



POSTER SESSION 11 – BRAIN 3
SEPTEMBER 17, 2021 – 13:00 – 14:30 CEST

ID 448 - EARLY NEURODEVELOPMENTAL OUTCOMES IN EXTREMELY PRETERM BORN INFANTS (<28 WEEKS' GESTATIONAL AGE) OVER 9 YEARS AT THE WILHELMINA CHILDREN'S HOSPITAL

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Background:

Extremely preterm infants (EPI) are at high risk of neurodevelopmental impairments (NDI). This study aims to describe the prevalence of NDI at two years of age in a large EPI sample, and evaluate the impact of GA, BW, maternal (MEL), and paternal educational level (PEL) on early neurodevelopmental outcomes (NDO).

Methods:

Between 2008 and 2016, 646 EPI were admitted to the Wilhelmina Children's Hospital's NICU. NDO was assessed at two years' corrected age using the Bayley-III-NL (M=100, SD=15) and CBCL (M=50, SD=10). Around 93 (14.40%) EPI died during this period. Due to various reasons, such as emigration, severe psychomotor retardation, cerebral palsy, and NDO assessment in another hospital, NDO could not be evaluated in 25 infants. Data regarding Bayley-III-NL and CBCL were available for 377 (71.40%) and 311 (58.90%) infants respectively.

Results:

Cognitive and motor delay were observed in 56 (14.85%) and 30 (7.96%) infants respectively, while 35 (11.25%), 28 (9.00%), and 48 (15.43%) infants had total, internalizing, and externalizing problems respectively. Using univariate regression we found that GA (b = 2.49, p = .001), BW (b = .02, p < .001), MEL (b = 11.71, p < .001), and PEL (b = 13.58, p < .001) were significantly associated with cognitive composite scores. GA (b = 1.75, p = .010), BW (b = .02, p < .001), and high PEL (b = 9.31, p = .006) were also associated with motor composite scores. Furthermore, high PEL was significantly and negatively associated with total and internalizing problems T-scores (b = -6.46, b = -5.34, p < .05 respectively). In the multiple regression model only high MEL (b = 9.02) and PEL (b = 8.32) were significantly and positively associated with cognitive composite scores (p < .05), whereas BW (b = .01, p = .008) and high PEL (b = 7.66, p = .035) were positively associated with motor composite scores.

Conclusion:

This study shows a rough overview of EPI's NDO. We confirmed the crucial role of MEL and PEL on this sample's early NDO. Further research is needed to untangle this relationship, taking clinical risk factors into account.

None declared



ID 436 - CLINICAL PROFILE AND OUTCOME OF BABIES DIAGNOSED WITH INBORN ERROR OF METABOLISM ADMITTED TO A REGIONAL TERTIARY NEONATAL UNIT IN THE UK OVER TEN YEARS

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Background:

Inborn errors of metabolisms (IEM) are a heterogeneous group of genetic disorders due to defects of single genes that code for enzymes that facilitate conversion of various substances (substrates) into others (products). Delay in the recognition and treatment can lead to significant consequences on the morbidity and mortality. As about 25% of IEMs can have manifestations in the neonatal period, neonatal practitioners consider these in babies with severe symptoms or low survival ability. Because of limited resources and expensive and complex nature of the investigations, a better understanding of clinical profile would help targeting the investigations to a specific set of babies. We carried out this study to improve our understanding of babies with positive metabolic work up.

Methods:

A retrospective review of case records from neonatal admissions between 2011 to 2020 was undertaken using looking for diagnosis of IEM or metabolic disorder. The data collected were analysed for clinical and laboratory profile. Follow-up and outcome data was captured.

Results:

A total of 16 infants were identified with IEM during the study period, making an incidence of 1 in 700 admitted infants. Out of these, 11 were males and 5 were females. 12 infants were term and 4 infants were pre-term with the youngest born at 29 weeks. 6 infants were born to a consanguineous parent and for another 4 of them, it remained unknown.

11 infants were unwell on admission to the neonatal unit with the common symptoms being hypoglycaemia (19%), respiratory distress (19%), metabolic acidosis (12%), hypotonia (12%) and hypothermia (6%). 12 (75%) infants were found to have raised ammonia and 5 (31%) babies with raised lactate. Commonest diagnosed metabolic disorder was organic acidemia which affected 6 (37.5%) babies. A breakdown of individual disorders is shown in table 1. 12 (75%) infants were discharged while 4 (25%) died.

Summary and Conclusion:

The study showed that while incidence remains rare, a common pattern identified from the clinical and laboratory profile would go a long way to facilitate focussing the tests on select group of infants.



Table 1:

Diagnosis	Number of babies	Outcome
Methylmalonic acidaemia (MMA)	5	3 discharged home; 2 died
Pyruvate carboxylase deficiency	1	Died
Medium-chain acyl-CoA dehydrogenase (MCAD)	1	Discharged home at 5 months of age
Carnitine palmitoyltransferase 1 (CPT 1) deficiency	1	Discharged home at 2 months of age
Propionic acidaemia	1	Discharged home
Non-ketotic hyperglycinemia	1	Discharged home at 1 month of age. Currently on ketogenic diet, epilepsy, global developmental impairment.
Ornithine transcarbamylase deficiency 1	1	Discharged home at 1 month of age. Doing well
D-bifunctional protein deficiency	1	Died at 30 weeks of age
Non specific metabolic disorder	4	3 discharged home; 1 died due to NEC

Table1 showing the number of babies in each metabolic disorder and the outcome
None declared



ID 508 - THE RELATIONSHIP BETWEEN PERINATAL OR NEONATAL CHARACTERISTICS AND SURGICAL OUTCOME IN PRETERM INFANTS ADMITTED FOR VENTRICULO-SUBGALEAL SHUNT INSERTION

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BACKGROUND

Post-haemorrhagic ventricular dilatation (PHVD) is a complication of severe intraventricular haemorrhage (IVH) in preterm infants. Surgical management of PHVD using ventriculo-subgaleal shunts (VSGS) may be required for infants with severe PHVD who are unsuitable for ventriculo-peritoneal shunts (VPS). We analysed the clinical and surgical data of all infants admitted for VSGS insertion and explored the relationship between perinatal or neonatal characteristics and surgical outcome.

