

## A DTI study of diffusion anisotropy on CRMP-1 knockout mice

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### Introduction

Collapsin response mediator protein-1 (CRMP-1), one of human genes, has been identified in brain and implicated in plexin-dependent neuronal function. CRMP-1 knock-out mice exhibited impaired performance in hippocampal-dependent spatial learning and memory tests, and disorganized MAP2 (microtubule-associated protein 2) staining in the distal dendrites of hippocampal CA1 pyramidal cells [1]. However, the invasive staining methods impede long-term researches on CRMP-1 knock-out mice. Magnetic resonance imaging (MRI), one of non-invasive imaging methods, offers detailed images to visualize the structure and function of brain. The diffusion MRI provides further microscopic information of brain structure within each voxel. In this study we use diffusion tensor imaging (DTI) [2] to noninvasively and quantitatively investigate the change of diffusion properties of the knock-out of the CRMP-1.

### Materials & Methods

MR images were acquired at a 3 Tesla MRI Biospec system (Bruker, Germany) with a phased array coil. DTI were acquired with 12 gradient encoding directions and 1 reference image using a pulse-gradient spin-echo sequence with TR/TE = 2000/52.1 ms, FOV = 25x25 mm<sup>2</sup>, matrix size = 216x216, and slice thickness = 1 mm,  $\Delta/\delta = 22.58/90$  ms,  $b = 1166$  s/mm<sup>2</sup>. Three mutant and CRMP-1 knock-out mice (C57BL/6) were obtained according to the processes using in [1] and another three mutant and wild-type mice were also used as controls. All mice were aged 8-12 weeks and sacrificed by overdose of chloral hydrate before MR scanning in order to avoid the motion artifacts from breath or heartbeat during DTI acquisition.

### Results

The FA maps, overlaid with 1<sup>st</sup> eigenvector, from a wild-type mouse (Fig. 1a) and a CRMP-1 knock-out mouse (Fig. 1b) were shown in Fig. 1. The structural difference of fiber orientations between CRMP-1 knock-out and wild-type mice was invisible in CA1. The FA values (Fig. 2a) in CA1 of CRMP-1 knock-out mice were significantly lower than that in wild-type mice using the statistical analysis of t-test with  $p = 0.016$  while the mean diffusivity (Fig. 2b), first eigenvalue (Fig. 2c) and radial diffusivity (Fig. 2d) showed no significant differences.

### Discussions & Conclusions

The similar results in mean diffusivity, first eigenvalue and radial diffusivity indicate the similar diffusion property of water molecules in CA1 of CRMP-1 knock-out and wild-type mice. Hence, the lower FA in CRMP-1 knock-out mice should be correspondent to the disorganization of the dendrites with unchanged mean diffusivity, first eigenvalue and radial diffusivity, which is consistent with disorganized MAP2 staining results shown in [1]. The unchanged fiber structures between CRMP-1 knock-out and wild-type mice implies the disorganization in the dendrite of CA1 pyramidal cells is not severe enough to affect the fiber orientation estimate. Further, previous study has shown lower FA was associated with impaired memory organization in schizophrenia [3] and offers a positive relationship between the impaired performance of spatial memory and lower diffusion anisotropy from our study. In conclusion, DTI can noninvasively and quantitatively evaluate the deficiency in CA1 of CRMP-1 knock-out mice and provides the possibility for long-term studies, such as development or aging.

### References

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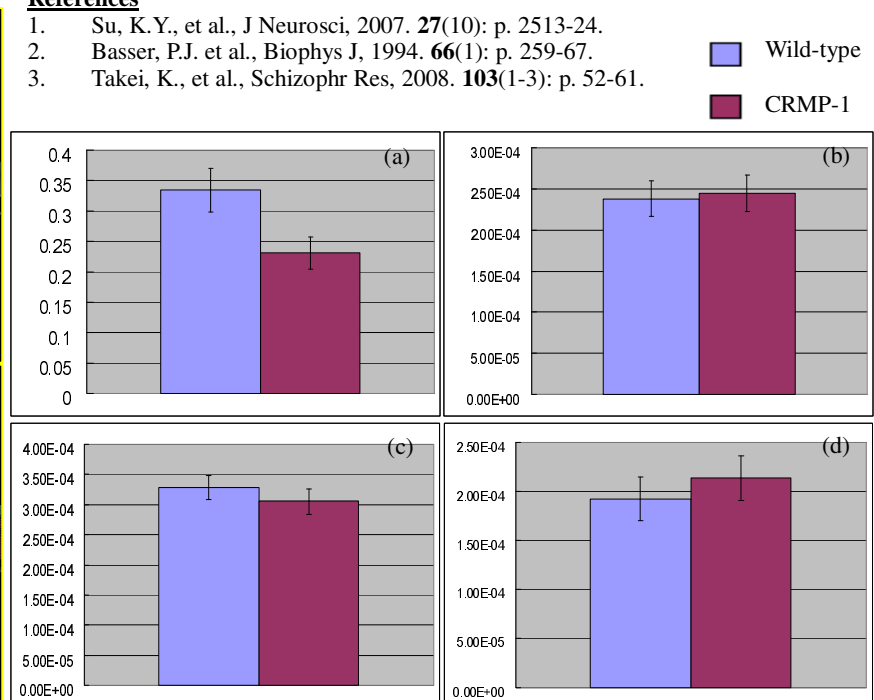
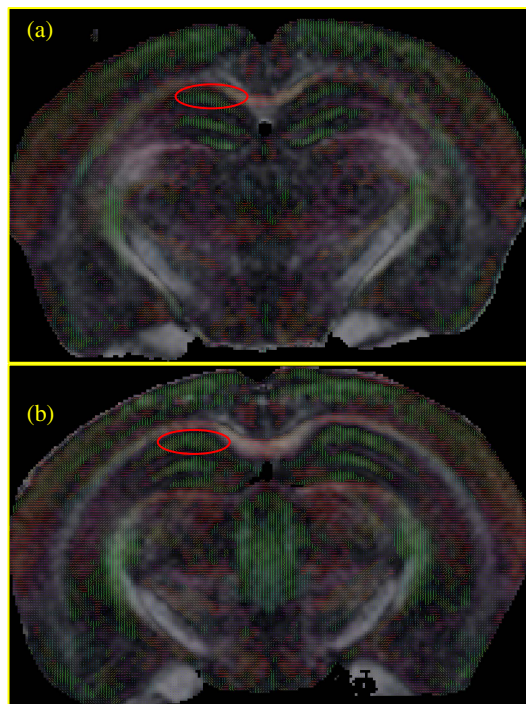


Fig. 1. The FA maps of a wild-type (a) and a CRMP-1 knock-out (b) mice, overlaid with 1<sup>st</sup> eigenvector results. Red ROIs indicate the region of CA1.

Fig. 2. The FA (a), mean diffusivity (b), first eigenvalue (c) and radial diffusivity (d) from wild-type (blue) and CRMP-1 knock-out (purple) mice. There is a significant difference for FA using t-test with  $p=0.016$  and no significant difference for mean diffusivity, first eigenvalue and radial diffusivity.