September 20th, 2023 08:30 - 9:00

POSTER WALK – BRAIN 1

ID 369.Translating a neurophysiological metric for infant nociception into a clinically-useful tool

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Background

Infants in neonatal intensive care units receive many potentially painful clinical procedures in a day, and this appears to impact their later development. However, we have limited ability to tell when an individual infant is in pain, which procedures they find more painful, or whether particular analgesics are effective.

Previous work with event–related EEG potentials has provided a metric for the nociceptive brain activity evoked by a procedure. The metric is promising as a direct measure of cortical activity in response to a noxious stimulus, but it is not easily usable clinically or in clinical trials. In this work, we aim to make this tool easier to implement and more robust to clinical–grade data quality issues, two pre–requisites for routine cotside clinical use.

Methods

1. By using machine learning, an automated method has been developed to identify artefact in low–channel infant EEG.
2. A flexible and reliable pipeline has been created to pre–process EEG data; automatically applying appropriate resampling, filtering, epoching and artefact identification (Figure 1).

3. To reduce noise variance, a method was developed of combining noxious-related EEG measurements with heartrate changes in response to noxious stimuli.
4. Software is developed to provide a graphical interface for users to quickly identify noxious-related brain responses in infants at the cotside.

Results

1. Our automated method for identifying EEG artefact identifies artefact in EEG data as accurately as experienced individual raters. It does so objectively, reproducibly and in a fraction of the time (balanced accuracy=0.81).
2. Our EEG data pipeline is currently being used in a clinical research setting to determine the primary outcome measure in a multi-centre clinical trial.
3. Our metric for pain in infants in a clinical setting performs well at differentiating clinically-necessary heel lances from equivalent vibro-tactile control stimulation.
4. We are developing software for incorporation into a medical device which we hope will make these methods available for use at the cotside.

Conclusion

We have developed new techniques which make it more feasible for researchers and clinicians to identify noxious-related responses at the cotside.

