Abstract 1011

Protein Mass Spectrometry analysis to help in interpreting T1-dispersion curves of FFC-NMR: applications in human cerebral tumours

Session Type: Scientific Session

Topic: Clinical Applications / Brain (excluding functional and MRS)

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Purpose / Introduction

Fast-Field-Cycling NMR (FFC-NMR) is a method that measures longitudinal relaxation T_1 over a large range of magnetic fields B_0, generally at low strength. T_1 versus B_0 is termed T_1-dispersion profile and informs on molecular dynamics[1]. Special features, termed Quadrupolar Peaks (QP), may appear in T_1-dispersion profile[2], especially in biological tissues[3,4] and diseases[5,6]. The links between T_1-dispersion profiles and pathologies are still poorly known. Here using human cerebral biopsies, we propose to compare FFC-NMR data with proteomic.

Subjects and Methods

Eight human brain biopsies (Table1) were obtained frozen from the Grenoble biobank, sampled twice while frozen over homogeneous regions and analysed by FFC-NMR and proteomics.

The T_1-dispersion profiles (SpinMaster relaxometer; Stelar s.r.l., Italy) were fitted using polymer and Lorentzian QP models[7,8]. Fit parameters were used for FFC-NMR sample clustering. Proteomic consisted in one-dimensional gel (SDS-PAGE) proteins digested with LysC/trypsin and peptide were analysed using LC-MS/MS (IMPACT II - QTOF Bruker Daltonics). Label-free quantitative analysis was performed in triplicate by block for each sample. After a Pearson correlation between all samples, proteomic hierarchical clustering (Ward method) and their corresponding biological pathways were obtained.

Results

The same clusters were independently found by FFC-NMR and proteomic data analysis (Table1). Glioma T_1-dispersion curves show smaller QP for sample A and exhibit 2 regimes for samples C and D instead of 3 for other samples (Figure1). Proteomics analyses quantified 3950 proteins, split into 4 clusters. The significant biological pathways of glioma clusters 1, 2 and 3 are shown in Table2.

