

PET-MR imaging of Tau and synaptic density in prodromal Alzheimer's disease

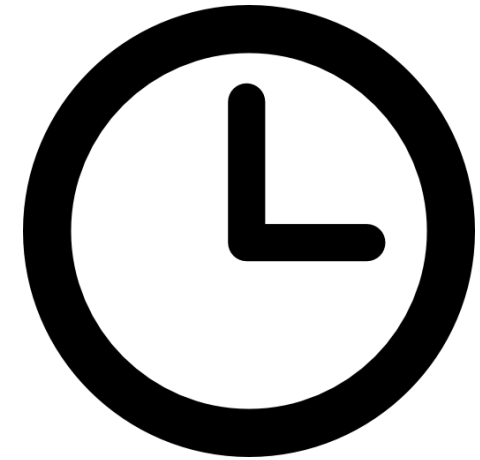
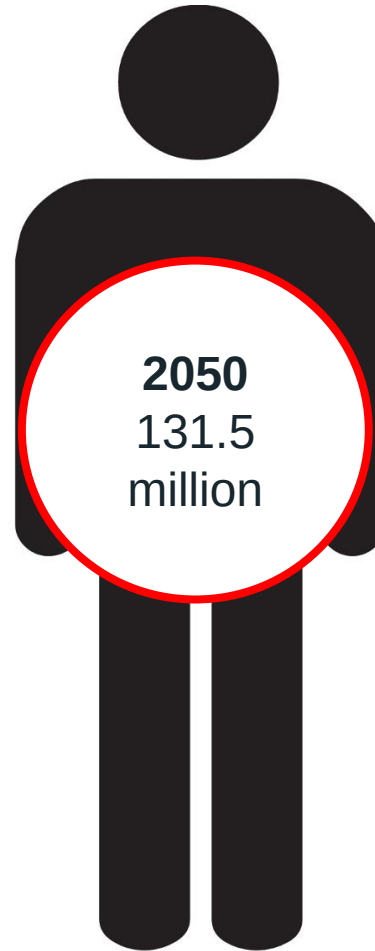
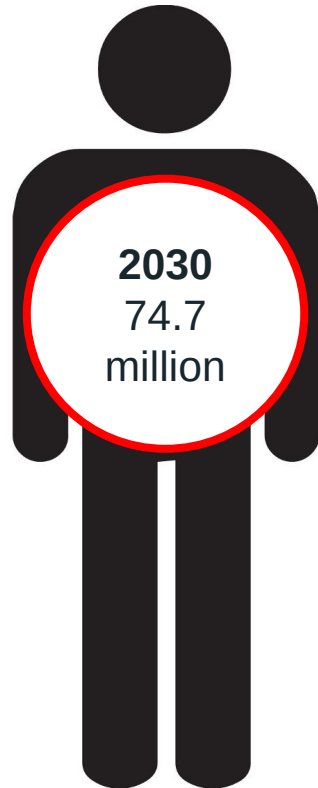
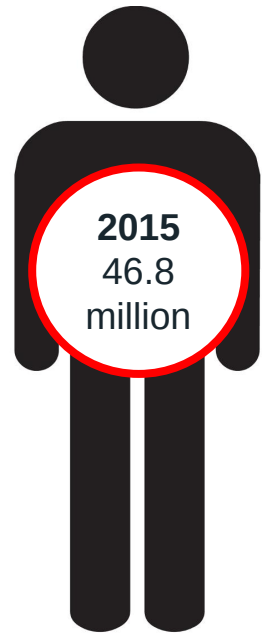
H. Vanhaute¹, J. Ceccarini¹, L. Michiels^{1,2}, M. Koole¹, S. Sunaert³, L. Emsell³,
R. Lemmens², M. Vandenbulcke⁴, K. Van Laere¹

¹ Nuclear Medicine, Department of Imaging and Pathology, ²Department of Neurology,
³Department of Translational MRI, ⁴Department of Old Age Psychiatry

