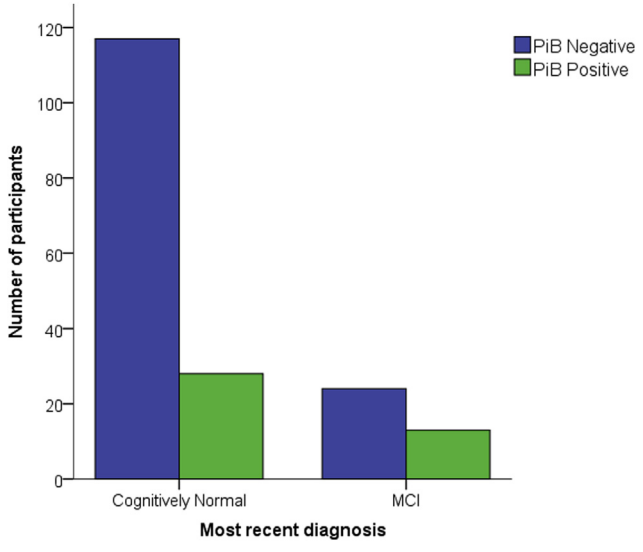
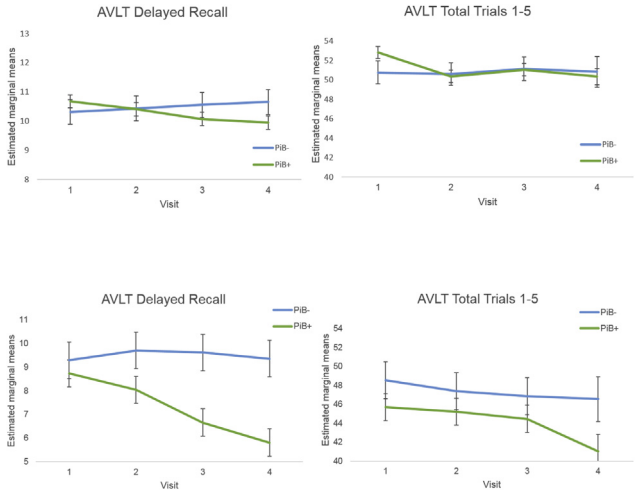
IC-P-015 HIGH AMYLOID LOAD IS ASSOCIATED WITH EPISODIC MEMORY DECLINE AND INCIDENT MILD COGNITIVE IMPAIRMENT IN MIDDLE-AGED ADULTS IN THE WISCONSIN REGISTRY FOR ALZHEIMER'S PREVENTION (WRAP)

Lindsay R. Clark[1,2], Annie M. Racine[3,4,5], Rebecca L. Koscik[2], Ozioma C. Okonkwo[1,2,6], Christopher R. Nicholas[1,6], Cynthia M. Carlsson[1,6], Sanjay Asthana[2,6,7], Mark A. Sager[2], Bradley T. Christian[8,9], Sterling C. Johnson[1,2,6,8], *[1]Wisconsin Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [2]Wisconsin Alzheimer's Institute, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [3]Institute on Aging, University of Wisconsin, Madison, WI, USA; [4]Neuroscience Training Program, University of Wisconsin, Madison, WI, USA; [5]Neuroscience and Public Policy Program, University of Wisconsin, Madison, WI, USA; [6]Geriatric Research Education and Clinical Center, Wm. S. Middleton Veterans Hospital, Madison, WI, USA; [7]University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [8]Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin-Madison, Madison, WI, USA; [9]University of Wisconsin, Madison, Madison, WI, USA. Contact e-mail: scj@medicine.wisc.edu*

Background: This study investigated the relationship between amyloid burden and cognition in a cohort of late middle-aged participants enriched for family history of Alzheimer's disease (AD) enrolled in the WRAP Study. **Methods:** 182 WRAP participants completed a PET-PiB scan approximately 5 years after baseline cognitive testing. A composite cortical measure of amyloid burden was calculated and a DVR cutpoint of 1.12 (derived from an ROC analysis) was used to classify participants as PiB+ (n= 41) or PiB- (n=141). Additionally, participants were classified as having psychometric mild cognitive impairment (MCI; n=37) if at least two neuropsychological performances within a cognitive domain or least one measure in three cognitive domains (immediate memory, delayed memory, executive functioning) were ≤ 1.5 standard deviations below the mean of a robust normative group. Rates of PiB positivity by cognitive group (MCI or cognitively normal [CN]) were compared and a linear mixed-effects regression model examined longitudinal trajectories on the Rey Auditory Verbal Learning Test (RAVLT) by PiB and MCI status. The model included fixed effects for amyloid group (PiB+/PiB-), amyloid group x time, age, and gender, and random effects for participant and time.





Outcome variables were either RAVLT total trials 1-5 or RAVLT delayed recall raw scores. **Results:** The MCI group had a greater proportion of PiB+ participants compared with the CN group (X2=4.23; p<.05; see Figure 1). Linear mixed-effects models revealed a significant interaction between amyloid group and time on RAVLT delayed recall (β = -.34, p<.05), indicating steeper decline in the PiB+ group (see Figure 2). Other significant fixed effects included age (β =-.08, p<.01) and female sex (β =2.14, p<.001). There was a trend in the same direction for the amyloid by time interaction on RAVLT total trials (β = -.84, p=.08; see Figure 2). Models were re-run in the MCI group only and again indicated a significant interaction between amyloid group and time on RAVLT delayed recall (β =-1.05, p<.01), but not on RAVLT total trials (see Figure 3). **Conclusions:** Greater amyloid burden in late middle-age is associated with increased rates of MCI and steeper memory decline.

IC-P-016 AMYLOID IMAGING IN THERAPEUTIC TRIALS: THE QUEST FOR THE OPTIMAL REFERENCE REGION

Victor L. Villemagne[1,2], Pierrick Bourgeat[3], Vincent Doré[4], Lance Macaulay[4], Robert Williams[5], David Ames[6], Ralph N. Martins[7], Olivier Salvado[3], Kewei Chen[8], Eric M. Reiman[8], Colin L. Masters[2], Christopher C. Rowe[1], *[1]Austin Health, Melbourne, Australia; [2]The Florey Institute of Neuroscience and Mental Health, Parkville, Australia; [3]CSIRO, Brisbane, Australia; [4]CSIRO, Melbourne, Australia; [5]The Florey Institute of Neuroscience and Mental Health, Melbourne, Australia; [6]National Ageing Research Institute, Melbourne, Australia; [7]Sir James McCusker Alzheimer's Disease Research Unit (Hollywood Private Hospital), Perth, Australia; [8]Banner Alzheimer's Institute, Phoenix, AZ, USA. Contact e-mail: victorlv@unimelb.edu.au*

Background: The reference region (RR) approach was initially proposed for the kinetic analysis of neuroimaging radiotracers to remove the need of a metabolite-corrected plasma input function. The RR was described as a brain region with similar cellular and blood flow characteristics as the target region but lacking specific (saturable) binding sites. It relied on two basic assumptions: that the degree of nonspecific binding and the volume of distribution of the free compartment were the same in the RR and target regions. The use of a RR was later applied to semiquantitative tissue ratio