The Neonatal Society

Autumn Meeting

Royal Society of Medicine, 1 Wimpole Street, London, W1G 0AE

5th November 2020

Autumn Meeting, 5th November 2020

Meeting Virtual Link: To be emailed to delegates on 3 November 2020

Session 1: Chair – Professor Andy Ewer. Moderator - Dr Ela Chakkarapani

10:00. M Pureza Laudiano-Dray, University College London
Quantification of neonatal procedural pain severity: a platform for estimating total pain burden in individual infants

10:15. L Fabrizi, University College London
Maternal contact alters how neonates process pain

10.30. L Boel, University Hospital of Wales, Cardiff
Temporal trends of care practices, morbidity, and mortality of extremely preterm infants over 10-years in South Wales, UK

10.45. R D'Souza, Evelina Children's Hospital, London
Leaving necrotic bowel in situ at NEC laparotomy leads to increased mortality

11:00. Q Yang, University of Bristol
The effect of insomnia on pregnancy and perinatal outcomes: a mendelian randomization study

11:15. Tea / coffee

Session 2: Chair – Professor Lucy Chappell.

11:45 **Keynote Lecture**
Professor Paul Leeson. Cardiovascular Clinical Research Facility. University of Oxford.
Early life determinants of cardiovascular and cerebrovascular health

12:45. **Annual General Meeting** (Open to members of the Neonatal Society)
Virtual breakout session

13.45. Lunch break

Session 3: Chair – Professor Helen Budge. Moderator – Dr Chris Gale

14:45. R Pang, University College London
High dose melatonin with erythropoietin and therapeutic hypothermia for perinatal hypoxia ischemia (EMPATHY study): a randomized pre-clinical piglet study

15.00. J Gibb, University of Bristol.
Cardiac function in school aged children cooled for neonatal hypoxic ischaemic encephalopathy

15:15. D Odd, University of Bristol
Antenatal inflammation is not associated with death or short-term morbidity in infants cooled for neonatal encephalopathy

15:30. N Goulding, University of Bristol
Investigating correlations in metabolite levels between pregnant mothers and cord-blood

15:45. TJ Robb, University of Bristol
Social communication development in children aged 6-8 years, without cerebral palsy cooled for neonatal hypoxic ischaemic encephalopathy

16.00. Afternoon Tea / Coffee

Session 4: Chair – Professor James Boardman

16:25. **Prize for best presentation by a trainee**

16:30. **Widdowson Lecture** – **Introduced by Professor James Boardman, President**
Professor Stephen Charnock-Jones. Department of Obstetrics and Gynaecology. University of Cambridge.
Human placenta has no microbiome but can contain potential pathogens.

17:30. Close of meeting

Self Certificate of Attendance

Please complete the form below and have it signed by a member of the neonatal society committee if you wish to claim RCPCH CPD points

Neonatal Society Autumn Meeting
London
5th November 2020

Name of person claiming CPD points:

(Block letters)…….

Place of Work:…….

Number of CPD points claimed :……
(1 point per hour of attendance – up to a maximum of 10 **CPD Points**)

Claimant's Signature……

Name and signature of Neonatal Society Committee member

……
Howard Clark/Helen Budge/James Boardman/Andrew Ewer/Karen Luyt/Chris Gale/Ela Chakkarapani/Lucy Chappell/Kevin Goss
(please delete as appropriate)

QUANTIFICATION OF NEONATAL PROCEDURAL PAIN SEVERITY: A PLATFORM FOR ESTIMATING TOTAL PAIN BURDEN IN INDIVIDUAL INFANTS

Maria Pureza Laudiano-Dray [1], Rebecca Pillai Riddell [2], Laura Jones [1], Rajeshwari Iyer [1], Kimberley Whitehead [1], Maria Fitzgerald [1], Lorenzo Fabrizi [1], Judith Meek [3]

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Institution(s)

[1] Department of Neuroscience, Physiology & Pharmacology, University College London
[2] Department of Psychology, York University (Toronto)
[3] Elizabeth Garrett Anderson Obstetric Wing, University College London Hospitals

Introduction *(include hypothesis)*

Long-term outcomes for infants born prematurely are adversely affected by repeated exposure to noxious procedures[1]. These interventions vary widely, for example, in the extent of damage caused and duration. Skin and tissue breaking procedures are therefore likely to each contribute differently to the overall pain burden of neonates, ultimately having a different impact on their development.