METHODS

This was a retrospective study of 75 preterm infants with median (range) gestational age 25.9 (23.14–33.71) weeks, who underwent VSGS insertion at Great Ormond Street Hospital, between October 2012 and April 2021. Data on perinatal, neonatal, and neurosurgical care were extracted from electronic patient records. Statistical analysis was performed on SPSS Statistics 27 using Chi-squared, Mann-Whitney U, Kruskal-Wallis, Spearman's correlation coefficient and paired T-tests.

RESULTS

In our cohort, 84.1% of mothers received antenatal steroids and 65.8% were given perinatal magnesium sulphate (MgSO₄). 72.2% of infants had suspected early onset sepsis (EOS), of which 19.2% were culture-positive. 49.3% of infants needed inotropic support postnatally. On admission for VSGS insertion, 40.5% of infants were ventilated. Haemoglobin dropped significantly from pre to post-VSGS insertion ($p=0.005$); 75.0% of infants required blood transfusions. Seizures post-VSGS insertion were suspected or confirmed in 21.7% infants. 78.7% required VPS insertion <1 year due to VSGS complications, including migration, obstruction, and infection. 55.9% of VPS were revised post-insertion.

Infants who received MgSO₄ perinatally had significantly lower 30-day VSGS complication ($p=0.045$) and seizure ($p=0.014$) rates. Those with larger ventricular indices at referral had higher 30-day complication rates ($p=0.047$) and required more VPS revisions ($p=0.001$). Infants with suspected or confirmed seizures post-VSGS insertion had higher 30-day VSGS complication rates ($p<0.001$), and those with culture-positive EOS had higher VPS revision rates ($p=0.017$). Infants ventilated on arrival and with lower weights at transfer had higher VPS revision rates ($p=0.034$, $p=0.027$ respectively).

CONCLUSION

This study showed that some perinatal and neonatal characteristics, including lack of perinatal MgSO₄ administration, larger ventricular indices at referral, mechanical ventilation, culture-positive EOS, and suspected or confirmed seizures were suggestive of poorer surgical outcome. Neuroprotection, brain monitoring, and a low threshold for sepsis screening may improve surgical outcomes.

On behalf of all authors, the corresponding author states that there is no conflict of interest.



ID 517 - MELATONIN TREATMENT FOR NEWBORNS WITH NEONATAL ENCEPHALOPATHY: A COCHRANE REVIEW

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Background

Melatonin is a promising adjunct therapy to therapeutic hypothermia (HT) in neonatal encephalopathy (NE). It is a potent antioxidant, anti-inflammatory, and anti-apoptotic agent. It easily crosses the blood-brain barrier and has an excellent safety profile in neonates. Melatonin treatment as an adjunct to HT in animal models of NE have demonstrated reduced cell death and improved outcomes. We examined the current evidence for melatonin treatment in neonates with NE.

Methods

A comprehensive search was run on 21 October 2020 in the databases CENTRAL, MEDLINE, clinical trials databases, and the reference lists of retrieved articles for randomised controlled trials (RCTs) and quasi-RCTs. The review was limited to include only RCTs and quasi-RCTs that compared melatonin to standard treatment or placebo. The primary outcome was a reduction in death or adverse neurodevelopmental outcome at ≥ 18 months of age. Secondary outcomes included differences in mortality, neurodevelopmental disability (NDD) and abnormalities on MRI brain. 2 reviewers independently screened the literature search results, completed the data extraction and assessed the quality of included studies. Standard Cochrane methodologies were used throughout the review.

Results

The literature search identified 82 results of which 11 were suitable for full text screening. 4 RCTs of melatonin treatment in NE were identified. 2 compared melatonin as an adjunct to HT and 2 compared melatonin monotherapy to placebo or standard treatment. All studies were judged to carry unclear risk of bias. All studies demonstrated improved outcomes with melatonin treatment, however there was significant variation in outcomes reported. Only 1 pilot study of 25 patients reported the primary outcome and did not detect any difference in death or NDD at 18 months, however it was not powered to detect a difference. The study reported improved cognitive outcomes for patients treated with melatonin compared to placebo. The review also identified 1 stage 3 RCT measuring the primary outcome, for which recruitment is ongoing.

Discussion

There is very low certainty evidence that melatonin may improve outcomes for patients with NE. Large stage 3 trials are urgently required as HT remains only partially effective in preventing adverse outcomes and further investigation of promising treatments should not be delayed.



Summary of findings:

Melatonin compared to standard therapy for newborns with neonatal encephalopathy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)
	Risk with standard therapy	Risk with melatonin			
Death or major disability in survivors	Jerez-Calero is the only study to report the effects of the intervention on the primary outcome of death or long-term major NDD. The 2 outcomes are presented separately. There was no difference in mortality nor in major long-term NDD between groups. This is a pilot study and the sample size was insufficient to measure the effect of the intervention on the primary outcome.			25 (1 RCT)	⊕○○○ VERY LOW ^{ab}
Mortality follow up: 1 month	282 per 1,000	96 per 1,000 (41 to 211)	OR 0.27 (0.11 to 0.68)	155 (4 RCTs)	⊕○○○ VERY LOW ^{bcd}
Neurodevelopmental disability follow up: 18 months	Jerez-Calero is the only study to report major NDD follow up to 18 months. There was no significant difference between groups in GMFCS classification or Tardieu scale. Only results of significance tests are presented, with no further information supplied. However, participants in the intervention group had significantly higher cognitive function (101.25 ± 21.51) at 18 months of age on BSID-III compared to the control group (85.56 ± 17.40). Participants in the intervention group also had higher language function (95.38 ± 24.47) compared to controls (83.22 ± 19.23) although the difference was not statistically significant (p = 0.06). Participants in the intervention groups also had higher motor function (96.13 ± 22.08) compared to controls (89.33 ± 26.12), although again the difference was not statistically significant (p = 0.35). This is a pilot study and the sample size was insufficient to measure the effect of the intervention on the incidence of major long-term NDD.			25 (1 RCT)	⊕○○○ VERY LOW ^{ab}
MRI abnormalities in PLIC or basal ganglia and thalamus	458 per 1,000	477 per 1,000 (228 to 741)	OR 1.08 (0.35 to 3.39)	50 (2 RCTs)	⊕○○○ VERY LOW ^{ab}
MRI abnormalities in the white matter	583 per 1,000	322 per 1,000 (101 to 652)	OR 0.34 (0.08 to 1.34)	50 (2 RCTs)	⊕○○○ VERY LOW ^{ab}

CI: Confidence interval; OR: Odds ratio; MD: Mean difference; PO: Per os (oral administration); IV: Intravenous; NDD: Neurodevelopmental disability; GMFCS: Gross motor function classification system

Summary of Findings (SOF) table
None declared



ID 586 - EYE-TRACKING AND THE GRIFFITHS III NEURODEVELOPMENTAL ASSESSMENT AT 18 MONTHS IN HEALTHY TERM INFANTS.