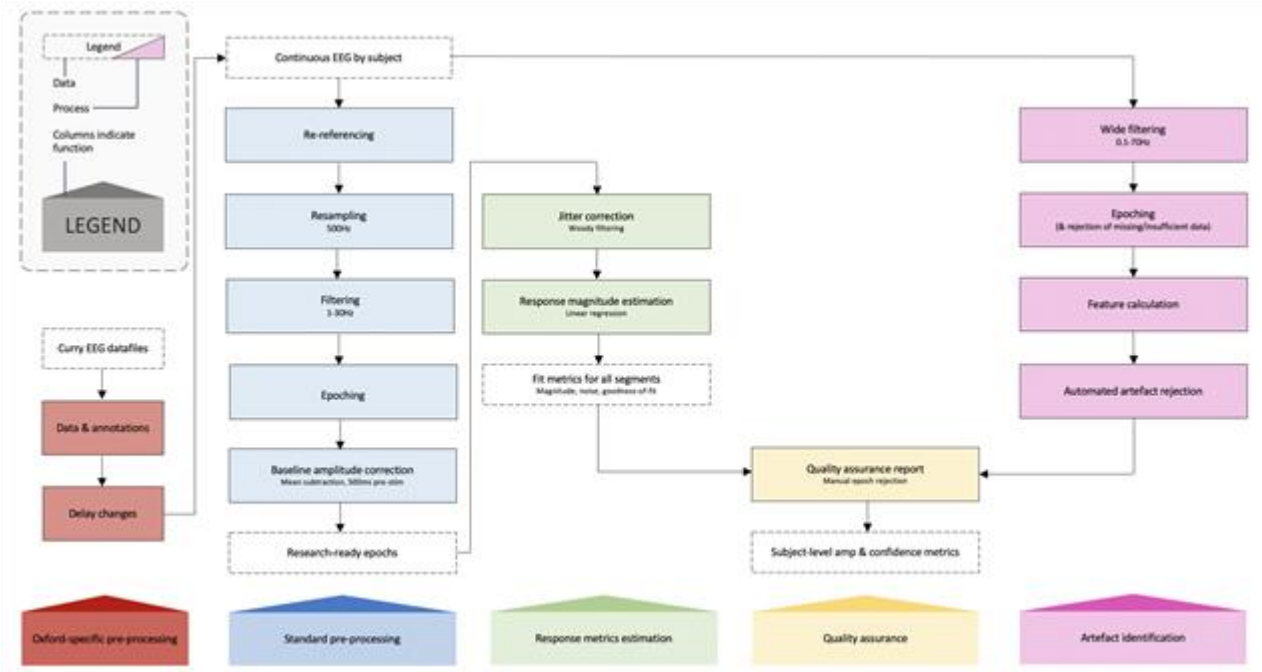

Fig1: outline of EEG processing steps. Each column represents a function: artefact identification (yellow; step 1), pre–processing (blue; step 2), noxious–specific (green; step 3) and user interface (yellow; step 4).

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This work was partly funded by Wellcome Trust, EPSRC, and Reckitt. No funder had involvement in study design or analysis. Part of this work is UK Patent Pending (Application 2116218.5).

ID 171. Factors Affecting Growth Pattern of Patients with Congenital Hypothyroidism at a Newborn Screening Continuity Clinic in Western Visayas Philippines

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Background: Congenital hypothyroidism (CH) is a common endocrine disease in newborns and affects approximately 1 in 2,000 to 4,000 live births with an increasing trend in Western and Asian countries. It is one of the most common treatable and preventable causes of intellectual disability in children. Delays in diagnosis and treatment of CH, may cause impairment in neurological development and intelligence quotient. The Newborn Screening Continuity Clinic – Western Visayas (NBSCC–WV) has managed newborns with congenital hypothyroidism but no data review on their growth patterns and the factors affecting it were done. The study determined factors that affected the growth patterns of patients diagnosed with congenital hypothyroidism at the NBSCC–WV for 5 years.

Methods: This retrospective cross–sectional study determined the factors that affected the growth patterns of patients diagnosed with CH at NBSCC–WV from 2014 to 2019. Thirty–five infants with congenital hypothyroidism were included in the study. A researcher–made data collection form was used that included factors such as clinico– clinico–demographic, laboratory, profile, and compliance to medication and follow–up.

Results: Majority were females within 33.5 to 44.5 months old from Iloilo Province and Capiz. Term patients whose newborn screening taken within 1–5 days after birth and were diagnosed within 4 weeks after birth predominated the study. Mean age for

the start of CH medications was 2.4 ± 1.1 weeks old. All patients had good compliance to follow-up and 86% have good medical compliance. Initial laboratory test results showed increased TSH and decreased FT4 levels. Increasing trend of patients with normal thyroid hormone levels after their follow-up consultations was attributed to good compliance to medications and good quality healthcare provided by NBSCC-WV. There was normal length, weight, and head circumference for age seen in majority of patients. Results however tend to plateau at z-score of 3 for length and head circumference for age.

Conclusion: There may be nutritional, socioeconomic, cultural, or geographical factors that have affected the clinical picture of patients despite their adherence to hormonal therapy.

Key Words: Congenital hypothyroidism, growth patterns, newborn screening, compliance, sociodemographic factors.
None declared

ID 821. Neonatal Screening for Biotinidase Deficiency in Turkey: A Preliminary Study

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Background: Biotinidase deficiency (BD) is an autosomal recessive metabolic disease caused by mutations in the BTD gene. Clinical presentation o BD is heterogeneous and early treatment with oral biotin prevents the onset of clinical symptoms. Neonatal screening for BD is successfully performed since 2008 in Turkey, enabling early diagnosis and treatment, and providing an excellent prognosis of this inborn error of metabolism. The frequency of BD (1/7.116) in Turkey is considerably higher than the frequency reported in the world (1/60.000). In this study, it was aimed to obtain a prediction about the frequency of BD in babies born in Acibadem Healthcare Group.

Methods: In addition to the National Newborn Screening Program, biotinidase activity is screened by the fluorometric method (546 nm) in the heel blood samples impregnated with the filter card of all newborn babies born in Acibadem Healthcare Group. According to the reaction result, the enzyme activity is reported as qualitatively positive, low positive and negative. Babies with low positive and negative results are recalled and clinical and laboratory evaluations are made.

