Investigating the Functional Diffusion-Signal Response (DfMRI) in Living, CA1 Pyramidal Neurons Undergoing Chemical Activation with Kainate

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Introduction

If the changes in compartmentation of intra and extra cellular water that take place during neuronal firing[1,2] could be detected using diffusion-based MR contrast, this mechanism would offer significant spatial and temporal improvements over blood-oxygen level dependent (BOLD) based methods. In order to better understand the cellular origins of DfMRI signal contrast, we conducted functional activation experiments at resolutions (15.6μm in-plane) high enough to quantify diffusion data from individual hippocampal lamina.

Experimental

Diffusion-weighted MR data (TR/TE = 2000/12.9, Δ = 6.5ms, δ = 1.3ms, b = 0 to 3200 s/mm^2, resolution = 15.6μm in-plane, avg = 4, scan time = 8.5min) were acquired (**Fig. 1**) using the 600MHz spectrometer in AMRIS. Scans were collected employing a micro perfusion and oxygenator system interfaced to a modified surface coil (200μm diameter) as described previously[3]. Acute, rat hippocampal slices (n = 6) were maintained over a time course of 3.3 h. Image series were collected before and after slices were activated with 100μM kainate and signal properties were compared in the strata oriens, pyramidale and radiatum.

Results and Discussion

The hippocampal layer containing the perikarya of pyramidal neurons (S.P., **Fig.2**) exhibited a significant change in diffusion properties between inactive and active states (p = 0.0043, **Fig.3**). This result maintained significance (CI = 95%) even when subjected to a Bonferroni correction (0.05/3 = 0.017; 0.0043 < 0.017).

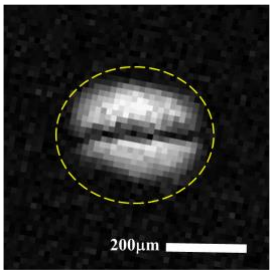

Fig.1 Representative DWI (b = 3200 s/mm^2) collected in the CA1 region of a living hippocampal slice. Dashed yellow line represents the equivalent tissue region highlighted in Fig. 2.

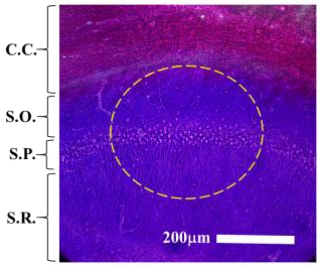

Fig.2 Fixed, Cresyl violet stained histology section detailing the lamellar organization of the CA1 region. Laminae include the corpus callosum (C.C.), stratum oriens (S.O.), stratum pyramidale (S.P.) and stratum radiatum (S.R.). The area excited by the 200μm diameter surface coil is highlighted (dashed yellow line).

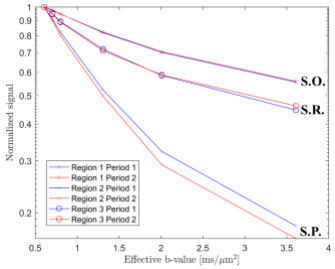

Fig.3 Diffusion signal decay measured in individual hippocampal lamina during periods of rest (Period 1, blue) and activation (Period 2, red). Divergence of the signal curves corresponding to increased diffusion weighting (S.P. layer) is indicative of changes in the diffusion properties of the tissue.

Conclusions

Although we report a significant, activation dependent change in the diffusion properties of neuronal soma occurring within the pyramidal cell layer of the rat hippocampus, an increase in diffusion signal—that is considered the hallmark of DfMRI signal contrast—was not observed. Given recent evidence that DfMRI contrast is absent from neural tissues undergoing non-pathological activity[4], these effects may be the result of neuronal swelling or gliosis rather than function.

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References

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