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Background:

Traditional neurodevelopmental assessment tools are heavily reliant on language, and are culture and administrator dependent. Eye-tracking (ET) tasks have been used in young infants to assess emerging social skills. No previous studies have examined its correlation with other developmental domains. This study aimed to examine the correlation between individual eye tracking tasks and language, motor and cognitive development at 18 months.

Methods:

Healthy term-born infants were prospectively recruited at birth. At 18 months, children had eye-tracking and Griffiths Scales of Child Development-3rd edition (Griffiths-III) assessments. Simple linear regression was used to investigate relationships between eye-tracking and Griffiths-III.

Results:

ET and Griffiths-III were completed in 57 infants (32male:25 female), mean (SD) age = 17.9(0.5) months. Correlations between individual tasks and developmental domains are shown in table 1. The most significant correlations were seen between the Happy task and Scale B (language and communication), and Scale D (Personal-Social and Emotional). The Happy task involves a woman's face displayed on the screen repeating positive phrases. Toddlers who had a quicker first fixation to the eyes of the Happy Task scored higher on scale A (Foundations of Learning), scale D (Personal-social-emotional), and General Development (GD) of Griffiths-III. More time spent fixated on the mouth of the Happy Task was associated with higher language and communication scores. None of the elements of the Happy task correlated with fine or gross motor development (Scale C and E). Followed gaze in joint attention task was associated with in lower gross motor (Scale E) and overall (GD) score.

Conclusion:

Elements of the Happy Face ET Task, in particular mouth fixation correlate strongly with the measured language development of a child at 18 months, and has the potential to aid in the assessment of language in the pre-verbal or non-English speaking child.



Table 1. Investigation of factors associated with Griffiths III Developmental Quotient Subscales outcome: Simple Linear Regression Results

	<i>n</i>	A	B	C	D	E
Happy Task						
TTFF Eyes (1s increase)	45	0.32*	0.428	0.095	0.21*	0.169
MD Eyes (1s increase)	45	-0.05	-0.651	0.177	1.11*	0.615
MD Mouth (1s increase)	53	0.997	3.7***	0.874	0.7*	-0.191
DP Eyes (1% increase)	56	-0.043	-0.17**	-0.017	-0.06*	0.008
DP Mouth (1% increase)	56	0.015	0.14**	0.004	0.039	-0.084
FF Mouth (Yes vs No)	56	2.098	7.29*	0.968	2.164	-2.052
Sad Task						
MD Eyes (1s increase)	47	-2.14*	0.417	-1.307	-0.011	1.199
MD mouth (1s increase)	51	0.657	1.76*	1.34*	0.41	0.019
DP mouth (1% increase)	54	0.047	0.11*	0.062	0.015	-0.037
Social Preference Task						
Mean DP FN (1% increase)	57	0.52*	0.71*	0.043	0.25	0.018
Mean TTFF Car (1s increase)	57	-1.896	0.542	-2.275	0.072	-3.18*
Joint Attention Task						
Followed Gaze (Yes vs No)	38	-4.781	-9.229	-3.917	-3.812	-21.37***
Visual Engagement Task						
Valid Trial Baseline (No./10)	56	0.77*	0.968	0.284	0.40*	-0.149
Valid Trial Gap (No./10)	57	0.384	0.85*	0.316	0.318	-0.238
Avg. SRT Gap (1s increase)	57	-0.04	-0.057	-0.027	-30.35*	-0.007

Coefficient values from simple linear regression. No./10 = Number out of 10, TTFF = Time to First Fixation, FF=First Fixation, MD = Mean Duration, DP = Duration Percentage, Avg. = average, SRT = Saccadic Reaction Time,

Table 1. Investigation of factors associated with Griffiths III Developmental Quotient Subscales outcome: Simple Linear Regression Results

None declared



ID 104 - BIRTH OUTSIDE OF COOLING CENTRES IS ASSOCIATED WITH ADVERSE OUTCOMES IN INFANTS WITH MODERATE OR SEVERE HYPOXIC ISCHAEMIC ENCEPHALOPATHY IN THE UK

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Introduction

Therapeutic hypothermia (TH) commenced within 6 hours of birth is associated with lower mortality and neurodisability in infants with moderate/severe (HIE). Active TH has been established within regional cooling centres (CCs), that are mainly tertiary neonatal centres in the UK. Infants born in non-cooling centres (non-CCs), where equipment to undertake active TH is not available, are usually passively cooled prior to upward transfer to a regional CC. It is unknown if birth in a non-cooling centre (non-CC) impacts short-term outcomes. We aimed to evaluate the relationship between birth in a non-cooling centre, without active TH, and short term outcomes.

Methods

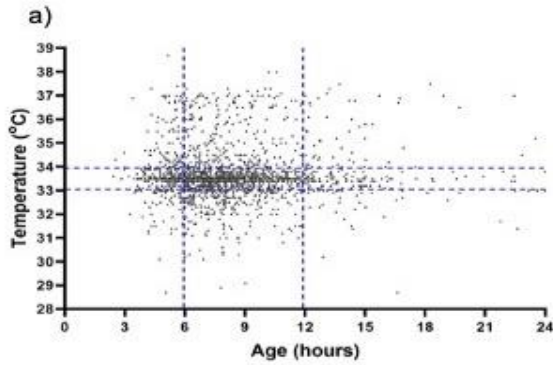
National cohort study using data held in the National Neonatal Research Database from prospectively completed records from infants 36 to 42 weeks gestational age admitted to UK neonatal units between 2011 and 2016 with a diagnosis of moderate/severe HIE and underwent TH. Infants who died within the first 48 hours of life with moderate/severe HIE but did not undergo TH, were also included. Propensity score-matching was used to provide balanced groups of infants to evaluate short term outcomes and mortality between infants born in a centralised centre with immediate access to active TH (CC) with those with no immediate access (non-CC).

