of cognition by committee (n=77 normal and n=15 MCI). **Results:** Nearly half (44/92) of non-demented older adults in this sub-study were PiB+ for amyloid. Amyloid deposition was associated with ba PWV and SBP. After adjustment for covariates, one standard deviation increase in ba PWV resulted in nearly a 2-fold increase in the odds of being PiB+. Additional adjustment for ApoE-4, mild cognitive impairment and SBP did not attenuate this association. Higher WMH volume was associated with increased central PWV (cf PWV ($p<0.01$) and hf PWV ($p=0.03$)) and SBP ($p=0.05$). Each standard deviation increase in ba PWV and cf PWV was associated with a 3 and 4-fold increase, respectively, in the odds of having both high amyloid and high WMH, relative to low amyloid and low WMH. **Conclusions:** This is the first study to show that PWV is associated with PiB-PET. Our results confirm initial reports showing associations between SBP and PiB-PET and extend this research by showing arterial stiffness is associated with in vivo amyloid deposition in non-demented individuals, independent of SBP and anti-hypertensive medication use. It will be important to determine if the prevention of elevated BP and vascular stiffness at middle-age will reduce amyloid deposition in the aging brain.

Table
The odds ratios for having structural brain abnormalities per one standard deviation change in arterial stiffness.

	Model 2				Model 2 + SBP			
	OR	95% CI		p-value	OR	95% CI		p-value
baPWV (cm/s)								
Both PIB+ and High WMH	2.79	1.35	5.80	0.0058	2.40	1.03	5.57	0.0418
PiB+ only	1.69	0.83	3.48	0.1505	1.27	0.56	2.90	0.5701
High WMH only	1.36	0.65	2.85	0.4218	1.04	0.45	2.40	0.9239
Neither	*referent*				*referent*			
cfPWV (cm/s)								
Both PIB+ and High WMH	3.83	1.46	10.06	0.0063	3.26	1.16	9.12	0.0248
PiB+ only	2.24	0.82	6.13	0.1183	1.48	0.49	4.50	0.4843
High WMH only	2.98	1.13	7.86	0.0277	2.41	0.86	6.75	0.0933
Neither	*referent*				*referent*			

Model 2 represents the odds of having brain amyloid deposition (PiB+) and white matter hyperintensities (WMH) per one standard deviation change in pulse wave velocity measures after adjustment for age, gender, body mass index and anti-hypertensive medication use (between 2000-2008).

IC-P-019 *IN VIVO* GD-STAINING MRI REVEALS EFFICACY OF ANTI-BETA-AMYLOID IMMUNOTHERAPY AFTER LONGITUDINAL STUDY IN A TRANSGENIC MOUSE MODEL OF ALZHEIMER'S DISEASE

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Background: Magnetic resonance imaging (MRI) combined with intra-cerebro-ventricular administration of Gadolinium (Gd-DOTA) contrast agents can be used to detect individual amyloid plaques in transgenic live mice (ICV-Gd-staining protocol [1]). Here, we used this protocol to evaluate, at a preclinical level, an anti-A β antibody specifically recognizing protofibrillar forms of Aβ. **Methods:** Fourteen APP/PS1 transgenic mice received a weekly injection of the anti-Aβ antibody (40mg/kg) from 3.5 to 8.5 months; 12 other APP/PS1 mice received a control antibody. Twenty amyloid-free control mice (PS1) received the same antibodies (10 vs. 10). Amyloid plaques detection was performed after ICV-Gd-staining, a protocol based on the use of a clinically approved MR contrast agent [1]. Three-D Gradient-echo MR images (resolution: 29x29x117µm 3) were recorded on each mouse at the age of 5.5 and 8.5 months. Amyloid plaque load was quantified on the basis of the MR images for each mouse on 8 brain slices evenly spaced [2]. After imaging, mice were sacrificed and amyloid plaque load was quantified from histological sections. **Results:** Gd-staining largely increased the signal to noise ratio in the brain of mice and allowed plaque detection (Fig. 1). The amyloid load increased between the age of 5.5 and 8.5 months for the group treated with the control antibody (3.4% to 7.5%, respectively) or with the anti-Aβ antibody (3.3% to 5.7%). However, this increase was significantly lower in the group treated with the anti-Aβ antibody ($p=0.004$; Fig. 1). The histological study performed in 8.5 month-old APP/PS1 mice confirmed amyloid load reduction in the mice treated with the anti-amyloid immunotherapy. **Conclusions:** In vivo amyloid plaque detection is critical to follow-up the efficacy of treatments against Alzheimer's disease at a preclinical stage. Here, we show that Gd-staining detects amyloid plaques in vivo with a very high resolution (29µm). It enables to follow-up the age-associated increase of amyloid plaques in transgenic mice and reveals treatment efficacy. It can be used as a reference method in anti-amyloid drug development trials. References: [1] Petiet et al., Neurobiology of Aging, 2012; [2] Jack et al., J Neuroscience, 2005.

