Chromium-Enhanced MRI of Myelinated Structures in Mouse Brain *In Vivo*

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Introduction

Specific chemical reactions to potassium dichromate have been used for a histologic staining of myelin. For example, controlled chromation of lipids allowed for a visualization of myelin sheaths of white matter tracts in rat brain [1]. The present work attempts to exploit such principles for MRI. The idea is based on the assumption that a reduction of Cr(VI) to paramagnetic Cr(V) or Cr(III) by lipid oxidation causes a shortening of the T1 relaxation time. The purpose of this mouse brain study *in vivo* was (i) to examine if a direct injection of a small amount of Cr(VI) results in a contrast enhancement detectable by T1-weighted 3D MRI, (ii) to determine the pattern of highlighted structures, and (iii) to characterize the time course of the enhancement.

Methods

Five mice received a single injection of Cr(VI) (0.4 µl of 10 mM $K_2Cr_2O_7$ dissolved in physiological saline) in the right lateral ventricle. MR images were acquired before as well as 3, 24, and 48 h after Cr(VI) administration. T1-weighted 3D MRI (rf-spoiled 3D FLASH, TR = 17 ms, TE = 7.6 ms, flip angle = 25°, 150 µm isotropic resolution, measuring time 75 min) was performed at 2.35 T (Bruker Biospin, Germany). RF excitation and signal reception were accomplished with use of a Helmholtz coil (100 mm) and an elliptical surface coil (20 x 12 mm), respectively.

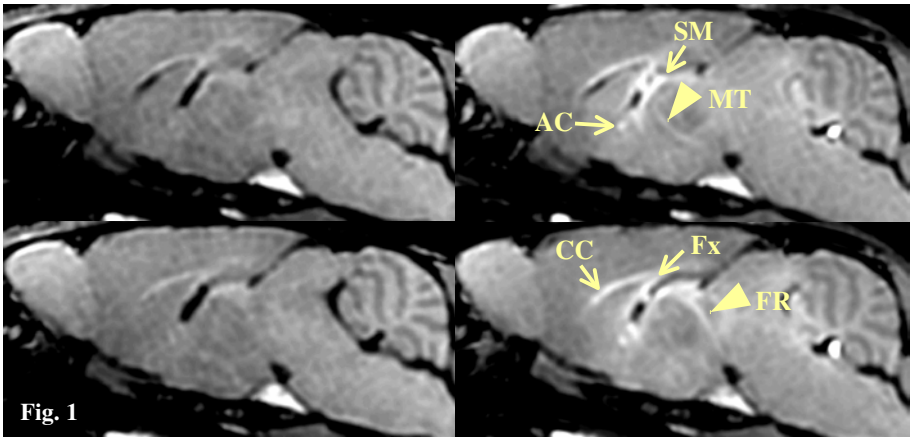

Fig. 1

Results

Intracerebroventricular administration of Cr(VI) selectively enhanced brain tissues in T1-weighted MRI. The results clearly indicate a tissue-specific reduction of diamagnetic Cr(VI) to paramagnetic Cr(V) or Cr(III) in structures known to consist of myelinated axonal fiber bundles. Apart from marked signal intensity increases around the injection site but not in cerebrospinal fluid (CSF), most pronounced enhancements were observed in white matter directly exposed to CSF in the lateral and third ventricle. Figure 1 shows parasagittal MR images of a mouse brain (left) before as well as (right) 24 hours after Cr(VI) administration. White matter tracts such as the anterior commissure (AC), stria medullaris (SM), corpus callosum (CC), and fornix (Fx) were strongly highlighted. In addition, the mammillothalamic tract (MT) and fasciculus retroflexus (FR) were readily delineated.

Figure 2 shows oblique sections along these tracts highlighting the corpus callosum (CC) as well as the enhanced MT and FR on both sides.

Figure 3 summarizes the time courses of the mean SNR increases for CC, MT, and FR in comparison with a cortical region (Cor). Whereas gray matter results in only a mild unspecific enhancement (13%), white matter yields SNR increases of 30 to 100 % at 24 hours after administration. The temporal stability of the SNR increases for up to 48 hours indicates retention of paramagnetic chromium.

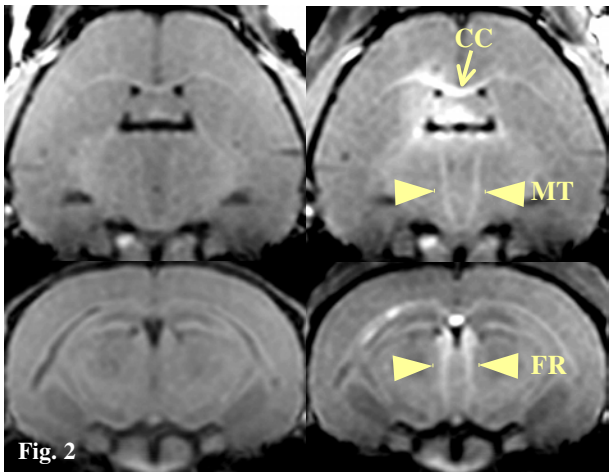

Fig. 2

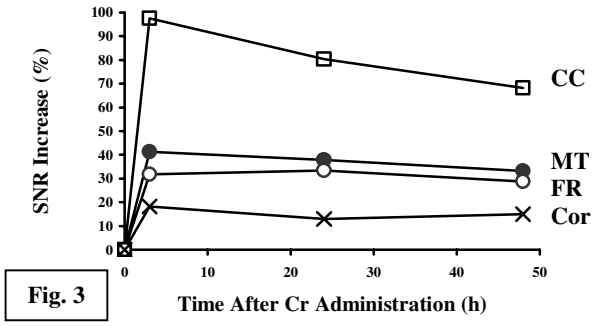

Fig. 3

Discussion

The present results show that Cr(VI) can be used to enhance T1-weighted MRI signal intensities predominantly of white matter tracts. These findings are in line with histologic staining techniques and the high lipid content of myelin. The suggested mechanism assumes the molecular diffusion of Cr(VI) ions in the CSF and extracellular fluid to be followed by the oxidation of myelin lipids and a reduction to paramagnetic forms as well as by a subsequent retention of the reaction products in the multilamellar structure. It may be concluded that chromium-enhanced MRI provides new insights into the histochemistry of reactive tissue elements that certainly differ from the information gathered by manganese-enhanced MRI. Obvious differences are the pronounced enhancement of the CC as well as the lack of any specific signal increases in gray matter structures such as the hippocampal formation (e.g., compare [2]). Further work will be required to support the notion that the functional mapping of neuroaxonal tissue by manganese may be complemented by an *in vivo* staining of myelin using chromium.

References

1. Pearse AGE. *Histochemistry*, vol. 2, 4th Ed. p811. Churchill Livingstone, NY (1985).
2. Watanabe et al. *NMR Biomed* 17:554-568 (2004).