Results: Biotinidase screening results of 61,845 newborns born between January 2018 and December 2022 in Acibadem Healthcare Group were evaluated. BD was detected in 500 newborns (0.08%) in the screening. Biotinidase activity was reported as negative in 17 of them and low positive in 483. It was observed that 31 of these newborns died, 439 of them had normal (positive) biotinidase activity in the control and 30 of them were started on biotin treatment and followed by a Pediatric Metabolism Department. According to the results of serum biotinidase activity, the rate of diagnosis of BD was found to be 1/2061.

Conclusion: In this pilot study, the frequency of BD was found to be higher than reported. In order to resolve the controversial issues related to the diagnosis of BD, the accuracy of the screening results of patients who are started on biotin therapy should be examined with large-scale studies including genetic analysis.

None declared.

ID 466. METABOLIC SECONDARY SYSTEMIC INSULT AMONG NEWBORNS WITH NEONATAL ENCEPHALOPATHY AND NEONATAL OUTCOME: A DESCRIPTIVE MONOCENTRIC COHORT STUDY

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Abstract

Purpose: To evaluate in newborn with neonatal encephalopathy (NE) the frequency of metabolic secondary systemic insult (mSSI) and its association with neonatal mortality.

Methods

This is a monocentric retrospective observational study of newborns with NE hospitalized from 01/01/2018 to 12/31/2020. mSSI were defined as abnormalities at least one time on glycemia, natremia and/or capnia taken during routine blood sampling in the first 3 days of life. Definition threshold were: Hypoglycemia (<2 mmol/l), hyperglycemia (>10 mmol/L); hypocapnia (pCO2<30 mmHg), hypercapnia (pCO2 >70 mmHg), hyponatremia (natremia<130 mmol/L) and hypernatremia (natremia>150 mmol/L). The cumulative number of mSSI was the addition of different types of mSSI. Primary outcome was in hospital mortality.

Results

Among the 109 newborns included, 22% patients presented no mSSI, 35% 1 mSSI, 28% 2 mSSI, 11% 3 mSSI and 4% 4 mSSI. The cumulative number of mSSI was significantly (p<.01) associated with the Apgar score at 5 minutes and the severity of HIE (respectively 8.3% – 24.3% – 42.3% and 53.8% for 0 — 1 — 2 and ⩾3 mSSI groups were graded Sarnat III). Mortality was significantly (p = .009) associated with

the cumulative number of mSSI affecting 0/24 patients for 0 mSSI group to 2/38 (5.3%) for 1 mSSI group, 3/31 (9.7%) of 2 mSSI group and 5/16 (31.3%) of ⩾3 mSSI group.

Conclusion: mSSI concerned 4/5 of neonates hospitalized for NE. The cumulative number of mSSI was significantly associated with mortality. Further studies are needed to evaluate the impact of the control of these mSSI on the prognosis

none declared

ID 596. NEURODEVELOPMENTAL ASSESSMENT AT 12 MONTHS OF CORRECTED AGE IN A COHORT OF PRETERM INFANTS: COMPARISON BETWEEN THE BAYLEY III SCALE AND THE DP-3 QUESTIONNAIRE

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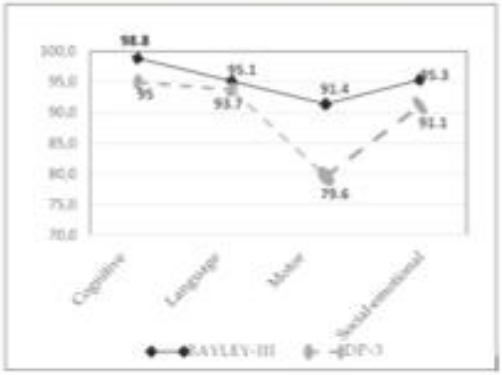
Background: the rising incidence of minor neurodevelopmental disorders in children born preterm represents a concern for their negative impact on quality of life. Bayley–III developmental scales are used to monitor, in the first 36 months of life, the neurodevelopment of preterm infants. The complementary use of indirect tools as the DP–3 standardized questionnaire for parents, which explores the four domains of the Bayley–III scale (cognitive, motor, language, social–emotional), may also provide relevant information. Objectives: to investigate the correlation between the scores obtained at 12 months of corrected age by administering the Bayley III and DP–3 scales to a cohort of ex–premature children and their parents.

