

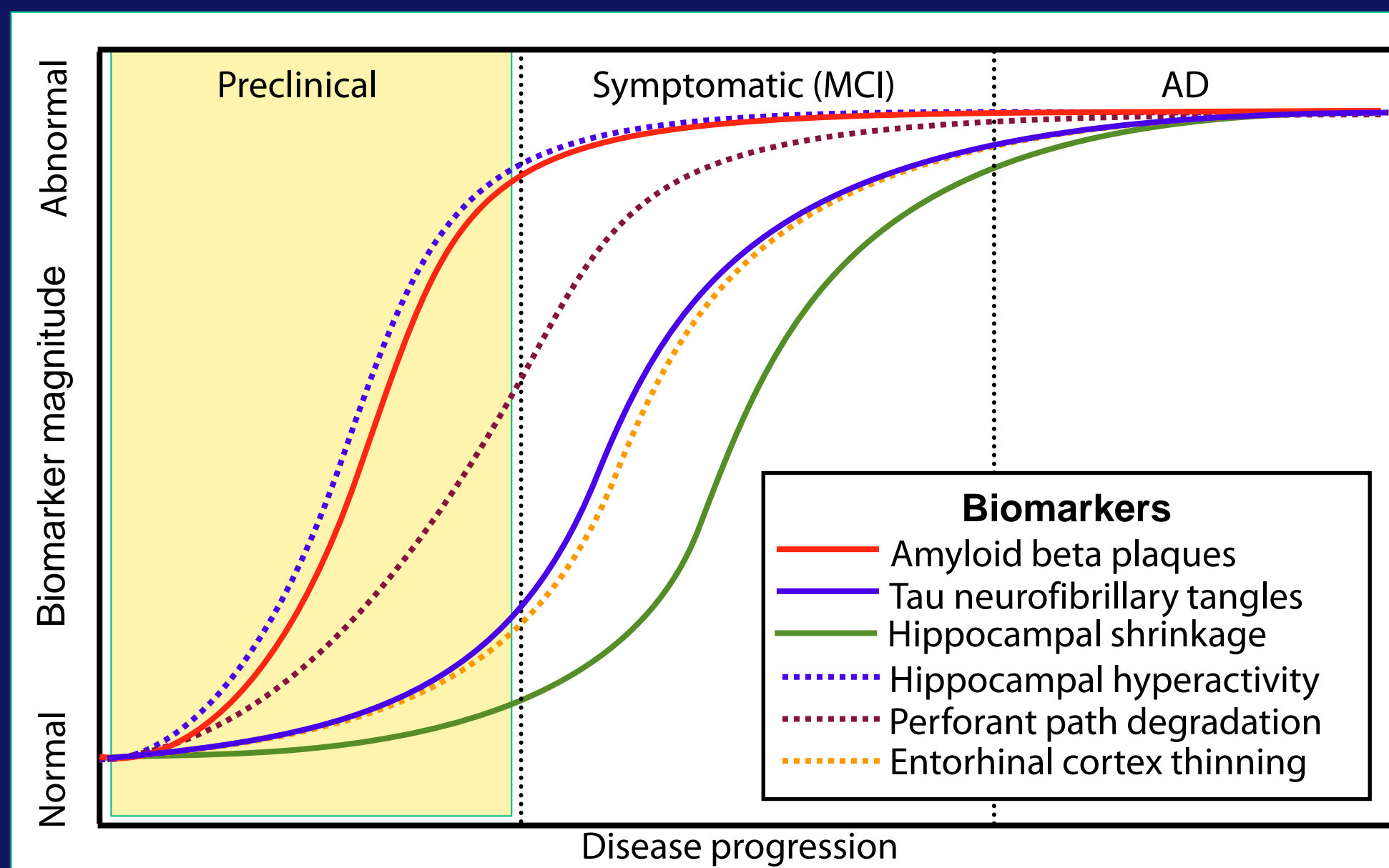
Neuroimaging Biomarkers for Preclinical Alzheimer's Disease

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Early Detection of Alzheimer's

Memory decline is a hallmark effect of aging, but is also a defining symptom of mild cognitive impairment (MCI) and Alzheimer's disease (AD). Current research points to a multitude of aging profiles, some of which end in a diagnosis of AD. *However, by the time someone arrives at a diagnosis, much of the damage has been done.*