Methods (*include source of funding and ethical approval if required)*

In order to quantify the total pain burden experienced by infants on NICU retrospectively, we aimed to estimate the pain severity of common NICU procedures using published pain scores. We extracted pain scores over the first minute (pain reactivity) from the literature, using 59 randomized controlled trials for 15 different procedures. We calculated the averaged mean scores per procedure and ran a hierarchical cluster analysis to see how they would be significantly separated into degrees of severity. The study was funded by MRC UK, IASP's Collaborative Research Grant and CHRP.

Results

The average pain scores clustered into five discrete severity groups; mild (n=1; eye drops instillation), mild to moderate (n=3; orogastric tube insertion, nasal prongs insertion for CPAP, urethral catheterization), moderate (n=7; heel lance, nasogastric tube insertion, tape removal, naso/oropharyngeal suction, venepuncture, endotracheal suction, eye examination), severe (n=3; intramuscular injection, endotracheal intubation, peripheral arterial puncture) and very severe (n=1; lumbar puncture). The estimate of the severity of individual procedures provided new insight into infant pain reactivity which is not always directly related to the invasiveness and duration of a procedure.

Conclusions

This estimate of procedural pain severity, based on pain reactivity scores, provides a novel platform for retrospective quantification of the total pain burden in NICU patients. Other measures that reflect the recovery from each individual procedure, such as brain activity and behaviour, would further improve pain estimation.

References *(include acknowledgement here if appropriate)*

[1] Grunau R. E. (2013). Neonatal pain in very preterm infants: long-term effects on brain, neurodevelopment and pain reactivitv. *Rambam Maimonides medical iournal*. *4*(4). e0025. doi:10.5041/RMMJ.10132

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Dr Judith Meek

MATERNAL CONTACT ALTERS HOW NEONATES PROCESS PAIN

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Laura Jones[1], Maria Pureza Laudiano-Dray[1], Kimberley Whitehead[1], Judith Meek[2], Maria Fitzgerald[1], Rebecca Pillai Riddell[3], Lorenzo Fabrizi[1]

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Introduction *(include hypothesis)*

Neonatal mammalian brain activity is dependent upon maternal interaction [1]. Maternal presence or absence is associated with brain states supporting attachment or threat learning respectively. The state in which the brain is at the time of a painful intervention is therefore likely to influence the perception of the stimulus. In human adults, cortical processing of a painful stimulus is dependent upon contextual factors [2], and maternal touch/massage and skin-to-skin care can alter neonatal behavioural and physiological reactions [3]. However, the effect of maternal contact on neonatal cortical pain processing is not known. We hypothesised that maternal contact during a clinically required painful procedure will alter the neonatal brain activity suggesting different cortical processing of the stimulus.

Methods (*include source of funding and ethical approval if required)*

EEG, facial expression and heart rate were recorded during a clinically-required heel lance across three age and sex-matched groups of neonates who were either in skin-to-skin, held while clothed, or in the cot. Ethical approval for this study was given by the NHS Health Research Authority. This work was funded by the Medical Research Council UK and an IASP Collaborative Research Grant.

Results

The lance was followed by a sequence of 4-5 event related potentials (ERPs), including a pain-specific ERP (nERP)[4], which was smallest for infants held skin-to-skin and largest for infants held while clothed (p=.016). The nERP was followed by additional and divergent long-latency ERPs (>750ms post-lance), not previously described, in each of the conditions. Behavioural (facial expression) and physiological (heart rate) responses to the lance did not differ between groups.

