DTI-based analysis facilitates the understanding of a peculiar neuropsychological dissociation in a patient with bilateral thalamic damage

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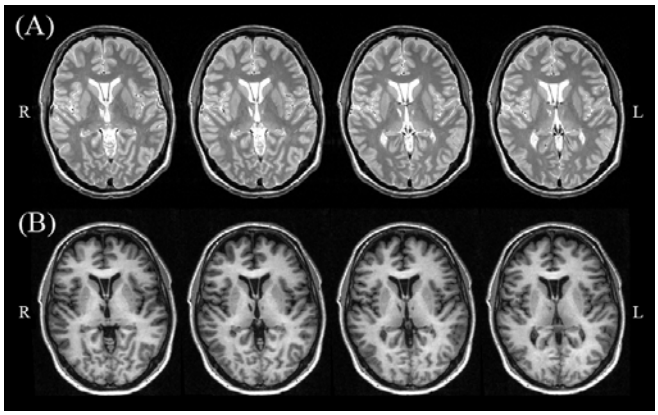
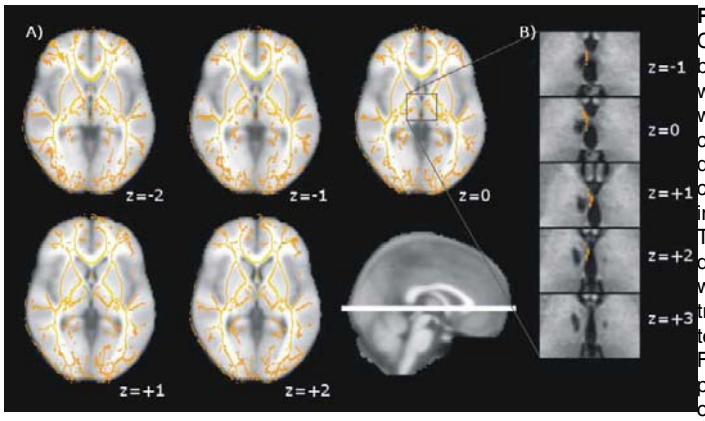
Introduction

A focal damage confined to the hippocampus may result in recognition deficits characterized by a dissociation between an impairment of recollection and a preservation of familiarity. We report here a single case of an amnesic patient with a bilateral damage of the anterior part of the thalamus, who presented with a neuropsychological profile suggestive for such a dissociation, in absence of any additional impairment of general cognitive functions. We hypothesized that this focal damage involved, at a different anatomical level than in patients with hippocampal lesions, the so called Delay and Brion's circuit, which has been theorized to subserve the episodic memory processes. However, conventional MR imaging did not highlight any white matter (WM) abnormality affecting this circuit, and its underlying fiber tracts are too small to be reliably reconstructed by conventional tractography. Nevertheless, a potential WM abnormality might be detected by a statistical comparison between the patient and a group of healthy subjects. We show how, using the TBSS (Tract-Based Spatial Statistics, [1]) method, it was possible to detect in this patient a focal damage of the WM involving the mammillo-thalamic tract with a preservation of the medio-dorsal thalamic nuclei.

Methods

We acquired MR data from twenty healthy men (age range 23-44 years) and the amnesic patient (38 years). Scans were obtained on a 3T Siemens Allegra MR scanner. Lesion localization for the patient was carried out on images obtained by dual echo acquisition proton density-T2 weighted spin-echo with a voxel size of $1x1x2mm^3$, and on 3D T1-weighted MPRAGE with a voxel size of $1x1x1mm^3$. Diffusion-weighted data were acquired using echo planar imaging (52 interleaved axial slices, field of view $192x192\ mm^2$, voxel size of $1.5x1.5x2mm^3$). The diffusion weighting was isotropically distributed along 12 directions with a b value of 1000 s/mm^2. For each subject, we acquired 8 sets of diffusion-weighted data, and for each of those sets we acquired two volumes with no diffusion weighting. Image analysis was carried out using tools from the FMRIB Software Library (FSL, www.fmrib.ox.ac.uk/fsl, [2]). FMRIB's Diffusion Toolbox was used to fit a diffusion tensor at each brain voxel in the diffusion data and to calculate voxel-wise values for FA. From the second and third eigenvalue (λ_2 and λ_3) of the diffusion tensor we calculated for each voxel the values of "perpendicular diffusivity" $D_{perp}=(\lambda_2+\lambda_3)/2$, a parameter which have been shown to be related with myelin degradation [3]. Voxelwise statistical analysis of the FA and D_{perp} data was carried out using TBSS. TBSS projects all subjects' FA data onto a mean FA tract skeleton, before applying voxelwise cross-subject statistics. In order to compare the values of FA and D_{perp} on the skeleton, we performed a nonparametric 2-sample t-test using the Randomise tool of FSL [2], considering the patient as a group of 1 subject.





Results

Conventional MRI showed the presence of ischemic infarcts in the thalamus bilaterally. No additional abnormalities were detectable on both PD-T2 and T1 weighted scans. In Figure 1 are presented axial dual-echo SE (A) and T1 weighted slices (B) showing the bilateral involvement of the thalamus. The combined TBSS-Randomise analysis detected areas of significant abnormal diffusion in white matter tracts of our amnesic patient compared to the healthy control group. The patient showed reduced values of fractional anisotropy and increased values of perpendicular diffusivity (P=0.047, for both FA and D_{perp}). These abnormalities, suggesting occult white matter micro-structural disorganization, were found adjacent to the right thalamic lesion, in areas whose MNI coordinates are compatible with the path of the mammillo-thalamic tract. Figure 2 shows (A) the mean FA skeleton superimposed on a MNI template, with the voxels resulting significant from the 2-sample t-test in blue. Figure 2 (B) shows the same results of decreased anisotropy and increased perpendicular diffusivity superimposed on the relevant normalized axial slices of the T1 mprage from the patient.

Discussion

Diffusion and fractional anisotropy abnormalities in fiber tracts proximal to the right-thalamic lesion, suggest a loss of structural organization secondary to occult WM damage in our patient. Recent animal and human studies show that an increase of perpendicular diffusivity may represent the underlying substrate for the low diffusion anisotropy usually related to chronic axonal damage and Wallerian degeneration. In our study, we identified a decrease of FA values with a concomitant increase of perpendicular diffusivity. It is likely that this structural disruption is due to white matter gliosis and myelin degradation associated to the ischemic lesion.

Conclusions

DTI-based analysis has facilitated the comprehension of the specific neuropsychological deficits observed in our patient. Moreover, our findings support the idea that the same functional specialization hypothesized for the different sub-regions of the hippocampus might be extended to the thalamus. Finally, this case supports recent theories, which regard recollection and familiarity as independent processes associated to different neural circuits.

Bibliography

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