Results

5059 infants were included with 2364 (46.7%) born in a non-CC. Following propensity matching, 4330 infants were well matched on key confounding factors. Birth in a CC was significantly associated with improved survival without seizures (35.1% vs 31.8%; OR 1.15, 95% CI 1.02–1.31; p=0.02), fewer seizures (60.7% vs 64.6%; OR 0.84, 95% CI 0.75-0.95, p=0.007) but no difference in mortality (15.8% vs 14.4%; OR 1.11, 95% CI 0.93-1.31, p=0.20) compared with non-CC births. Following transfer from a non-CC to a CC, only 1362 infants (67.1%) arrived with a temperature in the therapeutic range (Figure).

Conclusion

In the UK, infants with moderate/severe HIE born in a non-CC are less likely to survive without seizures and have delayed optimal TH treatment. With almost half of births occurring in non-CCs, consideration should be given to commissioning of active TH in these centres to provide optimal treatment and improve their outcomes.



b)

		Age at Admission		
		<6 Hours	6-12 Hours	>12 Hours
Temperature	>34°C	4.2% (n=86)	11.9% (n=242)	2.4% (n=48)
	33-34°C	12.7% (n=259)	48.3% (n=979)	6.1% (n=124)
	<33°C	2.5% (n=52)	10.3% (n=209)	1.3% (n=27)

- a) Individual plots for each infant divided into key zones as in table b
 b) Tabular data bases on admission temperature and time. Shaded blue area represents the optimal temperature in the 6 hour therapeutic window

Temperature on arrival at a cooling centre compared to time from birth for infants ≥ 36 weeks gestational age with moderate or severe hypoxic-ischaemic encephalopathy
 None declared



ID 197 -GENDER DIMORPHISM IN NEONATAL ENCEPHALOPATHY OUTCOMES

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Background

Neonatal encephalopathy (NE) is a devastating outcome of an otherwise healthy term delivery. Gender dimorphism exists in the neonatal period and throughout life in terms of morbidity and mortality. Perinatal brain damage, cerebral palsy, congenital deformities, stillbirth, meningitis and neonatal sepsis are more common in boys. Gender disparity has not been previously explored in NE infants regarding inflammation and outcome. Our aim was to explore the cytokine expression between male and female infants with NE in terms of MRI and developmental outcome.

Methods

Infants with neonatal encephalopathy were recruited from The National Maternity Hospital, Dublin with written informed consent (Table 1). Serum biomarkers (EPO and GM-CSF) were serially evaluated during the first 5 days of life and compared with MRI brain injury and Bayley Scales of Infant development (Bayley-III). Statistical analysis was carried out using R version 3.6.2.

Results

Sixty-six infants with NE (NE I=9, NE II =50, NE III=7) were recruited and had serum samples analysed. EPO at D3-5 strongly correlated with each of the three Bayley-III domains, cognitive ($p < 0.002$), language ($p < 0.002$) and motor ($p < 0.032$). The language score for GM-CSF at D3-5 is also highly significant ($p < 0.003$).

When evaluated according to gender we found that in male population, there is a significant relationship between cognitive and EPO levels at D1-2, however, there is not such relation in the female population. At D3-5, all three Bayley scores are significantly associated with EPO for males, in contrast to female population. For GM-CSF, the language score is statistically significant in the female population at D1-2 ($p < 0.02$) and D3-4 ($p < 0.04$). No significant associations were found between the cytokines and MRI outcome for either male or females.

Conclusion

Gender differences are evident in cytokine expression when measured in respect to neonatal outcome of Bayley Scale of Infant development (Bayley-III). Further research in the mechanisms of these observed sex differences in neonates is warranted with a view to consider gender as an important variable for treatment and improved outcomes.



		Male (n=45)	Female (n=21)
Gestational age (wks)		40.33 (1.57)	40.48 (1.42)
Birth weight (kg)		3.69 (0.66)	3.62 (0.73)
Apgar	1min	4 (0-9)	3 (0-9)
	5min	5 (0-9)	4 (0-8)
NE I/II/III		5/34/6	4/16/1
TH n (%)		34 (75)	15 (71)
MRI (abnormal %)		22 (49)	11 (52)
BSID	Cognitive	103 (17.8)	95.5 (19.9)
	Language	103 (19.8)	96.9 (23.5)
	Motor	103 (18.8)	98.8 (20.9)

Table 1: Patient demographics with mean \pm SEM.

None declared



ID 274 - MINOR NEUROLOGICAL DYSFUNCTION IS MORE FREQUENT AT AGE SIX AND A HALF THAN AT TWELVE IN CHILDREN BORN EXTREMELY PRETERM

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BACKGROUND

Children born extremely preterm (EPT) are at high risk for developing developmental coordination disorder (DCD) and minor neurological dysfunction (MND).

The Movement Assessment Battery for Children - 2nd ed. (MABC-2) is a tool used for assessing motor function. A modified version of Touwen's Neurological Examination (simplified Touwen) has been used to assess MND in primary school aged children born EPT. It has been shown that the total score of MABC-2 is strongly related to the severity of MND in these children.

The aims were (1) to test the inter-assessor reliability of the simplified Touwen when used in 12-year-old children born at term and EPT, (2) to examine how the simplified Touwen differentiate between typically developing children, at 12 yrs., and children born EPT, (3) to look at how MND correlates to motor function (MABC-2) and finally (4) to describe the trajectory of MND according to the simplified Touwen between 6,5 and 12 yrs. in children born EPT.

METHODS

Sixty-two children born EPT and 44 children born at term were included. The reliability part of the study consisted of 17 children born EPT and 30 born at term. The children had been examined at 6,5 yrs. and now again at 12 yrs. The assessments included the simplified Touwen assessment and MABC-2.