University Hospitals Leuven and KU Leuven, Belgium

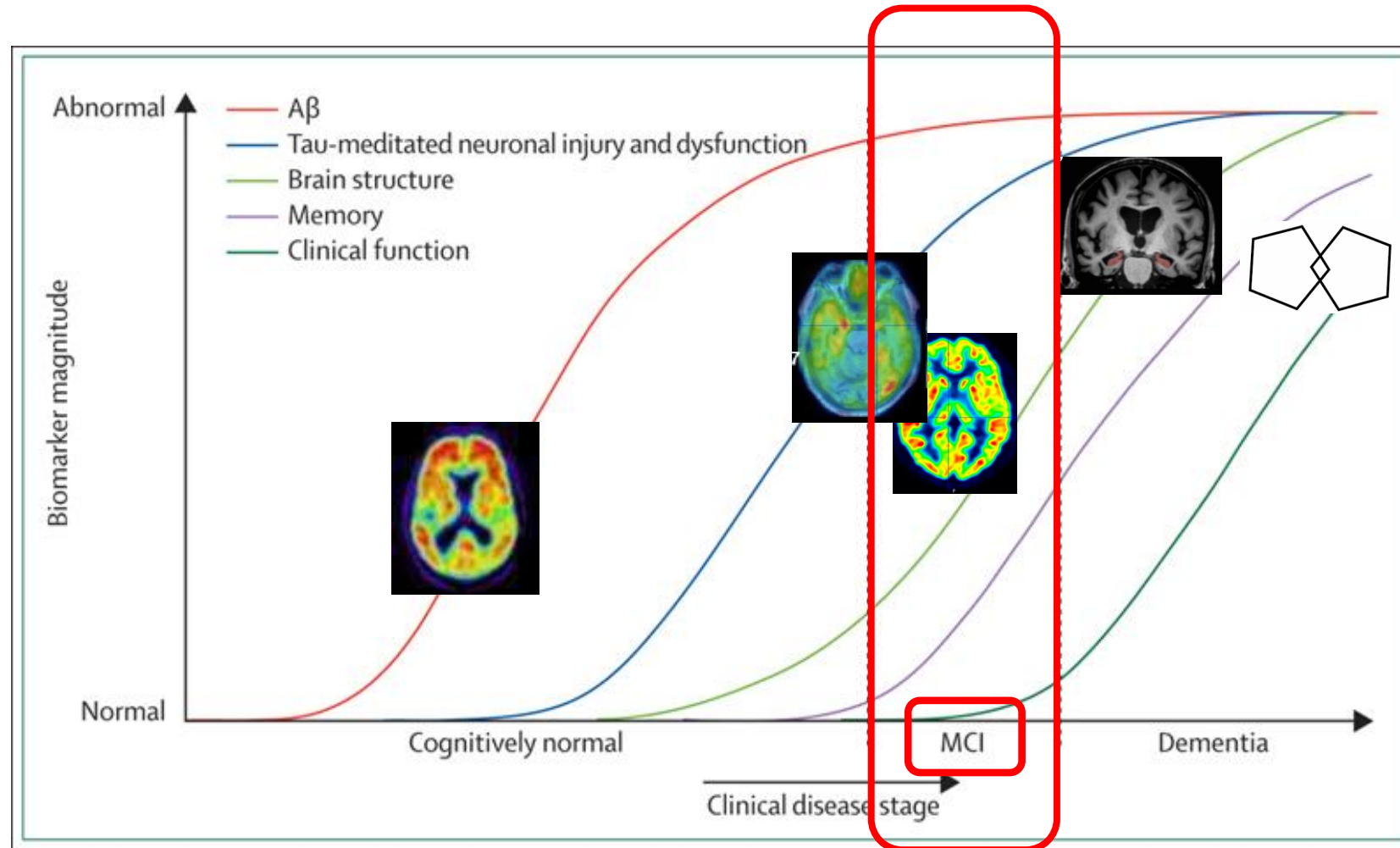


Global burden of dementia

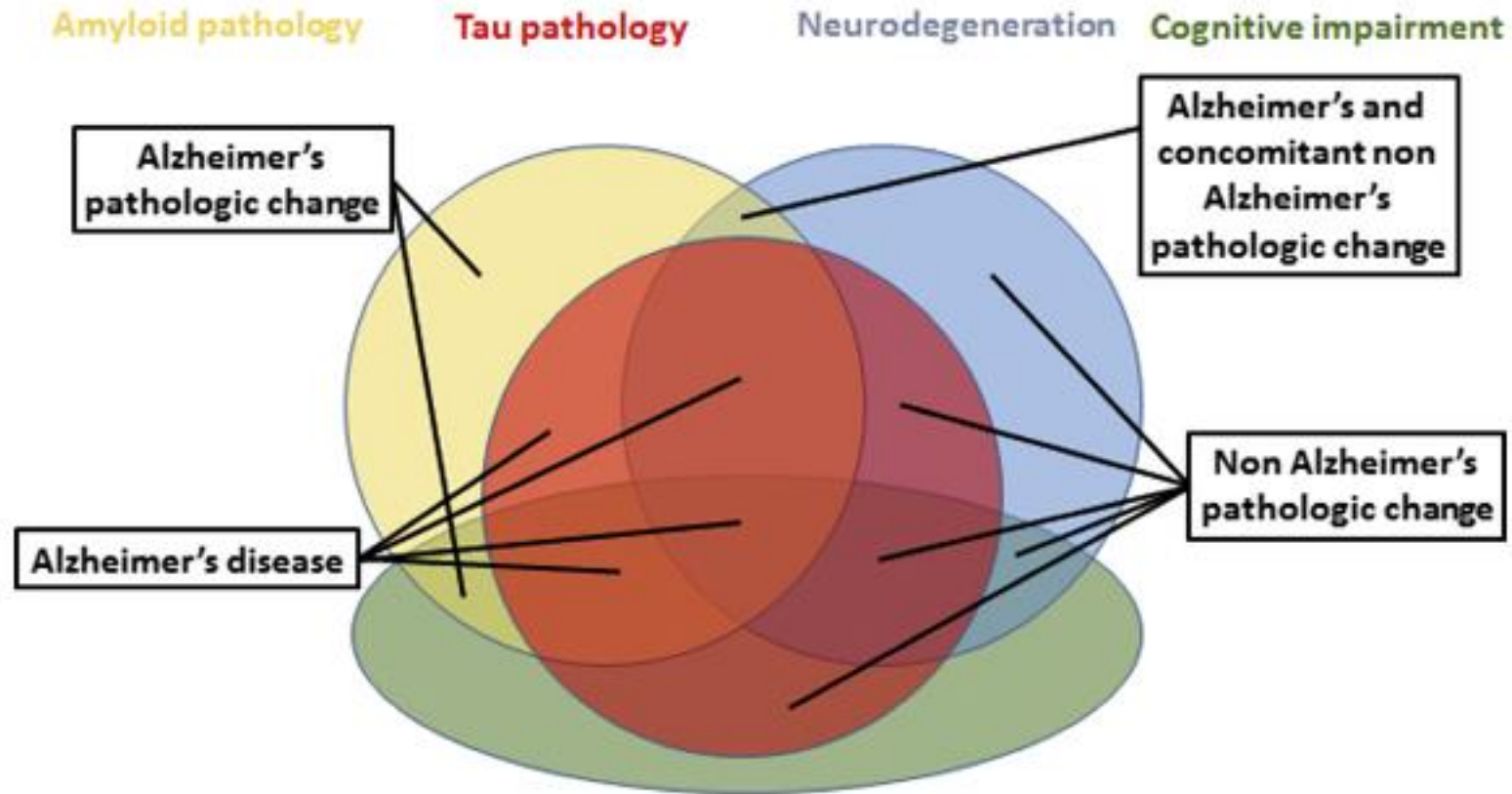


One every 3 seconds

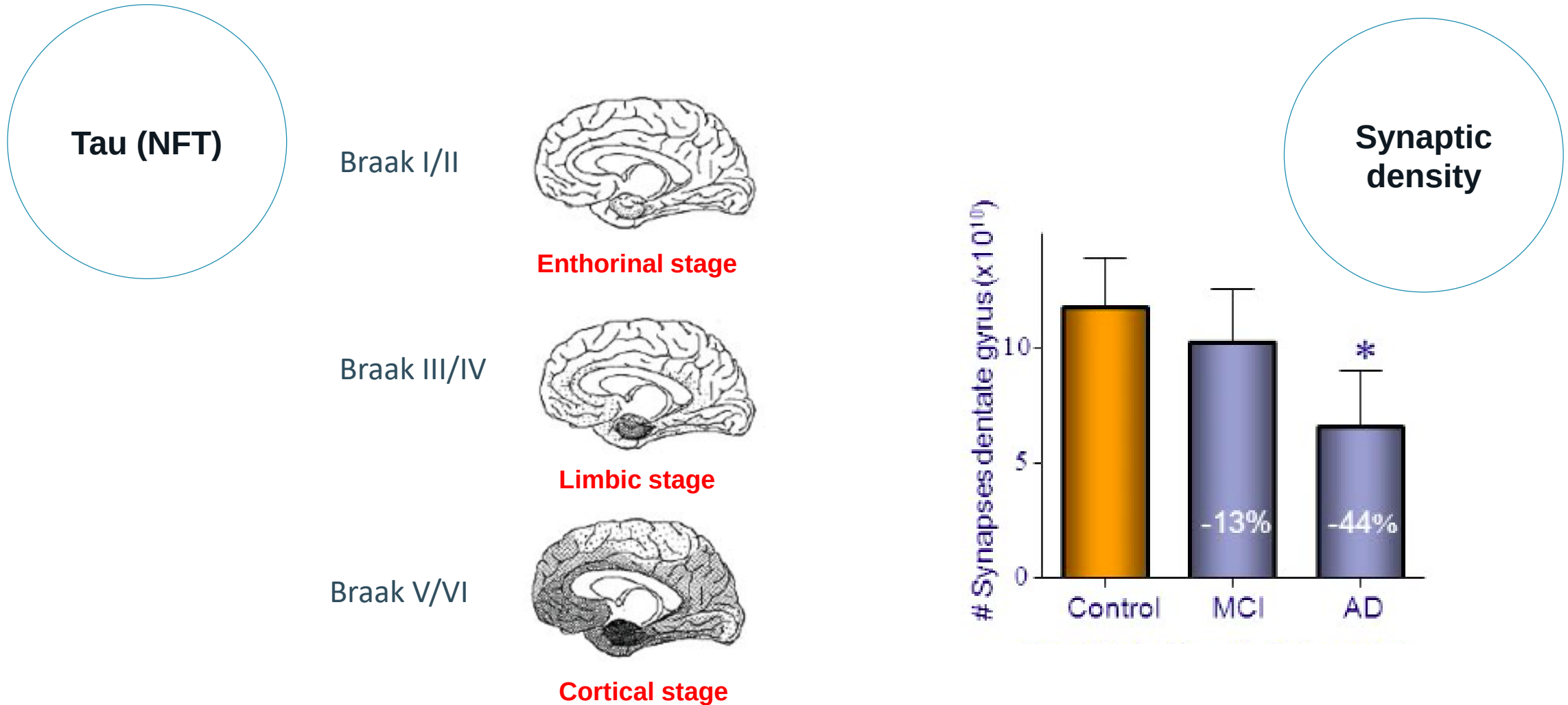
The quest for biomarkers in AD...



ATN-research framework

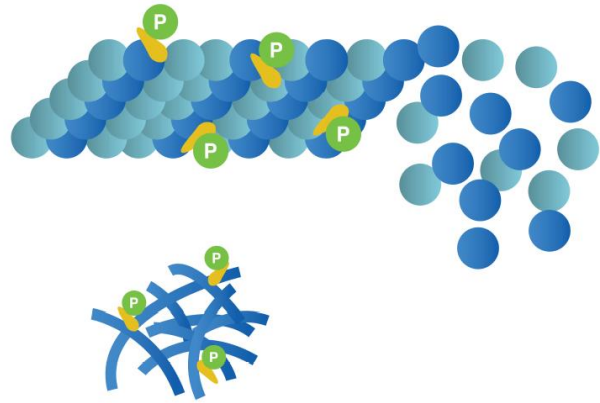


Earlier findings in (prodromal) AD: *in vitro*



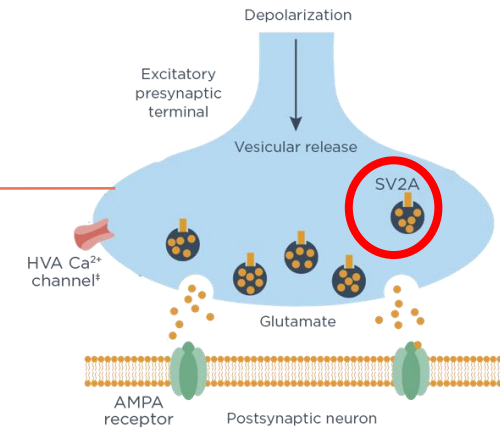
Promising PET tracers

^{18}F -MK-6240: NFT

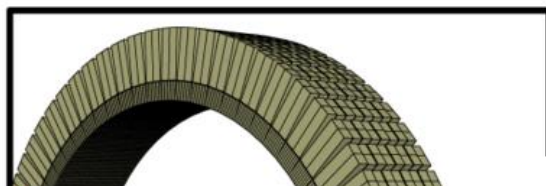


Early
pathological
changes
correlated with
cognitive decline

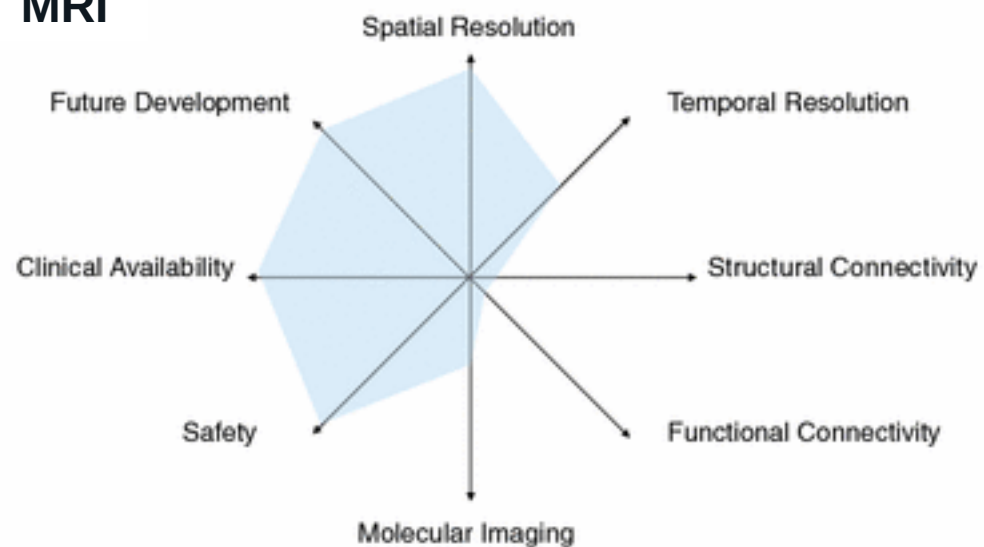
^{11}C -UCB-J: Synaptic loss



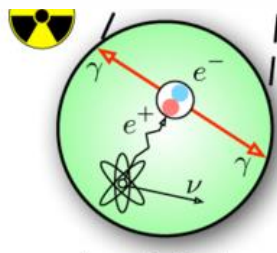
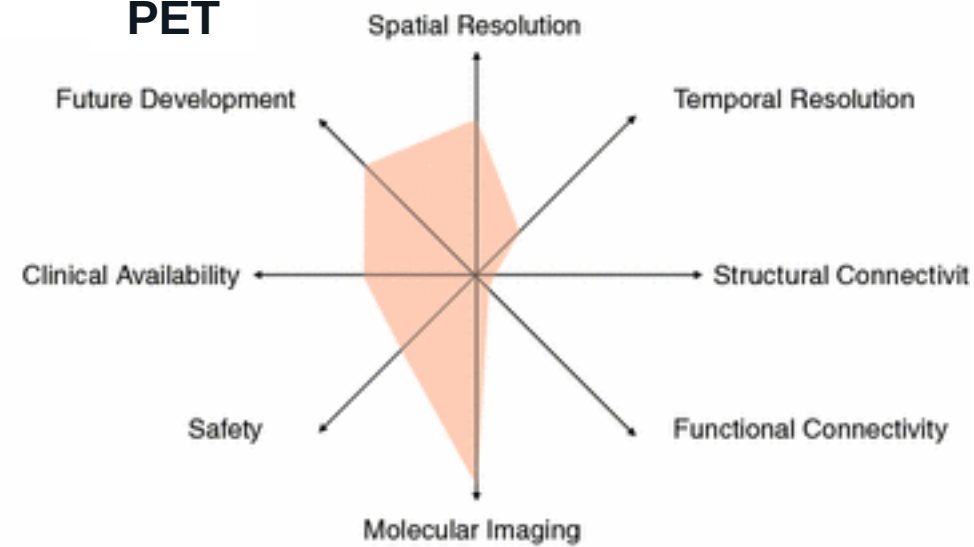
PET(-MR) scan



