ORIGINAL

Regional changes of fractional anisotropy with normal aging using Statistical Parametric Mapping (SPM)

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Abstract : Objective :There has been reports on the usefulness of diffusion tensor imaging (DTI) about age-or disease-related degradation. DTI is generally evaluated by the region of interest (ROI) methodology. In this study, we applied a statistical way using Statistical Parametric Mapping (SPM) to assess normal aging by DTI and compared results of these two methods.
Methods : Ten young and ten senior normal volunteers were examined. On SPM, tensor images were changed into normalized tensor images. They were compared between the two groups by t-test.
Results : In the senior group, fractional anisotropy (FA) values were higher on the basal ganglia, cingulated gyrus and other cortical gray matter, lower in the corona radiata, internal capsule, centrum semiovale and corpus callosum by using SPM. In the ROI method, the results were almost compatible except in the brain periphery.
Conclusions : Aging changes on water diffusion anisotropy was clearly shown by SPM method which would be useful to evaluate change of water diffusion anisotropy without operator bias even in clinical setting instead of ROI measurement. J. Med. Invest. 52 : 186-190, August, 2005

Keywords **:** *magnetic resonace imaging, diffusion tensor image, Statistical Parametric Mapping, normal aging*

INTRODUCTION

Recently magnetic resonance diffusion tensor imaging (DTI) of the brain has allowed visualization of neuronal projections or estimation of the neuronal changes of patients with neurological disease through a decrease in the fractional anisotropy (FA) values. Some studies have already proved changes of FA values in the normal aging and some neurodegenerative disease by ROI measurement of FA values on the tensor images. However, it is not easy to place ROI at the same regions in different subjects. The result of ROI measurement does not show the mapping area with statistical different value. In this study, in addition to the conventional ROI measurement, we tried the normalization of DTI to the template form of the brain and analyzed by pixel-by-pixel comparison with statistical method using SPM to investigate changes of FA values in normal aging.

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PATIENTS & METHODS

The subjects were twenty healthy volunteers including ten young normal volunteers (Young group : 4 men, 6 women, 20-29 years of age), and ten senior normal volunteers (7 men, 3 women, 60-69 years of age) without known disorders affecting the central nervous system. Informed consents were obtained from all of subjects. Magnetic resonance imaging (MRI) was done with a 3.0Tesla imager (Signa VHi, GE Medical system), The sequence for DTI was as following; TR

(repetition time)/TE(echo time)=10000/87 msec, slice thickness=4.0 mm, field of view=28 cm, matrix=128×128, b value=1000 s/mm^2, NEX=1, MPGdirections=6. FA is defined by the following formula.

$$FA = \sqrt{\frac{3}{2}} \frac{\sqrt{(\lambda_1 - \langle D \rangle)^2 + (\lambda_2 - \langle D \rangle)^2 + (\lambda_3 - \langle D \rangle)^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

$$\langle D \rangle = \frac{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}{3}$$

FA map derived from DTI was converted to Analyze format after sending to a workstation. The processing of realignment, normalization using our original FA template and smoothing was conducted to each FA map by statistical parametric mapping software (SPM99)

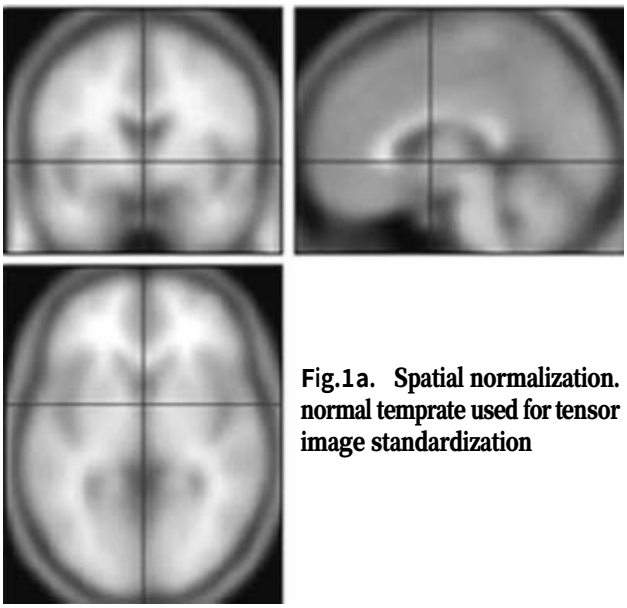

Fig.1a. Spatial normalization. normal temprate used for tensor image standardization

