NEonatal Sleep Talks
Abstract Booklet

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Clare College Cambridge

Cambridge Perinatal Group

AI-4-NICU

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EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

This is the 4th symposium on neonatal and early infant sleep and the first face-face meeting.

NEonatal **S**leep **T**alks brings together scientists and healthcare professionals to share and exchange ideas on all aspects of sleep and the developing brain.

Aim of the meeting to provide a comprehensive overview of sleep in the newborn and early infancy, from the basic science of sleep and the developing brain, to new technologies to assess sleep in the neonatal intensive care unit and the home, as well as investigating the impact of sleep on health and wellbeing, particularly in high-risk infants.

The meeting will encourage cross-disciplinary interaction and presentation of early-stage research to promote discussion and future collaborations.

Objectives of the meeting by the end of the meeting, delegates will have an understanding of:

- How sleep develops in utero and early infancy and its relationship to brain development.
- The importance of protecting sleep in the neonatal intensive care unit.
- Issues affecting sleep in early infancy.
- Technological developments in the assessment of sleep in the newborn.
- The development of circadian rhythms.
- Challenges of conducting research into infant sleep.

Who is it for Scientists (basic and applied) and healthcare professionals interested in neonatal and infant sleep.

Structure of the meeting The meeting will consist of keynote speakers and short submitted presentations from researchers as well as poster and breakout sessions.

The meeting is being organized by the **Cambridge Perinatal Group** (www.cambridgeperinatalgroup.org) and supported by funding from the

European Cooperation in Science and Technology (COST) as part of the AI-4-NICU grant (CA20124 - Maximising impact of multidisciplinary research in early diagnosis of neonatal brain injury).

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1. Active sleep as an early predictor of white matter development.

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[†]These authors contributed equally

Background and aim: White matter dysmaturation is commonly seen in preterm infants admitted to the neonatal intensive care unit (NICU). Animal research has shown that active sleep is essential for early brain plasticity. This study aimed to determine the potential of active sleep as an early predictor for subsequent white matter development in preterm infants.

Methods: Using heart and respiratory rates routinely monitored in the NICU, we first developed a machine learning-based automated sleep stage classifier in a cohort of 25 preterm infants. The automated classifier was then applied to a study cohort of 66 preterm infants to extract active sleep percentage over 5–7 consecutive days during 29–32 weeks of postmenstrual age. Each of the 66 infants underwent high-quality T2-weighted magnetic resonance brain imaging at term-equivalent age, which was used to measure total white matter volume. The association between active sleep percentage and white matter volume was examined using a multiple linear regression model adjusted for potential confounders.

Results: Using the automated classifier with a superior sleep classification performance (mean area under the receiver operating characteristic curve = 0.87, 95% CI = 0.83–0.92), we found that a higher active sleep percentage during the preterm period was significantly associated with increased white matter volume at term-equivalent age in human preterm infants (β = 0.30; 95% CI: 0.09–0.51; adjusted *P*-value = 0.020).

Conclusion: Our results extend the positive association between active sleep and early brain development found in animal research to human preterm infants and emphasize the potential benefit of sleep preservation in the NICU setting.

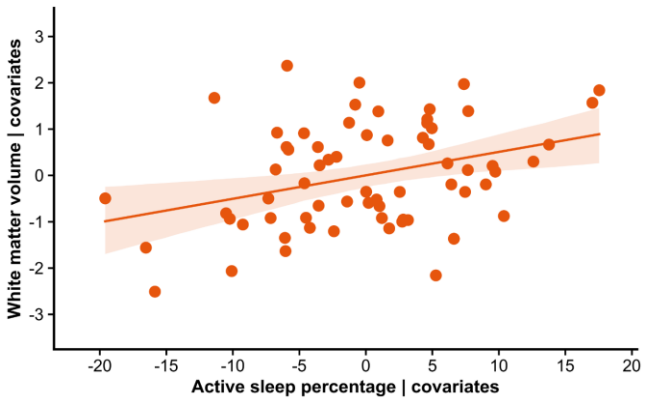

Figure. The relationship between active sleep percentage and white matter volume, after adjusting for covariates.

2. Metastability in the newborn brain during sleep and wakefulness.

Juliette Champaud, Mohammed Rupawala, Neelum Mistry, Tomoki Arichi, Lorenzo Fabrizi**

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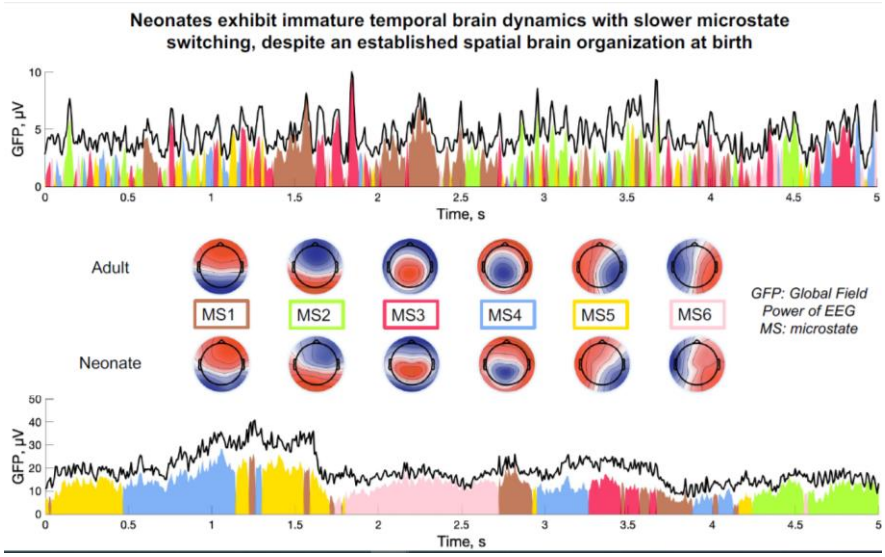
Evidence suggests that the neural activity underlying complex behavioural and cognitive functions involves brain networks transiently activating and switching on a spatial and temporal scale. We can model these metastable brain dynamics using neural microstates, which are metastable electrical topographies derived from spatio-temporal patterning of electroencephalography (EEG). Around 75% of adult resting brain activity is explained by four microstates whose temporal characteristics depend on their vigilance state. However, it remains unclear whether the spatial and temporal properties of microstates are present at birth, during the rapid development of the brain.

To assess this, we tested whether neonatal brain activity can also be described by distinct microstates and compared them to those in adults, controlling for their state of vigilance. Microstates were inferred from 150-second 20-channel EEG recordings from 36 neonates, 23 in quiet sleep and 13 awake (37.14-42.86 postmenstrual weeks), and 48 adults, 20 in N2 sleep and 28 awake (18-27 years old) using an adapted agglomerative hierarchical clustering algorithm. Microstate spatial and temporal characteristics were then compared across groups.

Initial analysis shows that both neonates and adults exhibited six similar microstates (spatial correlation r=0.85-0.96) which accounted for 59% and 61% of the EEG signal, respectively, regardless of vigilance state. However, microstates in neonates lasted significantly longer (131.6 milliseconds on average) and occurred less frequently (1 occurrence per second on average) compared to adults (27.2 milliseconds and 6 occurrences per second on average).