Methods: preterm neonates born at Sant'Eugenio and Policlinico Umberto I Hospitals in Rome between January 2020 and December 2021 enrolled in the neurodevelopmental follow–up program were considered for inclusion. We excluded patients with genetic syndromes, severe IVH (grade III–IV), PVL, and those with a major motor/sensory disability. The Bayley–III and DP–3 Scales were administered at 12–months of corrected age. The mean scores obtained were compared through the Pearson–Correlation–Coefficient–r.

Results: 53 children (23 females and 30 males) were enrolled. Mean BW and GA at

birth were 1354.9 ± 434.3 gr (range 629–2348) and 30 ± 2.2 weeks (range 26–34). The average stay in NICU was 53 ± 20.8 days (range 10–116). The scales were administered at a mean corrected age of 12.1 ± 0.7 months (range 10–14). Overall higher average scores (from a minimum of +1.4 to a maximum of + 11.8 points) were registered at the Bayley–III scale compared to the DP–3. Despite these differences, a statistically significant positive linear correlation was found in all the domains analysed (p values between 0.001 and 0.021), as shown in Table 1.

Conclusions: this study provides an innovative contribution by highlighting a correlation between the scores obtained with the two scales. The slightly lower performances of our preterm group in the DP–3 questionnaire, which expressed parental concerns, could predict developmental problems in later age. Early identification of neurodevelopmental delays allows to intervene when neuroplasticity is in its full potential through early enablement programs.



Domains	r	p
Cognitive Bayley-III vs DP-3	0.44	0.001**
Language Bayley-III vs DP-3	0.38	0.004**
Motor Bayley-III vs DP-3	0.40	0.003**
Social-emotional Bayley-III vs DP-3	0.31	0.021*

Table 1 Note: Normal scores for both scales: Mean (SD) = 100 (15); ** = p< 0.01; * = p< 0.05.

none declared

ID 755. SMALL VS. APPROPRIATE FOR GESTATIONAL AGE VLBW INFANTS <600G – A MATCHED GROUP STUDY

Doctor Raphaela Jernej[1], Mag. Dr. Renate Fuiko[1], Doctor Judith Rittenschober–Boehm[1], Doctor Katrin Klebermass–Schrehof[1], Doctor Agnes Grill[1], Doctor Angelika Berger[1], Doctor Katharina Goeral[1]

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Background: There are controversial data regarding the impact of small for gestational age (SGA) on mortality, morbidities and neurodevelopmental outcome within very low birth weight (VLBW) neonates. Additional data is required to offer evidence–based data supporting prenatal counselling.

Methods: The aim was to compare survival until discharge, short–term morbidities and neurodevelopmental outcome at two–three years corrected age of VLBW neonates SGA vs. appropriate for gestational age (AGA) infants. Retrospective single center matched cohort study including neonates born ⩾23 weeks GA between 2010 and 2022. A total of 130 SGA infants born ⩽600g were matched with AGA infants according to sex, year of birth and GA.

Results: Despite comparable mean GA at birth (26 weeks), SGA neonates received surfactant significantly more often (p=0.003)) and had a significantly higher risk for BPD (p=0.004). At discharge, median corrected GA was 40 weeks in SGA and 38 weeks in AGA neonates (p⩽0.001) and weight percentile was 2 in SGA and 23 in AGA infants. Half (55%) of SGA infants and 85% of AGA infants admitted to the NICU survived (p⩽0.001). Using Bayley Scales of Infant Development at two–three years corrected age 48% of SGA and 55% of AGA infants showed normal cognitive outcome (p=0.222), while 46% SGA and 55% AGA infants had normal motor development (p=0.214). Profound combined neurodevelopmental impairment (defined

as Bayley Scale <55, visual or hearing impairment with need of visual or hearing aid and, or, profound cerebral palsy with a GMFCS level 4—5) was present in 12 SGA (24%) and 17 AGA survivors (20%; p=0.310).

Conclusion: SGA infants showed a significantly higher risk of death before discharge with a relative survival difference of 54% compared to AGA neonates. In survivors, there was no significant difference in cognitive or motor development outcome as well as in profound combined neurodevelopmental impairment between groups (24% in SGA, 20% in AGA).

