POSTER SESSION 1 – BRAIN 1
SEPTEMBER 15, 2021 – 13:00 – 14:30 CEST

ID 446 - INVESTIGATING CHANGES IN CEREBRAL MICROVASCULAR BLOOD FLOW AND MITOCHONDRIAL METABOLISM TOGETHER AT THE COT-SIDE IN NEONATAL ENCEPHALOPATHY.

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Background:
Perinatal injury to the developing brain continues to remain a significant cause of neonatal morbidity and mortality. The availability of early cot-side markers of neuronal injury that correlate with disease severity and are predictive of outcome would likely facilitate a more targeted therapeutic approach using adjunctive therapies. To answer this need, we developed a photonic platform that brings together broadband near-infrared spectroscopy (BNIRS) and diffuse correlation spectroscopy (DCS); allowing the synchronous measurement of (i) haemoglobin oxygenation changes, (ii) mitochondrial function through measurements of the oxidation state of cytochrome-c-oxidase (oxCCO) and (iii) cerebral blood flow index (BFI).

Methods:
The Florence system is composed of a BNIRS and a DCS instrument. The BNIRS consists of a tungsten halogen lamp light source with a 700nm longpass filter, and a micro spectrometer as a detector. The DCS system, consists of a 785nm long coherence diode laser as a source, and 4 avalanche photodiodes with a correlator as detectors. Optical fibres are used to connect the instrument with infant’s head using a custom 3D printed probe holder (source-detector separation of 3cm and 2cm for BNIRS and DCS respectively). The Florence measurements include the changes in concentration of oxy- deoxy- haemoglobin (HbO2, HHb) (from which we can derive changes in brain oxygenation (HbDiff=HbO2-HHb) and brain blood volume (HbT=HbO2+HHb)), changes in the oxidation state of cytochrome-c-oxidase (oxCCO) and cerebral blood flow index (BFI).

Results:
We are currently investigating the impact of hypoxic ischaemic brain injury on cerebral metabolism, haemodynamics and oxygenation in infants with neonatal encephalopathy (NE) with an aim to develop an index of brain tissue health that will be able to assess injury severity and prognosticate outcome. Figure 1.a presents this new instrument operating in the NICU. With Figure1.b presenting a typical dataset collected by the instrument on day 1 of life.

Conclusions:
We have demonstrated that a combined BNIRS-DCS system is able to monitor useful real time information regarding cerebral blood flow, mitochondrial metabolism and cerebral oxygenation relating to the evolving pathophysiological changes in infants with NE. It promises to be a useful tool in NICU.
Figure 1. Photograph a) shows the photonic instrument operating in the NICU with b) presenting a typical dataset collected by the instrument on day 1 of life.

None declared.
ID 454 - THE RELATION AMONG INTERHEMISPHERIC SYNCHRONY, MICROSTRUCTURAL DEVELOPMENT OF THE CORPUS CALLOSUM IN EXTREMELY PRETERM INFANTS

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Background:
Amplitude integrated electroencephalography (aEEG/EEG) is a valuable tool allowing non-invasive, inexpensive and bedside evaluation of brain functional status in the newborn. Bursting interhemispheric synchrony (bIHS) in the newborn’s cortical activity is considered a key feature of EEG maturation. This study aims to examine whether bIHS, in the first week of life of infants born extremely preterm, is associated with microstructural development of the corpus callosum (CC) on term equivalent age MRI scans.

Methods:
A total of 25 extremely preterm infants admitted to the NICU of the Wilhelmina Children's Hospital were monitored with the continuous 2-channel EEG during the first 72 hours and after 1 week from birth. bIHS was analyzed using the Activation Synchrony Index (ASI) algorithm. Infants underwent MRI, with DTI, to assess white matter integrity at ~30 and ~40 weeks of postmenstrual age (PMA). Microstructural development of the CC was assessed using fractional anisotropy (FA) measurements, adjusted for PMA at scan. Multivariable regression analyses were used to assess the primary and secondary aim. Analyses were adjusted for important clinical confounders: morphine, birth weight z-score, white matter injury score.

Results:
ASI (measured as the AUC of the time-points of interest) was not significantly associated with FA of the CC at 30 weeks PMA and at 40 weeks PMA (p > 0.5) (Fig1). ASI was positively associated with the administration of morphine (p < 0.05) (Fig2). In particular, infants who received morphine had higher ASI values compared to infants who did not receive it at one week after birth.

Conclusion:
Early cortical synchrony is affected by morphine and is not associated with the microstructural development of the CC, at 30- and 40-weeks of GA. More studies are needed to evaluate the long-term effects of neonatal morphine treatment in order to optimize sedation in this high-risk population and to positively impact preterm brain development.
Figure 1, Association of ASI with (a, c) 30- and (b, d) 40-week scan of FA_CC, morphine (a, b) administration and (c, d) dosage. Figure 2, Relationship between ASI, BW-Z, and morphine (a) administration or (b) dosage.
ID 89 - ASSOCIATION OF VENTRICULAR VOLUME TO OUTCOME IN POST HAEMORRHAGIC VENTRICULAR DILATATION

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Background
Linear measurements of the lateral ventricles are frequently used to diagnose and monitor post haemorrhagic ventricular dilatation (PHVD) in the preterm infant. Ventricular volume (VV) can be estimated through manual segmentation on 3D US and it can be accurately estimated from linear measurements in 2D US: ventricular index (VI), anterior horn width (AHW) and thalamo-occipital distance (TOD). However, it is yet to be determined if VV could have a potential role in PHVD. We aim to study the association of VV to intervention group and outcome in a subpopulation of patients from the ELVIS trial.

Methods
We included 3D US of those patients recruited in the ELVIS trial. The different ventricular indices were collected and manual segmentation of VV and total brain volume (TBV) was performed. Accounting for repeated measures, we used general estimated equations to study the association of linear measurements and VV to cognitive scores at 2 years.

