Diffusion-weighted Spectroscopic Imaging of Multiple Metabolites in Rat Brains after Middle Cerebral Artery Occlusion

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Introduction

Diffusion-weighted spectroscopy (DWS) and diffusion-weighted spectroscopic imaging (DWSI) are expected to provide useful information about tissue microstructures and functions [1]. DWSI has an advantage in acquiring spatial information; however, it has a disadvantage in accuracy, especially concerning larger motion artifacts, compared to DWS. To overcome this disadvantage, we previously developed diffusion-weighted echo-planar spectroscopic imaging with a pair of bipolar gradients (DW-EPSI with BPGs) [2]. After that, to investigate specific changes in neurons, we used the DW-EPSI with BPGs for acquiring the change in apparent diffusion coefficient (ADC) for N-acetylaspartate (NAA) after a middle cerebral artery occlusion (MCAO) in rat brains [3].

In the present study, to investigate changes in neurons and glial cells after MCAO in rat brains, we expand that previous study to analysis of multiple metabolites including creatine (Cr) and choline (Cho). To the best of our knowledge, the changes in ADC maps for NAA, Cr and Cho after MCAO were acquired for the first time. We analyzed the acquired data by using a Gaussian mixture distribution, which can handle many spatial pixels acquired simultaneously by DWSI. The analysis result demonstrates the advantage of acquiring spatial ADC maps for multiple metabolites by DWSI.

Methods

As previously reported [3], a 7-T MRI for small-animal study was used to measure seven male Sprague-Dawley rats with a right permanent MCAO and three normal ones. Each rat was cyclically measured by using a set of techniques, where each set was composed of DW-EPSI with BPGs and diffusion-weighted echo-planar imaging (DW-EPI). The measurement time for each set was 30 minutes, and the number of sets was 12. The measurement parameters of DW-EPSI with BPGs 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 eight. A pair of bipolar diffusion gradients was added in the x, y, and z directions at $b = 3000\times10^6$ s/m^2 and $\delta/\Delta = 12/12$ ms. ADC for NAA, Cr and Cho (ADC_{NAA}, ADC_{Cr} and ADC_{Cho}) were acquired by DW-EPSI with BPGs, and that of water (ADC_{water}) was acquired by DW-EPI. A two-term two-dimensional Gaussian mixture distribution was used to analyze changes in pairs of ADC_{water} and either of ADC_{NAA}, ADC_{Cr} or ADC_{Cho} after MCAO. An expectation-maximization algorithm was used to calculate parameters of the distribution fitted to each two-dimensional pair of ADCs of water and each metabolite for all pixels in the rat brains. Two-dimensional analysis was used because the number of pixel was not enough for four-dimensional analysis.

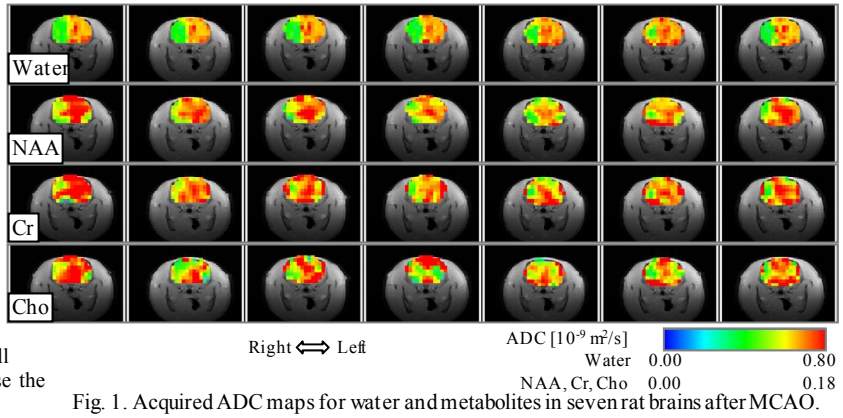

Fig. 1. Acquired ADC maps for water and metabolites in seven rat brains after MCAO.

