antenatal Steroids (complete course) (%)	88 (82)	99 (77)	0.354
IVH (%)	43 (40)	29 (23)	0.004*
Grade 1-2 IVH (%)	27 (25)	16 (12.5)	0.012*
Grade 3-4 IVH (%)	17 (16)	13 (10)	0.190
PHVD requiring surgical intervention (%)	5 (5)	2 (2)	0.162

Table 1. Cohort demographics and incidence of Intraventricular Haemorrhage

Table 1. Cohort demographics and incidence of Intraventricular Haemorrhage

None declared

ID 924. The Effects of Socioeconomi Status on Preterm White-Matter Microstructure: An exploratory TBSS study

Miss Julianna Lopez[1], Miss Rita de Lima[1], Doctor Maria Luisa Tataranno[1], Doctor Corine Koopman-Esseboom[1], Doctor Henriette F.N. Swanenburg de Veye[2], Miss E. Janson[1], Miss E.R. de Groot[1], Doctor Femke Lammertink[1], Doctor Floris Groenendaal[1], Doctor Niek E. van der Aa[1], Doctor Jeroen Dudink[1], Professor Doctor Manon J.N.L. Benders[1]

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Background — Preterm infants are vulnerable to adverse neurodevelopment, making it essential to pinpoint early predictors. Increasingly more studies find that socio-environmental factors such as socioeconomic status (SES) can have a significant effect on brain development and neurodevelopmental outcomes. The objective of this study was to study the effects of SES on white matter microstructure at term equivalent age (TEA) in extremely preterm born infants using tract-based spatial statistics (TBSS).

Methods — Retrospective data of 97 infants born before 28 weeks of gestation (between 2013-2016) were included. SES was measured by parental education level on a scale of 3 and SES-indicators based on the Dutch Central Bureau of Statistics' postal-code data. Additionally, sex, gestational age (GA) at birth, age at TEA scan (PMA40), days of ventilation, birthweight z-scores, parental presence (PP), and kangaroo care (KC) were analysed as covariates. Whole-brain analyses were performed using TBSS on white matter fractional anisotropy maps. First simple

analyses were performed with each individual parameter adjusted for PMA40. Based on the significance of results, analyses were repeated adjusting for the remaining covariates. Additional exploratory analyses were done to test the association between the other covariates and FA maps.

Results — No significant associations were found between SES and FA. Significant positive and negative correlations were found between FA and GA at birth, and the latter was sustained when including more covariates. Negative correlations were found in crossing-fibre regions in crossing-fibre regions corona radiata with the superior longitudinal fasciculus and the corpus callosum. Interestingly, higher SES was found to be positively correlated with KC and PP.

Conclusion — SES was not associated to extremely preterm white matter microstructure at TEA in this study. Based on previous literature, this study speculates that SES effects on preterm white matter development might only arise in post-NICU period. Furthermore, SES might influence grey matter development or indirectly influence brain development during NICU-stay via association with other NICU variables that are associated with brain development. Several important limitations should be considered, especially regarding SES in our study, and suggestions for future research are made.

None declared

ID 143. Effect of Early Postnatal Hydrocortisone Treatment on ROP Outcome in Extremely Preterm Infants

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Background

Retinopathy of prematurity (ROP) affects primarily extremely preterm infants and is characterized by a first phase of arrested retinal vascularisation after birth. In severe cases, ischemia and inflammation in the peripheral avascular retina cause pathologic neovascularisation and, in the worst case, retinal detachment and blindness. Due to their anti-inflammatory and antiproliferative effects, corticosteroids have been widely used in ophthalmology to treat adult proliferative retinopathy.

Postnatal low-dose hydrocortisone treatment for bronchopulmonary dysplasia (BPD) has recently been introduced in neonatal care to prevent the harmful effects of inflammation on developing lungs in preterm infants.

We aimed to evaluate retrospectively the effect of early postnatal low-dose Hydrocortisone treatment on the severity and outcome of ROP among extremely preterm infants.

Methods

This retrospective study at The Queen Silvia Children's Hospital, Gothenburg, Sweden included preterm infants born before gestational age (GA) 28 weeks from 2016–2022. We compared the ROP outcome between preterm infants (born September 2020 – August 2022) treated with low-dose Hydrocortisone intravenous to prevent BPD with preterm infants (born September 2016 – August 2020) who had no Hydrocortisone treatment. Intravenous Hydrocortisone for preventing BPD was administered postnatally during the first ten days with the following dose: 0.5 mg/kg twice daily for seven days, followed by 0.5 mg/kg per day for three days.