Results
We included 12 patients recruited at our study centre, 6 randomized to the low and 6 randomized to high threshold group. We found no differences in perinatal characteristics among both groups. We measured 212 ultrasounds from 10 patients that were evaluated at 2 years (one patient died and another was lost to follow up). Linear measurements were not associated to cognitive outcome except for TOD in the high threshold group, where those with good outcome had lower TOD (25.8 mm[22.3- 28.4] vs.32.2 mm[31.7- 32.5]; P=0.002). VV was associated to outcome in the high threshold group (18.2 cm3[14.0- 28.6] good vs. 36.2 cm3[30.2- 41.2] adverse outcome; P= 0.008) as was VV/TBV index (0.1[0.08- 0.11] vs. 0.18 [0.15- 0.21]; P=0.0001).

Regarding linear measurements, TOD and randomization group were significantly associated with outcome, accounting for repeated measurements and postmenstrual age. VV and VV/TBV are associated to outcome independently from threshold group (Table 1).

Conclusions
VV and VV/TBV are associated with adverse outcome in patients with PHVD. ELVIS trial proposed threshold and TOD are related to 2-year outcome while VI and AHW are not. Further studies are needed to address the potential role of VV estimation in PHVD.
<table>
<thead>
<tr>
<th>Measurements</th>
<th>Coefficient</th>
<th>P value</th>
<th>Coefficient</th>
<th>P value</th>
<th>Coefficient</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular index</td>
<td>0.08</td>
<td>0.33</td>
<td></td>
<td></td>
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<tr>
<td>Anterior horn width</td>
<td>-0.07</td>
<td>0.27</td>
<td></td>
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<td></td>
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<tr>
<td>Thalamo-occipital distance</td>
<td>0.04</td>
<td>0.03</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Ventricular volume (VV)</td>
<td></td>
<td></td>
<td>0.02</td>
<td>0.003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VV/TBV</td>
<td></td>
<td></td>
<td></td>
<td>3.99</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Postmenstrual age</td>
<td>0.02</td>
<td>0.6</td>
<td>0.16</td>
<td>0.0001</td>
<td>0.16</td>
<td>0.0001</td>
</tr>
<tr>
<td>Threshold group</td>
<td>-0.47</td>
<td>0.008</td>
<td>-0.06</td>
<td>0.673</td>
<td>-0.07</td>
<td>0.6</td>
</tr>
</tbody>
</table>

N.Obs= 60; N. groups=6 P=0.002
N.Obs=53 N. groups=5 P=0.0001
N.Obs=53 N. groups=5 P=0.0001

Table 1. Association of lineal measurements, ventricular volume (VV) and VV/total brain volume (TBV) to cognitive outcome at 2 years, including intervention group and postmenstrual age.
None declared
ID 546 - OPIOIDS AFFECT THE AMPLITUDE-INTEGRATED EEG (aEEG) BACKGROUND IN PRETERM INFANTS ≤ 28 WEEKS

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Background:
Early abnormal aEEG tracings (burst suppression -BS-, continuous low voltage, inactive) have been shown to predict adverse short-term outcomes (defined as severe intraventricular hemorrhage -IVH-, periventricular hemorrhagic infarction -PVHI-, and/or death) in very premature infants. However premature infants with adverse short-term outcome are more likely to have respiratory and hemodynamic instability within their first days of life and need sedation. We assessed whether opioid sedation affects the predictive value of the aEEG background in these infants.

Methods:
aEEG monitoring of preterm infants ≤ 28 weeks of gestational age (GA) started within the first 24 hours of life and continued up to 72-96 hours was performed. A visual qualitative analysis (Hellstrom-Westas classification) of the aEEG recordings was performed in 6h epochs. Opioids use data were collected and aEEG background changes were assessed after their administration. Short-term adverse outcome was defined as the presence of IVH grade III, PVHI and/or death.

Results:
Recordings of 49 infants with a mean GA of 26.6 weeks (±1.4) were assessed. 17/49 (34.7%) infants received opioids. Infants given opioids required more mechanical ventilation and cardiovascular support compared to non-sedated infants (p <0.001). After sedation, 16 of 17 had a BS with a high burst density pattern (BS+). Of these 16, 3 initially had a BS with a low burst density (BS-) or had an inactive pattern. For isolated IV boluses, the BS+ pattern lasted between 5 and 15 hours, and for continuous IV perfusion it was maintained throughout the treatment. None of the non-sedated infants had a BS+ pattern. 14/49 (28.6%) infants had an adverse short-term outcome. Among the infants given opioids, 8/17 (47%) had an adverse short-term outcome (p=0.05).

For predicting short-term adverse outcome, the presence of a BS+ pattern in at least 1 epoch had a PPV of 50% and a NPV of 81%.

Conclusion:
Sedating extremely preterm infants with opioids affects brain function, regardless of the presence or absence of brain injury. Thus, opioids alter the predictive value of an abnormal aEEG background to determine adverse short-term outcome in this population.

None declared
Background
Hypoxic-ischaemic encephalopathy (HIE) is a significant cause of infant mortality and morbidity in term neonates. Recently, several studies have focused on identifying early markers of brain damage and their predictive role in the severity of neurological outcomes. The aim of our study is to assess the prognostic role of continuous somatosensory evoked potentials (SEPs-c) monitoring during video-electroencephalogram (VEEG) in HIE treated with hypothermia.

Methods
This prospective study enrolled neonates with HIE who had received therapeutic hypothermia. They underwent VEEG and continuous SEP recording for one hour under normothermic conditions. The SEP-c were scored as follows: bilateral normal responses (zero), bilateral monotonous responses (one), bilateral hypovolted-monotonous and/or increased latency responses (two), unilateral absent responses (three) and bilateral absent responses (four) (fig.1).