None declared

ID 549. Cerebellar Pathologies in Extremely Preterm Infants with Intraventricular Hemorrhage: Outcome at Two-Years of Age

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Background

Extremely preterm birth and intraventricular hemorrhage (IVH) are known risk factors for adverse neurodevelopmental outcomes. As IVH is often associated with cerebellar hemorrhage (CBH), the influence of these posterior fossa abnormalities is warranted.

Methods

This retrospective study analyzed cMRI data at term-equivalent age of patients <28 weeks gestational age with intraventricular hemorrhage between 2011 and 2021. Cerebellar hemorrhages (graded after Kidokoro et al) and further pathologies, as well as cerebellar voluminal, were studied and the correlation of these injuries to the outcome at 2 years of age (analyzed with Bayley tests) was evaluated.

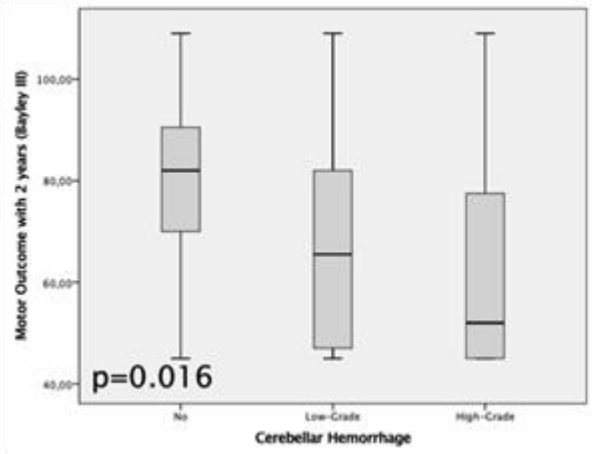
Results

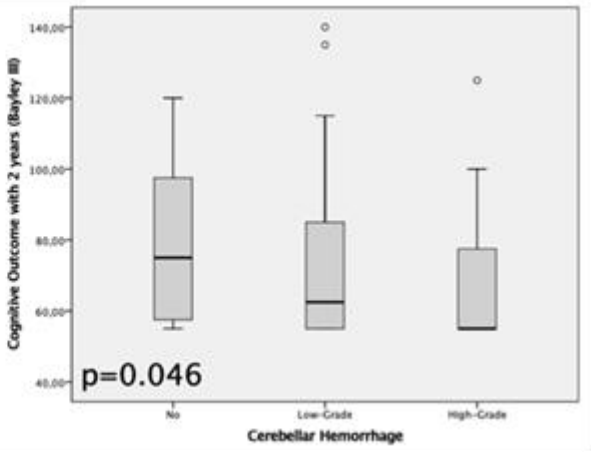
A total of 103 cMRI scans were available for analysis. Out of these 69 (67.0%) showed cerebellar hemorrhage with a median Kidokoro grade of 1 (0-3). At two years of age, CBH was associated with significantly impaired motor outcome [84 (IQR 67.92) vs 60 (IQR 45.81), p=0.031]. With increasing grade of CBH, motor and cognitive outcomes were significantly worse (motor p=0.004; cognitive p=0.0034). Altogether, 30 (29.1%) infants had cerebellar atrophy of at least one hemisphere, which was associated with significantly impaired composite outcome scores (motor

p=0.010; cognitive p=0.042, language p=0.021). Increasing cerebellar size significantly correlated with better motor development (p=0.04).

Conclusion

Two-thirds of all extremely preterm infants with IVH had a concomitant CBH, which was associated with significantly worse motor scores at two-years of age. Extent of cerebellar pathology was associated with poorer outcome. This study might support prediction of long-term outcome and parental counseling in patients with IVH.





None declared.

ID 1005. Extra-uterine growth in preterm: an independent factor for neurological outcome.

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Background: Extrauterine growth restriction (EUGR) is common in preterm and is a risk factor for worse long term neurological outcome. We report our experience in a large population of very low birth weight (VLBW) neonates.