Results

Totally 276 preterm infants were included. Sixty-five infants were treated with Hydrocortisone from September 2020 – August 2022, and 211 had not received any Hydrocortisone treatment during the previous four-year period (September 2016 – August 2020). There was no significant difference in gestational age (GA) between the two groups (25,5 versus 25,7 weeks, p=0,47). The infants treated with Hydrocortisone had lower birth weight (BW) (752 versus 807 grams, p=0,033) and male sex was less common (43,1% versus 59.2%, p=0.032). In the group of infants treated with Hydrocortisone, 35.4% (23/65) developed severe ROP (stage 3 and treated) compared to 40.3% (85/211) in the control group (p=0.57). There was no significant difference in ROP outcome between the two groups.

Conclusions

Early postnatal treatment with low-dose intravenous Hydrocortisone showed no significant effect on ROP severity and outcome among extremely preterm infants.

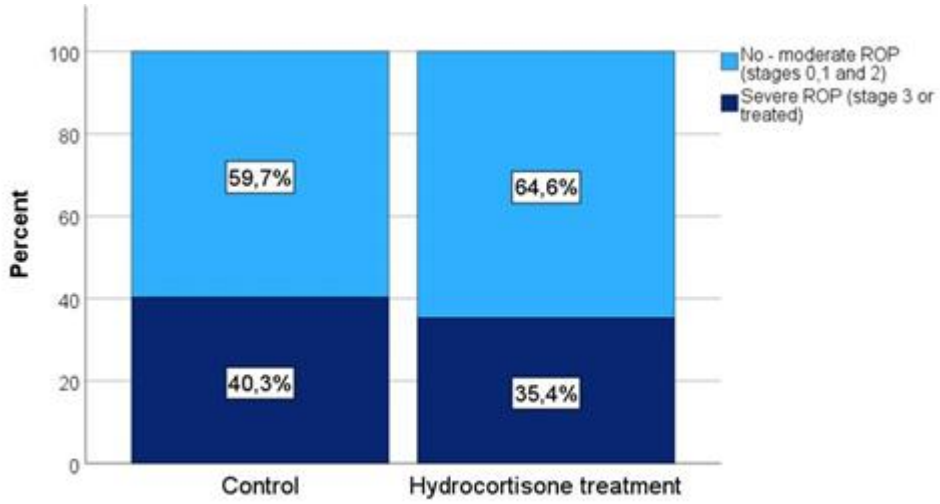

Fig.1 Comparison between ROP outcome in preterm infants treated with Hydrocortisone early postnatally and control group

Fig.1 Comparison between ROP outcome in preterm infants treated with Hydrocortisone early postnatally and control group

The authors declare no financial interests.

ID 96.Effectiveness of levetiracetam as add–on therapy in the treatment of neonatal seizures

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Background:
There is no agreement about the effectiveness of add–on therapy with levetiracetam (LEV) in the treatment of neonatal seizures. The efficacy of LEV in achieving seizure cessation within 24 hours varied from 17% to 82% in various studies. The aim of this study was to evaluate the effectiveness of add — on therapy with LEV, in a clinical setting, for achieving >80% seizure reduction.

Methods:
Single–center retrospective cohort study in full–term neonates, who were admitted to the neonatal intensive care unit between 1st of January 2012 and 2023 and had neonatal seizures despite 3 loading doses of phenobarbitone (total 40 mg/kg) as first–line therapy. All newborns were continuously monitored with 2 channel amplitude–integrated electroencephalography (aEEG). The total seizure burden 2 hours before and 4 hours after administration of LEV was calculated using raw EEG. The primary outcome was the effectiveness of LEV in achieving > 80% seizure reduction. Secondary outcomes were achieving > 50% seizure reduction, 24–, 48– and 72–hour seizure freedom, and the need for additional antiseizure medication (ASM) after the administration of LEV. In cases where lidocaine (LIDO) was used in addition to LEV, the effectiveness was measured as well.

Results:

A total of 47 neonates were included (mean gestational age 39+5 weeks, birthweight 3570 grams). The seizures etiologies were hypoxic–ischemic encephalopathy (n=11), hemorrhagic stroke (n=9), central nervous system infection (n= 8), genetic disorder (n=8), arterial ischemic stroke (n=7), metabolic disorder (3) and unknown (n=1). The mean loading dose of LEV was 20 mg/kg, and the mean total dose was 40 mg/kg. The data showed that LEV achieved >80% seizure reduction in respectively 21.7% (10/46), 13.2% (5/38), and 9.1% (1/11) of the cases for the first, second, and third dose. After the administration of LIDO 23/25 newborns achieved > 80% seizure reduction (Table 1).