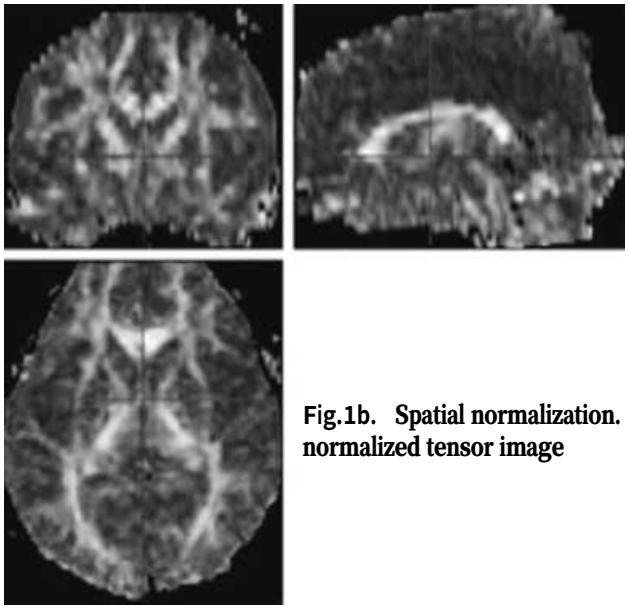

Fig.1b. Spatial normalization. normalized tensor image

(Fig.1a). Normalized FA images (Fig.1b) were compared between the two groups ; by t-test. The area with the significant difference ($p<0.05$) was depicted by colored portion on red and fused on T1 weighted template image of the brain.

As the evaluation by ROI measurement, we measured FA values of areas of depicted portions by statistical mapping analysis on SPM (by putting the ROI on white matter ; posterior limb of internal capsule/corona radiata/centrum semiovale/genu and splenium of corpus callosum/cerebeller hemisphere, gray matter ; basal ganglia/cingulate gyrus/cortical gray matter in the posterior lobe and frontal lobe as shown in (Fig. 2). FA values were measured in bilateral hemispheres except corpus callosum. The results of ROI measurement derived from two groups were statistically compared by the analysis of variance (ANOVA) and the statistical significance was determined at $p<0.05$.

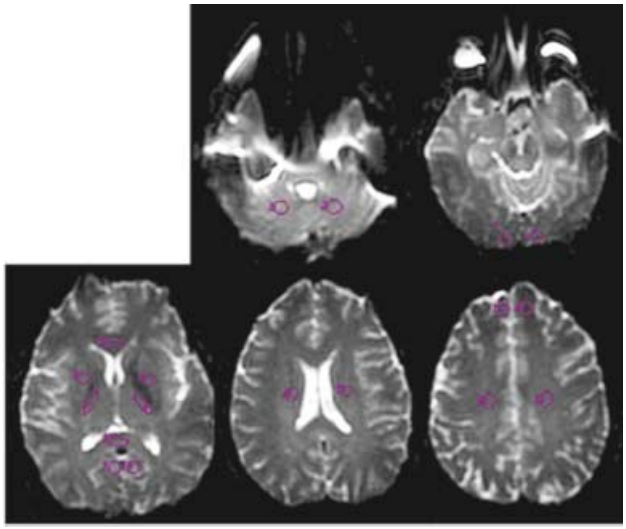

Fig.2. Depiction of ROIs in this study.
ROIs were drawn in the cerebeller hemisphere (1, 2), cortical gray matter in the posterior lobe (3, 4), basal ganglia (5, 6), posterior limb of the internal capsule (7, 8), cingulate gyrus (9, 10), corpus callosum (11, 12), coronara radiata (13, 14), centrum semiovale (15, 16), cortical gray matter in the anterior lobe (17, 18). All lesion except corpus callosum was measured bilaterally. Corpus callosum was measured both genu and splenium.

