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FUNCTIONAL CAPILLARY DENSITY IN THE FIRST MONTH OF LIFE IN PRETERM NEONATES

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Background: Orthogonal polarization spectral (OPS) imaging is a novel method to examine the microcirculation non-invasively.

Methods: Red blood cell velocity (RBC vel), vessel diameter (Diam) and functional capillary density (FCD) were measured daily in the first month of life on the upper arm in neonates with gestational age less than 30 weeks. OPS images were recorded on videotape and analysed off-line with the CapiScope program.

Results: In 25 preterm infants (median (95% CI): gestational age of 28 (26.18–27.58) weeks; birth weight 900 (807.9–992.8) g) Diam ranged from 7 to 24 μm, RBC vel from 171.8 to 726.3 μm/s with no significant change. RBC vel correlated with hemoglobin levels ($r^2 = 0.25$, 95% CI (0.14–0.74), $p = 0.0083$) and inversely with mean systolic blood pressure ($r^2 = 0.36$, 95% CI (-0.8 to -0.29), $p = 0.0009$). FCD decreased significantly from day 7 (mean 236.4 μm/s; 95% CI 218.5–254.2) to day 28 (mean 206.9 μm/s; 95% CI 190–223.3; $p = 0.0028$). FCD correlated directly with hemoglobin levels ($r^2 = 0.58$, 95% CI (0.54–0.89), $p < 0.001$). There was an inverse correlation between FCD and heart rate ($r^2 = 0.39$, 95% CI (-0.8 to -0.32), $p < 0.001$) and systolic blood pressure ($r^2 = 0.32$, 95% CI (-0.78 to -0.24), $p = 0.0021$). Clinical variables, such as blood pressure, heart rate or body temperature did not change significantly. Hemoglobin decreased significantly over time ($p < 0.0001$), which explains the concurrent decrease in FCD. Preterm neonates from 23 to 26 and from 28 to 30 weeks did not differ in RBC, Diam and FCD.

Conclusion: We have shown that tissue perfusion can be monitored reliably by OPS imaging in premature infants in the first month of life.

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EARLY QUANTITATIVE ELECTROENCEPHALOGRAPHIC MEASURES OF CONTINUITY ARE ASSOCIATED WITH NEURODEVELOPMENTAL OUTCOME AT 18 MONTHS IN PRETERM INFANTS

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Background Early outcome prediction for preterm infants is inadequate. Discontinuity on early conventional electroencephalography (EEG) is associated with poorer outcomes. However, the complexity of EEG interpretation has limited incorporation into routine clinical practice. Cotside EEG monitors are becoming increasingly available and some produce quantitative measures from the EEG to assist interpretation.

Aim To examine the ability of quantitative measures of continuity from cotside EEG recordings performed on preterm infants in the first four days after birth to predict neurodevelopmental outcome at 18 months.

Methods Preterm infants with birthweights <1500g had cotside EEG monitoring (research BRM, BrainZ Instruments Ltd, Auckland, New Zealand) within four days of birth. Sixty minute portions of EEG were analysed offline for quantitative continuity measures. Continuity was calculated as the percentage of each minute that the EEG amplitude was above a 10, 25 or 50μV threshold and left and right values averaged. Infants had a Bayley-II examination at 18 months chronological age. The relationships between continuity measures and mental/psychomotor developmental indices (MDI/PDI) were explored using simple linear regression. Significant associations were further tested using multiple regression taking into account gestation, birthweight Z score and age at EEG (hours).

Results Forty-four infants were studied with a median (range) gestation of 26(24–31)weeks and birthweight of 925(540–1360)grams. EEG recordings were performed at a median (range) of 26(3–92)hours after birth. Average continuity was related to PDI at each threshold (10μV r-squared=0.21, p=0.0018; 25μV r-squared=0.17, p=0.0048 and 50μV r-squared=0.16, p=0.0067) and to MDI at the 10 and 25μV thresholds (r-squared=0.19, p=0.0032 and r-squared=0.10, p=0.04 respectively). In multiple linear regression analyses continuity at the 10μV threshold remained an independent predictor of PDI (r-squared=0.47, p=0.05) and MDI (r-squared=0.26, p=0.009).