Our findings indicate the presence of a well-established brain organisation at birth and suggest that neonatal brain networks are capable of transient activation, albeit at a slower pace compared to adults, regardless of their state of vigilance. This difference in timing may be attributed to ongoing synaptogenesis and immature myelination during the neonatal period, potentially impacting the flexibility and efficiency of information processing in neonates.



3. Understanding the combinatorial effect of sleep deprivation and early inflammation on future cognitive and neuroimmunological outcomes.

C. Sam, N. Haidar, R. Rua

Centre d'Immunologie de Marseille-Luminy, Aix Marseille Université, Inserm, CNRS, Marseille, France

Interdisciplinary research of neuroscience and immunology is necessary to understand common cases of perinatal inflammation and sleep deprivation as they occur in hospitals. Currently, we are aware that both inflammation and sleep deprivation can independently disrupt perinatal brain development, leading to a higher risk of cognitive deficits at a later time point in life. However, we do not know what the combinatorial effect of these two early-life stressors is. In order to create a clear view of how the combined conditions of inflammation and sleep deprivation can alter early brain development, our team wants to study three groups of mice that will be either (A) inflamed by lipopolysaccharide (LPS) injections from post-natal day (PND) 3 to PND5, (B) sleep deprived from PND3 to PND5, or (C) sleep deprived during the induced inflammation from PND3 to PND5. The cognitive and neuroimmunological outcome later in life (starting at PND45) will be scoped with different behavioral tests for anxiety (Open Field Test), memory (Contextual Fear Conditioning), depression (Tail Suspension Test) and social behavior (Three Chamber Test, Social Odour test). The cognitive differences found between the conditions will be correlated with the cytokine expression and immune cell count changes in the brain and the meninges, using flow cytometry and qPCR techniques, since the meninges around the brain deeply influence cognitive functions and are particularly sensitive to early-life stressors. Furthermore, the cognitive differences in the three groups will be correlated with deficits in neurogenesis and synaptic formations using histology.

Overall, with a new understanding of the effect of early inflammation and sleep deprivation in hospitalized preterm neonates, the issue of more sleep regulation will be pressed, hopefully leading to new health care protocols prioritizing sleep during inflammation.

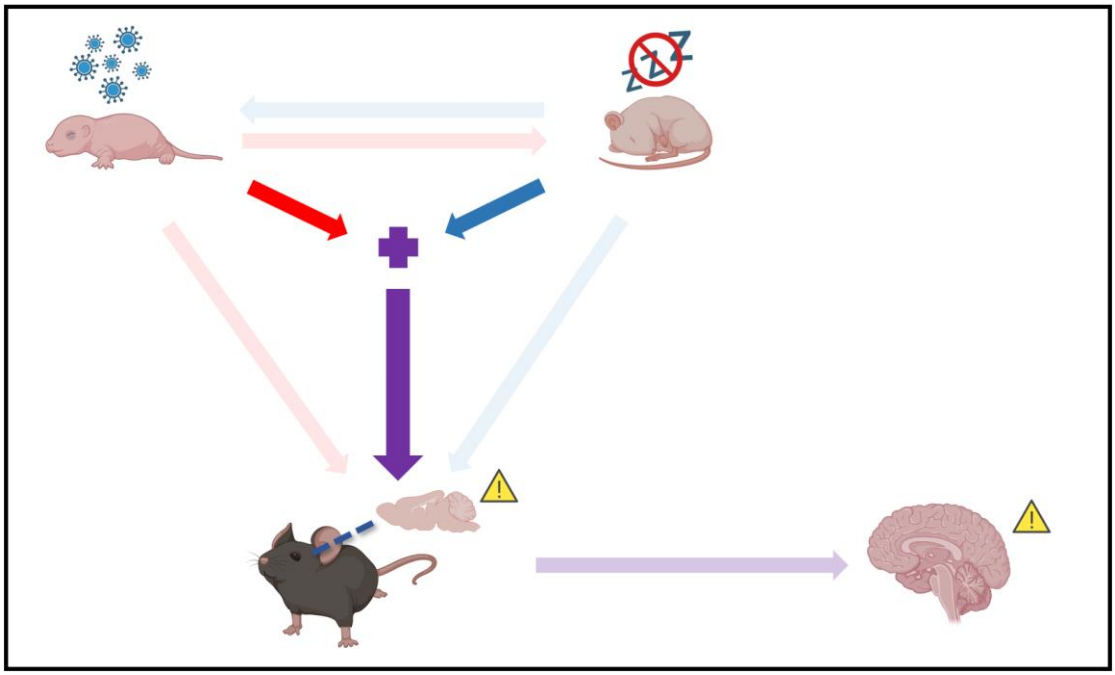


Figure 1 - The study proposal to discover the combinatorial effect of early inflammation and sleep deprivation on neuroimmunological and cognitive functions later in life. The light coloured arrows represent findings from previous research: early inflammation and sleep deprivation affect each other and independently affect cognition later in life. The dark red, blue and purple arrow represent the unanswered research question in this proposal, which will finally (light purple arrow) help to understand human brain development.

4. Quantitative analysis of quiet sleep in moderate to late preterm infants with a normal developmental outcome at 18.

M. A. Ryan[a,b]

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Background Moderate to late preterm (MLP) infants are at risk of adverse outcomes. Brain function can be measured using electroencephalography (EEG). Inter-burst intervals (IBI) are a specific feature of quiet sleep (QS) and a marker of brain maturation.

Aim This study aims to describe IBI features of MLP infants at 36 weeks postmenstrual age (PMA) with a normal developmental outcome at 18 months.

Methods Quantitative analysis of EEG (qEEG) was performed using an IBI detection algorithm adapted for use in the MLP infant group. Five quantitative features of IBI were extracted (maximum IBI length, median IBI length, IBI variability, number of IBIs/minute and percentage of epoch that was IBI) for each infant.

Results There were no significant differences between the algorithm and reviewer estimate of the five summary IBI features (p>0.05 from Wilcoxon signed rank test for all features) which supports strong performance of the algorithm.

The median (IQR) features of IBI features of MLP infant (n=60) were: IBI maximum length 6.89(5.97-7.86) secs, median length 3.00(2.60-3.27) secs, IBI length variability 2.49(2.00-2.90) secs, number of IBIs per minute 5.58(4.81-5.88) and percentage IBI 32.90(24.68-39.02) %. With the exception of IBI median length IBI values decreased with advancing PMA except (p=0.02-0.08). All IBI features were significantly longer/higher for infants nursed in incubators. Infants from multiple pregnancies had longer IBI length maximum (p=0.030), IBI length variability (p=0.043) was independently associated with pregnancy type than infants from singleton pregnancies**.**

Conclusion We have described for the first time, detailed quantitative features of IBIs in QS of the MLP infant with a normal developmental outcome at 18 months PMA. This normative data which can be used in future studies of infants at risk of abnormal development. Automated analysis may be a useful pre-discharge screening tool for all preterm infants.