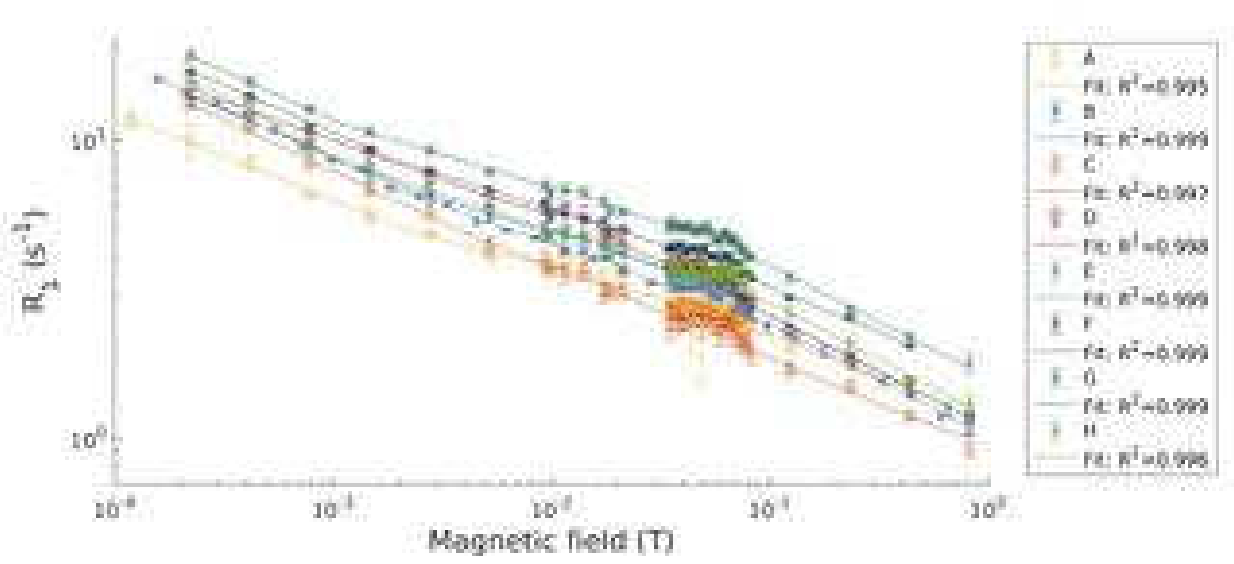
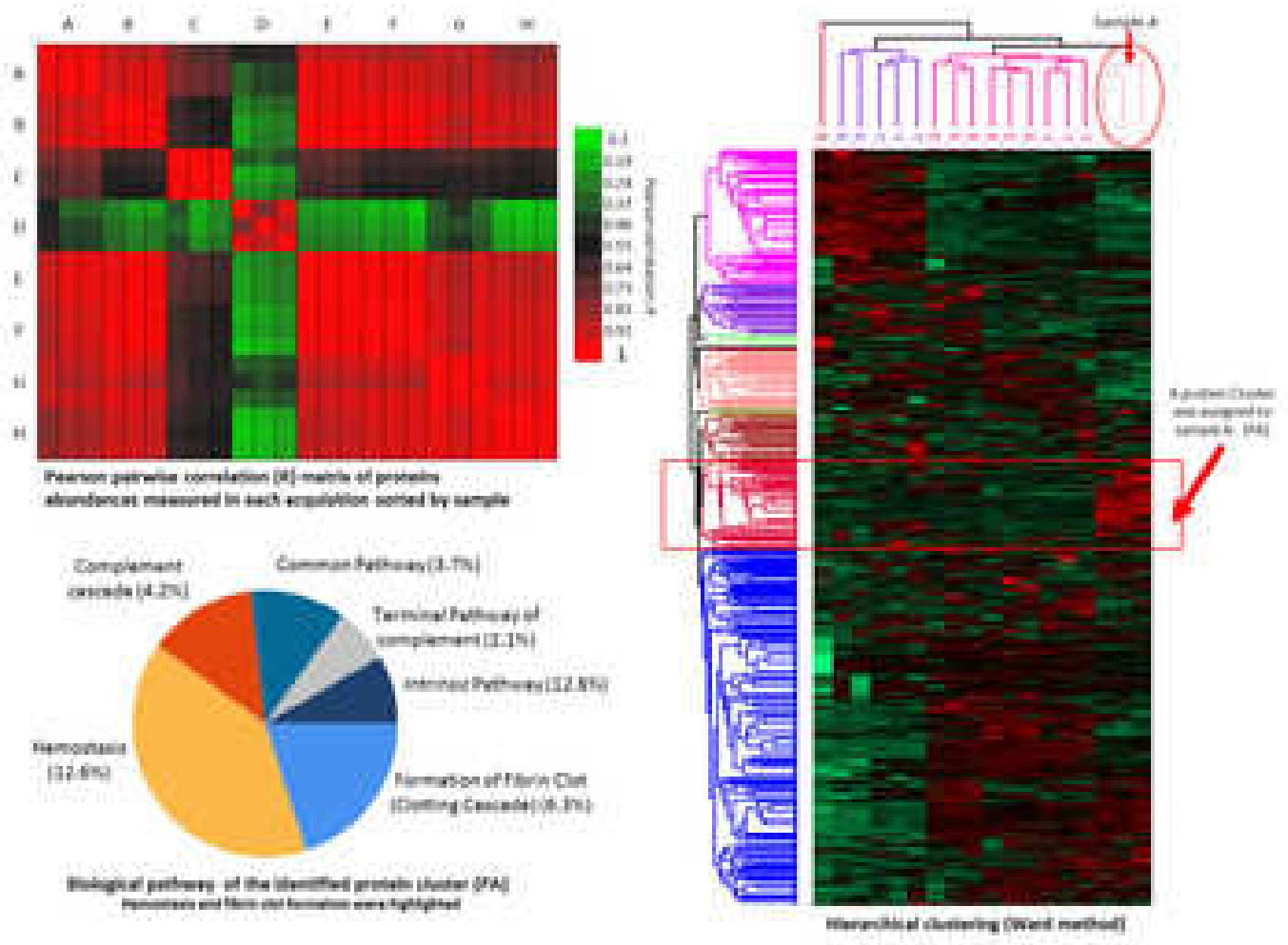


Table 1: clustering data

Patient code	A	B	C	D	E	F	G	H
Pathology	Glioma	Epileptic	Glioma	Glioma	Epileptic	Meningioma	Epileptic	Epileptic
T_1-dispersion cluster	1	4	2	3	4	4	4	4

Proteomic cluster	1	4	2	3	4	4	4	4



Discussion / Conclusion

Glioma T_1-dispersion features appear associated to specific biological pathways. Reduced QP in sample A was correlated to hemostasis, a result which appears coherent since QP amplitude is known to increase as the amount of immobilised fibrin increases[5]. The reduced QP is certainly due to the enzymatic activity of haemostasis, probably increasing the molecular dynamic of the proteins of the sample as fibrins. In samples C and D, T_1-dispersion parameters (slopes, transitions at low/high magnetic field regimes, Table 2) appear related to metabolic activities and probably to tumour aggressiveness. These preliminary results are relevant, since the fibrinolysis and metabolic pathways are of great interest in neuro-oncology, but need confirmation and works are in progress.

References

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