Conclusions

The maternal/infant context can modulate the magnitude of pain-specific brain activity following a heel lance procedure, highlighting the importance of environmental factors in altering neonatal pain processing. Indeed, the longest latency ERPs are dependent upon maternal/infant interaction and suggests that the more complex processing of the painful stimulus is altered. This work has demonstrated, for the first time in human neonates, that maternal presence can attenuate pain-related cortical activity as well as alter underlying neural processes following a painful procedure.

References *(include acknowledgement here if appropriate)*

[1] Debiec & Sullivan (2017). Neurobiol. Learn. Mem. **143**: 49-58.
[2] López-Solà et al. (2018). Psychosom. Med. **80**: 814–825.
[3] Pillai Riddell et al. (2015). Cochrane Database Syst. Rev. **12**: CD006275.
[4] Fabrizi et al. (2011). Curr. Biol. **21**: 1552–1558.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Dr Judith Meek

TEMPORAL TRENDS OF CARE PRACTICES, MORBIDITY, AND MORTALITY OF EXTREME PRETERM INFANTS OVER 10-YEARS IN SOUTH WALES, UK

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Lieve Boel [1], Sujoy Banerjee[2], Megan Clark[3], Annabel Greenwood[1], Alok Sharma[1], Nitin Goel[1], Gautam Bagga[4], Chuen Poon[4], David Odd[5] Mallinath Chakraborty[1, 6] (Member introducing the author to the Society: J. Calvert)

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Institution(s)

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Introduction *(include hypothesis)*

Contemporary outcome data of preterm infants are essential to commission, evaluate and improve healthcare resources and outcomes while also assisting professionals and families in counselling and decision making. We analysed trends in clinical practice, morbidity, and mortality of extremely preterm infants over 10 years in South Wales, UK.

Methods (*include source of funding and ethical approval if required)*

This population-based study included live born infants <28 weeks of gestation in tertiary neonatal units between 01/01/2007 and 31/12/2016. Patient characteristics, clinical practices, mortality, and morbidity were studied until death or discharge home. Temporal trends were examined by adjusted multivariable logistic regression models and expressed as adjusted odds ratios (aOR) with 95% confidence intervals (95% CI). A sensitivity analysis was conducted after excluding infants born at <24 weeks of gestation.

Results

In this population, overall mortality for infants after live birth was 28.2% (267/948). The odds of mortality (aOR 0.93, 95%CI [0.88, 0.99]) and admission to the neonatal unit (0.93 [0.87, 0.98]) significantly decreased over time. Non-invasive ventilation support during stabilisation at birth increased significantly (1.26 [1.15, 1.38]) with corresponding decrease in mechanical ventilation at birth (0.89 [0.81, 0.97]) and following admission (0.80 [0.68 - 0.96]). Medical treatment for patent ductus arteriosus significantly decreased over the study period (0.90 [0.85, 0.96]). The incidence of major neonatal morbidities remained stable, except for a reduction in late-onset sepsis (0.94 [0.89, 0.99]). Gestation and centre of birth were significant independent factors for several outcomes. The results from our sensitivity analysis were compatible with our main results with the notable exception of death after admission to NICU (0.95 [0.89, 1.01]).

Conclusions

Significant improvements in survival and reduction of late-onset sepsis in extreme preterm infants. Sensitivity analysis suggests that some of the temporal changes were driven by improved outcomes in the most preterm infants. Clinical practices in respiratory support have changed, but significant variation between centres.

Check box if presenting author is a trainee: **basic science trainee** ☐ **clinical trainee** ☒

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Mallinath Chakraborty

LEAVING NECROTIC BOWEL IN SITU AT NEC LAPAROTOMY LEADS TO INCREASED MORTALITY

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Rashmi D'Souza1, Caroline Pardy1, Joe Davidson1,2, Grenville Fox1, Iain Yardley1

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Institution(s)

1. Evelina Children's Hospital, London, UK
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Introduction *(include hypothesis)*

Necrotising enterocolitis (NEC) is the commonest surgical emergency in neonates with a high mortality rate. There are various surgical strategies at laparotomy and no consensus as to which offers the best outcomes. We aim to determine outcomes in neonates undergoing laparotomy for NEC in our tertiary unit.

