In-vivo Detection of Intracortical Myelinated Fibers in Human Hippocampal Formation: Submillimeter Resolution Diffusion Tensor Imaging Compared with Histological Findings

Takashi Yoshiura[1], Akio Hiwatashi[1], Satoshi Suzuki[2], Tsuyoshi Okamoto[3], Osamu Togao[1], Koji Yamashita[1], Kazufumi Kikuchi[1], and Hiroshi Honda[1]

[1]Department of Clinical Radiology, Kyushu University, Fukuoka, Japan, [2]Department of Neuropathology, Kyushu University, Fukuoka, Japan, [3]Department of Advanced Medical Initiatives, Kyusuh University, Fukuoka, Japan

Introduction

Along with the cytoarchitecture, intracortical myelinated fiber (ICMF) is an essential component to characterize microarchitecture of the cerebral cortex. Visualization of ICMF by diffusion tensor (DT) imaging may be of clinical value in characterizing and diagnosing neurological diseases that primarily affect cerebral cortex. For example, Alzheimer's disease is known to affect ICMFs including those in the perfornat pathway in its early stage. However, typical in-plane spatial resolution of the clinical DT imaging is approximately 2 mm, which is comparable with the cortical thickness. To observe the intracortical microstructures, submillimeter in plane resolution is required. Our purpose was to test the feasibility of detecting ICMF in the human hippocampal formation by in-vivo high-resolution DT imaging.

Materials and Methods

Eleven healthy subjects (M/F = 9/2; mean age = 31 years) were studied using a 3T clinical whole-body MR scanner (Quasar Dual, Philips Medical Systems, Best, the Netherlands) and an 8-channel head array-coil. DT images of the left temporal lobe were obtained with an acquisition in-plane resolution of 0.85x0.85mm^2 (0.56 x 0.56 mm^2 after interpolation) using the small field-of-view (FOV) technique [1]. The imaging slices (3mm-thick, 15 slices) were placed perpendicular to the long axis of the hippocampus. The small FOV technique was used to maintain image quality of high-resolution single-shot echo-planar images for DT imaging by reducing the number of phase-encoding steps. Other imaging parameters were as follows: TR/TE=4132 ms/53 ms, b factors=0 and 700 s/mm^2, 6-directional MPG, acquisition matrix = 64x64, SENSE factor = 1.8, FOV = 54 mm, number of averaging = 44 (b = 700)/22 (b = 0), imaging time = 39min 50s. Mean fractional anisotropy (FA) values were measured within regions-of-interest (ROIs) drawn over 3 cortical regions within the hippocampal formation: subiculum (SUB), cornu ammonis (CA)1 and CA4/dentate gyrus (CA4/DG) according to a modified version of previously proposed methods [2,3]. As a gold standard, myelin-stained histological specimens obtained from 5 male patients were prepared to create whole slide images (so-called "virtual slides"). The mean ICMF density was quantitatively estimated in the 3 cortical regions (SUB, CA1 and CA4/DG) as a pixel value in the gray-scaled image of the specimens (lower pixel values corresponded higher myelin density). Comparisons of FA and myelin density among the 3 cortical regions were performed using the least square mean Student t-test at a significance level of $P < 0.05$.

Results

An example of FA mapping of the hippocampal formation is shown in Fig 1. Fig 2 shows photomicrographs of a myelin-stained specimen in the corresponding region. In DT imaging, FA in SUB was significantly higher than those in CA1 and CA4/DG ($P < 0.05$, respectively) (Fig 3A). In the histological evaluation, ICMF density in SUB was significantly higher than those in CA1 and CA4/DG ($P < 0.05$, respectively) (Fig 3B). Histological inspection revealed abundant ICMF running in SUB (Fig 2).

Discussion

High-resolution DT imaging revealed higher FA values in SUB, corresponding to histologically confirmed denser ICMF in the same cortical region. Our results suggested that in-vivo detection of ICMF using high resolution DT imaging is feasible. High-resolution DT imaging may be useful in detecting early pathological changes in neurological diseases affecting the cerebral cortex such as Alzheimer's disease and temporal lobe epilepsy.

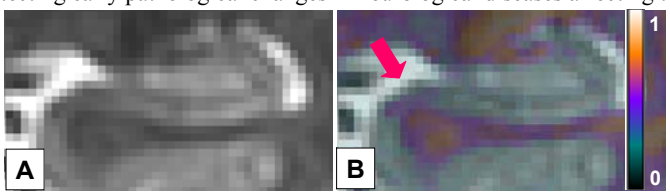

Fig 1: High-resolution DT images of the hippocampal formation. An echo-planar image obtained at b=0 s/mm2 (**A**) shows the anatomy. A color-coded FA map (**B**) shows a high FA area in the SUB (**arrow**).

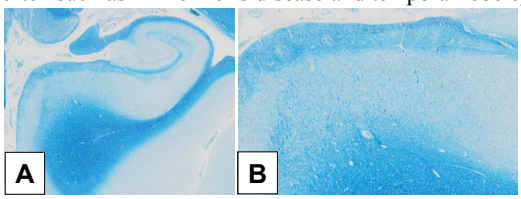

Fig 2: A myelin-stained specimen (**A**) shows dense ICMF in SUB. A close-up image of SUB is also shown (**B**).

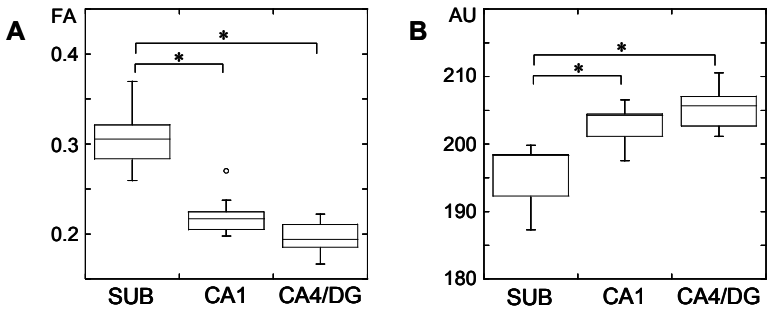

Fig 3: A: FA comparison among 3 cortical regions. FA in SUB was significantly higher than those in CA1 and CA4/DG. **B:** Comparison of histological ICMF density. ICMF density in SUB was significantly higher than those in the other 2 regions. Notice that lower gray scale values represent higher ICMF density.

References

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