ID: 129

TITLE: ULTRASOUND MEASUREMENTS OF INTRACRANIAL STRUCTURES IN GROWTH-RESTRICTED NEONATES WITH EVIDENCE OF FETAL REDISTRIBUTION

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CONTENT:

Fetal growth restriction (FGR) is an important cause of perinatal mortality and morbidity, and long-term neuro disabilities. Fetal circulatory redistribution is a common cause of delivery of the “at risk” FGR neonate. The impact of this “brain sparing” on corpus callosum, cerebellum and lateral ventricle measurements has not been well studied.

Aim: To compare corpus callosum, cerebellar, and ventricular measurements of FGR neonates with fetal redistribution (abnormal antenatal umbilical/middle cerebral artery Dopplers) with those of gestation-matched appropriately grown for age (AGA) neonates.

Prospective observational study conducted at a tertiary neonatal unit in Melbourne, Australia. Cranial ultrasound was done between D 1-3 of life in FGR (with fetal redistribution necessitating delivery) neonates born at a gestational age between 24 – 42 weeks, and gestation-matched AGA neonates. Measurements of different brain structures (Lateral ventricles (width and depth), corpus callosum (length, fastigium length, antero-posterior diameter of the genu, width of genu, body and splenium), and cerebellum (vermis height and antero-posterior diameter, transverse cerebellar diameter) and extra-axial space) were done in both groups of neonates and the measurements were subjected to statistical analysis.

Cranial ultrasounds on 20 FGR [mean (SD) gestation: 31.4 (3.1) weeks, mean (SD) weight 1205 (463) grams] and 20 AGA neonates [31.1 (3.0) weeks; 1667 (490) grams] were done. Corpus callosum length (mean ± SEM) was significantly decreased in FGR neonates [35.4 ± 0.91 vs. 37.9 ± 0.76 mm, p=0.01] as compared to AGA neonates, but corpus callosum fastigium length (mean ± SEM) was similar [40.37 ± 0.99 vs. 41.6 ± 0.93 mm, p=0.6]. Similarly, FGR neonates showed decreased transverse cerebellar diameter (mean ± SEM) [35.06 ± 1.09 vs. 37.49 ± 1.33 mm, p=0.03] as compared to AGA neonates, but cerebellar vermis height and antero-posterior diameter were comparable. Bilateral lateral ventricle volume, corpus callosum genu, body and splenium thickness and extra-axial space measurements were comparable between the groups.

 Corpus callosum and cerebellar measurements seem to be most affected in FGR neonates with fetal redistribution. This may have implications for their future neurodevelopmental outcomes.

COI: None declared
TITLE: ADVANCED MRI ANALYSIS TECHNIQUES TO STUDY BRAIN INJURY IN GROWTH RESTRICTED NEWBORN LAMBS

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CONTENT:

Fetal growth restriction (FGR) is a serious pregnancy complication associated with increased risk of perinatal morbidity and adverse neurodevelopment. Conventional brain imaging in the neonatal period is relatively insensitive for detection of subtle changes in brain microstructure in FGR infants. We examined whether advanced MRI analysis techniques can detect early neonatal brain injury caused by chronic hypoxia-induced fetal growth restriction in preterm lambs.

Background on lamb model: Surgery was undertaken in twin bearing pregnant ewes at 88 days gestation (term, 147 d) to induce FGR in one fetus. At 127 days gestation (~32 weeks human brain development), FGR and control (appropriate for gestational age, AGA) lambs were delivered by caesarean section, intubated, sedated and commenced on ventilation. (Reference: Malhotra A, et al. Neuropathology as a consequence of neonatal ventilation in premature growth restricted lambs. Am J Physiol Regul Integr Comp Physiol 2018 Dec; 315(6): R1183-1194)

Brain imaging was conducted within the first two hours of life using a 3T MRI (Siemens Skyra, Erlangen, Germany). T1 and T2 structural imaging, magnetic resonance spectroscopy (MRS), and diffusion MRI (dMRI) data were acquired. Advanced analysis techniques, including fixel-based analysis of 3-tissue constrained spherical deconvolution (CSD) of the dMRI data, were applied to compare brain scans from FGR and AGA lambs. Diffusion tensor imaging (DTI) modelling of dMRI included the following brain regions of interest (ROI): subcortical white matter, periventricular white matter, hippocampus, corpus callosum and thalamus. Lambs were euthanized immediately after the scans and brain histology was performed the regions of interest to confirm FGR related injury.

Six pairs of FGR and AGA lamb (body weight, mean(SD): 2.2(0.5) vs. 3.4(0.3) kg) brain scans were studied. Brain histology confirmed subtle white matter injury in FGR lambs. There were no differences observed between the groups in conventional T1, T2 or MRS brain data. Axial, mean and radial diffusivity and fractional anisotropy indices obtained from DTI modelling of the dMRI data also did not show any differences in any ROI. Fixel-based analysis of 3-tissue CSD revealed a decrease in fibre cross-section (FC, p<0.05) but not in fibre density or combined fibre density and cross-section (FD or FDC) in FGR vs. AGA lamb brains. The specific tracts that showed a decrease in FC were in the region of the periventricular white matter and hippocampus, and were associated with histological evidence of white matter loss, inflammatory cell infiltration and microbleeds in FGR lamb brains.

The neuropathology associated with FGR in neonatal preterm lambs is subtle and requires advanced MRI and tract-based analysis techniques for detection on imaging. Fixel-based analysis of 3-tissue CSD offers new avenues to measure tract-specific differences in brain microstructure, not seen on conventional imaging or voxel-based analysis. These findings may inform analysis of similar brain pathology in neonatal infants.
COI: None declared
ID: 260  
TITLE: PERINATAL HYPOXIC-ISCHEMIC INJURY OF THE CEREBELLUM: ANTEMORTEM DIFFUSION WEIGHTED IMAGING VERSUS POSTMORTEM HISTOLOGY  
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AFFILIATIONS: 1 Department of Neonatology, Wilhelmina Children’s Hospital, University Medical Centre Utrecht, University Utrecht, the Netherlands.  
2 Brain Centre Rudolf Magnus, University Utrecht, the Netherlands.  
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4 Department of Pathology, University Medical Centre Utrecht, University Utrecht, the Netherlands.  