Methods (*include source of funding and ethical approval if required)*

Neonates with NEC undergoing laparotomy between May 2015 and March 2019 were identified and NEC totalis excluded. Demographic data and surrogate markers of severity of NEC were recorded including gestation, birthweight, inotropic or ventilatory support, and inflammatory markers. Cases were classified according to whether necrotic bowel was resected (R) or left in-situ (LIS). Primary outcome was survival. Secondary outcomes included ongoing inflammatory burden (CRP levels over 14 days post-operatively) and time to enteral autonomy

Results

50 patients were included (21 LIS vs 29 R). Groups were comparable with regard to both demographic and severity characteristics. Patients with all necrotic bowel resected were more likely to survive, (R vs. LIS, 5/29(17%) vs. 13/21(62%), OR 7.8[2.1-28.8], $p<0.005$). Those patients with necrotic bowel left in-situ who survived were less likely to achieve enteral independence (6/9(66.7%) vs. 24/25(96.0%), OR 12[1.05-136.8], $p<0.05$). Among survivors, post-operative inflammatory burden was higher in patients with bowel left in situ (1191[417-1818] vs. 504[277-1080], $p=0.05$). On logistic regression, leaving necrotic bowel in-situ was strongly associated with mortality (OR 8.67[1.86-40.42], $p<0.01$).

Conclusions

Overall mortality at our centre appears comparable to previous studies, however, cases with necrotic bowel left in situ have more than double the mortality rate of those undergoing total resection. Additionally, leaving necrotic bowel in situ does not improve the likelihood of achieving enteral autonomy.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☒

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Iain Yardley / Grenville Fox

THE EFFECT OF INSOMNIA ON PREGNANCY AND PERINATAL OUTCOMES: A MENDELIAN RANDOMIZATION STUDY

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Qian Yang,[1,2] M. Carolina Borges,[1,2] Eleanor Sanderson,[1,2] Kate Tilling,[1,2,3] Deborah A Lawlor[1,2,3] on behalf of the MR-PREG consortia

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Introduction *(include hypothesis)*

Insomnia is common during pregnancy and has been linked with higher risks of adverse pregnancy and perinatal outcomes in previous observational studies using multivariable regressions.[1] However, it remains unclear whether those associations are causal. We aim to test whether insomnia is causally associated with pregnancy loss, gestational diabetes, hypertensive disorders in pregnancy, perinatal depression, preterm birth and low/high offspring birthweight using two-sample Mendelian randomization (MR).[2]

Methods (*include source of funding and ethical approval if required)*

We randomly split individual-participant data from UK Biobank (N=208171), and conducted a two-sample MR study with 81 genetic variants for a lifelong difference in having insomnia (usually versus sometimes to never) to investigate its effects on outcomes. We compared MR results to those from multivariable regressions of insomnia in pregnancy in Avon Longitudinal Study of Parents and Children (N=11748). Funding sources include MRC, Wellcome Trust, NIH, ERC and BHF. Ethical approvals were received from NREC for both cohorts.

Results

In the main (inverse variance weighted) two-sample MR, insomnia related to higher risks of any pregnancy loss (odds ratio [OR] 1.44 95% CI: 1.07-1.93), miscarriage (OR 1.43, 95% CI: 1.01-2.02), perinatal depression (OR 3.33, 95% CI: 1.25-8.85) and low offspring birthweight (OR 2.96, 95% CI: 1.55-5.68). There was no evidence of effects with other outcomes. Sensitivity analyses suggested that results for perinatal depression and low offspring birthweight might have been biased by unbalanced horizontal pleiotropy. In multivariable regressions, insomnia at 18 weeks of gestation was associated with higher risks of pregnancy loss (OR 1.27, 95% CI 1.10-1.45), stillbirth (OR 2.19, 95% CI 1.18-4.07), miscarriage (OR 1.32, 95% CI 1.13-1.55) and perinatal depression (OR 3.17, 95% CI 1.13-1.55) after adjusting for potential confounders. Estimates were similar for insomnia at 32 weeks of gestation.

