



Neonatal Society Spring Meeting
15th March, 2019
Royal Society of Medicine
1 Wimpole Street, London, W1G 0AE

Spring Meeting, 15th March 2019

Royal Society of Medicine, 1 Wimpole Street, London, W1G OAE

09.30 Coffee

Session 1: Chair – Dr Chris Gale, Committee Member

10.00. L Mills, Imperial College London

Macronutrient content of donor milk from a regional human milk bank: variation with donor mother-infant characteristics

10.15. A Lok, Bradford Neonatal Unit

Early Extubation Success in Extreme Preterm Infants – Yorkshire ODN Experience

10.30. S. Sakonidou, Imperial College London

Interventions to improve parent satisfaction with care in neonatal intensive care units: a systematic review

10.45. H Hunt, University of Exeter

“They’ve walked the walk”: A systematic review of quantitative and qualitative evidence for parent-to-parent support for parents of babies in neonatal care

11.00. Tea / coffee

Session 2: Chair –Dr Ela Chakkarapani, Committee Member

11.30. T Sproat, Institute of Cellular Medicine, Newcastle University

Investigating the immune system of preterm babies and the effect of diet

11.45. E Fitzgerald, University of Edinburgh

LPS and hypoxia affect transcription and 5' hydroxymethylation of SLC7A5 in the developing mouse brain

12.00. W Lee, University of Nottingham

Vibration induced brain injury in the developing brain: a double hit mechanism?

12.15 **Keynote Lecture**

Professor Olivier Baud. Professor of Paediatrics, Université Paris-Diderot and University of Geneva
Hydrocortisone for Improving Outcome after Extremely Preterm Birth

13.15. Lunch break

Session 3: Chair – Professor James Boardman, President

14.45. S Datir, Stoke Mandeville Hospital, Aylesbury and Neonatal Intensive Care Unit, John Radcliffe Hospital, Oxford.

Interpretation of cerebral function monitor traces: Comparison of skills in paediatric registrars in the Oxford deanery after a decade

15.00. J Crowell, University of Bristol

White matter integrity at school age in children from the DRIFT randomised controlled trial of neonatal post haemorrhagic ventricular dilatation

15.15. G Sullivan, University of Edinburgh

Structural connectivity measures correlate with language outcomes in preterm infants at 2 years of age

15.30. Afternoon Tea / Coffee

Session 4: Chair – Professor Andrew Ewer, General Secretary

16.00. A Glazewska-Hallin, Department of Women and Children's Health, King's College London

Efficacy of vaginal cerclage in women with prior emergency caesarean section

16.15. D Stoye, University of Edinburgh

Reduced maternal glucocorticoid clearance is associated with higher serum cortisol and reduced offspring birthweight

16.30. **Prize for best presentation by a trainee**

16:35. **McCance Lecture**

Professor Bo Jacobsson. Professor in Obstetrics and Gynaecology, Gothenburg and Senior Researcher, Institute of Public Health, Oslo.

A genetic perspective of preterm delivery - is it the mother or the child or both?

17:35 Drinks reception and close of meeting

Macronutrient content of donor milk from a regional human milk bank: variation with donor mother-infant characteristics

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

Luke Mills, Lynda Coulter, Emma Savage, Neena Modi

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Institution(s)

Imperial College London, Academic Neonatal Medicine

Introduction (*include hypothesis*)

Better understanding of the variation in macronutrient content of human donor milk (HDM) potentiates targeted nutrition for preterm babies. This study describes the relationship of maternal age, parity, lactation time, volume of milk donated, sex, gestation, birthweight, and sex specific birthweight adjusted for gestational age z scores, with macronutrient content of HDM.

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

Samples from 1175 mother-infant pairs and 2966 donations to the UK North West Human Milk Bank between 2011-2017 were analysed. A stepwise multiple regression was performed using the predictor variables above on the outcome macronutrient value determined using mid infrared spectroscopy. Mean macronutrient content was also compared by gestational age, and small or appropriate for gestational age (SGA) (z score <1.28) or (AGA) (z score ≥ 1.28) categories.

Results

Mean (sd) protein, fat, carbohydrate, and calculated energy, were 0.89 (0.24) g/dl, 2.99 (0.96) g/dl, 7.09 (0.44) g/dl, and 60.37 (8.41) kcal/dl respectively. Lactation time and z score negatively predicted protein and fat. Lower gestational age predicted fat, but not protein. There were no differences between preterm gestational age categories but highest levels of protein, fat and energy were found in preterm compared to term, and SGA compared to AGA HDM in the first 3 months of lactation, with the biggest differences seen between preterm SGA and term AGA groups.

Conclusions

SGA status, as well as prematurity, may be an important determinant of macronutrient content in early lactation. As bioavailability of macronutrients from HDM is uncertain, studies evaluating growth and body composition in preterm and SGA babies fed HDM are warranted.

