Table 1
Characteristics of the sample by HbA1c Trajectory group

Variable	Lower Stable* N=227	Higher Stable* N=365	Lower Increasing N=123	Higher Increasing N=46	Lower Decreasing N=59	Higher Decreasing N=15	Total N=835	*P* value
Years in Diabetes Registry	8.35 (2.58)	8.35 (2.81)	9.36 (2.32)	8.88 (2.57)	10.13 (1.7)	10.95 (0.56)	8.70 (2.64)	<0.0001
HbA1c at entry into Diabetes Registry	5.96 (0.67)	6.84 (0.94)	7.26 (0.84)	7.76 (0.95)	9.19 (1.4)	10.73 (0.97)	6.95 (1.32)	<0.0001
Mean HbA1c During Follow-Up	6.01 (0.28)	6.70 (0.23)	7.45 (0.23)	8.35 (0.34)	7.61 (0.36)	9.22 (0.45)	6.82 (0.77)	<0.0001
Current age	72.99 (4.75)	72.91 (4.66)	72.52 (4.46)	70.78 (4.16)	73.63 (4.48)	69.73 (3.35)	72.75 (4.63)	0.0027
Education (years)	13.43 (3.47)	13.21 (3.71)	13.12 (3.18)	12.59 (2.8)	12.75 (2.71)	12.00 (2.80)	13.17 (3.45)	0.3857
HDL	48.39 (11.24)	48.06 (10.68)	47.93 (11.58)	43.97 (8.35)	46.73 (9.44)	44.98 (11.8)	47.76 (10.82)	0.1427
LDL	102.15 (19.12)	103.69 (19.82)	98.38 (19.22)	97.84 (27.38)	95.56 (14.46)	93.89 (22.7)	101.42 (19.9)	0.0050
Total cholesterol	179.65 (24.69)	182.69 (25.96)	180.14 (23.61)	182.28 (28.45)	172.31 (18.34)	167.58 (27.52)	180.46 (25.12)	0.0184
Systolic BP	133.4 (8.86)	134.88 (9.11)	135.45 (9.42)	137.70 (9.98)	135.38 (12.04)	133.99 (8.01)	134.74 (9.39)	0.0659
Diastolic BP	76.85 (4.74)	77.40 (4.81)	76.90 (4.52)	77.52 (4.66)	75.15 (5.84)	76.18 (5.54)	77.00 (4.85)	0.0319
GFR	80.38 (23.87)	81.71 (27.13)	79.33 (25.98)	83.31 (32.5)	77.82 (25.73)	91.43 (24.42)	80.99 (26.29)	0.4852
GDS	1.00 [0-9]	1.00 [0-11]	2.00 [0-9]	2.00 [0-10]	1.00 [0-14]	1.00 [0-9]	1.00 [0-14]	0.3249
Diabetes medication group								
Oral antidiabetic Only	164 (72%)	324 (89%)	103 (84%)	25 (54%)	45 (76%)	2 (13%)	663 (79%)	<0.0001
Insulin Only	3 (1%)	2 (1%)	2 (2%)	1 (2%)	1 (2%)	0 (0%)	9 (1%)	
Insulin+Oral antidiabetic	3 (1%)	6 (2%)	17 (14%)	20 (43%)	13 (22%)	12 (80%)	71 (9%)	
None	57 (25%)	33 (9%)	1 (1%)	0 (0%)	0 (0%)	1 (7%)	92 (11%)	

sociodemographic, cardiovascular, diabetes-related covariates and depression. Subjects averaged 72.8 years of age. Six trajectories of HbA1c were identified, characterized by HbA1c level at entry into the DR (Higher/ Lower), and trend over time (Stable/Decreasing/Increasing). Both groups with a trajectory of decreasing HbA1c levels had high HbA1c levels at entry into the DR (9.2%, 10.7%), and high, though decreasing, HbA1c levels over time. They had the worst cognitive performance, particularly in overall cognition ($p<0.02$) and semantic categorization ($p<0.01$), followed by that of subjects whose HbA1c at entry into the DR was relatively high (7.2%, 7.8%) and increased over time. Subjects with stable HbA1c over time had the lowest HbA1c levels at entry (6.0%, 6.8%) and performed best in cognitive tests. Glycemic control trajectories, which better reflect chronicity of T2D than a single HbA1c measurement, predict cognitive performance. A trajectory of stable HbA1c levels over time is associated with better cognitive function.

