Three-dimensional MRM of the Drosophila brain at high resolution

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Introduction

The small fruit fly *Drosophila melanogaster* has many advantages for performing genetic studies, including evolutionarily conserved neuronal function and innate behaviors [1]. The fruit fly brain is also an ideal model for developing 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.

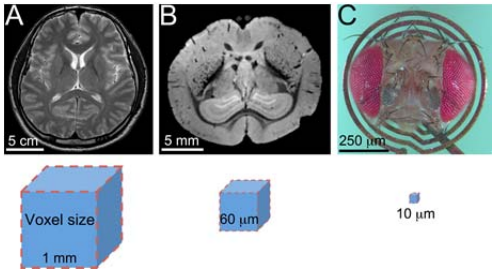

Figure 1. MRI specimens and voxel size. A, Human brain imaged at 1 mm resolution. **B,** Mouse brain imaged at 60 µm. **C,** *Drosophila* head mounted on a 500 µm planar microcoil for imaging at 10 µm. Voxels not at scale.

Experimental

We aimed to image a complete brain at the highest possible resolution by MR. We selected *Drosophila* because they have the smallest fully organized brain among the laboratory models and has the additional advantage of introducing genetic modifications of brain anatomy and/or function. We selected a planar 500 µm in diameter RF microcoil optimized to the Drosophila head (Fig. 1) and two complementary sequences, FLASH and DWI. We imaged the heads at 10 µm isotropic resolution, almost an order of magnitude higher than previous MRM imaging in fruit flies (***Fig. 2A***) [2,3].

Results and Discussion

FLASH produced high signal of most internal head structures, including the retina, the lamina, and the brain, but the neuropil showed homogeneous signal (***Fig. 2B***). The DWI signal was weak in the retina and the lamina, but 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. 2C***). The images produced by FLASH and DWI were almost complementary, allowing the segmentation and 3D reconstruction of the *Drosophila* brain (***Fig. 2D).*** This MRM model closely mimicked widely used models generated by optical microscopy despite the difference in resolution and z-step.

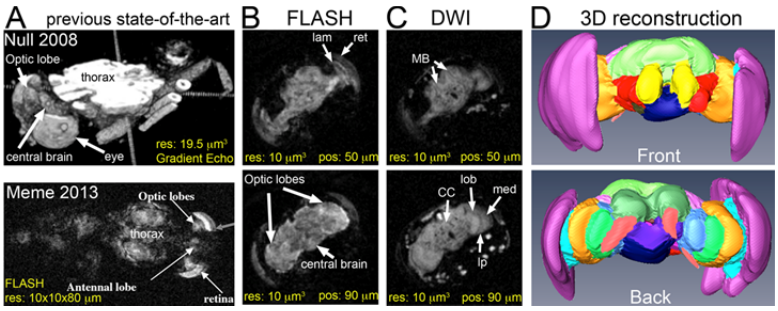

Figure 2. 3D MRM reveals the anatomy of the *Drosophila* brain. **A**, Published MRM images of *Drosophila*. Note the lack of anatomic details in the brain. res: resolution; pos: position along the A-P axis. **B,** FLASH reveals the retina (ret, pink) and lamina (lam, cyan). **C**, DWI generates exquisite contrast in the neuropil: mushroom bodies (MB), central complex (CC), medulla (med, orange), lobula (lob, blue), and lobula plate (lp, green). **D**, 3D brain model.

Conclusions

Overall, these images reflect the highest resolution and contrast of any complete 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 structural and tractography signatures associated with brain pathologies.

Acknowledgements

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References: [1] Bellen HJ, *et al.* (2010) Nat Rev Neurosci 11: 514-522; [2] Meme S, *et al.* (2013) Magn Reson Imaging 31: 109-119; [3] Null B, *et al.* (2008) PLoS One 3: e2817.