References (*include acknowledgement here if appropriate*)

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: Neena Modi

Early Extubation Success in Extreme Preterm Infants – Yorkshire ODN Experience

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

Aishin Lok, C Hudson, C Vasudevan, S Seal. Introduced by Dr Ela Chakkarapani

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Institution(s)

Bradford Neonatal Unit

Introduction (*include hypothesis*)

Prolonged mechanical ventilation in the extremely preterm infant is associated with many morbidities and mortality. There are no measurements with satisfactory levels of sensitivity and specificity to predict the optimal moment for extubation. We aim to explore extubation practices in the extremely preterm /extremely low birth weight (ELBW) infants in 4 tertiary neonatal units across Yorkshire Neonatal Network and to assess composite outcome of mortality and predefined major morbidities.

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

A retrospective cohort study of extremely preterm infants (<27 weeks gestational age) or ELBW infants (birth weight <1000g) requiring mechanical ventilation at birth in 2016. Successful extubation is defined as not requiring reintubation for 72 hours post extubation.

Results

195 infant's data were analysed. Wide variation of practices was found. Between 39% and 89% of infants were extubated in the first 72 hours of life. Earlier extubation is not found to have increase rate of major morbidities. It is not associated with higher rate of extubation success. Extubation success rate increases with GA (5% for 23 weeks GA vs 75% for 27 weeks GA). Successful extubation was associated with a higher birth weight and pre-extubation conditions such as higher pH and lower pre-extubation oxygen requirement.

Use of morphine pre-extubation, incomplete antenatal steroids and haemoglobin levels of less than 12 were positively associated with extubation failure. Infants who failed extubation had a higher mortality rate before discharge, retinopathy of prematurity, longer duration of respiratory support and hospitalisation.

Conclusions

Early extubation is feasible in the extremely preterm infants if pre-extubation conditions are optimised. Results of this study has helped to inform current neonatal extubation practice and warrant the development of regional guidelines for early extubation of the extreme preterm infants.

References (*include acknowledgement here if appropriate*)

Acknowledgement: Leeds Neonatal Unit, Hull Neonatal Unit, Jessops Neonatal Unit.

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 C Vasudevan

Interventions to improve parent satisfaction with care in neonatal intensive care units: a systematic review

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)

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Introduction (include hypothesis)

Healthcare staff increasingly use satisfaction with neonatal care as a parent experience measure and service quality indicator. Interventions aimed at improving parent satisfaction can help reduce parent stress, and potentially improve parent-infant bonding (1) and infant outcomes (2). Objective: To conduct a systematic review of interventions to improve parent satisfaction with neonatal care.

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

We conducted a literature search (MEDLINE, EMBASE, PsychINFO, Cochrane Central, CINAHL, HMIC, Maternity and Infant Care), 1/1/1946-1/10/2017. We included studies of parents of babies receiving neonatal care and interventions aiming to improve parent satisfaction; randomised controlled trials and non-randomised comparative studies assessing ≥ 1 quantitative outcome were eligible. We extracted interventions, their impact on parent satisfaction, parent satisfaction definitions and measurements, and parent input into design of the interventions. We assessed methodological quality with the Cochrane Collaboration risk of bias tool (randomised) and the ROBINS-I tool (non-randomised studies). Funding: NIHR Fellowship grant (2017-10-172).

Results

We identified 32 studies with parent satisfaction measures from over 2900 parents and grouped interventions into 5 themes: parent involvement (e.g. parental presence at clinical rounds); parent emotional support (e.g. narrative writing); clinical care (e.g. co-bedding infants in incubators); information provision (e.g. Short Message Services (SMS) for parents); other (e.g. free parent parking). Of 32 studies 18 (56%) reported higher parent satisfaction in the intervention group. The theme with most studies reporting higher satisfaction was parent involvement (10/14). Parent satisfaction was measured by 334 different questions in 29 questionnaires (23/29 partially or completely unvalidated). Five (5/32, 16%) studies reported involving parents in intervention design. We assessed all studies as having high risk of bias.

Conclusions

Many interventions, commonly relating to parent involvement, are reported to improve parent satisfaction with neonatal care. However, inconsistency in definition and measurement of parent satisfaction and high risk of bias in all studies makes this low quality evidence. Standardised definitions and validated parent satisfaction measures are needed, as well as higher quality trials of parent experience.

