Project Details	
Project Code	MRCNMH25Ex Poorun
Title	Mapping Preterm Sleep Microstructure and EEG Biomarkers for Early Neurodevelopmental Risk Assessment
Research Theme	Neuroscience & Mental Health
Summary	Sleep is crucial for early brain development, yet preterm infants often have disrupted sleep patterns that may impact their long-term outcomes. This project will use advanced EEG analysis to map the development of sleep microstructure in preterm babies and relate this to preschool neurodevelopmental milestones. By identifying sleep EEG biomarkers of brain vulnerability, we aim to enable earlier detection of infants at risk, informing personalised care strategies to protect and nurture the preterm brain. The project combines advanced signal processing, longitudinal clinical assessments, and a multidisciplinary perspective to shed new light on the complex interplay between sleep and neurodevelopment.
Description	Background: Preterm birth affects 10% of live births globally, with survivors at increased risk of neurodevelopmental impairments [1]. This project will focus on moderate to late preterm infants, born between 32 and 36 weeks gestation, who compromise about 84% of all preterm births [2]. Despite being considered lower risk than very preterm infants, moderate to late preterm infants are known to have poorer neurodevelopmental outcomes compared to term-born peers. These infants face increased risks of cognitive deficits, language delays, attention problems, and behavioural issues [3,4]. For instance, they have a 36% higher risk of developmental delay or disability at age 2 compared to term-born infants [5]. Sleep is critical for early brain development, but preterm infants have significantly disrupted sleep patterns compared to term-born infants [6]. These abnormalities persist across the neonatal period and may contribute to adverse neurodevelopmental outcomes, possibly by impairing brain connectivity during critical windows [7,8]. However, the specific mechanisms linking preterm sleep disruption to impaired outcomes remain poorly understood. Traditional sleep analysis methods lack the resolution to capture prognostically relevant features. Recent advances in EEG signal processing and machine learning enable automated, high-resolution analysis of sleep microstructure, offering new possibilities to identify early biomarkers of neurodevelopmental risk [9,10]. Key Research Question: Can quantitative metrics of sleep microstructure in the neonatal period, derived through advanced EEG signal analysis, provide novel prognostic information about neurodevelopmental risk in moderate to late preterm infants (32 to 36 weeks gestation)? Is altered sleep organisation associated with impaired functional connectivity development? Specific Objectives: 1. Characterise the longitudinal development of sleep microstructure in preterm infants from birth to term-equivalent age using sleep EEG and quantitative signal analysis. This will involve serial

	EEG recordings, sleep state classification, and extraction of microstructural features [11]. 2. Evaluate the prognostic utility of neonatal sleep EEG metrics for predicting preschool neurodevelopmental outcomes across cognitive, language, motor and behavioural domains. Advanced statistical and machine learning techniques will be used to develop predictive models and assess their added value over clinical factors alone [12,13]. 3. Explore relationships between sleep microstructure and functional brain connectivity development in preterm infants using advanced EEG connectivity analysis. The project will assess whether there are critical periods when sleep disruption maximally impacts connectivity, and if altered connectivity mediates sleep-related neurodevelopmental impairments [14,15]. Areas for Student Ownership: • Selection and optimisation of EEG processing and machine learning techniques • Exploration of novel EEG biomarkers of neurodevelopmental risk • Development of hypotheses and analytic strategies for probing sleep-connectivity-outcome relationships • Formulation of recommendations for clinical translation of findings into care pathways References: [1] Chawanpaiboon, S., et al. (2019). Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. The Lancet Global Health, 7(1), e37-e46. [2] Shapiro-Mendoza, C. K., & Lackritz, E. M. (2012). Epidemiology of late and moderate preterm birth. Seminars in Fetal and Neonatal Medicine, 17(3), 120-125. [3] Cheong, J. L., et al. (2017). Association between moderate and late preterm birth and neurodevelopment and social-emotional development at age 2 years. JAMA Pediatrics, 171(4), e164805. [4] Vohr, B. (2013). Long-term outcomes of moderately preterm, late preterm, and early term infants. Clinics in Perinatology, 40(4), 739-751. [5] Woythaler, M. A., McCormick, M. C., & Smith, V. C. (2011). Late preterm infants have worse 24-month neurodevelopmental outcomes than term infants. Pediatrics, 127(3), e622-e629. [6] Dereymaeker, A., et al. (2017). Review of sleep-EEG in preterm and term neonates. Early Human Development, 113, 87-103. [7] Graven, S. N., & Browne, J. V. (2008). Sleep and brain development: the critical role of sleep in fetal and early neonatal brain development. Newborn and Infant Nursing Reviews, 8(4), 173-179. [8] Holditch-Davis, D., et al. (2004). Sleep and developmental outcomes in infants born preterm. Infant Behavior and Development, 27(4), 428-445. [9] O'Toole, J. M., et al. (2016). Estimating functional brain maturity in very and extremely preterm neonates using automated analysis of the electroencephalogram. Clinical Neurophysiology, 127(8), 2910-2918. [10] Koolen, N., et al. (2017). Automated classification of neonatal sleep states using EEG. Clinical Neurophysiology, 128(6), 1100-1108.

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