Whole Brain Fractional Anisotropy Analysis in HIV Patients with Elastic Registration

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Introduction

Diffusion tensor imaging (DTI) provides insights into the local diffusitivity of water molecules within the tissue, allowing for evaluation of micro-structural integrity and the orientation of white matter non-invasively. Therefore, DTI can potentially play a pivotal role in the investigation of white matter related diseases. White matter pallor is one of the major neuropathological features of HIV-1 infection, especially in the advanced stages of the disease. Few studies have explored the neurological effects of HIV infection with the DTI approach. The previous studies have examined the anisotropy and diffusitivity changes (1, 2) by manually drawing ROIs within 2D image slices. Filippi et al have found that FA was significantly decreased in the splenium and genu of HIV patients (1). In addition, significantly decreased FA at the frontal lobes and increased FA at the internal capsules were reported (2) by Pomara et al. In this abstract, a 3D elastic image registration approach was developed and utilized to co-register the DTI images of 11 HIV patients to a normal white matter atlas generated from 10 healthy volunteers. Subsequently, group comparisons of FA maps between HIV patients and normal volunteers are made voxel-by-voxel for the whole brain.

Materials and Methods

A 3D bi-directional elastic registration approach based on FA was developed and utilized to co-register the DTI images of 11 HIV patients to a normal white matter atlas constructed from 10 healthy volunteers. Two 3D B-spline models are used for characterizing the forward (from the source to the target) and backward (from the target to the source) transformations. The transformation between the image pair were found through the minimization of a cost function which includes the similarity between the FA map pair, the consistency between the forward and backward transformation and the regularization term on the two transformations.

10 healthy volunteers (age 26.9±3.5) and 11 HIV patients (age 43±7.6) were recruited with written consent. The HIV patients were divided into three different stages based on clinical criteria: HIV associated dementia (HAD), minor cognitive motor dysfunction (MCMD) and subclinical MCMD. The DTI images were acquired by using a single shot EPI DTI sequence with diffusion gradients applied in six directions. All images were acquired with a Siemens 3T Allegra system with imaging parameters as follows: b=1000 s/mm^2, voxel size is 2*2*2 mm^3. DTI images obtained from one of the healthy volunteers were chosen randomly as the template to which DTI images obtained from the remaining subjects were registered. Group comparisons were made between the normal (n=10) and each of the patient groups (HAD, n=3; MCMD, n=6; and subclinical MCMD, n=6) as well as between the normal and all of the HIV patients as a single group (n=11). Student t-test was performed to assess the statistical significant level.

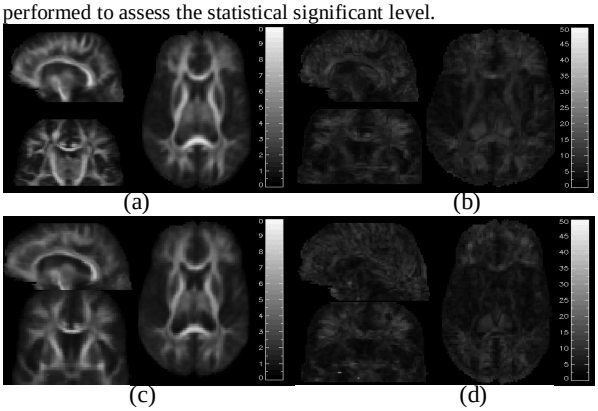

Figure 1.The FA mean and standard deviation of normal (n=10) (a,b) and HIV group (n=11) (c,d). The scale of the mean FA is from 0 to 1, while the scale of the standard deviation of FA is from 0 to 0.5.

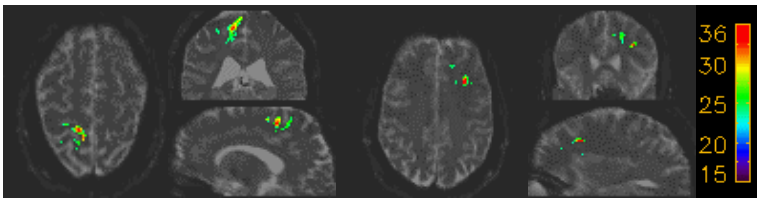

Figure 2. Reduced FA is seen in two regions are at the precentral gyrus (left) and anterior prefrontal (right) regions in three different views (transverse, coronal and sagital views). The t score is color coded and superimposed on T2 anatomical images. Color bar shows t score (×10) from 1.5 to 3.6. (T score above 2.09 show statistical significance with 95% confidence level.)

In most of the white matter, the FA from HIV patients in HAD, MCMD and subclinical MCMD groups were different from the normal group. However, these differences were not significant due to the limited sample size for each subgroup. Similar patterns in FA were found in focal brain regions in all three groups. Since there was no significant difference between the HIV subgroups, they were pooled for this analysis. The mean and standard deviation of FA of normals and HIV patients were shown in Fig 1. Two signifcantly reduced FA regions were observed, in the precentral gyrus and anterior prefrontal area, corresponding to the motor and premotor region, respectively, as shown in Figure 2. (T score above 2.09 show statistical significance with 95% confidence level.)

Discussion

We have demonstrated that a whole brain voxel by voxel FA comparison can be obtained between HIV patient group and a normal white matter atlas constructed from normal subjects by using a 3D elastic registration approach. Reduced FA is observed in the precentral gyrus and anterior prefrontal area, corresponding to the motor and premotor regions. Interestingly, the neuro-psychological tests have found different levels of cognitive motor dysfunction in these patients. It is suggested that the reduced FA in the motor and premotor region may correlate with the motor dysfunction. One potential limitation of this study is the age difference between the normal and patient groups. Abe et al have demonstrated only significant decreased FA is observed in genu with increased age (3). In this work, significantly different FA is observed when all patients were grouped together. However, results were not significant at various clinical stages due to the limited sample size in each patient groups. The comparison between the all patient and normal groups may only show pathophysiological changes presented in all clinical stages. This study is ongoing at our institution and additional patients will be available to further increase the sample size, allowing for the subgroup analysis in the future.

References

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