Table 1 Quantitative analysis of IBI features on EEG in quiet sleep overall and by gestational age group, birth weight, sex, location, mode of feeding and pregnancy type at 36 weeks PMA(n=60)

n=60	IBI length Maximum (secs) Median (IQR)	p-value[1]	IBI length Median(secs) Median (IQR)	p-value[1]	IBI length variability(secs) Median (IQR)	p-value[1]	IBI number/min Median (IQR)	p-value[1]	IBI percent (%) Median (IQR)	p-value[1]
Overall	6.89(5.97-7.86)		3.00(2.60-3.27)		2.49(2.00-2.90)		5.58(4.81-5.88)		32.90(24.68-39.02)	
Birth GA (weeks)		**0.960**		**0.789**		**0.953**		**0.569**		**0.813**
32 (n=11)	6.88(5.68-8.21)		2.98(2.63-3.34)		2.49(1.91-3.07)		5.65(4.90-5.90)		32.95(23.44-39.86)	
33 (n=11)	7.17(6.34-7.86)		3.09(2.76-3.35)		2.61(2.31-2.76)		5.66(4.80-6.25)		37.22(25.55-39.22)	
34 (n=20)	6.84(5.26-7.98)		2.90(2.40-3.27)		2.40(1.81-2.85)		5.46(4.53-5.64)		32.10(22.67-37.38)	
35 (n=9)	6.89(5.67-7.75)		2.64(2.46-3.25)		2.48(1.93-3.02)		5.64(4.79-5.99)		30.95(23.78-39.26)	
36 (n=9)	6.51(6.22-7.95)		3.07(2.82-3.30)		2.31(2.21-2.85)		5.61(4.76-5.71)		30.53(25.71-36.84)	
Birth Weight		**0.317**		**0.336**		**0.545**		**0.226**		**0.232**
<1.5 (n=3)	7.89		3.00		2.93		5.73		30.04	
1.50-1.99(n=25)	7.17(6.09-8.08		3.03(2.64-3.35)		2.53(2.01-3.100		5.65(4.93-6.16)		35.16(29.93-39.46)	
2.00-2.49(n=23)	6.84(5.68-7.74)		3.02(2.54-3.24)		2.58(1.98-2.87)		5.55(4.70-5.70)		32.61(24.31-37.62)	
2.50-2.99(n=7)	6.31(5.65-6.89)		2.73(2.22-3.00)		2.27(1.92-2.50)		4.88(4.08-5.50)		27.10(19.51-30.95)	
>3.00(n=2)	6.81		2.93		32.41		5.20		5.20	
Sex		**0.544**		**0.905**		**0.472**		**0.290**		**0.440**
Male (n=25)	6.84(5.36-7.79)		3.02(2.47-3.33)		2.50(1.85-2.83)		5.43(4.39-5.89)		31.58(21.09-38.50)	
Female (n=35)	6.89(6.03-7.89)		3.00(2.63-3.20)		2.49(2.05-3.02)		5.61(4.90-5.88)		33.36(25.31-39.10)	
Mode of feeding[2]		**0.433**		**0.088**		**0.173**		**0.256**		**0.183**
Oral (n=37)	6.84(5.38-7.71)		2.87(2.43-3.20)		2.49(1.87-2.87)		5.60(4.41-5.78)		32.61(22.54-37.66)	
Mixed(n=22)	6.96(6.00-8.05)		3.05(2.86-3.37)		2.63(2.23-3.05)		5.50(4.90-6.16)		35.49(28.19-39.13)	
Location		**0.024**		**0.014**		**0.014**		**0.048**		**0.026**
Cot (n=45)	6.68(5.68-7.67)		2.87(2.52-3.20)		2.49(1.93-2.74)		5.48(4.54-5.71)		31.58(23.87-38.14)	
Incubator(n=15)	7.73(6.31-8.55)		3.07(3.00-3.69)		2.91(2.31-3.26)		5.88(5.38-6.16)		37.22(29.77-43.75)	
Pregnancy		**0.030**		**0.038**		**0.043**		**0.188**		**0.089**
Singleton (n=30)	6.39(5.67-7.10)		2.82(2.45-3.10)		2.29(1.92-2.64)		5.43(4.55-5.70)		30.28(24.17-35.83)	
Multiple (n=30)	7.54(6.15-8.07)		3.10(2.80-3.37)		2.70(2.24-3.07)		5.64(4.82-5.91)		35.98(27.12-39.28)	

IBI: inter-burst interval, IQR: interquartile range. Max: maximum, GA: gestational age. [1] The p-value calculated from the Kruskall- Wallis test was used for gestational age and weight and a p-value calculated from Mann-Whitney U test was used for sex, location and mode of feeding and pregnancy type. A p-value<0.05 is statistically significant. A mixed mode of feeding included both oral and nasogastric tube feeds. [2] One infant fed exclusively via nasogastric tube and was eliminated from the mode of feeding analysis.

5. Sleep state organisation of moderate to late preterm infants in the neonatal unit.

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b. INFANT Research Centre, University College Cork, Cork, Ireland

Background Sleep supports neurodevelopment and sleep architecture reflects brain maturation. This prospective observational study describes the nocturnal sleep architecture of healthy moderate to late preterm (MLP) infants in the neonatal unit at 36 weeks postmenstrual age (PMA).

Methods MLP infants, in the neonatal unit of a tertiary hospital in Ireland from 2017 to 2018, had overnight conventional electroencephalography (cEEG) with video for a minimum 12 hours at 36 weeks PMA. The total sleep time (TST) including periods of active sleep (AS), quiet sleep (QS), indeterminate sleep (IS), wakefulness and feeding were identified annotated and quantified.

Results 98 infants had cEEG with video monitoring suitable for analysis. The TST in the 12-hour period was median (IQR) 7.09 (IQR 6.61-7.76) hrs 4.58 (3.69-5.09) hours in AS, 2.02 (1.76-2.36) hours in QS and 0.65 (0.48-0.89) hours in IS. The total duration of AS was significantly lower in infants born at lower GA (p= 0.007) whilst the duration of individual QS periods was significantly higher (p=0.001). MLP infants who were exclusively fed orally had a shorter total sleep time (p<0.001) and less AS(p=0.001) compared to infants with a mixed mode of feeding. (Table 1)

Conclusion Overnight cEEG with video at 36 weeks PMA showed sleep state architecture is dependent on birth GA. Active sleep (AS) is the dominant sleep state. Quantitative changes in sleep states occur with advancing gestational age (GA) Infants with a lower birth GA have less AS and more QS which may have implications for later neurodevelopment.