Methods: we selected all VLBW patients born between 2012 and 2018 that performed an MRI scan at term age. Patients with congenital malformations or major brain lesions were excluded, patients with low grade IVH, punctate lesions, micro–cerebellar hemorrhage were included. Neurological outcome were evaluated with Griffiths scale (GMDS) at 2 and 3 year of age. Perinatal and neonatal risk factors as gestational age (GA), born weight, Apgar score, sepsis, NEC, bronchopulmonary dysplasia and surgery was collected. Weight growth was evaluated at term age, 6 and 12 month of correct age. Multivariate analysis was done.

Results: Of 498 VLBW, 210 were exclude (severe brain lesions, malformation or incomplete data). Statistical analysis was performed in 288 patients (mean GA 28,9 weeks, range 23–34,6 weeks). EUGR (defined as weight z–score < 1.28 or <10°

percentile) was found in 43.8% at term age, 46.2% at 6 months, 48,3% at 12 months. Multivariate analysis showed that higher weight z–score at 6 month is protective for neurological outcome at 2 year of age (OR 0.74; CI 0.59–0.93; p=0,01). In particular, EUGR patients at 6 months had an higher risk for motor deficit (OR 1,87, CI 1,05–3,29, p=0,03); language deficit (OR 1,87; CI 1,05–3,29 p=0,02) and adaptive behavior deficit (OR 1,94; CI 1.12–3.37, p=0,02) at 2 year GMDS. These data are not confirmed at 3 year of age except for language deficit (OR 1.63; CI 0.99–2.69 p=0,055). NEC (OR 2,55; CI 1.11–5.86 p=0.03) and male sex (OR 1.94; CI 1.16 – 3.24 p=0,01) seems to be the major risk factors for lower GMDS at 3 year.

Conclusion: EUGR has a high incidence in our population of preterm. A lower weight at 6 month of age seems to be an independent risk factor for neuro–developmental delay at 2 years. A significant negative effect remains at three years for language impairments. Nutrition after hospital discharge probably deserves major attention in VLBW in preterm infants.

None declared

ID 666. Neurodevelopmental Outcome of the Infants with Transient Hypothyroxinemia of Prematurity

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Background

Transient hypothyroxinemia of prematurity (THoP) is defined as a free thyroxine level below the reference values despite normal TSH in preterm infants. THoP occurs in 35–50% of preterm births. Clinicians experience contradictions in management of THoP due to the lack of long–term data. Therefore, this study aimed to evaluate the clinical and neurodevelopmental outcome of infants with THoP.

Methods

This prospective study included newborns who were born between 28–36 weeks of gestation (GW) and were admitted to the neonatal intensive care unit (NICU). Newborns with maternal thyroid disease, severe intracranial problems, and with congenital anomalies were excluded.Study group consisted of infants with THoP.Infants without THoP formed the control group. Subgroups of study group were determined as the infants with levothyroxine use and the others without replacement. First TFT were taken at 10–20th days of life. Neonatal demographics, replacement status, and morbidities including RDS, BPD and NEC were all evaluated comparatively. Ages and Stages Questionnaire (ASQ) and Ages and Stages Questionary–Social–Emotional (ASQ:SE) developmental screening tests were administered to the entire study population at the corrected age of 2 years.

Results

A total of 70 newborn infants were included in this study. Study group consisted of 40 patients, 53,7% (n=22) male and 62%(n=18) female. Control group consisted of 30 infants 46,3%(n=19) male and 37,9% (n=11) female. Mean GW of study group was 34,4 ± 3,8, was 37,2 ± 2,3 of control group (p=0,69). Mean birth weight was 1640±428gr. Levothyroxine (L–T4) replacement was started in only 12infants (30%). Groups didn't differ in terms of demographic characteristics. BPD and ROP were significantly higher in the treated group (p=0,01). No difference was found in the comparison of the ASQ and ASQ:SE results of the study and control groups(p=0,75). ASQ and ASQ:SE results did not differ between those with THoP who received and did not receive replacement (p=0,14).

Conclusion

This study showed that although levothyroxine replacement therapy was associated with higher BPD and ROP rates, it did not improve long–term neurological outcomes in infants with THoP. Prospective controlled studies with larger sample sizes are needed to clarify the role of levothyroxine replacement in THoP.