The effect of SEP abnormalities on Bayley Scales of Infant and Toddler Development - Third Edition at 24 months was measured; positive (PPV) and negative (NPV) predictive value, sensitivity and specificity were calculated.

Results
The analysis comprised 25 full-term neonates. When it came to continuous SEPs-c, 10 infants had a score of zero (40%), 7 scored one (28%), four scored two (16%), none scored three and four scored four (16%). Three of newborns scored four died for the HIE. Our results showed that altered SEPs-c (score ≥ 1) had for neurodevelopmental impairment (NDI) in cognitive area a PPV of 0.36 (95% CI: 0.15 to 0.64), NPV of 0.90 (95% CI: 0.50 to 0.99), sensitivity 0.80 (95% CI: 0.37 to 0.98), and specificity 0.56 (95% CI: 0.33 to 0.76). The altered SEPs-c showed for NDI in language area a PPV of 0.72 (95% CI: 0.43 to 0.90), NPV of 0.90 (95% CI: 0.59 to 0.99), sensitivity 0.88 (95% CI: 0.56 to 0.99), and specificity 0.75 (95% CI: 0.46 to 0.91) while for NDI in motor area a PPV of 0.18 (95% CI: 0.03 to 0.47), NPV of 1.00 (95% CI: 0.72 to 1.00), sensitivity 1.00 (95% CI: 0.17 to 1.00), and specificity 0.52 (95% CI: 0.31 to 0.72).

Conclusion
Continuously monitoring SEPs could provide important prognostic information in neonates with HIE, especially with regard to disorders of the language area.
Fig. 1: Example of a continuous SEP score
None declared
ID 406 - CREATING AN OPTIMAL BEHAVIORAL SLEEP STATE CLASSIFICATION SYSTEM FOR VERY AND EXTREMELY PRETERM INFANTS.

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Background:
Sleep serves both a protective and constructional purpose in the preterm brain. Preterm sleep consist of active and quiet states. Monitoring the underdeveloped preterm brain can function as a diagnostic and predictive tool for neuronal health. Currently, no behavioral classification scale is validated for extremely preterm infants (born < 28 weeks GA). The current study aims to develop a new, high-quality, reliable and verified visual sleep state classification system for extremely, to very preterm infants, within the first postnatal days of life.

Methods:
The sleep state classification went through four evaluation cycles, with different research teams over two years (Figure 1). In each cycle, reliability was checked using Cohen’s and Fleiss’ kappa. Furthermore, each cycle led to adaptations to the method according to new insights from the team improving usability. The final version was developed based on all adaptations and difficulties experienced. This final behavioral sleep state classification will be checked on the interrater agreement (Cohen’s and Fleiss’ kappa), expert and construct validity.

Results:
The classification methods were based 10033 minutes of observed behavior (62 infants), with 3794 minutes AS (37,82%), 2654 minutes QS (26,45%), 2663 minutes IS (26,54%), and 957 minutes W (9,54%). For the three different versions of the sleep state classification method, an interrater agreement of respectively .76, .56 and .46 was reached between observers.

The final version is currently under development and will include an extensive section on all expected behaviors during the sleep states. Besides, heart rate and respiratory frequency characteristics are considered differently depending on age. Furthermore, a transitory state (IS) is added, as transitions between sleep states do not always occur instantly. Moreover, the score includes confidence scores for observers to indicate per epoch. Finally, a section on smoothing is added, in order to adapt classifications afterwards to increase accuracy. To improve usability, a decision flow-chart has been created.

Conclusion:
To promote sleep in extremely preterm infants, it is important to perform research using a validated sleep state classification method. We have developed a method that is easy to learn and use for all healthcare providers. This will make future research more comparable, valid and replicable.
Figure 1. Overview of the methodology used to develop the behavioral sleep state classification method. Each column represents a different research team (highlighted by different colors).

None declared
ID 413 - CYTOMEGALOVIRUS INFECTION AND PRENATAL ULTRASOUND

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BACKGROUND:
Transplacental viral infections were widely investigated in last decades. Embryo–fetal infections have been reported to cause recurrent spontaneous abortions, and fetal malformations. The aim of the study was to evaluate the prevalence of Cytomegalovirus (CMV) infections in cases of ultrasound anomalies in the second trimester of pregnancy.

METHODS:
Serological examinations were carried out in 612 cases with anomalies detected by fetal ultrasound examinations, to test for CMV infection, at the Department of Obstetrics and Gynecology. The authors examined the levels of IgG and IgM, and the ratio of new CMV infections. In the second part of the study in 107 cases they performed amniocentesis because of recent CMV infections for CMV-PCR examination. The authors examined the ultrasound anomalies during pregnancy of these cases with genetic amniocentesis.

RESULTS:
In 75 cases (12.3%) recent CMV infection was detected by serological examination. In 326 cases of ventriculomegaly 41 (12.6%), and in 20 cases of brain calcification 3 CMV (15%) infections were detected. In 50 cases of increased liver echogenity there was only 1 CMV (2%) infection. In 110 cases of echogenic bowels they found 17 CMV (15.5%) infections. In 15 cases of intestinal dilation 4 CMV (26.7%) infections were detected. In 32 cases of cystic placenta there were 6 CMV (18.8%) infections.
Out of 107 cases with amniocentesis because of fresh CMV infections they found 9 positive PCR results. According to ultrasound anomalies out of 23/107 cases there were cranial, and in 34/107 cases there were abdominal ultrasound anomalies in the fetuses.

CONCLUSIONS:
Fetal ultrasonography during pregnancy plays an important role in prenatal diagnostics. In cases with atypical ultrasound findings suspicious for CMV infection, the serological examination is reasonable, and in cases of new infection genetic counseling and genetic amniocentesis for CMV-PCR is recommended.

