ID: 475
TITLE: MONITORING SLEEP THROUGH EEG IN PREMATURE INFANTS: THE 'SLEEPI' STUDY
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CONTENT:

Sleep is essential for neurosensory cortical development, physical growth and brain formation in the preterm infant. Deprivation of sleep has been associated with impaired development and loss of brain plasticity. In the NICU emphasis is on recording of cardiorespiratory vitals with less placed on monitoring neurodevelopment. Electroencephalogram (EEG) makes a valuable contribution to assessment of neurologic status when infant is sleeping. The aim of this study is to assess the number of overnight sleep wake cycles (SWC) in mid to late preterm infants (MLP) and to quantify the number of forced versus spontaneous awakenings during active and quiet sleep and the reason for same.

This is a single centre observational study (pilot) carried out in southern Ireland. Participants were healthy /clinically stable MLP infants (32-36+6 weeks gestation), admitted to the neonatal unit at birth. An overnight video EEG was carried out before 36+6 week’s gestation and prior to discharge. Lifelines EEG monitors were used for all recordings. A modified neonatal version of the international 10/20 system was used, which provided recordings from 11 electrodes: F4, F3, C4, Cz, C3, T4, T3, O2, O1, reference and ground. ECG and respiratory activity were also monitored. A standardised 12 hour time period was analysed and annotated for all recordings commencing with the onset of active sleep. Standard of care was not altered whilst recordings were in progress.

The mean gestational age of MLP at birth was 34.48 ± 1.29 weeks and weight recorded at 2.12 ± 0.37 (Kg). Whilst the majority of infants were nursed in a cot during monitoring (60%), the high numbers nursed in incubators were in part attributed to the fact that 20% (6) underwent phototherapy during monitoring. A median (IQR) of 4 (4-4) feeds were given to each infant during EEG. 46.7% of infants fed orally, 10% via nasogastric tube and 43.3% a mixture of both. Throughout recording only 20% of infants woke/ left to wake spontaneously for all feeds.

A median (IQR) of 6(5-7) SWCs were identified for each infant on EEG. In total, 51 forced awakenings were seen in the 30 recordings, with a median (IQR) of 2(1-3) per infant - the greater majority of which occurred during active sleep (70%). Feeding was the main reason for forced awakenings (66.7%) with parental handling also provoking awakenings.

This study provides baseline information regarding sleep and feeding in pre discharge MLP infants. Further study is required to determine the most favourable strategy for feeding in terms of sleep optimisation and developmental impact, and consider whether forced or spontaneous awakening for feeds pre discharge serve the best interest of the MLP infant. Routine EEG monitoring for MLP’s is a valuable adjunct to a pre discharge clinical assessment.

COI: None Declared
ID: 524

**TITLE:** PRENATAL STRESS HAS STRAIN-SPECIFIC EFFECT ON SERUM CORTICOSTERONE LEVELS

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**CONTENT:**

Prenatal exposure to stress is associated with an increased risk for neurodevelopmental disorders such as anxiety, schizophrenia, autism spectrum disorder, and attention deficit hyperactivity disorder. Results from human and animal research show that early-life exposure to stress affects the regulation of the neuroendocrine response to stress and thus represents an important risk factor for a broad range of pathologies. Although most research is performed on male subjects, a sexually dimorphic response to the programming of the hypothalamic-pituitary-adrenal (HPA) axis has been found in animals. The mechanisms remain to be elucidated, but the interaction between HPA and hypothalamic-pituitary-gonadal (HPG) axes seems to be involved. Similarly, few studies report differences in the response to stress in different strains of mice. Glucocorticoids are tightly regulated by the HPA system and play a pivotal role in stress response. Corticosterone, the main stress steroid produced in non-human animals, is a major indicator of stress. The aim of this study was to determine the effect of prenatal stress on strain and gender in a mouse model of prenatal stress.

The effect of prenatal stress was examined in a mouse model using CD1 and C57Bl6 mice. Beginning on gestational day 14, pregnant dams were subjected to an 8-day schedule of variable stressors including restraint, swim stress, social stress, bedding-free cage, and alteration of light and dark cycles. A variable stress paradigm was implemented to prevent habituation. Body weights and blood from pups and mothers were obtained. Serum corticosterone levels were measured in duplicate by immunoassay (Corticosterone Enzyme Immunoassay, Arbor Assays). DNA was extracted for PCR sex determination. Behavioral testing performed at set times in young adult offspring. All procedures were approved by the Institutional Animal Care and Use Committee at Biomedical Research Institute of New Jersey.

We have analyzed data for 8 litters; 4 exposed to prenatal stress and 4 controls. Pups exposed to prenatal stress had decreased weight at P1 compared to controls. In CD1 pups, prenatal stress was associated with an increased serum corticosterone on P1 (527 pg/mL v 143 pg/mL, p < 0.001). No such effect was seen in C57 mice (706 pg/mL v 392 pg/mL, p=0.29). There was no difference in serum corticosterone levels between males and females after exposure to prenatal stress in either CD1 (609 pg/mL v 374 pg/mL, p = 0.50) or C57 mice (965 pg/mL v 1153 pg/mL, p= 0.29). When accounting for birth weight, prenatal stress increased serum corticosterone in FEMALE CD1 mice (743 pg/mL v 150 pg/mL, p= 0.0004) but not in FEMALE C57 mice (564 pg/mL v 1183 pg/mL, p = 0.099).

