Brain tissue damage in Dementia with Lewy bodies: a Diffusion Tensor MRI study in vivo.

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Synopsis

Demetia with Lewy bodies (DLB) has been recognized as the second most diffuse form of dementia after Alzheimer's disease (AD) in several pathological studies (1). In 1996 consensus criteria for clinical diagnosis of DLB were introduced (2). Nevertheless, a relevant percentage of missed diagnoses is reported and the patho-physiological mechanisms underlying DLB remain largely obscure. Conventional Magnetic resonance imaging (MRI) studies reported conflicting results assessing neuro-radiological features of DBL. Conversely, SPECT studies have reported diffuse cortical hypoperfusion and hypometabolism particularly involving the occipital lobe (3,4). Aim of the present study was to assess in vivo the presence and the distribution of microscopic brain tissue damage from patients with DLB using Diffusion Tensor Imaging (DTI) by a Region of Interest (ROI) analysis applied to mean diffusivity (MD) and fractional anysotropy (FA) maps.

Methods

Eleven patients diagnosed with DLB by consensus criteria (2) (6 probable, 5 possible) and 8 sex- and age-matched healthy subjects were studied using MR. The following scans were obtained: a) dual-echo turbo spin echo (TSE) (TR/TE/NEX=3300/16-98/ 1; number of slices: 20, contigous, 6 mm thick); b) pulsed-gradient spin-echo echo-planar (EPI) pulse sequence (inter-echo spacing=0.8, TE=123); number of slices: 20, contigous, 6 mm thick), with diffusion gradients applied in 8 non collinear directions. (maximum b factor: 1044 sec mm-2). For both, TSE and EPI scans, the 20 slices were acquired with the same orientation and positioned parallel to corpus callosum in order to cover the entire brain. After correction for eddy current induced distortion, the diffusion tensor was estimated linearly for every voxel, assuming a mono-exponential relationship between the signal attenuation and the elements of the tensor matrix. After diagonalization of the matrix, mean diffusivity (MD) and fractional anisotropy (FA) maps were derived for every voxel.

Two experienced observers, unaware to whom the scans belonged, identified by consensus the pathological T2 hyperintensities in patients and controls. Subjects with more than 4 macroscopic periventricular or any other hyperintensities were excluded from analysis. For any subject, anatomical white matter (WM) ROIs were selected on the b0 step of DTI scans and then transferred on the MD and FA maps in order to measure the corrispondent regional quantities (Fig. 1). A Student's t test for non-paired data was used to compare MD and FA values of the regional WM from DLB patients and controls. Bonferroni's correction for multiple comparisons was applied (only $p \leq 0.005$ were considered as statistically significant)

Results

The selected WM ROIs and the corrispondent mean MD and FA derived quantities from patients and controls are reported in Tab 1, including the statistical p value for any comparison. Patients with LBD have shown statistically significant higher values of the MD in the parietal lobes, in the caudate nucleus, in the corpus callosum and pericallosal areas and statistically significant decreases of FA in the parietal and occipital lobes, in the pericallosal areas and in the caudate nucleus when compared to controls. MD increases in the frontal and occipital lobes and in putamen and FA decreases in the frontal and temporal lobes and in the corpus callosum showed a trend towards a statistically significant difference comparing LBD patients to controls.

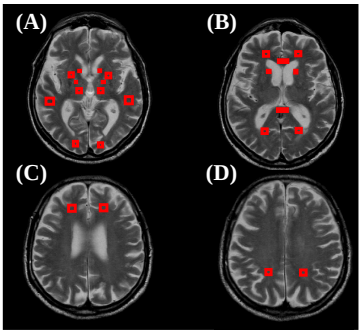

Fig1. Location of the WM ROIs in a patient with LBD. (A) Internal capsule, putamen, thalamus, temporal and occipital lobes; (B) genu and splenium of the corpus callosum, anterior and posterior pericallosal areas, caudate nucleus; (C) frontal lobes; (D) parietal lobes.

	Controls	Patients with LBD	p (*)	Controls	Patients with LBD	p (*)
	Average MD (SD)			Average FA (SD)		
Frontal lobes	0.87 (0.04)	0.95 (0.08)	NS (0.029)	0.30 (0.03)	0.25 (0.05)	N.S. (0.008)
Parietal lobes	0.83 (0.05)	0.96 (0.09)	**0.003**	0.39 (0.03)	0.28 (0.07)	**0.002**
Temporal lobed	0.88 (0.03)	0.93 (0.08)	N.S (0.13)	0.27 (0.03)	0.21 (0.05)	N.S. (0.01)
Occipital lobes	0.80 (0.03)	0.88 (0.09)	N.S (0.02)	0.40 (0.02)	0.32 (0.03)	**< 0.001**
Corpus callosum	0.79 (0.07)	1.00 (0.15)	**0.002**	0.75 (0.06)	0.61 (0.13)	**0.005**
Pericallosal areas	0.80 (0.04)	0.98 (0.12)	**0.001**	0.40 (0.06)	0.29 (0.05)	**0.001**
Internal capsule	0.83 (0.05)	0.85 (0.03)	N.S (0.17)	0.48 (0.04)	0.44 (0.04)	N.S (0.13)
Thalamus	0.86 (0.02)	0.90 (0.09)	N.S (0.20)	0.29 (0.05)	0.26 (0.02)	N.S (0.16)
Caudate nucleus	0.79 (0.04)	0.90 (0.08)	**0.004**	0.31 (0.06)	0.21 (0.04)	**<0.001**
Putamen	0.85 (0.06)	0.92 (0.06)	N.S (0.05)	0.21 (0.02)	0.21 (0.03)	N.S (0.73)

Table1. Mean (SD) MD (expressed in units of $m^2s^{-1}x10^{-9}$) and FA values of the selected WM areas from LBD patients and controls. * Student's t test for non paired data. Only Bonferroni corrected p values ≤ 0.005 were considered as statistically significant.

Discussion

Consistently with the results obtained previously in AD (5), the location of WM microstructural abnormalities in regions (corpus callosum and pericallosal areas) with a high prevalence of fibre tracts connecting cortical associative areas, suggests the presence of Wallerian degeneration secondary to neuronal loss in the associative cortex. Such abnormalities might contribute to the neuropsychological impairment in patients with DLB. Conversely, patients with LBD showed a less prominent involvement of temporal and frontal lobe WM, consistently with the assessment of a relative preservation in global neuro-psychological measures and memory tasks, at least in the early stage of the disease. The selective involvement of the occipital lobe fits with previous SPECT studies (3,4) suggesting a possible distinctive marker for and a putative explanation for visual hallucinations which represent one of the cardinal diagnostic symptoms of DLB (2). The microscopic abnormalities found in the caudate nucleus are consistent with a previous PET study which showed a decrease of FDOPA accumulation in the caudate nucleus and putamen (6), suggesting DLB and Parkinson's disease might share a similar nigro-striatal involvement which might be caused by common patho-physiological mechanisms.

Refereces

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