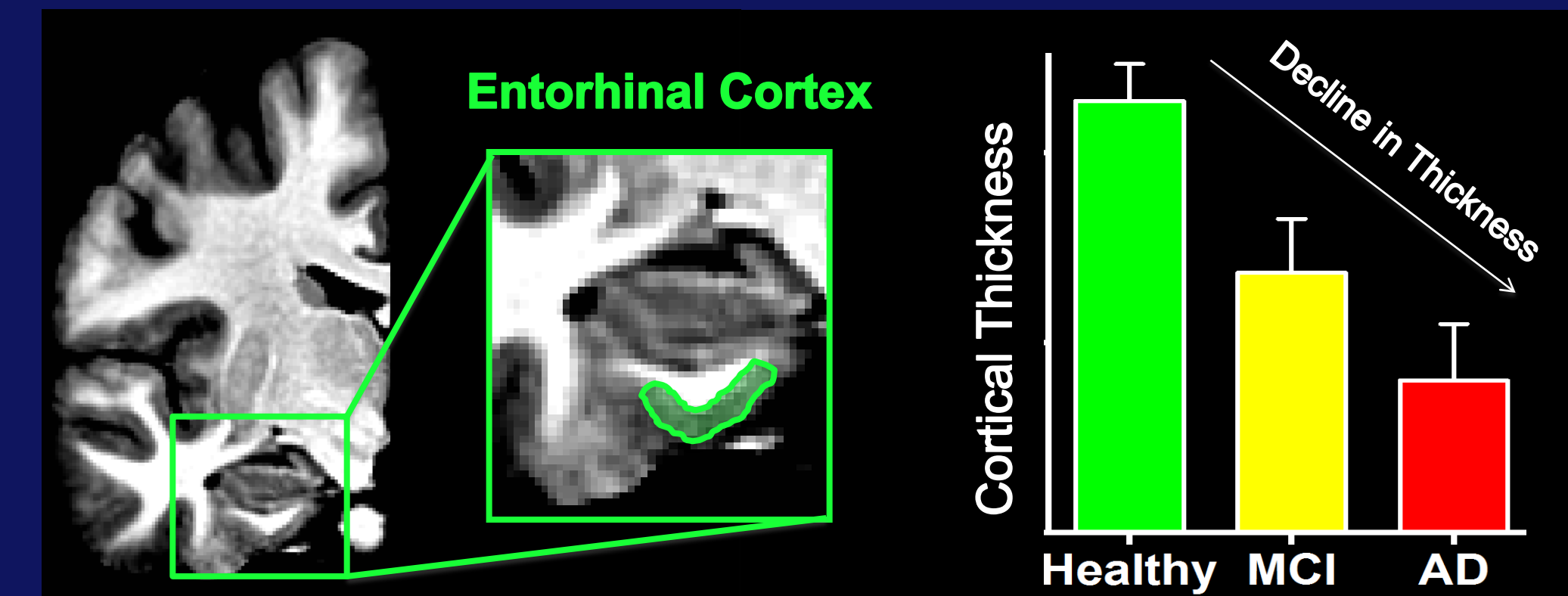


We identify sensitive brain imaging biomarkers for AD in the medial temporal lobes (MTL) which include the hippocampus and nearby entorhinal cortex. *Our goal is to identify AD in the preclinical stage so treatments and interventions can begin earlier and be more effective for at-risk patients.*

Key Questions

1. Are there subtle structural changes to brain tissue that predict conversion to AD?
2. Do connections between brain regions in the MTL predict MCI and AD status?
3. Are there subtle changes in MTL function that predict healthy aging vs. MCI and AD?