Table 1 Total duration of each sleep state expressed in hours and as a percentage of total sleep time

	TST (hours) median (IQR)	p-value[1]	AS (hours) median (IQR)	p-value[1]	% AS median (IQR)	p-value[1]	QS (hours) median (IQR)	p-value[1]	% QS median (IQR)
Overall	7.09(6.61-7.76)		4.58(3.69-5.09)		**63.07(56.25-67.43)**		2.02(1.76-2.36)		**27.88(24.26-**
Birth Gestational Age group (weeks)		0.143		0.007		0.097		0.825	
32(n=19)	6.96(6.06-7.34)		3.86(3.28-4.38)		56.22(49.43-64.79)		2.07(1.88-2.50)		33.33(26.63-
33(n=12)	7.09(6.84-8.01)		4.76(4.09-5.15)		63.01(58.49-68.29)		2.07(1.70-2.46)		29.14(24.68-
34(n=36)	6.96(6.30-7.84)		4.45(3.45-5.09)		64.11(51.20-68.33)		2.04(1.78-2.23)		27.65(23.39-
35(n=15)	7.50(6.91-7.82)		4.87(4.60-5.08)		64.94(60.49-66.86)		1.98(1.70-2.35)		26.19(22.43-
36(n=16)	7.17(6.83-8.16)		4.95(4.14-5.48)		65.91(57.62-69.35)		1.92(1.43-2.55)		26.15(21.53-
Sex		0.606		0.457		0.2		0.089	
Male (n=52)	7.06(6.59-7.73)		4.59(3.70-5.24)		64.55(55.40-69.52)		1.95(1.71-2.28)		26.55(23.08-
Female(n=46)	7.21(6.70-7.83)		4.40(3.68-5.06)		61.76(56.25-65.73)		2.14(1.88-2.49)		29.59(25.84-
Accommodation		0.271		0.79		0.335		0.073	
Cot(n=80)	7.03(6.52-7.73)		4.49(3.70-5.15)		63.78(56.23-68.22)		1.99(1.71-2.31)		27.88(23.62-
Incubator(n=18)	7.30(6.83-7.83)		4.75(3.60-4.98)		60.98(55.44-65.10)		2.24(1.93-2.51)		27.88(26.18-
Mode of feeding[2]		<0.001		0.001		0.433		0.291	
Oral(n=61)	6.91(6.30-7.35)		4.29(3.45-4.86)		63.25(52.19-68.05)		2.01(1.75-2.33)		27.90(24.62-
Mixed(n=36)	7.57(6.94-8.20)		4.94(4.47-5.32)		63.09(59.31-67.01)		2.04(1.73-2.52)		27.65(22.76-

TST: total sleep time, AS: active sleep, QS; quiet sleep, IS: Indeterminate sleep, IQR: interquartile range. The percentage (%) for each infant is the percentage of time spent in each sleep state.

[1]The Kruskal- Wallis test was used for gestational age and the Mann-Whitney U test was used for sex, accommodation and mode of feeding

[2]One infant fed exclusively via NGT tube and eliminated from the mode of feeding analysis (n=97). p<0.05 is considered statistically significant.

6. Sound(a)sleep – Pilot study investigating the acoustic landscape on NICU and its effect on sleep behaviour in premature neonates.

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2. Department of Engineering, University of Cambridge;
3. Evelyn Perinatal Imaging Centre, Cambridge University Hospitals NHS Foundation Trust;
4. Department of Paediatrics, University of Cambridge

Background Impaired sleep-wake cycling has been shown to affect the functional connectivity of the neonatal brain. Preterm infants display impaired functional brain connectivity and disturbance of sleep-wake cycling may further exacerbate it. We hypothesised that the native acoustic landscape on NICU would alter sleep behaviour in premature neonates and developed a method to measure this effect.

Methods A prospective pilot study of 6 preterm infants on NICU was carried out following informed parental consent. Infants were observed for 3 hours each and their behaviour was recorded using a novel iPad interface recording the timing of each event. This was based on the Behavioural Sleep Stage classification for Preterm Infants. Sound level (frequency range 6.3 Hz – 20 kHz) was recorded by two sound meters in the cot and the environment at a constant distance from the cot. Vital signs were extracted from monitoring devices. Data was analysed on a second-by-second basis using generalised linear modelling for the increased occurrence of gross body movement (GBM) in response to increased sound level of different frequencies.

Results In three infants, the probability of GBM increased significantly with increasing environmental and cot sound. In two infants, one of whom was in a sound-proof incubator, this relationship was only significant for cot sound. One infant, who was ventilated and sedated at the time of observation, did not show any relationship. 5/6 infants showed a steeper relationship with A-weighted sound, assigning greater weight to sound audible to the human ear, as opposed to the flat Z-weighted trace. Furthermore, the proportion of time spent performing GBM seemed to increase with A-weighted peak sound pressure level (ns).

Conclusion This pilot data suggests the NICU acoustic landscape alters the sleep behaviour of preterm neonates, and a larger prospective study is planned to relate sleep behaviour and development of functional connectivity.

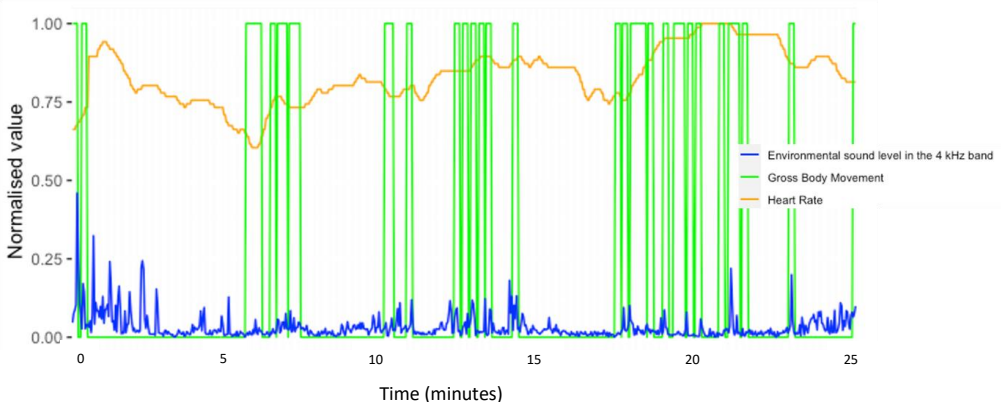

Figure 1 - Example trace showing behavioural correlations with sound. The occurrence of GBM is quantified as either 1 (present) or 0 (absent) with vertical lines representing state change. Heart rate and sound level are plotted as normalised values for ease of presentation.

7. Cortical activity depression and potential sleep-related recovery following hypoxia-ischaemia.

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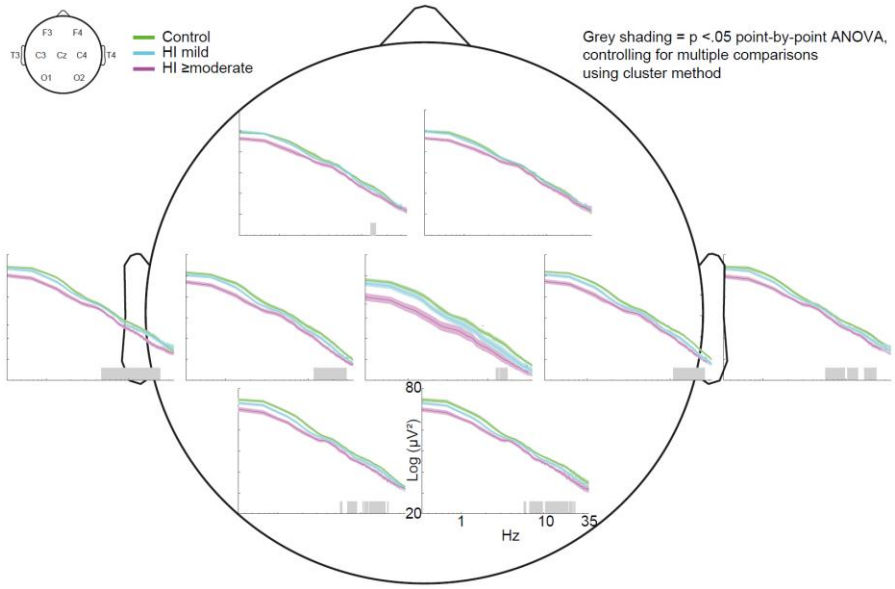
Background In young mammals, experience-dependent synaptic plasticity - including after an insult - requires appropriate cortical activity and sleep. In human infants recovering after a hypoxic-ischemic insult, excessively high amplitude cortical activity and abnormal sleep are independent predictors of adverse neurodevelopmental outcome, but it is unknown how they interact.

