# Diffusion Tensor Spectroscopic Imaging of Multiple Metabolites in Rat Brains

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## Introduction

Diffusion tensor spectroscopy (DTS), which measures diffusion tensors of metabolites, is expected to provide specific information about tissue microstructures of neurons and glial cells [1,2]. Diffusion tensor spectroscopic imaging (DTSI), which measures diffusion tensor images (DTIs) of metabolites, has been developed recently [3] using diffusion-weighted echo-planar spectroscopic imaging with a pair of diffusion gradients (DW-EPSI with BPGs) to reduce motion artifacts [4]. DTI of N-acetylaspartate (NAA) in normal rat brains has been measured by using this technique [4]; however, the DTIs of metabolites except for NAA have not been reported to be measured.

In the present study, the DTSI was applied to obtain DTIs of NAA, creatine (Cr) and choline (Cho) in normal rat brains, and these DTIs of metabolites were compared to the DTI of water. The DTIs of NAA and Cr were successfully measured and are very similar to the DTI of water in most brain regions but show differences in the detail, i.e. cortex and corpus callosum (CC). The DTI of Cho was deteriorated by gradually decreasing the signal of Cho during measurement and is not very similar to the DTI of water. Further investigation is needed from the views of measurement technique and biophysical meaning; however, this result demonstrates DTSI may become a useful tool for investigating tissue microstructures.

## Methods

A 7-T MRI for a small animal study, equipped with a linear birdcage transmit coil, a surface receive coil and actively shielded gradient coils, was used. Three normal male Spraque-Dawley rats, with weights of 248 to 264 g, were measured. The DTSI uses DW-EPSI with BPGs with changed amplitude and direction of BPGs [3]. The measurement parameters were TR/TE of 3000/136 ms, spectral bandwidth of 7.24 ppm (128 points), FOV in the x and y directions of 40 mm (16 pixels), slice thickness of 2.5 mm, and number of acquisitions of 8. The pair of BPGs, with $\delta/\Delta$ of 12/12 ms and interval of 30 ms, was added. Diffusion-weighting measurements were done with *b*-vectors of 500, 1000, 2000, and 3000 × $10^6$ s/m$^2$ in 13 directions, and non-diffusion-weighting measurements were done 5 times. The DTIs of NAA, Cr and Cho were calculated by taking the logarithm of the signal peak intensities of each metabolite and multiplying it by the inverse matrix of *b*-vectors. To obtain the DTI of water, single-shot diffusion-weighted echo-planar imaging with a pair of BPGs was used. The parameters of the BPGs were the same as those stated above except for *b*-vectors of 333, 667, 1333, and 2000 × $10^6$ s/m$^2$. The total measurement time for DTSI and DTI was about 7 hours.

To compare the DTIs of metabolites and DTI of water, they were resized to have the same spatial resolutions. The obtained DTIs were analyzed by calculating tensor correlation coefficient (TCC) and difference of fractional anisotropy (FA) [3]. The TCC $r$ between diffusion tensors $\Lambda$ and $\Omega$ is defined as the following equation:

$$r(\Lambda,\Omega)=\sum_{i=1}^{3}\sum_{j=1}^{3}\lambda_i\omega_j(v_i\cdot w_j)^2\Big/\sqrt{\lambda_1^2+\lambda_2^2+\lambda_3^2}\sqrt{\omega_1^2+\omega_2^2+\omega_3^2}\ ,$$

where $\lambda_i$ and $v_i$ are eigenvalues and eigenvectors of $\Lambda$, $\omega_j$ and $w_j$ are eigenvalues and eigenvectors of $\Omega$, and · denotes the inner product of two vectors.. The FA difference was calculated as $FA_{metabolite} - FA_{water}$, where each FA was calculated from the corresponding diffusion tensor.

## Results and Discussion

The obtained DTIs of NAA and Cr show radial diffusivity in the cortex and right-left diffusivity at CC in the same manner as the DTI of water (Fig. 1). The calculated mean TCCs of NAA and Cr are very similar to water, and the TCC maps of NAA and Cr show high TCC in most regions, except near cortex, base and CC. The FA difference maps of NAA and Cr show that the FAs of NAA and Cr are higher than the FA of water in most regions, except at CC. These differences in TCC and FA between the metabolites and water may be caused by cellular localization of metabolites. The difference between NAA and Cr is not so large; thus, further investigation is needed to make clear the different localization between NAA and Cr. The DTI of Cho shows a low TCC and a high FA difference; however, gradually decreasing the signal of Cho during the long measurement time affected the result. This suggests that a faster measurement technique is needed to improve the accuracy.

## Conclusion

DTIs of NAA and Cr of normal rat brains were obtained by using DTSI. The obtained DTIs of NAA and Cr showed similar aspect to DTI of water but showed difference in detail, possibly reflecting specific tissue microstructures.

## References

[1] Ellegood et al. MRM 2006;55:1. [2] Upadhyay et al. MRM 2007;58:1045. [3] Bito et al. ISMRM 2011:408. [4] Bito et al. ISMRM 2010:24.

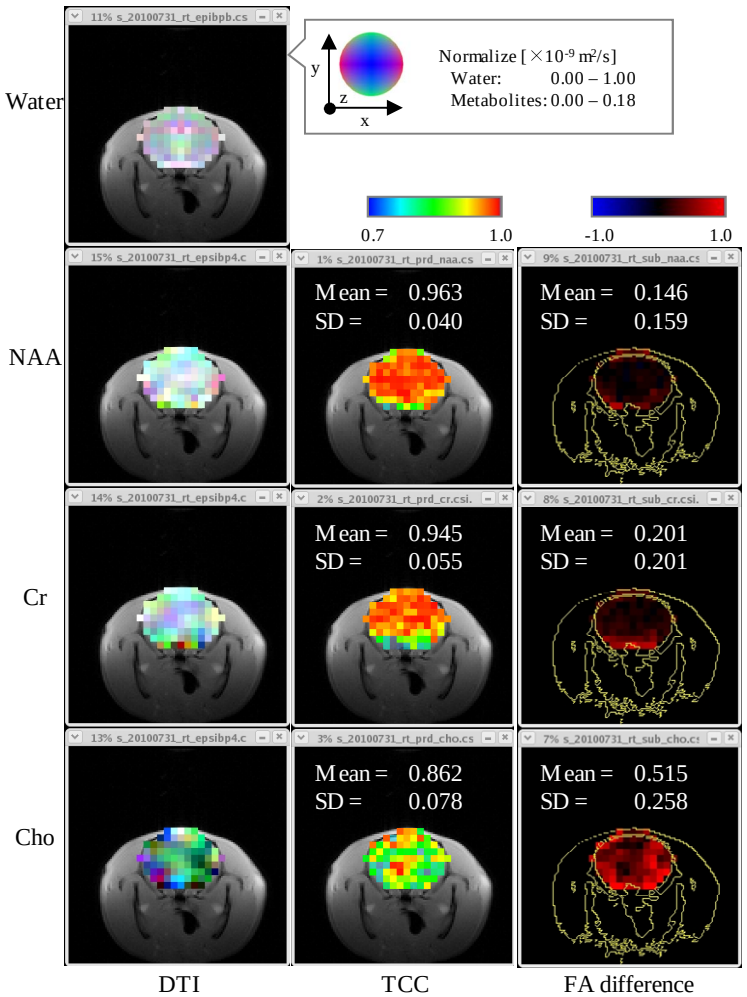


Fig. 1. Color maps of acquired DTI, TCC and FA difference of metabolites and water of a typical rat brain. Overlaid mean and SD were calculated using three rat brains.