None declare
ID 456 - HIGH SEIZURE BURDEN AMONGST INFANTS WITH NEONATAL ENCEPHALOPATHY RECEIVING CONTINUOUS EEG MONITORING IN UGANDA: A FEASIBILITY STUDY

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¹ INFANT research centre, University College Cork, Cork, Ireland, ² MRC/UVRI & LSHTM Uganda Research Unit, Entebbe, Entebbe, Uganda, ³ London School of Hygiene & Tropical Medicine, London, UK, ⁴ University College London Hospitals NHS Trust, London, UK, ⁵ Kawempe National Referral Hospital, Kampala, Uganda, ⁶ Makerere University, Kampala, Uganda

Introduction

Neonatal encephalopathy (NE) is a major cause of mortality and morbidity worldwide, with highest burden in low-income countries, however data from the highest burden settings is lacking. Continuous EEG (cEEG) is the gold standard for seizure detection and provides prognostic value, but is technically challenging. We examined the feasibility of cEEG amongst Ugandan neonates with NE.

Methods

cEEG was recorded on neonates with NE at Kawempe National Referral Hospital, Kampala, Uganda using Lifelines iEEG (Lifelines Neuro, UK) as part of the wider ‘Baby BRAiN’ cohort study. Neonates with NE were recruited by the clinical research team with cEEG training, technical support, and analysis provided remotely by the INFANT Research Centre, University College Cork. Post-acquisition analysis included seizure burden and semiology, and background EEG grade. Neurodevelopmental follow-up to 18 months is ongoing.

Results

Of 51 recruits with NE, 50 underwent cEEG of diagnostic quality. The cEEG was recorded for a median (IQR) duration of 71 (53-72) hours. 26/50 (52%) had cEEG seizures and 13/26 (50%) had status epilepticus. Infants with seizures had a high median (IQR) seizure burden of 246 (44-430) mins which was highest in those with moderately abnormal EEG (Fig 1). EEG grades showed a strong correlation with Thompson score (Pearson .676, p<0.01). Background EEG score predicted survival (p<0.01); 9 of 11 babies with an inactive trace died in the neonatal period. Neither status epilepticus (p=0.703) or seizure burden (p=0.668) predicted survival.

Conclusion

It was feasible to record cEEG in this setting. An inactive EEG predicted death in the neonatal period, but status epilepticus and seizure burden did not; possibly as the most severely affected neonates had electrical brain activity that remained profoundly supressed. A very high seizure burden was seen; more than 3 times higher than recorded in cooled infants in a high-income country setting. This is of particular concern given the increasing evidence that high seizure burden contributes to poor outcome. However, as seizure burden was highest in the moderate group who tend to survive the neonatal period, this study highlights the potential to reduce morbidity in this group with early recognition and treatment of seizures.
Fig 1. Seizure burden for infants grouped by worst EEG background grade during EEG. *P<0.05, **P<0.01
None declared
Background
Hypoxic-ischemic encephalopathy (HIE) is the leading cause of neurological damage in the term newborn. Since the introduction of therapeutic hypothermia (TH), there has been a decrease in the rates of death and severe neurological disability. However, 40% of children still die or suffer moderate to severe disability. Therefore, it is crucial to be able to identify those patients who are going to present more severe neurological damage. An understudied tool after the introduction of HT is somatosensory evoked potentials (SEPs).

Methods
Retrospective study of neonates ≥ 36 weeks of gestational age with HIE and TH in our center with SEPs performed in the first 14 days, between 2009 and 2019. SEPs from the median nerve were performed at the wrist with a stimulation frequency of 1 Hz and duration of 0.2ms. The intensity used was increased until the first finger movement was observed. The electrodes were placed at Erb’s point and on the parietal region opposite to the stimulated side. At least 300-400 responses were averaged. Uni or bilateral absence of N20 or latency ≥ 36 ms uni or bilaterally was considered pathological. All newborns underwent a brain MRI, which was evaluated by a blinded neuroradiologist.

Results
169 patients received TH for HIE, of which 85 patients were excluded: 28 presented some exclusion criteria, 57 did not have SEPs or were performed after 14 days. The median gestational age was 39.7 (IQR 38.1-40.7). With respect to EHI degree: 13.1% had mild-moderate, 71.4% moderate and 15.5% had severe EHI. TH was initiated at a median age of 6 (IQR 4-7) hours. SEPs were performed with a median age of 8 days (IQR 6-10). Altered SEPs were associated with increased risk of MRI injury for the predominant lesion and also globally since there are patients with mixed patterns of involvement (table).

Conclusions
SEPs are useful for assessing neurological damage in the EHI patient undergoing TH. In our study, the best predictive capacity was for the gangliothalamic region and the internal capsule. Further studies are needed to clearly establish their predictive capacity, alone and in combination with other tools.
### Table: Risk of presenting lesion on MRI for pathologic SEPs

<table>
<thead>
<tr>
<th>Location and severity of the lesion</th>
<th>Odds Ratio CI95%</th>
<th>p</th>
<th>S</th>
<th>E</th>
<th>VPP</th>
<th>VPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganglion-thalamic moderate-severe</td>
<td>91.2 (10.9-762.2)</td>
<td>&lt;0.001</td>
<td>95%</td>
<td>82.8%</td>
<td>65.5%</td>
<td>98%</td>
</tr>
<tr>
<td>Whitte matter moderate-severe</td>
<td>15.8 (5.03-49.3)</td>
<td>&lt;0.001</td>
<td>75%</td>
<td>84%</td>
<td>72.4%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Cortical moderate-severe</td>
<td>6.9 (1.2-39.03)</td>
<td>0.02</td>
<td>71.4%</td>
<td>73.4%</td>
<td>22.7%</td>
<td>95.9%</td>
</tr>
<tr>
<td>Internal capsule: unio bilateral</td>
<td>91.2 (10.9-762.2)</td>
<td>&lt;0.001</td>
<td>95%</td>
<td>82.8%</td>
<td>65.5%</td>
<td>98%</td>
</tr>
<tr>
<td>Brainstem</td>
<td>8.95 (1.75-45.8)</td>
<td>0.03</td>
<td>80%</td>
<td>69.1%</td>
<td>27.6%</td>
<td>95.9%</td>
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<tr>
<td>Pathological MRI (any location and degree of injury)</td>
<td>7.9 (2.7-22.5)</td>
<td>&lt;0.001</td>
<td>61.1%</td>
<td>83.3%</td>
<td>75.9%</td>
<td>71.4%</td>
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</table>
ID 158 - FUNCTIONAL BRAIN MATURATION AND SLEEP ORGANISATION IN NEONATES WITH CONGENITAL HEART DISEASE