Methods Infants who underwent EEG following perinatal hypoxia-ischemia (median blood pH 6.91 and Apgar 3 (clinical condition at birth, scale 0-10)) were divided into i) ≥moderate (n = 15) and ii) mild clinical encephalopathy (n = 14). To examine how cortical activity was acutely affected, we compared the first 11 minutes of artefact-free EEG during the 14 hours post birth, excluding segments within 6 hours after anti-epileptic drug administration or during seizures, to that of EEG mean 20 hours post birth in a control group matched by age, intensive care nursing, and recording system (n = 8, median blood pH 7.28 and Apgar 9).

To characterise the dynamics of recovery, we also analysed the occurrence and amplitude of cortical activity bursts during the full EEG length, stratified by sleep state (in the 'mild' group so far, analysis of the full cohort in progress). Statistical significance was set at $p<0.05$.

Results and conclusion Hypoxia-ischemia acutely depressed cortical activity in a severity-dependent manner (Figure). Burst rate was lower in active than quiet sleep, while average burst amplitude did not differ. There was no consistent direction of change during the EEG for burst rate, but average burst amplitude declined across all channels, and there was a trend for the slope of this change being more negative for active than quiet sleep.

In sum, hypoxia-ischemia acutely depresses cortical activity, even when the brain insult is little behaviourally expressed. Preliminary results also indicate that normalisation of cortical activity may interact with sleep.



8. Neonatal sleep physiology and executive function in preterm infants.

Anneleen Dereymaeker, Tim Hermans, Bieke Bollen, Katrien Jansen, Els Ortibus, Maarten De Vos, Gunnar Naulaers

Department of Neonatology & ESAT STADIUS
University Hospitals Leuven & KULEUVEN

Objective To test the hypothesis that neonatal sleep is related to 2 years neurodevelopmental outcome and executive function (EF) assessment.

Methods Preterm neonates (n= 108, mean GA 30w, without severe IVH or PVL) underwent EEG-polysomnography before discharge. The distribution of sleep states (LVI, ASI, QS-HVS, QS-TA), percentage of total sleep and unexpected transitions were quantified with an automated sleep staging algorithm.

We examined EF tests and BSID-III at 24 months, in relation to neonatal sleep parameters, adjusting for confounders (GA, PMA, gender, birthweight), factors related to outcome (IVH grade I-II, postnatal infection, total days of ventilation, skin breaking procedures, maternal education) and total amount of Kangaroo Care (KC) in a series of hierarchical multiple regression models.

Results Eighty-four children returned for assessments. The median scores for BSID-III cognitive (105, IQR 100-110), language (97, IQR 89-106) and motor outcome (107, IQR 100-115) were within the normal range. For EF composite score (n= 76), we found a median of 0.13 (IQR -0.38-0.43), a more negative score reflects worse EF. EF scores were positively associated with the percentage of sleep at discharge (stB= 0.3, p 0.002) adjusted for GA, PMA, sex and total amount of KC (adj R^2: 0.39, p<0.001) and mom education. None of the other medical factors improved the model. Motor scores were positively associated with the percentage of total sleep and QS-HVS (stB= 0.2, p=0.04, stB=0.3, p=0.02), adjusted for mom education and PMA (adj R^2: 0.26, p<0.001). Language scores were negatively associated with a higher number of unexpected transitions during sleep (stB= -0.49, p <0.001) and positively with higher amount of KC (stB= 0.32, p=0.007, adj R^2: 0.28, p<0.001). Cognitive scores were positively correlated with the amount of KC, no significant relationship with sleep physiology was evident.

Conclusions This prospective study suggests that inefficient neonatal sleep, e.g. lower percentage of sleep, unexpected transitions, and the percentage of HVS is associated with respectively lower early EF scores, language and motor development. This may represent signs of maladaptive brain maturation even in a relatively stable preterm cohort.

9. Sleep trajectories and 24-month neurobehavioral outcomes.

Abstract for Neonatal Sleep Talks – Claire College – Cambridge, UK

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Growing evidence points to a role of sleep and circadian rhythmicity in modulating neurobehavioral development. The overall aim of this study was to examine longitudinal trajectories of objectively-measured sleep duration patterns in relation to neurobehavioral functioning, specifically executive function, across the first 24 months of life. Participants were 325 infants of the Rise & SHINE (Sleep Health in Infancy & Early Childhood study) with measurements from ankle actigraphy of sleep duration at age 1, 6, 12 and 24 months, and neurobehavior, assessed by the Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P) at age 24 months. We applied latent class mixture modeling to three distinct sleep parameters, namely night sleep duration, longest nighttime sleep and daytime sleep duration. The aim of this approach is to characterize heterogeneity in sleep development over time via distinct "classes", each with a distinct sleep trajectory shape. Each sleep parameter had either two or three classes with a total of eight sleep trajectories. We then used multivariate linear models to examine associations between sleep trajectory groups and four main BRIEF-P composite outcomes. In multivariable models, infants belonging to a **sl**ow rising, **s**hort **l**ongest nighttime **s**leep trajectory class (SOSLS) were more likely to have impaired executive function abilities, e.g., worse scores for inhibitory self-control (2.97 points, 95% CI: 0.07, 5.86), flexibility (2.43 points, 95% CI 0.33, 4.53), and emergent metacognition (3.59, 95% CI: 0.50, 6.67) compared to a slow rising, long longest nighttime sleep trajectory. Our results suggest a critical role of sleep consolidation in children's later executive functions. Here, it should be noted that the ability of infants to sleep for longer continuous sleep periods at night is usually considered as sleep consolidation. Future research should investigate these links with experimental designs and interventional trials. '

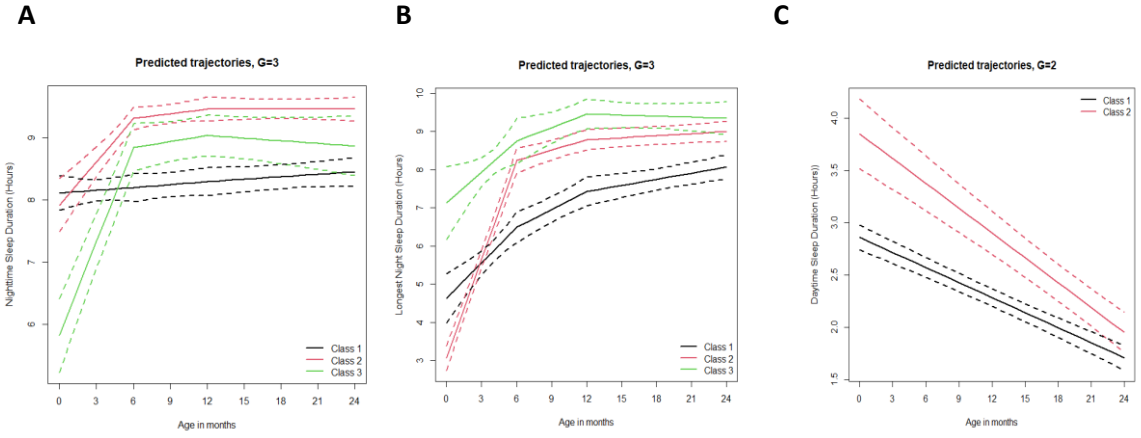

Figure 1. Latent classes of night sleep duration trajectory (A), longest nighttime sleep trajectory (B) and day time sleep trajectory (C)

10. The effect of moderate to late preterm birth on EEG sleep markers of development in early infancy.

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Introduction Moderate-to-late preterm (MLP) infants show higher morbidity and mortality than term infants, but their developmental trajectory has received far less attention compared to their more preterm counterparts. In this study, we compared multiple sleep EEG biomarkers of brain maturation between MLP and term-born infants at 4 months corrected age.