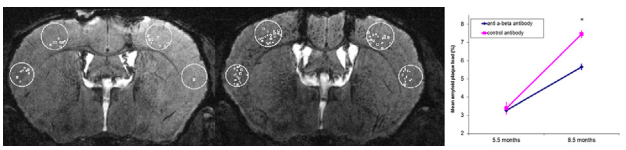

Fig. 1. Longitudinal follow-up of amyloid plaque load in APP/PS1 mice. Left – *In vivo* ICV-Gd-staining MRI of a control APP/PS1 mouse at 5.5 month-old. White circles are ROIs where amyloid load was quantified. Spots identified as plaques are visible within the cortex and drawn in white into the ROIs. Center – MRI of the same APP/PS1 mouse at the age of 8.5 months. Right - Comparison of amyloid plaque load measured on APP/PS1 mice treated with the anti-Aβ antibody or with the control antibody. Error bars stand for standard error of the mean.

IC-P-020 PERIPHERAL BLOOD PLASMA PROTEIN LEVELS ARE ASSOCIATED WITH PITTSBURGH COMPOUND B-BINDING IN THE BRAIN

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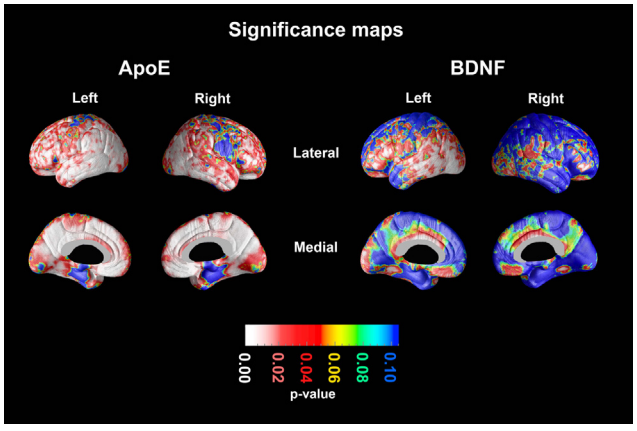
Background: Biomarkers are the only feasible approach to diagnose Alzheimer's disease (AD) in its presymptomatic stages, when a disease-modifying agent will have the greatest impact. Blood-based markers, that are inexpensive and easily obtainable, could become useful for presymptomatic diagnosis. Pittsburgh compound B is a positron emission tomography (PET) radiotracer that binds to fibrillar A b in the brains of symptomatic and presymptomatic AD subjects. Here we examined the association between several AD-relevant blood plasma proteins and PIB binding in the brain. **Methods:** Our dataset consisted of 18 AD, 56 mild cognitive impairment and 3 normal control Alzheimer's Disease Neuroimaging Initiative

(ADNI) subjects with available [11 C] PIB and peripheral blood protein data. MRI-coregistered PET data was smoothed with a 15 mm kernel and convected onto the 3D hemispheric models along the warping deformations computed in cortical pattern matching of the associated MRI scans. We applied linear regression to examine in 3D the associations between apolipoprotein E (ApoE), apolipoprotein J (ApoJ), brain-derived neurotrophic factor (BDNF), interleukin 6 receptor (IL6R), interleukin 13 (IL13) and tumor-necrosis factor a (TNF a) and PIB SUVR, while adjusting for age and sex. We used permutation statistics thresholded at $p<0.01$, for multiple comparisons correction. **Results:** Plasma ApoE showed significant negative association with PIB SUVR throughout the brain, except in the sensorimotor and entorhinal cortex (left p corrected =0.004, right p corrected =0.008). Plasma BDNF levels showed significant negative associations with left greater than right amyloid burden in the lateral temporal, inferior parietal, inferior frontal, anterior and posterior cingulate, and orbitofrontal regions (left p corrected =0.03). ApoJ, IL6R, IL13 and TNF a failed to show significant associations with PIB SUVR. **Conclusions:** Lower peripheral blood levels of proteins that are involved in A b degradation and clearance (ApoE) and neuroprotection against A b toxicity (BDNF) showed a significant widespread association with severity of brain amyloidosis. This further establishes the role of these two proteins in AD. The lack of association between IL6R, IL13 and TNF a may be explained by their stronger relevance to the neuroinflammatory aspects of AD, which are not directly measured by amyloid imaging.