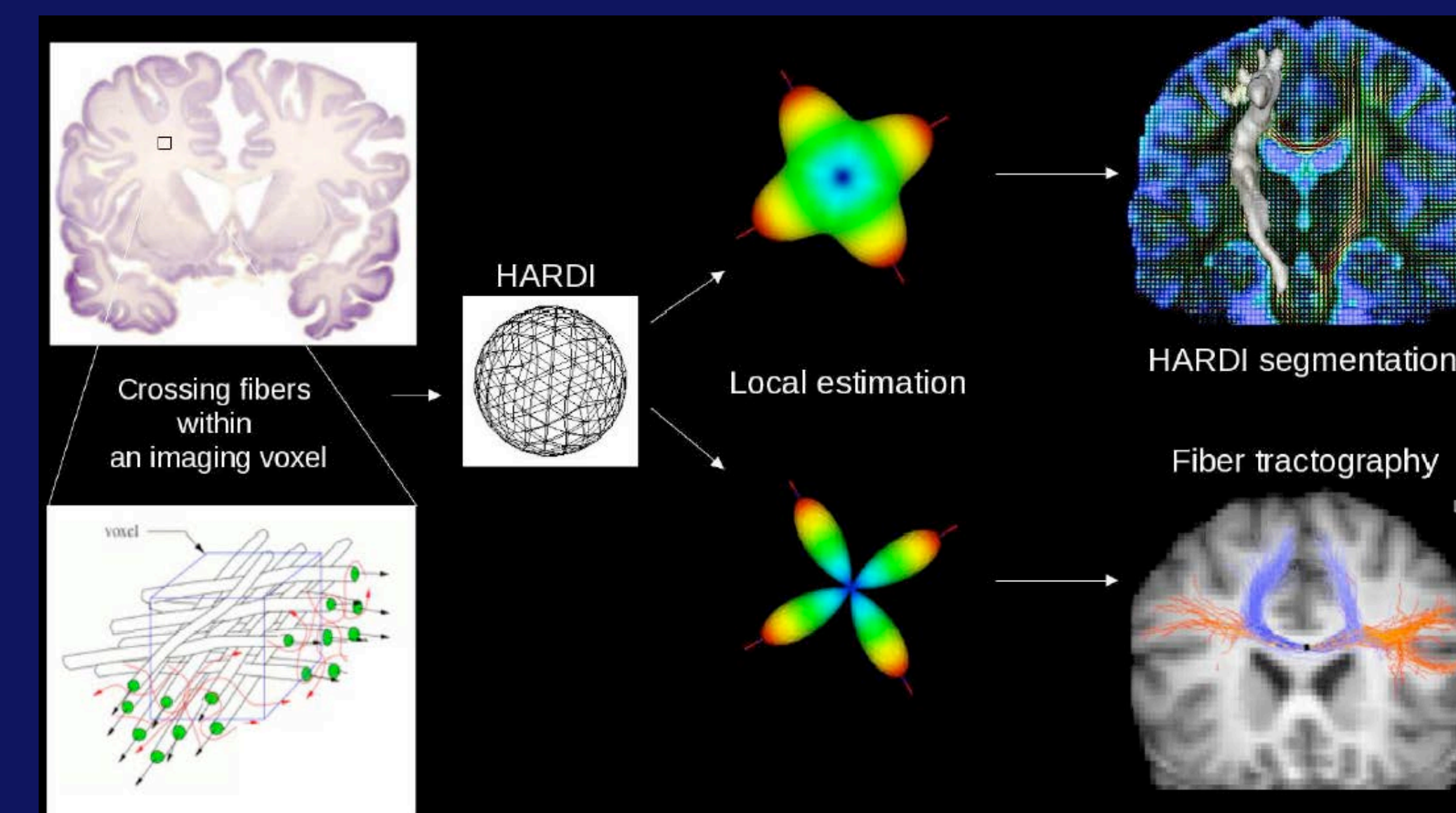
Structural MRI – Brain Tissue



Structural MRI shows that the thickness of brain tissue in the entorhinal cortex predicts clinical status and rate of shrinkage predicts decline in MCI (Yassa and Gallagher AAlC 2013). We are developing improved techniques with higher resolution to detect cortical thinning at the earliest stages (Leal and Yassa Hippocampus 2014).

