Longitudinal Diffusion Tensor Imaging of the Rat Brain after Hexachlorophene Exposure

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Purpose

Accidental ingestion of hexachlorophene (HC) is known to cause brain edema and spongy degeneration of white matter [1]. Several instances of HC exposure, its neurotoxic effects and various other conditions including anorexia, convulsions and cardiovascular disturbances have been well documented in the Toxicology Data Network database [2]. While HC is known to cause significant white matter damage and its effects have been studied using histopathological methods [4], there is a lack of clarity of the life cycle of these changes in vivo. Diffusion Tensor Imaging (DTI) has the ability to tease out information about white matter damage and also provide specific measures that can relate to axonal and myelin degeneration (fractional anisotropy, FA; axial diffusivity, AD; radial diffusivity, RD). In this report, we studied the HC effects in the rat brain using longitudinal DTI MRI.

Methods

The animal use protocol was approved by the NCTR IACUC. Adult male Sprague-Dawley rats (N = 12, 364 ± 40 g) were either given HC (30 mg/kg, N = 10) or vehicle (corn oil, 1 ml/kg, N = 2) orally, once a day, for 5 consecutive days. In vivo DTI was performed at Day 0 and at days 3, 6, 13, and 20 following HC administration. MRI was performed using a 7 tesla Bruker Biospec AV III equipped with 4-channel array rat brain RF coil. Animals were anesthetized with isoflurane (3% induction, 1-2% maintenance in oxygen) and the body temperature was kept at 37.3 ± 0.6°C. A spin-echo 3D EPI-DTI sequence was used (FOV = 3.84 × 3.84, B Value = 1300, TR = 2 s, NA = 2, 30 diffusion directions). Apparent diffusion coefficient (ADC), FA, AD and RD images were obtained after processing the data using DTIStudio software. Region of Interest (ROI) analysis was performed on the quantitative DTI images on 4 different brain areas (Internal capsule, Fimbria, Corpus Collosum and Anterior + Posterior Commisures). Group comparisons of the ROI metrics were performed using two-way repeated measures ANOVA.

Results

Figure 1 shows a snapshot of the longitudinal DTI metrics for FA, AD and RD. Visually and statistically the FA images do not show differences but the AD and RD clearly indicate changes in white matter (especially at day 6). Significant differences were observed between groups in all 4 chosen locations similar to the internal capsule data shown in Figure 2.

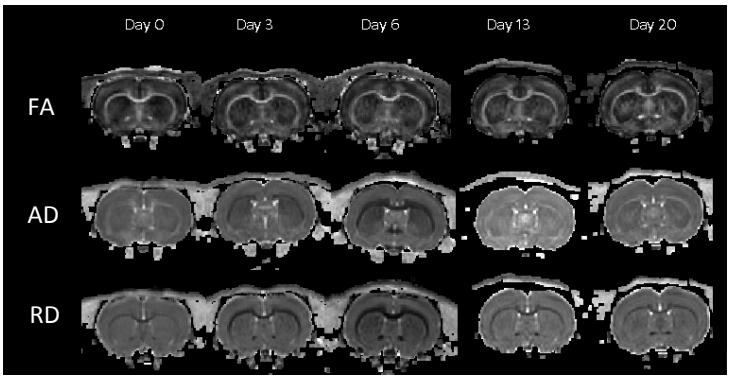

Figure 1. Representative longitudinal FA, AD and RD images, derived from DTI

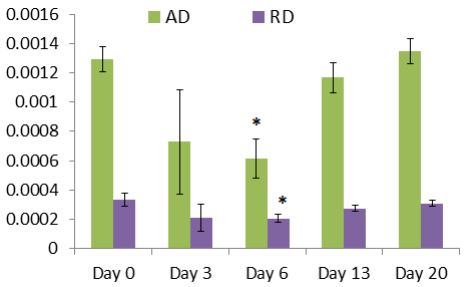

Figure 2. Group comparison of AD and RD data over time.
* - statistical difference with day 0, P < 0.05

Discussion

While changes in AD and RD clearly demonstrate myelin perturbations consistent with edema, the lack of FA changes suggest that the anisotropic diffusivity structure of the myelin is not disrupted significantly by HC. Follow-up longitudinal histopathological studies are warranted to test this hypothesis.

References

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4. Hanig J., et al. Regul Toxicol Pharmacol. 2014, S0273-2300(14)00215-3.