MAGNETIC RESONANCE MICROSCOPY OF THE DROSOPHILA BRAIN AT 10 MICRON ISOTROPIC RESOLUTION

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INTRODUCTION

Understanding the complex brain architecture and functional connectivity using MRI has been a major interest in neuroscience. Based on the capability of MR microscopy (MRM) to visualize the mammalian and human cells (1, 2), the desire to map the entire human brain circuit at the resolution high enough to visualize cell-level structures is becoming a reality. Studies of a simpler brain, i.e. *Drosophila*, are significant due to its high genetic tractability together with high degree of conservation with humans at the genetic and cellular levels. There have been two recent attempts to image *Drosophila* with MRM; however, the details of the internal brain anatomy could not be discriminated such as the subdomains within the central brain (3, 4). In an attempt to visualize the neuronal circuitry in the small *Drosophila* brain, we acquired MRM of that brain at 10 µm isotropic resolution by using the optimal sized RF coil and strong/fast-switching gradients, which together facilitated the delineation of the microarchitecture in this highly complex (10^5 neurons) but very small brain (600x300x100 microns in volume). 3D fast low angle shot (FLASH) displays different contrast between cell bodies in the cortex and modular neuropil in the center; on the other hand, diffusion weighted imaging (DWI) describes the high contrast among brain compartments, providing the unprecedented details of the complex brain neuropil. Both of them were verified by the confocal and immuohistochemical images respectively and with 3D volumetric data sets.

METHODS

MRM was carried out with a 500 µm ID micro surface-coil (Bruker Biospin, B6370/0001) in a 600 MHz (14.1T) vertical-bore magnet (Oxford Instruments) interfaced with Bruker consoles. The benefits of a high strength gradient were maximized by employing a newly-designed planar gradient system by Bruker (Z110828, B6406) whose maximum amplitude reached up to 66T/m. For comparative fluorescence images of the *Drosophila* brain, we generated flies expressing panneurally a reporter GFP transgene localized to the synapse (Elav-Gal4; UAS-GFP-Syt). The histological sections were performed in a Leica microtome at 1 µm, collected in a slide, stained for 5 min with toluidine blue, washed, air dried, and mounted in mounting medium. 3D volume rendering of MRM was done by using AMIRA 5.4.0 (Visage Imaging Inc.) where individual architecture was manually segmented for each slice.

RESULTS

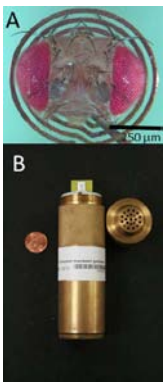
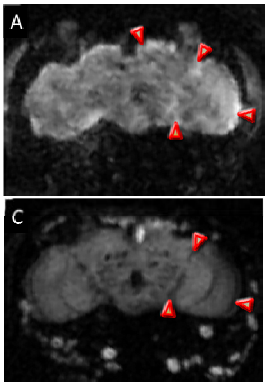


Figure 1.



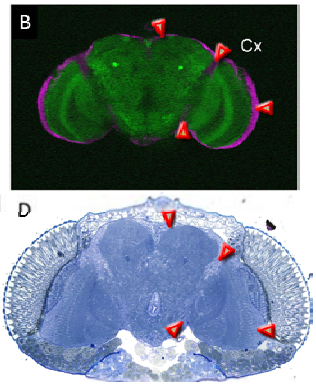


Figure 2.

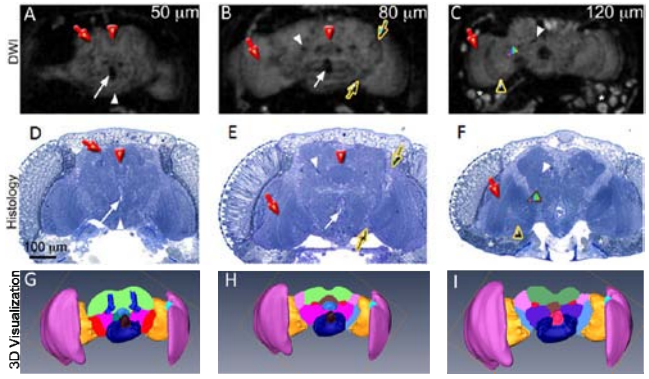


Figure 3.

Figure 1. Photograph of a fly brain on the RF micro surface-coil (A) and the planar gradient (B).

Figure 2. MRM of cell bodies in a *Drosophila* brain (A and C) with corresponding confocal (B) and histological image (D). (A) FLASH image showing hyperintense signal in cortical brain areas, and the gaps between optic lobes and central brain (arrow head). (C) DWI image showing hypointense signal correlated by the confocal and histological images showing the cell bodies (B and D).

Figure 3. MRM of neuropil microarchitecture in the *Drosophila* brain with corresponding histological and 3D-rendered images. MRM images of neuropil structures: in (A), mushroom bodies (MB, red arrow), ellipsoid body (EB, red arrowhead), oesophagus (Oe, white arrow), suboesophageal ganglion (SEG, white arrowhead); in (B), medulla (red arrow), peduncles (white arrowhead), ellipsoid body (red arrowhead), oesophagus (white arrow), cell bodies (yellow arrow); in (C), medulla (red arrow), lobula plate (yellow arrowhead), lobula (blue arrowhead), peduncles (white arrowhead) with corresponding histological (D-F) and 3D visualization (G-I).

DISCUSSION and CONCLUSIONS

This abstract represents the first MRM to delineate the individual subdomains of the *Drosophila* brain, e.g. internal architecture of the central complex and optic lobe, with endogenous contrast at 10 micron isotropic resolution, the highest reported to date in an animal sample. We conclude that FLASH, which can reduce the measuring time in 3D acquisition, has a potential to show the functional connectivity between cell bodies in the periphery and in-between brain lobes and a modular neuropil in the center of the brain; in contrast, DWI, which has high clinical specificity to detect pathophysiological features such as ischemic stroke in human, extracted exquisite details of the modular neuropil. Additionally, it showed the capability of MRM to make this small fly as a potent model for the study of human diseases including congenital disorders, aging, cancer, and neurodegenerative diseases non-invasively.

REFERENCES and ACKNOWLEDGEMENTS

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