Methods MLP and term infants were recruited at birth at Cork University Maternity Hospital and daytime sleep EEGs were recorded at 4 months of age. Sleep was staged according to AASM criteria, and the analyses were based on the first sleep cycle. Groups were compared for sleep stages duration, latency to sleep and REM. Sleep spindles were identified manually, and groups were compared for spindle density, number, symmetry, synchrony, spectral power, frequency, and duration. Groups were also compared for relative and absolute spectral power and connectivity as measured by inter- and intra-hemispheric coherence.

Results Fifty-nine MLP (30/59 females) born at a mean (SD) age of 34.5 (1.3) and 96 term-born infants (40/96 females) born at 39.8 (1.2) weeks were included in the study.

MLPs had fewer sleep spindles (MLP: median (IQR) 212.00 (137.50-280.00); term-born: 253.00 (213.00-293.00), p=0.029), and a shorter N2 sleep stage (MLP: 2.75 (1.88-4.63); term-born: 4.50(2.50 to 6.50) minutes, p<0.001]. MLPs also had higher power in delta 1 frequency [MLP: 702.49 (557.46-840.67)μV^2; term-born: 593.34 (449.21-749.36)μV^2, p=0.011], and delta 2 [MLP: 245.31 (194.17-327.77)μV^2, term-born: 215.32(164.78-283.39)μV^2, p=0.028] and lower relative gamma power during NREM [MLP: 0.0016 (0.0013-0.0019)%; term-born: 0.0018 (0.0015-0.0022)%, p=0.034]. Differences in connectivity were also seen, with a general increase of frontal and lower interhemispherical parieto-occipital coherence in the MLP group.

Conclusion Moderate to late preterm infants show multiple EEG sleep biomarker alterations in comparison to term born infants, reflecting changes in brain organisation and function.

11. Effect of auditory stimulation on sleep.

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Undisturbed sleep is important, especially during development, when sleep is necessary for healthy brain maturation. However, during sleep we are still receiving and processing sensory input from the environment, awaking if necessary. The brain needs to achieve the right balance between processing sufficient input and protecting underlying processes from sensory disturbance. Sensory processing atypicalities are one of the core symptoms of autism. The ability the gate sensory information during wakefulness is reduced in infants at elevated likelihood for autism. With this study we want to explore whether and how sensory stimulation affects sleep in infancy. Additionally, we ask whether increased sensory sensitivity is associated with worse sleep (both in terms of behavioral and EEG markers of sleep) and/or whether sensory sensitivity affects sleep particularly when there is increased external stimulation. We are particularly interested in sleep spindles and slow waves, as both are thought to serve as protective factors from external disturbance during sleep.

To do so, EEG was measured in 8-11 month-olds who were invited to take a nap in the lab twice, once with and once without auditory stimulation. In total, 44 infants visited the lab, of which 40 infants managed to fall asleep. Statistical analyses were performed using Mixed Effects Models.

The results so far show that auditory stimulation significantly decreases nap duration (Est = 11.56, p = .041), but does not significantly impact sleep stage distribution (Est = . 01, p= 0.66) or sleep spindle density (Est =-.28, p = .10). Sensory sensitivity does not significantly influence nap duration, nor does it affect nap duration from baseline to stimulation (Sensitivity: Est =. 996, p = .89; SensitivityxCondition: Est = 7.29, p= 0.589). In further analysis will look at other features of sleep spindles and slow wave activity.

12. Sleep in ex-preterm infants.

Dr Jayne Spiller

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This talk describes the extant literature on the sleep architecture, sleep duration, sleep quality in children born preterm following discharge from the NICU relative to children born at term. The role of parent-reported night waking and snoring in inattention, hyperactivity and emotional symptoms at age 11 in children born <27 weeks of gestation will be discussed using data from the EPICure2 cohort. Children born <27 weeks of gestation (n=165) had greater habitual snoring (adjusted odds ratio 6.8; 95% confidence interval 2.3, 20.3), less frequently fell asleep within 20 minutes (Cohen's *d* 0.33), higher night wakings (*d* 0.44) and daytime sleepiness scores (*d* 0.40) than term-born children (n=121); there was no between-group difference in sleep duration scores. It was found that an additional 5-13% of the variance in behavioural and emotional problems was explained by night waking in children without severe disabilities. Less variance in behavioural symptoms was explained by habitual snoring (1-5%). The talk will conclude with reflections on research questions on sleep in childhood following preterm birth which remain outstanding.

13. A robust pipeline for reliable automated sleep staging from neonatal EEG.

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Background: Automated sleep analysis is a promising application of automated neonatal EEG processing. Although algorithms for automated sleep classification from neonatal EEG have already been proposed, they require further enhancements in terms of robustness and reliability to enable fully automated use in clinical practice. We aim to develop a robust algorithmic pipeline for reliable automated neonatal sleep analysis.

Methods: We propose a multi-step algorithm that produces a hypnogram from EEG data. First, artefacts are automatically detected, and the EEG data is cleaned where possible. Then, a state-of-the-art sleep classifier is applied to the cleaned EEG data, which produces a sleep stage prediction for each 30 seconds of data. Subsequently, these predicted sleep stage probabilities are post-processed by a novel hidden Markov model (HMM), improving the temporal sequence of predicted sleep stages. Then, the reliability of each segment's prediction is determined by looking at the presence of artefacts in the EEG segment, the novelty of the EEG segment (using an isolation forest), and the class-probabilities predicted by the sleep classifier. Finally, everything is combined with a set of heuristic rules that constructs the hypnogram.

Results: The algorithm processes a recording of 17 hours in approximately 2m14s on a regular laptop. The data cleaning and HMM post-processing steps improve the classification accuracy, whereas the reliability analysis removes unreliable predictions, such that the persisting predictions can be trusted with higher confidence. Visual analysis confirms that the hypnograms obtained with the novel pipeline are more reliable than the hypnograms obtained without the proposed additional steps.

Conclusion: We proposed a robust pipeline for fully automated sleep staging. Novel pre- and postprocessing steps improved the robustness and reliability of the resulting hypnogram. Nevertheless, the proposed method takes implementation of automated sleep detection methods one step closer towards clinical practice.

