Cerebral metabolite differences in adolescents with low birth weight. Assessment with In Vivo Proton MR Spectroscopy

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Introduction:

Very low birth weight children (VLBW) are especially at risk of later development problems, while infants born at term, small for gestational age (SGA), are also at some risk. The objective of this study was to evaluate possible differences in brain metabolites among VLBW and control adolescents.

Subjects and methods:

The study is part of a population based follow up at 14 years of age of VLBW and term SGA adolescents compared to controls (1, 2). 18 subjects from each group was randomly selected for the work presented here; control, birth weight ≥ 10th percentile for gestational age (10 girls/8 boys), SGA, birth weight ≤ 10th percentile for gestational age (11 girls/7 boys) and VLBW, birth weight≤1500 g (10 girls/8 boys). Proton in vivo MR spectroscopy was performed using a whole-body 1.5T system (Siemens Symphony). The volume was positioned in the left frontal lobe, containing mainly white matter. The size of the voxel was 1.5×1.5×2.5 cm. Acquisition was done by point-resolved spatially localized spectroscopy (PRESS, TE 135 ms, TR 2000 ms, 128 scans). The FIDs were zero-filled (1024K) and a Lorentzian filter of 2Hz was applied before Fourier Transform. The time-domain data were analyzed with the AMARES algorithm (MRUI), and the resulting peak areas were used to calculate the ratio of n-acetyl aspartate to creatine (NAA/Cr) and total choline to creatine (Cho/Cr). In order to perform multivariate analysis, the spectra were converted to ASCII format, peak aligned, and all areas corresponding to baseline was removed. Only the chemical shift region containing the resonances from NAA, Cho and Cr were utilized in the multivariate analysis. The resulting matrix thus comprised 54 samples (rows) and 70 variables (columns) corresponding to the relative peak intensities. The spectra were used as input for probabilistic neural network (PNN) analysis (3). The training of the PNN was performed applying a genetic adaptive component for network optimisation and cross-validation. Partial least squares discriminant analysis (PLS-DA) was applied to the same data matrix for an independent evaluation.

Results:

Typical 1H MR spectra from the study protocol are given in Figure 1. No significant difference in metabolite ratios could be demonstrated between the groups applying non-parametric Mann-Whitney or Kruskal Wallis tests. PNN classified 52 of the 54 samples with a sensitivity and specificity exceeding 93% for all groups (Table 1). However, two samples with spectra considered too different from the training data were not classified. PLS-DA also separated the groups, but SGA samples were found to be more similar to the controls than to the VLBW (Figure 2).

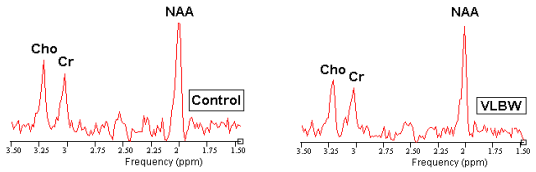

Figure 1: In vivo 1H MR spectrum from a control and VLBW subject.

	Actual Control	Actual VLBW	Actual SGA	Total
Classified as control	15	0	1	16
Classified as VLBW	0	17	0	17
Classified as SGA	1	1	17	19
Total	16	18	18	52
Sensitivity (%)	93.8	94.4	94.4	
Spesificity (%)	97.2	100	94.1	

Table 1. Results from PNN classification.

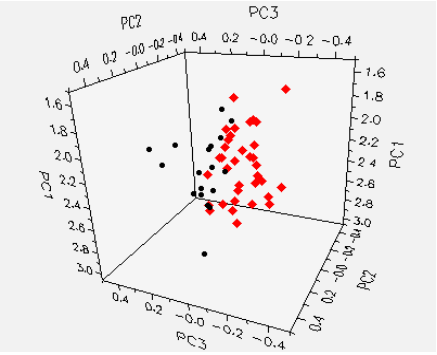

Figure 2: 3D score-plot from PLS-DA showing that SGA samples are more similar to the controls (squares) than the VLBW (filled circles).

Discussion and conclusion:

Small, yet systematic, variations in metabolite distributions were found to be associated with VLBW and term SGA compared to control adolescents using PNN. Similarly, discrimination among these groups was also achieved through the application of PLS-DA. Further work will focus on prediction of clinical variables, such as motor skills and psychiatric symptoms, from the in vivo MR spectra.

References: 1 Indredavik MS et al, Arch Dis Child Fetal Neonatal Ed. 2004, 89, F445-50; 2 Evensen KAI et al, Arch Dis Child Fetal Neonatal Ed. 2004, 89, F451-5; 3 Specht. Neural Networks 1990, 3, 109