patients and age-matched healthy controls (HC). **Methods**: Five mild AD subjects (MMSE 24±3, CDR 1) and 5 HC (MMSE >28) underwent PET imaging over 3 hours after injection of 300 MBq of the ^{18}F-ligand. Distribution volume ratios (DVR) were calculated through graphical analysis using the cerebellum as input function. **Results**: All AD subjects showed neocortical binding, greatest in the precuneus/posterior cingulate and frontal cortex, followed by lateral temporal and parietal, with relative sparing of sensorimotor cortex. HC showed no binding in cortical or subcortical grey matter and their scans were clearly distinguishable from AD subjects. Cerebellar cortex showed no retention in either group. Significantly higher neocortical DVRs were observed in AD (1.84 ± 0.20) when compared with HC (1.3 ± 0.17, p = 0.009). Cortical uptake to cerebellar cortex ratio (SUVR) at 90-120 minutes post-injection gave similar results to DVR. **Conclusions**: Our results show that Aβ burden can be quantified in AD with a novel F-18 labelled PET ligand. The pattern of binding closely matches that reported with ^{11}C-PIB. This ligand may permit wide application of amyloid imaging by centralized production and distribution not possible with a C-11 labelled Aβ ligand.

O1-04-03 AMYLOID BURDEN IN AGEING SUBJECTS WITH AND WITHOUT COGNITIVE DECLINE

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Background: Up to 30% of healthy persons aged over 75 years show Aβ deposition at autopsy. It is postulated that this represents preclinical Alzheimer's disease (AD). **Objectives:** We evaluated the relationship between Aβ burden as assessed by PIB PET and cognitive decline in a predominantly normal elderly population. **Methods:** PIB PET and cognitive tests were performed on 33 elderly participants (age 73 ± 6) from the longitudinal Melbourne Healthy Ageing Study (MHAS). Subjects were classified as being cognitively "stable" or "declining" by an independent behavioral neurologist based on clinical assessment and annual word-list recall scores from the preceding six years. Rates of decline were calculated from the word-list recall scores. Aβ burden was quantified using Standardized Uptake Value normalized to cerebellar cortex (SUVR). **Results:** Nine subjects were classified as declining. At the time of the PET scan, three subjects had MCI, one had Alzheimer's disease (AD), and six were declining but remained in the normal range for age on cognitive tests. Seven of the 9 declining subjects and 3 of the 24 stable subjects, had cortical PIB binding. Aβ burden correlated with memory impairment in the declining group (SUVR vs CVLT II delayed recall: r = -0.69, p < 0.0001) and with the rate of decline (r = -0.57, p = 0.0004). **Conclusions:** Declining subjects are much more likely to show cortical PIB retention than stable subjects. Aβ burden as assessed by PIB PET correlates with memory impairment and the rate of memory decline in the ageing population. These observations suggest that Aβ deposition is not part of normal ageing and is likely to represent preclinical AD. Further longitudinal observation is required to confirm this hypothesis.

O1-04-04 THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE: PROGRESS REPORT

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Background: As disease modifying treatments are developed, it is desirable to identify "validated" biomarkers which have high power to quantify progression. **Objectives:** The goals of ADNI are: 1) Develop improved methods and uniform standards for longitudinal multisite MRI, PET, blood and CSF biomarker data in patients with Alzheimer's disease (AD), mild cognitive impairment (MCI), and elderly controls. 2) A public data repository, which describes longitudinal clinical, cognitive, blood and CSF biomarkers, brain structure and glucose metabolism. 3) Determine methods, which provide maximum power to distinguish treatment effects in clinical trials. **Methods:** Enrolling subjects at 58 sites: AD (n=200), MCI (n=400) and 200 controls with clinical/cognitive assessments and 1.5 T structural MRI every 6 months for 2-3 years; 50% of subjects will also have FDG PET scans and 25% 3T MRI at each time point. Blood, urine and CSF samples will be analyzed. All ADNI data is available: www.loni.ucla.edu/ADNI. **Results:** The tables show baseline characteristics of 668 subjects currently enrolled (AVL is auditory verbal learning test). We expect to complete patient enrollment in May 2007. By the Prevention meeting we expect to have 1 yr rate of change data on 105 controls, 126 MCI, and 56 AD, as well as 6 month rate of change data on 192 controls, 270 MCI, and 129 AD. MRI scans are being analyzed by a number of methods including hippocampal volumes, brain boundary shift integral, tensor based morphometery, voxel based morphometry and cortical thickness. FDG PET scans are being analyzed using region-of-interest and voxel based methods. Statistical analyses will compare the various methods to detect rates of change in the 3 subject groups, and to validate each method by correlating with change of clinical measures. **Conclusions:** ADNI provides a large set of data quantifying change in controls, AD and MCI and validates imaging and biomarkers for clinical trials.