CONTENT:  
Cerebellar injury is frequently seen in postmortem pathological examination in infants with severe hypoxic-ischemic encephalopathy (HIE), but is, in contrast to supratentorial damage, less visible on diffusion weighted imaging (DWI). The primary aim of this study was to investigate the correlation between the cerebellar apparent diffusion coefficient (ADC)-values on DWI and the extent of histological cerebellar injury in infants with HIE. The secondary aim was compare ADC-values in the cerebellum of infants with HIE to neonates without brain injury.  

In this retrospective study, (near-)term infants with HIE with postmortem autopsy and antemortem DWI within 7 days after birth (median 4) were included. ADC-values were measured in the cerebellar vermis, hemispheres and nucleus dentatus (ND) using Horos Imaging software. ADC-values were also measured in a group of neonates with congenital non-cardiac anomalies and normal postoperative MRI (range 3-13; median 7.5) without underlying syndromes. Mean ADC-values were compared using the Mann-Whitney-U test. Histological HLA-DR and CD68 stains of the cerebellar hemispheres, vermis and ND were binarized using ImageJ software. The mean CD68 and HLA-DR positive areas were calculated for these structures. The correlation between ADC-values and the CD68 and/or HLA-DR positive area was calculated.  

Thirty-three infants with HIE and 22 infants without brain injury were included. ADC-values in the cerebellar hemispheres were comparable between infants with HIE and the infants without brain injury. ADC-values in the vermis (HIE=786±114 x10-6mm2/s; controls=859±72 x10-6mm2/s; p=0.021) and ND (HIE=1004±152 x10-6mm2/s; controls=1142±79 x10-6mm2/s; p<0.001) were significantly lower in infants with HIE. There were no significant correlations between ADC-values and the CD68 or HLA-DR positive area in the cerebellum vermis, hemispheres or ND.  

Infants with HIE with lower ADC-values did not have more microglia activation and macrophage influx. ADC-values in the vermis and ND in patients with severe HIE were significantly lower than in controls. ADC-values in the cerebellar hemispheres were not decreased in infants with HIE. Hematoxylin and eosin stains are currently analysed to study Purkinje cell injury in HIE.  

COI: Floris Groenendaal is expert witness in cases of perinatal asphyxia, the other authors have no conflict of interest to declare.
ID: 384

TITLE: NEUROPROTECTIVE EFFECT OF REMOTE ISCHEMIC POSTCONDITIONING AND THERAPEUTIC HYPOTHERMIA IN A PIGLET MODEL

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CONTENT:

Therapeutic hypothermia (TH) is a safe and efficient treatment of neonates with hypoxic ischemic encephalopathy. However, TH only reduces part of the acquired brain damage and additional treatments are needed to improve outcome. Remote ischemic postconditioning (RIPC) has been shown to be neuroprotective in rats and piglets. It is unknown whether there is any additional neuroprotective effect when combining RIPC with TH.

A total of 33 piglets <12 hours of age were anesthetised. A global hypoxic-ischemic insult was induced by reducing FiO2 during a 45-minute period to achieve aEEG <7μV and a mean blood pressure <70% of baseline for at least 5 minutes. In total, 26 animals were randomized to TH+RIPC or TH while 7 animals were subjected to hypoxia only. RIPC was induced by occluding blood flow to both hind limbs for five minutes followed by five minutes of reperfusion in four cycles. The primary outcome was lactate/n-acetylaspartate-ratio measured by magnetic resonance spectroscopy (MRS) in the thalamus, white matter, frontal- and occipital cortex. Secondary outcomes were thalamic oedema, oxygenation, and perfusion measured by magnetic resonance imaging (MRI). MRS/MRI was performed at 6, 12, and 24 hours.

We present preliminary results from the first 24 animals subjected to TH vs. RIPC+TH. Insult severity was comparable in the two groups with respect to duration of aEEG suppression (median; 26.2 vs. 26.8 min.), duration of hypotension (median; 5.5 vs. 5.7 min.), and post-insult metabolic acidosis (median; pH 6.99 vs. 7.05). Three animals died in the TH+RIPC group and four died in the TH group. There was no difference in lactate/n-acetylaspartate-ratio in any of the four brain regions at any time point (Fig. 1A). Further, we found no difference between the two groups in MRI measures of intracellular oedema or oxygenation at any time point (Fig 1B).

These preliminary results showed no additional neuroprotective effect after adding RIPC to TH. Results from the last nine animals and measurements of cerebral perfusion are pending and will be presented at the conference.

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Figure 1. Magnetic resonance spectroscopy (A) and imaging data (B) from the first 24 animals at 6, 12, and 24 hours after the hypoxic insult. ADC; apparent diffusion coefficient. BOLD; Blood oxygenation level dependent. NAA; n-acetylaspartate. Data are median with interquartile range.

COI: None declared
**ID:** 422  
**TITLE:** EARLY CEREBRAL OXYGENATION AND ELECTROCEREBRAL ACTIVITY IN ANEMIC AND NON-ANEMIC TERM INFANTS WITH MODERATE TO SEVERE HYPOXIC-ISCHEMIC ENCEPHALOPATHY  
**AUTHORS:** Willemien S. Kalteren, BSc 1; Leanne de Vetten, MD 1; Hendrik J. ter Horst, MD PhD 1; Arend F. Bos, MD PhD 1; Elisabeth M.W. Kooi, MD PhD 1  
**AFFILIATIONS:** 1 Department of Pediatrics, Division of Neonatology, Beatrix Children’s Hospital, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands  

**CONTENT:**  
Perinatal anemia may lead to brain injury by impaired oxygen delivery, causing hypoxic-ischemic encephalopathy (HIE). Previously we found perinatal anemia in HIE to be associated with high mortality rates. Neurodevelopmental outcome (NDO) of survivors, however, appeared to be favorable compared with survivors from other causes for HIE. To understand the pathogenesis of these findings, we now aimed to explore the course and interrelation of cerebral oxygenation and electrocerebral activity during the first days after birth, comparing term infants with HIE due to perinatal anemia and term infants with HIE due to other causes.  
1 Kalteren WS et al., Neonatology, 2018.  

All HIE infants treated with therapeutic hypothermia (2010-2017) were retrospectively included. We measured cerebral tissue oxygen saturation (rcSO2), using near-infrared spectroscopy. We used amplitude-integrated electroencephalography (aEEG) to assess background patterns (BPs), sleep-wake cycling (SWC) and epileptic activity during the first 96 hours after birth. Burst suppression, continuous low voltage and flat trace were considered as abnormal. Additionally, cerebral fractional tissue oxygen extraction (cFTOE) was calculated. Anemic infants (initial Hb<7 mmol/L) were compared with non-anemic infants in both deceased and survived infants. We calculated odds ratios (ORs) to determine whether cFTOE and aEEG were associated with mortality.  