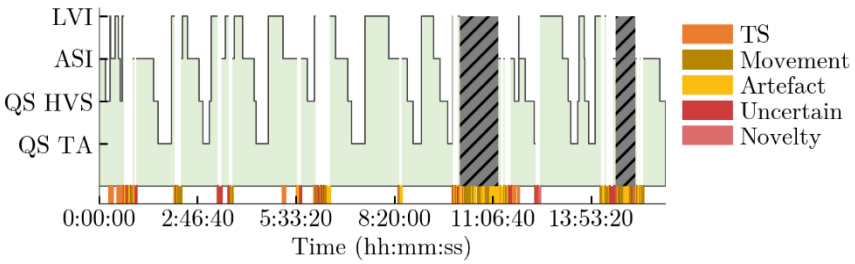

Figure 1 Example of an automatically constructed hypnogram.

14. Automatic sleep assessment from eye cues in videos of strongly occluded preterm infants.

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Monitoring the sleep patterns of preterm infants is crucial for understanding their development and ensuring appropriate care. In this study, we explore the potential of leveraging eye cues and convolutional neural networks (CNNs) to automate sleep assessment using low-end RGB cameras. Specifically, we focus on consistently extracting eye regions from videos of occluded preterm infants and training CNNs to identify different eye states.

We constructed labeled datasets using videos recorded at the neonatal intensive care unit of the University Medical Center Utrecht. Through our experiments, we demonstrate that CNNs can be effectively trained on these eye regions to accurately classify eye states. Our binary CNN achieved a remarkable test accuracy of 96.3% in distinguishing between opened and closed eyes. Additionally, by employing a sliding window and a binary 3D CNN, we successfully identified rapid eye movements (REMs) with a test accuracy of up to 74.5%.

To translate these eye state predictions into sleep stages, we aggregated eye states on a per-minute basis and employed a random forest classifier. Remarkably, we achieved an accuracy of 92.2% in discriminating between wake, active sleep, and quiet sleep stages solely based on eye cues. However, certain challenges and limitations persist, which we thoroughly discuss in this study. Furthermore, we propose potential solutions to enhance the performance of our automated sleep assessment system.

The findings of this study underscore the potential of using eye cues and CNNs to automate sleep assessment in preterm infants. By eliminating the need for manual assessment, this approach can provide valuable insights into the sleep patterns of preterm infants, enabling timely interventions and optimized care. Future research should focus on addressing the remaining challenges and refining the proposed framework to further improve its accuracy and applicability.

15. Influences of neonatal medical factors on automated derived sleep-wake architecture in preterm infants.

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Background: Integration of sleep assessment in the NICU is gaining attention. Sleep curtailment by different neonatal perturbations such as noxious stimulation, cardiorespiratory instability, or exposure to the extra-uterine environment, may be detrimental for further brain maturation and plasticity. The aim of this study is to identify risk factors for impaired sleep organization and to distinguish protective measures in preterm babies by automated reporting of neonatal sleep parameters.

Methods: In a prospective cohort study, N=108 preterm infants (median GA 30 weeks), underwent overnight multichannel-polysomnography before discharge home. The sleep staging algorithm runs the EEG in five sequential steps: artefact detection, data cleaning, sleep state classification, reliability analysis and hypnogram construction. The algorithm identifies the segments (30s) corresponding to sleep and classifies each of these segments as one of four sleep states: AS-LVI, AS-ASI, QS-HVS or QS-TA. Kaplan-Meier survival curves of automated derived sleep bout durations are constructed. Multiple variable regression is used to assess the causal effect of clinical risk factors (total days of ventilation, skin breaking procedures, intraventricular hemorrhage, and kangaroo care, adjusting for confounding factors (GA, PMA, gender) on neonatal sleep behavior.

Results: A significant effect of PMA on sleep bout duration is found for AS, QS, QS-HVS and QS-TA. The duration of QS-TA bouts decreases, while the duration of HVS bouts increases with PMA. More SBP in early life are negatively correlated with the total percentage of sleep. Preterm neonates exposed to a higher number of SBP have significantly longer QS-TA bouts, corrected for PMA, the more immature and discontinuous QS state at term equivalent age and less AS. Preterm neonates with a higher total amount of KC during NICU stay have a higher percentage of mature QS-HVS. The total days of ventilation negatively influence the amount of AS-ASI.

Conclusion: Normative modelling approaches can characterize typical population variation in a data-driven fashion. By mapping datasets from different neonatal cohorts, we can detect perinatal factors that have the highest impact on neonatal sleep architecture, which can support interventions and serve as tool for post-outcome measures.

16. Napping pants (NAPPA): An open wearable solution for monitoring infant's sleeping rhythms, respiration and sleeping position.

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Objective: To develop a non-invasive and practical method for a long-term tracking of infant's sleeping behaviour using wearable technology.

Methods: An infant smart wearable, napping pants (NAPPA), was constructed by combining diaper cover and a movement sensor that can record internally or to a mobile phone. The recordings were used for training a sleep state classifier using hypnogram from concomitant polysomnography (PSG) recordings as the benchmark. A cohort of N=33 infants aged 1-18months were co-recorded with NAPPA and PSG, and a feature-based sleep classifier was trained for three vigilance states: wake, N1/REM, and N2/N3. Finally, computation of the signal features was embedded into the sensor microcircuitry to allow a stand-alone recording of infant sleep for extended periods of time.

Results: A combination of six computational features estimated from the gyroscope and accelerometer signals was sufficient to train a sleep state classifier with an overall classification accuracy of 70% (range 64-74%). Sleep state trends (SST) created from the classifier outputs showed sleep depth fluctuations that were highly comparable to those observed in the hypnograms in all infants. Standalone recording without mobile phones by embedding feature computation directly into the wearable sensor yielded comparable SST outputs.

Conclusions: It is practical and feasible to track infant's sleeping behaviour using a wearable solution that measures a combination of respiration, body orientation and activity. While providing assessment of sleep rhythms, the solution will also allow accurate assessment individual features (body position, respiration rate, activity level) each of which have an independent clinical information value.

Significance: An open-source wearable solution of this kind allows out-of-hospital, large scale, quantitative assessment of infant's sleeping and related behaviour.

Keywords: wearable, infant, sleep, non-invasive monitoring, human activity recognition, respiration

17. Binarized approximate entropy for classification of term neonates with seizure.

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Background: Machine-learning support tool could help in identification of neonates that have seizures. Approximate entropy (ApEn) quantifies irregularities of time series, and it is highlighted as good choice of features for predicting epileptic seizures based on scalp EEG [2]. ApEn requires the stationarity condition to be fulfilled, it is computationally demanding, so it is applied to short-term EEG. Binarized approximate entropy (*BinEn*) [1], is derivate from ApEn, and it is performed on differentially coded time series, which significantly speeds up the estimation of entropy value and makes the time series more stationary. *BinEn* turned out to be a useful feature in the prediction of epileptic seizures in pediatric subjects [3].

Objective: Investigate ability of *BinEn* to make distinction between term neonates that have seizures and seizures free group.

Methods: The quadratic discriminant (QD) classifier is applied to test the ability of *BinEn* features in classification neonates with seizures from seizures free subjects. We use open datasets available in [4], with median recording of 74 minutes. For testing and training QD classifier, we select only EEGs that have at least 90% consensus of three medical experts that denote each second of recorded EEG. Total number of EEG data is 55. *BinEn* is estimated one channels of EEG, without dividing data on short-term segments.