References (include acknowledgement here if appropriate)

1. Lopez-Maestro et al. Quality of attachment in infants less than 1500g or less than 32 weeks. Related factors. Early Hum Dev. 2016;104:1-6 2. Charpak N, Tessier R, Ruiz JG, Hernandez JT, Uriza F, Villegas J, et al. Twenty-year Follow-up of Kangaroo Mother Care Versus Traditional Care. Pediatrics. 2017;139(1)

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: X

Senior author supporting presentation on day of meeting: Dr Christopher Gale

"THEY'VE WALKED THE WALK": A SYSTEMATIC REVIEW OF QUANTITATIVE AND QUALITATIVE EVIDENCE FOR PARENT-TO-PARENT SUPPORT FOR PARENTS OF BABIES IN NEONATAL CARE.

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

Harriet Hunt, Rebecca Abbott, Kate Boddy, Rebecca Whear, Alison Bethel, Sue Prosser, Andrew Collinson, Jennifer Kurinczuk, Christopher Morris, Leanna Wakely, Jo Thompson Coon (*proposer Andy Ewer if accepted*)

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Institution(s)

University of Exeter; Supporting Neonatal Users and Graduates (SNUG); Royal Devon and Exeter Hospital; Royal Cornwall Hospital, Treliske; National Perinatal Epidemiology Unit, University of Oxford

Introduction (*include hypothesis*)

Parents of babies admitted to neonatal units experience an arduous emotional journey which may lead to anxiety, depression and post-traumatic stress and can persist long after discharge from the unit. Support from a parent with first-hand experience able to empathise with problems and challenges may help. This systematic review identified the quantitative and qualitative evidence that explored the experiences and effects of parent to parent (P2P) support, from the perspective of those giving, receiving, or implementing it.

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

We worked with a Parent Advisory Group (PAG) of parents with relevant and varied lived experience of having a baby in neonatal care and experience of providing peer support. Using best practice, we undertook a systematic review of P2P support. Thirteen electronic databases were searched and independent double screening and quality appraisal was undertaken. Studies were included if they described the effects or experiences of P2P support. We excluded studies relating to interventions delivered by professionals offering instruction or training to parents rather than support. The protocol was registered: PROSPERO CRD42018090569.

Results

The search identified 4593 records. After abstract and full text screening, 15 papers from 14 studies were included: 7 quantitative and 8 qualitative. No studies from the UK were found: 6 were from Canada, 8 from the USA and 1 from Finland. Quality of the evidence was mixed, with few studies rated as high quality. Ten studies related to general P2P support, and 5 related specifically to breastfeeding. Quantitative outcomes were grouped into 5 categories: psychological, perceptions of care and support, interaction and parenting behaviours, knowledge and understanding, and breastfeeding rates and attitudes. P2P support was found to increase perceptions of support, reduce maternal stress, and increase maternal confidence in the ability to care for their baby. From the qualitative data, 26 sub-themes (e.g. shared experience, reassurance and non-judgmental understanding) were identified resulting in 4 main themes: trust, hope, information, and connecting. Few negative experiences or outcomes were reported, and data on the experiences of fathers was lacking.

Conclusions

Whilst the rich qualitative evidence suggested mostly positive experiences from all perspectives of P2P support, robust trial evidence for this was lacking. Furthermore, the difference in models for implementing P2P support meant we were unable to draw solid recommendations to guide best practice.

References (*include acknowledgement here if appropriate*)

This research was funded by the Research for Patient Benefit (RfPB) Programme ref. PB-PG-0416-20032, and supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care South West Peninsula (NIHR CLAHRC South West Peninsula). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care

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: Rebecca Abbott

INVESTIGATING THE IMMUNE SYSTEM OF PRETERM BABIES AND THE EFFECT OF DIET

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

T Sproat^{1,2}, J Spegarova¹, R Payne¹, CJ Stewart¹, J Berrington^{1,2}, N Embleton^{1,2}, S Hambleton^{1,2}

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Institution(s)

1. Institute of Cellular Medicine, Newcastle University
2. Newcastle Upon Tyne Hospitals NHS Foundation Trust

Introduction (*include hypothesis*)

Enteral diet in preterm babies is associated with diseases such as necrotising enterocolitis (NEC) and late onset sepsis (LOS). NEC and LOS are both associated with an inappropriate immune response, as well as changes in the gut microbiota. ¹

We aimed to determine the impact of an exclusive human milk diet on gut microbiota and development of T lymphocytes. We hypothesised that there will be an association between diet and mucosal-associated immune cell (MAIT, iNK T, Treg) populations, and that T cell populations change over time.

