Double-PFG MR imaging of the CNS: probing underlying grey matter microstructure

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Introduction. Single-Pulsed-Field-Gradient (s-PFG) MR methods such as diffusion tensor imaging (DTI)1 and q-space imaging2 have become the methods of choice for characterizing white matter tissues in central nervous system (CNS) tissues owing to their ability to portray diffusion anisotropy in coherently organized structures having ensemble anisotropy (eA). However, conventional s-PFG methodologies are extremely limited when anisotropic compartments are randomly oriented (such as grey matter); in these cases, diffusion appears isotropic in s-PFG and the underlying microstructural information is completely lost. Recently, angular double-PFG (d-PFG) experiments were performed on a variety of specimens ranging from coherently organized microcapillaries3 to randomly oriented pores4 and even grey and white matter tissues5,6, showing the possibility of obtaining unique microstructural information.

Aims. To explore the possibility of revealing microstructural features within grey matter tissues using d-PFG MRI.

Methods. All experiments were performed on a 7T Bruker Biospec equipped with a gradient system capable of producing up to 40 G/cm in all directions. A double-Pulsed-Gradient-Spin-Echo (d-PGSE) MRI sequence with EPI readout was written in-house. First, the d-PFG MRI was performed on a phantom comprised of microcapillaries having a diameter of 20 ± 1 μm that were aligned with their main axis pointing towards the z-direction. The in-plane resolution was 280 μm isotropic, and the slice thickness was 15 mm. Experiments were performed on ex vivo rat brains where the in-plane resolution was 141 μm isotropic, and the slice thickness was 1.2 mm. Further experiments were performed on pig spinal cord, where the in-plane resolution was 100 μm isotropic, and the slice thickness was 2 mm. For the phantom, Δ1=Δ2=55 ms, Δ3=2 ms, and t=2.2 ms were selected, and the experiment was performed at 2q=510 cm⁻¹. For the spinal cord Δ1=Δ2=25 ms, Δ3=4 ms, and t=4.2 ms were used. For the rat brain, the same parameters were used except Δ1=Δ2=20 ms. These experiments were performed at 2q=1090 cm⁻¹. The angular d-PFG experiment6 was performed in the X-Y plane and the angle ψ was incremented in 30º steps between 0º and 360º. The E(ψ) images were co-registered and then all of the images were normalized to a reference image Eref=ψ=0º, yielding normalized E(ψ) images. To search for patterns within the 13 ψ values, multiparametric clustering was performed using the kmeans clustering algorithm as previously described11.

Results and Discussion. Figure 1 shows the normalized data (E(ψ)/Eref) of the d-PFG MRI images of the phantom. The expected angular profile for microcapillaries shows marked differences, demonstrating that water is diffusing in randomly compartments of different eccentricities; orange clusters show characteristics of more coherent ordering, like one would expect from areas with more white matter contribution. These findings show underlying microstructural heterogeneity of the cortex. While there is no reason to expect that these data will exactly correspond to different functional regions (since they only convey microstructural differences), there seems to be some similarities to the Paxinos and Watson atlas, especially in the more lateral cortex. Figure 3C shows data from the striatum. Here, although the clustering algorithm finds different behaviors, the E(ψ) plots are quite similar to one another, suggesting little microstructural heterogeneity at this slice of the striatum. Of course, this could be to some extent a manifestation of partial volume effects, and it is highly likely that signal from more anterior parts, where the striatum is more uniform, contribute substantially to the similarity of the E(ψ) plots. Histological studies are underway to corroborate the d-PFG MRI findings. Similar observations were made in the grey matter of spinal cords (data not shown).

Conclusions. These findings suggest that d-PFG MRI may become a very useful means to characterize grey matter underlying microstructure.

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