Comparing the Structural Integrity of the Perforant Path in Young and Aged Rats

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Introduction

Advanced aging has been linked to deterioration of parahippocampal white matter tracts in the human brain including the perforant path [1-3]. This structure is responsible for connectivity between the brain's entorhinal cortex and a multitude of hippocampal regions including the dentate gyrus, CA fields 1, 2, and 3, and the subiculum. To aid in a correlative model of functional deficits related to aging, our group investigated structural integrity in the perforant paths of aged and young rats. This was accomplished by comparing fractional anisotropy data (FA) in these regions calculated from 21 direction, diffusion tensor MRI datasets.

Experimental

Male Fischer 344 x Brown Norway F1 Hybrid rats from the National Institute on Aging (NIA) colony were employed in our aging studies. Young (4 month old, n = 3) and old (24 month old, n = 4) animals were perfusion fixed using 4% formaldehyde and their brains removed. Whole, fixed brains were washed for a period of no less than 14 days in phosphate buffered saline (PBS) with multiple wash volume changes to reduce fixative levels in the tissue. Diffusion tensor MRI datasets (TR/TE = 1000/20ms, b = 1200s/mm^2, δ = 1.2ms, Δ = 10ms, Res = 47μm in-plane, 21 direction, Avg = 4, Time = 12h31min) were collected on a 750MHz (17.1T) ultra-wide bore spectrometer. Fractional anisotropy (FA) measurements were calculated from FA maps using regions of interest (ROIs) selected from areas comprising the subjects' perforant pathways. Mean FA values were then calculated for both aged and young cohorts.

Results

Selected 2D fractional anisotropy maps detail the ROI selection (magenta) of the perforant pathway used in our FA analysis (**Fig.1**) The FA values calculated for each voxel are assigned a specific value denoted by the included color bar. Mean FA values in the perforant path calculated from groups of aged (n =4) and young (n = 3) rats are reported (**Fig.2**)

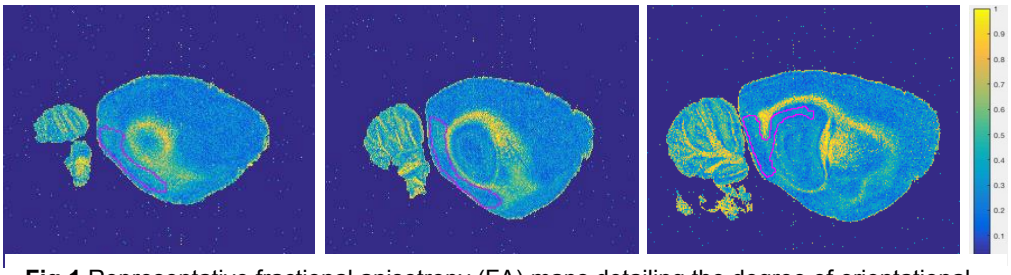

Fig.1 Representative fractional anisotropy (FA) maps detailing the degree of orientational preference to water diffusion in each voxel across the brain. Areas comprising the perforant path are indicated within the magenta ROIs. Color bar denotes FA values from low (0.0, dark blue) to high (1.0, bright yellow).

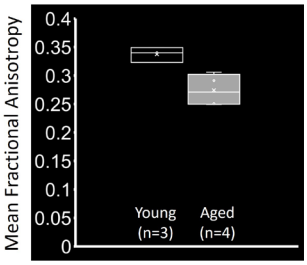

Fig.2 Fractional anisotropy (FA) group means for young (black, n = 3) and aged (grey, n = 4) rats.

Conclusions

Analysis of the perforant path in rats revealed a clear reduction in the calculated fractional anisotropy of aged animals as compared to their younger counterparts. This finding corroborates data in human studies which describes age related deterioration of parahippocampal white matter [1-3]. Such measures will be used as a metric for tissue integrity in future work investigating the effects of aging and perforant path function on discrimination-based memory tasks.

Acknowledgements

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References

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