Evolution of Fractional Anisotrophic Changes In An Animal Model of Ischemic Stroke: Relative Contribution of Anisotropic Versus Magnitude Diffusivity

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Introduction

The diffusion tensor imaging (DTI) parameter, fractional anisotropy (FA), is now widely used as a numerical index of water molecular diffusion anisotropy to reflect microstructural changes in white matter diseases. Since FA is computed from a division of the standard deviation of the three eigenvalues (q = $q = \sqrt{(\lambda_1 - D)^2 + (\lambda_2 - D)^2 + (\lambda_3 - D)^2}$) by their root-mean-square value (L = $L = \sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}$), changes in FA under pathological conditions may not be specific [1]. In ischemic stroke, FA can be paradoxically higher in ischemic region than that of contralateral normal brain, and then declines rapidly over the ensuing time course [2]. Although the FA changes in acute ischemic stroke can potentially be of value in term of therapeutic window indicators, it is unclear whether the changes are mostly attributed to reciprocal alterations in q or L, and whether the changing patterns differ between early and late ischemic phases. Therefore, the aim of our study is to investigate the differential behaviors of q and L in the ischemic penumbra versus the infarct core using a longitudinal rat stroke model.

Materials and Methods

Intraluminal thread occlusion of one middle cerebral artery (MCA) was performed on eight rats as the model of ischemic stroke. DTI was performed at 7T (PharmaScan 70/16; Bruker, Germany) with six non-collinear diffusion-encoding gradients at a b factor of 1,100 s/mm^2 plus one b = 0 T2-weighted reference. The signal readout module was a multi-shot echo-planar imaging (TR = 10000 ms, TE = 31 ms, NEX = 4) with navigator-echo correction. To investigate the longitudinal changes of q and L, the scan was executed at 0.5, 1.5, 2.5, 3.5, 4.5, 5.5, and 6.5 hours after stroke onset, thus seven time points were obtained. Perfusion-weighted imaging was also performed sequentially using the dynamic susceptibility-contrast technique at 2 second temporal resolution (total 40 time frames) with bolus injection of Gd-DTPA via the left femoral vein. Analysis of the imaging data was carried out separately for the ischemic core and the penumbra regions, using in-house software. The ischemic core (IC) and ischemic penumbra (IP) were defined based on the diffusion-perfusion mismatch concept, where IC was determined as tissues showing reductions of 62% or more in the cerebral blood flow (CBF) [3] and a drop of 30% or more in the apparent diffusion coefficient (ADC) [4] compared with the contralateral hemisphere, and IP as tissues showing perfusion deficit but the ADC reduction was less than 30%. Diffusion tensor parameters *q* and *L* were then derived, and with the diffusion tensor ellipsoids shown to provide visualization of the dynamic morphological alterations.

Results

Figure 1 shows the longitudinal evolutions of *q* and *L* in the ischemic core (Fig.1a) and in the ischemic penumbra (Fig.1b), respectively, expressed as percentage changes relative to the contralateral tissue. In both IC and IP, a more prominent temporal changes in the numerical value of *q* is found than in *L*, suggesting that post-ischemic changes in FA is largely dominated by the anisotropic diffusivity *q* rather than by the magnitude diffusivity *L*. In addition, both *q* and *L* remained declined stably in the penumbra (Fig.1b), unlike in the ischemic core where the anisotropic diffusivity is seen to reduce continuously to approximately –40% up to 6.5 hours (Fig.1a). Figs.2a-2g show the graphical changes of the diffusion tensor ellipsoids at the seven time points following ischemic onset. Although visually somewhat less obvious, the cigar-shaped diffusion tensor ellipsoid in the ischemic core shows slow deformation into a disc shape. Changes in *q* plotted versus *L* in Fig.2h shows two well-separated clusters corresponding to the ischemic core and penumbra.

Discussion

It has been shown that in acute cerebral ischemia, FA in the ischemic region can be higher than that of the contralateral normal brain tissue, and then declines rapidly over the time course observed [2]. Results from our animal model study suggest that this FA trend seems to be mainly determined by the pure anisotropic diffusivity *q*. The magnitude diffusivity, on the other hand, decreased immediately at the onset of ischemia and no longer exerted substantial influence on the trend of FA changes. This behavior suggests that *q* may detect stroke-related abnormality with a higher sensitively than *L*. The relative stable q in ischemic penumbra may provide insight into the definition of salvageable brain tissue in hypoperfused brain at acute setting.

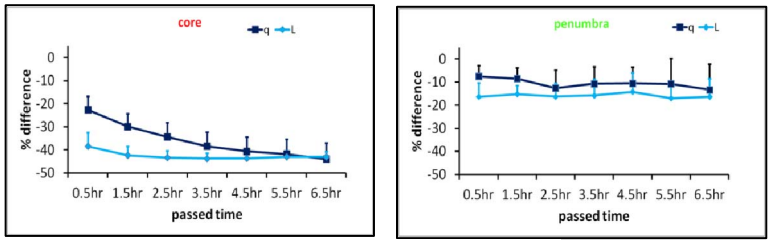

Fig. 1 Temporal evolutions of *q* and *L* from 0.5 to 6.5 hours after stroke onset for the ischemic core (a, left) and the penumbra (b, right), showing that the changes in *q* (dark blue) seem to dominate the FA alterations.

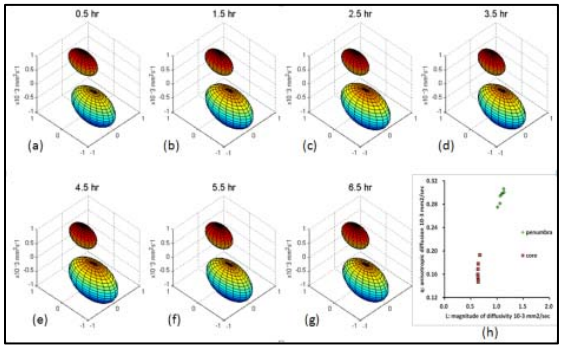

Fig. 2 (a-g) Evolution of diffusion ellipsoids in IP (big ones) and in IC (small ones) from 0.5 to 6.5 hours after stroke onset, respectively. (h) q plotted versus L shows two well-separated clusters corresponding to IP and IC. The L values remain largely unchanged.

References

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