One-hundred-eighteen term infants were included of whom 24 were anemic at birth. In total 25 infants (21%) died (88% withdrawal of care). Out of the 24 anemic infants, nine (38%) died versus 16 from 94 (17%) non-anemic infants, p=0.03. Anemic infants had significantly lower rcSO2 and higher cFTOE during the first 48-hours than non-anemic infants (Figure 1). Twenty-one (88%) anemic infants showed abnormal aEEG BPs at some point, compared to 65% of the non-anemic group, p=0.03. SWC was present in six (25%) anemic infants, while 49 non-anemic infants (52%) showed SWC, p=0.03. Seizures were less common in anemic infants (33%) compared to non-anemic infants (55%), p=0.045. The OR for mortality of an abnormal aEEG BP at 12 hours after birth was 32.6 (4.11-258), p<0.01. In the group of survivors, anemic infants had lower rcSO2 and less seizures than non-anemic infants.  

Perinatal anemia in HIE infants is associated with lower cerebral oxygenation and more infants showing abnormal aEEG BPs, but less seizures. Abnormal aEEG BPs, whatever the cause of HIE, resulted in higher mortality risks. The lower rcSO2 in anemic infants was not associated with mortality, nor with seizure activity in survivors. Further studies are required to investigate whether these findings are associated with better NDOs.  

**IMAGES:**  
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**COI:** None declared
ID: 425

TITLE: THE ROLE OF NEUTROPHILS IN NEONATAL HYPOXIC-ISCHEMIC BRAIN INJURY

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AFFILIATIONS: Department of Paediatrics I, University Hospital Essen, Essen, Germany

CONTENT:

Neonatal encephalopathy caused by hypoxia-ischemia (HI) is a major cause of death and disability in newborns. Therapeutic hypothermia is the only recommended therapy. However the therapeutic window of 6 hours is very short. Infiltration of myeloid cells has been linked to worse outcome after neonatal HI, but the specific role of neutrophils as potential therapeutic target is still controversially discussed. The aim of the present study was to characterize the temporal and spatial dynamics of neutrophil infiltration followed by analysis of its functional role in the post-hypoxic disease phase through delayed neutrophil depletion.

Nine day old C57BL/6 mice were exposed to HI through ligation oft the right common carotid artery followed by 1 hour hypoxia (10% oxygen). Infiltration and activation of neutrophils was assessed by immunohistochemistry and flow cytometry 1, 3 and 7 days post HI, which was correlated to HI-induced neuronal loss. The functional role of neutrophils was evaluated by intraperitoneal (i.p.) injection of a neutrophil-depleting anti-Ly6G antibody (clone 1A8, 10 µg/g body weight). Depletion efficacy was determined in naive animals via flow cytometry 6, 12, 24 and 48 hours post injection. According to infiltration and depletion dynamics anti-Ly6G was injected 12 hours after HI followed by analysis of brain injury via histology and immunohistochemistry 36 hours later.

Analysis of cerebral neutrophil infiltration revealed a biphasic infiltration pattern peaking at 1 and 7 days after HI, with most pronounced infiltration in severely injured brain regions (e.g. hippocampus). The amount of activated CD86 positive neutrophils in the brain increased from 7% to 40% between 1 and 7 days after HI, contrasting results from the blood where less than 5% of activated neutrophils were determined up day 7 after HI. Efficacy of neutrophil infiltration by i.p. injection of anti-Ly6G reached its maximum with 90% 12 hours after injection. Aiming to exactly hit the first infiltration peak of neutrophils 24 hours after HI, we initiated neutrophil depletion 12 hours post HI resulting in significantly reduced hippocampal tissue loss and cellular degeneration.

These data suggest a detrimental role of acute cerebral neutrophil infiltration in neonatal HI. Importantly, the therapeutic time window seems larger than the only available therapy HT. Thus, inhibition of neutrophil infiltration by therapeutic pharmacological approaches might present a novel therapeutic option in addition or as alternative to HT.

COI: None declared
ID: 470

TITLE: KEY FEATURES OF THE PRENATAL FUNCTIONAL CONNECTOME

AUTHORS: Elise Turk a,b,c; Manon J.N.L. Benders a,b; Roel de Heus b; Arie Franx b; Moriah E. Thomason d,e,; Martijn P. van den Heuvel f

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CONTENT:

The functional connectome is a complex network of interconnected communicating brain regions. Network development is governed by biological rules to make a trade-off between neural wiring cost and efficiency, resulting in small world topology to balance out efficient global communication and local organization. The last stages of pregnancy are a critical phase in brain development, and emerging evidence supports the notion that functional connectome formation and re-organization already starts as early as the second trimester. We aim to identify which first principles of functional connectome organization are already developed in utero.

A sample of 105 women participated in fetal resting-state fMRI studies during pregnancy (fetal gestational age between 20 and 40 weeks) at Wayne State University, Detroit, MI. Functional connectivity was inferred by measuring fMRI signal covariance across cortical regions. Brain regions were selected using a special made version of the Freesurfer’s Desikan Killiany atlas constructed that was manually fine-tuned on a 32-week preterm neonatal brain template. Group-based and individual graph analysis and permutation testing were used to analyze weighted network characteristics. For a better interpretation of common functional resting-state networks we examined the overlap with the adult resting-state functional connectome.

We identified efficient network features including high clustering (1.20 times higher than in random networks, p < 0.001), short path length (1.14 times higher than random networks, p < 0.001), and small-world index higher than 1 (1.05 times higher than random networks, p < 0.001). Rich club hubs can already be pointed out and have widely distributed communication paths across the cortex. We also identified an overlap of 61.67% (Mantel test p < 0.001) between the fetal and adult network.

Within the fetal brain, we observe efficient functional dynamics, such as small world topology and proto-networks of generally known functional modules, network structures that are known to be key features of the adult connectome. Mapping and understanding the healthy fetal functional connectome may bring opportunities for early detection of functional alterations of the vulnerable developing brain.