Offspring exposed to prenatal stress showed abnormal behavioral testing consistent with depression.

Exposure to stress during gestation caused a reduction in the birth weight of the offspring. Behavioral test results in early adulthood in our rodent model validate our model and confirm reports that prenatal stress exposure can cause depressive-like behavior in mice.

Our findings show a strain difference in the neuroendocrine response to prenatal stress in P1 mice. No difference was observed on corticosterone levels between males and females.
PAIN, STRESS AND SLEEP

Oral Presentations Abstracts

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COI: None declared
ID: 733

TITLE: EARLY EXPOSURE TO PROCEDURAL PAIN IS ASSOCIATED WITH DEVELOPMENT OF THALAMO-INSULA CONNECTIVITY IN VERY PRETERM NEONATES

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CONTENT:

INTRODUCTION: Early exposure to procedural pain in very-preterm (VPT) neonates (<32 weeks’ gestational age [GA]) represents a major concern in the NICU. Recent data suggest that early procedural pain exposure predicts disrupted thalamocortical development. In adults, the anterior insula is central for sensory and affective pain processing, yet the cortical representation of pain in the preterm brain remains unknown. We hypothesized that early procedural pain in VPT neonates would be associated with impaired thalamo-insula connectivity. Our objective was to determine whether neonatal pain is associated with development of functional connectivity between thalamus and insula in VPT neonates.

METHODS: Fifty-one neonates (median[IQR] GA 27.6[2.0] weeks) underwent 3 serial MRIs including functional resting-state MRI at median postmenstrual weeks: 29.4, 31.9, and 41.1. Time courses from the independent-component maps in the thalamus and in the anterior and posterior insula were extracted, and correlation coefficients between subcortical and cortical areas were calculated. Pain was operationalized as the total number of invasive procedures over the NICU stay. Generalized Estimating Equations, accounting for repeated measures, assessed the association of procedural pain with functional connectivity between thalamus and insular cortex. Models accounted for postmenstrual age at MRI and clinical factors: GA, days of mechanical ventilation, sepsis, morphine and dexamethasone doses.

RESULTS: High-quality serial fMRI data were available for 27 subjects with a total of 60 scans. Over the period of neonatal intensive care, functional connectivity increased as measured by the strength of correlated activity between thalamus and anterior insula (r=0.46, p<0.001), and thalamus and posterior insula (r=0.52, p<0.001). Procedural pain negatively predicted functional connectivity between thalamus and anterior insula over time (interaction term: invasive procedures and postmenstrual age; p=0.004), independent of relevant clinical factors. This relationship was not observed in the posterior insula.

CONCLUSIONS: Robust maturation of thalamo-cortical functional connectivity was observed in the insula over an early sensitive period of brain development. Early exposure to procedural pain was associated with impaired development of thalamo-insular functional connectivity with anatomic specificity, suggesting a role for these specific thalamo-cortical projections in early-life pain processing.

IMAGES:

The graph shows the functional correlated activity between the thalamus and the anterior insula (cubic transformation of the values) by postmenstrual age at MRI, stratified in 2 groups divided by the median number of invasive procedures.
COI: None declared
ID: 822

TITLE: NOISE EXPOSURE REMAINS A SIGNIFICANT PROBLEM FOR PRETERM INFANTS UNDERGOING AMBULANCE TRANSFER

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CONTENT:

Excess noise can cause neonatal instability with elevation in heart rate, blood pressure and desaturations. Preterm infants have decreased autonomic self-regulatory mechanisms, predisposing them to instability and fluctuations in cerebral blood flow with loud noxious stimuli, potentially increasing their risk of IVH. The maximum recommended sound level for neonatal units is 45dBA. In the UK, >16,000 neonatal transfers occur per year and it has been known for >30 years to cause excess noise exposure. Inter-hospital transfer of preterm infants is associated with an increased risk of IVH. We aimed to establish current noise exposure on the NICU and during inter-hospital ambulance transfer.

Preterm babies <32 weeks gestation and <72 hours old who either received their early neonatal care at NUH NICU (inborn arm) or were transported to NUH within the first 72 hours of life (transported arm) were included in this cohort study. Sound exposure was recorded both inside and outside the incubator for the duration of the transport journey in the transported group (n=5), or 1.5 hours in the inborn group (n=15). Total A weighted amplitude (1/3 Oct Leq dB), peak amplitude (LCPeak) and amplitude of 1/3 octave band (20-20000Hz) exposure was recorded using a calibrated Svantek sound device. Results were analysed using Prism GraphPad software.

Total A weighted sound exposure outside the incubator and peak sound exposure, in the transported group were elevated compared to the inborn group (p<0.001). However, total A weighted sound within the incubator was higher for the inborn group (p<0.001) limited to 20-4000Hz, with sound reduced to less than 30dB above 8000Hz and almost undetectable by 16,000Hz. However, within the incubator this attenuation was not seen with sound >45dB at 20-8000Hz, remaining >30dB from 10,000-20,000Hz.

Noise exposure continues to be excessive particularly during transport with peaks potentially contributing to stress and higher risk of IVH. In addition, within the incubator babies are exposed to a greater frequency range than within their environment indicating sound generation within the incubator. These interim results indicate that noise suppression during transport needs to focus at the baby interface as well as incubator design.

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Table 1. Mean and peak sound exposure inside and outside the incubator for transported and inborn babies.

COI: no conflicts of interest