Conclusions

Results from MR and multivariable regression were in agreement, despite different sources of biases. Our findings suggest insomnia may increase the risks of pregnancy loss, perinatal depression and low offspring birthweight. Further replication of these findings in a large Norwegian birth cohort is planned.

References *(include acknowledgement here if appropriate)*

1.Warland J, et al. *Sleep Med Rev.* 2018; 41:197-219. 2.Lawlor DA. *Int J Epidemiol.* 2016; 45: 908-15.
This research was conducted using the UK Biobank resource under application number 23938.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

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Senior author supporting presentation on day of meeting: Prof Deborah A Lawlor

HIGH DOSE MELATONIN WITH ERYTHROPOIETIN AND THERAPEUTIC HYPOTHERMIA FOR PERINATAL HYPOXIA ISCHEMIA (EMPATHY STUDY): A RANDOMIZED PRE-CLINICAL PIGLET STUDY

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Raymand Pang[1], Adnan Avdic-Belltheus[1], Chris Meehan[1], Kathryn Martinello[1], Magdalena Sokolska[2], Francisco Torrealdea[2], Mariya Hristova[1], Alan Bainbridge[2], Xavier Golay[3], Sandra Juul[4], Nicola J Robertson[1]*

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Introduction *(include hypothesis)*

Not all babies with neonatal encephalopathy (NE) benefit from therapeutic hypothermia (HT). High dose melatonin (MEL) and erythropoietin (EPO) have been studied as adjunct therapies in pre-clinical models (1) and phase II/III clinical trials (2) and each has shown additional benefit over HT, with different mechanisms of action. We hypothesized that: (i) the addition of MEL and EPO to HT would augment brain protection compared to HT alone; and (ii) triple therapy (HT+MEL+EPO) would lead to best neuroprotection overall.

Methods (*include source of funding and ethical approval if required)*

The study was funded by MRC (MR/P025978/1) and conducted according to UK Home Office [Animals (Scientific procedures) Act, 1986]. Forty nine Large White male piglets underwent hypoxia ischemia (HI) by carotid artery occlusion and reduction in FiO2 to 6% followed by randomization to: (i) HT+vehicle (V) (n=12), (ii) HT+MEL** (n=12), (iii) HT+EPO (n=13) or (iv) HT+MEL+EPO (n=12). Piglets received HT for 12h from 1-13h after HI. Cerebral activity was monitored with aEEG and thalamic and white matter (WM) ^{1}H MRS *Lac/NAA was acquired at 30h and 66h at 3T. Animals were euthanised at 72h and immunohistochemistry assessed.

Results

Baseline variables, insult parameters and inotropic requirements were similar across groups. Therapeutic levels were achieved within 30mins of the EPO 3,000U/kg bolus and after 2h of the MEL 20mg/kg infusion. aEEG recovery was observed with HT+MEL ($p=0.02$) and HT+EPO ($p=0.033$) at 25-30h and HT+MEL+EPO ($p=0.042$) at 55-60h compared to HT+V. We observed a rise in Lac/NAA from 30h to 66h ($p<0.05$) in HT+V; thalamic Lac/NAA was lower in HT+MEL ($p=0.01$), HT+EPO ($p=0.07$) and HT+MEL+EPO ($p=0.03$) versus HT+V. In HT+MEL, we observed reduced TUNEL-positive cells in sensorimotor cortex ($p=0.017$) and increased Olig2-positive counts in hippocampus ($p=0.014$) and periventricular WM ($p=0.039$). There was no reduction in TUNEL with HT+EPO, but an increase in Olig2-positive counts in cingulate cortex ($p=0.029$), hippocampus (0.024), periventricular WM ($p=0.005$), internal capsule ($p=0.046$) and thalamus ($p=0.047$). No difference in aEEG, MRS or TUNEL was observed comparing the 3 adjunct treatment groups (HT+MEL,HT+EPO, HT+MEL+EPO).