Conclusion Cotside monitoring devices with automated quantitative neurophysiologic analyses may assist clinicians with earlier prediction of neurodevelopmental outcomes in preterm infants. MB is a consultant for BrainZ Instruments Ltd.

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COMPARISON OF QUANTITATIVE MEASURES AND NEUROPHYSIOLOGIST ASSESSMENT USING COTSIDE EEG MONITORS TO PREDICT OUTCOME IN PRETERM INFANTS

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Background Conventional electroencephalography (EEG) may help predict outcome in preterm infants, but requires specialist interpretation. Some cotside EEG devices provide quantitative analyses assisting non-specialists with interpretation.

Aim To compare quantitative measures of continuity with interpretation by a neurophysiologist using early cotside EEG recordings to predict outcome of preterm infants.

Methods In infants <32 weeks gestation 60 minute epochs of EEG recorded using research BRM cotside monitors (BrainZ Instruments Ltd, Auckland, New Zealand) were analysed for continuity (percentage of each minute with EEG amplitude >10μV) and categorised as normal (100%, 62% of cohort), moderate (80–99%) or low (<80%, lowest 10% of cohort). The same portion of EEG was graded by a neurophysiologist, blinded to infant outcome, as 'normal' or 'abnormal' using interburst interval and seizure activity. Surviving infants had Bayley-II examinations at 18 months. Outcome was 'poor' if the infant died or had a Mental or Psychomotor Developmental Index (MDI/PDI) <70, 'moderate' if MDI or PDI=70–84, and 'normal' if MDI and PDI>=85.

Results Analyses were performed for 29 infants with median (range) gestation at delivery 26(24–31)weeks, birthweight 910(605–1250)grams and postnatal age at EEG 22(2–53)hours. Outcomes were 'poor' in 7 (3 died, 4 had PDI<70), 'moderate' in 8 and 'normal' in 14. Three infants with low continuity had 'poor' outcome. Moderate continuity was found in 2/7 infants with 'poor' outcome, 3/8 infants with 'moderate' outcome and 5/14 with 'normal' outcome. The remainder had normal continuity (Cramer's V=0.43, Chi-squared p=0.03). The neurophysiologist graded traces as abnormal in 6/7 infants with 'poor' outcome, 1/8 with 'moderate' and 0/14 with 'normal' outcome (Cramer's V=0.82, Chi-squared p<0.0001). Categorisation by continuity measures and neurophysiologist assessment were dissimilar, Chi-squared p=0.19.

Conclusion Both techniques offer some potential, but continuity measures performed less well than neurophysiologist interpretation in predicting outcome from early cotside EEG recordings. MB is a consultant for BrainZ Instruments Ltd.

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ECHOCARDIOGRAPHIC BLOOD FLOW MEASURES ARE ASSOCIATED WITH QUANTITATIVE EEG PARAMETERS IN PRETERM INFANTS IN THE FIRST 48 HOURS AFTER BIRTH

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Background Low superior vena caval (SVC) flow over the first 24hrs after preterm delivery is associated with adverse outcome at three years(1). Low spectral edge frequency (SEF) on early electroencephalography (EEG) recordings correlates with white matter injury on term MRI(2). However, the relationships between echocardiographic flow measures and EEG are unknown.

Aim To examine the relationships between echocardiographic flow measures and quantitative EEG parameters in the first 48hrs after birth in preterm infants.

Methods Infants <31 weeks gestation had echocardiographic measures of SVC flow, left and right ventricular output (LVO and RVO) at 5, 12, 24 and 48hrs after birth. SEF, median and minimum amplitude, and continuity (percentage of each minute with EEG amplitude >10, 25 or 50μV) were quantified on 60 minute segments of EEG recorded using the research BRM monitor (BrainZ Instruments Ltd, Auckland, NZ) immediately before or after echocardiography.