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

Extremely preterm (<30 weeks gestation) infants were recruited and randomised within 72 hours of age to a dietary intervention until 34w corrected age. All infants received mother's own milk but were randomised to supplementation with either human (Prolacta Biosciences) or bovine milk products (Nutriprem C&G). Daily stool samples, as well as 500ul blood were collected (2 time points). Lymphocytes were isolated and stained with a 39 antibody mass cytometry (CyTOF) panel as well as a conventional 7 channel flow cytometry panel (defining major lymphocyte subsets). ISRCTN doi.org/10.1186/ISRCTN16799022 Funding: Prolacta

Results

We present preliminary data on 25 lymphocyte profiles from 17 preterm infants (mean; gestational age 27w, birthweight 973g). An average of 186,000 leucocytes were analysed using mass cytometry. As expected, the proportion of major lymphocyte populations were similar between flow and mass cytometry. Conventional T cells were mostly naïve, therefore we focused on the innate-like lymphocyte subsets. Our data shows an increased abundance of V-alpha 7.2 CD161- cells (CD4+ and CD8+) as % of T cells in neonates compared to adults (mean 2.9% vs 1.13% (p<0.001)). Further characterisation of these cells may improve the understanding of the development of mucosa-associated invariant T (MAIT) cells (V-alpha 7.2+CD161+). Furthermore, the population of invariant NK (iNK) T cells is heterogenous, expanded in neonates compared to adults, and has a predominance of chemokine receptor 4 expression in neonates.

Conclusions

Mass cytometry enables a broader description of immune development and is a valuable tool to characterise immune cell populations in preterm babies. Our data is some of the first to clearly identify circulating mucosal associated T cells in preterm infants, suggesting major differences in the size and composition of this compartment. Further study will enable correlation with clinical, dietary, and microbiome data.

References (*include acknowledgement here if appropriate*)

1. M. A. Mara et al. Innate and Adaptive Immunity in Necrotising Enterocolitis. *Seminars in Fetal and Neonatal Medicine* 23 (2018) 394–399

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:

LPS AND HYPOXIA AFFECT TRANSCRIPTION AND 5' HYDROXYMETHYLATION OF SLC7A5 IN THE DEVELOPING MOUSE BRAIN

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

Eamon Fitzgerald¹, James P Boardman² and Amanda J Drake¹

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Institution(s)

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Introduction (*include hypothesis*)

Preterm birth (PTB) is associated with alterations in DNA methylation at sites that influence neurodevelopment including SLC7A5, an amino acid transporter linked to autism spectrum disorder (ASD)¹, but the environmental exposures that drive epigenetic modification are uncertain. Preterm infants may be exposed to infection and hypoxia, both of which can modify the epigenome². We tested the hypothesis that exposure to LPS and/or hypoxia affects SLC7A5 expression in the developing mouse brain mediated by altered cytosine modifications.

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

C57/Bl6 mice were culled at P0-P1 and 300µm forebrain slices cultured, with 4 experimental groups: (1) control (no intervention); (2) LPS (100ng/ml for 5 hours), (3) hypoxia (1% oxygen for 24 hours); and (4) LPS + hypoxia (5 hours LPS then 24 hours hypoxia). RNA/DNA was extracted, then qPCR, and 5-hydroxymethylated DNA (5hmC) immunoprecipitation-qPCR performed. N=6-12 mice (1 slice/condition) for all experiments. Animals were kept, and procedures carried out in accordance with the University of Edinburgh's policy and Home Office regulations. Funding provided by Medical Research Scotland and Aquila Biomedical.

Results

Exposure to LPS + hypoxia (group 4), but not LPS (group 2) or hypoxia (group 3), resulted in increased expression of SLC7A5 ($p=0.01$) and in increased expression of the DNA demethylases Tet1 and Tet2 which convert 5-methylcytosine (classically associated with gene silencing) to 5hmC (associated with active transcription) (both $p<0.05$). LPS (group 2) and LPS + hypoxia (group 4) associated with increased 5hmC within a well-conserved region of SLC7A5 ($p=0.04$), with no effect of hypoxia (group 3), $p=0.531$.

Conclusions

LPS + hypoxia associates with altered expression of a candidate gene for ASD, SLC7A5. LPS and LPS + hypoxia is associated with increased 5hmC at SLC7A5. As such we propose, the effect of LPS to sensitise to subsequent hypoxia, as seen in animal models of perinatal brain injury, is at least partly mediated by 5hmC.

References (*include acknowledgement here if appropriate*)

1.Sparrow, S. *et al.*. *Transl. Psychiatry* **6**, e716 (2016). 2.Brigati, C. *et al.* *Mediators Inflamm.* 2010, 263914
We thank Dr Veronique Miron and Graeme Ireland for initial development and characterisation of the model.

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: Prof James Boardman

Vibration induced brain injury in the developing brain: a double hit mechanism?

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)

Academic Child Health, School of Medicine, University of Nottingham

Introduction (include hypothesis)

Inter-hospital transfer of preterm infants is associated with worse neurological outcomes⁽¹⁾. Chronic whole-body vibration [WBV] causes neurovascular injury, but it is unknown the impact it has on the developing brain as a potential mechanism of neuronal injury. Using our new rodent model of a single acute WBV exposure, as experienced during neonatal ambulance transfer, we have previously demonstrated outer cortical neuronal injury. We now hypothesise that the preterm phase of neuronal development is more susceptible to WBV induced traumatic brain injury [TBI] and aimed to explore neuronal injury in the whole developing brain.

