IMPROVING IN VIVO BRAIN TUMOR PHENOTYPING WITH MRS PATTERN PERTURBATION AND PATTERN RECOGNITION ANALYSIS

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INTRODUCTION:

MRS pattern recognition analysis is becoming an invaluable tool for the non-invasive classification of human brain tumors [1] but still fails to fully discriminate between certain types and grades. Based on the reproducible effects of hyperglycemia in a mouse model of brain glioma, as monitored by ^{1}H MRS, we have recently suggested MRS pattern perturbation as a potential tool for increasing the dynamic range for brain tumor classification *in vivo* [2]. Here we show preliminary results that point towards pattern recognition analysis as a fast and accurate method for discriminating MRS patterns upon such metabolic challenge.

PURPOSE:

To show the potential of pattern recognition analysis for fast and accurate discrimination between mouse brain and brain tumor MRS patterns upon a hyperglycemic challenge.

METHODS:

14 C57BL6 mice were used in this study: 7 were control animals and the rest (7) harbored a brain tumor, induced by intracranial sterotactic injection of GL261 murine glioma cells (xenografts) [2]. All animals underwent MR exploration at 7T (*PharmaScan*, Bruker, Germany), as previously reported [2]. Briefly, dynamic ^{1}H-MRS (MRS_{dyn}) was carried out at 12 and 136 ms TE, using single-voxel PRESS, 12 min time resolution, 3x3x3 mm (27 µl) voxel size and 128 scans. The MRS_{dyn} protocol consisted in acquiring consecutive 12-136ms TE MRS "shots" during a period of acute hyperglycemia, which was induced by *i.p.* bolus injection of D-Glucose (250 µl at 25% w/v). MRS data were post-processed and exported in ASCII format with *MestRec* (Mestrelab R, Spain) and *R* v2.3.0 (GNU, USA) was used for spectral averaging. Multivariate analysis of the data (ASCII files normalized to unit length) was performed with SPSS 14.0 (SPSS Inc., USA). 12ms TE spectra were used for this purpose and collected from three groups: normal brain parenchyma in euglycemia ($Normal_{Eug}$, control), n = 7; GL261 tumor in euglycemia ($GL261_{Eug}$, acquired before hyperglycemia was induced), n = 7; GL261 tumor in hyperglycemia ($GL261_{Hyp}$, acquired at 60 min post-injection of glucose), n = 7. Features from these 21 MRS patterns (4.5-3.1 ppm region, 859 data points) were first explained by principal components (PC) and those were used for classification with linear discriminant analysis (LDA), using leave-one-out (LOO) crossvalidation.

RESULTS:

Since MRS pattern changes were detected at 12 ms TE (but not at 136 ms TE), as described [2], only spectra collected at this TE were used for further analysis. Three principal components (PC) explained 74 % of the variance among the 21 patterns studied. The resulting classification space is shown in Figure 1, as well as average spectra (12 ms TE), with superimposed SD (grey), of the data used for classification in each group. 100% of the cases were correctly classified (95.2% with the LOO crossvalidation).

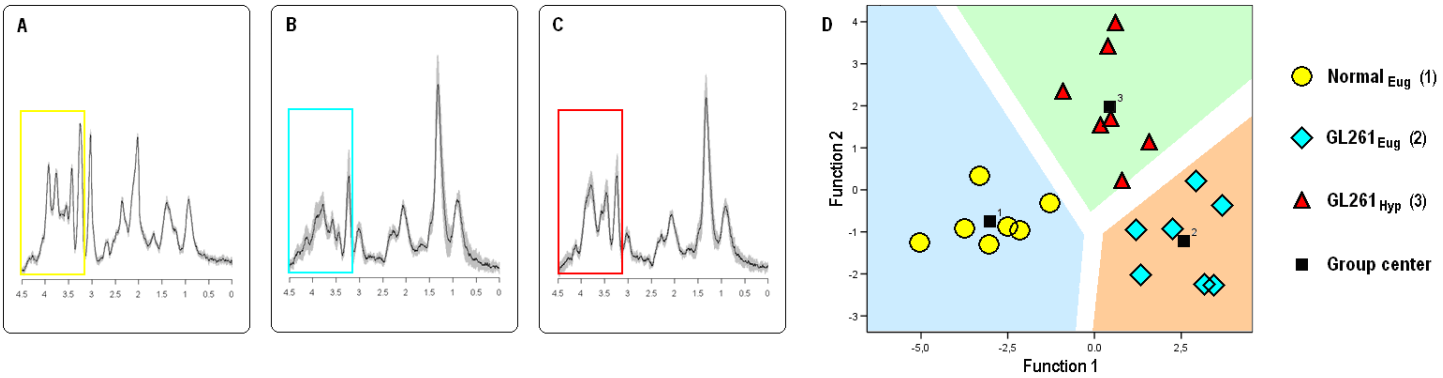

Figure 1 – From A to C, 12 ms TE average spectra, with superimposed SD (grey), of the data used for pattern recognition analysis (the rectangle insert highlights the region used for PCA – 4.5-3.1 ppm): Normal brain in euglycemia, n=7 (A); GL261 tumor in euglycemia, n=7 (B); GL261 tumor in Hyperglycemia, n=7 (C). D, LDA classification space of the 21 spectral patterns recorded (spheres, rhombus and triangles); white lines define class boundaries.

CONCLUSIONS:

Here we show that pattern recognition analysis easily distinguishes MRS "perturbed patterns". This makes pattern recognition analysis of these patterns a potentially useful tool for detection of metabolic perturbations in other *in vivo* systems by MR.

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