Magnetic Resonance Diffusion and Spectroscopy abnormalities in different forms of Creutzfeldt-Jakob disease

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Introduction

Creutzfeldt-Jakob disease (CJD) is a rare and fatal neurodegenerative disorder caused by abnormal prion protein accumulation in the brain (1). A number of subtypes are recognized. The most common is sporadic (sCJD) which has an incidence of about one per million annually. Rarer forms include iatrogenic CJD (iCJD), transmitted by CJD-infected neurosurgical instruments, tissue or hormone preparation, and familial CJD (fCJD) associated with mutations of the prion protein gene. In 1996, a new form was described and named variant CJD (vCJD). vCJD is believed to occur by transmission of the prion from bovine spongiform encephalopathy to humans through infected beef products. If most patients have been residents of the United Kingdom, few cases have recognized in France and in another countries (1). Early and accurate diagnosis of vCJD is important for prognostic and epidemiologic purposes and furthermore, for therapy development. If definite vCJD can be only made by neuropathologic examination, either by *in vivo* biopsy of brain tissue or at post-mortem examination, diagnostic test of sCJD include characteristic EEG periodic discharges and raised CSF 14-3-3 protein levels. In addition to these features, MR imaging constitutes the most promising and non invasive approach for diagnosis and therapy evaluation (2). The purpose of this study is to evaluate a new treatment based on the intra cerebro-ventricular infusion of Pentosan polysulfate (PSP) by biological, electrophysiological, clinical and MRI examinations every 6 weeks (3).

Material and Methods

The first MR examination of the protocol was performed on 6 male patients (age=44±10y) with different form of CJD (2 iatrogenic, 1 variant, 1 sporadic, 2 genetic) using a 1.5 T Sonata imager (Siemens, Germany) system before starting the PSF treatment. For control, six normal subjects were examined (age=38±8y). Conventional imaging sequences includes an isotropic 3D T1 MPR (TE/TR=4/2010ms, FOV=320 mm, thickness=1mm) acquisition of 4 min using a 8 channel headcoil and parallel imaging, transverse fast SE T_2-weighted images (TE/TR=132/5680ms, 25 slices, thickness=3mm, FOV=240mm) and FLAIR images (TI/TE/TR=2200/105/8000ms, 25 slices, thickness=3mm, FOV=240mm) acquired in the AC-PC axis. Diffusion-weighted EPI images were acquired with three b values (0, 500, 1000 s/mm^2) sequentially in the x, y and z directions (TE/TR=84ms/3300ms, 25slices, thickness=5mm, FOV= 240mm) and ADC maps calculated. Six single voxel spectra were localized using PRESS sequence (TR=1500 ms, 128 scans) with short echo time (TE=30 ms) from the anterior cingular cortex, the right and left side of the lenticular and the pulvinar areas, and the vermis. MR images were read by a neuroradiologist (M.H.). ADC values were measured in seven regions: right and left heads of caudate nuclei, putamen nuclei, and pulvinar areas, anterior cingular cortex, and vermis. The spectra were analyzed using the Siemens spectroscopic software. All peaks were fitted (lipids, NAA, glutamate, glutamine, creatine, choline, inositol (Ino)) and metabolite ratios were calculated using creatine (Cr) as reference.

Results

Visual analysis of the T2w, FLAIR and Diffusion Weighted images showed hyper-intensities at various degrees depending on the region and the CJD form. As shown in Fig.1, DWI showed typical hyperintensities “hockey sign” in the pulvinar area of the vCJD patient while the iCJD patient presented further increase in the caudate and putamen nuclei. Compared to normal values obtained from six volunteers, the ADC was significantly decreased in caudate, putamen and pulvinar regions of the patients (Table 1). NAA/Cr ratio was decreased in cortex, pulvinar and vermis regions while the Ino/Cr ratio was increased in the lenticular region.

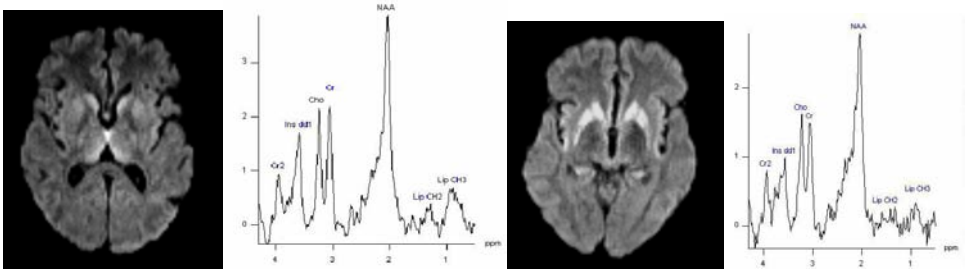

Fig.1. DWI in the variant CJD patient showing lesion in the pulvinar and its spectrum (left) and in a iatrogenic CJD patient showing lesion in lenticular nuclei and its spectrum (right).

	Controls	Patients
Caudate	809 ± 25	661 ± 101*
Putamen	735 ± 19	584 ± 81*
Pulvinar	801 ± 46	715 ± 83*
Ant.Cingular	874 ± 24	838 ± 60
Vermis	751 ± 33	785 ± 28

Table 1: ADC values (Mean ± SD x 10^{-6} mm^2/s) in different regions (* p<0.0001).

Conclusion

These preliminary results demonstrated that both DWI and MRS provide complementary patterns of lesions and metabolic abnormalities to characterize CJD and constitute both sensitive and specific tools for non invasive therapeutic follow-up.

References

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