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

Female Sprague-Dawley rats, at neurodevelopmental stages equivalent to the 32w preterm [postnatal day 7] or post-term [postnatal day 21] infant, were randomised into control [C] and WBV [V] groups. V groups were vibrated at 2m/s² for 90 minutes⁽²⁾. 24 hours post-exposure, whole brain tissues were sectioned and TUNEL stained for apoptotic cells. Blinded histological quantification of apoptotic cells was performed within 4 cortical and 4 subcortical regions of interest and analysed using Mann-Whitney U test with significance set at P<0.05. This study was conducted in accordance to the Animal Act 1986.

Results

Day 7 V pups had significantly more apoptotic cells in the outer cortex, mid-outer cortex, and corpus callosum/hippocampus regions compared to the C group [Table]. Amongst day 21 pups, only the outer cortex of the V group showed significantly more apoptosis. In both V groups, apoptosis was maximised at the outer cortex and decreases toward deeper regions. Overall, more brain regions were significantly affected and at greater extent in day 7 V group than in day 21.

	% TUNEL +ve cells					
	Day 7			Day 21		
	C [n=8]	V [n=8]	Fold change	C [n=8]	V [n=8]	Fold change
Outer cortex	1.6 [0.0-3.0]	15.5** [4.1-29.4]	9.7	1.9 [1.1-2.9]	4.7* [2.4-14.0]	2.5
Mid-outer cortex	0.4 [0.0-0.5]	1.5*** [0.8-3.4]	3.8	1.7 [0.9-2.3]	1.2 [0.7-1.6]	0.7
Mid-inner cortex	0.7 [0.4-1.4]	0.9 [0.5-2.3]	1.3	2.2 [1.0-3.2]	1.1 [0.8-3.7]	0.5
Inner cortex	0.4 [0.1-0.9]	1.3 [0.1-5.0]	3.3	2.2 [0.5-3.2]	1.5 [0.2-2.9]	0.7
Corpus callosum/ Hippocampus	0.8 [0.3-1.1]	3.3** [1.0-6.9]	4.1	1.0 [0.8-1.6]	1.0 [0.6-1.2]	1.0
Caudate Putamen	0.6 [0.3-0.8]	1.4 [0.4-0.7]	2.3	0.6 [0.5-1.2]	0.8 [0.6-1.1]	1.3
Lateral septum/ Thalamus	0.2 [0.0-3.8]	1.0 [0.1-3.0]	5.0	0.9 [0.6-1.7]	0.9 [0.8-1.4]	1.0
Nucleus accumbens/ Hypothalamus	0.2 [0.0-0.4]	0.6 [0.2-0.4]	3.0	0.4 [0.3-0.7]	0.5 [0.2-0.7]	1.3

Data expressed as median [IQR].

Statistical significance:
***p<0.001 C vs V,
**p<0.01 C vs V,
*p<0.05 C vs V

Conclusions

Ambulance equivalent WBV induces microscopic TBI within the developing brain, appearing particularly susceptible in the outer cortical layers. Deeper regional injuries in the corpus callosum and hippocampus could be related to poor stress response and subsequent poor cerebral autoregulation. These microscopic injuries could impact the long-term neurodevelopment of transported neonates even in the absence of intraventricular haemorrhage.

References (include acknowledgement here if appropriate)

1. Mohamed MA, Aly H. Arch Dis Child Fetal Neonatal Ed. 2010;95(6):403–7.
2. Blaxter L, Yeo M, McNally D, Crowe J, Henry C, Hill S, et al. J Eng Med. 2017;231(2):99–113.

INTERPRETATION OF CEREBRAL FUNCTION MONITOR TRACES: COMPARISON OF SKILLS IN PAEDIATRIC REGISTRARS IN THE OXFORD DEANERY AFTER A DECADE

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)

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Introduction (include hypothesis)

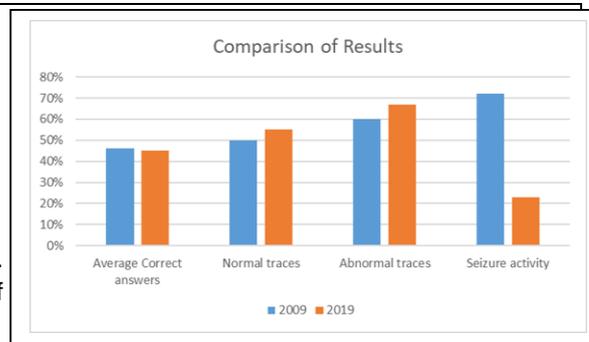
Cerebral Function monitoring (CFM) is an established tool in the early evaluation of infants with hypoxic injury, during therapeutic hypothermia and in the detection of seizures (1,2). We have previously shown that trainees at the registrar level have limited skills in identifying abnormal patterns on CFM (3). This is a repeat survey conducted to assess the CFM interpretation skills of ST4+ Paediatric trainees in the Oxford deanery with the results compared to the previous survey.

