On the Application of Anomalous Diffusion Metrics in Animal Stroke Models

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Target Audience

This abstract evaluates the stretched-exponential model as a biomarker of stroke lesions and is of interest for researchers and clinicians dealing with brain pathologies and applications of advanced diffusion MRI methods.

Purpose

In recent years, non-Gaussian diffusion methods, such as diffusion kurtosis imaging[1] (DKI) or anomalous diffusion imaging based on the stretched-exponential model[2] (SEM), have gained increasing interest in brain research. Several applications of both methods have been reported to provide enhanced information on microstructural properties of healthy and pathological tissue. In particular, striking enhancement (by factor 2 to 3) of the kurtosis metrics in stroke lesions was observed by Jensen et al. (2010) in humans and by Grinberg et al.[3] in animals. Promising SEM application to investigation of brain tumours have been reported by Bennett et al. (2004). The purpose of this work is to investigate the applicability and sensitivity of the SEM metrics as biomarkers of ischemic lesions in the animal stroke models.

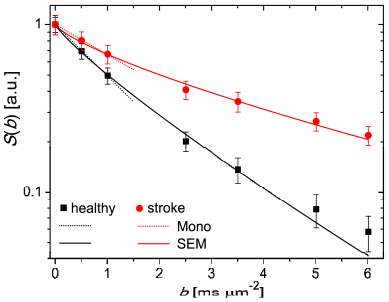

Figure 1. Diffusion-weighted signal as a function of *b*-values.

Materials and Methods

The details regarding the MR experiments and animals used in this study are described elsewhere[3]. Diffusion-weighted signal S in the range of b-values ≤ 6 μm^{-2} ms was analysed in terms of the SEM[2]

$$S(b) = \exp\left\{-(b \times DDC)^{\alpha}\right\},$$

with two free parameters: the distributed diffusion coefficient, DDC, and the stretching exponent, α, characterising deviations from the mono-exponential behaviour (the so-called heterogeneity index). For the Gaussian model, α=1. Satisfactory fits were obtained as shown in Figure 1 in the large range of signal attenuations exceeding one order of magnitude. The SEM metrics are compared to the mean diffusivity MD evaluated by conventional DTI. Diffusion anisotropy in grey matter lesions was very low, therefore fractional anisotropy is not considered.

Results and Discussions

Figure 2 (left) shows the maps of MD, DDC and α for two selected slices, all maps providing a clear contrast of two ischemic lesions located in the cerebral cortex (CT) and in the cauduate putamen (CPu). Interesting findings here are that the DDC-maps provide even larger contrast than MD-maps (considered to be the gold standard in stroke assessment), and that α-maps exhibit more structural details than the diffusivity maps. The observed contrasts are substantiated by the significant shifts of the parameter histograms observed in lesions, Figure 2 (right).

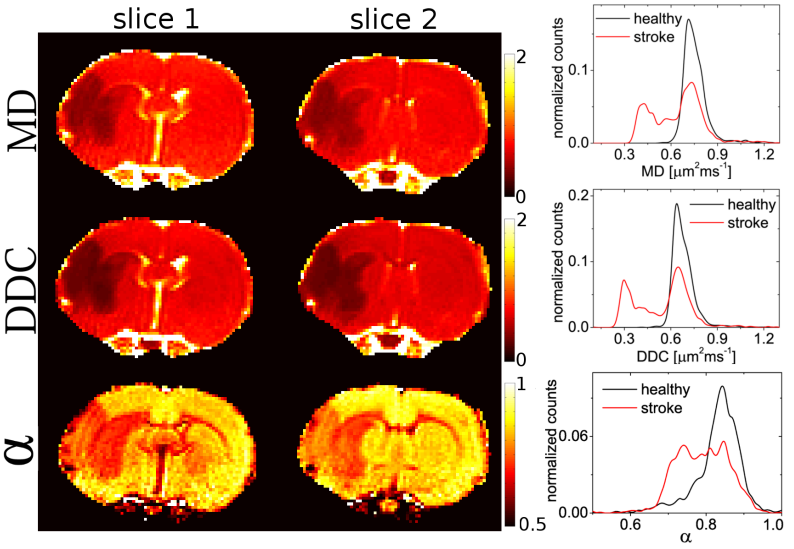

Figure 2. The maps of MD, DDC, and α in two selected slices (left) and the corresponding averaged histograms (right).

In frame of the anomalous diffusion and fractal model approaches proposed by Özarslan et al. (2006), Hall and Barrick (2008), and Zhou et al. (2010), lower α values indicate increasing disorder of the microenvironment in which the molecules diffuse. The observed decrease of α values in lesions can be related to the cell swelling and beading (focal enlargements) of cellular projections accompanying the cascade of pathological processes in stroke. Thus, the SEM metrics provide complementary means to infer valuable microstructural information.

Figure 3 summarises the relative quantitative changes (first 24 hours after reperfusion) of MD, DDC and α averaged over total of 12 slices (4 slices in 3 animals) with respect to the healthy contralateral tissue. Among the latter parameters, the largest change (54%) was observed for DDC and the smallest change (13%) was observed for α. In difference, two other non-Gaussian models, DKI and LNDF (log-normal distribution function), considered in the previous works[2] exhibit much stronger change of the parameters characterising non-Gaussianness (kurtosis, MK, and σ for LNDF), than the parameters characterising diffusivities (D_K for DKI and D_{ld} for LNDF), compare the data in Figure 3.

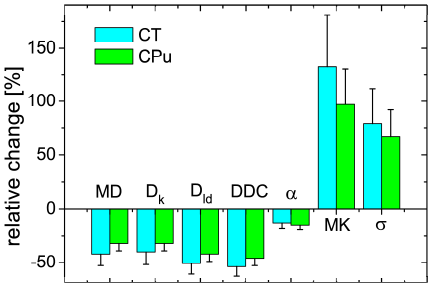

Figure 3. Relative average changes of the values of MD, D_K, D_{LD}, DDC, α, MK and σ in ischemic lesions with respect to healthy tissue averaged over 12 slices (4 slices in 3 animals).

Conclusions

In conclusion, anomalous diffusion imaging based on the stretched-exponential model provides promising results in terms of stroke assessment and better understanding of pathological microstructural changes in the ischemic lesions.

References

[1] J.H. Jensen, J.A. Helpern, A. Ramani, H. Lu, K. Kaczynski, Magn. Reson. Med., 53 (2005) 1432–1440; [2] K.M. Bennett, K.M. Schmainda, R.T. Bennett, D.B. Rowe, H. Lu, J.S. Hyde, Magn. Reson. Med., 50 (2003) 727-734; [3] F. Grinberg, L. Ciobanu, E. Farrher, N.J. Shah, NMR Biomed., 25 (2012) 1295-304.