COI: None declared
**ID:** 536  
**TITLE:** SEX DEPENDENT CRP RESPONSE IN COOLED INFANTS WITH ADVERSE OUTCOME FOLLOWING NEONATAL ENCEPHALOPATHY  
**AUTHORS:** Thomas Robb 1; Hemmen Sabir 2; Marianne Thoresen 1; Ela Chakkarapani 1  
**AFFILIATIONS:** 1 Dept of Neonatology, St Michael’s Hospital, University of Bristol, Bristol, United Kingdom  
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**CONTENT:**

Hypoxic-ischaemic brain injury results in cellular inflammation. Cytokine responses are increased in infants with adverse outcome (death or disability), compared to infants with good outcome, following cooling for neonatal encephalopathy (NE). However, the relationship between adverse outcome and clinically used inflammatory markers; C-reactive protein (CRP), white blood cell count (WBC) and neutrophil count is not known. Furthermore, sex and risk factors for chorioamnionitis (rf-chorio) may influence inflammatory profiles. Therefore, we investigated whether clinical outcome, sex and rf-chorio were associated with the temporal course of inflammatory markers in infants cooled for NE.

Of 225 infants cooled for NE between 2006-2017 in a single centre, 39 were excluded due to lack of data, or additional diagnoses accounting for NE. In 186 infants (106 male), we recorded data on survival, sex, birthweight, Apgar10min, worst pH within 1 hour of life, meconium aspiration, rf-chorio (prolonged rupture of membranes >18hours, maternal fever >38°C, group B streptococcus vaginal colonisation), and CRP, WBC and neutrophil count 12 hourly until 168 hours (end of rewarming period). High CRP response was defined as median CRP(0-168hours) > 10mg/L. Bayley-III assessment was performed at 18–22 months. Adverse outcome was defined as death or Bayley-III cognitive/language composite score <85, or cerebral palsy (Gross Motor Function Score 3-5) or severe hearing/visual impairment.

Of 186 infants, 11 died and 157 underwent Bayley examination. 44/186 infants had adverse outcome. In the favourable outcome group, infants with rf-chorio had higher CRP values compared to infants without rf-chorio (fig 1A). CRP values were higher in infants with adverse outcome compared to infants with favourable outcome (fig 1B). In the adverse outcome group, females had a significantly lower CRP (fig 1C) and higher WBC and neutrophil count compared to males. In the adverse outcome group, females had significantly lower median CRP values ($\beta$: -29.2 mg/L, 95%CI: -48.1, -10.3), lower maximum CRP ($\beta$: -38.5 mg/L, 95%CI: -67.2, -9.7) and a delay in reaching the maximum CRP value ($\beta$:18.6h, 95%CI:5.0, 32.2) independent of confounders. Logistic regression showed that in infants with high CRP response, male gender was significantly associated with adverse outcome (OR: 2.8, 95% CI 1.0, 7.5).

CRP response in newborns with adverse outcome following cooling for NE was found to be sex dependent. Females with adverse outcome had a lower CRP and higher white blood cell count response compared to males, independent of clinical risk factors for chorioamnionitis or severity of NE.

**IMAGES:**
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**COI:** None declared
ID: 572
TITLE: THE NEONATAL PRETERM BRAIN: A CONNECTOME ANALYSIS
AUTHORS: Joana Sa de Almeida 1; Serafeim Loukas 1,2; Lara Lordier 1; Alexandra Adam-Darque 1; François Lazeyras 3; Petra Hüppi 1
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CONTENT:

Premature birth exposes the maturing brain to environmental stressors during a key period of development. Preterm infants have been shown to evidence later neurodevelopmental impairments, which might have their origin in structural brain alterations, englobing altered brain connectivity already present in the newborn period. Diffusion-weighted imaging is a non-invasive MRI method that allows in vivo visualization and quantification of white matter microstructure and structural connectivity. Using a whole-brain connectome analysis approach, we aimed to study the impact of prematurity on neonatal brain structural network organization.

13 full-term (FT) and 24 very preterm newborns (VPT) at term age underwent an MRI exam comprising T2-weighted and Diffusion-weighted image acquisitions. T2-weighted brain volumes were segmented and cortical brain parcellation was obtained by non-linear registration of ALL neonatal atlas propagated to each subject space. Structural networks were constructed using Mrtrix3 anatomically-constrained tractography with spherical-deconvolution algorithm and weighted per number of streamlines counts (SCw), fractional anisotropy (FAw) or SCw masked by FA (threshold 0.1) (SC*FAw). Graph analysis and network connectivity strength statistical comparison using FDR were performed to compare brain network organization of premature vs full-term newborns.

Graph analysis revealed that both FT and VPT infants’ brain networks presented a typical small-world organization. We identified 9 hubs in FT and 14 in VPT infants, with similar regions between both groups, mostly in basal ganglia, cingulate, insula and precuneus. In comparison to FT, VPT infants’ networks presented an increased characteristic path length, reduced global efficiency, reduced average closeness centrality and reduced nodal strength in 10 nodes, mostly located in frontal but also limbic and subcortical regions (Fig. 1A, 1B).

Statistical comparison of connectivity strength between groups, using FDR analysis, revealed that, in comparison to FT, VPT infants presented 66 networks with significantly decreased connectivity strength, englobing mainly cortico-cortical and cortico-subcortical intra-hemispheric connections mostly in frontal and limbic and temporal regions (Fig. 1C).

Results show a preserved hallmark organization of the human brain connectome in both FT and VPT infants at term. VPT infants’ structural networks have a less optimal topological organization, resulting in a global reduced capacity to integrate information across brain regions and evidence alterations in subnetwork structural maturity mainly in frontal-subcortical and limbic networks.

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Fig.1. – A: 54 nodes with diminished closeness centrality in VPT infants in comparison to FT; B: 10 nodes with diminished nodal strength in VPT infants in comparison to FT. C: Representation of the 66 connections presenting diminished
connectivity strength in VPT in comparison to FT infants, both at term age. Nodes are color coded representing the degree, from yellow (low degree) to red (high degree) colour range. For abbreviations, consult UNC Infant 0-1-2 atlases online documentation.

COI: None declared
**ID:** 658  
**TITLE:** CORRELATION OF VALIDATED MRI SCORING SYSTEMS IN NEONATAL ENCEPHALOPATHY  
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8. Our Lady’s Children’s Hospital Crumlin, Ireland  

**CONTENT:**

Predicting long term outcomes in neonatal encephalopathy (NE) remains challenging. Magnetic Resonance Imaging (MRI) is the gold standard of neuroimaging that best defines the nature and extent of brain injury in NE. There are a number of different validated MRI brain scoring systems to predict long term outcome in neonatal brain injury at term. The scoring systems have different levels of complexity and detail. The different patterns of injury seen on MRI have been correlated to neurodevelopmental outcome. These scoring systems have never been compared and it is unclear if any is superior.