Conclusions

MEL and EPO combined with HT were safe and augmented HT neuroprotection based on improved aEEG recovery, reduced Lac/NAA and reduced cell death and/or increased oligodendrocyte survival. There was no benefit of triple (HT+MEL+EPO) versus double therapy (HT+MEL or EPO) over these 72h studies. The different effect of MEL and EPO on immunohistochemistry may reflect their different mechanisms of action.

References *(include acknowledgement here if appropriate)*

[1] Robertson NJ, *Brain*. 2013;160(4):544-552. [2] Juul SE, *Neonatology.* 2018;113(4):331-338
* Lac+Threonine/total NAA ** Proprietary Melatonin formulation supplied by Chiesi Pharmaceuticals

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Senior author supporting presentation on day of meeting: Professor Nicola Robertson

CARDIAC FUNCTION IN SCHOOL AGED CHILDREN COOLED FOR NEONATAL HYPOXIC ISCHAEMIC ENCEPHALOPATHY

Authors

Jack J. C. Gibb[1], Richard Lee-Kelland[1,2], Beverly Tsai-Goodman[3], Owen Burgess[1], Marianne Thoresen[2,3], Ela Chakkarapani[1,2]

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4. Institute of Physiology, University of Oslo, Norway.

Introduction *(include hypothesis)*

Objective Whether neonates with hypotension or high cardiac troponin I (cTnI) levels during therapeutic hypothermia (TH) for neonatal hypoxic-ischaemic encephalopathy (HIE) have abnormal cardiac function at childhood is unknown. We investigated the cardiac function at childhood for neonates with or without hypotension or high cTnI during TH and examined association between cTnI and cardiac function.

Methods (*include source of funding and ethical approval if required)*

Design Prospective observational study between October 2015 and August 2016.
Setting Bristol Children's Hospital, UK.
Patients 15 children aged 6-8 years who underwent TH for HIE and were classified based on receiving inotropic support for hypotension and cTnI threshold of 0.087ng/ml within 12 hours of life.
Main outcome measures Echocardiographic left ventricle (LV) and right ventricle (RV) systolic and diastolic function

Results

High cTnI (n=10) compared to low cTnI (n=5) group had significantly lower median (IQR) pH(6.87 (6.80, 6.90) vs 6.97 (6.90, 7.05), P = 0.036) and base excess (-23.0 (-26.4, -19.5) vs -13.4 (-16.2, -12.0), P=0.005) perinatally. Inotrope (n=8) versus non-inotrope (n=7) group, and high versus low cTNI group did not differ in the LV and RV systolic or diastolic measures. LV global longitudinal strain z score was <<-2 in 7%; global circumferential strain z scores were >+2 in 33.3-93% from basal to apical level. Correlations between peak cTnI and cardiac function did not survive multiple testing correction.

Conclusions

Abnormalities in LV function might occur in children who had myocardial injury during cooling for HIE. Longitudinal evaluation of infants with imaging evidence of neonatal cardiac dysfunction are required to identify persisting cardiac abnormalities.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ✓

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ✓

Antenatal inflammation is not associated with death or short-term morbidity in infants cooled for neonatal encephalopathy.

Odd D[3], Sabir H[2], Jones S A[3], Gale C[4], Chakkarapani E.[1]

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Introduction *(include hypothesis)*

Pre-clinical studies[1] and small single center studies[2] report conflicting degrees of neuroprotection with therapeutic hypothermia (TH) following inflammation prior to hypoxia-ischemic encephalopathy (inflammation-sensitized HIE). Therefore, we aimed to determine the independent effect of inflammation-sensitization on death and nasogastric (NG) tube feeding at discharge, and its association with major organ dysfunction, length of stay and time to full oral feeds in cooled HIE infants from the larger UK national neonatal research database (NNRD).