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

26 trainees in the middle grade (ST4 and above) took part in a survey conducted in a group setting. The questionnaire was a designed test interpretation of 10 commonly seen CFM traces in clinical practice. Five of the traces were normal, two were moderately abnormal, five showed seizures and three were classed as severely abnormal (4). Additional information collected included neonatal experience and formal CFM training. Results of the survey were compared to an identical exercise that was done in 2009, which used the same questionnaire set.

Results

All the trainees claimed to have been exposed to the use of CFM in 2019 compared to 87% in 2009. In 2019, 80.7% of the trainees had at least 6 months of level III experience as registrars and 23% had formal training in the use of CFM. The performance of trainees in the two time periods remained similar. An abnormal trace was missed by 40% of trainees. The overall correct interpretation over a range of CFM traces remained at 40%. In 2019, 80% of trainees failed to recognise the presence of seizures on a CFM tracing.



Conclusions

Only 23% of trainees undergo some form of formal training in the interpretation of CFM. Skills in interpreting CFM amongst trainees remain poor and have not improved over 10 years. This may have implications for patient care and highlights the need for making formal training in CFM interpretation widely available.

References (include acknowledgement here if appropriate)

1) Azzopardi D, TOBY study group. Predictive value of the amplitude integrated EEG in infants with hypoxic ischaemic encephalopathy: data from a randomised trial of therapeutic hypothermia. Arch Dis Child Fetal

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 Amit Gupta

WHITE MATTER INTEGRITY AT SCHOOL AGE IN CHILDREN FROM THE DRIFT RANDOMISED CONTROLLED TRIAL OF NEONATAL POST HAEMORRHAGIC VENTRICULAR DILATATION

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)

¹University of Bristol, Bristol, ²CRICBristol, ³St. Michael's Hospital UHBristol NHS Trust.

Introduction (*include hypothesis*)

Drainage, Irrigation, and Fibrinolytic Therapy (DRIFT) was developed to improve the neurodevelopmental outcomes of preterm infants with Intraventricular Haemorrhage (IVH) and post-haemorrhagic ventricular dilatation (PHVD), a complication which causes significant neurodisability in survivors. Our aim was to identify and characterise white matter asymmetries between patients given DRIFT treatment compared to those with standard treatment using Tract Based Spatial Statistics (TBSS) on Diffusion Tensor Imaging (DTI) data and brain volume differences in grey and white matter from high resolution MRI scans performed at 10-year follow-up.

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

TBSS voxelwise statistical comparison of fractional anisotropy (FA) was used to compare mean regional FA and left-right hemispheric asymmetries between the two treatment groups. Two-sample t-tests were performed for groupwise contrasts with statistical significance set at $p < 0.05$, corrected for multiple comparisons. To examine differences in grey and white matter tissue volumes, Voxel Based Morphometry (VBM) was performed and Two-sample t-tests utilised to compare treatment groups. Of the patients scanned at 10 years post treatment ($n=28$), 22 were able to complete the Diffusion Tensor Imaging (DTI) sequence. Standard Treatment Group $n=9$, DRIFT Treatment Group $n=13$.

Results

TBSS symmetry analysis L>R showed the DRIFT treatment group to have statistically significant differences in homotopic white matter tracts across hemispheres compared to the Standard treatment group. Tracts showing greater symmetry in the DRIFT vs Standard treatment groups included the anterior thalamic radiation, forceps minor, superior and inferior longitudinal fasciculus and corticospinal tract (all $p < 0.05$ corrected). No significant differences in volume were found in the VBM analysis in either white or grey matter tissue between the two treatment groups at $p < 0.05$ corrected.

Conclusions

The significant hemisphere asymmetries between groups suggest that in specific white matter tracts the DRIFT treatment group has better hemispheric symmetry in white matter connectivity compared to the standard treatment group (Smith et al 2007). Further research is needed to fully understand the implications of regional white matter asymmetries between treatment groups and whether this relates to functional outcomes.

References (*include acknowledgement here if appropriate*)

Smith et al. Acquisition and voxelwise analysis of multi-subject diffusion data with tract-based spatial statistics. Nat Protoc. 2007;2(3):499-503.
This project was funded by the National Institute for Health Research HTA 12/35/61. NHS Research Ethics approval was granted.