MRI

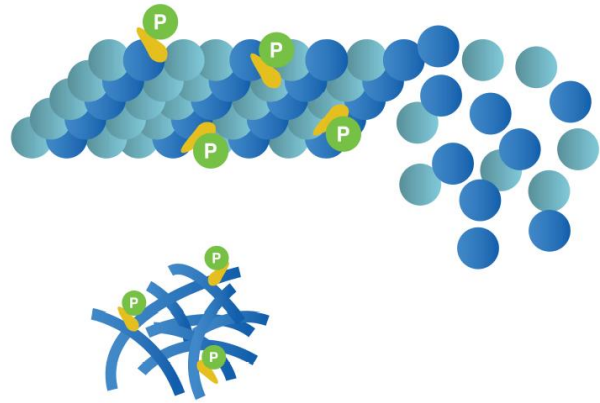


PET



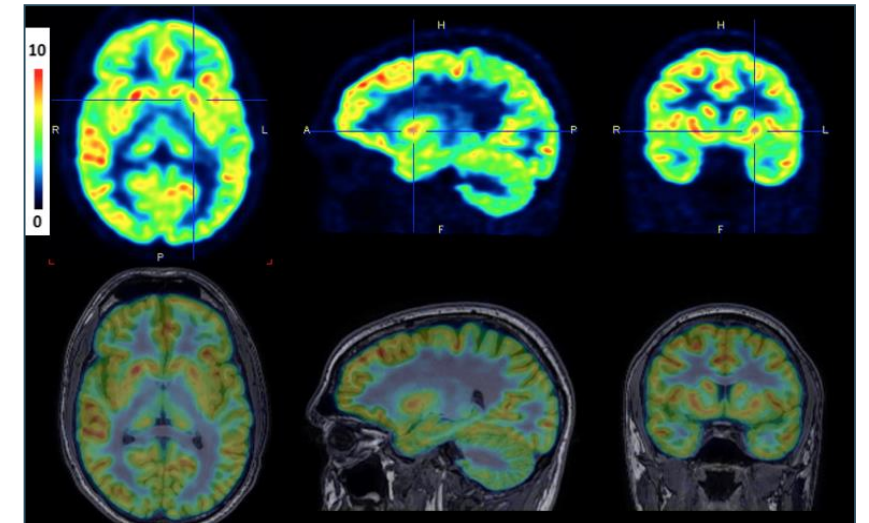
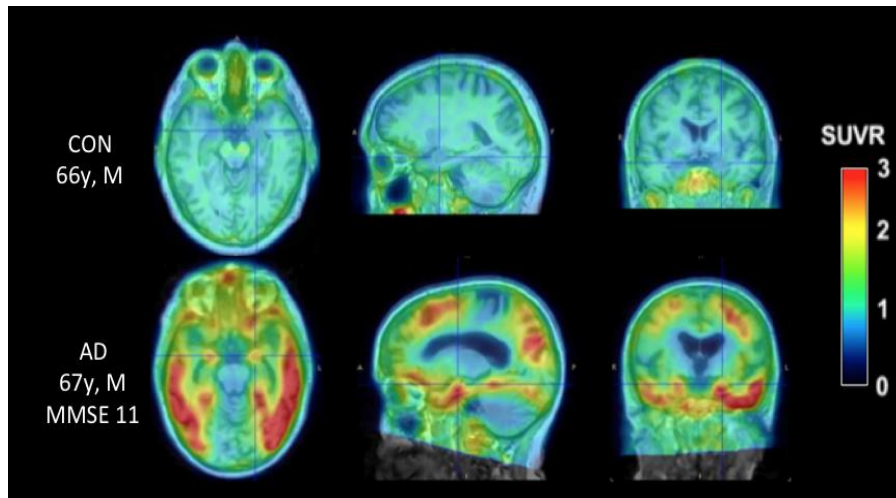
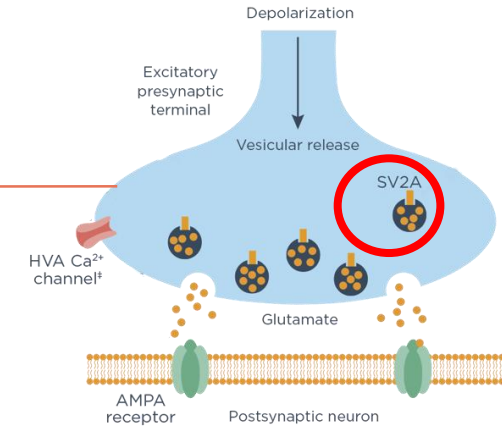
Promising PET tracers

^{18}F -MK-6240: NFT



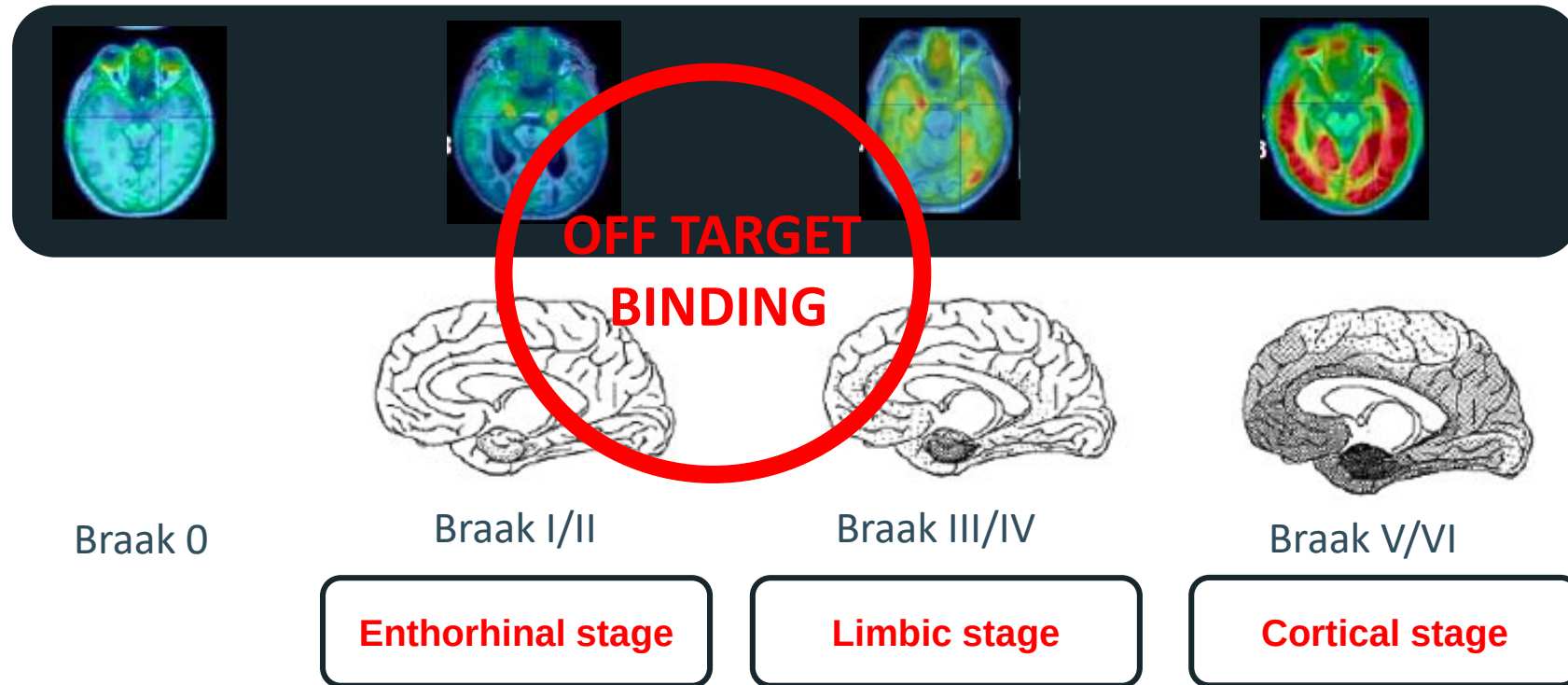
Early pathological changes correlated with cognitive decline

^{11}C -UCB-J: Synaptic loss



Earlier findings in (prodromal) AD: *in vivo*

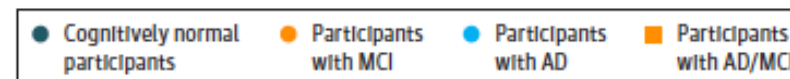
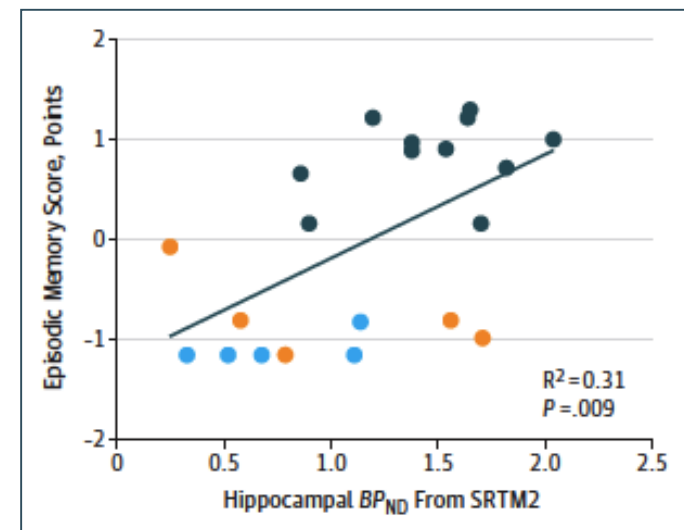
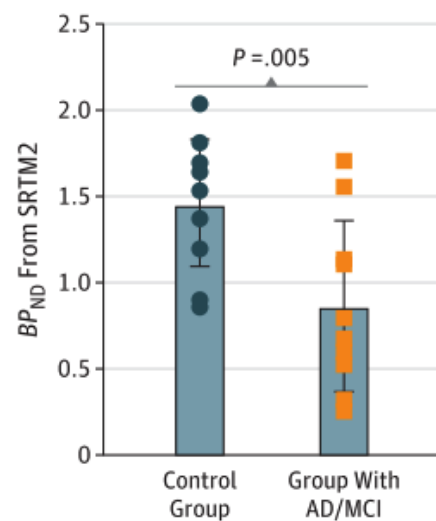
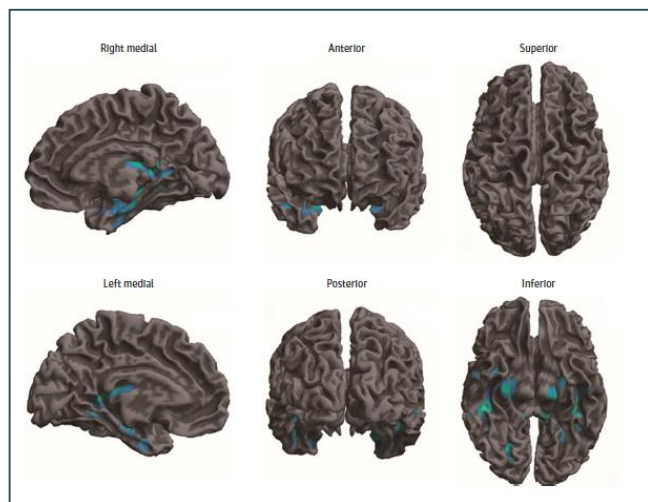
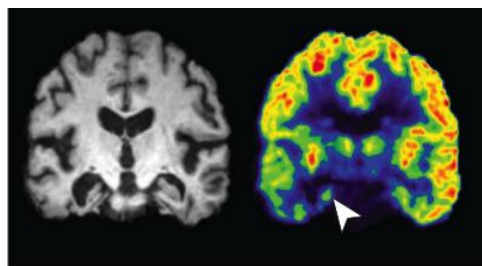
TAU-PET in MCI/AD



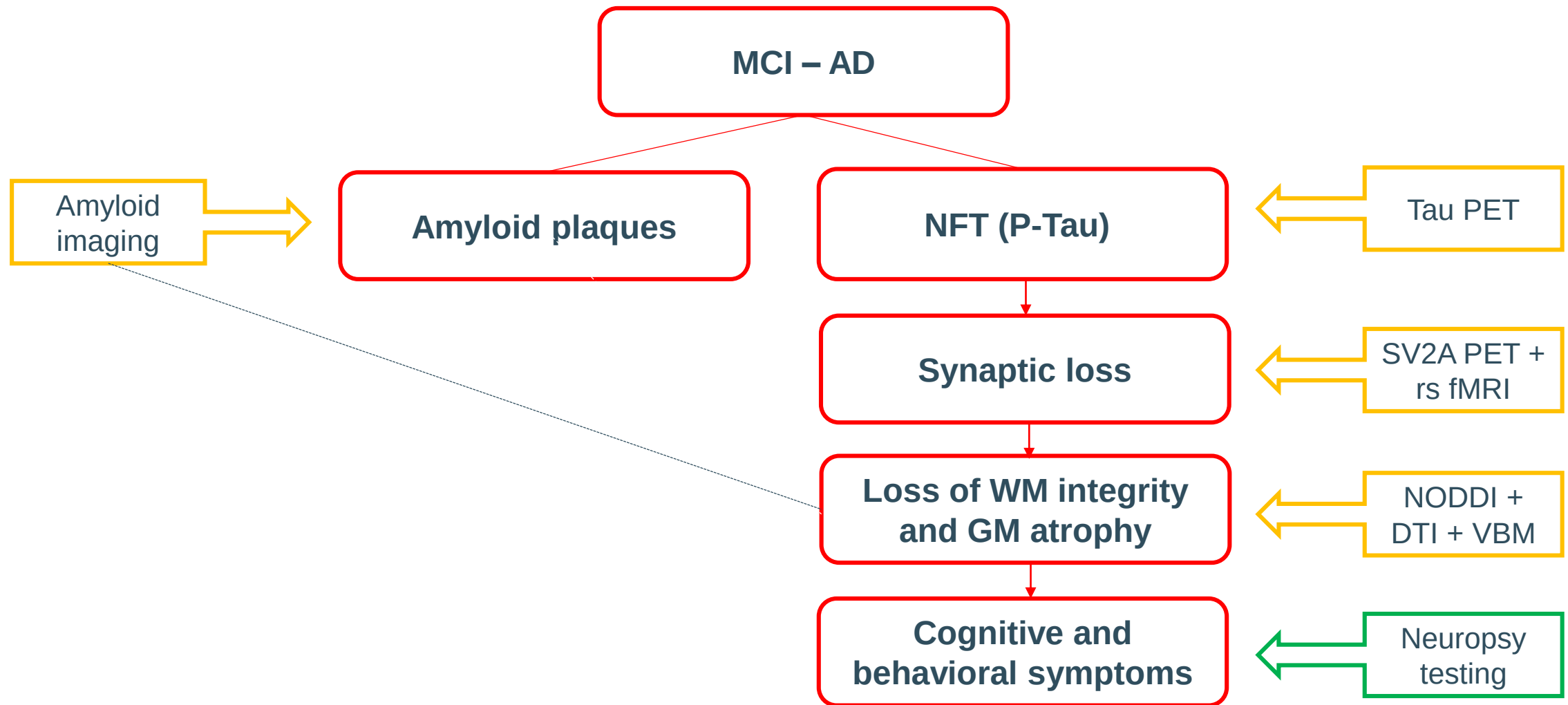
Earlier findings in (prodromal) AD: *in vivo*

