What can the transcriptome tell us about hippocampal subregion differences?

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OUR FOCUS

Identify the transcriptional differences between selected hippocampal sub-regions
Aging is associated with cognitive decline

The hippocampal formation is known to be particularly vulnerable

Each sub-region within the hippocampus has unique susceptibilities and possesses unique anatomy and molecular physiology

CA1 → particularly susceptible to AD-related pathology
CA3 → more vulnerable to stress/glucocorticoids
DG → reduced neurogenesis with aging
Do the transcriptional differences across the hippocampal sub-regions throughout the lifespan (i.e. ignoring age-related changes) help explain their unique age-related susceptibilities?
Only considered genes that met correction for all of our parallel hypotheses [B&H FDR p<0.05]

Must be statistically significant across both sites
APPLES TO APPLES
CROSS SITE CORRELATION

R-squared = 0.827
GENES DETECTED

Genes detected in 750,000 counts

Sample

Genes detected (raw counts > 5)
Significantly (B&H) different vs. CA1 and CA3 at both sites
TOP HITS – DG SPECIFIC (meta p-value, Fisher’s combined)

DG = 2,532 transcripts
CA1 = 1,068 transcripts
CA3 = 1,200 transcripts
PLK5

Kinase-deficient in humans, role in differentiation?

Mouse
CA3 = no strong **uniquely** expressed genes
So... WHAT ABOUT AGING?

CA1 – particularly susceptible to AD-related pathology

Pathway analysis of the CA1 differentially expressed transcripts “synaptic vesicle” transcripts are associated in CA1 but not the other sub-regions
Thanks

Funding: McKnight Brain Research Foundation

Collaborators: UA / UF / UAB
DISCORDANT GENES

N≈450 genes that were consistently detected at UF [Ion Proton]

75 genes were explained by the use of a stranded library prep kit

Remaining have no explanation as of yet [chr / biotypes / etc...]