

Sex differences in region-specific hippocampal areas in Alzheimer's Disease: an animal-based approach

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Background: Atrophy in the hippocampus is responsible for memory and cognitive decline in Alzheimer's Disease (AD). Progression and presentation of AD in men and women are different, and the hippocampus and its subregions could be affected differently. By identifying what areas of the hippocampus are affected by sex, diagnostic tools can be better used to clinically identify and treat AD.

Aims: The goals of the proposed research are: (1) use in vivo MRI techniques to isolate the hippocampus in a mouse model, (2) use data analysis to compare the volume of the hippocampus and its subregions in 5xFAD mice, and (3) see if sex plays a role in differing hippocampal volume, and (4) assess the translational utility of using structural MRI to measure hippocampal integrity for future in vivo human brain studies/clinical practice.

Methods: We used the imaging software FSLeaves to examine MRI images and isolate hippocampal subregion masks. MRI images were taken at the 2-month age period when amyloid-B deposition begins in the forebrain. Upon isolation of the hippocampal mask of each MRI, group classification was identified, and quantitative analysis was performed to compare groups.

Results: We found significant lower spatial volume in Stratum Granulosum (SG) of the hippocampus in female mice compared to male mice. The SG contains dentate granule cells, responsible for spatial memory. Apart from this, the data that we obtained was nonsignificant but did show that female mice contained mainly smaller hippocampus subregions and total volumes despite TICV being larger in females.

Conclusion and Impact: More data is needed to observe the degeneration of SG over a lifetime and assess if it is the reason why males retain spatial memory in AD as opposed to females. Otherwise, analyzing hippocampal volume in the early stages of AD doesn't appear to be sufficient in explaining outstanding sex differences in AD presentation and progression.