None declared.

ID 899. NEUROMOTOR AND NEUROSENSORY DEFICITS DETECTED AT POSTNATAL DAY 2 IN PRETERM RABBIT PUPS WITH GLYCEROL-INDUCED INTRAVENTRICULAR HEMORRHAGE

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Background: Intraventricular hemorrhage (IVH) is a pronounced morbidity in extreme preterm infants often resulting in long–term neurodevelopmental impairment, including cerebral palsy, intellectual disability and other cognitive and movement disorders. Neurobehavioral assessments can be used to characterize the deficits originating from an IVH, as well as follow the progression of the disease, and to investigate new therapeutic strategies.
In this study we investigated the usefulness of assessing neuromotor and neurosensory outcomes in the preterm rabbit model of glycerol–induced IVH on postnatal day (PND) 2. The preterm rabbit pup reflects many traits of preterm systemic physiology, including underdeveloped lungs and brain. Furthermore, the preterm rabbit pup model of IVH display essential aspects of the development of IVH in the preterm human infant.

Methods: Preterm rabbit pups were delivered by cesarean section on E29 (term 32 days), corresponding to a human brain maturation of approx. 24–28 weeks of gestation. IVH was induced by intraperitoneal administration of a 50% glycerol solution at 3 hours post–partum and verified by high–frequency ultrasound (HFU) at PND1.
At PND2 neurobehavioral tests, based on a scoring protocol by Derrick et al. (1), were performed. The pups were evaluated inside an infant incubator on a delineated arena

by blinded operators. Motor function, including tone, motor activity, locomotion, righting reflex and gait were evaluated. Sensory function was examination by touching the whiskers and introducing milk and ethanol (aversion) to the nose. All assessments were recorded and evaluated in a blinded procedure.

Results: Evaluation showed a significant difference in motor activity, displayed as decreased duration of activity and righting reflexes, in pups with IVH compared to control animals. In the sensory tests a difference (lower scores) in suckling response and head movements during feeding was detected in pups with IVH.

Conclusions: We show that neurobehavioral assessment established by Derrick et al. can be a useful tool for characterizing early neurosensory and neuromotor deficits in preterm rabbit pups with IVH. This assessment has the potential to be guiding in interventional therapies directed towards prevention and treatment of perinatal brain damage following IVH.

1. Derrick et al. J of Neuroscience, 2004, 24 (1) 24–34.

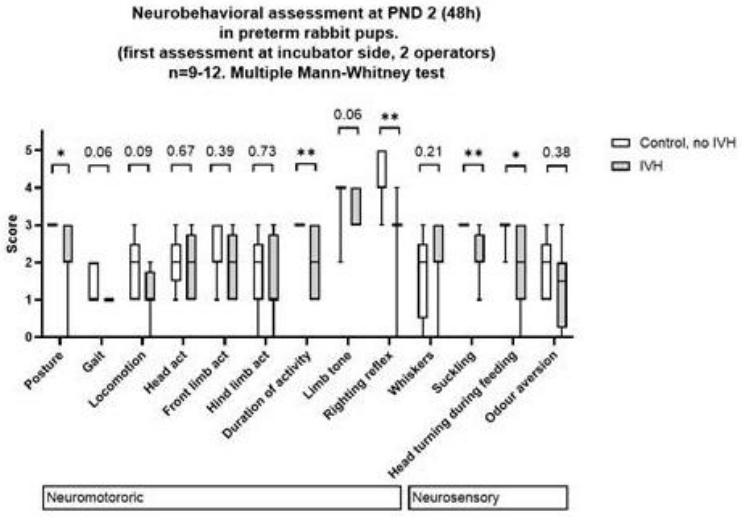

Figure. Neurobehavioral assessment at postnatal day 2 of preterm rabbit pups.

Figure. Neurobehavioral assessment at postnatal day 2 of preterm rabbit pups.

