Influence of b Factor on ADC Sensitivity in Creutzfeldt-Jakob Disease

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Introduction: Creutzfeldt-Jakob Disease (CJD) is the most notable form of human prion diseases, characterized on MRI by local diffusion reductions in basal ganglia and cortex (see illustrative cases in Fig. 1a). All but one previous studies[1] of DWI (Diffusion-Weighted Imaging) in CJD were conducted at b-values of 1000 s/mm^2 or less. Higher b values have been reported to offer greater sensitivity for stroke[2], white matter damage[3] and vascular dementia[4]. Here we calculated ADC values (Apparent Diffusion Coefficient) and examined the sensitivity of two b values in detecting CJD.

Methods: 15 healthy subjects (7 male/8 female, mean age=57 ± 10 years, range 43 to 80) and 13 probable CJD subjects (8 male/5 female, mean age=60 ± 8 years, range 45 to 75, 5 sporadic and 8 familial CJDs) were included in the study. Scanning was performed on a 1.5T GE Signa system with a standard quadrature head coil. MRI sequences included single-shot echo-planar spin echo DWI along 3 orthogonal directions (acquired resolution 1.88 x 1.88 x 3.0 mm, 48 axial slices, TR/TE 5000/85 for b=1000 s/mm^2 and 5000/100 for b=2000 s/mm^2) and anatomical T1-weighted SPGR sequences (104 contiguous axial slices, TR/TE/FA 28/6/40, voxel dimensions 0.94 x0.94 x1.50 mm). ADC was derived from the commonly used Stejskal and Tanner equation. We used SPM5 for voxel-wise analyses, and FIRST (FSL 4.0) for a VOI analytic approach[5, 6, 7]. In the voxel-wise analyses, ADC maps were coregistered with SPGR, and were spatially normalized using the normalization parameters estimated from SPGR followed by isotropic Gaussian smoothing of 4mm. Smoothed and normalized images were submitted to group level random effect model of ANCOVA with diagnosis (Dx) as a grouping factor and age as covariate (results displayed at p<.001, k>5 thresholds). In FIRST, default parameters were entered, and 4 anatomical structures (caudate, putamen, thalamus, pallidus) were parcellated as shown in Fig. 1b. We used the parcellated image as a mask to extract mean ADC values, and analyzed the data by a repeated-measures MANOVA with Dx as grouping factor and the b value (1000 Vs 2000) as repeated measure (age covariance did not change the findings).

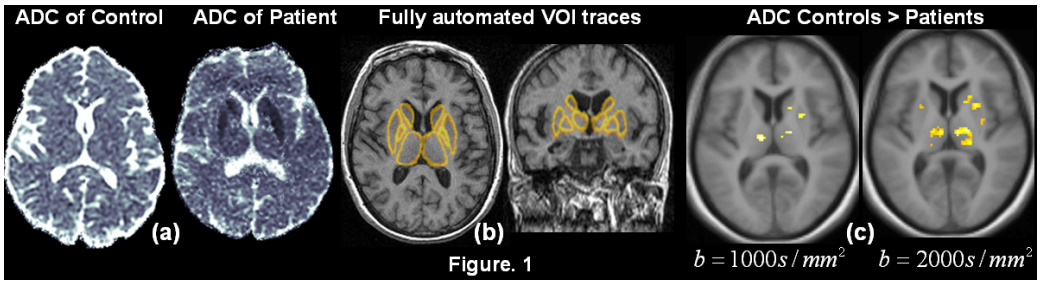

Figure. 1

Results: In all comparisons and all areas, ADC calculated by b=2000 was significantly lower (by 5-15%) than the b=1000 values. SPM findings of reduced diffusion in CJD patients are depicted in Fig. 1c. At b=1000, putamen and caudate nucleus were found to be significant unilaterally while thalamus (medial dorsal nucleus and ventral lateral nucleus) was significant bilaterally. Compared to controls, the ADC in patients was reduced by 17~18% in caudate, 18% in putamen, and 13%~14% in medial dorsal nucleus and ventral lateral nucleus. At b=2000, all of the clusters seen in b=1000 were also significant but larger, and the pulvinar was also significant. Regarding the anatomical VOIs, results are shown in Figure. 2. In the putamen, caudate and thalamus, but not the globus pallidus, patients had significantly lower ADC than controls (p<.05). Additionally, in the CN (p<.01) and thalamus (p<.01), but not putamen, there was a significant interaction between b and Dx, showing that the differences between patients and controls were greater at b=2000.

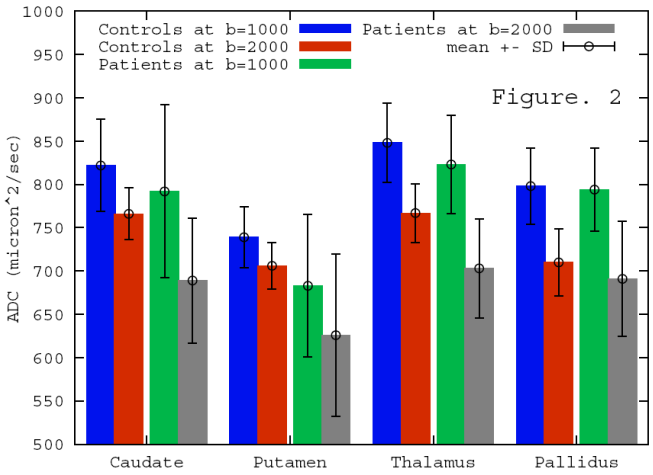

Figure. 2

Discussion: As CJD associated vacuolation has been reported to be significantly correlated with the diffusion deficit[8] and the diffusion length (~20 micron) also becomes comparable to the vacuoles radius, higher b factors may allow detection of larger vacuoles. However, we estimate that the increase of b from 1000 to 2000 s/mm^2 only extends the diffusion length by ~9%. A more likely explanation is the predominance of multi-exponential decay at b=2000, resulting in better discrimination of normal and diseased tissue diffusion. While DWI hyperintesities are clinically useful and often correlated with reduction in ADC, DWI images at b=2000 are inherently noisier than b=1000, and their applicability to clinical practice remains to be proven in future studies.

References:

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