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 K. Luyt

STRUCTURAL CONNECTIVITY MEASURES CORRELATE WITH LANGUAGE OUTCOMES IN PRETERM INFANTS AT 2 YEARS OF AGE.

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

Gemma Sullivan, Paola Galdi, Manuel Blesa, Emma Telford, Sarah Sparrow, Margaret Evans, Alan Quigley, Scott Semple, Mark Bastin, James P. Boardman

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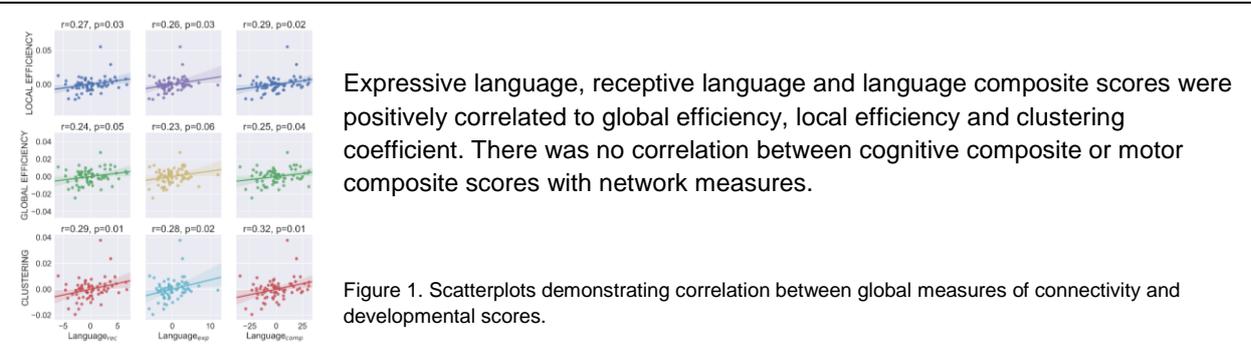
Introduction (include hypothesis)

Preterm birth is associated with altered white matter tract microstructure and dysmaturation of developing neural networks resulting in long term neurological, cognitive and behavioural impairments. Magnetic resonance imaging (MRI) markers allowing early identification of infants at risk of neurodevelopmental problems may enable targeted early intervention or provide an opportunity to study the effect of new therapies. *Hypothesis:* Global measures of structural connectivity are correlated with motor, language and cognitive outcomes in preterm infants at 2 years of age.

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

Participants: 73 preterm infants with mean PMA 29⁺⁰ weeks, range 23⁺¹ to 33⁺⁰. Ethical approval was obtained from the UK Research Ethics Committee. *MRI:* Structural and diffusion MRI were acquired at term-equivalent age. Connectomes were generated using the Melbourne Crib neonatal atlas¹ followed by tractography construction using BedpostX and ProbtrackX. Edges were weighted using fractional anisotropy (FA) and structural connectivity calculated using 5 network parameters²: Global efficiency (GE), local efficiency (LE), clustering coefficient (CC), modularity (Q) and small world propensity (SWP). *Development:* All participants had a neurodevelopmental assessment performed at a mean age of 24 months (range 23-28 months), corrected for prematurity, using the Bayley Scales of Infant and Toddler Development, Third edition (BSID-III). *Analysis:* Pearson's correlation was performed to identify relationships between network measures and Bayley scores following removal of the confounding effects of GA at birth, PMA at scan, birthweight, gender, chorioamnionitis and bronchopulmonary dysplasia using multiple regression.

Results



Conclusions

These findings suggest that global measures of network integration at term-equivalent age may be useful predictors of early language development in premature infants at 2 years of age.

References (include acknowledgement here if appropriate)

- Alexander B. et al. A new neonatal cortical and subcortical brain atlas: the Melbourne Children's Regional Infant Brain (M-CRIB) atlas. Neuroimage 2017.
 - Rubinov M., Sporns O. Complex network measures of brain connectivity: uses and interpretations. Neuroimage 2010.
- Acknowledgement: Thorsten Feiweier at Siemens Healthcare collaborated with Works-in-Progress Package for Advanced EPI Diffusion Imaging.

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: James P. Boardman

EFFICACY OF VAGINAL CERCLAGE IN WOMEN WITH PRIOR EMERGENCY CAESAREAN SECTION

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

A Glazewska-Hallin, M Hickland, J Carter, H Watson, L Story, A Shennan

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Department of Women and Children's Health, King's College London

Introduction (*include hypothesis*)

Preterm deliveries have multiple aetiologies and management is dependent on cause. A recent under-recognised association, likely to be causative, has been made to full dilatation Caesarean sections (FDCS). These carry a 6-fold increased risk of early premature birth and late miscarriage(1). 14% of women with this history are in the risk group (2), approximately 8000 women annually in the UK. Data is limited regarding efficacy of transvaginal cerclage (TVC) in this cohort and the risk following emergency Caesarean sections.