^{11}C -UCB-J in MCI/AD

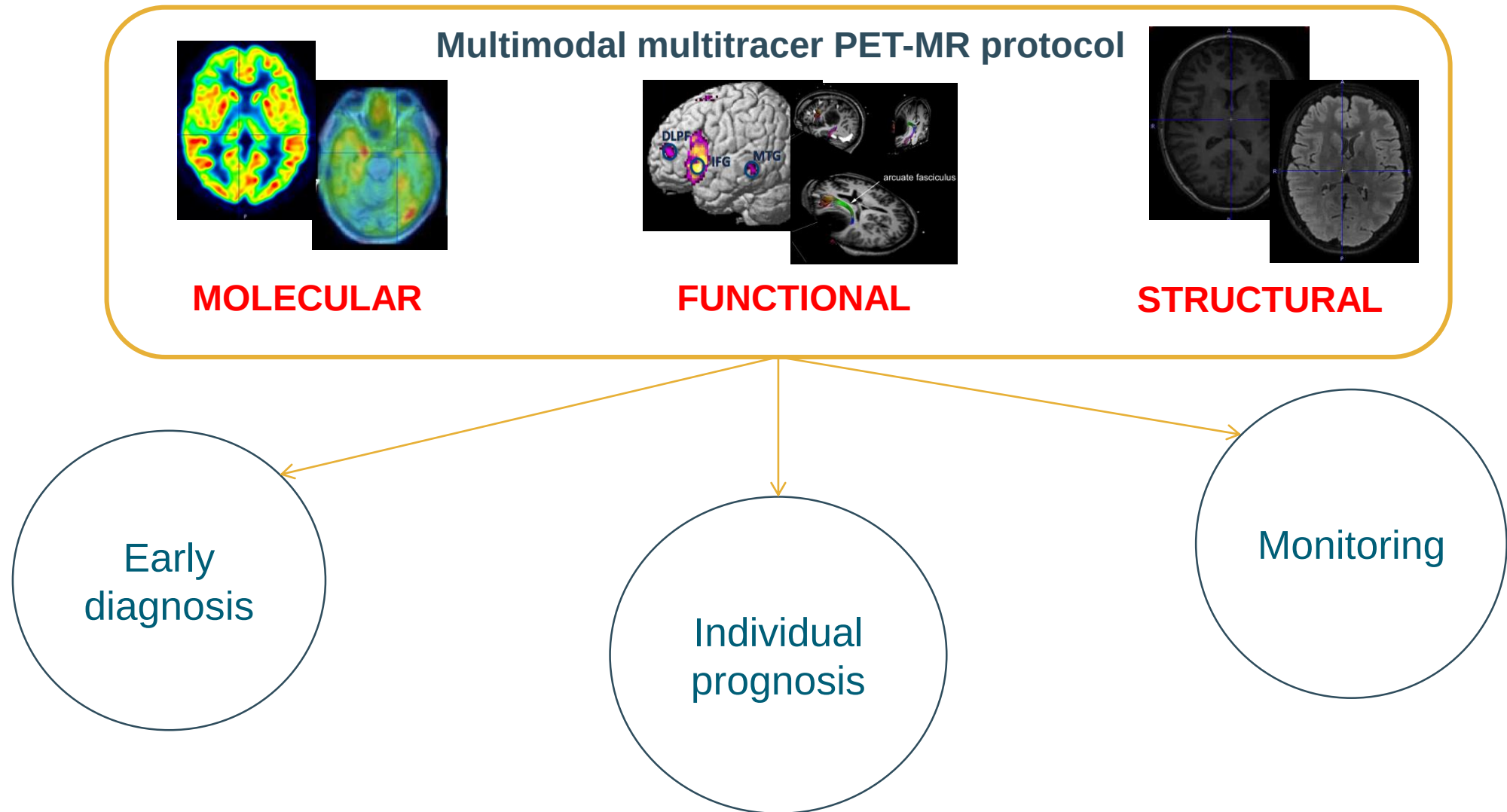
Hippocampal loss of SV2A

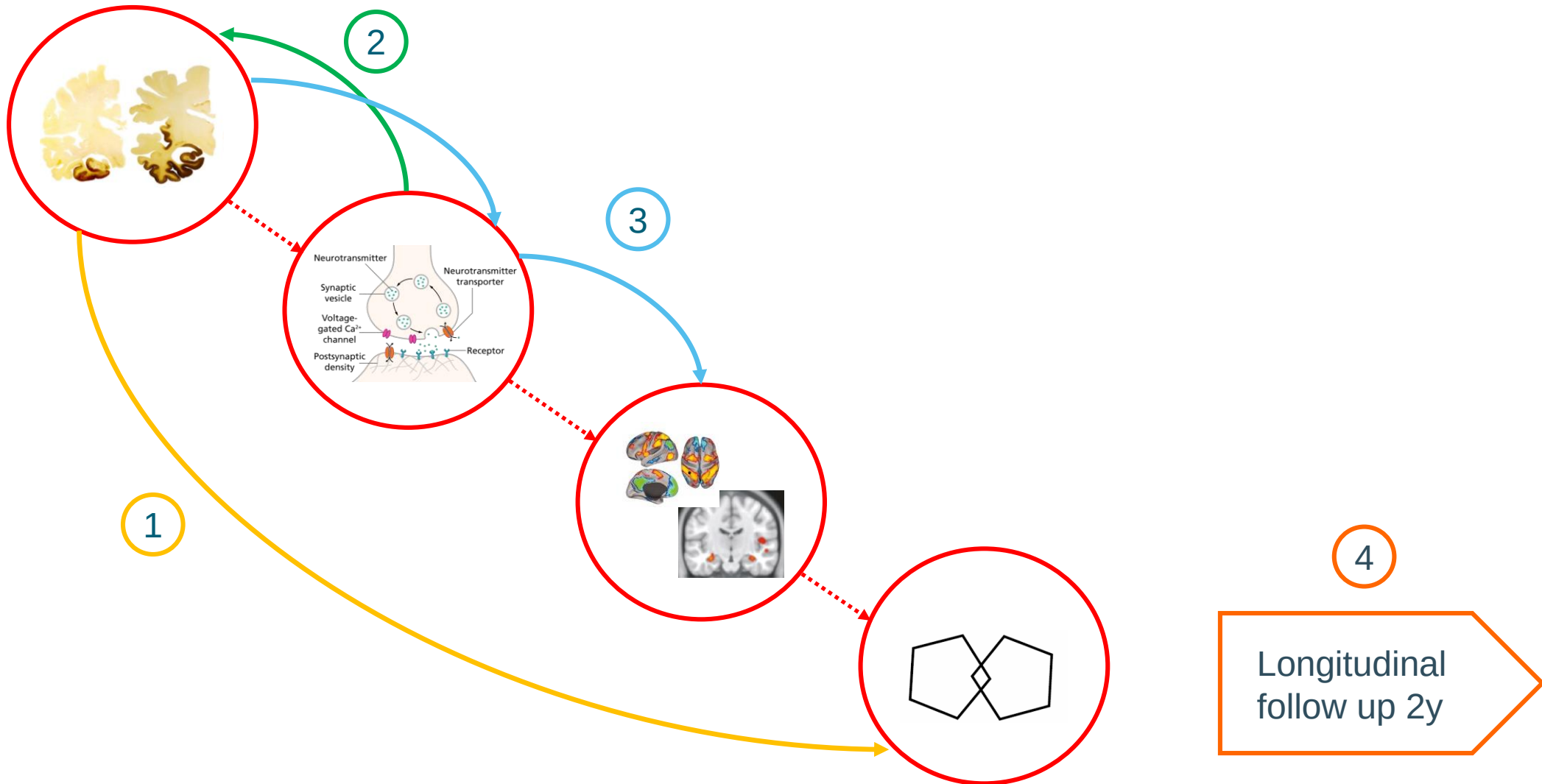


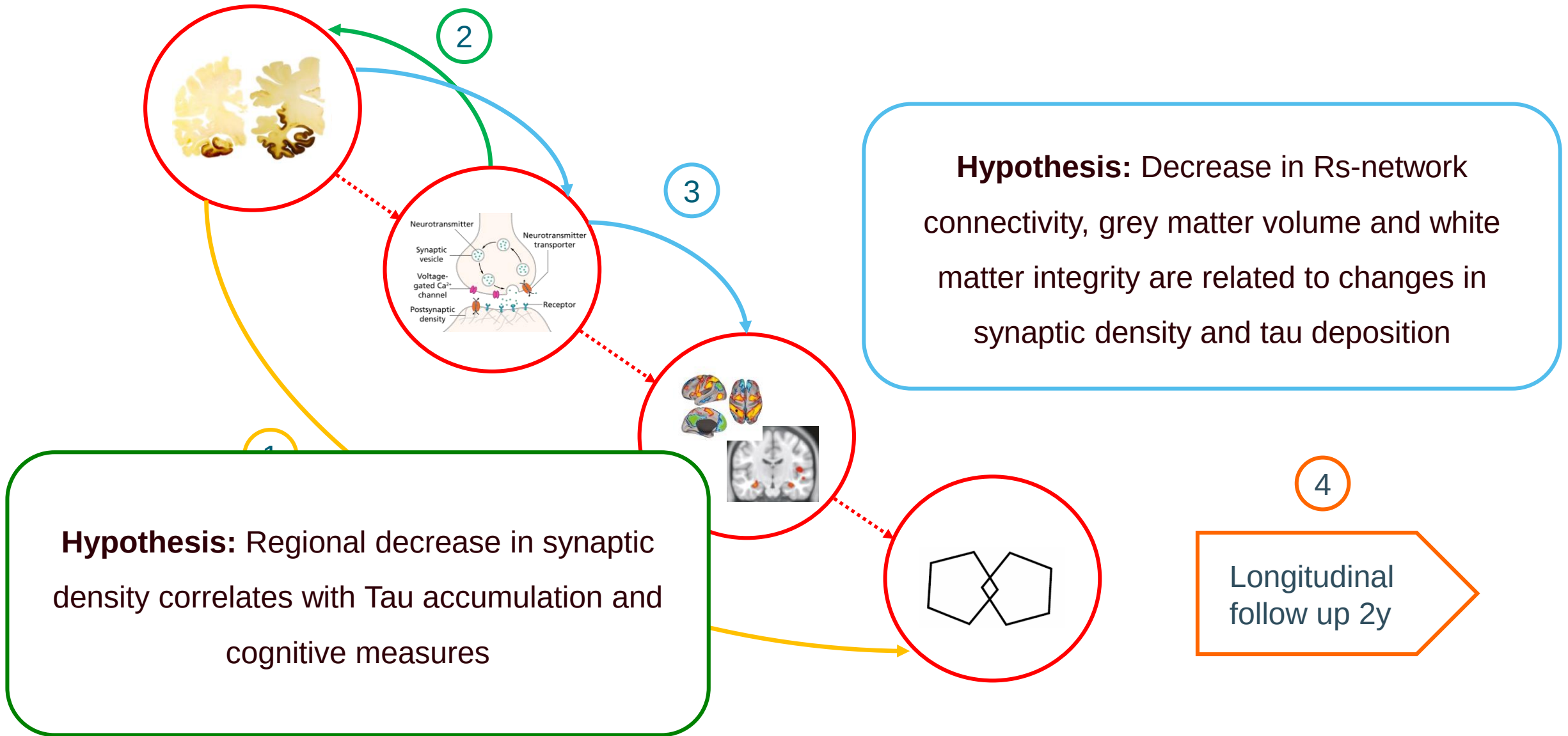
Study objective