Results: The QD was able to achieve an average sensitivity 87.5%, specificity 84.2 %, balanced accuracy 86%, and false positive rate 12.5% in classification of term neonates with seizures.

Conclusions: The results obtained reveals potential of application *BinEn* in classification seizures and nonseizers subject. The main limitation of the study is the limited data set. To confirm practical application in neonatal intensive care it is necessary to validate proposed the method on a larger data set.

Acknowledge: The work is within the framework of CA20124 - “Maximising the impact of multidisciplinary research in early diagnosis of neonatal brain injury“.

References:

[1] T. Skoric, O. Mohamoud, B. Milovanovic, N. , Japundzic-Zigon, D. Bajic, “Binarized cross-approximate entropy in crowdsensing environment,” Comput Biol Med, vol. 80, pp. 137-147, Jan. 2017.

[2] S. M. Usman, S. Khalid, R. Akhtar, Z. Bortolotto, Z. Bashir, H. Qiu, “Using scalp EEG and intracranial EEG signals for predicting epileptic seizures: Review of available methodologies,” Seizure, vol. 71, pp. 258-269, 2019.

[3] T. Skoric and D. Bajic, “Epileptic seizures prediction of pediatric subjects in health-care pervasive environments”, ICC 2023, pp. 1716-1720 (in press)

[4] Stevenson, N., Tapani, K., Lauronen, L. *et al.* A dataset of neonatal EEG recordings with seizure annotations. *Sci Data* **6**, 190039 (2019). https://doi.org/10.1038/sdata.2019.39

18. Levetiracetam monotherapy for the treatment in neonates with hypoxic-ischemic encephalopathy.

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Introduction: Neonatal seizures are one of the most commonly neurological emergencies and about two-thirds of cases of neonatal seizures are due to Hypoxic ischemic encephalopathy (HIE). Phenobarbital is the commonly used anticonvulsant for neonatal seizures. However, long-term use of it is associated with impaired neurodevelopmental outcome. Levetiracetam is a new generation anti-epileptic drug and has been widely used off-label in the management of neonatal seizures. The aim of this study was to determine the efficacy of levetiracetam as monotherapy in treatment of neonatal seizures due to hypoxic ischemic encephalopathy.

Methods: This retrospective cohort study was conducted consisting of 109 newborns with HIE.

Results: Of 109 patients, 68.8% (n=75) were diagnosed as stage 1, 17.4% (n=19) stage 2, and 13.8% (n=15) stage 3 HIE. Anti-seizure treatment was started in a total of 42 patients (38.5%). Of the 42 patients in whom anti-seizure treatment was initiated, 62% (n=26) received LEV monotherapy and 24% (n=10) polytherapy. The efficacy of levetiracetam monotherapy was found to be significantly higher in patients with stage 1 and 2 HIE than in patients with stage 3 HIE (p=0.04). It was found to be significantly lower in the LEV-failure group in terms of Apgar scores (p=0.02; 0.07). Clinical seizure and abnormal brain MRI findings were higher in the LEV-failure group (p=0.01). Levetiracetam-monotherapy was found to be more effective in patients receiving hypothermia treatment (p=0.001).

Conclusion: According to our results, levetiracetam is an effective, well tolerated agent for the treatment of newborns seizure with stage 1-2 HIE, with normal brain MRI and in patients receiving hypothermia treatment.

19. The story about a sleepless newborn.

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Introduction Angelman Syndrome (AS) occurs with frequency from 1:12,000 to 1:30,000 live births and is characterized by developmental delay, hyperactivity, speech impairment with the need for using augmentative and alternative communication, gait ataxia and happy appearance. Up to 80 % people with AS may experience sleep disturbances. Making diagnosis is difficult as phenotype features are more visible when the baby is 1 - 2 years old and developmental delays are present. AS genetical diagnostics need many tests due to complexity of genetics mechanisms causing AS. Early diagnosis is crucial for implementing interventions and treatment suited for AS. For lack of standard newborn screening tests, screening sleep quality and sleep patterns in infants could be taken under consideration.

Method Case presents a 22 days old newborn with hiperactivity, hiperarousal, abnormal sleep pattern manifested as inability to fall asleep, feeding difficulties, bursting with laugher and chaotic type in Prechtl General Movement Assessment. Typically sleep takes from 11 to 19 hours in a 24-hour day at the beginning of infancy. Lack of sleep affects not only a baby but family as a whole system as well.

Results Presented patient had 1 - 2 episodes of sleep per day, 30 minutes each. Performed EEG did not register sleep pattern. Onset of drug resistant epilepsy occured in age of 4 months - different treatment as polytherapy of anti epileptic drugs, MCT oil, melatonin or ketogenic diet have failed. Currently the patient is given clobazam, levetiracetam, valproic acid and still experiences epilepsy. Multiple EEG was performed since the diagnosis was made - none recorded sleep pattern. Patient now is 3 1/2 years old and has inharmonious, delayed development even though he is taken care by early intervention specialist since the 2nd month of life. He is able to sit, stand up in verticalizer, turn over on both ways and grab small objects. He in nonverbal and uses alternative sign communication with a few words.

Conclusions Sleep disturbances can be present in many genetic diseases but also developmental delays can precipitate sleep problems. As lack of sufficient sleep can impaire cognitive functions, memory and learning potential a need for screening sleep quality in newborn and infants is crucial.

20. Towards a stratified approach to the diagnosis of neonatal seizures: combining electroencephalography (EEG), magnetic resonance imaging (MRI) and rapid whole genomic sequencing (WGS).

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Background & Aims Neonatal seizures are difficult to identify and pose diagnostic and management challenges. The aim was to see how the combination of a short duration EEG, rapid WGS and MRI influenced management.

Methods A single centre, retrospective review was undertaken of infants aged 32 - 44 weeks corrected gestation admitted to a tertiary level neonatal unit between 2016 and 2021 with suspected clinical seizures. Only infants who had standard short duration EEG (1 hour), MRI and WGS were included in further analysis.

Results Of 196 charts screened (Figure 1) 45 patients were stratified into 5 groups: suspected HIE (30/45); seizures of uncertain aetiology (7/45); perinatal stroke (1/45); infection (4/45); and congenital brain anomaly (3/45).

6/18 infants with suspected HIE demonstrated seizures on EEG, of which 4/6 had electrographic only seizures. MRI findings were confirmatory of HIE (14/30); normal (10/30), atypical for HIE (2/30) and haemorrhage (4/30).

In the group with seizures of uncertain aetiology (7/52), WGS identified genetic epilepsy (n=3), and metabolic diagnosis (n=1); EEG confirmed myoclonus (n=1); MRI identified positive findings in the remaining 2.

In the infant with perinatal stroke EEG was suggestive of a diagnosis. EEG identified seizures in 1/4 infants with infection and excluded seizures in all the infants with congenital brain anomaly.

Conclusions In neonates with clinically suspected seizures, short duration EEG has a low diagnostic pick-up rate; continuous EEG is likely to improve diagnostic accuracy. Rapid WGS and MRI can help inform the diagnosis and subsequent management, especially when aetiology is unclear.