O2-09-05 VITAMIN B12 AND FOLATE IN RELATION TO THE RATE OF BRAIN ATROPHY IN SUBJECTS AT RISK OF DEMENTIA: A LONGITUDINAL POPULATION BASED STUDY

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Project Description: Low vitamin B12 and folate status are common conditions in the elderly and have been linked to a greater risk of Alheimer's disease. Our objective was to examine the association of plasma vitamin B12 and red blood cell (RBC) folate status with cerebral volumes in a longitudinal population-based cohort of older adults. 501 dementia-free subjects at baseline (aged 60-97 years; 298 women and 203 men) from the Swedish National Study of Aging and Care in Kungsholmen (SNAC-K), with repeated structural brain magnetic resonance imaging (MRI) scans at 2-3 occasions over 6 years, were recruited. The association of baseline vitamin B12 and RBC folate with the rate of brain volume loss was examined with the use of linear mixed models. After adjusting for several potential confounders including age, sex, education, the use of vitamins supplements, RBC folate levels, chronic conditions, hemoglobin, and plasma albumin, higher baseline plasma vitamin B12 concentrations were associated with decreased rate of total brain tissue (TBT) and grey matter (GM) volume loss over 6 years. β coefficient and standard error (SE) were 0.0020 (0.001), $p = 0.002$ for TBT; and they were 0.0013 (<0.001), $p = 0.016$ for GM. These associations remained significant even after excluding 28 incident dementia cases [β (SE): 0.0019 (<0.001); $p = 0.003$ for TBT and 0.0014 (<0.001); $p = 0.010$ for GM]. RBC folate levels had no longitudinal relationship with cerebral volumes. These results indicate that higher plasma concentrations of vitamin B12 are associated with decreased rate of brain volume loss. Randomized controlled trials are needed to determine the impact of vitamin B12 supplementation on preventing cognitive decline in older adults.

O2-09-06 DRUNKENNESS AND RISK OF COGNITIVE DECLINE

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Project Description: A J-shaped relationship between mean alcohol consumption and risk of cognitive decline has been noted repeatedly but we know little about how other potential harmful drinking patterns, such as getting drunk, affect cognitive function over time. We used data on adults aged ≥65 from the English Longitudinal Study of Ageing (ELSA), a population-based study of community-dwelling older adults in England. Between 1998 and 2001 participants were asked how many times they had been drunk in the preceding three months. A battery of cognitive function tests was administered in 2002 and again in 2008. We examined the relationship between frequency of drunkenness and change in cognitive function scores between 2002 and 2008 (using linear regression models) and being in the lowest 25% of cognitive function scores in 2008 (using generalized linear models to calculate relative risks). Models were adjusted for potential confounding by age, gender, level of education, smoking status, number of depressive symptoms, and mean baseline level of alcohol consumption. Among 1,221 drinkers, 48 (3.9%) reported having been drunk one or more times in the preceding three months. In adjusted models, compared to those who had had not been drunk in the preceding three months those who had been drunk two or three times had a follow-up cognitive function score -0.23 standard deviations lower (95% Confidence Interval [CI] -0.69 to 0.23) and those who had been drunk four or more times had a score 0.51 standard deviations lower (95% CI -0.95 to -0.08). The relative risk of being in the lowest quarter of scores at follow-up associated with being drunk two or three times was 2.12 (95% CI 0.62 to 7.27) and 3.35 (95% CI 1.15 to 9.80) with being drunk four or more times. These results suggest frequent episodes of drunkenness in

older adults are associated with a greater risk of cognitive decline. Given the likelihood of underreporting and underrepresentation biases in our data these findings warrant attention as well as replication in other cohorts.

MONDAY, JULY 14, 2014
ORAL SESSIONS
O2-10
NEUROIMAGING: COGNITIVE CHANGES AND COMPLAINTS IN HEALTHY OLDER ADULTS—IMAGING CORRELATES

O2-10-01 BRAIN BETA-AMYLOID, VASCULAR FACTORS, AND COGNITION: 54-MONTH FOLLOWUP RESULTS FROM THE AIBL STUDY

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Background: There is great interest in interplay between cerebrovascular disease (CVD) and amyloid in mediating cognitive decline. Vascular disease risk factors increase risk for dementia, however whether this is synergistic or additive to concurrent AD-pathology is unclear. **Methods:** 287 participants from the Australian Imaging, Biomarkers and Lifestyle Study of Ageing, ranging from normal cognition through MCI to AD dementia, assessed four times over 54 months with 11C-PiB PET, 3T-MRI and neuropsychology assessment. 174 also had SWI MRI for microbleeds and 80 had carotid intima-media thickness (CIMT) measurement. Linear mixed models regression was used to compare outcome (cognitive score, PET SUVR, atrophy) between groups with and without significant PiB and CVD burden over time. Subanalyses also tested whether greater carotid intima-media thickness (CIMT) or lobar microbleeds (LMB) influenced change in PiB. **Results:** 21/151 NC and 24/32 MCI had declined (e.g. NC-MCI, MCI-AD) by 54 months. A similar proportion of PiB+CVD+ and PiB+CVD- NC declined at 54 months (25.0% vs 26.7%) compared with PiB-CVD+ (14.3%) and PiB-CVD- (9.1%) (X 2 =6.3, p=0.01). For MCI, 100% (4/4) of PiB+CVD+ MCI vs 69.2% of PiB+CVD- declined, 2/2 PiB-CVD+ and 1/10 PiB-CD- (X 2 =15.3, p=0.002). Both PiB+ and CVD+ were associated with cognitive decline in univariate models, however after correcting for age, E4, gender and education, PiB+ remained significant, whereas CVD+ was not. In mixed models analyses adjusted for age, education and E4 status, PiB and CVD were additive, but not interactive, in influencing longitudinal change in episodic memory (CVLT-long delay) and global cognitive function (CDR-SOB). There was no significant difference seen in the accumulation of PiB over time between CVD+/-, nor in subanalyses by CIMT or lobar microbleeds. **Conclusions:** In this sample, PiB and CVD were additive but not interactive processes in mediating cognitive decline, and no association was seen between markers of vascular pathology and longitudinal PiB accumulation.

