Diffusion Tensor Imaging of Time-Dependent Axonal and Myelin Degradation After Carbon Monoxide Intoxication: White Matter Tract-Specific Quantification by Tract Probabilistic Map

C-Y. Lo[1], W-C. Lin[1,2], C-H. Wang[1], A-L. Hsu[3], and C-P. Lin[1,3]

[1]Institute of Biomedical Imaging and Radiological Sciences, National Yang Ming University, Taipei, Taiwan, [2]Departments of Diagnostic Radiology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung, Taiwan, [3]Institute of Brain Science, National Yang Ming University, Taipei, Taiwan

Introduction

Morbidity following carbon monoxide (CO) poisoning includes neurologic sequelae, neurobehavioral changes, and cognitive impairments [1-2]. After acute CO intoxication, patients may develop progressive white matter (WM) demyelination [3]. The damage might cause disconnection between cortex area and lead to functional disintegration of neurocognitive networks, a process likely related to delayed CO encephalopathy. Diffusion tensor imaging (DTI) is a quantitative and noninvasive method that permits clinicians to delineate the anatomy of WM pathways. However, fiber tracking are sensitive to noise, partial volume effects, and convolution of axonal structures with different orientations within a voxel [4-5]. Diseased brains often have altered DTI parameters that could affect the tractography results. In this study, we created WM parcellation atlas-based probabilistic maps of 5 major WM tracts derived from the DTI data from 55 normal subjects. Using these probabilistic maps, automated tract-specific quantification of DTI parameters were performed to evaluation WM tract damage and the chronologic change in 17 patients with CO intoxication.

Materials and Methods

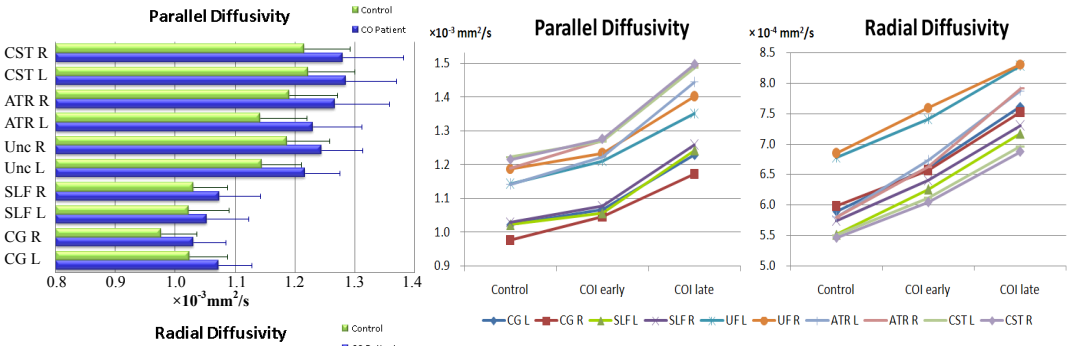
In order to construct standard MNI space probabilistic tract atlas, 55 healthy subjects (27 males, 29 females, 24±3.6 year-old) were enrolled from Taipei Veterans General hospital in Taiwan. The details of imaging acquisition and image processing procedure were the same as our previous article [6]. 17 patients with delayed sequelae after CO intoxication (8 males, 9 females, 44±12 year-old) were evaluated with both imaging and clinical at baseline and 22 matched healthy subjects (10 males, 12 females, 40±10 year-old) were recruited in this study. For the following study, 9 patients in this group were imaged approximately 3 months later. DTI datasets of CO participants with 25 noncollinear directions (b=1000 s/mm2) and one non-diffusion T2 weighted images were acquired at 3T scanner (Signa Excite HD; GE Healthcare, Milwaukee, Wis, USA) by using a single shot spin-echo echo planar imaging (EPI) sequence (TR=7000 ms, TE=72 ms, FOV=24×24 cm2, slice thickness=5 mm, matrix=128×128, NEX=6). Non-diffusion weighted T2 image of each participant was registered to the standard space EPI template image which was available in SPM2 package by using nonlinear normalization algorithm (Wellcome Department of Cognitive Neurology, London, UK). In order to calculate inverse transformation metrics that comes from previous step, the Deformation toolbox available in SPM2 was used. Then, all five tract probabilistic maps were inverse transformed to each individual participant's native space by nonlinear warping. To keep major fiber bundle and remove out variance of different tract trajectory, these tract probabilistic maps were set at a threshold with probability > 20%. Moreover, the FA value of each voxel lower than 0.2 were ruled out for statistic analysis due to the higher uncertainty of diffusion orientation. These tract probabilistic maps provided the location information of the fiber atlas and were used to compute weighted ROI averages of DTI indices.

Results

The following 5 white matter tracts were reconstructed for this study: Cingulum of the Cingulate cortex (Cg), Corticospinal tract (CST), Superior Longitudinal Fasciculus (SLF), Uncinate fasciculus (Unc), and Anterior Thalamic Radiation (ATR). In patients with CO intoxication, both fractional anisotropy (FA) decreased, and mean diffusivity (MD) increased significantly in the ATR, Cg, CST, SLF, and Unc in contrast with the corresponding fibers of healthy controls. To investigate potential mechanisms for changes in white matter integrity in CO intoxication, both parallel ($\lambda\|$) and radial ($\lambda\perp$, $[(\lambda 2+\lambda 3)/2]$) diffusivities were extracted (Fig1&Fig2). The results revealed that decreasing FA were primarily driven by increasing $\lambda\perp$, which appeared to be more strongly correlated with demyelination in the initial presentation. The Mini Mental State Examination showed a positive correlation with the FA of SLF (p=0.012, left and right) and FA of ATR (p=0.026, left and p=0.017, right) in correlation analysis. During follow-up, repeat studies in 9 patients showed progressive increase of MD. However, FA of all fiber tracts was not significantly different from that in initial DTI study. Further analysis showed significant increase in $\lambda\|$ and $\lambda\perp$. It suggested an advancing axonal and myelin damage.

Discussions

White matter damage in patients with CO intoxication is variable and causes the demyelination and axonal destruction to disconnect the cortex. With conventional MRI, WM lesions are identified in 12–37% of patients, but the findings are not related to the severity of intoxication. By using atlas-based probabilistic maps, tract specific damage that we demonstrated in patients with CO intoxication was extensively. It started from WM demylination process and followed by progressive global gliosis. The high correlation between MMSE score with FA of SLFs and ATRs, supports the hypothesis that WM microstructural changes of CO intoxication may contribute to the decline in cognitive functions. Furthermore, the statistical template can be applied to individual patient data for automated white matter parcellation and for repeated tract-specific quantification of MR parameters.



◀*Fig.1 Weighted mean of parallel diffusivity (PD) and radial diffusivity (RD) in control subjects and patients with left and right tract probabilistic map. Voxels with FA less than 0.2 were excluded. Significant difference exists in PD and RD of all fiber tracts between two groups (all of p<0.005).*

▲*Fig.2 Chronological changes of the mean DTI indices in control subjects and patient with first and second observation. The mean of parallel and radial diffusivities increases comparing with control subjects and patients after CO intoxication with early (COI early) and late (COI late) effect.*

Conclusion

Atlas-based probabilistic maps appears to be a sensitive tool for identifying the neuropathological and neuropsychological changes associated with CO intoxication. Our study supplements previous MRI studies by adding a level of anatomic detail to the relationship between white matter damage and cognitive dysfunction.

References

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