Conclusion:

Although the loading dose of LEV was low and the group of infants studied was heterogeneous, the effectiveness of LEV as add–on therapy for the treatment of acute neonatal seizures was limited based on the low rates of seizure reduction and seizure freedom, as well as a high need for additional ASM.

Outcome Measures	*Patients (n, %)*
Effectiveness of levetiracetam	
First dose	
Reduction >80% in seizure burden	10/46 (21.7%) *
24-hours seizure freedom	2/47 (4.3%)
Other ASM within 4 hrs of administration.	29/47 (61.7%)
Second dose	
Reduction >80% in seizure burden	5/38 (13.2%)
24-hours seizure freedom	2/38 (5.3%)
Other ASM within 4 hrs of administration.	20/38 (52.6%)
Third dose	
Reduction >80% in seizure burden	1/11 (9.1%)
24-hours seizure freedom	0/11 (0%)
Other ASM within 4 hrs of administration	5/11 (45.5%)
Effectiveness of lidocaine	
Reduction >80% in seizure burden	23/25 (92%)
24-hours seizure freedom	14/25 (56%)
Need for other ASM within 4 hrs of administration	1/25 (4%)

*In one neonate the seizure reduction was not assessed for the first dose due to logistical reasons.

Table 1. Effectiveness of levetiracetam and lidocaine.

A comprehensive overview of the important outcome measures, including >80% seizure reduction, 24–hours seizure freedom and need of other ASM within 4 hours.

Table 1. Effectiveness of levetiracetam and lidocaine.

A comprehensive overview of the important outcome measures, including >80% seizure reduction, 24–hours seizure freedom and need of other ASM within 4 hours.

None declared

ID 618. Serum neurofilament reference database for individual diagnostics in neonatal and paediatric care

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Background

Neurological conditions represent a significant driver of neonatal and paediatric disability burden worldwide. Measurement of serum neurofilament light chain (sNfL) concentrations, a specific marker of neuroaxonal injury, has the potential to

substantially contribute to management of children with such conditions. In this context, recently, the European Medicines Agency declared introducing age-adjusted reference values for sNfL a top research priority.

Methods

sNfL values were measured in healthy children and adolescents that were included as control groups in two large cohorts: The Coronavirus antibodies in Kids from Bavaria (CoKiBa) and a US paediatric case-control Multiple Sclerosis cohort. The distribution of sNfL concentrations as function of age-related physiological changes was modeled to derive percentile and Z score values via a generalised additive model for location, scale, and shape. The clinical utilisation of the new reference dataset was assessed in children with various neurological diseases, including epilepsy, traumatic brain injury and bacterial CNS infections.

Results

Samples from 2667 healthy children and adolescents constituted the newly established reference dataset covering neonatal age to adolescence. On average, sNfL concentrations decreased by 6.8% every year until the age of 10.3 years and remained relatively stable thereafter. Independent of age, weight did not considerably impact sNfL concentrations. Age-adjusted sNfL Z scores were higher in children with neurological conditions compared to healthy children ($p<0.001$) with higher effect size metrics (Cohen $d=1.56$) compared to the application of raw sNfL concentrations ($d=1.28$). To allow for a worldwide utilisation in the scientific community, we have implemented an online App free of charge to generate Z scores for subjects younger than 18 years old.

Conclusion

Establishing normative values for sNfL for neonatal and paediatric cases paves the way towards clinical application of sNfL in this population. The utilisation of the sNfL Z score was associated with higher effect size metrics and allowed for more accurate estimation of the extent of ongoing neuroaxonal damage in individual patients.

None declared

ID 273. Brain injury occurring during or soon after birth: a national report on rates of brain injuries in 2020

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Background

Conditions that injure the brain during the perinatal period are leading causes of neonatal mortality and morbidity. In this report we describe the rates of brain injury and underlying causes in the entire livebirth population in England in 2020. We compare rates of brain injury at the national level since 2012 and describe how rates of brain injury differ by gestational age, deprivation and ethnicity.