Doctor Anneleen Dereymaeker, Ir Tim Hermans, Doctor Liesbeth Thewissen, Professor, Doctor Marc gewillig, Doctor Bjorn Cools, Professor Katrien Jansen, Ir Kirubin Pillay, Professor, Ir Maarten De Vos, Professor, Ir Sabine Van Huffel, Professor, Dr Gunnar Naulaers

1University Hospitals Leuven, Ku Leuven, Leuven, Belgium, 2Division STADIUS, Department of Electrical Engineering (ESAT), KU Leuven (University of Leuven), Leuven, Belgium, 3Department of Cardiovascular Science, Paediatric Cardiology, University Hospitals Leuven, KU Leuven (University of Leuven), Leuven, Belgium, 4Department of Development and Regeneration, Child Neurology, University Hospitals Leuven, KU Leuven (University of Leuven), Leuven, Belgium, 5Department of Paediatrics, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom, Oxford, UK

Background:
Neuroimaging studies have demonstrated structural delays in brain development in neonates with Congenital Heart Disease (CHD). To evaluate whether this is also reflected in early alterations of functional brain maturation on EEG, analysis of Functional Brain Age (FBA) and sleep organisation during the neonatal period is investigated.

Methods:
We compared prospectively 15 neonates with CHD who underwent multichannel EEG, pre- and postoperatively, with healthy term newborns of the same postmenstrual age (PMA). Subgroup analysis for d-Transposition of the Great Arteries (d-TGA) was performed (n=8). To estimate FBA, a prediction tool using quantitative EEG features as input, was applied. Second, the EEG was automatically classified as Active Sleep Stage 1 (AS1), Quiet Sleep Tracé Alternant (QS-TA), Quiet Sleep High Voltage Slow Wave Sleep (QS-HVS) and Active Sleep Stage 2 (AS2). Neonates with CHD underwent neurodevelopmental testing at 24 months with Bayley Scale of Infant Development (BSID-III).

Results:
The pre-operative FBA was delayed in the CHD infants (n=15) and more so in the d-TGA infants. The FBA was positively correlated with BSID-III motor scores.
Sleep organisation was also significantly influenced during the first days in neonates with CHD. The duration of the sleep cycle and the proportion of AS1 was decreased, again more marked in the d-TGA infants. Neonates with d-TGA spent less time in QS-HVS and more in QS-TA compared to healthy terms. Both FBA and sleep organisation normalised post-operatively to be similar to control infants. Duration of QS-HVS was positively correlated with higher motor scores in d-TGA infants.
The FBA could also be predicted on reduced channel montage.

Conclusion:
Altered early brain function and sleep is present in neonates with CHD, with significant changes after early interventions which improved cerebral oxygenation delivery. Identifying how these rapid alterations in brain function are mitigated through early surgery, drugs and nutrition may have relevance for clinical practice and long-term outcome.

None declared
ID 261 - THE RELATIONSHIP BETWEEN MOTOR PERFORMANCE AND BRAIN VOLUMES INVOLVING MOTOR AREAS IN EXTREMELY PRETERM AND TERM BORN CHILDREN AT CHILDHOOD

Phd student Lina Broström, MD, PhD Nelly Padilla, PhD student Hedvig Kvanta, PhD student Daniela Nosko, PT, PhD Maria Örtqvist, PhD, MD Ulrika Ådén

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Background
Preterm birth is associated with significant motor impairment persisting throughout childhood affecting function in everyday life. Neuroimaging studies have shown that very preterm children have smaller brain volumes compared to term born controls. Studies on the relationship between brain volumes and motor function in extremely preterm born children are lacking. The aims were 1) to compare the volumes of the brain areas involved in motor function between extremely preterm and term children at 10 years of age and 2) to define differences in motor areas of the brain in extremely preterm children with and without motor abnormalities.

Methods
42 children born < 27 weeks’ gestation and 25 term born controls born in Sweden. Children with cerebral palsy were excluded. Assessment in motor function was done at 12 years with Movement Assessment Battery for Children-2 (<5 percentile was set as cut off for impairment). The MRI data were acquired 3T MRI scanner at 10 years of age, specific brain regions involving motor function were analysed. MANCOVA (with correction for multiple comparisons) was performed to compare brain volumes and Pearson’s was used for correlation analyses.

Results
There were significant differences in all motor areas between preterm and term children after adjusting for intracranial volume and survived for multiple comparison (table 1, p<0.001). There were no significant differences in volumes of brain regions involving motor function after adjusting for birth weight in the preterm group in children with motor problems (mean 226.3 ± SD 14.9 cm³) and without (mean 230.8 ± SD 15.1 cm³), p=0.81. There were no correlation between total motor score and volume of motor regions in the preterm group, p=0.56.