Infants with NE, Sarnat Grade II and III, (n=35) were prospectively recruited into an observational study. All underwent therapeutic hypothermia (TH) and had early MRI scan (mean (SD) 8.9 (4.2) days). The MRI scans were scored by paediatric radiologists, blinded to patient outcome using three validated scoring systems – Barkovich, NICHD and de Vries. The relationships between the scoring systems were assessed using the Spearman rank correlation to assess the strength of association between them.

Adequate MRI images to complete assessment by all scoring systems were available for 31 patients. A high proportion of patients had normal scans using all 3 scoring systems – 13/31 Barkovich (13/31), NICHD (13/31) and de Vries (12/31) in keeping with previous validation studies of these scoring systems. There was a high level of correlation between all scoring systems. The strength of association between NICHD and Barkovich scores measured by Spearman rank correlation (SRC) was 0.9303 with a 95% confidence interval (95% CI) of 0.86 to 0.97 (Figure 1). Similarly the strength of association between de Vries and Barkovich scores measured by SRC was 0.93 with 95% CI of 0.86 to 0.97. The strongest correlation found was between de Vries and NICHD scores, with a SRC of 0.96 and a 95% CI of 0.92 to 0.98. The p values for each comparison was <0.001.

There is high correlation between each of the scoring systems. They vary in complexity and consequently level of time and detail required to complete each one. Our study suggests that the Barkovich scoring system that requires the least time resource is as informative as the others. Correlation between the MRI scoring systems and with the infants neurodevelopment will be done when infants are aged 2.

**IMAGES:**  
[https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=1d9c4d07d6f66f00ad236756accf562-MjAxOS0wNSM1Y2UyNjY2Y2IzNWQ3](https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=1d9c4d07d6f66f00ad236756accf562-MjAxOS0wNSM1Y2UyNjY2Y2IzNWQ3)

Figure 1. Relationship between MRI brain predictive scoring systems in NE. Figure 1a. Relationship between NICHD and Barkovich Score. A significant correlation was observed by the Spearman rank correlation (r=0.93, 95% CI 0.86-0.97, p<0.001). 1b. Correlation between de Vries and Barkovich Score. A significant correlation was observed by the Spearman rank correlation (r=0.96, 95% CI 0.92-0.98, p<0.001).
rank correlation ($r=0.93, 95\% \text{ CI } 0.86-0.97, p<0.001$). 1c. Correlation between de Vries and NICHD Score. A significant correlation was observed by the Spearman rank correlation ($r=0.96, 95\% \text{ CI } 0.92-0.98, p<0.001$).

COI: nil
**ID:** 660  
**TITLE:** QUANTITATIVE EEG TO DETECT INTRA-VENTRICULAR HAEMORRHAGE IN VERY PRETERM INFANTS  
**AUTHORS:** John M. O’Toole 1,2; Clodagh Walsh 3; Daragh Finn 1,4; Geraldine B. Boylan 1,2; Eugene M. Dempsey 1,2  
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**CONTENT:**

Postnatal adaption to extra-uterine life for preterm infants presents many challenges. Up to 1 in 3 infants born <32 weeks of gestation may develop brain injuries, such as intra-ventricular haemorrhage (IVH). We aim to determine if quantitative analysis of the EEG, coupled with machine learning algorithms, can detect the presence of IVH on day one.

Continuous EEG was recorded within hours after birth for infants born <32 weeks of gestation. EEG epochs of 1-hour were pruned at 6 and 12 hours after birth. Epochs with poor signal quality were rejected from further analysis. A common channel to all EEG records, C3–C4, was analysed with quantitative EEG (qEEG). First, an automated method removed segments of the EEG distorted by artefacts. Second, a set of qEEG features were then extracted; these features included spectral power, range-EEG, and inter-burst intervals. Cranial ultrasound was performed within 48 hours of birth to determine the presence of IVH. qEEG features were combined to detect IVH (any grade) using a gradient-boosting machine. A leave-one-baby-out cross-validation scheme was used for training and testing.

Forty EEG epochs were available at the 6-hour time point and 43 were available at the 12-hour time point. Fourteen out of the 43 infants developed IVH. Preliminary analysis showed that relative spectral power at the 6-hour time point—with frequency bands 0.5–3 Hz, 3–8 Hz, 8–15 Hz, and 15–30 Hz—as the best-performing feature, with a maximum area under the receiver operator characteristic (AUC) of 0.72 (95% confidence interval, CI: 0.55–0.88). Cross-validation testing results for combining the 4 features of relative spectral power over the 2 time points yielded an AUC of 0.90 (95% CI: 0.80–0.99).

Machine learning methods using qEEG can detect IVH within 12 hours of birth. Automated analysis of the EEG could enable rapid identification of IVH and direct timely interventions to ensure the best possible outcomes for this high-risk population.

**COI:** None declared
ID: 682

**TITLE:** EARLY PREDICTIVE BIOMAKERS FOR GRADE AND SEIZURES IN NEONATAL ENCEPHALOPATHY

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**CONTENT:**

Hypoxic-Ischaemic Encephalopathy (HIE), is a major cause of morbidity and mortality worldwide. One of the challenges we face today is predicting as early as possible the degree of the brain injury (HIE grade) and the risk of seizures after perinatal asphyxia. Clinical examination is often used to guide therapeutic intervention, however, an infant’s condition at birth does not always correlate well with the degree of the injury, nor with the risk for seizures.

The aim of our study was to assess the ability of a combination of early biomarkers to predict HIE grade and the development of EEG confirmed neonatal seizures. Predictive ability was examined using machine learning techniques.

This was a secondary data analysis from two European multicentre cohort studies (BiHiVe/ANSeR 1 and ANSeR 2 studies). Infants born >36 weeks gestational age (GA), needing continuous EEG monitoring for clinical concerns were included. Infants with a diagnosis of clinical and electrographic HIE were included in this analysis. All grades of HIE were included. All EEG recordings were assessed by a clinical neurophysiologist for grade of HIE and presence of seizures. The early features used for the analysis were: GA, birth weight (BW), occurrence of intrapartum complications, Apgar at 1, and 5 minutes, lowest cord pH, post resuscitation pH, base deficit and lactate, most intensive level of resuscitation at birth. Logistic regression was performed with repeated 10-fold cross validation.

