Three-Dimensional MRM of the Drosophila Brain at High Resolution

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Introduction

Here, we propose to push the limits of MR microscopy (MRM) resolution using the *Drosophila* brain as a small, but highly complex model system. For decades, the fruit fly *Drosophila melanogaster* has proved a powerful model system and has played a key role in our understanding of neuronal specification and function [1]. The genetic tractability of *Drosophila* has made this small fly a potent model for the study of human diseases. *Drosophila* is also a powerful model for understanding brain organization with the continuous development of novel tools for neuronal tracing, which help link circuits with behaviors. The fruit fly brain is an ideal model for developing non-invasive imaging technologies because it combines a small size (600 x 300 x 100 µm) with high complexity (10^5 neurons). Two recent publications failed to reveal details of the microarchitecture of the *Drosophila* brain using MRM [2,3], hinting that this small brain was not accessible by MRM. Thus, we undertook the challenge of demonstrating that MRM can deliver enough resolution to dissect the well-known microarchitecture of the Drosophila brain.

Experimental

We recently imaged a fixed Drosophila head at 10 µm isotropic resolution using endogenous contrast with the 14.1T AMRIS magnet. We collected data by two MRI modalities, FLASH and DWI, on the same sample, resulting in high contrast and the identification of several microdomains.

Results and Discussion

FLASH produced high signal of most internal head structures, including the retina, the lamina, and the brain (***Fig. 1B, F***). However, the neuropil showed a fairly homogeneous signal. Although the DWI signal was weak in the retina and the lamina, the contrast within the neuropil was extraordinary, allowing the identification of several known microdomains, including the central complex, the pedunculus, the suboesophageal ganglion, the medulla, and the lobula (***Fig. 1C, G***). Remarkably, FLASH showed a brighter halo in the periphery of the brain corresponding to the cortex containing the cell bodies of the brain neurons (***Fig. 1D-F***, arrowheads). However, DWI showed weaker signal in areas containing the cell bodies, resulting in a pattern complementary to FLASH (***Figs. 1G***, arrowheads). The strong contrast of DWI allowed us to segment the images and create a 3-dimensional reconstruction of the *Drosophila* brain that closely reproduced the known spatial distribution of its internal structures (***Fig. 1H, I)***.

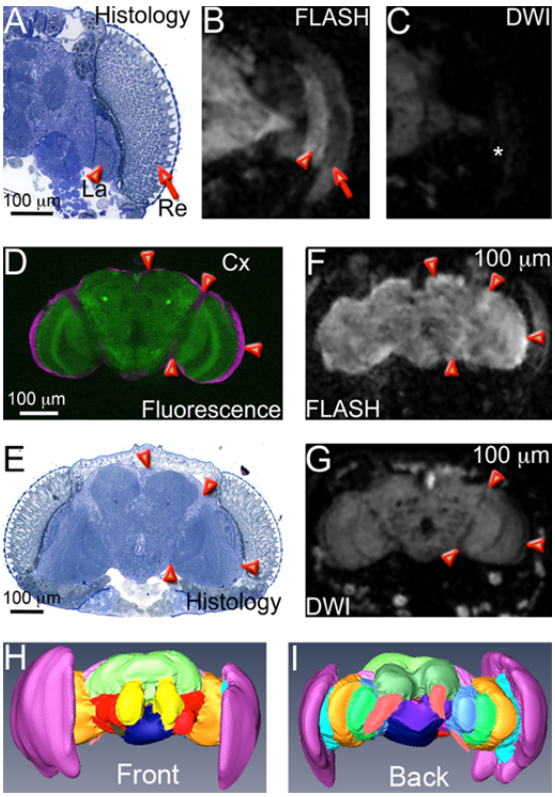

Figure 1. The Drosophila brain by MRM. **A-C**, The histological section exposes the iterative organization of retina and lamina. FLASH imaging identifies both structures, although the lamina is stronger. DWI is mostly hypointense in these structures. **D, E**, Comparative sections in a fluorescent brain and in a brain section. **F, G**, Same brain imaged by FLASH and DWI. The cortex (Cx, red arrowheads) is hypointense in DWI and hyperintense in FLASH. **C**, 3D reconstruction of the brain using the 3D MRM images

Conclusions

Overall, these images reflect the highest resolution and contrast of the *Drosophila* brain by non-invasive microscopy reported so far. We believe we can push for higher resolution by taking advantage of the AMRIS facilities and apply these advances to identify the early signatures of brain pathologies.

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