Results Forty infants with median (range) birthweight 945(510–1900)grams and gestation 27(24–30)weeks had paired measurements; at 5, 12, 24 and 48hrs in 24, 27, 30 and 31 infants respectively. At 12hrs RVO was related to minimum amplitude (r-squared=0.29, p=0.002) and median amplitude (r-squared=0.18, p=0.015). At 48hrs LVO was related to continuity at 25μV (r-squared=0.15, p= 0.018) and at 50μV (r-squared=0.18, p=0.01). Significant relationships remained after adjustment for gestation, birthweight Z-score and CRIB-2 scores for minimum amplitude at 12hrs (r-squared=0.53) and continuity at 25 and 50μV at 48hrs (both r-squared=0.3). At 24hrs 8 (27%) infants had low continuity at 10μV (continuity<100%). These infants had lower SVC flow (p=0.03) and LVO (p=0.003) at 5hrs and lower RVO at 12hrs (p=0.004) compared with those having 100% continuity at 10μV at 24hrs.

Conclusion Early echocardiographic measures of blood flow are related to quantitative EEG parameters from cotside monitoring in preterm infants over the first 48hrs after birth.

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CEREBRAL ALANINE INCREASES DURING THE EVOLUTION OF SECONDARY ENERGY FAILURE FOLLOWING TRANSIENT HYPOXIA-ISCHAEMIA IN NEWBORN BRAIN

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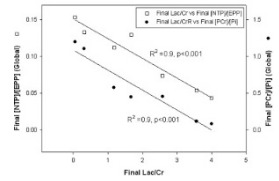
Background: Alanine (Ala), a nonessential amino acid, is present in normal brain at a concentration of ~0.5 mmol/kg. During acute hypoxia-ischaemia (HI) Ala increases due to decreased flux of pyruvate through the Krebs cycle and the activity of alanine transaminase (AAT). Brain Ala increases in proportion to the severity of HI and may be detected using proton (^{1}H) magnetic resonance spectroscopy (MRS).

Aim: To investigate relationships between the severity of secondary (delayed) energy failure (SEF) and late brain Ala metabolite ratios following transient cerebral HI in the newborn piglet.

Design/Methods: Seven newborn piglets (<24 hrs old) were studied under general anaesthesia (isoflurane & morphine) before, during and for up to 48 hours following transient HI (reversible bilateral carotid occlusion and 12% FiO2 for 45 min). Whole-brain pulse-acquire phosphorus (^{31}P; repetition time (TR) 10 s) and localised ^{1}H (PRESS, thalamic, echo time 270 ms, TR 5 s) MRS data were acquired serially before, during (^{31}P only), and following HI. Spectra were analysed using AMARES (^{31}P) and LCModel (^{1}H).

Results: In two piglets SEF was not observed. In the remaining 5 SEF ranged between mild and severe as quantified by delayed reductions in [phosphocreatine]/[inorganic phosphate] ([PCr]/[Pi]) and [nucleotide triphosphate]/[exchangeable high-energy phosphate pool] ([NTP]/[EPP]) and increases in lactate/total creatine (Lac/Cr).

Ala was only detected in the 5 SEF piglets. During SEF evolution we observed progressively increasing thalamic Ala/Cr and Lac/Cr. When the final measurements were compared both Lac/Cr and Ala/Cr separately showed inverse linear correlations with [NTP]/[EPP] and [PCr]/[Pi] (all $p<0.05$) (Figure 1).



Conclusions: Both Ala/Cr and Lac/Cr increased concomitant with the development and proportional to the severity of SEF. These observations are consistent with decreased pyruvate flux through the Krebs cycle and increased flux through lactate-dehydrogenase and AAT during the evolution of SEF leading to concomitant accumulation of Lac and Ala respectively.