266 infants with HIE were included in this analysis, 31.2% mild, 46.2% moderate and 21.1% severe. Mean (SD) GA was 40.05 ± 1.30 weeks, BW 3522.46 ± 601.03g, male:female ratio = 59.4%:40.6%. Mean Apgar scores were 2 and 4, at 1 and 5 minutes respectively, mean (SD) cord pH 7.03 ± 0.19, 63.2% needing PPV at 10 minutes; 79.3% received therapeutic hypothermia, 34.2% had electrographic seizures with a total seizure burden (TSB) 121.48 ± 130.26. HIE grade prediction was done using data from 254 infants with an overall accuracy (95%CI) of 0.54 (0.44 – 0.64). Seizures occurred in 131 infants (49.2%). After looking at the predictive ability of each feature individually, the best prediction was achieved with a combination of Apgar score at 5 minutes with the value of the post resuscitation lactate, which gave a PPV 67.57%, NPV 76.99%, and AUROC (95% CI) 0.7269 (0.66-0.80).

Our study shows that early clinical markers for neonatal encephalopathy are not reliable predictors of the grade of encephalopathy. A combination of these clinical markers improved the prediction of seizures, compared with individual feature prediction, but are not robust enough to guide treatment. Additional predictive power may require additional physiological or biochemical markers.

**COI:** None declared
ID: 835

**TITLE:** ALTERATIONS IN UMBILICAL CORD BLOOD MESSENGER RNA EXPRESSION IN NEONATAL HYPOXIC-ISCHAEMIC ENCEPHALOPATHY AND LONG-TERM OUTCOME

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**CONTENT:**

Hypoxic-ischaemic encephalopathy (HIE) remains an important cause of neonatal death and long-term neurological disability. It remains challenging to classify infants eligible for therapeutic hypothermia (TH) within the short postnatal therapeutic time window of 6 hours. No objective and robust biological marker is available in the clinical setting. The purpose of this study was to explore the predicted downstream messenger RNA (mRNA) targets of validated microRNA in the whole blood across our two independent BiHiVE cohorts and to assess their ability to predict grade of HIE and neurodevelopmental outcome.

This study included two cohorts. The discovery cohort recruited full-term infants with PA at birth to the BiHiVE1 study in Cork, Ireland (2009-2011). Encephalopathy grade was defined using early EEG and Sarnat score. The BiHiVE2 multi-centre validation study (2013-2015) recruited full-term infants in Cork and Karolinska Huddinge, Sweden, the study recruited infants with PA along with healthy control infants using identical recruitment criteria to BiHiVE1. Umbilical cord blood was processed and biobanked in Tempus tubes at delivery. Infants were assigned a modified Sarnat score at 24 hours. Candidate mFZD4 and mNFAT5 were measured using quantitative real-time polymerase chain reaction. The outcome was assessed at 2-3 years using the Bayley Scales of Infant Development III.

126 infants were included in the analysis. BiHiVE1 included 55 infants(controls n = 16, PA n = 19, HIE n = 20) and BiHiVE2 included 71 infants(controls n=22, PA n=25, HIE n=24). Both cohorts had a mean age = 40 wks[IQR = 39-41 wks] and included 82 males/44 females. In HIE severity, mFZD4 levels were increased in severe HIE(RQ = 2.98 (IQR = 2.23-3.68)) vs both moderate HIE (1.05 (0.81-1.20)), P = 0.003, and mild HIE(0.88 (0.46-1.37)), P = 0.004. Neurodevelopmental outcome was available in 56 infants. mNFAT5 levels were increased in severely abnormal(1.26 (1.17-1.39)) vs normal outcome(0.97 (0.83-1.24)), P = 0.036, and in severely abnormal(1.26 (1.17-1.39)) vs mildly abnormal outcome(0.96 (0.80-1.06)), P = 0.013. mFZD4 levels were increased in severely abnormal(2.51 (1.60-3.56)) vs mildly abnormal outcome(0.97 (0.75-1.34)), P = 0.026 and normal outcome(0.74 (0.48-1.49)), P = 0.004.

Altered mFZD4 expression was observed in umbilical cord whole blood of neonates with severe HIE; both mNFAT5 and mFZD4 expression were increased in infants with a severely abnormal outcome at 2-3 years. These mRNA could aid current measures as early objective prognostic markers of HIE severity at delivery.

**COI:** None declared
ID: 878

TITLE: ULTRA-HIGH FIELD MAGNETIC RESONANCE IMAGING: SAFETY AND FEASIBILITY IN NEONATES.

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CONTENT:

A high number of neonates admitted to the NICU is at risk of brain injury. Cerebral MRI is the gold standard to assess brain injury and maturation, and to predict long-term neurodevelopmental outcome. Currently, in neonates MRIs are performed with a magnetic field strength of 3 Tesla (T). In adults however, a growing number of studies have shown the added diagnostic value of 7T MRI including improved quality of arterial spin labelling (ASL), susceptibility weighted imaging (SWI) and magnetic resonance spectroscopy (MRS). The aim of the study is to investigate the safety of 7T imaging in neonates and to assess the feasibility of obtaining good quality images at 7T.

In this prospective study, 5 of the planned 20 infants have been examined. Clinically stable infants can be included if they have a clinical indication for MRI between term (equivalent) age and 3 months of (corrected) age. They will undergo 7T MRI immediately after their routine 3T MRI scan (Philips, Best, the Netherlands). Prior to the study, power deposition (as quantified by the specific absorption rate (SAR)) was simulated in a baby model. Safety will be determined by measuring the infant’s vital parameters, temperature and comfort scales before, during/between and after MRI. Since this is the first time that 7T MRI will be performed in neonates, the 7T scan protocols will be developed and optimized whilst scanning the first patients.

The global SAR and peak local SAR levels did not exceed the SAR levels in the adult head for the same settings. Scanning at maximum permissible SAR for normal operation, results in an average SAR deposition of 0.94 W/kg in the baby model in centre position. So far, five preterm born infants were scanned at term equivalent age. No major adverse events occurred and the vital parameters and comfort scales were not statistically different before, during and after 3T and 7T MRI scans. Importantly, no increase in temperature was observed. It was feasible to obtain good quality imaging at 7T. SWI showed better visualisation of the deep venous circulation (Figure 1). Proton MRS showed additional metabolite peaks at 7T compared to 3T, such as N-acetyl aspartyl glutamate. Phase contrast angiography and T2-weighted imaging were of comparable quality, T1-weighted imaging still needs to be improved.

