Possible Compensatory Plasticity of Anterior Thalamic Nucleus to Memory Impairment In Normal Pressure Hydrocephalus Patients Manifested As Increased Anisotropy and Fiber Density

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Introduction

Idiopathic normal pressure hydrocephalus (NPH) is manifested clinically with classic triad of gait disturbance, incontinence and dementia [1]. Unlike other types of dementia, the memory impairment in NPH can be reversed with early intervention. On the other hand, the main pathway for human brain memory is Papez circuit [2] in which the anterior nucleus (AN) receives afferent fibers from the mammillo-thalamic tract and sends efferent projection fibers to the cingulate gyrus. AN plays an important role in the modulation of memory and alertness. Recent advances in diffusion tensor imaging (DTI) allow specific tracking of fibers to their destination of nuclei [3]. Quantification of anisotropy in terms of metrics such as the fractional anisotropy (FA) offers insight into microstructure alternations. The purpose of this study is to examine the diffusion tensor parametric behavior of anterior thalamic nucleus in response to memory impairment in normal pressure hydrocephalus.

Method

10 NPH patients (4 men and 6 woman, mean age 73.5±13) and 10 normal controls (age- and gender-matched) were enrolled in this study. NPH patients were diagnosed according to Japanese guidelines for management of idiopathic NPH [4]. Memory were evaluated on the Chinese version of Wechsler Memory Scale—Third Edition (WMS–III) Word List subtest (Verbal) and Rey Complex Figure Test (Non-Verbal). DTI was performed on a 1.5T scanner (GE, Signa HDx, USA) using single-shot echo-planar imaging technique with parameters as follows: TR=10000 ms; TE=85.3 ms; flip angle=90o; b values=0, 1000 seconds/mm2; diffusion directions=15; FOV=240; matrix size=128×128 (zero-filled to 256×256); section thickness=4 mm; section gap=0 mm; and NEX=2. Fiber-tracking was performed using MRtrix software package (Brain Research Institute, Melbourne, Australia, http://www.brain.org.au/ software), based on probabilistic streamlines method. The region of AN was hence identified by tracking mammillo-thalamic tract using two deterministic seeds for propagation of fibers: one was placed at the mammillary body and the other at the proximal end of the anterior limb of the internal capsule (fig 1A). This method improves the AN identification while avoids the displacement effects by the dilated ventricles. Track density of AN was derived from the track-density maps in which the numbers of track voxels were obtained by randomly distributing 2,500,000 seeds in the entire brain(fig 1B). Tensor parametrics (λ 1=axial diffusivity, λ 2=radial diffusivity, λ 3=radial diffusivity, MD=mean diffusivity, q = diffusion anisotropy, L = diffusion magnitude, FA, and fiber density) for each subject was calculated by averaging measurements from both hemispheres.

Results

In verbal memory test, NPH patients had average 35% decrease in immediate memory and 44 % decrease in delayed memory while non-verbal test means showed less than 5% of normal score. Figure 2 shows significant increase in FA, q and fiber density in NPH patients as compared to control. In short, the FA increase seems to be dominated by the increase of q, considering the relative stable of L. The increase of fiber density is twice than that of the control. There was no significant difference of the tensor metrics, includingλ1, λ2, λ3, MD, and L, between NPH patients and the control.

Discussion

Previous DTI studies on NPH patients were mostly in motor tract analysis [5]. Our study aimed at memory pathway at AN, which dictates all input from mammillary bodies. The increased FA and fiber density may imply two folds: first, the impaired memory cognitive functions at high cortical levels were compensated by supplemental recruitment regulated by Papez circuit; second, the dilated lateral and third ventricles might have compressive effects on the neighboring fiber bundles and nuclei, leading to condensed fibers. In conclusion, we have shown for the first time that, alternations of diffusion tensor metrics can be measured in thalamic nucleus responsible for memory in NPH patient. Our findings have potential clinical implications for responses monitoring at microstructure level in NPH patients under treatment.

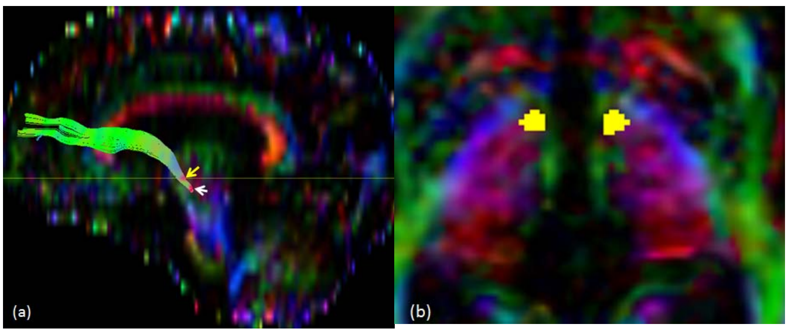

Fig1 (a) Fiber tracking based on probabilistic streamline. White arrow indicates mammillary body and yellow arrow indicates anterior nucleus of thalamus. A horizontal line shows the axial plane in figure 1(b) where the tensor metrics of AN (yellow regions) were calculated.

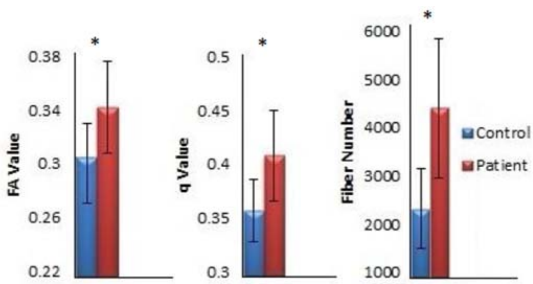

Fig. 2 Significant increase in FA, q value and fiber numbers in AN of NPH patient as compared to the control subjects.

References

[1] Williams MA, et al. Neurol Clin Pract. 2013 Oct;3(5):375-385. [2] Vertes RP, et al. Neuroscience. 2001;104(3):619-25. [3] Yamada K, et al . AJNR 2010 Apr;31(4):732-5 [4] Ishikawa M, Neurol Med Chir (Tokyo). 2008;48 Suppl:S1-23. [4] Kim MJ, et al. AJNR 2011 32: 1496-1503.