Conclusion
Extremely preterm children have smaller brain volumes involving motor function but there were no association between these motor regions at 10 years and motor performance.
<table>
<thead>
<tr>
<th>Brain region</th>
<th>Preterm (n=42)</th>
<th>Term (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precentral gyrus</td>
<td>41.8 ± 2.69</td>
<td>44.6 ± 2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supplementary motor area</td>
<td>27.9 ± 1.79</td>
<td>29.8 ± 1.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>46.6 ± 2.97</td>
<td>49.7 ± 3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Precuneus</td>
<td>41.7 ± 2.65</td>
<td>44.6 ± 2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thalamus</td>
<td>12.9 ± 0.82</td>
<td>13.8 ± 0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Basal_ganglia</td>
<td>27.9 ± 1.8</td>
<td>29.8 ± 1.81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Superior-frontal gyrus medial</td>
<td>30.8 ± 1.97</td>
<td>32.8 ± 1.99</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 1. Comparison of brain volumes at childhood between extremely preterm and term born children
None declared
ID 525 - THE EFFECT OF DEXAMETHASONE AND HYDROCORTISONE ON CEREBELLAR GROWTH IN PREMATURE INFANTS

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BACKGROUND

Chronic lung disease (CLD) of prematurity is often treated with glucocorticoids. Associated neurological side effects, such as impaired brain growth, seem to be stronger for dexamethasone than for hydrocortisone. The effect on the vulnerable preterm cerebellum has not been extensively studied, though impaired cerebellar growth may have serious adverse effects in later life. This study aimed to compare postnatal cerebellar growth in premature infants who received dexamethasone or hydrocortisone for CLD or no medication.

METHODS

Retrospective case-control study in premature infants (GA <29 weeks) admitted to two level III neonatal intensive care units between 2006 and 2020. Cases were treated with dexamethasone (unit 1) or hydrocortisone (unit 2) for CLD. Controls (unit 1) did not receive postnatal glucocorticoids. Sequential head circumference (HC) and ultrasound measurements of transcerebellar diameter (TCD), biparietal diameter (BPD), corpus callosum-fastigium length (CCFL) were assessed until 40 weeks postmenstrual age (PMA). Linear mixed models were created to determine the effect of treatment on brain growth correcting for PMA at measurement, sex, and HC z-score at birth. Differences before starting treatment were assessed using linear regression.

RESULTS

346 premature infants were included (68 dexamethasone, 37 hydrocortisone, 241 control) with a mean GA at birth of 25.43, 26.35, and 27.15 weeks, respectively (p < 0.001 for each treatment group compared to control group). Before starting treatment, TCD, BPD, and HC measurements for infants in each treatment group did not differ significantly from matched measurements in the control group; CCFL measurements in the hydrocortisone group were higher than in the control group (p = 0.008). After starting treatment, dexamethasone had a significant negative effect on TCD, BPD, HC (p < 0.001), and CCFL (p = 0.007). Hydrocortisone displayed a significant negative effect only on TCD (p = 0.003) and BPD (p < 0.001).

CONCLUSION

Both dexamethasone and hydrocortisone were associated with impaired cerebellar growth in premature infants. This effect was seen after initiation of treatment, but the effect size seemed smaller for hydrocortisone. In addition, dexamethasone was also associated with smaller measurements of BPD, CCFL, and HC, whereas hydrocortisone was only associated with smaller measurements of BPD.

None declared
ID 168 - EXPECTATIVE MANAGEMENT OF A PATENT DUCTUS ARTERIOSUS: PAYS THE BRAIN THE PRICE?

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Background:
Due to increasing concerns about the adverse effects of an invasive PDA-closure and the lack of evidence that early closure is superior, an expectant policy towards closure of a hemodynamically significant patent ductus arteriosus (hsPDA) is usually preferred. However, based on earlier research (Lemmers et al, Pediatrics 2016), we hypothesize that a prolonged duration of a hsPDA can induce suboptimal brain growth.

Aim:
To investigate relation between duration of hsPDA and cerebral oxygenation with MRI-determined brain volume and neurodevelopmental outcome at two years.

Patients/Methods:
All preterm infants born <29.0 wk gestation (GA), admitted to our NICU and subject to surgical ductal closure between 2008 and 2018 were included. NIRS-monitored cerebral oxygen saturation (rScO2) during and up to 48 h after ductal closure was continuously monitored, a volumetric MRI of different brain regions at term equivalent age and a Bayley Scales of Infant and Toddler Development III test at two years of age was performed.

Results:
90 of the 94 infants fulfilled the inclusion criteria (GA mean[range]:25.9 wk [24.0-28.9]; birth weight 864 g [540-1350]). Days of a hsPDA ranged from 1-to-41 and postnatal age at surgery ranged from 3-to-47 days. Regression analysis showed that duration of hsPDA (days) had a negative relation with cerebellar volume (p<0.05) and motor-and cognitive outcome at two years of age p<0.05). 30% of the patients had a cerebral oxygenation <45% just before surgery. Delayed recovery (>24h) of rScO2 after surgical ductal closure to values >55% (-2SD normal range) had a negative relation with motor outcomes at two years of age (p<0.05).

Discussion:
Prolonged duration of hsPDA negatively affects cerebellar growth and neurodevelopmental outcome. Delayed normalization of cerebral oxygenation after ductal closure was negatively associated with neurodevelopmental outcome. The mechanisms behind these findings may be related to adverse hemodynamic effects of a hsPDA: a compromised left ventricle (LV) contractility after a longstanding duct has been suggested by several reports (Baumgart et al, Pediatr Res 2018). In case of delayed ductal closure, it may therefore be essential to be informed about LV-function and oxygenation of vital organ systems, particularly the immature brain.