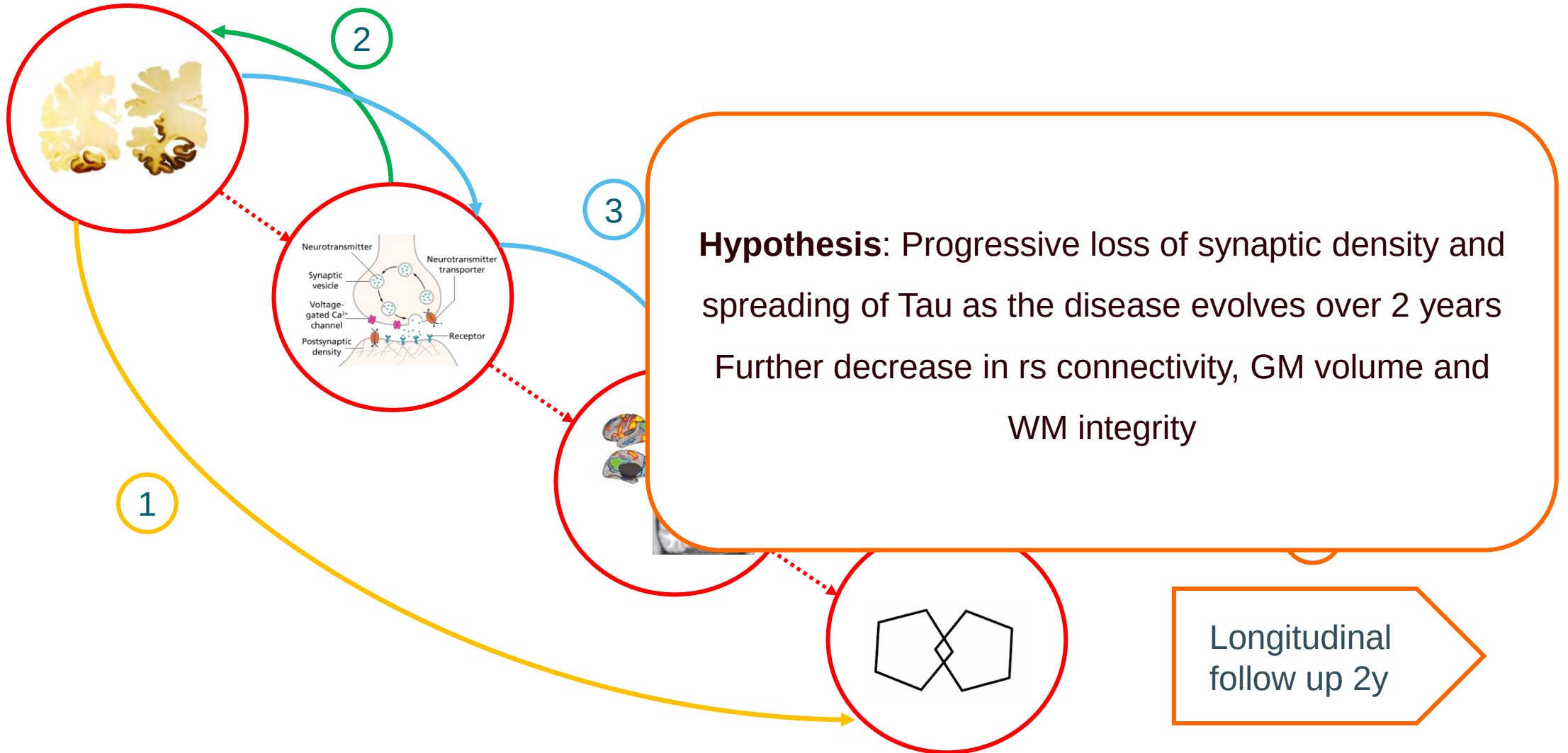


Study objective

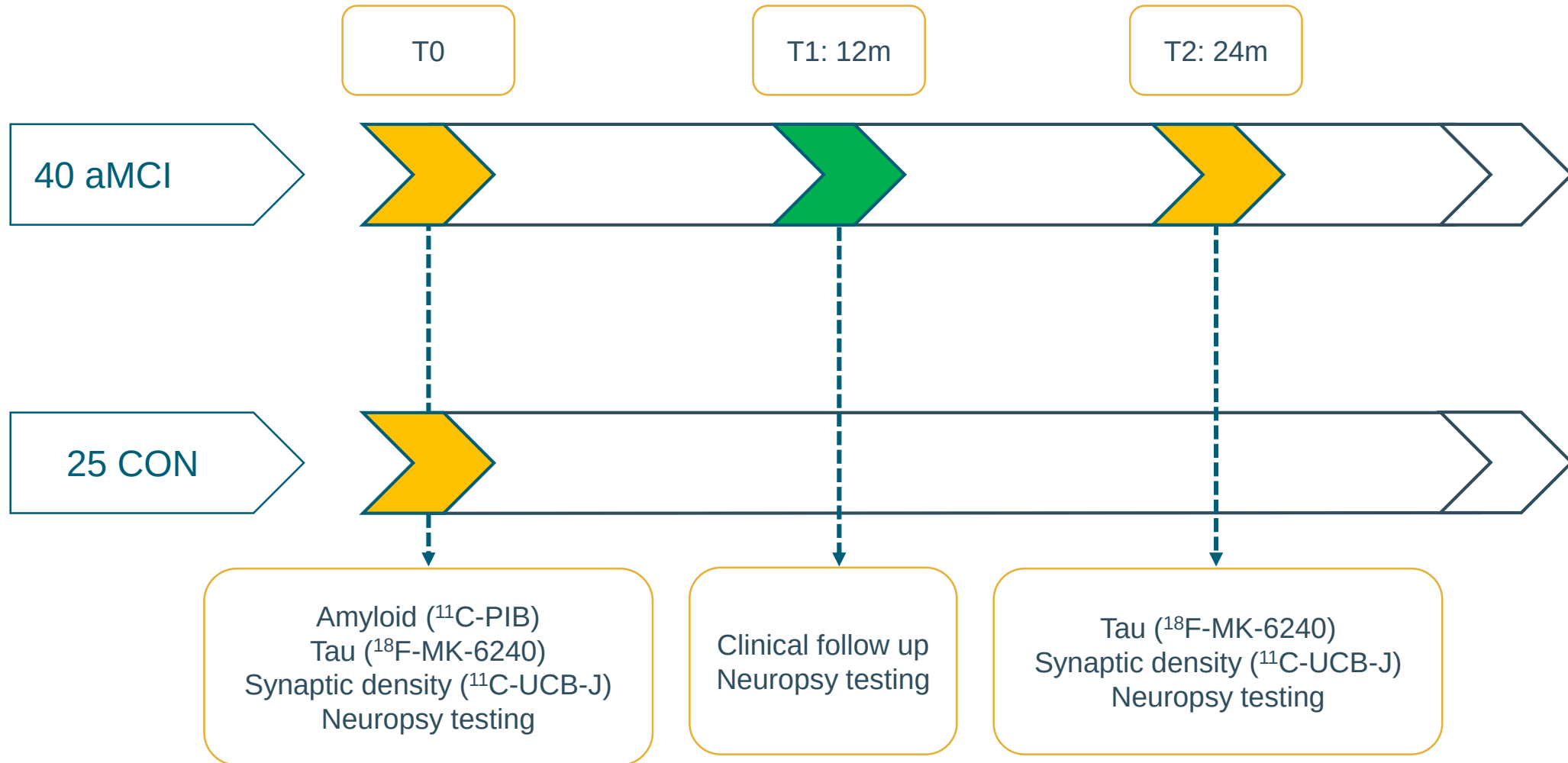




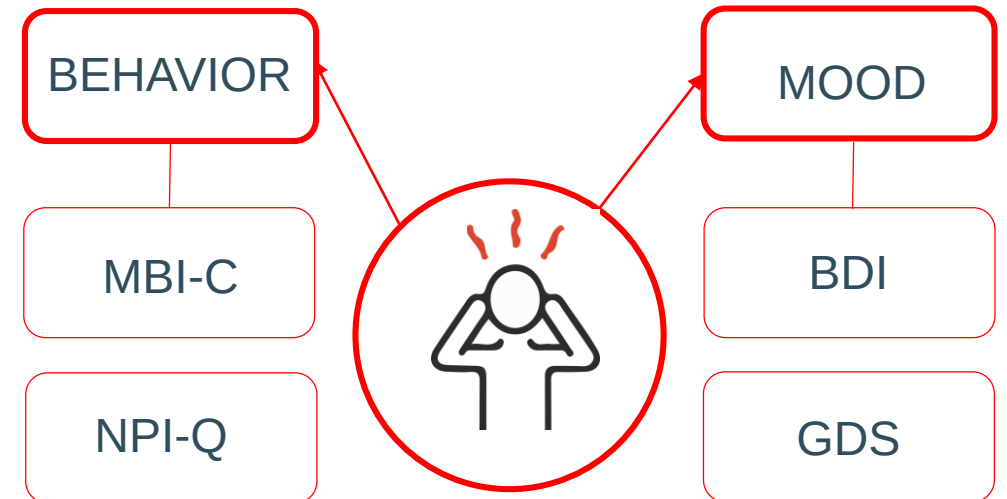
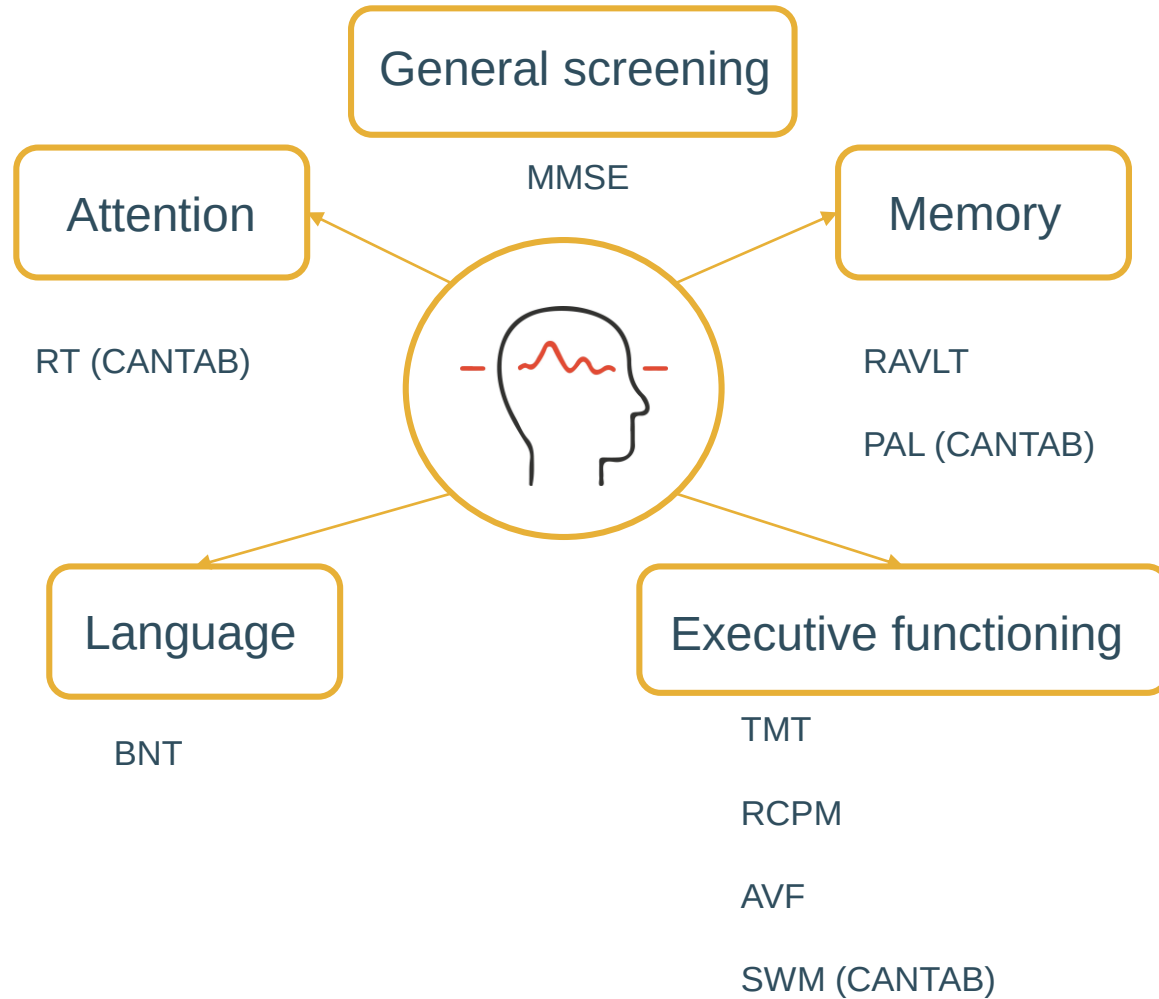




