

Correlation of Fractional Anisotropy and Mean Diffusivity in Rhesus Monkey with Age and Parkinson's Disease

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INTRODUCTION: Parkinson's disease (PD) is a common neurodegenerative disease characterized by loss of motor control. PD belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing neurons in the substantia nigra (SN). It is often difficult to diagnose the early stages of PD due to the overlap of its symptoms with normal aging. Understanding the biological changes in the brain which accompany PD and normal aging such as motor slowing are major goals of this research. The imaging data set generated in this project will enable the testing of multiple hypotheses. Specifically, we hypothesize that depletion of the dopamine neurons in the SN that affect white matter tracts connecting the SN to the putamen will be detectable using diffusion tensor imaging (DTI). Second, we are analyzing the DTI data for the effects of age on fractional anisotropy (FA) and mean diffusivity (MD).

METHODS: We studied a group of sixteen research naïve rhesus monkeys between the ages of 16 and 21 using DTI. Rhesus monkeys are frequently used to study the effects of PD as well as aging. Their brain organization is very similar although a factor of eight smaller than that of a human. The animals were grouped into middle aged, and a group of hemi-parkinsonian (HP) rhesus monkeys aged matched to the middle aged animals. This latter group was made hemi-parkinsonian through the unilateral injection into the carotid artery with the selective neurotoxin MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). The animals were anesthetized with pentobarbital or isoflurine and imaged on a 3T Siemens Trio imager. A custom-built, single channel, receive-only coil was built on a fiberglass frame and used to enhance the received signal. Imaging consisted of double echo, diffusion-weighted, echo planar images with a spatial resolution of 1.25×1.25×2.0 mm³. Forty-eight diffusion directions with b = 500 s/mm² and six with b = 0 were acquired. In a separate analysis a group of 26 research naïve rhesus between the ages of 7 and 21 were imaged with a similar sequence to examine the effects of age on FA and MD. Seventy-eight diffusion directions with a b = 1000 s/mm² and six with b = 0 were acquired. All images were analyzed using FSL. Specifically, the images were corrected for susceptibility and eddy current distortions using a gradient echo field-map and non-linear registration to bring all animal's images into a common space.

RESULTS: The monkeys were grouped as follows: middle aged (n=6) 19.95 ± 2.4 yr and a hemi-parkinsonian group (n=10) 18.59 ± 3.0 yr which were not significantly different in age than the middle aged group. The monkeys from the second age analysis: 7.90 to 21.26 (n=26).

In the first analysis comparing the effects of the MPTP treatment, the MA group exhibited greater FA than the HP group in the corpus callosum in the MPTP treated (right) side. (See Figure 1) Additionally, higher FA was found in sections of the corpus callosum in the HP group in the untreated (left) side. In the second analysis of age, a positive correlation was found between age and FA in the Splenial Fibers (Clusters 1, 2) and the Inferior Longitudinal Fasciculus (Clusters 3, 4). (See Figures 2 and 3) A plot of FA versus age for the 26 monkeys is provided in Plot 1.

DISCUSSION: These results are consistent with the hypothesis that the denervation of the SN by the MPTP treatment will lead to a loss of associated motor neurons on the treated side. The increased FA seen on the left side may be explained by compensation of the left hemisphere due to the degradation of the treated right hemisphere. An increased FA with age in the second age analysis may be attributed to continuous myelination through adulthood.

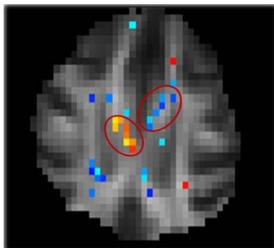
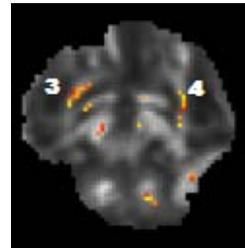
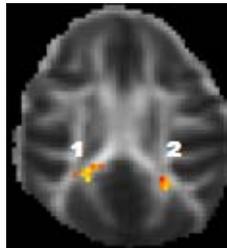
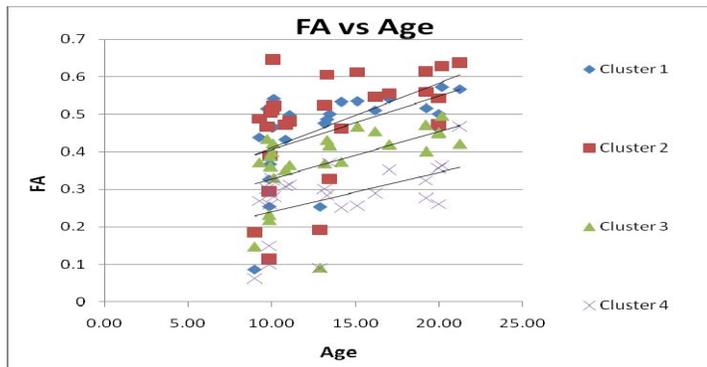


Figure 1. Significant pixels discovered comparing HP vs MA animals. Warm Colored Voxels = greater FA in the HP group (significance red < yellow); Cool colored Voxels = greater FA in the MA group (significance blue < light blue)



Figures 2 and 3. Second Age Analysis, Significant pixels discovered during regression of FA vs Age. Bi-lateral positive correlation between FA and Age.



Plot 1 Second Age Analysis, Scatter Plot of FA vs Age