RESULTS

Inter-assessor reliability of the simplified Touwen showed almost perfect agreement (Cohens kappa 0,947). MND was significantly ($p=0.001$) more common in children born EPT than in children born at term at 12 yrs. Worse results of the simplified Touwen in children born EPT were associated with lower MABC-2 total test scores ($p=0.001$) at 12 yrs. Between 6,5 and 12 yrs. the number of children with simple and complex MND decreased significantly ($p=0.007$) for children born EPT.

CONCLUSION

The simplified Touwen can be used reliably to assess MND in middle school aged children, both born EPT and at term. It can also differentiate between children born EPT and at term and is associated with impaired motor outcome with MABC-2. The number of MND decreases with age.

None declared



ID 365 - SCHOOL PERFORMANCE OF PRETERM CHILDREN. RESULTS OF THE POPULATION-BASED COHORT STUDY IKIDS

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Background

Around 9% of children are born preterm in Germany. Several international studies conducted in the 1980s through 1990s suggest that children, who were born at a gestational age (GA) below 37 weeks have an

increased risk of poorer school performance. Since medical progress may have led not only to higher survival rates, but also to an improved neurodevelopmental outcome of preterm infants, our aim is to describe the association between GA and school performance in a current population-based sample of first graders.

Methods

Data from the population-based prospective cohort study ikidS were used. For ikidS, 2,003 first graders from the city of Mainz and the surrounding district of Mainz-Bingen (Rhineland-Palatinate, Germany) were enrolled. Data of the preschool health examination in 2015 (including GA) were provided by the regional Department of Public Health. Competencies in mathematics and science as well as school-related attention (i.e., concentration skills and perseverance) were assessed by classroom teachers at the end of first grade. Outcomes were rated on a 5-point Likert scale ranging from “much poorer” (-2) through “much better” (+2) than other children of the same age. Potential confounding variables were obtained by parental questionnaires. Associations between GA and each outcome were assessed by linear mixed regression models adjusted for confounding variables. Missing values for GA and confounding variables were multiply imputed.

Results

1,463 children (52% male) had at least one rating and were included in the analysis. Of these, 8% were born prematurely (i.e., GA <37 weeks). Mean (SD) mathematical competencies were 0.31 (1.04), science competencies were 0.25 (0.87), and school-related attention was 0.06 (1.13). In the adjusted analysis, GA was positively associated with competencies in mathematics (mean increase per week GA: 0.04 points on the Likert scale; 95%CI 0.01 to 0.07) but not with competencies in science and school-related Attention (see table 1).

Conclusion

Despite medical advances, lower GA is still associated with poorer school performance in mathematics. Reasons for this are unclear but the uptake and benefit of early special educational support may be further evaluated in first graders born preterm.

Dependent variable	n	Mean increase per week GA (SE)	[95% CI]
Mathematical competencies	1457	0.04 (0.01)	[0.01; 0.07]
Science competencies	1426	0.02 (0.01)	[0.00; 0.05]
School-related attention	1461	0.03 (0.02)	[-0.01; 0.06]

CI - confidence interval; GA - gestational age; SE - standard error.

Table 1: Associations between gestational age and school performance.

None declared



ID 590 - EYE-TRACKING FOR THE ASSESSMENT OF COGNITIVE DEVELOPMENT IN FULL-TERM AND MODERATE-TO-LATE PRETERM INFANTS AT 18 MONTHS

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Background:

Preterm infants are at increased risk for language, sensory, motor, and cognitive deficits. Long-term outcomes for preterm infants below 32 weeks' gestation have been extensively studied; in contrast, outcome studies for moderate-to-late preterm (MLPT) infants are sparse. These infants account for up to 74% of the preterm population and warrant careful follow-up. This study compares the neurodevelopment of term-born and MLPT infants at 18 months using both the Griffiths III and eye-tracking assessments.

Methods:

Full-term (≥ 37 weeks gestation) and MLPT infants (32–36+6 weeks gestation) were prospectively recruited at Cork University Maternity Hospital, Cork, Ireland. Follow-up assessments occurred at 18 months of age (corrected where appropriate) using the Griffiths-III and eye-tracking assessments. Eye-tracking assessed visual disengagement, working memory, joint attention, and other aspects of social cognition. Figure 1 provides an example of eye-tracking data captured during a social preference task. The Griffiths-III assessment measures Foundations of learning (subscale A), Language and communication (subscale B), Fine Motor (subscale C), Personal-social-emotional (subscale D), Gross motor (subscale E) and a general development (GD) measure. Differences between the groups were investigated using Mann-Whitney U-test, Fisher's exact test and ANOVA.

Results:

The term group ($n=57$) scored significantly higher than the MLPT group ($n=36$) on the overall GD measure ($p=0.028$) of the Griffiths-III assessment and in two subscales; Eye and Hand coordination (C) ($p=0.012$), Gross motor (E) ($p<0.001$). No significant differences were seen between the term and MLPT group on any of the administered eye-tracking tasks.

Conclusions:

We have confirmed that MLPT infants are at increased risk of developmental delay, however this delay is greatest in the fine and gross motor domains. ET tasks are focused on cognitive and social development and thus did not detect differences in this group.

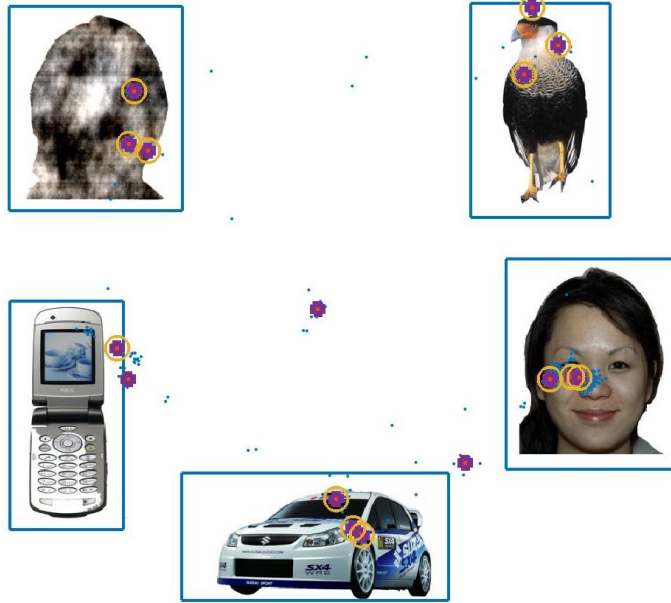


Figure 1: Example of the eye-tracking data captured during a pop-out task.