None declared
ID 293 - EVALUATION OF ANATOMICAL AND VASCULAR ASPECTS BY CRANIAL ULTRASONOGRAPHY VIA TRANSFONTANELLAR IN NEWBORNS OF WOMEN INFECTED WITH SARS-COV-2 DURING PREGNANCY

Doctor Geraldo Fernandes1, Doctor David Araújo Jr1, Doctor Felipe Motta1, Doctor Maria Eduarda Castro1, Mr. Rodrigo Nery1, Doctor Licia Mota1, Doctor Alexandre Soares1, Doctor Rosana Tristão1

1Universidade De Brasília, Brasília - DF, Brazil

Background:
Vertical transmission of SARS-CoV-2 is described as uncommon, because in the pathophysiology of the disease, the expression of receptors involved in the undeveloped process (angiotensin converters and transmembrane proteases 2) However, American data report that 1-3% of newborns have positive RT-PCR in the first days of life suggesting vertical transmission. It is inferred that the cascade of cytokines resulting from SARS-CoV-2 infection may interfere with the anatomical and physiological development of target organs in these babies. Placental transfer of maternal antibodies can induce a state of hyperinflammation, still in intrauterine life, altering the formation and development of the fetal neuroaxis.

Methods:
Sampling consisting of patients born to mothers with documented SARS-CoV-2 infection, regardless of the trimester, with negative TORCHS serologies and who have normal morphological USG. The presence of congenital anomalies was an exclusion criterion. Cranial ultrasonography via transfontanellar was performed during the routine pediatric consultation, for the evaluation of anatomical and vascular aspects through a color Doppler and Spectral study in the intracranial arteries. Data such as birth conditions, neonatal ICU admission and severity of maternal illness were collected.

Results:
144 transfontanellar ultrasound scans were performed, with 11 exams showing changes. Full-term patients, suitable weight for gestational age and without the need for admission to the Neonatal ICU. Of the alterations, 6 were compatible with leukomalacia, 1 with bilateral Papille grade I intracranial hemorrhage. Another 5 babies showed hemodynamic changes with redistribution of flow in the intracranial arteries.

Conclusion:
Slight brain changes were found in the deep white matter and signs of redistribution of intracranial blood flow in some patients. Such findings raise the possibility of hemodynamic changes related to the systemic inflammatory reaction or even as a consequence of obstruction in the microvasculature - events known to be triggered by SARS-CoV-2 infection.

None declared
ID 79 - WHAT ARE THE COMPONENTS OF AN EVIDENCE-BASED CARE BUNDLE TO REDUCE INTRAVENTRICULAR HAEMORRHAGE IN PRETERM NEONATES?

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Background
Intraventricular haemorrhage (IVH) is a significant complication of premature birth. It occurs in 20% to 25% of neonates born before 30 weeks of gestation or with a birth weight of <1500 grams. IVH carries a risk of adverse long-term neurodevelopment outcomes in very low birth weight (VLBW) infants.

Methods
A systematic literature review was performed to develop an IVH care bundle. A regional team of expert clinicians including 247 neonatal health care professionals were identified. They were requested to review components of the draft care bundle (and some distractor sham components) and rate the evidence supporting them. In order to obtain a standard consensus from the expert panel, a Delphi process with two rounds of surveys was conducted using an online ‘survey monkey’ questionnaire. The results of the Delphi consensus process were used to modify the draft care bundle and produce a final IVH reduction care bundle. After the second round, panellists were asked to nominate ‘top three’ items to put in the care bundle.

Results
54 out of 247 members responded to the first round and 30 out of 54 to the second round of survey. Alongside the best available evidence, the results from both rounds were reviewed and analysed. The results showed that majority of the panellists correctly identified measures supported by good evidence, for example, use of antenatal corticosteroids, antenatal magnesium sulphate, maintaining blood pressure, and optimising thermoregulation which attributes to the standard existing practices. In contrast, the study revealed that only a few of them identified measures such as management of maternal chorioamnionitis and delayed cord clamping having strong evidence in reducing IVH.

Conclusion
Despite recognising IVH as a major complication there is a lack of awareness regarding some of the best practices and this necessitates the need for a standardised evidence-based IVH care bundle. A multidisciplinary team approach along with staff education is required to implement the care bundle. Conclusively, a quality improvement study would be needed to assess the outcome measure of IVH rates being reduced after the implementation of the bundle.
**Figure 1: Intraventricular haemorrhage Care Bundle**

**Delivery room interventions**
- Use of antenatal corticosteroids
- Use of antenatal magnesium Sulphate
- Identifying and treating Maternal chorioamnionitis

**Interventions at birth**
- Physiological Cord Clamping
- Optimise Thermoregulation
- Volume targeted ventilation plus early surfactant administration

**Stabilisation in Neonatal intensive care**
- Mini-bundle* within my Bubble
- Respiratory care including transcutaneous CO₂ monitoring
- Cardiovascular care - Administer volume slowly (if stress is evident), monitoring of invasive blood pressure

*Mini-bundle in my Bubble:
- Minimise pain and stress, Use Sucrose
- Avoid environmental triggers like noise and light
- Maintain midline supine head positioning at 15° degree for 72hrs
- Minimal handling: Cluster cares by coordinating with the team

Aesha Mohammedi, amohammedi@nhs.net

**None declared**
Background
Neonates who are born preterm are susceptible to a number of acquired brain injuries, which can be detected with cranial ultrasound imaging. It is recommended that preterm neonates born before 32 weeks gestation are screened using cranial ultrasound. The aim of our study was to determine the frequency of abnormalities demonstrated on cranial ultrasound images in a cohort of very preterm infants.

Methods
A retrospective study of a five-year period between mid-2015 to mid-2019 was performed at Monash Children’s Hospital, Melbourne, Australia. Preterm neonates born before 33 weeks gestation during this period, at our institution, who had cranial ultrasounds were included in the study. Frequency of cranial ultrasound abnormalities was recorded at various time points in neonatal life.

