A TRACT BASED SPATIAL STATISTIC STUDY OF FRACTIONAL ANISOTROPY ALTERATIONS CAUSED BY SIMIAN IMMUNODEFICIENCY VIRUS INFECTION

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Target audience:

Neuroimaging researchers and AIDS researchers.

Purpose:

Using Tract Based Spatial Statistic (TBSS) analysis to study Fractional Anisotropy (FA) alterations caused by Simian Immunodeficiency Virus (SIV) infection.

Methods:

Four male rhesus monkeys were utilized from a HIV project at Beijing YouAn Hospital, Capital Medical University. DTI was acquired in one setting and obtained at the baseline (2 weeks before virus inoculation) and in the weeks of 12, 24 post virus inoculation. Blood samples, for quantitation of peripheral blood $CD4^+$ and $CD8^+$ T cells, were collected before each DTI scan. One of the 4 animals terminated in the 13th week post-inoculation due to terminal AIDS. After Fractional Anisotropy (FA) was calculated from DTI, the TBSS[1] was used to identify the centers of all major white matter tracts presented in all subjects. To examine the main effect of time post-inoculation, repeated measures ANOVA was analyzed on TBSS results. ANOVA results were thresholded at P<0.005 (uncorrected, cluster size≥20). Regions survived the threshold were considered as regions of interest (ROIs). Mean and max FA values in each ROI of all the FA images were calculated. Furthermore, we investigated the relationship of the mean and max FA values with the $CD4^+$ T cell counts, $CD8^+$ T cell counts and $CD4^+/CD8^+$ ratio.

Results:

Significant FA changes were observed in two regions in the inferior temporal regions (area TE). One was at the ventral subregion of posterior TE (TEpv, P<0.005, uncorrected, 31 voxels), and the other was at the dorsal subregion of posterior TE (TEpd, P<0.005, uncorrected, 20 voxels). Results were displayed in the T1 template from Wisconsin 112RM-SL rhesus atlas[2], which is in the coordinate space of Saleem-Logothetis rhesus brain stereotaxic atlas[3] (as showed in Figure1). In TEpv, no significant correlation was found. In TEpd, mean and max FA values were significantly negatively correlated with $CD4^+/CD8^+$ ratio (r=-0.816, P=0.025 for mean FA; r=-0.85 P=0.015 for max FA, scatter diagram is showed in Figure2). Mean and max FA values in TEpd were negatively correlated with $CD4^+$ T cell counts and positively correlated with $CD8^+$ T cell counts, but didn't show significance.

Discussion:

In our longitudinal study, we used TBSS to access white matter integrity degeneration with the advance of disease. We found that white matter integrity in the inferior temporal regions was vulnerable to the SIV infection. The results are consistent with previous studies on HIV affected patients[4, 5], which discovered both white matter and grey matter alterations in the inferior temporal regions. Our findings cross-validate that AIDS leads to impairments in the inferior temporal regions. Area TE is on the ventral visual pathway and associated with visual cognition[6]. We infer that SIV may impair the ventral visual pathway, causing disability or low efficiency of information transmission. We also found that FA was significantly negatively correlated with $CD4^+/CD8^+$ ratio in TEpd. Lower FA values were correlated with higher $CD4^+/CD8^+$ ratio. $CD4^+/CD8^+$ ratio is routinely used to evaluate and track the progression of HIV infection in clinic[7]. The significant correlation suggests that FA may characterize the disease development of HIV infection.

Conclusion:

With the advance of disease, SIV impairs macaque white matter integrity in the inferior temporal regions selectively, and may cause damage to the ventral visual pathway. Our MRI findings indicate that FA may be a potential marker for monitoring the disease progression.

References:

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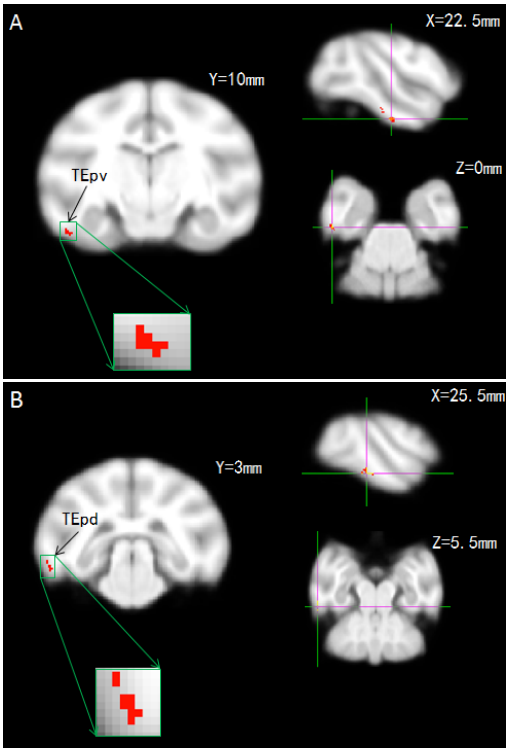

Figure 1. 3×1 repeated measures ANOVA results showing the main effect of time post-inoculation.
(A) Ventral subregion of posterior TE (TEpv, uncorrected, P<0.005, 31 voxels).
(B) Dorsal subregion of posterior TE (TEpd, uncorrected, P<0.005, 20 voxels).

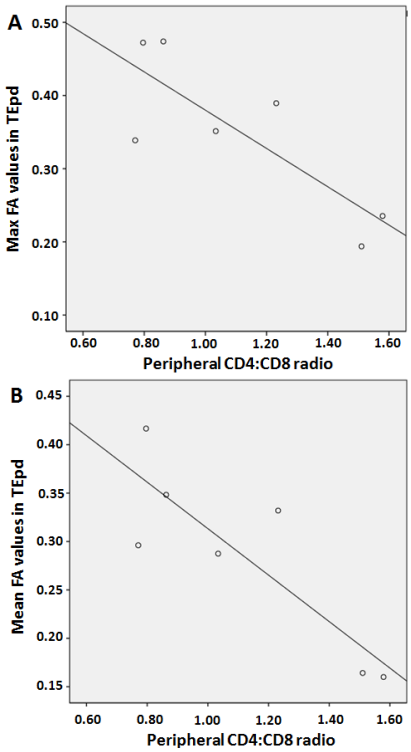

Figure 2. FA values in TEpd were negatively correlated with peripheral blood $CD4^+/CD8^+$ ratio.
(A) Max FA values in TEpd were negatively correlated with $CD4^+/CD8^+$ ratio (r=-0.816, P=0.025, R^2=0.665).
(B) Mean FA values in TEpd were negatively correlated with $CD4^+/CD8^+$ ratio (r=-0.85, P=0.015, R^2=0.723).