None declared



ID 108 - IS NEUROPROTECTIVE MAGNESIUM SULFATE AS EFFECTIVE IN TWINS AS IN PRETERM SINGLETONS INFANTS?

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Background:

In observational studies, maternal administration of magnesium sulfate (MgSO₄) has been associated with a subsequent reduction in the risk of intraventricular hemorrhage, cerebral palsy, and mortality. However the knowledge is scarce how MgSO₄ effect in preterm infants born from multiple gestation.

Methods:

Preterm infants with gestational age <32 weeks, born in a tertiary center were retrospectively evaluated. Twins who received neuroprotective MgSO₄ or did not, were compared in terms of early neurological outcomes including IVH and seizures. Furthermore twins who received MgSO₄ were compared with singletons.

Results:

Data from 108 twin infants were analyzed, 63 (58.3 %) twins received MgSO₄ treatment and 45 (41.6%) of them did not. Demographic characteristics of the groups are summarized in table 1. Severe IVH (12.5% vs. 7.3%, p = 0.51), intrapranchymal hemorrhage (5.4% vs. 4.9%, p>0.05), periventricular leukomalacia (10.9 % vs. 10.5%, p>0.05) and seizure incidence (5.1% vs. 4.8% p>0.05) were comparable in twins who received MgSO₄ or not despite the significantly lower antenatal steroid rates in twins who did not received MgSO₄ treatment (60% vs. 82.5%, p = 0.015). Furthermore twins were compared with singletons (n=161) who received MgSO₄ and no significant difference observed between the groups in terms of severe IVH (12.5 % vs.9.4 %, p = 0.6) and IPH (5.4% vs. 5.8%, p>0.05), PVL (10.9 % vs. 10.7%, p>0.05) and seizure rates (5.1 vs. 3.3% p = 0.68). However the birth weight of singletons (1039 ±391g) were significantly lower when compared with twins (1157±368g) (p=0.04).

Conclusion:

The established favorable effects of MgSO₄ could not be demonstrated in twins who received the treatment may be due to the small sample size in this study. The incidence of neonatal morbidities are increased in multiple pregnancies and protective strategies such as MgSO₄ may be less effective when compared singleton pregnancies. These results and the optimum regimen of neuroprotective MgSO₄ in multiple pregnancies needs to be confirmed with large randomized controlled trials.



Table-1 Demographic characteristics' of the twins who received MgSO₄ or not			
	MgSO₄ (+)	MgSO₄ (-)	p
GW (week, mean±SD)	28,3±2,4	28±2,6	0,567
BW (g, mean±SD)	1157±368	1245±444	0,281
APGAR (mean)	4,5	4,8	0,414
ANS % (n)	82,5 (52)	60 (27)	0,015
Preeclampsia % (n)	6,3 (4)	2,2 (1)	0,399
Maternal DM % (n)	4,8 (3)	0	0,069
PPROM % (n)	17,5 (11)	20 (9)	0,804
Chorioamnionitis % (n)	7,9 (5)	2,2 (1)	0,201
IUGR % (n)	6,3 (4)	6,7 (3)	0,947
Gender % (n)			0,692
-Male	57,1 (36)	62,2 (28)	
-Female	42,9 (27)	37,8 (17)	
Delivery type (C/S) % (n)	98,4 (62)	97,8 (44)	0,809
RDS % (n)	76,2 (48)	75,6 (34)	0,939
Surfactant % (n)	57,1 (36)	66,7 (30)	0,423
PDA % (n)	42,9 (24)	48,8 (20)	0,680
NEC % (n)	6,8 (4)	0 (0)	0,145
Severe ROP % (n)	10 (5)	0 (0)	0,078
BPD % (n)	37,2 (16)	30 (9)	0,619
Mortality % (n)	32,8 (20)	38,6 (17)	0,543

Table-1
None declared



ID 126 - EARLY DIAGNOSIS OF CEREBRAL PALSY IN LOW- AND MIDDLE-INCOME COUNTRIES

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Background and Aims:

Cerebral palsy describes a group of permanent disorders of movement, motor function and posture that occur due to non-progressive insults to the developing brain¹. Cerebral palsy can be accurately diagnosed as early as three to four months of age in high-risk infants, helping to facilitate access to early, targeted interventions and support². Despite a higher rate of cerebral palsy reported in low- and middle-income countries^{3, 4} the majority of evidence supporting the early diagnosis of cerebral palsy originates from studies conducted in high income countries. This study analyses the literature related to early diagnosis of cerebral palsy from low- and middle-income countries.

Methods:

A scoping review of Google Scholar, OVID Medline and PubMed was performed to identify studies on the early diagnosis of cerebral palsy in low- and middle-income countries. For the purpose of this review, "early" diagnosis was defined as diagnosis prior to 12 months of age, and countries were classified as low and middle income using the World Bank classification system. Articles published in English between February 2011 and February 2021 were included in this review.

Results:

We identified 11 studies relating to early diagnosis of cerebral palsy in low- and middle-income countries. Prechtl's General Movement Assessment was the most frequently studied tool for the early diagnosis of cerebral palsy (55% of studies), followed by the Hammersmith Neonatal Neurological Examination (18%) and Hammersmith Infant Neurological Examination (18%). One study (9%) assessed the use of cranial ultrasound to assist in the diagnosis of cerebral palsy. None of the identified studies assessed the use of neonatal MRI for cerebral palsy diagnosis. Two cerebral palsy registries (Bangladesh and Sri Lanka) were identified in low- and middle-income countries.

Conclusions:

There is paucity of published research on the early diagnosis of cerebral palsy in low- and middle-income countries. Further research is needed to determine whether the tools used to diagnose cerebral palsy early in high-income countries are accurate and feasible for use in low- and middle-income countries.

