A Resting State Functional Connectivity Analysis of fMRI Correlates for Cognitive Dysfunction in Mouse Models with Alzheimer's Disease

Anjali Reddy[1] , Hae Sol Moon[2] , Alexandra Badea[3], PhD
[1] NCSSM; [2] Duke BME; [3] Duke Radiology

Background:
Alzheimer's Disease is detected too late for treatments to be effective, thus we must understand risk factors and act upon them.

Research Question:
What are the fMRI correlates of risk factors (age, APOE genotype, female sex, immunity) of cognitive dysfunction in Alzheimer's Disease mouse models?

Objectives:
Examine the impact of risk factors for Alzheimer's disease on learning, memory and functional brain networks.

Methods:
Morris Water Maze tested spatial learning and memory using probe trials, statistical ANOVA analysis of risk factors, Conn Toolbox fMRI analysis.

Results:
Mice with APOE4 allele exhibit poorer learning and memory and altered connectivity with risk factors, such as diet.

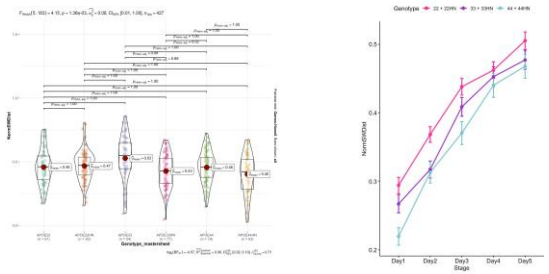
Conclusions:
Mice with risk factors of old age and APOE4 genotype are at most risk of Alzheimer's Disease.

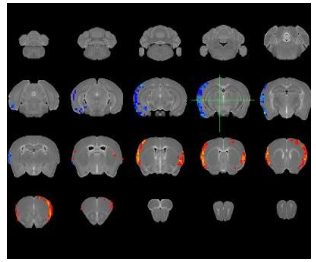
Future Directions:
Validating findings in human populations and improved community understanding of AD risk.

ANOVA Analysis of all Morris Water Maze (MWM) results.

P-value statistically significant (less than 0.05) for genotype, sex, diet, line type, and age

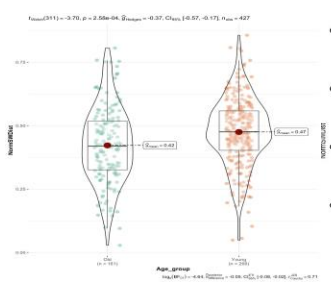
	Sum Sq	Mean Sq	NumDF	DenDF	Fvalue	Pr(>F)
Geno	1878.347	939.1737	2	372.8673	28.29901	3.61E-12
Sex	135.4353	135.4353	1	372.8667	4.080911	0.044085
Diet	1157.544	578.772	2	372.8643	17.43945	5.75E-08
Line_type	2266.211	2266.211	1	372.8667	68.28505	2.51E-15
Age_group	2989.558	2989.558	1	372.8667	90.08082	2.79E-19
Stage	128700.7	32175.18	4	8012.92	969.4966	0

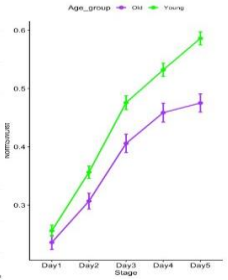




Implications:
Alzheimer's Disease results from multiple interacting factors and not one single cause. Differences in mouse genetics and physiology make these results not fully translatable to humans but enable us to study risk factors and interactions in a controlled way.

Memory
= high risk
= low risk

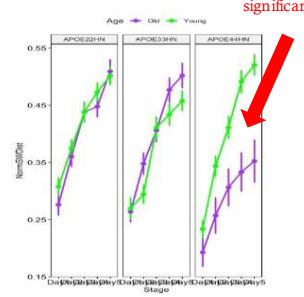




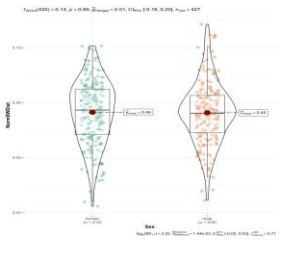
Learning
= high risk
= low risk

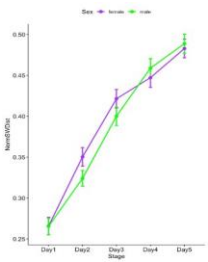
Age: Old Young

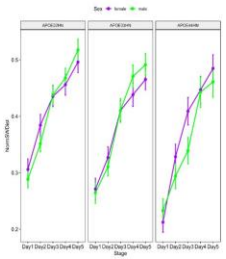
Most significant



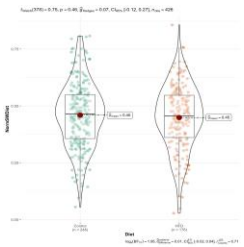
Sex: Female Male

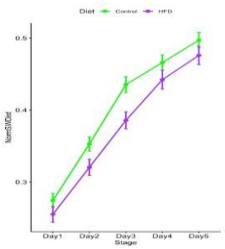


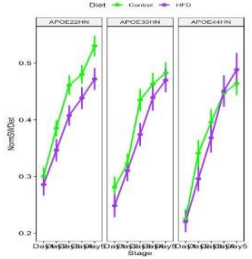




Diet: HFD CTRL







Immunity: Humanized NOS Mouse