OCULAR INTEGRITY FOLLOWING MANGANESE LABELING OF THE VISUAL SYSTEM FOR MRI

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Introduction:

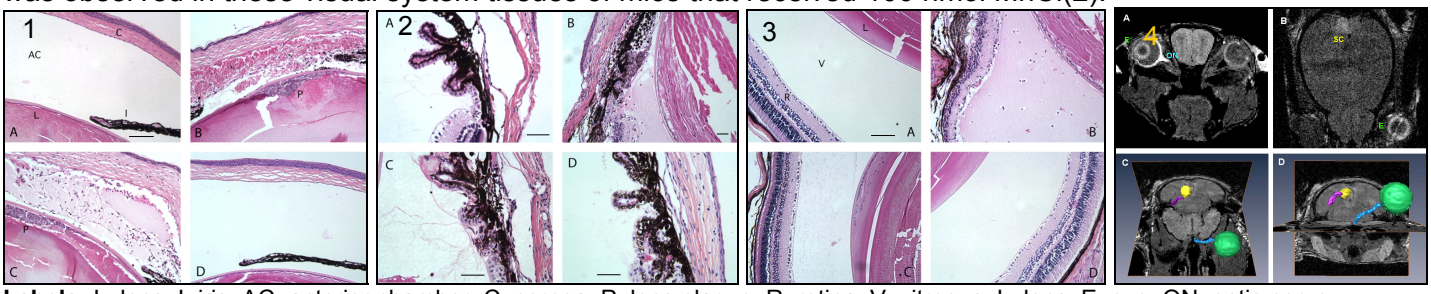
Injection of manganese as MnCl(2) into the eye can increase contrast in visual system neuronal pathways when imaged by MRI (MEMRI). As an in-vivo technique, MEMRI has the potential to be used for repeated studies. However, MnCl(2) is known to be neurotoxic and limited published data exists on how toxic MnCl(2) is to different ocular structures when injected into the eye (1,2). This is of particular importance for experiments that use this approach to longitudinally follow degenerative changes in models of neuronal disease or injury related responses. This study determines the effect of a range of MR visible MnCl(2) doses upon the integrity of various ocular structures.

Methods:

25 C57Bl/6 mice were used for this study. Anesthetized mice received ocular anterior chamber injections of 50 – 500 nmols of MnCl(2) solution in a volume of 1.0 μl. One week later, the eyes were fixed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Six additional animals received 50 nmols or 100 nmols of MnCl(2) injected into the anterior chamber, and were imaged at 24 hours using a Bruker 7T scanner and a T1-weighted imaging protocol (3D FLASH sequence with TR/TE of 11.2/5.5 ms, 20° flip angle). Measurements of image intensity within the visual system were obtained as previously described (3).

Results:

Following 500 and 300 nmol MnCl(2), the corneal stroma and endothelium were degenerated, the anterior chamber contained a dense fibrin matrix with extensive inflammatory cell infiltration, a plaque often formed on the anterior lens (Figure 1 B,C), and significant retinal degeneration was observed (Figure 3 B,C). Following 100 nmol MnCl(2) retinal preservation of ocular structures was significantly better than at higher doses, and retinal cell counts showed no difference from vehicle control retina in each of the three cell layers. However, there was thinning of the outer plexiform layer in the peripheral retina, as well as in the photoreceptor outer segment layer (not shown). Following 50 nmol MnCl(2), the anterior chamber was clear, the ciliary body was largely normal, and the retina was unchanged compared to vehicle control eyes (Figures 1 D, 2 D,3 D). Visual system elements labeled on MRI of mice that received 100 nmols MnCl(2) included the retina, optic nerve, lateral geniculate nucleus, and superior colliculus (Figure 4). Significantly enhanced MR signal (p= 0.02-0.006) was observed in these visual system tissues of mice that received 100 nmol MnCl(2).



Labels: L, lens; I, iris; AC, anterior chamber; C, cornea; P, lens plaque; R, retina; V, vitreous; L, lens; E, eye; ON, optic nerve.
Figure 1. The anterior chamber of a control eye (**A**), and eyes one week following injection of 500 nmol MnCl(2) (**B**), 300 nmol (**C**), or 50 nmol (**D**). **Figure 2.** Ciliary body from a control eye (**A**), from eyes that had received 500 nmol MnCl(2) (**B**), 300 nmol (**C**), or 50 nmol (**D**). **Figure 3.** Vitreous, lens and retina within an un-injected control eye (**A**), and one week following injection of 500 nmol MnCl(2) (**B**), 300 nmol (**C**) 50 nmol (**D**). **Figure** (**4**) MR images after 100 nmol MnCl(2) (**A .B**), and 3D reconstruction visual tract (**C,D**).

Discussion:

These results indicate that 50-100 nmol MnCl(2) injection into the anterior chamber may be useful for MRI labeling of the retina, optic nerve, and optic nerve target nuclei where preservation of other ocular tissues is desired, and may be suitable for longitudinal studies, though this is near the level of detection with MRI.

References: (1) Thuen: JMRI 2008;855-865, (2) Bearer: Neuroimage 2007;37:S37-S46, (3) Lindsey: Neuroimage 2007;34:1619-1626.