Coherence Index measures of DTI reveal gender differences following methamphetamine exposure: technical aspects

Y. Natsuaki[1,2], T. E. Nordahl[2,3], R. E. Salo[2,3], M. H. Buonocore[2,4]

[1]Biomedical Engineering, UC Davis, Davis, CA, United States, [2]Imaging Research Center, UC Davis Medical Center, Sacramento, CA, United States, [3]Psychiatry, UC Davis Medical Center, Sacramento, CA, United States, [4]Radiology, UC Davis Medical Center, Sacramento, CA, United States

Introduction

Coherence Index (CI) computed from the images obtained in DTI measures the local alignment of neighboring axonal tracts [1], and can be used to detect axonal damage. Lower CI values reflect less coherent axonal tracts, thus serving as a marker of neuronal damage. One important application of CI, and perhaps other DTI-derived images, is the measurement of the effects of drug exposure (e.g. cocaine) in human brains. Animal and human studies suggest that damage following exposure to methamphetamine (MA) occurs primarily in frontal/terminal axonal regions [2], and the data from animal studies suggest that the gender differences may exist following MA exposure, with male mice exhibiting greater evidence of damage compared to female mice [3]. One would predict that CI values would be lower in these regions in humans, and that the severity of the axonal damage may differ across genders.

The purpose of the current study is to investigate gender differences in CI in humans following MA exposure using MRI-DTI techniques. CI measures are obtained in the anterior callosal white matter adjacent to Anterior Cingulate Cortex (ACC).

Materials and Methods

36 subjects (17 males and 19 females; 20 controls, 16 MA exposed (ME)), matched for demographic characteristics, were scanned with 1.5T GE Signa LX at Imaging Research Center (Sacramento, CA). The DTI data were then processed offline to calculate CI.

CI, first proposed by Klingberg et al [4], is defined as a mean dot-product of the main eigenvector (v) in voxel at (i,j) and v in its eight neighboring voxels at (r,c):

$$CI_{ij} = \frac{1}{8}\left(\sum_{r=i-1}^{i+1} \sum_{c=j-1}^{j+1} v_{ij} \bullet v_{rc} - 1 \right).$$

Since eigenvectors are defined with unit length, the dot product $v_{ij} \bullet v_{rc}$ is the cosine of the angle between v_{ij} and v_{rc} (i.e., the cosine of the angle between the primary directions of the fibers in the adjacent pixels), and CI values varies between 0 and 1. CI has been then rescaled to 0-1000.

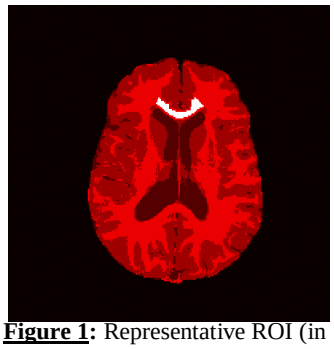

Figure 1: Representative ROI (in white) on the segmented brain.

A Region of Interest (ROI) is drawn on an oblique AC/PC slice. Oblique AC/PC slices are acquired to minimize the variability across subjects of image appearance and ROI sampling. The ROI is determined from a segmented brain map (based on dual-echo WM/GM/CSF brain segmentation). The WM region adjacent (posterior) to ACC (see Figure 1) is manually selected. The selected ROI is further reduced (via erosion) to avoid the edge of the WM/GM. CI pixel values corresponding to the selected ROI are collected, and the mean CI values (CImean) are calculated. Statistical analysis (ANOVA and simple t-test) are performed to observe the interaction between sex (male or female) and group (control or ME) with CImean.

Results and Discussion

Figure 2 reveals a significant difference in CI images. The Male MA exposed group (Figure 2(a)) displays incoherence at ROI (i.e. "breakage" in CI), while the two other groups show strong coherence (i.e., no "breakage", Figure 2(b)).

The average CImean values are listed on Table 1. A 2 (sex: male and female) x 2 (group: control and ME) ANOVA is performed on CImean, and the interaction is statistically significant [F(1,32)=4.622, p=0.0392]. Also, a simple t-test reveals that the gender differences are limited to the ME group, indicating the male ME has lower average CImean values (714.3) than ME female (813.7), [F(1,17)=6.09, p=0.024]. However, the effect of gender does not reach statistical significance in the control group, p=0.991.

Preliminary results from the CI analysis provide evidence of gender differences in sensitivity to MA toxicity. Consistent with animal studies, this data provides preliminary evidence that males are more sensitive to MA exposure than females.

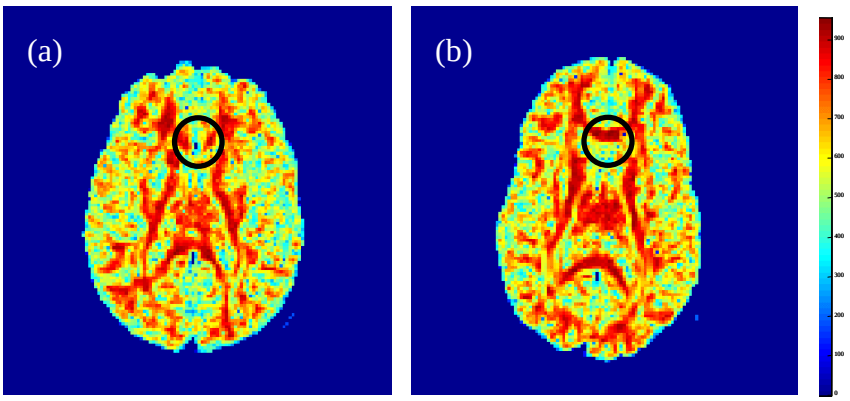

Figure 2: Coherence Index Images for representative (a) ME Males and (b) other groups, with red=highest (1000) and blue=lowest (0). Circles show the evidence of incoherence (i.e., "breakage" within our ROI) in ME males and strong coherence (i.e., no "breakage") in the others.

Table 1: mean table of CImean

	Count	Mean	SD	SE
Female, Control	9	815.0	32.2	10.7
Female, ME	11	813.7	47.6	15.0
Male, Control	8	815.3	47.9	17.0
Male, ME	8	**714.3**	**122.3**	**43.2**

References

1. Pfefferbaum et al, 2000
2. Nordahl et al, 2003
3. Wagner et al, 1993
4. Klingberg et al, 1999