Methods

We obtained denominator data from the Office for National Statistics and MBRRACE–UK, and numerator data (including neonatal characteristics and diagnosis data) from the National Neonatal Research Database. We calculated rates of brain injury per 1,000 live births and compared rates by gestational age at birth, ethnicity (using maternal ethnicity) and deprivation (using the Index of Multiple Deprivation decile for maternal postcode). This work was funded by the UK Department of Health as part of a commissioned service evaluation.

Results

The annual rate of neonatal brain injuries in England in 2020 (4.2 per 1,000 live births: 95% CI 4.0, 4.3) has not reduced from the rate in 2012 (4.3 per 1,000 live births: 95% CI 4.1, 4.4). Rates of brain injury are higher in preterm infants (24.1 per 1,000 live births) than term (2.5 per 1,000 live births). The three most common diagnoses were

hypoxic ischaemic encephalopathy, seizures and intracranial haemorrhage. Rates of brain injury were higher in the most deprived decile rates were 4.88 per 1,000 livebirths (95% CI: 4.42, 5.40) while in the least deprived decile rates were 3.4 per 1,00 livebirths (95% CI: 2.91, 4.03). Rates also varied by maternal ethnicity: in Black Caribbean populations the rate was 6.34 per 1,000 livebirths (95% CI: 4.49, 8.97) while in White British populations the rate was 3.15 per 1,000 livebirths (95% CI: 2.97, 3.34).

Conclusions

Rates of neonatal brain injury have not decreased, and variation exists with higher rates in deprived populations and some ethnic groups. This may be related to the increased rates of preterm birth in these groups. However, if the entire population had the same risk of brain injury as the least deprived, the overall rate would reduce by 18%.

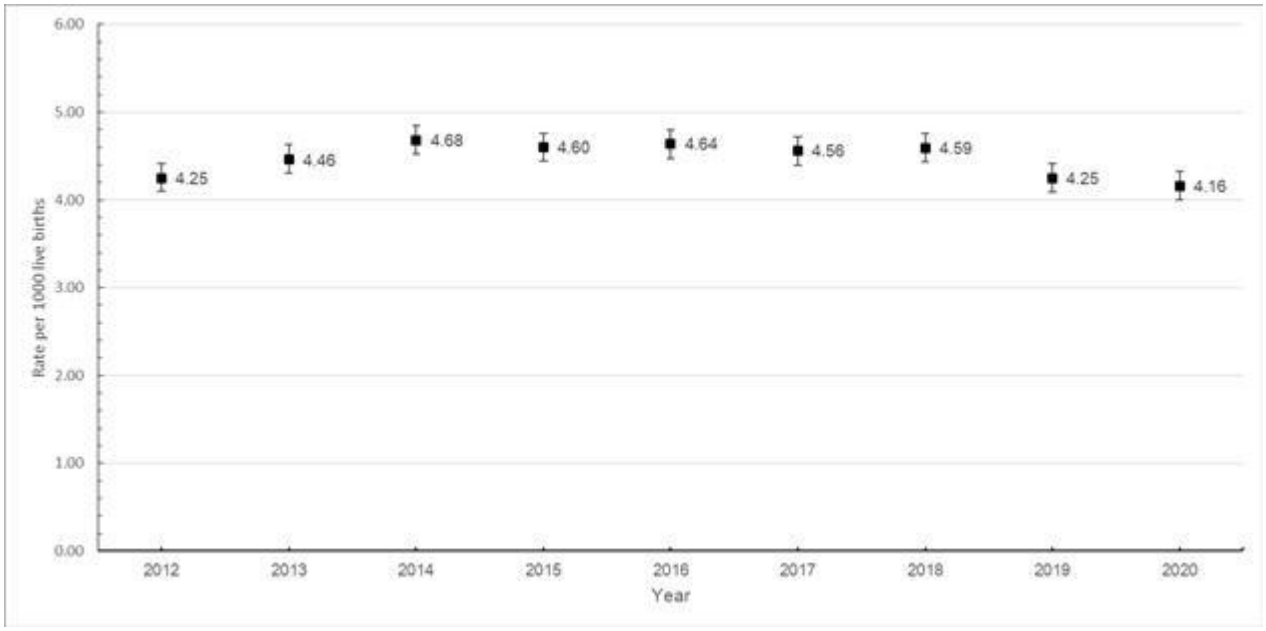

Figure 1: Annual rates of brain injury occurring during or soon after birth in England (all gestational ages) 2012–2020; error bars indicate 95% confidence intervals

Figure 1: Annual rates of brain injury occurring during or soon after birth in England (all gestational ages) 2012–2020; error bars indicate 95% confidence intervals

None declared