7T MRI was demonstrated to be safe in the first five neonates scanned at term equivalent age with no major adverse events. It was feasible to obtain good quality proton MRS and SWI which provided additional information at 7T. In the following months more neonates will be included whilst further improving the protocol. Demonstration of safety and feasibility in neonates paves the way for larger cohort studies.
Figure 1. A: SWI image at 3T MRI in a preterm born neonate at term equivalent age. B: SWI image of the same patient at 7T MRI. At the 7T MRI more details of the deep venous circulation are visible.

**COI:** Fredy Visser is as well an employee of the UMC Utrecht as of Philips. The other authors have no conflict of interest to declare.
ID: 902

**TITLE:** ELEVATED SERUM INTERLEUKIN-10 IS ASSOCIATED WITH INCREASED SEVERITY OF ENCEPHALOPATHY AND ADVERSE 2-YEAR OUTCOMES IN UGANDAN INFANTS WITH NEONATAL ENCEPHALOPATHY

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**CONTENT:**

Traditional biomarkers that predict neurodevelopmental outcome in neonatal encephalopathy (NE) are not widely available in low-income countries. Cytokine levels predict outcome in NE, however studies have focussed on infants in high income settings and are limited to small numbers, excluding those with co-existing infection. Infection and inflammation are independent risk factors for NE in Ugandan infants[1]. In this cohort, we aimed to characterise the cytokine profile that predicts longer-term outcomes. We hypothesised that IL10 levels predict NE outcome, based on findings in a hypoxia-ischaemia piglet model[2].


Infants were recruited to the ABAaNA study investigating risk factors for[1], and outcomes from NE at Mulago Hospital, Uganda. Serum IL1α, IL6, IL8, IL10, TNFα and VEGF were measured at <36h in 159 NE and 157 non-NE infants. NE severity was graded (Sarnat score). Infants were assessed at 2 years using Griffiths Mental Developmental Scales II and Hammersmith Infant Neuropathological Examination(HINE). Adverse outcome included death, Griffiths developmental quotient <70, HiNE<67 or cerebral palsy.

Cytokines for NE and non-NE infants were compared. The association between cytokines, NE severity and 2-year outcome were assessed using Kruskal Wallis and Mann Whitney U. Logistic regression assessed ability of cytokines to predict poor outcome, adjusting for neonatal bacteraemia, sex and sample time.

In NE infants, 91% had moderate-severe encephalopathy and 59% had adverse 2-year outcomes. NE was associated with higher maternal c-reactive protein(CRP) (>90thcentile OR 3.82 p97thcentile OR 4.19 p=0.03) and incidence of neonatal bacteraemia (OR 3.86, p=0.17) compared with controls.

Infants with NE had higher IL10 (median 6.7pg/ml (IQR 0.6-25) control 1.0 (IQR 0-3.2) p<0.001), lower TNF (median 5.2pg/ml (2.6-10) control 7.8 (4.2-15) p=0.001) and lower VEGF (median 92pg/ml (17-201) control 203 (82-367) p<0.001).

Higher IL10 was associated with increased NE severity (mild 0.1pg/ml (IQR 0-5.4) moderate 6.7 (IQR 1.1-24) severe 8.5 (IQR 1.3-30), p=0.01) and adverse 2-year outcomes (median difference +10.9pg/ml compared with good outcome group, p<0.01) (Figure). After adjusting for covariates, IL10 remained a significant predictor of poor outcome (aOR 2.4 p<0.01).

In Ugandan infants with NE, elevated serum IL10 on day 1 is associated with NE severity and is a significant predictor of adverse 2-year outcome. IL10 levels were elevated and TNF and VEGF were lower in NE compared to non-NE infants. These findings concur with pre-clinical piglet studies where IL10 at 24-48h correlates with injury assessed using magnetic resonance spectroscopy, and adds weight to the use of serum cytokines to predict NE outcomes.
Fig: Cytokine profile of infants with NE by severity of encephalopathy according to Sarnat Classification (A) and 2-year outcomes(B). Box and whisker plot showing median, 25th, 75th quartiles and range on log10 scale. Mann Whitney U or Kruskal Wallis *p<0.05 **p<0.01

COI: None declared
ID: 973

**TITLE:** THE IMPACT OF MAGNESIUM SULFATE-ENHANCED THERAPEUTIC HYPOTHERMIA ON SELECTED BIOCHEMICAL MARKERS OF ASPHYXIA IN NEONATES WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY.

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**CONTENT:**

In recent years therapeutic hypothermia has become a standard method of neonatal hypoxic-ischemic encephalopathy treatment. At present, research focuses on finding ways to increase the therapeutic effect of hypothermia. Magnesium sulfate is promising as a potentially neuroprotective drug. It is possible that magnesium sulfate, used together with therapeutic hypothermia, may enhance its beneficial effect. Magnesium sulfate is a very interesting option as a neuroprotective drug also because of its easy availability. The drug can be administered to the patient in the birth hospital while the neonate is being prepared for the transport to the center with therapeutic hypothermia.

Prospective RCT was conducted at three perinatal centers. Neonates born at ≥36 GA, with perinatal asphyxia and confirmed moderate or severe HIE were included to the study. All neonates were treated with therapeutic hypothermia (for 72 hours). Neonates in study group (TH+MG) received three doses of MgSO4 (250 mg/kg) as iv infusion in addition to therapeutic hypothermia. Serum Mg level was analyzed in the 1st, 2nd, 4th day of life, whereas S100B protein, ceruloplasmin, MDA and iron serum concentration were assessed in the 1st, 2nd, 6th day of life. All measurements in the blood samples (except the Mg and iron concentrations) were assessed in the central laboratory. For this purpose blood serum frozen at -70°C was sent by a special transport dedicated for bioassays under cooling conditions.

