The effects of myelin in FA and QSI indices: control vs. Long Evans shaker rat brains

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Introduction. Water diffusion in neuronal tissues was found to be anisotropic more than a decade ago.[1] Various structural components of the white matter (WM) tissue determine this anisotropy, i.e., myelin sheaths, axonal membranes, microtubules and neurofilaments[2], but even now the relative importance of myelin in determining this anisotropy is still under debate[3]. Conventional DTI uses low diffusion weighting in the characterization of white matter tissue, and assumes Gaussian diffusion of a single component[4]. It is known that at sufficiently high diffusion weighting, more than one diffusion component can be observed in neuronal tissues[5]. The q-space approach has been suggested as an effective means for analyzing such high b-value DWI data in neuronal tissues[6]. In the present study we used high b-value q-space diffusion MRI to characterize, for the first time, the diffusion characteristics of Long Evans shaker (*les*) rat brains and their age matched controls. We evaluated the effect of myelin on three MRI diffusion indices; displacement, probability and kurtosis at three different maturation stages.

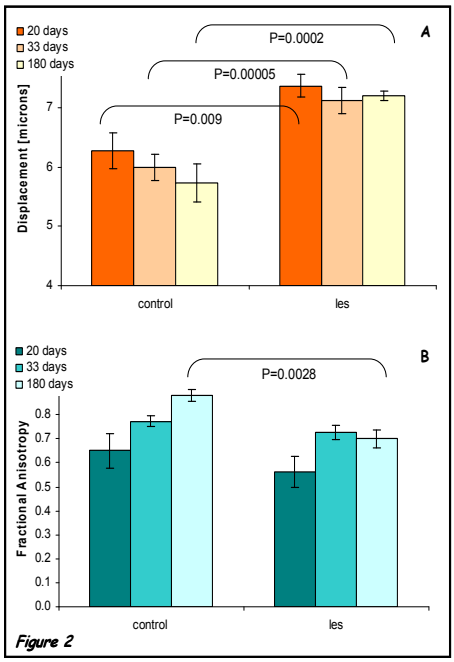

Figure 2

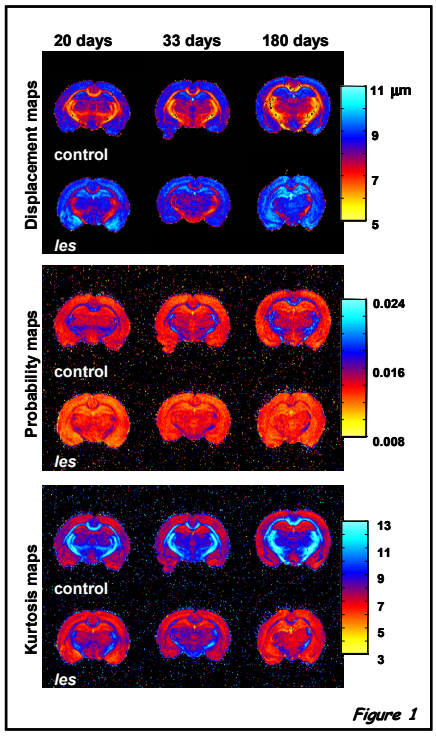

Figure 1

Methods. MRI experiments were performed on a 7T/30 cm BioSpec System (Bruker, Germany) equipped with a BGU20 gradient system capable of producing pulse gradients of up to 40 gauss cm-1 in each of the three dimensions. Formalin fixed brains of 20, 33 and 180 days old *les* brains and their age matched controls were used in this study. Ten coronal continuous 1 mm slices were acquired with a protocol that included T2 weighted MR images (TR/TE = 3000/80 ms) and high b-value QSI.[6] The following parameters were used when acquiring the QSI: TR/TE =2500/20 ms, Δ=100 ms, δ=4 ms, an FOV of 1.92 x 1.92 cm, a matrix of 128 x 64 (zero filled to 128 x 128) and 4 averages. The diffusion gradient was incremented from 0 to 36 G/cm in 13 equal steps for all 6 directions, resulting in maximal b- and q-values of 13,850 s/mm^2 and 613 [cm^{-1}], respectively.

Results and Discussion. Figure 1 depicts the displacement, probability and kurtosis maps, obtained from the q-space diffusion MRI experiments of representative control and *les* brains at three different time points. For the displacement maps, the smallest mean displacement value out of the six diffusion directions was selected for each voxel. For the probability maps, the highest probability for zero displacement out of the six directions was selected for each voxel. For the kurtosis maps, the highest kurtosis value, which characterizes the deviation from Gaussian diffusion, i.e., maximum restriction, out of the six diffusion directions, was selected for each voxel. All of the diffusion indices suggest that there is more restriction in the WM of the control brain. Figure 2 shows quantitative ROI analysis of the internal capsule in the control and *les* brains of all three age groups. Figure 2A shows the average displacement values and Figure 2B shows the Fractional Anisotropy (FA) as extracted from the low b-value regime of the QSI data. The displacement values are significantly bigger in the *les* rat brains as compared to their age matched controls, suggesting that there is more water diffusion and less restriction in the WM of the *les*. In addition, for the control brains, the displacement values become smaller as the rat matures, although differences are not statistically significant. This suggests that the mature brains are more structured and myelinated, therefore, more restriction is observed. The fractional anisotropy, calculated from the low b-value regime of the QSI data, depicts higher values in the control brains but in a significant manner only for the 180 days age group, showing higher power of high b-value QSI to distinguish between the two groups. Figure 3 shows histological images of proteolipid protein (PLP) and myelin basic protein (MBP) immunostained 28 days old control and *les* brains. The *les* brains show mild staining with PLP and no staining with MBP. In agreement with the MRI results, this figure shows that a *les* brain of about 30 days of age lacks one of the main genes for myelin.

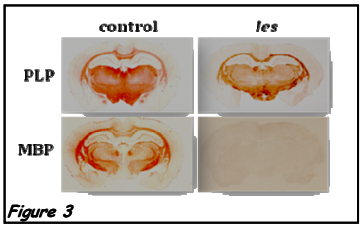

Figure 3

Summary. This study shows that the lack of myelin affects the diffusion indices obtained from the high b-value q-space DWI. Quantitative analysis of the displacement values shows significant differences between the *les* and control groups in all age groups. In addition, we found that FA blurs the differences between the two groups. Significance is observed only in the older rats (180 days) where the difference in myelin content is the biggest. Therefore, high b-value q-space DWI should be considered as a means for achieving better distinction between *les* and control brain tissues.

References. [1]Moseley ME et al., Radiology, 1990; 176: 439-445. [2] Beaulieu C., Allen P.S. Magn Reson Med 1994; 31: 394-400. [3] Beaulieu C, NMR Biomed, 2002; 15: 435-455. [4] Basser PJ, Pierpaoli C, Magn Reson Med, 1998; 39: 928-934. [5] Assaf Y., Cohen Y. Magn Reson Med 2000; 43: 191-199. [6] Assaf et al., Magn Reson Med, 2000; 44, 713-724