IC-P-021 IMAGE-DERIVED ARTERIAL INPUT FUNCTION FOR PIB QUANTIFICATION

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Background: Deposition of β-amyloid (Aβ) plaques in the brain is one of the earliest indicator of Alzheimer's disease (AD) pathology. In vivo quantification of Aβ load using positron emission tomography (PET) is critical to further our understanding of disease mechanisms, to develop early diagnostic techniques, and to identify suitable surrogate indicators for treatment monitoring and efficacy evaluation in drug trials. The mainstream quantification techniques of Aβ imaging use a reference tissue based approach; however, the reference may not be valid under various circumstances. On the other hand, absolute quantification requires arterial sampling, which is invasive and noisy. Recently, we developed an image-derived arterial input function (IDAIF) technique that allows us to do absolute quantification without arterial sampling and we evaluated this technique in this abstract. **Methods:** A total of 24 individuals (8 PIB+ based on a mean cortical binding potential of 0.18) were included in this study. Each participant underwent PIB PET imaging, anatomical T1-weighted MR imaging and time-of-flight (TOF) MR angiography (MRA). The three images were co-registered using a vector-gradient technique and the arterial input function (AIF) was estimated based on the PET and TOF-MRA using a previously described technique. Metabolites correction was done using population data. For PIB quantification using IDAIF, volume of distribution (V T) was calculated using Logan plot. Distribution volume ratio (DVR) was calculated by taking the ratio of regional V T over cerebellum V T as well as the Logan reference tissue technique. **Results:** DVR calculated using IDAIF and Logan reference tissue model strongly correlates with each other for both global index (r=0.999 for mean cortical DVR) and locally (r=0.999 for precuneus). The mean V T for the PiB- group were 3.38, 3.92, 3.56, for cerebellum cortex, precuneus and mean cortical respectively; and 3.39, 6.02, 5.48 for the PIB+ group. **Conclusions:** The IDAIF technique generated comparable V T estimation as literature reported values using arterial sampling. Strong correlation in DVR between the IDAIF and Logan reference tissue technique indicates the feasibility of using IDAIF technique for PIB quantification. Further investigation is ongoing to further validate this technique.

IC-P-022 THE IMPACT OF BETA-AMYLOID DEPOSITION AND VASCULAR RISK FACTORS ON CORTICAL THICKNESS AND COGNITION

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Background: Vascular risk factors such as hypertension, diabetes and cholesterol are well known risk factors for Alzheimer disease. Recent data suggest that some of them may be associated with beta-amyloid deposition and reduction of gray matter integrity. The objective of this study was to investigate how beta-amyloid affects the relationships between vascular risk factors and brain structure and to examine their association with cognition. **Methods:** The study included 67 persons from the Aging Brain cohort, a study recruiting cognitively normal and mild cognitive impairment patients at increased risk for vascular diseases. Subjects were categorized as PIB+ (n=22; age=80 $\pm$ 5.9; MCI=14) or PIB- (n=45; age=78 $\pm$ 6.9; MCI=18) based on their cortical PIB uptake (DVRs values; cerebellar reference region). Cortical thickness was measured using Freesurfer and 3T MRI data. Vascular risk was measured with the Framingham Coronary Risk Profile (FCRP) index and a MANCOVA was conducted to assess the individual contribution of each factor (age, gender, LDL cholesterol, HDL cholesterol, systolic blood pressure, diabetes and smoking) to cortical thickness. Cognition was evaluated using standardized composite scores of episodic memory and executive functions. **Results:** Among the FCRP factors, age (p =.023) and HDL cholesterol (p =.020) were correlated with cortical thickness. Both increased age and low HDL cholesterol were associated with thinner frontal and temporal cortex; low HDL was also associated with thinner parietal cortex. When subjects were divided by amyloid status, both high vascular risk (FCRP total score) and low HDL cholesterol were associated with thinner frontal and temporal cortex in both PIB- and PIB+ subjects. In PIB+ subjects, high vascular risk and low HDL cholesterol were also associated with thinner parietal cortex (Figure). Finally, higher beta-amyloid and higher vascular risk were associated with lower memory performance and cortical thickness mediated these relationships. **Conclusions:** While vascular risk and HDL cholesterol affect cortical thickness in frontotemporal cortex regardless of amyloid status, individuals with