There were 37 study subjects in the control and 38 in the study group. No statistically significant differences according to demographic data and clinical characteristic between the groups were observed. The body weight (mean, ± SD) was 3173.8 ±590.5g and 3321.9±524.0g in the control and study group respectively. The GA amounted to 38.6; ±1.9, and 38.7 ±1.7 (control vs study group). In this study, 2-fold lower S100B concentrations were observed in subsequent days of treatment in group (TH+MG). Statistically significant difference was confirmed in S100B protein concentration in the 1 day of life; 9.38±11.98 vs 3.93±7.07ug/L (p-value 0.017), as well as at all the measured points considered together (S100B protein p-values 0.014). No significant differences in iron, ceruloplasmin and malondialdehyde concentrations were observed.

Magnesium sulfate is promising potentially neuroprotective drug. It is also possible that magnesium used together with therapeutic hypothermia may enhance its beneficial effect.

Herein reported twofold reduction of protein S100B serum concentration, although with only tendency for statistical significance, may encourage further research on neuroprotective properties of magnesium in newborns with hypoxic ischemic encephalopathy.

**IMAGES:**

https://www.eisevereverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=9609e1a0f2f2ddfbad145c56bce82ac-MjAxOS0wNSM1Y2UyNyMjY2ZDM4Yjkz

Comparison of biochemical markers between neonates treated with hypothermia or hypothermia combined with magnesium sulfate.
COI: None declared
ID: LATE BREAKER
TITLE: TWO-YEAR OUTCOMES OF THERAPEUTIC HYPOTHERMIA IN PERINATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY AT CHIANG MAI UNIVERSITY HOSPITAL
AUTHORS:
AFFILIATIONS:

CONTENT:

Two-year outcomes of therapeutic hypothermia in perinatal hypoxic-ischemic encephalopathy at Chiang Mai University Hospital
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Background: Therapeutic hypothermia (TH) is a standard treatment of moderate to severe hypoxic-ischemic encephalopathy, which is a consequence of perinatal asphyxia. The outcomes of TH in Thailand have never been reported.
Objective: To report clinical outcomes, including death, severe developmental delay, severe neurological impairment, severe hearing deficit and blindness at 2 years of age in perinatal hypoxic-ischemic encephalopathy (HIE) infants who underwent therapeutic hypothermia (TH) at Chiang Mai University (CMU) Hospital
Method: At 2 years of age, the eligible infants who admitted at the CMU Hospital during February 2014 and December 2016 were recruited. Developmental assessment was performed by a developmental pediatrician, using Bayley Scales of Infant Development (BSID-III), gross motor function was classified by gross motor classification scale (GMFCS). Hearing was evaluated by auditory brainstem response (ABR) and blindness was evaluated by a pediatrician or ophthalmologist. Demographic data and clinical course during TH were drawn from electronic medical records.
Results: Of which 23 eligible patients, 4 (17.4%) died before discharge. At 2 years of age, overall death rate was 31.5% (6/19) and death or severe disability was 58.8% (10/17). Among the survivors, 11 patients were followed at median age (IQR) of 27 (19) mo. Weight<P3, Height<P3 and OFC<P3 were 18.1% (2/11), 45.5% (5/11) and 71.4% (5/7), respectively. Severe developmental delayed (<-2SD), severe motor disability (GMSCF3-5), blindness and profound hearing loss were 36.4% (4/11), 36.4% (4/11), 27.3% (3/11), and 0% (0/8), respectively. The patients who died and/or had severe disabilities at 2 years of age had significantly higher blood lactate on day 3 of life than those who survive without severe disability. (5.2 vs .2.4 mmol/L, p=0.03)
Conclusion: TH for perinatal HIE infants reduced death and combined death and/or severe disability at 2 years of age. To enhance these outcomes, improving supportive care and augmenting therapeutic hypothermia with neuroprotective agent should be considered.
Keywords: hypoxic ischemic encephalopathy, perinatal asphyxia, therapeutic hypothermia, low-to middle-income country, death and severe disability
ID: LATE BREAKER
TITLE: MATERNAL LCPUFA PROFILE AND THEIR NEWBORN INFANTS’ MRI BRAIN VOLUMETRICS
AUTHORS:
AFFILIATIONS:

CONTENT:

Background: Links between maternal nutrition and the developing brain’s health is rapidly translating from bench to human clinical practice. This study is first showing a relationship between maternal prenatal blood essential fatty acid profile and their newborn infants’ brain volumes measured using brain magnetic resonance imaging (MRI) scan. We previously showed for the first time that brain specific long chain polyunsaturated fatty acids (LCPUFA) supplementation of pregnant women increased newborn total and sub-regional MRI-measured brain volumes, (Ogundipe et al; PLEFA 2018). Large mammalian study found that various brain regions were rich in LCPUFAs essential for human brain development, primarily specific omega-3 and omega-6 LCPUFA derived from maternal stores.

Methods: Hypothesis was that maternal LCPUFA status in early pregnancy correlates to newborn infants’ brain volumes measured on MRI scan. 300 pregnant women enrolled in triple blinded placebo RCT (FOSS trial) had maternal blood erythrocyte fatty acids taken at enrolment measured using FOLCH technique. Brain MRI scans performed at a neonatal MRI centre on 3-T Philips Achieva MRI system (Best, The Netherlands) used an eight-channel phased-array head coil on infants with parental consent. Pulse oximetry and full monitoring was undertaken throughout the MRI scan procedure with ear protection using mask and silicone-based putty earplugs. MRI scan images were analysed by a paediatric neuroradiologist. Maternal fatty acids levels were statistically correlated to the newborn brain MRI volumetrics. Statistical analyses utilised Pearson’s correlation co-efficient (r) analyses using SPSS and significance level taken at p <0.05.

Results: Eighty nine scans were analysed; 49 (57%) male. Gestation (r=0.82; p<0.0001), birthweight (r=0.67; p<0.0001), birth length (r=0.32; p=0.007), head circumference(r=0.40; p=0.001) and 5 minute Apgar scores (r=0.50; p<0.0001) all correlated positively with infant brain volumes on MRI. Higher essential brain fatty acids in maternal blood at booking correlated positively with their newborn infants’ MRI measured brain volumes (p <0.0001). Of note, maternal lipid markers of essential brain fatty acids deficiency correlated with the newborn infants brain MRI volumes with lower grey matter (p<0.0001) and also lower white matter volumes (p <0.0001).

Conclusions: This is the first study to show that maternal levels of the essential brain LCPUFAs in early pregnancy is related to newborn infants’ total and sub-regional brain volumes determined by MRI scan. Maternal LCPUFA status predicts anatomically measured brain size and better neonatal outcome measures.