None declared

ID 823. ULTRASOUND ASSESSMENT OF SUBVENTRICULAR ECHOGENICITY IN PRETERM INFANTS WITH NECROTIZING ENTEROCOLITIS OR BACTERIAL SEPSIS

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Background: The pathological dysregulation of the physiological regression of the germinal matrix (e.g. subventricular injury (SVI)), can in its early stages be detected through cerebral ultrasound by observing increased echogenicity of the germinal matrix, also referred to as subventricular echogenicity (SVE). The purpose of this study is to examine the relationship between the development of SVE and two systemic inflammatory diseases in preterm infants: necrotizing enterocolitis (NEC) and gram–negative sepsis.

Methods: Cranial ultrasounds (CUS) of 56 extremely or very preterm infants with NEC or gram–negative sepsis were retrospectively evaluated. Following pre–defined

sonographic criteria, each infant was assessed as negative, equivocal, or positive for SVE at two-time points: pre-disease and post-disease. Paired sample T-tests were performed to assess any differences in SVE findings pre- and post-disease.

Results: Of the 47 neonates that were negative for SVE at pre-disease CUS, 23 became positive for SVE presence at the post-disease CUS, revealing a correlation between acute systemic inflammatory disease (NEC and gram-negative sepsis) and the subsequent occurrence of SVE ($p<.001$). Even when the two events are considered separately, both gram-negative sepsis ($p<.001$) and NEC ($p<.001$) appear to be significantly associated with the appearance of SVE. In most cases, the lesion manifested itself in the days immediately following the diagnosis and lasted for several weeks.

Conclusion: In our retrospective cohort, we saw an increase in the presence of SVE following NEC or sepsis. This result is in line with the hypothesis that acute systemic inflammation is an important etiopathological agent in the development of SVE. Future prospective ultrasound case-control studies (using standardized coronal planes) are crucial because it eliminates potential variations in imaging techniques and operator-dependent biases. These studies would allow a comprehensive evaluation of SVE characteristics, including its temporal dynamics and potential predictive value for long-term neurodevelopment.

	Negative N (%)	Equivocal N (%)	Positive N (%)
Total (n = 47)	14 (29,79)	10 (21,27)	23 (48,94)
NEC cohort (n = 32)	10 (31,25)	5 (15,62)	17 (53,13)
Sepsis cohort (n = 15)	4 (26,67)	5 (33,33)	6 (40)

Prevalence of subventricular echogenicity in post-disease cranial ultrasounds.
Prevalence of subventricular echogenicity in post-disease cranial ultrasounds.
None declared

ID 489. Investigating the onset of intraventricular haemorrhage in preterm neonates: a systematic review and meta-analysis

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Background
Our objective is to investigate the time distribution of onset of IVH in preterm neonates (VLBW, ⩽1500g/GA<32 weeks) during the first week of life.
Intraventricular haemorrhage (IVH) is a devastating complication of preterm infants with a pooled estimate of 34.3% for GA <28 weeks. IVH typically occurs during early postnatal hours (HOL), however, the exact onset of IVH is unknown.

Methods
MEDLINE, Embase, CENTRAL and Web of Science were searched until late 2022. The overall occurrence of IVH among preterm infants was calculated. The meta–analysis included 58 studies. Occurrences with standard errors of IVH were calculated and pooled at different time intervals 0–6, 0–24, 0–48, 0–72 HOL. In a subgroup analysis results of studies conducted before and after 2007 were compared. The majority of the articles in the subgroup before 2007 were included in the previous meta–analysis by Sameer Al–Abdi in 2014.

Results

The overall occurrence of IVH in all preterm neonates was 35% [30–41%] (as point estimate [95% CI limits]) before 2007 and 30% [25–36%] afterwards. The proportion of IVH occurrence at different time intervals among all preterm neonates in the subgroup before and after 2007: up to 6 HOL* was 12% [7–18%] and 5% [2–11%], up to 24 HOL* was 18% [13–26%] and 10% [6–16%], up to 48 HOL* was 28% [21–36%] and 17% [11–24%], up to 72 HOL was 27% [20–36%] and 21% [15–29%] The remaining cases occurred beyond 72 HOL. (*: $p<0.05$)

Conclusion

The overall occurrence of IVH among preterm infants has not changed significantly, while time distribution pattern reflects some delay of onset of IVH in studies after 2007 compared to studies before 2007.

There was high heterogeneity across studies suggesting a need for standardised reporting for CUS and known risk factors of IVH as well.

None declared