O2-10-02 PRACTICE EFFECTS AND LONGITUDINAL COGNITIVE CHANGE AS A FUNCTION OF AMYLOID AND NEURODEGENERATIVE IMAGING BIOMARKERS IN COGNITIVELY NORMAL INDIVIDUALS

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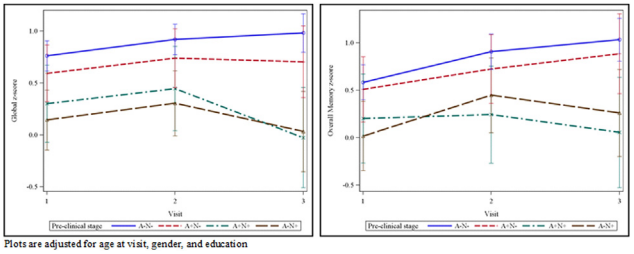
Background: We previously showed that practice effects and longitudinal cognitive change in four cognitive domains and a global index of cognition differed in individuals who remained clinically normal vs. those who developed incident mild cognitive impairment (MCI) or dementia. The aim of this study was to examine practice effects and cognitive trajectories in clinically normal individuals as a function of amyloid and neurodegenerative imaging biomarker status. **Methods:** Participants were 153 individuals, aged 70 years and older, from the Mayo Clinic Study of Aging diagnosed as cognitively normal at their baseline evaluation and re-evaluated at approximately 15-month intervals. We used study coordinator and physician ratings (but not neuropsychological test scores) to classify subjects as clinically normal. All participants completed MRI, FDG-PET and PiB-PET at their baseline evaluation. We divided subjects into four groups based on neuroimaging measures of amyloid (PiB-PET SUVR $\geq$ 1.5 [A+ or A-]) and neurodegeneration (abnormal hippocampal volume or FDG-PET hypometabolism in "Alzheimer signature" regions [N+ or N-]). Ninety-three participants were classified as A-N-, 25 A+N-, 22 A-N+, and 13 A+N+. We used linear mixed effects modeling to test for differences in z-scores between time points in four cognitive domains and a global score for each of the four imaging groups. **Results:** The A-N- group showed a practice effect (i.e., significant improvement at Visit 2) in memory, attention and the global score. The A-N+ group also showed a practice effect in memory. At the 30-month visit (Visit 3), the A-N- group showed further improvement in memory and the global score. The A+N- group also showed improvement in memory relative to baseline whereas the A+N+ group showed a decline in language and the global score. Between-group comparisons showed a divergent pattern by the 30-month follow-up, with the A-N- and A+N- groups performing better than the A-N+ and A+N+ groups on all cognitive domains and the global score. (See Figure.) **Conclusions:** The presence of amyloid alone did not have an adverse impact on the practice effects or 30-month cognitive trajectories of normal individuals. In contrast, participants with neurodegeneration (either A-N+ or A+N+) had worse performance at the 30-month follow-up.



Plots are adjusted for age at visit, gender, and education

O2-10-03 HIGHER AB BURDEN IN HEALTHY APOE-E4 CARRIERS IS ASSOCIATED WITH SUBJECTIVE MEMORY COMPLAINTS: RESULTS FROM THE FLUTEMETAMOL AND PIB AIBL COHORTS

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Background: The underlying pathological process, diagnostic utility and prognostic value of subjective memory complaints (SMC) in relation to Alzheimer's disease (AD) remains unclear. The relationship between SMC, Apolipoprotein E-e4 allele (e4) status and Aβ-burden was compared in two healthy control (HC) cohorts in the Australian Imaging Biomarkers and Lifestyle study of ageing (AIBL). **Methods:** 134 new HC (age 74.4$\pm$5.6) AIBL participants were recently imaged with 18 F-flutemetamol