Diffusion-weighted Spectroscopic Imaging of 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]. DWS has been used for several studies [2-4]; however, DWSI has not yet been used in biophysical or clinical studies mainly because an accurate measurement technique that overcomes the issues of long measurement time, low signal-to-noise ratio, and large motion artifacts has not yet been developed [5]. To overcome these issues, we developed diffusion-weighted echo-planar spectroscopic imaging with a pair of bipolar gradients (DW-EPSI with BPGs), and showed its effectiveness in reducing motion artifacts in normal rat brains [5]. However, its effectiveness in biophysical studies has not yet been clarified.

In the present study, we applied the previously developed DW-EPSI with BPGs to investigate the change in apparent diffusion coefficient (ADC) of N-acetylaspartate (NAA) after a middle cerebral artery occlusion (MCAO) in rat brains. To the best of our knowledge, the changes in ADC maps of NAA after MCAO were acquired for the first time. The acquired data were analyzed by using a Gaussian mixture distribution, which can handle many spatial pixels acquired simultaneously by DWSI. The obtained result was consistent with a prior reported result obtained by using DWS after MCAO in rat brains [4], and it demonstrated the usefulness of acquiring spatial maps by DWSI.

Methods

A 7-T MRI for small-animal study, equipped with a surface receive coil and actively shielded gradient coils, was used. Ten male Sprague-Dawley rats, seven with right permanent MCAO and three normal ones, were used. Each rat was cyclically measured by using a set of techniques, where each set is 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 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. An ADC map of NAA was calculated by using DW-EPSI with BPGs, and that of water was calculated by using DW-EPI. A two-term two-dimensional Gaussian mixture distribution was used to analyze changes of ADC of NAA (ADC_{NAA}) and ADC of water (ADC_{Water}) after MCAO. An expectation-maximization algorithm was applied to calculate parameters of the distribution fitted to the acquired two-dimensional pair of ADC_{NAA} and ADC_{Water} for all pixels in the rat brains.

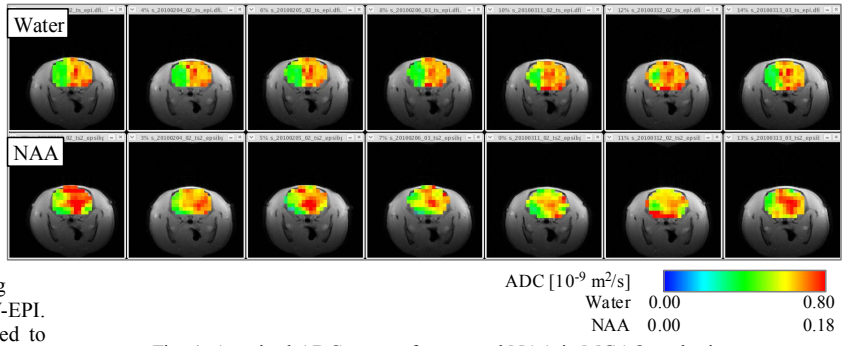

Fig. 1. Acquired ADC maps of water and NAA in MCAO rat brains.

Results and Discussion

Figure 1 shows reductions of ADC_{NAA} and ADC_{Water} in the right hemisphere of all rats after MCAO. The calculated two-term Gaussian mixture distribution shows that single term is almost sufficient to fit the normal data and two terms are needed to fit the MCAO data (Fig. 2 and Table 1). The reductions of ADC are about 60% for water and 77% for NAA. The difference in these reductions may mean that ADC_{NAA} is influenced by only some of the causes that reduce ADC_{Water} because NAA exists mostly in neurons. These values agree well with the previously reported values in one previous study [4] but less well with the values in another study [3] using DWS. More validation of the results may be needed because ADCs of NAA and water are influenced by measurement parameters such as *b*-values, time, and direction of diffusion gradients. Furthermore, ADC_{NAA}, ADC_{Water} and fraction of the first and second terms of the Gaussian mixture distribution were calculated for each cycle (Fig. 3). The figure suggests that ADC of each term does not change so much, but the fraction of each term changes with time. This result may mean the time taken by the biophysical change in a pixel was shorter than the measurement time for each set. A faster measurement technique may thus be needed to track such fast changes precisely. These results show that DW-EPSI with BPGs is effective for investigating spatially varying changes in a brain. They also show that retrospective analysis combined with DW-EPSI is useful in biophysical studies because spatial information can be taken into account after the measurements.