Methods (*include source of funding and ethical approval if required)*

Retrospective cohort study utilizing NNRD between Jan 2008 and Feb 2018. Population: infants ≥36wks gestation with HIE undergoing TH. Exposure: inflammation-sensitization defined as 1/more of: rupture of membranes >18hrs, maternal group B streptococcus colonization, chorioamnionitis, maternal pyrexia or intrapartum antibiotics. Primary outcome: death and or NG feeds/nil by mouth at discharge. Secondary outcomes: major organ dysfunction; length of stay; intraventricular haemorrhage; days &no. of anticonvulsants. We used a multilevel regression model (by birth year) and adjusted for demographics and intrapartum factors.

Results

Of 7265 eligible infants, 998 (13.7%) had evidence of antenatal inflammation-sensitization. Inflammation-sensitized group were heavier, mature, differed in mode of delivery, had higher cord pH and a lesser proportion of grade 3 HIE. Primary outcome occurred in 20.3% of inflammation-sensitized group and 23.1% in non-exposed group (p=0.05). Death occurred in 13% of inflammation-sensitized and 14% of non-exposed group (p=0.321). Multivariable association showed results compatible with the univariable analysis (OR 0.87 (0.71-1.08)). There was no difference in the secondary outcomes of major organ dysfunction, length of stay and intraventricular haemorrhage. Inflammation-sensitization group compared to non-exposed group were more likely to achieve full oral feeds earlier (means (95% CI): 7.1 (6.8-7.5) vs 7.8 (7.6-8.0), p<0.001), and received fewer anticonvulsants (1.36 (1.31-1.41) vs 1.43 (1.41-1.45, p=0.008) for fewer days (2.8 (2.6-3.0) vs 3.2 (3.1-3.3), p=0.006).

Conclusions

Infants developing HIE after inflammation-sensitization did not have increased risk of death or NG feeding at discharge than other HIE infants, and in some domains have better outcomes. Objective measurement of inflammation-sensitization may identify the role of antenatal inflammation on developmental outcomes in HIE.

References *(include acknowledgement here if appropriate)*

1. Falck M, et al. Dev Neurosci 2017;39 (1-4):238-247.
2. Hakobyan et al., Neonatology. 2019;115(2):127-133.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☐

Senior author supporting presentation on day of meeting: Dr Ela Chakkarapani

INVESTIGATING CORRELATIONS IN METABOLITE LEVELS BETWEEN PREGNANT MOTHERS AND CORD-BLOOD

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

1 MRC Integrative Epidemiology Unit, University of Bristol (UoB); 2 PHS, UoB; 3 Dept of Obstetrics and Gynaecology, St Michael's Hospital, Bristol; 4 THS, UoB; 5 Bradford Institute for Health Research, Bradford Teaching Hospitals NIHS Foundation Trust; 6 Bristol NIHR Biomedical Research Centre

Introduction *(include hypothesis)*

For most metabolites, it is not known whether or how they cross the placenta. We are not aware of research exploring associations of multiple maternal metabolites with the same measures in cord blood. Our hypothesis is that examining these associations will provide some insights into how metabolites cross the placenta.

Methods (*include source of funding and ethical approval if required)*

Data from the Born in Bradford cohort were used.[1] 6614 maternal gestational (24-28 weeks) and matching cord-blood samples were analysed for 84 NMR metabolite levels and ratios. For 12 measures there was a high proportion of cord-blood samples with levels below the limit of quantification (LOQ). Pearson correlations between mothers and cord-blood metabolites were calculated with (i) replacing with LOQ (N = 5726 to 6614) and (ii) complete case analyses (N = 3066 to 6611). We also stratified on ethnicity[1] and sex.
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Results