Study design

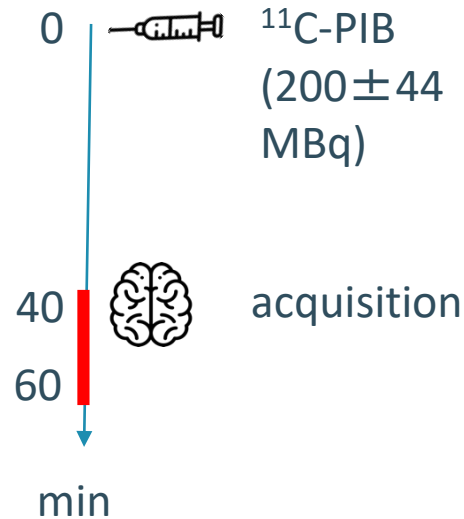


Methodology: data acquisition



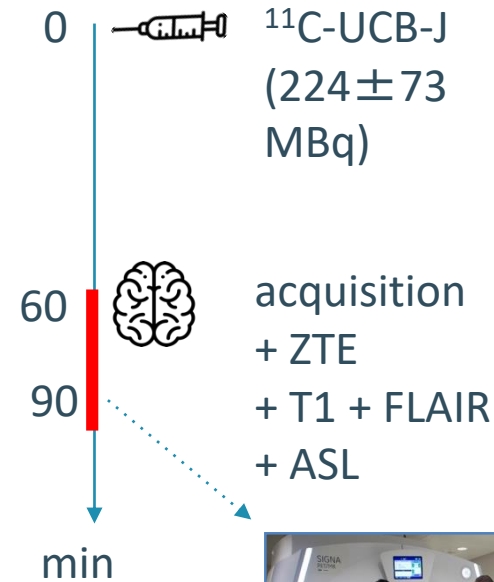
Methodology: data acquisition

DAY 1

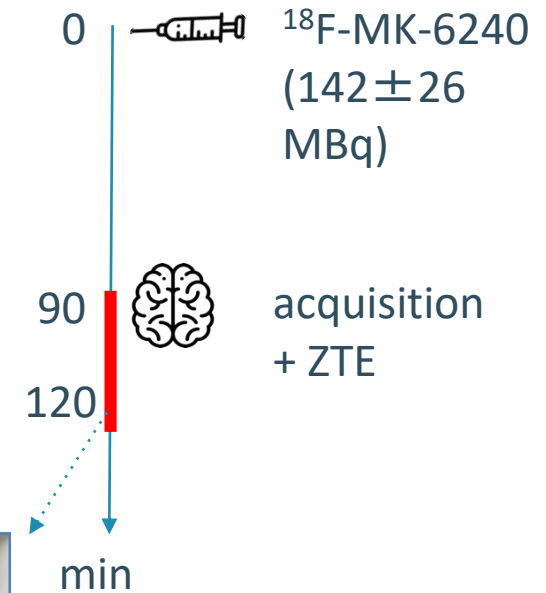


Siemens Truepoint PET-CT

DAY 2



DAY 3

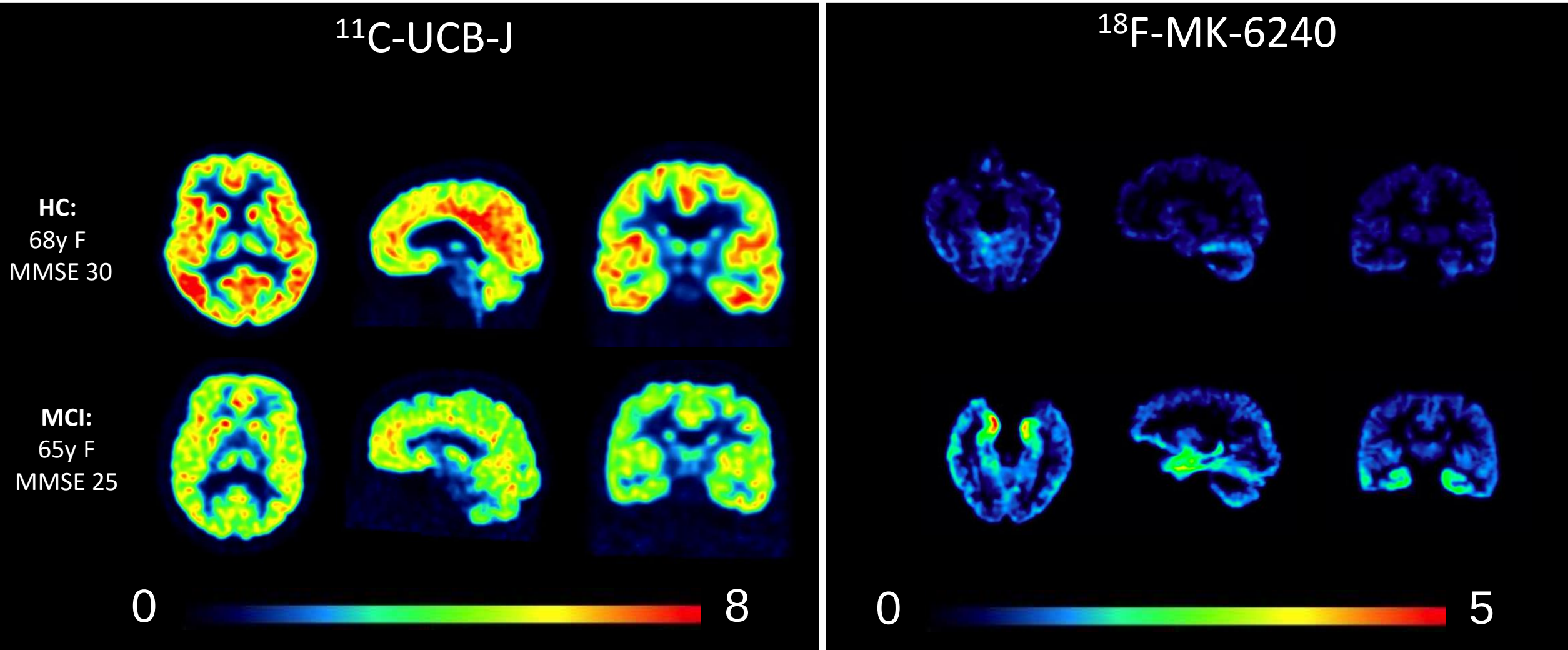


GE Signa 3T PET-MR

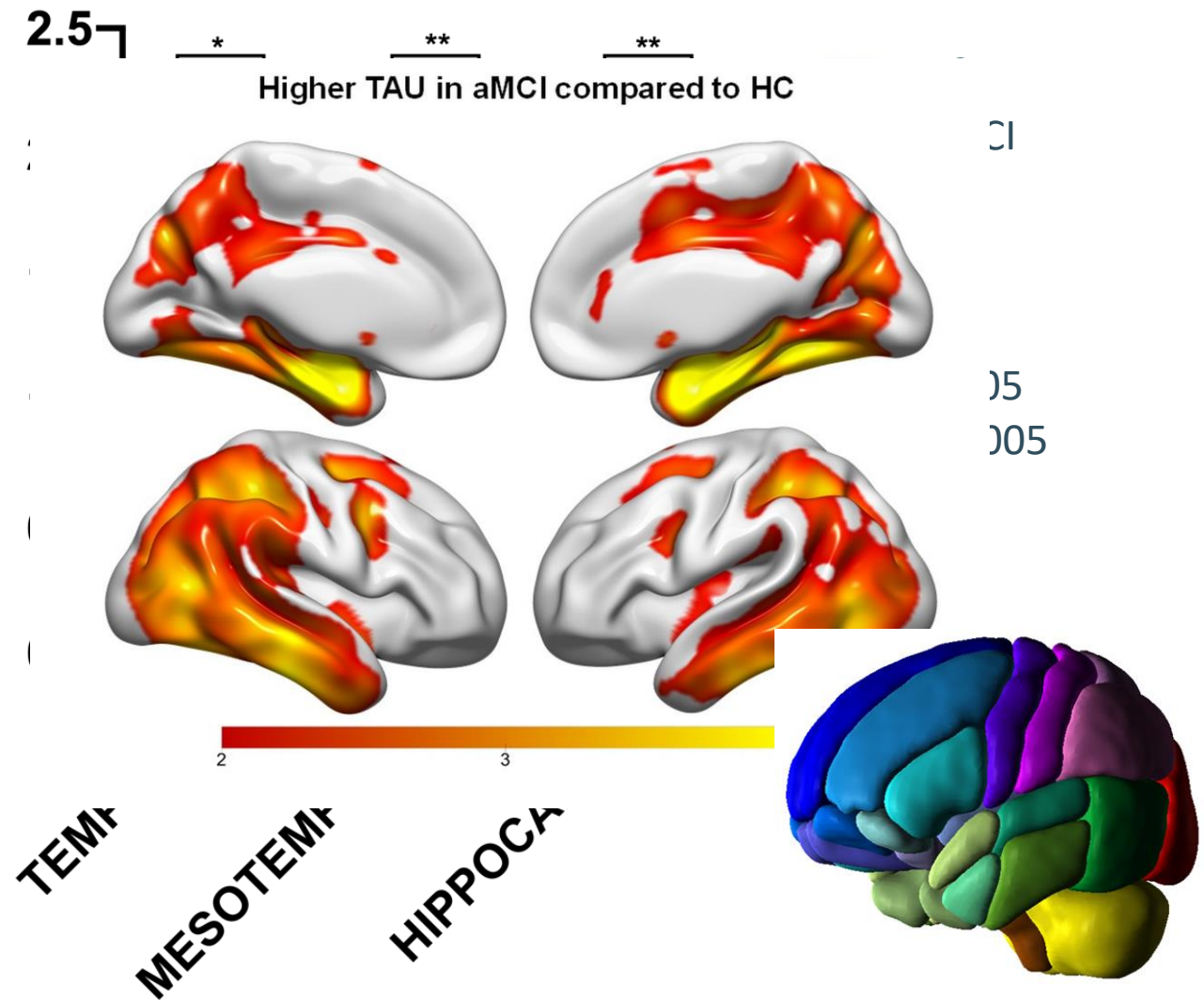
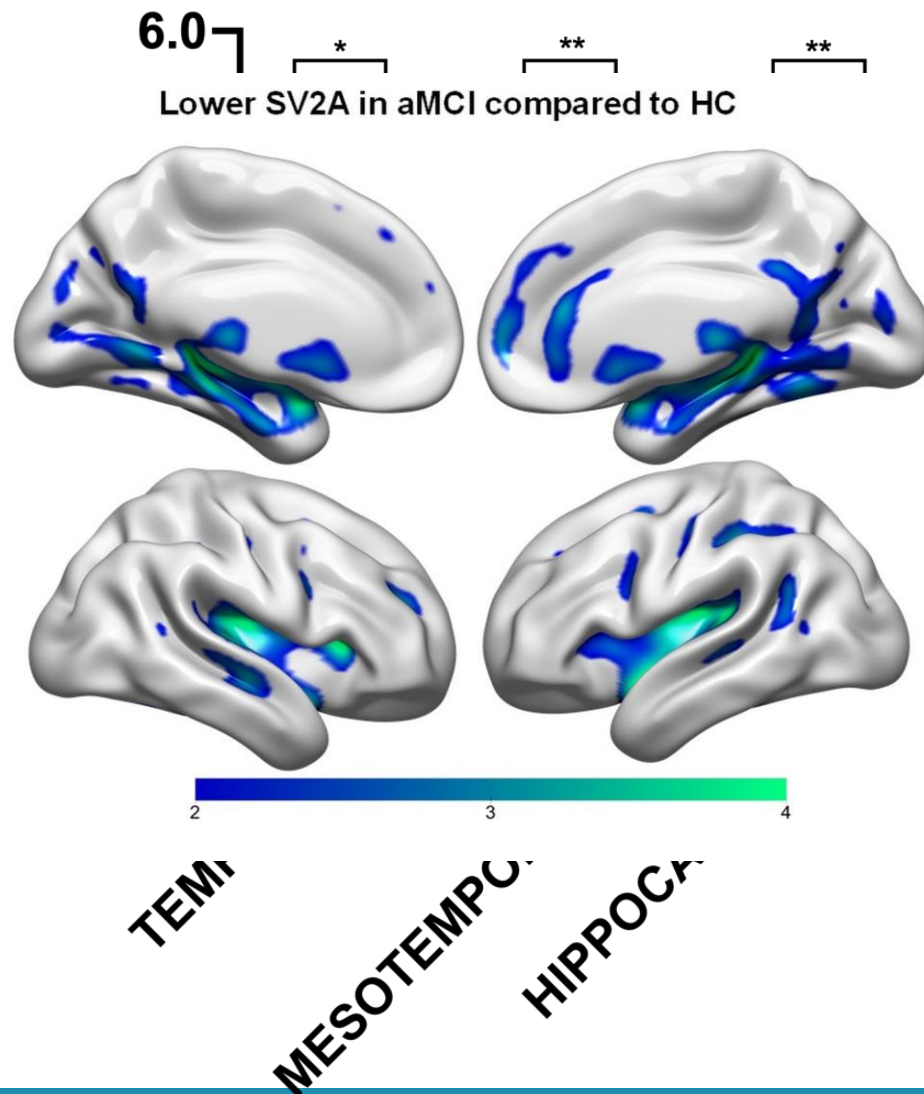
Results: characteristics