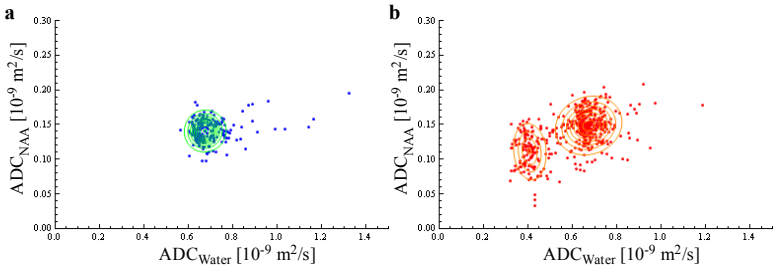

Fig. 2. ADC_{NAA} vs. ADC_{Water} in normal (a) and MCAO (b) rat brains. Scatter plots represent all spatial pixels and contour plots represent probability density function of fitted two-term Gaussian mixture distribution.

Table 1. Mean and covariance of ADCs of fitted two-term Gaussian mixture distribution in normal and MCAO rat brains. "1" and "2" represents each term of the distribution.

		(a) Normal rats			(b) MCAO rats		
		Mean [10^{-9} m^2/s]	Covariance [10^{-20} m^4/s^2]		Mean [10^{-9} m^2/s]	Covariance [10^{-20} m^4/s^2]	
1	ADC_{Water}	0.673	0.0190	0.0001	0.673	0.0552	0.0019
	ADC_{NAA}	0.141	0.0001	0.0020	0.149	0.0019	0.0045
2	ADC_{Water}	0.862	0.2619	0.0199	0.407	0.0186	-0.0015
	ADC_{NAA}	0.145	0.0199	0.0051	0.111	-0.0015	0.0060
Fraction 1:2		0.882 : 0.117			0.734 : 0.266		

Conclusion

Changes in ADC map of NAA was acquired after MCAO in rat brains by using DW-EPSI with BPGs. This technique is effective in investigating spatially varying ADC changes of metabolites. It may be also useful for understanding intra-cellular dynamics of neurons by using NAA as a probe.

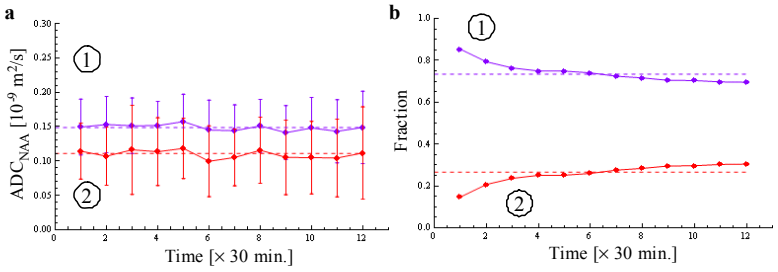

Fig. 3. Mean ADCs of NAA and their fractions of calculated two-term Gaussian mixture distribution with time after MCAO in rat brains. "1" and "2" represents each term of the distribution and dotted line represents average of corresponding values with time.

References

[1] Nicolay et al. NMR Biomed 2001;14:94. [2] Wick et al. Stroke 1995;26:1930. [3] Toorn et al. MRM 1996;36:914. [4] Dreher et al. MRM 2001;45:383. [5] Bito et al. ISMRM 2010;24.