There was no/very weak correlation (-0.03 to 0.20) between metabolite levels of mothers and cord-bloods for 79 (94%) of the NMR metabolites analysed in the whole sample. This included the correlation of maternal to cord glucose (R= 0.04). Creatinine, valine, glutamine, histidine and % Omega-3 fatty acids showed weak-moderate positive correlation (0.20 to 0.34). Creatinine (a measure of renal function) was the only metabolite to show noticeable differences in correlations for samples segregated by sex and/or ethnicity, ranging from 0.10 for White British boys to 0.34 for South Asian boys. A large proportion of cord-bloods (22% - 54%) were < LOQ for total lipids and particle concentration for very large and extremely large VLDL, small, medium and large LDL and large HDL. Repeating analyses on complete data treating these as missing (method (ii)) produced extremely similar results.

Conclusions

In general, there is very low correlation between NMR metabolite levels of mothers and cord-bloods. There is evidence of a moderate positive correlation for creatinine and some amino acids.

References *(include acknowledgement here if appropriate)*

1 Taylor K *et al*. Differences in pregnancy metabolic profiles and their determinants between White European and South Asian women: Findings from the Born in Bradford Cohort. *Metabolites* 2019; **9**: 190

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☐

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☒

Senior author supporting presentation on day of meeting: Professor Deborah A Lawlor

Social communication development in children aged 6-8 years, without cerebral palsy cooled for neonatal hypoxic ischaemic encephalopathy.

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

School-age children without cerebral palsy (CP), who were treated with therapeutic hypothermia for neonatal hypoxic ischaemic encephalopathy (HIE), have worse cognitive and behavioural scores compared with peers.[1] Communication abilities in these children have not been studied. Given the impaired cognitive skills, we hypothesised that school-aged children without CP cooled for HIE will have impaired communication abilities compared with peers.

Methods (*include source of funding and ethical approval if required)*

Parents and caregivers completed the validated communication screening questionnaire, the Children's Communication Checklist (CCC-2), for 51 children without CP who were cooled for HIE between 2008-2013 (case) and 43 age, sex and social class matched controls during an assessment day. The CCC-2 consists of 10 subscales. Sum of 8 subscales yield general communication composite (GCC) with mean (SD) of 80(15). GCC<55 indicates clinically significant communication problems.[2] Children with permanent hearing loss were excluded. Case-control group differences in GCC and subscale scores were compared using unpaired *t*-tests.

Results

Case children did not differ from controls for age (mean (SD): 83.84 months (6.86) vs 84.56 (6.3)), sex (female: 39% vs 49%) and social class. Two case children with permanent hearing loss were excluded. Cases had significantly lower mean (SD) GCC scores than controls (75.2 (19.6) vs 83.06 (17.0), p=0.04). There was a higher proportion of case children with GCC<55 than controls (14.2% vs 4.6%). In considering the subscales of the CCC-2, cases had a significantly lower median (IQR) 'Syntax' (structural language awareness) subscale score (10, (7.5, 12) compared to controls (12 (9,12), p=0.02. Cases compared with controls also had a significantly lower median (IQR) 'inappropriate initiation' subscale score (9 (7,11) vs 10 (9,12), p=0.04) and 'Interests' (restricted interests) subscale score (9 (7,10) vs 10(8,11), p=0.04).

Conclusions

Our findings indicate that children without CP who were cooled for neonatal HIE are at increased risk of subtle communication difficulties compared to matched controls and therefore ongoing monitoring of communication-specific abilities is recommended in childhood and adolescence.

References *(include acknowledgement here if appropriate)*

1. Lee-Kelland R, et al. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2020 Jan 1;105(1):8-13.
2. Norbury C F, et al. Int J Lang Comm Dis 2004; 39 (3): 345-364.

Check box if presenting author is a trainee: basic science trainee ☐ clinical trainee ☒

All authors have approved the abstract, actual or potential conflicts of interest have been declared to the meetings secretary, and the abstract has not been presented previously: ☐

Senior author supporting presentation on day of meeting: Dr Ela Chakkarapani