RESULTS

Using SPM, statistically significant increased FA regions were identified in bilateral basal ganglia, bilateral cingulate gyrus and other cortical gray matter in posterior and frontal lobe in the senior group (Fig. 3a). Statiscally significant decreased FA regions were identified in the white matterof bilateral cerebeller hemisphere, bilateral corona radiata, bilateral posterior limb of internal capsule, the genu and splenium of the

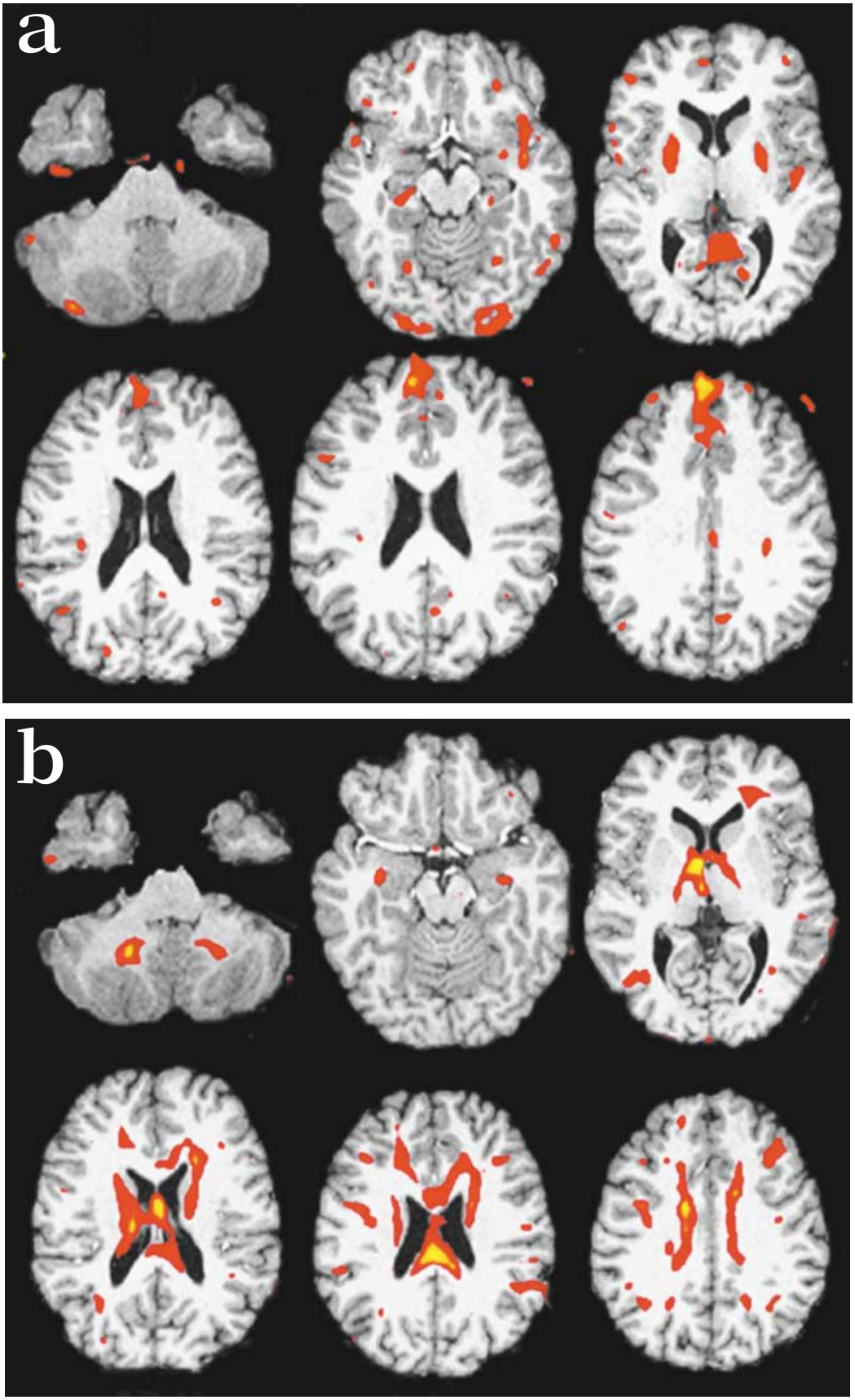

Fig. 3. Normalized tensor images were compared between the young and senior group by t-test. The area where the significant difference ($p<0.05$) was seen was colored in red and fused with T1 weighted image.

a. Statistically significant regions of increased anisotropy in the senior group. They were identified basal ganglia, cingulate gyrus and other cortical gray matter in posterior and frontal lobe.

b. Statistically significant regions of decreased anisotropy in the senior group. They were identified bil.cerebeller hemisphere,bil.corona radiata, bil.posterior limb of internal capsule, and the genu and splenium of the corpus callosum.