None declared



ID 181 - THE EFFECT OF THERAPEUTIC HYPOTHERMIA ON LEUKOCYTES AND CYTOKINES IN A NEWBORN PIGLET MODEL OF INFLAMMATION-SENSITIZED HYPOXIA-IS- CHEMIA

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Background

Therapeutic hypothermia (TH) is the standard treatment of moderate to severe neonatal hypoxic-ischemic (HI) encephalopathy. However, some studies indicate that TH is without neuroprotective effect when an infection or inflammation have occurred before the HI insult. This may be due to an impaired immunomodulating effect of TH in these instances. To pursue this hypothesis, we aimed to investigate concentrations of leukocytes and cytokines in newborn piglets with inflammation-sensitized HI treated with and without TH.

Methods

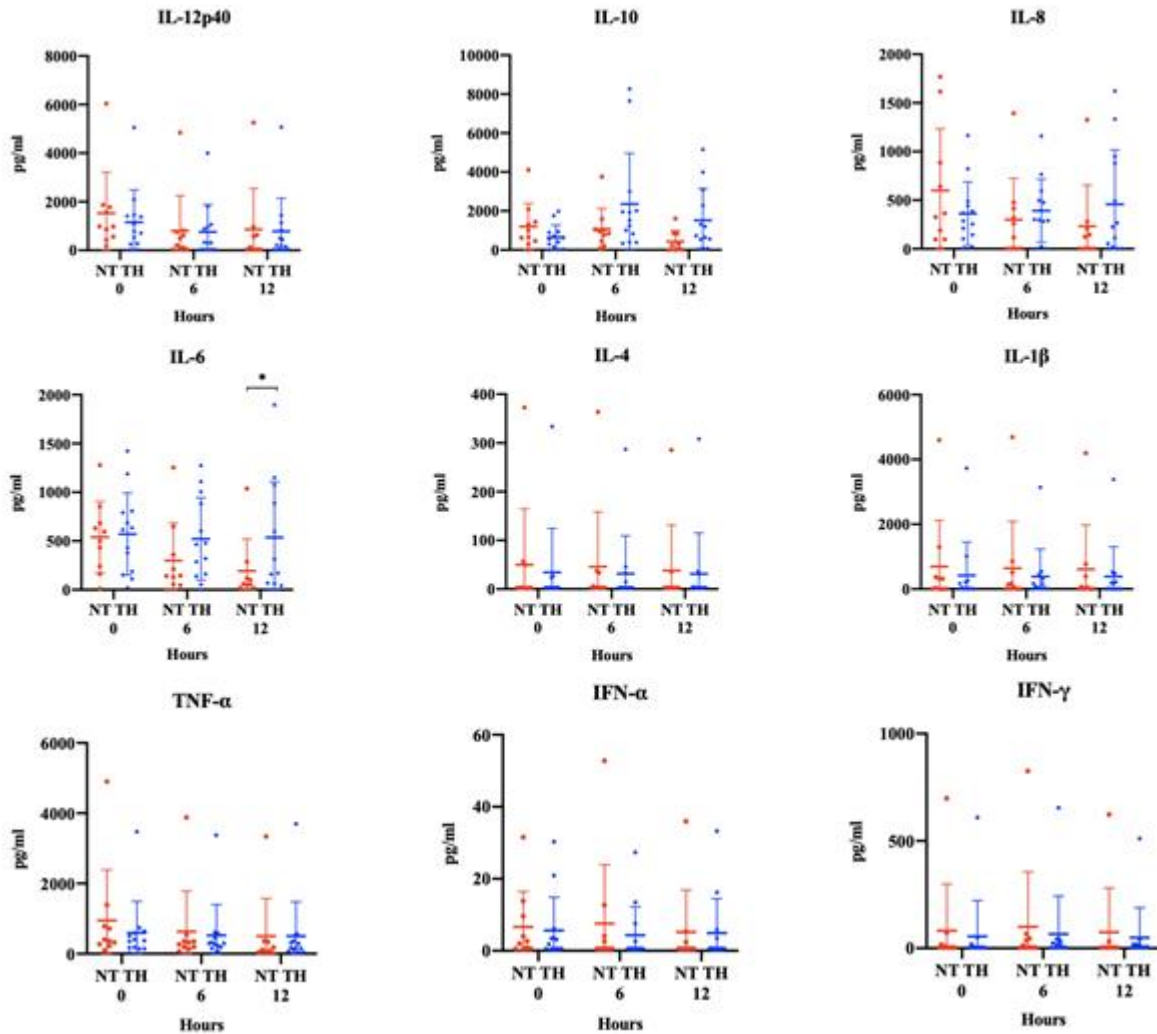
Thirty-two piglets were included in the study. Lipopolysaccharides from *Escherichia coli* were continuously infused throughout the experiment. After four hours of infusion, a 45-minute global HI insult was initiated. After HI, the piglets were randomized to treatment during normothermia (NT) or TH. Arterial blood samples were collected immediately after-, 6 hours after-, and 12 hours after HI. A veterinary hematology analyzer was used to assess concentrations of leukocytes including total white blood cells, neutrophils, lymphocytes, and monocytes. By multiplex-analysis, plasma concentrations of cytokines were assessed including IL-1 β , IL-4, IL-6, IL-8, IL-10, IL-12p40, IFN- α , IFN- γ , and TNF- α

Results

Severity of the HI insult was similar between the two groups. Due to death and logistic problems, leukocyte analysis was performed in 19 piglets (NT = 10, TH = 9) and cytokine analysis in 23 piglets (NT = 10, TH = 13). We found no overall difference in concentrations of leukocytes and cytokines between piglets treated with and without TH. By uncorrected multiple comparisons, we found higher concentrations of IL-6 after 12 hours in piglets treated with TH with a mean difference of 365 pg/ml (95% CI: 1-730) (Figure 1).

Conclusion

TH showed no overall immunomodulating effect in newborn piglets with inflammation-sensitized HI measured by leukocytes and various cytokines. We observed an increased concentration of IL-6 after 12 hours in piglets treated with TH. However, further investigations are needed to assess whether this have any clinical significance – or whether it was a finding by chance.



Plasma concentrations of cytokines from piglets with inflammation-sensitized hypoxia-ischemia treated with-
out (NT) and with therapeutic hypothermia (TH).
None declared



ID 140 - LONG-TERM NEUROLOGICAL CONSEQUENCES IN VERY LOW BIRTH WEIGHT INFANTS WITH CONGENITAL BACTERIAL INFECTION

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Background.

