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Axon Initial Segment Loss is not Observed in the Hippocampus of Experimental Autoimmune Encephalomyelitis Mouse Models

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Multiple Sclerosis

Incidence: 2.3 million people worldwide diagnosed with MS

Immune-mediated disorder of the CNS where healthy myelin tissues are damaged

Symptoms:
- Cognitive dysfunction
- Visual disturbances

Background

The axon initial segment (AIS) is fundamental for neuronal communication and action potential modulation, a characteristic which has been shown to be disrupted in inflammatory diseases such as Multiple Sclerosis. Previous work has portrayed evidence of AIS breakdown in layer 5 of the cortex, which was independent of demyelination in experimental autoimmune encephalomyelitis (EAE) induced mice. It has also been found that AnkyrinG, is an essential cytoskeletal scaffolding protein necessary for proper AIS function. It further promotes clustering of necessary AIS proteins and voltage-gated sodium channels. AnkyrinG deficiency results in a non-functional AIS. Therefore, AIS stability is critical for neuronal function. Furthermore, in order to determine if the pathology is specific to the cortex or affects other regions of the brain in the EAE model, we investigated the hippocampus, a region associated with cognitive dysfunction in several inflammatory diseases.

AIS Stability in EAE Hippocampus

![Image](image-url)

Figure 4. AISs are observed in the dentate gyrus (A,B) and CA1 (C,D) of the hippocampus. No overt differences were observed in the number of AISs in these region between Naive and EAE mice. Quantitative analysis was inviable due to extensive overlapping and clustering of the AISs (ankyrinG, red). Western blots of hippocampal homogenates from Naive, Late EAE, and Chronic EAE reveal no breakdown of Beta IV Spectrin (E).

Conclusion

- Immunohistochemical (HC) labeling for ankyrinG combined with laser confocal microscopy display an inefficient method of quantifying AISs in the hippocampus
- Preliminary data illustrates no breakdown of AISs in the hippocampus as observed in the cortex
- Western blots display Beta IV Spectrin breakdown in the cortex, but not in the hippocampus

Future Directions

- Micropigrial morphology in the hippocampus will be assessed to determine if a difference in activation results in AIS breakdown or preservation
- Micropigria are enigmatic and are known to play different roles in different regions of the brain. Therefore, we are interested in isolating these cells from the hippocampus and from the cortex to compare microglial expression profiles
- Findings from these studies should shed light on the role microglia play in different brain regions during disease.

Acknowledgements

This work was supported in part by the NMSS pilot grant and Veterans Affairs Merit Grants (1IO1BX002365 – JD and 101B0003759 – GHDV). Microscopy was performed at the VCU Department of Anatomy and Neurobiology Microscopy Facility with funding from an NIH-NINDS center core grant (5P30NS047463).

I would like to express my gratitude to Dr. Jeffrey Dupree, my mentor, for allowing me to work in his lab. And would like to extend my appreciation to Kareem Clark, Savannah Benusa, and Nick George for helping me conduct a successful research project.