Table 1. Measured FA by ROI methodology was compared by t-test between two group. No statistically significance were seen between the rt and lt.regions both young and senior group. Our data showed a statistically significant decrease of FA in lt. cerebeller hemisphere, bil.corona radiata, bil.posterior limb of the internal capsule, and the genu of the corpus callosum, and increase of FA in rt.basal ganglia with age.

	mean FA value				t-test			
	Young group		Senior group		Young vs Senior		Right vs Left	
	Right	Left	Right	Left	Right	Left	Young	Senior
Cerebeller hemisphere	0.622	0.646	0.562	0.55	n.s.	0.004	n.s.	n.s.
Cortical gray matter (posterior lobe)	0.261	0.318	0.306	0.344	n.s.	n.s.	n.s.	n.s.
Basal ganglia	0.18	0.184	0.215	0.207	0.015	n.s	n.s.	n.s.
Internal capsule	0.668	0.669	0.619	0.63	0.001	0.036	n.s.	n.s.
Cyngulate gyrus	0.21	0.248	0.243	0.261	n.s	n.s	n.s.	n.s.
Corona radiata	0.612	0.614	0.575	0.549	0.03	0.049	n.s.	n.s.
Corpus callosum	0.757	0.787	0.696	0.741	0.036	n.s	n.s.	n.s.
Centrum semiovalle	0.555	0.534	0.493	0.486	n.s.	n.s	n.s.	n.s.
Cortical gray matter (frontal lobe)	0.258	0.269	0.263	0.296	n.s.	n.s	n.s.	n.s.

corpus callosum and bilateral centrum semiovale in the senior group (Fig 3b).

By the ROI method, significant FA decline was observed in the bilateral posterior limb of internal capsule (right : p=0.001, left : p=0.036), corona radiata (right : p=0.03, left : p=0.049), genu of the corpus callosum (p=0.036) and left cerebeller hemisphere (p=0.004) in the senior group. Significant FA increase was seen in the right. basal ganglia (p=0.015) with increase of age. Other cortical gray matter (frontal and posterior lobe and cingulated gyrus) where the significant difference was seen using SPM has no significant difference in the ROI measuring method (Table 1).

DISCUSSION

Using SPM, our data showed significant FA decline in bilateral cerebeller hemisphere, bilateral posterior limb of the internal capsule, bilateral corona radiata and genu and splenium of the corpus callosum, and FA increase in the bilateral basal ganglia and diffusely at the periphery of the brain especially in frontal and posterior lobe and cingulate gyrus with advantage age. About FA decline with aging, there were some reports, Nusbaum *et al.*(1) showed statistically significant decrease in FA with increasing age in the periventricular white matter, frontal white matter and genu and splenium of the corpus callosum, Abe *et al.*(2) showed FA decrease only in the genu of the corpus callosum, Pfefferbaum *et al.* (3) showed it in the frontal and parietal pericallosal regions, genu of the corpus callosum, and centrum semiovale, Edith V *et al.* (4) showed it in the genu of the corpus callosum and bilateral frontal and parietal pericallosal white matter. Common features of these reports were age related FA decline in the genu of the corpus callosum. According the past reports, since myelination of the splenium of the corpuls callosum precedes that of the genu of the corpus callosum, the anterior structure may result in greater or earlier degeneration than the posterior structure. Our results also agreed with those reports. Our study and Nusbaum's study in which similar methods of standardized tensor images were used demonstrated that FA decline was seen not only in the genu but also in the splenium of the corpus calloum. But in ROI measueing method, there was no significant defference in the splenium of the corpus callosum. As there was CSF near splenium of the corpus callosum, it was possible that partial volume effect may have arisen in ROI meseasuring. Other results about FA decline were mostly compatible with past reports.

Using statistical method, we found the statistically significant FA increase with advantage age in the bilateral basal ganglia and diffusely at the periphery of the brain, especially in frontal and posterior lobe. But in cortical gray matter where significant FA increase was seen, no significant difference was seen in ROI measuring method. It was mostly considered that this discrepancy might be caused by mis-registration of CSF space and cerebral cortex, i.e., contamination of CSF in pixels of cerebral cortex associated with brain atrophy on transformation to the template brain shape. These phenomenon was also seen in the study by Nusbaum *et al.*, they said because with aging, the cortical sulci are deeper and CSF-brain boundaries

more prominent, the cortical rim might have spu- r iously higher anisotropy values in older individuals.

In conclusion, we use SPM in standardizing diffusion tensor images and performed group analysis by t-test in this study. Although it should be recognized that this procedure may include technical error such as mis-registration on normal transformation, SPM method was considered to have some advantage in diminishing operator's bias and showing more visual demonstration of different FA areas than ROI measurement.

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