Results and Discussion

ADC_{water} clearly decreases in the right hemisphere of all rats after MCAO, however, ADC_{NAA}, ADC_{Cr}, and ADC_{Cho} do not decrease as much as ADC_{water} (Fig. 1). The calculated two-term Gaussian mixture distribution shows that the major term is almost sufficient to fit the normal data, and two terms are needed to fit the MCAO data (Fig. 2). The reductions in ADC in descending order are as follows: water (60%), NAA (89%), Cr (93%), and Cho (96%). The significant difference in the ADC reductions for metabolites and water may mean that the ADCs of metabolites are influenced by only some of the causes that reduce ADC_{water} because these metabolites exist mostly in cells. The differences between the ADC reductions for the metabolites may be caused by a difference in local environments; namely, NAA exists mostly in neurons, but Cr and Cho exist in both neurons and glial cells. However, the differences in ADC reductions for the metabolites are so small, and the percentages do not agree well with the values in either of the previous studies using DWS [4, 5]. More validation of these results may be needed because ADCs of metabolites and water are influenced by measurement parameters such as *b*-values, time, and direction of diffusion gradients. Nevertheless, it is shown that DW-EPSI with BPGs is effective for investigating spatially varying changes of ADC for multiple metabolites simultaneously.

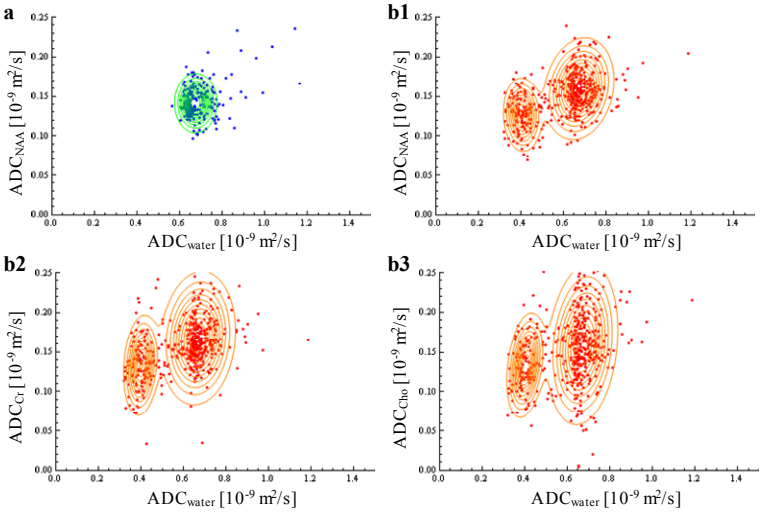

Fig. 2. (a) ADC_{NAA} vs. ADC_{water} in normal rat brains. (b1) ADC_{NAA}, (b2) ADC_{Cr}, and (b3) ADC_{Cho} vs. ADC_{water} in rat brains after MCAO. Scatter plots represent all spatial pixels and contour plots represent probability density function of fitted two-term Gaussian mixture distribution.

Table 1. Mean and standard deviation of ADCs of fitted two-term Gaussian mixture distribution in normal and MCAO rat brains. ADC reduction rate due to MCAO is calculated as (b)/(a) since minor term of MCAO rats represents ischemic lesion.

	Normal rats		MCAO rats		Rate
	Major term (a)	Minor term	Major term	Minor term (b)	(b)/(a)
Water	0.672±0.013	0.838±0.049	0.670±0.024	0.404±0.013	60.1%
NAA	0.142±0.005	0.170±0.013	0.160±0.009	0.127±0.007	89.4%
Cr	0.143±0.008	0.181±0.015	0.167±0.008	0.133±0.009	93.0%
Cho	0.138±0.007	0.156±0.007	0.159±0.015	0.133±0.009	96.3%
Fraction	0.849	0.151	0.742	0.256	

Conclusion

Changes in ADC maps for NAA, Cr and Cho after MCAO in rat brains were acquired by using DW-EPSI with BPGs. This technique is effective for investigating spatially varying ADC changes for metabolites. It may be useful for understanding intra-cellular dynamics and diffusion environment in specific cells such as neurons and glial cells by using appropriate metabolites as probes.

References

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