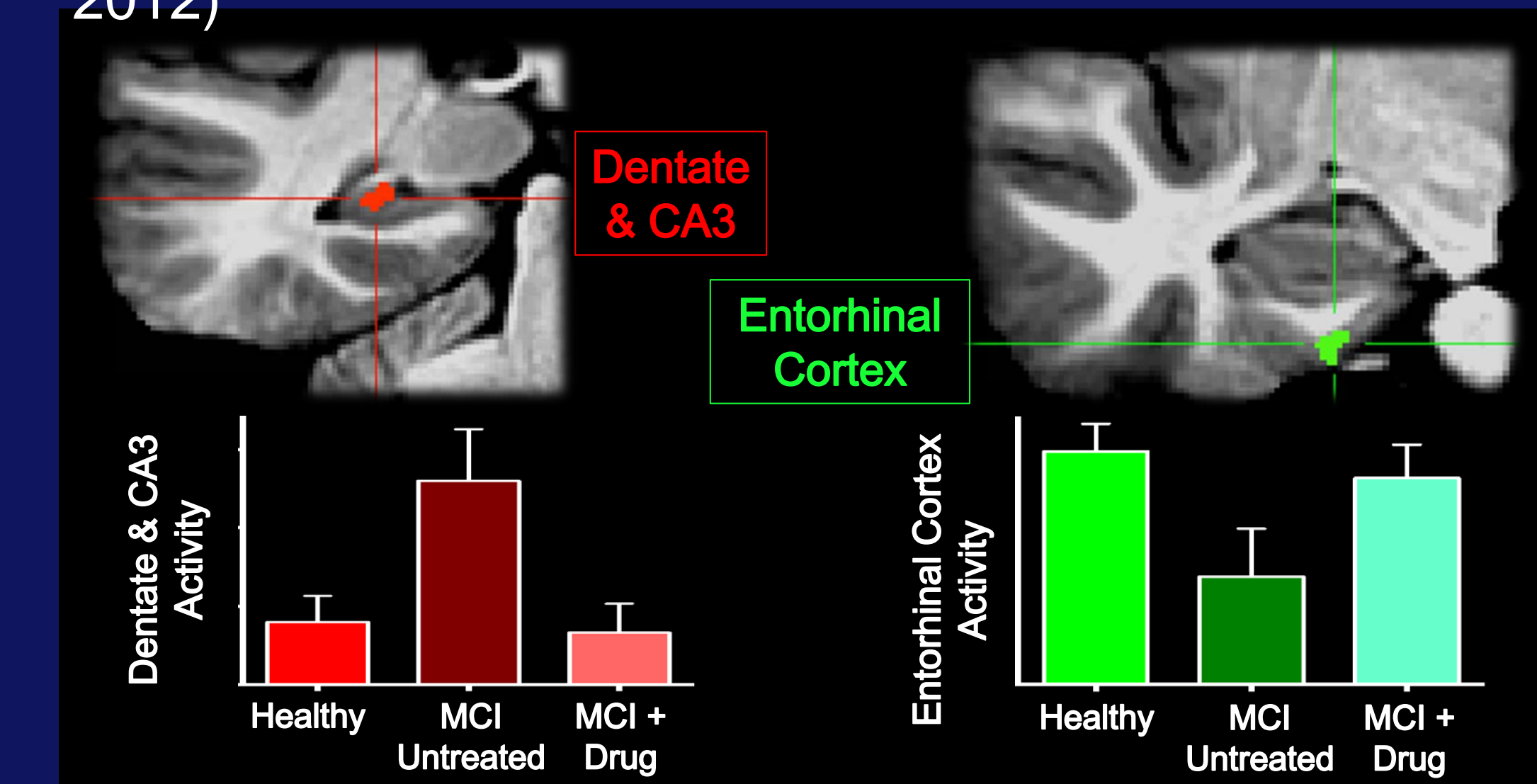
Diffusion MRI – Connections

High-resolution diffusion tensor imaging (DTI) shows that the perforant path, connecting the hippocampus to the entorhinal cortex, degrades with age-related memory loss (Yassa et al. PNAS 2010; PNAS 2011). We are now developing state-of-the-art High Angular Resolution Diffusion Imaging methods to detect subtle changes in connectivity (Schwab et al. IPMI 2013).



Functional MRI – Abnormal Activity

Memory deficits in MCI and AD are associated with *hyperactivity in the dentate & CA3 region of the hippocampus, and hypoactivity in the entorhinal cortex* (Yassa et al. Neuroimage 2010). A systemic low-dose anti-epileptic drug (levetiracetam) was found to *reverse abnormal brain activity and rescue memory impairments in MCI* (Bakker et al. Neuron 2012).



We are now developing new sensitive memory tasks and imaging techniques to target functional abnormalities in preclinical AD as well as ways to test therapeutics aiming to reverse or slow down AD.

Research Team

Our research team consists of Dr. Michael Yassa (PI), Ms. Elizabeth Murray (Program Manager), and Ph.D. students Stephanie Leal, Zachariah Reagh, Jared Roberts, and Rebecca Stevenson. We additionally collaborate closely with Dr. Craig Stark's lab. Our aging and AD biomarker work is supported by the National Institute on Aging (NIA).

References

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