	HC (n=10)	aMCI (n=10)
Sex		
M/F	5/5	6/4
Age, years	67.2 (± 6.5)	69.6 (± 5.4)
MMSE score	29.4 (± 0.8)	24.3 (± 1.8)
RAVLT		
Total: sum trial 1-5 (0-75)	55.2 (± 7.4)	26.3 (± 7.3)
Delayed recall (0-15)	12.3 (± 2.3)	2.6 (± 2.1)
GDS (0-30)	3.4 (± 2.8)	7.7 (± 7.8)
BDI (0-63)	4.3 (± 3.5)	6.0 (± 7.8)
Amyloid positive PET scan	1/10	9/10
Injected dose in MBq		
^{11}C -PIB	214.0 (± 38.2)	176.1 (± 46.7)
^{11}C -UCB-J	237.2 (± 60.6)	200.4 (± 85.8)
^{18}F -MK-6240	131.5 (± 29.1)	153.4 (± 13.5)

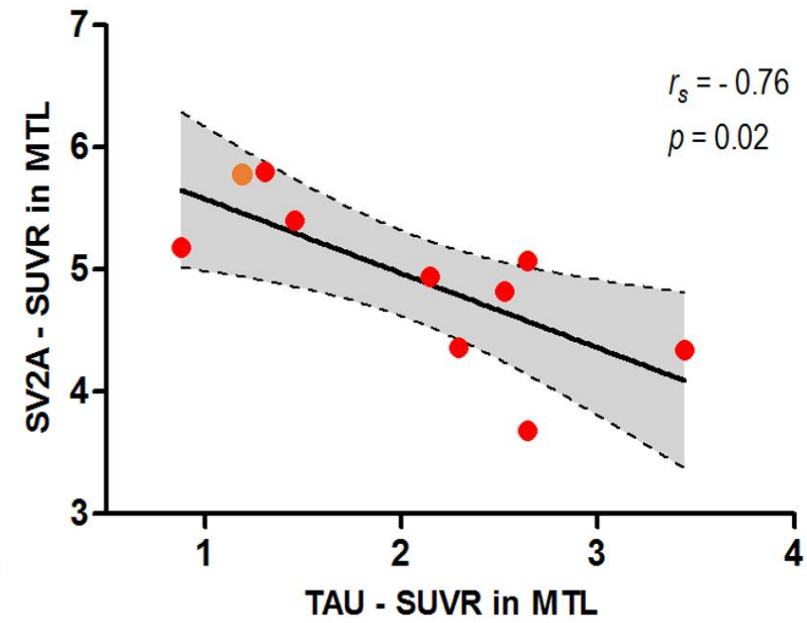
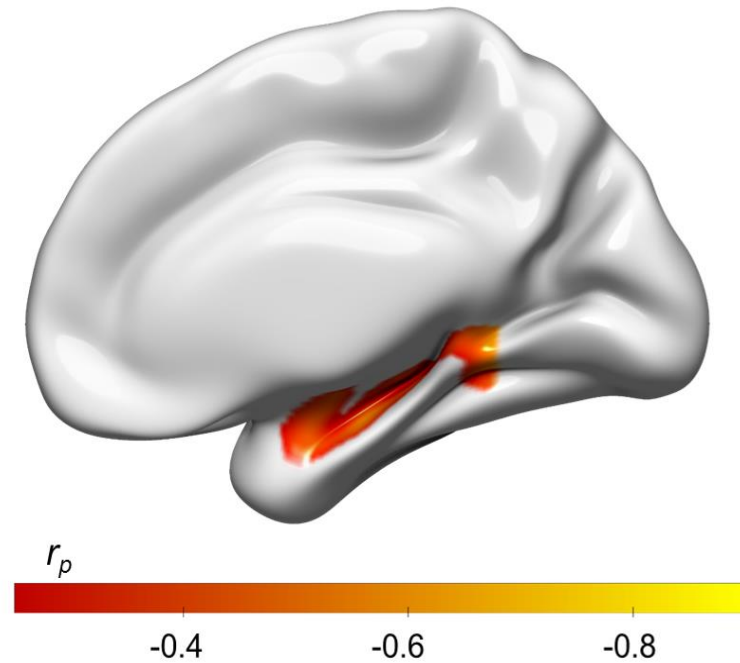
Results: representative SUVR ^{11}C -UCB-J and ^{18}F -MK-6240



Results: decreased SV2A and increased tau

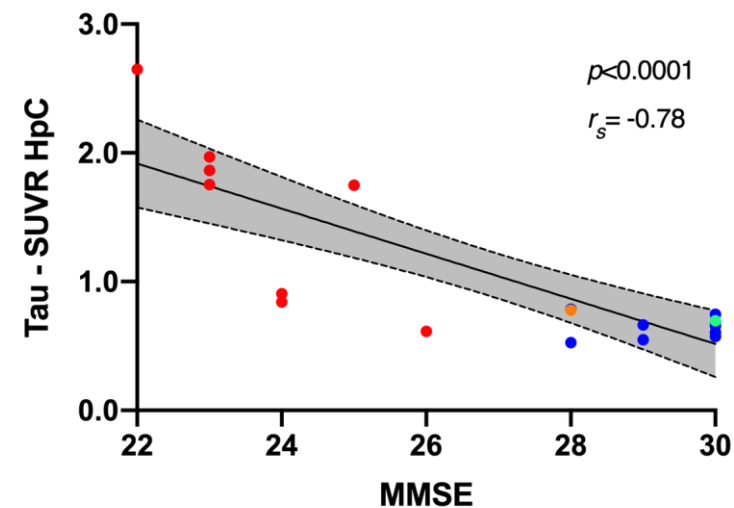
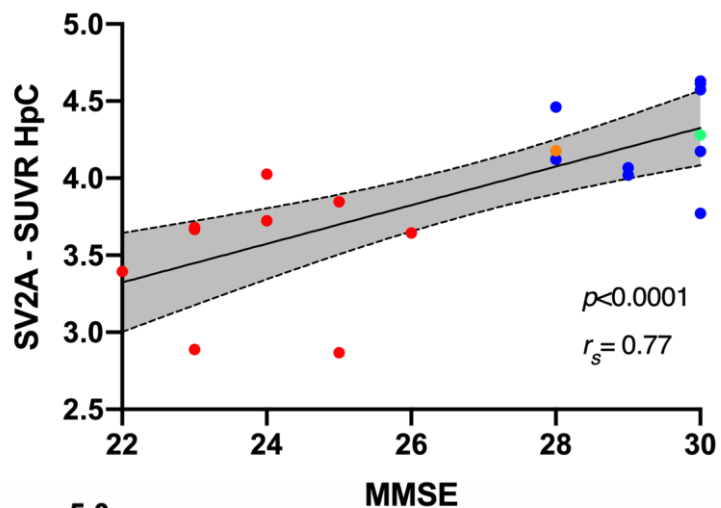


Results: SV2A/Tau correlation in MTL

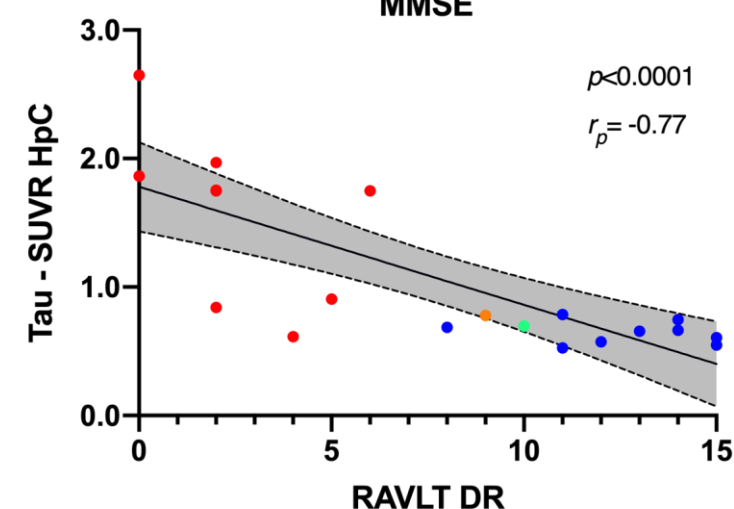
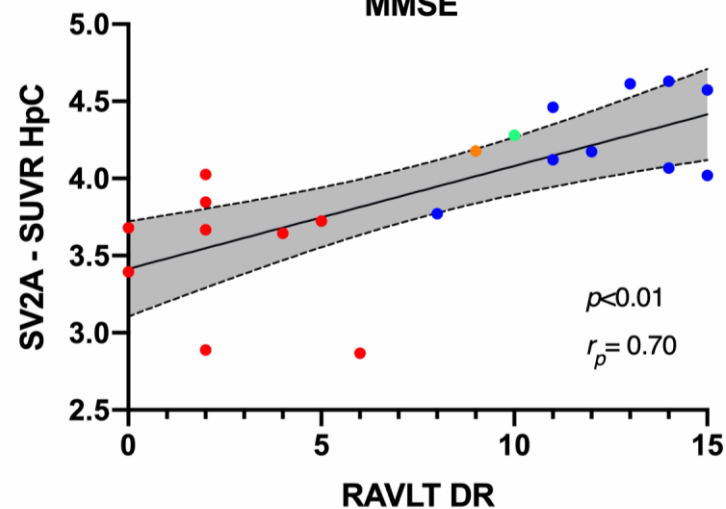