The data available in the literature on the frequency of long-term neurological consequences in very low birth weight infants with congenital bacterial infection are limited. The goal of the study is to evaluate neurological outcomes in very low birth weight infants with early neonatal sepsis (ENS) and congenital bacterial pneumonia (CBP) at the age of 3, 6 and 12 months of corrected age (CA).

Methods.

A prospective study was performed on patients who were born with birth weight ≤ 1500 g at 26 to 32 weeks' gestation age, who had ENS (N=13) or CBP (N=22). The comparison group (N=45) consisted of children with respiratory distress syndrome (RDS), without signs of congenital bacterial infection.

Results.

Disorders of muscle tone were statistically significantly more often detected in children with ENS and CBP in 3,6,12 months of CA compared to children with RDS ($p < 0,01$, $p < 0,05$, respectively). Cerebral palsy was more common in children with ENS compared to children with RDS ($p < 0,05$). At 6 and 12 months of CA children with ENS had a statistically significant delay in Griffith scale for psychomotor development compared to children with CBP and with RDS ($p < 0,05$). At 3, 6 and 12 CA months porencephaly was more often detected in children with ENS compared to children with RDS ($p < 0,05$) according to cranial ultrasonography and MRI. Periventricular gliosis was more common in children of the groups with ENS and ENP compared to children with RDS ($p < 0.001$ and $p < 0.05$, respectively) according to MRI.

Conclusion:

Very low birth weight infants with congenital bacterial infection and, in particular, those who have undergone early neonatal sepsis are at high risk for developing neurological disorders, including cerebral palsy. These children require long-term dynamic observation and an integrated approach to assessing psychomotor development in order to conduct timely therapy and rehabilitation.

None declared



ID 556 - PROSPECTIVE COHORT STUDY ON THE ASSOCIATION BETWEEN PORTEIN INTAKE IN THE FIRST WEEK OF LIFE AND NEURODEVELOPMENTAL OUTCOMES AT TWO YEARS OF CORRECTED AGE IN LATE AND MODERATELY PRETERM INFANTS

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Background and aim:

Late and moderately preterm infants (LMPT) are possibly at risk for neurodevelopmental delay. This study aims to identify the association between early protein intake during the first week of life and the neurocognitive development at two years of age.

Study Design and Methods:

In this prospective cohort study, daily actual nutritional intake during hospital admission after birth was collected. At two years of corrected age (CA), children underwent a cognitive, language and motor assessment using the BSID-III-NL. To evaluate the association between protein intake in the first week of life and scores on the BSID-III-NL at two years CA, we used multivariable linear regression analyses.

Results:

We followed 100 LMPT (mean gestational age 34+2 weeks, mean birthweight 2267g). The mean protein intake in the first week of life was 13,38 g/kg/w \pm 3,98. The mean score for the cognitive composite was 103,1 points (100,8-105,2 95% CI), for the language composite 101,1 points (98,0-104,1 95% CI) and for the language composite 100,8 points (98,9-102,7 95% CI) on the BSID-III-NL.

1g/kg/w of extra protein gave a lower score of 0,793 points (-1,630-0,045 95% CI) for the cognitive composite, a lower score of 0,657 points (-1,788-0,474 95% CI) on the language composite and a lower score for the motor composite of 0,446 points (1,088-0,197 95% CI) on the BSID-III-NL. These outcomes were all statistically not significant (respectively $p=0,064$, $p=0,254$ and $p=0,174$).

Conclusion:

In our prospective cohort study we found a possible negative association between protein intake in the first week of life during hospital admission and neurodevelopmental outcome at two years (CA) in moderately and late preterm infants. Our outcomes were statistically not significant, but potentially clinically relevant.

None declared



End tidal carbon dioxide monitoring in neonates receiving therapeutic hypothermia for hypoxic ischemic encephalopathy

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BACKGROUND: The consistent findings of the association between hypocapnia and adverse outcomes in infants with hypoxic-ischemic encephalopathy (HIE) suggest that the continuous carbon-dioxide (CO₂) monitoring should be encouraged. End tidal (etCO₂) monitoring enables the prevention of undesired PCO₂ levels by facilitating immediate intervention. The primary aim was to evaluate the agreement between etCO₂ and temperature corrected PCO₂ values in patients with HIE receiving hypothermia (TH).

METHODS: In this prospective observational single center trial, infants receiving TH for HIE at the 1st Department of Pediatrics, Semmelweis University between 2020 December to 2021 May were enrolled. Neonates during TH are mechanically ventilated as per local protocol. The level of etCO₂ was monitored via Capnostream 35 portable respiratory monitor using sidestream end tidal capnography with 20/s sampling rate. The mean etCO₂ was determined over 10 min periods preceding the time of the blood gas. Arterial, capillary blood samples were collected as part of routine care, based on the decisions of the attending physicians. The agreement between etCO₂ and temperature corrected PCO₂ was analyzed by using the Bland Altman plot.

RESULTS: Eighteen mechanically ventilated infants with HIE were assigned to the trial, and were monitored for etCO₂ for a median 67.6 hours, starting from a median 12.0 hours of life until 83.1 hours of life correspond to hypothermia and rewarming. A total of 119 paired etCO₂ and temperature corrected PCO₂ measurements were analyzed including 53 arterial and 66 capillary samples. The etCO₂ was closely related to the arterial PCO₂ with the average difference of -3.4 mmHg (limit of agreement -13.9; 7.0 mmHg), whereas for capillary samples the average difference was -8.9 mmHg (limit of agreement -20.4; 2.6 mmHg). Hypocapnia was frequent based on continuous etCO₂ measurements, neonates spent a median 26.7% [IQR17.9; 37.1] of time below the target etCO₂ range of 35-55 mmHg. Hypercapnia (> 55 mmHg) was rare, occurring in less than 1% of time.

CONCLUSION: The routine use of continuous etCO₂ monitoring has the potential to improve the intensive care of newborns with HIE by avoiding the extreme levels of CO₂ and optimize long-term neurological outcomes.

The current project was funded by ESPR Young Investigator START-UP Awards 2019.