Results
The search found 1009 very preterm infants who were eligible for inclusion in the study. Table 1 outlines the frequency of brain injury seen on cranial ultrasound at the time points day 3 (D3), day 8 (D8) and day 42 (D42) which are currently the minimum screening time points at our institution. A scan performed in the middle of the first week of life, at D3, demonstrated a number of babies had haemorrhages; germinal matrix haemorrhage (GMH) or intraventricular haemorrhage (IVH). The frequency of haemorrhage increased in the scans done early in the second week (D8) indicating it is worthwhile performing a second early scan at this time. White matter injury is seen on ultrasound as increased periventricular echogenicity (PVE) across the neonatal period although this was more frequent on early scans. The evolution of parenchymal atrophy or white matter volume loss demonstrated as extra axial space (EAS) enlargement and ventriculomegaly were seen more in the later scans.

Conclusions
GMH/IVH was maximally seen at D8 examinations, while changes attributed to white matter loss, though rare, were reported more frequently on D42 scans.
<table>
<thead>
<tr>
<th>Type of abnormality demonstrated on cranial ultrasound</th>
<th>Day of postnatal life</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D 3</td>
</tr>
<tr>
<td>Germinal matrix haemorrhage (GMH)</td>
<td>103/911</td>
</tr>
<tr>
<td></td>
<td>(9.4%)</td>
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<tr>
<td>Intraventricular haemorrhage GRADE 2</td>
<td>42/908</td>
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<tr>
<td></td>
<td>(4.6%)</td>
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<tr>
<td>Intraventricular haemorrhage GRADE 3</td>
<td>13/907</td>
</tr>
<tr>
<td></td>
<td>(1.4%)</td>
</tr>
<tr>
<td>Periventricular haemorrhagic infarction (PVHI)</td>
<td>16/911</td>
</tr>
<tr>
<td></td>
<td>(1.8%)</td>
</tr>
<tr>
<td>Periventricular echogenicity (PVE)</td>
<td>121/907</td>
</tr>
<tr>
<td></td>
<td>(13.3%)</td>
</tr>
<tr>
<td>Periventricular leukomalacia (PVL)</td>
<td>7/907</td>
</tr>
<tr>
<td></td>
<td>(0.8%)</td>
</tr>
<tr>
<td>CEREBELLAR HAEMORRHAGE</td>
<td>10/907</td>
</tr>
<tr>
<td></td>
<td>(1.1%)</td>
</tr>
<tr>
<td>VENTRICULOMEGALY</td>
<td>24/907</td>
</tr>
<tr>
<td></td>
<td>(2.6%)</td>
</tr>
<tr>
<td>EAS ENLARGEMENT</td>
<td>7/906</td>
</tr>
<tr>
<td></td>
<td>(0.8%)</td>
</tr>
<tr>
<td>SSS THROMBUS</td>
<td>2/909</td>
</tr>
<tr>
<td></td>
<td>(0.2%)</td>
</tr>
</tbody>
</table>

**Table 1**
Frequency of brain injury seen on cranial ultrasound at time points day 3 (D3), day 8 (D8) and day 42 (D42)

None declared
ID 551 - ASSOCIATIONS BETWEEN INTRA-VENTRICULAR HEMORRHAGE SEVERITY, MEAN ARTERIAL PRESSURE AND CEREBRAL OXYGENATION PARAMETERS IN PRE-TERM NEONATES: A SINGLE CENTER-STUDY

Doctor Melinda Matyas1, Mrs Anca Man3, Doctor Mihaela Iancu2, Doctor Monica Hasmasanu1, Doctor Ligia Blaga1, Professor Gabriela Zaharie1

1Neonatology Department, University Of Medicine And Pharmacy Cluj Napoca, Cluj Napoca, Romania, 2Medical Informatics and Biostatistics Department, University of Medicine and Pharmacy Cluj Napoca, Cluj Napoca, Romania, 3Pediatrics Department, County Emergency Hospital, Targu Mures, Targu Mures, Romania

Background
Near infrared spectroscopy (NIRS), point-of-care ultrasound are very important aid to diagnose specific condition of preterm newborn and in making decision. NIRS, head ultrasound can provide important information for the clinician in preterm neonate healthcare.

The objective of our study was to determine the association between intra-vetricular hemorrhage (IVH), mean arterial pressure and cerebral rcSO2 and FTOE in preterm neonates.

Methods
We conducted a prospective study in the Neonatology Department of 1st Obstetrics Clinic, Cluj Napoca. Were enrolled 46 preterm neonates, with gestational age ≤ 30 weeks. Head ultrasound and RI (resistivity index) measurement, blood pressure monitoring and cerebral oximetry in the first 72 hours was done.

Results:
the sample of preterm were divided into two groups: 23 with IVH (median gestational age [25th percentile, 75th percentile]: 28 weeks [26.0, 29.0], mean birth weight, 968 g, range 580 to 1600 g) and 23 preterm without IVH (median gestational age [25th percentile; 75th percentile]: 29 weeks [26.5, 30.0], mean birth weight, 1159 g, range 580 to 1770 g). We found no significant differences in means of FTOE and rStO2 in preterm with and without IVH (0.37 ± 0.11 vs. 0.32 ± 0.11, p=0.120); (59.48 ± 10.56 vs. 64.52 ± 10.19, p=0.106). We found no significant linear correlation between FTOE or rStO2 and mean arterial blood pressure measured on DOL 1, 2 and 3 in preterm without IVH (p>0.05) but there was a significant negative linear correlation between FTOE and mean arterial blood pressure measured on DOL 1 (r = −0.49, p=0.018) and DOL 3 (r = −0.45, p=0.032) in preterm neonates with IVH. There was a significant positive linear correlation between the rStO2 and mean arterial blood pressure measured on DOL 1 (r = 0.52, p=0.011) and 3 (r = 0.46, p=0.027).

We found no linear correlation between RI and FTOE or rStO2.

Conclusion
The FTOE and rStO2 calculated based on NIRS correlates with blood pressure of preterm neonates with IVH. This can be helpful in clinical and treatment decision making.

None declare