Results: correlations hippocampal Tau/SV2A and cognitive outcome measures

MMSE



RAVLT
(Episodic
memory)



Discussion

- Increased tau-deposition was seen in aMCI in the MTL and adjacent association cortex (Braak II-IV)
 - Correlations were seen with decreased performance on cognitive tests
 - Hippocampus allows for discrimination between HC and aMCI
- SV2A-PET findings correspond to previous research
 - Hippocampus as most prominent region of synapse loss, correlating with cognitive decline

Discussion

- In the MTL an increase of NFT is inversely related to loss of synaptic density confirming in vitro findings
- Tau deposition seems more widespread as compared to synapse loss
 - Pathological Tau as key driver of loss of synaptic function
 - Dynamic synaptic reorganization
 - Specific target of both tracers

Conclusion

- Preliminary evidence linking **an increased Tau deposition** to a **loss of synaptic density** *in vivo* in the **MTL**
- **Longitudinal** SV2A/Tau-PET imaging in prodromal AD is needed to acquire **temporal information** on the relation of AD hallmarks
- **Future goal:** identify an optimal, simplified combination of PET-MR imaging biomarkers for early assessment and/or risk stratification in de novo patients

Thank you for your attention

- **Nuclear Medicine**

- K. Van Laere, MD, PhD, DSc
- J. Ceccarini, Ir, PhD
- M. Koole, DSc, PhD
- L. Michiels, MD
- J. Van Aalst
- D. Van Weehaeghe, MD
- N. Mertens, MSc

- **Radiology**

- S. Sunaert, MD PhD
- L. Emsell, PhD

- **Neurology**

- L. Michiels, MD
- R. Lemmens, MD, PhD

- **Old age psychiatry**

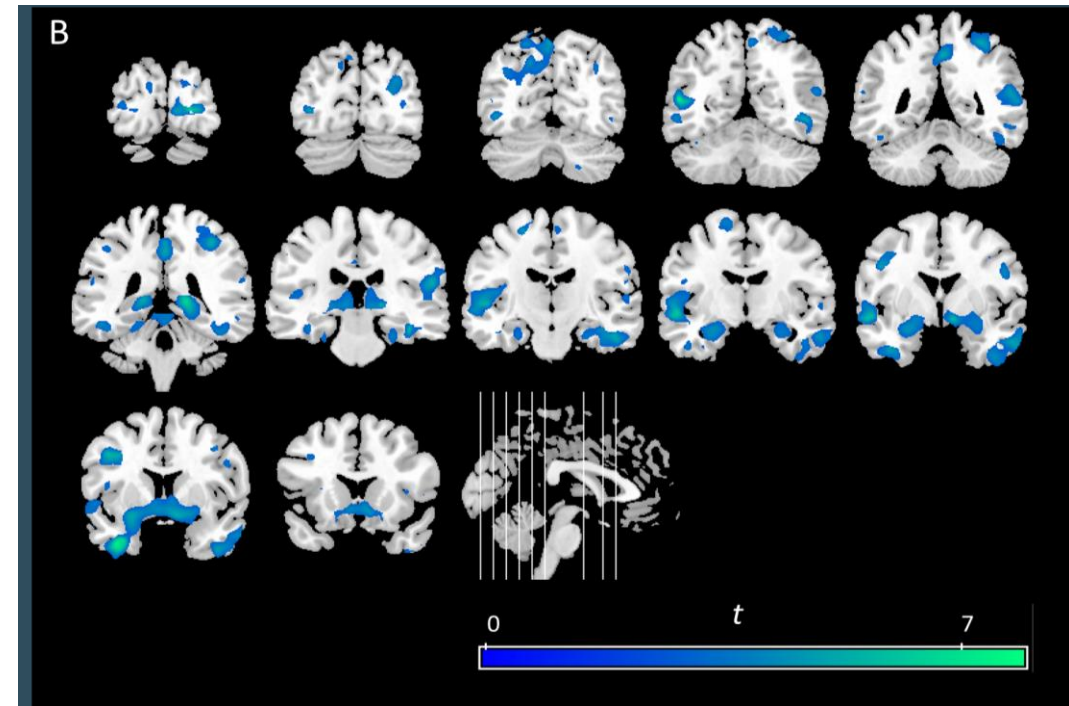
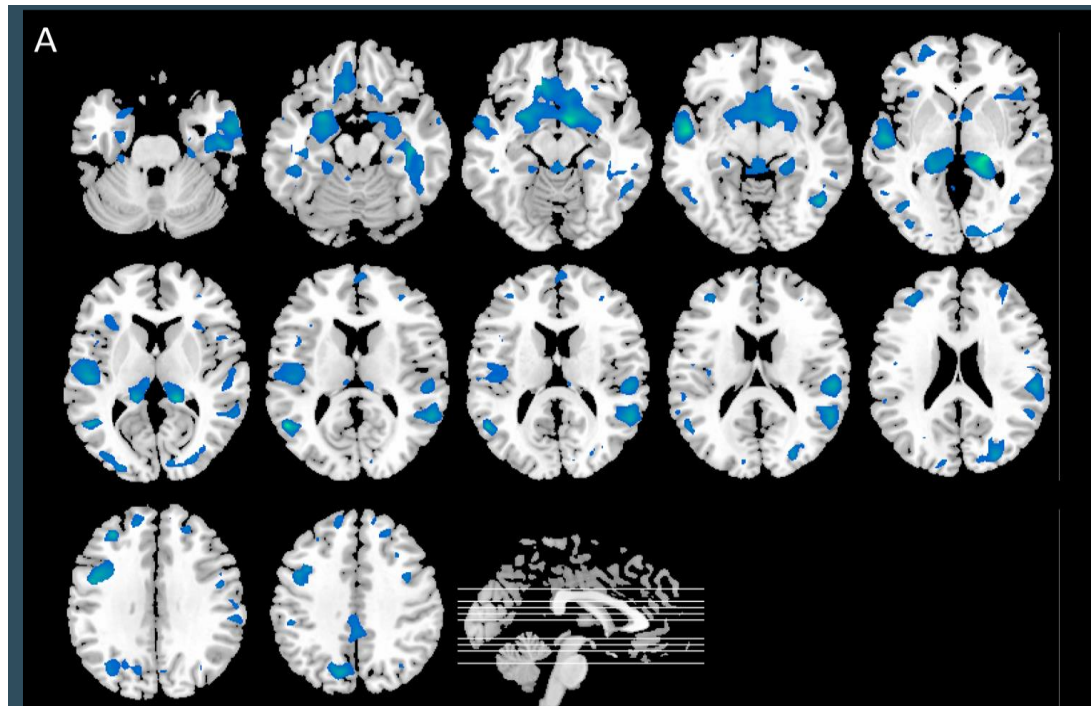
- M. Vandenbulcke, MD, PhD

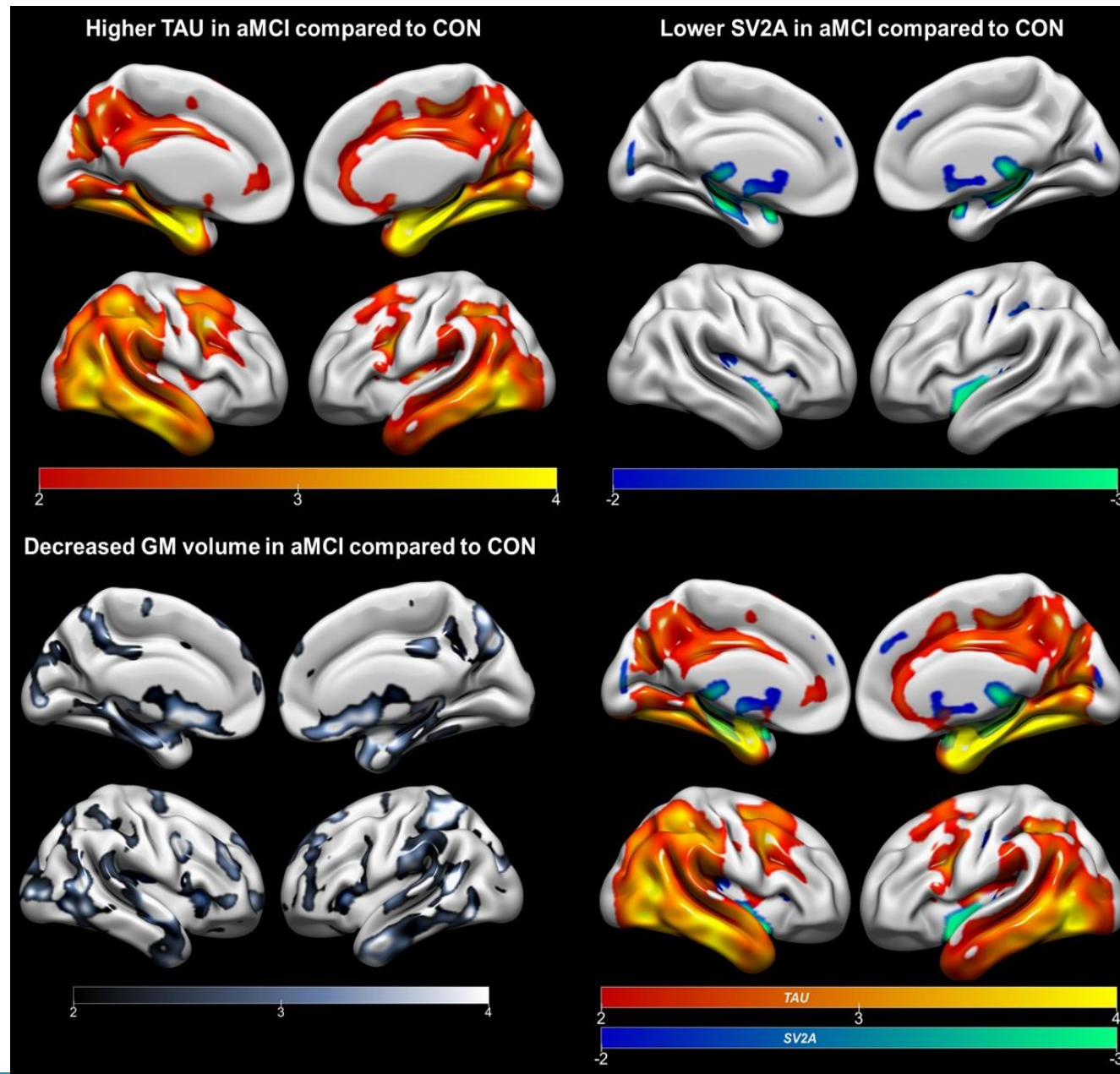


Stichting Alzheimer Onderzoek
Onderzoek geeft hoop!

Additional slides

Voxel based morphometry (VBM)





Correlations hippocampal tau/SV2A and cognitive outcome measures: aMCI group