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

A retrospective data analysis of women attending preterm surveillance clinic at St Thomas' Hospital. Women who had a preterm birth or late miscarriage following a full dilatation Caesarean section and emergency Caesarean sections were identified. The control group comprised of women with a previous spontaneous preterm birth or late miscarriage with any mode of delivery. The primary outcome was delivery prior to 30 weeks gestation. A fisher's exact test was used to compare groups.

Results

189 women experienced a subsequent spontaneous preterm birth or late miscarriage following an emergency Caesarean of which 64 received a TVC. There were 942 controls, of which 154 received TVS and 5/154 delivered <30 weeks (3%). 19/54 women in the FDCS group received a vaginal cerclage in their third pregnancy (including both history and ultrasound indicated) and significantly more of these women delivered before 30 weeks compared to controls (53% vs 3%, $p < 0.0001$). In the emergency Caesarean group, 31/64 with a TVC delivered prior to 30 weeks, significantly less than controls (48% vs 3%, $p < 0.0001$).

Conclusions

Both first stage emergency Caesareans and FDCS increase the risk of subsequent preterm birth, with a high incidence of delivery prior to 30 weeks. There is a higher TVC failure rate in these women. Further research is necessary to elucidate if ultrasound or MRI can predict outcome. Both preventative and therapeutic measures need to be investigated in this cohort of women who are at risk of recurrent, early preterm birth in spite of management.

References (*include acknowledgement here if appropriate*)

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2. Watson HA, Carter J, David AL, Seed PT, Shennan AH. Full dilation cesarean section: a risk factor for recurrent second-trimester loss and preterm birth. Acta Obstet Gynecol Scand. 2017;96(9):1100-5.

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 Karen Luyt

REDUCED MATERNAL GLUCOCORTICOID CLEARANCE IS ASSOCIATED WITH HIGHER SERUM CORTISOL AND REDUCED OFFSPRING BIRTHWEIGHT

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*)

Glucocorticoids play a critical role in directing fetal maturation. High levels of maternal cortisol, measured in serum or saliva, are associated with offspring growth restriction and adverse neurodevelopment¹. After release from the adrenal gland most cortisol is metabolised and excreted in urine. We hypothesised that variation in this peripheral metabolism and excretion influences maternal serum cortisol levels, and fetal growth.

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

151 women with mean age 30.5 ± SD 5.0 years and BMI 27.6 ± 7.1 kg/m², performed 24 hour urine collections in the 2nd and 3rd trimesters at gestational age (GA) 17.3 ± 2.4 and 33.9 ± 1.2 weeks, respectively. Maternal serum was sampled at GA 16.7 ± 2.4 and 33.3 ± 1.1 weeks. 24 hour-total urinary glucocorticoid metabolites (TUG) were measured by gas chromatography triple quadrupole mass spectrometry (GC-MS/MS). Associations of log-transformed TUG with serum cortisol and birthweight Z-score were tested with Pearson's correlation and linear regression adjusting for potential confounders. Study approval was provided by the Institutional Review Boards of each of the Measurement of Maternal Stress (MOMS) study's 4 sites.

Results

During the 3rd trimester there was a negative correlation between TUG and serum cortisol ($r=-0.179$, $p=0.029$). 2nd trimester, 3rd trimester and mean TUG were all positively associated with offspring birthweight Z-score in adjusted and unadjusted models (Table 1).

2 nd Trimester TUG		3 rd Trimester TUG		Mean TUG	
Unadjusted	Adjusted model	Unadjusted	Adjusted model	Unadjusted	Adjusted model
$\beta=-.221^2$	$\beta=-.199^1$	$\beta=-.169^1$	$\beta=-.192^1$	$\beta=-.258^2$	$\beta=-.312^2$

Table 1. ¹ $p \leq 0.05$, ² $p \leq 0.01$ Adjusted model variables: Gestation urine samples collected, ethnicity, smoking, maternal age, pre-eclampsia, hypertension, diabetes, maternal BMI, parity

Conclusions

Reduced maternal urinary glucocorticoid excretion was associated with both increased serum cortisol levels and reduced offspring birthweight. Variation in peripheral metabolism and clearance of cortisol from maternal peripheral tissues may serve as a novel mechanism influencing fetal glucocorticoid exposure and somatic growth.

References (*include acknowledgement here if appropriate*)

1. Duthie L, Reynolds RM. Changes in the maternal hypothalamic-pituitary-adrenal axis in pregnancy and postpartum: influences on maternal and fetal outcomes. *Neuroendocrinology*. 2013;98(2):106-15.

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 James Boardman

Self Certificate of Attendance

Neonatal Society Spring Meeting
Royal Society of Medicine, London
15th March, 2019



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