	n	Age	Education	%Female	%LP Consent	AVL (sum of trials 1-5)	AVL Delayed recall (\%)
NL	203	76.00 (4.98)	16.00 (2.89)	46.31%	62.07%	42.92 (8.93)	64.56 (27.97)
MCI	318	74.50 (7.54)	15.82 (3.01)	33.96%	63.21%	30.06 (8.42)	29.74 (30.49)
AD	147	75.52 (7.31)	14.77 (3.04)	46.26%	63.27%	23.37 (7.82)	11.81 (22.03)
Overall	668	75.18 (6.83)	15.65 (3.01)	40.42%	62.87%	32.58 (11.23)	36.71 (34.42)
		MMSE	CDR	CDR SOB		Logical Memory (Immediate)	Logical Memory (Delayed)
NL	203	29.09 (0.98)	0.00 (0.00)	0.03 (0.12)		13.68 (3.47)	12.77 (3.44)
MCI	318	26.91 (1.81)	0.50 (0.00)	1.59 (0.89)		6.88 (3.11)	3.67 (2.67)
AD	147	23.28 (2.01)	0.74 (0.25)	4.28 (1.59)		4.07 (2.95)	1.18 (1.80)
Overall	668	26.78 (2.66)	0.40 (0.30)	1.71 (1.80)		8.33 (4.89)	5.88 (5.42)

O1-04-05 SIX-MONTH CEREBRAL METABOLIC DECLINES IN ALZHEIMER'S DISEASE, AMNESTIC MILD COGNITIVE IMPAIRMENT AND ELDERLY NORMAL CONTROL GROUPS: PRELIMINARY FINDINGS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

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Background: In a previous FDG PET study, we found that patients with Alzheimer's disease (AD) had one-year declines in the regional cerebral metabolic rate for glucose (CMRgl), and we used that information to estimate the number of patients needed to evaluate putative disease-slowing treatments in one-year clinical trials (Alexander et al, 2002). **Objec-tive(s):** To characterize approximately six-month CMRgl declines in patients with AD, patients with amnestic mild cognitive impairment (MCI)

and elderly normal controls (NC), and to estimate the number of AD and MCI patients needed to evaluate a putative disease-slowing treatment in a six-month clinical trial, using PET images from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu\ADNI). **Methods:** Baseline and approximately six-month follow-up ADNI PET images were compared in separate analyses of 16 AD patients, 27 MCI patients and 27 NC using SPM5. Using the atlas coordinate with the maximally significant CMRgl decline in the respective AD and MCI comparison, power analyses were performed to estimate the number of patients needed to evaluate a putative primary prevention therapy in a six-month multi-center clinical trial. **Results:** There was a trend for approximately six-month MMSE declines in the AD patients ($P=0.06$) and MCI patients ($P=0.06$) but not in the NC ($P=0.86$). The AD patients had six-month CMRgl declines in left temporal, parietal and precuneus regions (maximal reduction 3.0%), the MCI patients had six-month CMRgl declines in bilateral temporal, right parietal and right frontal regions (maximal reduction 2.0%), and the NC had had six-month declines in the left temporal cortex ($P<0.001$, uncorrected for multiple comparisons). Using the maximal, left temporal CMRgl declines in each patient group, we estimate the need for at least 224 AD patients or 642 MCI patients per treatment arm to detect a putative disease-slowing treatment efficacy to reduce six-month CMRgl declines by 25% with 80% power (one-tailed $P=0.005$, uncorrected for multiple comparisons) in a multi-center clinical trial. **Conclusions:** This study provides preliminary information about six-month CMRgl declines in AD and MCI patients and a preliminary estimate of the number of patients needed to detect CMRgl effects in six-month clinical trials of putative disease-slowing treatments.

