NMR plasma profiling of newborns with low weight at birth

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Purpose/Introduction:

Beginning at birth, blood pressure values, as well as changes in blood pressure, provide information about the impact of intrauterine life on the risk of developing hypertension later in life. Additionally, blood pressure is significantly lower in those children with low birth at weight as compared to those in the other groups. Evaluation of metabolic profiles of newborns may provide new insights into the metabolic consequences and metabolic alterations of low weight at birth. In general, NMR spectroscopy has been successfully applied to metabolic profiling studies and the classification of different physiological and pathological states by the study of blood plasma. In this communication we present a study of human blood plasma NMR spectra for detecting the metabolic differences between low and normal weighted newborns.

Subjects and methods

Samples: Plasma was obtained from 51 newborns, of which 20 exhibit weight at birth below 2800 g and 18 were delivered by cesarea. The amount of blood plasma analyzed for each subject was 500 uL.

NMR spectroscopy: The whole study was performed at 37C. The spectra were recorded in a Bruker-AVANCE600 spectrometer. NMR 1D-presaturated single pulse spectra were obtained for all samples. Additionally, 2D experiments were collected in selected samples for assignment purposes. All spectra were preprocessed with 0.3Hz line broadening. Alanine doublet was used for spectral referencing.

Data analysis: Statistical multivariate analysis was performed using the PLS toolbox multivariate analysis library. Statistical multivariate analysis, relevant metabolite detection and peak fitting over the spectra were performed using in-house MATLAB scripts and the PLS Toolbox statistical multivariate analysis library. This analysis was applied to full spectral vector.

Results and discussion

PLSDA provided an insight over the metabolic differences between between low and normal weighted newborns blood plasma. Average NMR spectra from plasma of newborns were very similar. Differently to adult plasma spectra, fatty acids signals were very low and differences between females and males were not detected.

Metabolic profiling of newborn blood plasma reveals some statistically significant differences ($p < 0.05$) between low and normal weighted subjects. Some of these differences are less pronounced when adjusting the data for type of delivery (vaginal vs cesarean). Additionally, several metabolites suggestive of inflammatory processes also exhibit some correlation with the type of delivery, mainly phospholipids and fragments of glycoproteins. Most relevant metabolites correlating with the weight at birth include phenylalanine, citrulline, glutamine, glycerol and glucose. Interestingly, some of these metabolites are present in significant amounts in breast milk.

References

1. Brindle JT, Antti H, Holmes E, Tranter G, Nicholson JK, Bethell HW, Clarke S, Schofield PM, McKilligin E, Mosedale DE, Grainger DJ. Rapid and noninvasive diagnosis of the presence and severity of coronary heart disease using 1H-NMR-based metabonomics. Nat Med. 2002 Dec;8(12):1439-44.
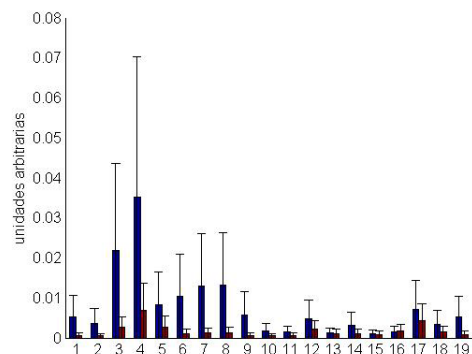
Figure 1. Relative levels of most relevant spectral regions for differentiating between NMR plasma profiles of newborns with loew (blue) and normal (red) weight at birth.
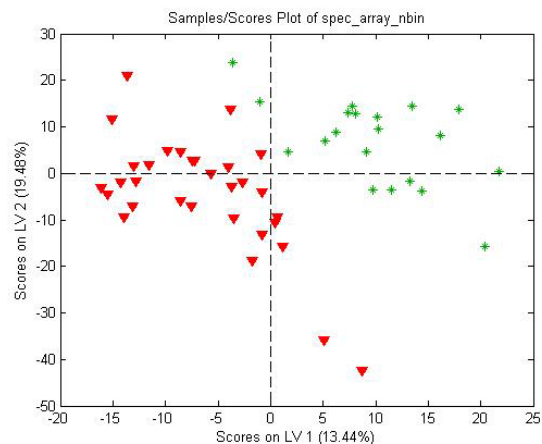

Figure 2. Scores plot for PLS-DA of plasma NMR 1D spectra showing the differences between individuals with low (green stars) and normal (red triangles) weight at birth.

Acknowledgements