Project Details	
Project Code	MRC23NMHBr Chakkarapani
Title	Early predictors of cognition in children cooled for neonatal hypoxic-ischaemic encephalopathy
Research Theme	Neuroscience and Mental Health
Summary	Cooling infants after birth asphyxia reduces death and cerebral palsy however around 1/3 of cooled infants have cognitive impairment at school-age. Early markers of later cognitive performance are needed for targeted early interventions. This study will determine relations between early movement and later cognition and examine the association of serial EEG with early movement and early social cognitive ability in a prospective cohort of cooled infants.
Description	Each year in the UK 2-3/1000 newborn babies born at term (> 36 weeks gestation) undergo cooling therapy for Hypoxic Ischaemic Encephalopathy, (HIE) (brain damage due to birth asphyxia) to reduce disability.(1,2) Of the survivors 18-20% will develop cerebral palsy (CP)(3) and over 1/3 will have cognitive impairment at school-age.(4) Cognitive deficits affect educational attainment and future employability, impacting personal and national economy.(5) Early identification of risk of cognitive deficits and targeted early intervention(6) could improve cognitive outcomes and later educational performance. Whilst the risk of CP in children cooled for HIE can be reliably predicted using General Movement Assessment (GMA) at 3 months(m)(7), there are currently no reliable early predictors of future cognitive performance. In preterm infants (born <37w gestation), GMA is associated with intelligence at school age(8) however its ability to predict cognitive performance in children cooled for HIE is unclear. We have shown that impaired cognition is associated with abnormal brain connectivity at school-age in children who were cooled for HIE.(9) Some of these children had mild brain injury on MRI performed in the neonatal period. It is unclear whether these brain injuries will affect the evolution of brain connectivity during infancy impacting the cognitive development at 2 years(y) of age. Research questions: Are GMA and brain connectivity during infancy associated with cognition in children cooled for HIE? How does residual brain injury following cooling therapy affect the evolution of brain connectivity during infancy? Specific objectives: In children cooled for HIE, to examine -whether GMA at 1w or 3m of age predict cognition at 18-24m and 6-8y of age -the trajectory of brain connectivity using EEG at 3-4, 6-8 and 12m in infants cooled for HIE -the association between brain connectivity during infancy and cognitive scores at 24m Methodology: This proposal includes data analysis on a retrospective cohort and a prospective observational study. We have routinely collected GMA video recordings at 3m of age and cognitive assessments at 2y (n=250) and at 6-8y (n=50) in children cooled for HIE. After obtaining ethics approval, the student will be trained in quantifying GMA and examine the association between the GMA at 3m and later cognition. In a prospective cohort of infants cooled for HIE (n=30) recruited from neonatal follow up clinics at University Hospital Bristol NHS Trust, Cardiff& Vale NHS Trust and across Wales collaborating in early intervention service (Cerebral Palsy Cymru), the student will be supported to develop skills in acquiring EEG, quantifying early infant

	movement and in developing commonly used functional social cognitive tasks during EEG recording at 3-4; 6-8 and 12m of age. Parents from the prospective cohort will complete a validated cognition questionnaire (PARCA-R) at 24m of age. Student will be trained to apply and interpret EEG data in infants and to develop an age-appropriate social communication task. Student will gain experience in recruiting families to the study, handling infants within a neuroimaging context, interacting with families and conducting statistical analyses. Successful students will be able to contribute to the scope, design and development of the social cognition task, take ownership of analyses of brain connectivity and develop their own research direction. References: 1)Gale C, et al Arch Dis Child Fetal Neonatal Ed 2018 2)NICEIPG347, 2010 3)Azzopardi D, et al New England Journal of Medicine 2014 4)Lee-Kelland R et al Arch Dis Child Fetal Neonatal Ed, 2020 5)Trickett J et al Child Neuropsychol 2022 6)Hutchon B et al Dev Med Child Neurol 2019 7)Robinson R et al Early Hum Dev 2021 8)Bruggink JL et al Pediatrics 2010 9)Spencer APC et al Neuroimage Clin. 2021
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