O1-04-06 CORRELATION OF MEMORY DYSFUNCTION AND AMYLOID BURDEN IN MILD COGNITIVE IMPAIRMENT

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Background: Mild cognitive impairment (MCI) carries a high risk of conversion to Alzheimer's disease (AD). The relationship between amyloid ($A\beta$) burden and severity of impairment in AD is controversial and has not been explored in MCI. **Objectives:** We examined the relationship between memory impairment and $A\beta$ burden as measured by PIB-PET. **Methods:** 34 healthy controls (HC) (age 71 ± 7; MMSE >28), 44 MCI subjects (age 72 ± 9; MMSE 26.6 ± 3) and 44 subjects with mild to moderate AD (age 73 ± 10; MMSE 21.3 ± 4) were studied. All subjects underwent cognitive assessment including MMSE and California Verbal Learning Test II long delay (CVLT). $A\beta$ burden was quantified using Standardized Uptake Value normalized to cerebellar cortex (SUVR) 40-70 min.PI. The mean of frontal, posterior cingulate, parietal, lateral temporal and occipital regions was used for analysis. **Results:** SUVR was 1.40 ± 0.33 in HC, 1.81 ± 0.59 in MCI and 2.39 ± 0.39 in AD and correlated negatively across all subjects with cognitive measures (MMSE $r = -0.43$, $p<0.0001$). When groups were examined separately, only the MCI cohort showed a correlation with cognition (CVLT $r = -0.53$, $p < 0.001$). At a SUVR thresh-hold of 1.6 (the 75th percentile of HC), cortical PIB binding was present in 100% of AD, 60% of MCI and 23% of HC. In MCI, but not in HC, PIB +ve subjects performed worse than PIB -ve subjects on memory measures (CVLT 2.9 ± 0.9 vs 7.2 ± 1.1, $p = 0.004$). Correlation between $A\beta$ and memory impairment in MCI persisted after removing the PIB -ve subjects (CVLT $r = -0.49$, $p = 0.01$). **Conclusions:** Our data supports a pathogenic role for $A\beta$ accumulation in AD by showing a relationship to mild cognitive impairment. This relationship is lost in later stages of disease as dementia develops. These findings may have implications for anti-amyloid therapy.

O1-04-07 CSF AND MRI PERFUSION BIOMARKERS IN MIDDLE-AGED ADULTS AT RISK FOR ALZHEIMER'S DISEASE: INFLUENCE OF APOE4 ALLELE

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Background: *APOE4* allele and vascular risk factors in midlife are independently associated with an increased risk of Alzheimer's disease (AD) in later life. It is unclear how *APOE4* and vascular factors interact to affect β-amyloid ($A\beta$) metabolism and cerebral perfusion - two key processes that become dysregulated early in preclinical AD. **Objective:** To describe the relationship of *APOE4* allele and vascular risk factors with CSF $A\beta$ levels and quantitative cerebral blood flow (qCBF) in asymptomatic adult children of persons with AD. **Methods:** In a cross-sectional analysis of 42 middle-aged adults at risk for AD, CSF $A\beta40$ and $A\beta42$ (n=27), vascular risk factors (n=42), and quantitative *T2**-weighted perfusion MR images (n=20) were measured (5 subjects with both CSF and MRI). CSF $A\beta$ levels were measured using ELISA. *T2**-weighted perfusion MR images were obtained on a GE 1.5 T MR scanner with echo planar capability. **Results:** Participant characteristics are shown in the Table. In subjects with CSF data, vascular risk factors did not correlate with CSF $A\beta40$ or $A\beta42$ levels. However, *APOE4* interacted with systolic blood pressure (SBP) and body mass index (BMI) to predict CSF $A\beta$ levels (Figure 1). In *APOE4* carriers, increased SBP and BMI were associated with CSF $A\beta40$ and $A\beta42$ levels and $A\beta40/42$ ratios suggestive of preclinical disease progression. This relationship was not noted in *APOE4* non-carriers (Figure 1). In MR perfusion analyses (n=20), *APOE4* carriers had lower qCBF in the middle temporal gyrus compared to non-carriers (*APOE4* carriers 39.3 ± 18.8 vs. *APOE4* non-carriers 59.6 ± 15.9 ml/100g/min, $p=0.023$, Figure 2). While *APOE* group differences in qCBF did not reach statistical significance in the superior frontal gyrus, parietal lobe, posterior cingulate, parahippocampus, and hippocampus (all $p>0.3$), the overall pattern suggests lower qCBF in these regions in *APOE4* carriers compared to non-carriers (Figure 2). **Conclusions:** In asymptomatic middle-aged adult children of persons with AD, *APOE4* allele may influence the relationship of vascular risk factors with $A\beta$ metabolism as well as CBF in brain areas known to be hypometabolic in symptomatic AD. Further studies are needed to confirm and clarify the clinical implications of these findings.

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Table
Participant Characteristics

Characteristic (n=42)	Value (Mean ± SD)
Age, y	54.5 ± 8.0
Women, n (%)	29 (69)
APOE4 carriers, n (%)	15 (36)
Total cholesterol, mg/dL (mmol/L)	195.8 ± 35.2 (5.07 ± 0.9)
LDL cholesterol, mg/dL (mmol/L)	107.8 ± 37.9 (2.8 ± 1.0)
Systolic blood pressure, mm Hg	119.0 ± 13.0
Body mass index (BMI), kg/m^2	27.2 ± 5.0
Diabetes mellitus, n (%)	0 (0)
Current tobacco use, n (%)	4 (10)