Layer-Specific manganese-enhanced MRI of the retina associated with light and dark adaptation at 11.7T

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INTRODUCTION: Light and dark adaptation of the retina remains of significant interest. Oxygen tension, electrical activity and oxygen and glucose consumption, and blood flow have been reported associated with light and dark adaptation [1]. There is consensus that the neuronal activity in the outer retina increases in dark relative to light. Choroid blood flow, which predominantly supplies the outer retina, does not differ between light and dark [2], although exception has been noted [3]. By contrast, the inner retina activity and retinal blood flow in light versus dark adaptation are controversial. One popular non-invasive technique to study light and dark adaptation is laser Doppler flowmetry, but it is limited to either the optic nerve head which is dominated by large retinal vessels or the fovea which are void of retinal vessels.

The goal of this study was to explore high-resolution functional manganese-enhanced MRI (MEMRI) to study the retina during light versus dark adaptation. We implemented two identical radio frequency transceiver coils (one for each eye) to allow interleaved acquisitions. We found differential activities among different layers of the rat retina during light versus dark adaptation.

METHODS: In Study #1 (n=3 Sprague Dawley rats), both eyes were light adapted. Rats were anesthetized for intravenous $MnCl_2$ administration (88 mg $MnCl_2 \cdot 4H_2O$/kg) over 1hr and allowed to recover under ambient room light. To confirm peak assignments, the intravascular agent MION (5mg/kg) was injected.

In Study #2 (n=7 Sprague Dawley rats), one eye was randomly assigned to be patched (dark adaption) with Elizabethan collar, and the other eye not patched (light adaptation). Animals were allowed to recover from anesthesia and adapted for 2hrs [4], then re-anesthetized for intravenous manganese administration over 1 hour and allowed to recover in housing cage under ambient room light.

After 5hrs, animals were anesthetized, intubated, and mechanically ventilated at ~1% isoflurane. In dim red light, eye patch was removed, atropine and lubricating eye drops were applied and pancuronium was administered (4mg/kg/hr, i.p.). MEMRI was performed on an 11.7T/16cm Bruker magnet with two identical surface coils, FLASH sequence, TR=150ms, TE=5.1ms, FOV=7.5x7.5mm, thk=0.7mm, NT=10, matrix= 384x384 (20x20μm). Time-series data were coregistered and averaged and profile analysis was performed [5]. Intensity profiles were normalized with respect to vitreous of each eye in homologous regions for each eye.

RESULTS: *In vivo* MEMRI results of two-light adapted eyes from the same rat showed 3 distinct peaks (**Figure 1**). Their SNR and intensity profiles were overall similar. Following MION injection, peak #1 and #3 were attenuated (**Figure 2**). MION does not cross the blood-retina barrier and should thus to outline the retinal and choroid vascular layer bounding the retina. Peak #1 was thus assigned as the inner retina which includes embedded retinal vessels, Peak #2 the avascular outer nuclear layer and peak #3 the choroid vascular layer. Intensity profiles of dark adapted and light adapted eyes from the same rat (**Figure 3**) showed that the choroid peaks had similar intensity between light and dark adapted eyes. The inner retina in dark had slightly lower intensity relative to light while the outer retina peak had higher intensity relative to light. Group-average peak data normalized to the vitreous signals (**Figure 4**) showed that the choroid peaks were iso-intense between dark and light ($P>0.05$), the outer retina was hyperintense relative to light ($P<0.03$) whereas the inner retina under dark was hypointense relative to light ($P<0.05$).

DISCUSSION: These findings are consistent with the notion that the outer retina in dark utilizes more energy (dark current) compared to light [6]. It is also consistent with majority of the studies that the inner retina utilizes more energy in light than dark [7]. The choroid is not expected to differ between light and dark. Our findings contradicted a previous report of MEMRI layer assignments and activities in the retina during light and dark [8]. These discrepancies could be due to differences in image spatial resolution and/or different normalization used. Future studies will aim to improve spatial resolution to visualize additional retinal layers and apply MEMRI to investigate retinal diseases, such as diabetic retinopathy, and retinal degeneration.

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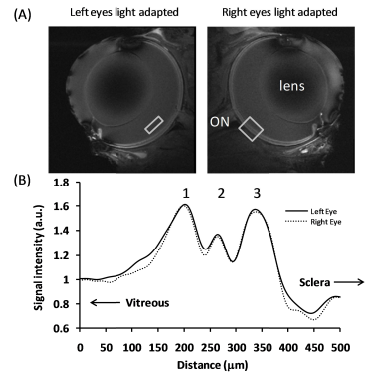

Fig 1. (A) MEMRI of light adapted eyes in the same rat. Vitreous and retina rectangle ROIs were used in analysis. ON: optic nerve. **(B)** Normalized intensity profiles show 3 peaks.

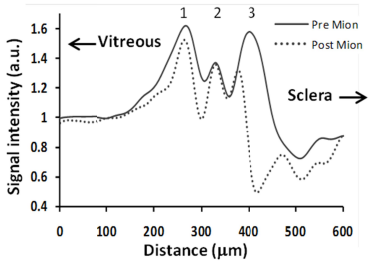

Fig 2. Intensity profiles before and after MION injection of two-light adapted eyes.

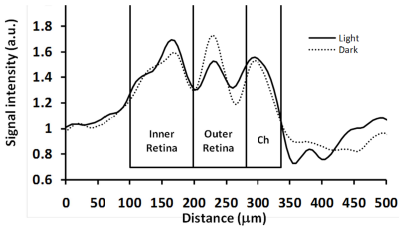

Fig 3. Intensity profiles of light and dark adapted eyes from same rat. The vertical lines outline the inner, outer retina, and choroid.

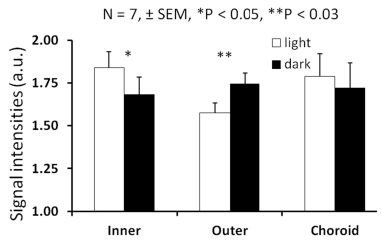

Fig 4. Group-averaged peak intensity values normalized with respect to vitreous.