Table
Changes in the diagnostic confidence between scenarios and over the time.

	T00	T06	T12	T06-T00		T12-T06		T12-T00	
Variables	mean (SD)	mean (SD)	mean (SD)	mean_diff (SD_diff)	Cohen's *d*	mean_diff (SD_diff)	Cohen's *d*	mean_diff (SD_diff)	Cohen's *d*
Befief (0-10)	5.86 (1.47)	6.29 (1.59)	7.00 (2.02)	0.43 (1.35)	*0.32*	0.71 (1.60)	*0.45*	1.14 (1.87)	*0.61*
Scenario 1 (0-100%)	54.29 (31.55)	66.21 (31.85)	55.50 (30.30)	11.93 (31.57)	*0.38*	-10.71 (26.84)	**-0.40**	1.21 (38.72)	0.03
Scenario 2 (0-100%)	67.14 (25.17)	55.00 (30.57)	71.07 (29.96)	-12.14 (26.10)	**-0.46**	16.07 (32.74)	*0.49*	3.93 (11.45)	*0.34*
Scenario 3 (0-100%)	23.33 (26.71)	20.48 (23.34)	18.09 (18.06)	-2.86 (33.66)	-0.08	-2.38 (25.19)	-0.09	-5.24 (24.06)	**-0.22**

Values for the three scenarios refer to percentages. Cohen's *d* is an index of effect size: defined as the difference between two means divided by a standard deviation for the data. Mean_diff is the difference between two time points, SD_diff is calculated with the following formula: SD_pre*sqrt(2*(1-rho)), where rho is the correlation coefficient. Values are in italics or bold when the Cohen's *d* is at least 'small' ($\geq$ 0.20): italics for positive difference and bold for negative.

as covariate. Effect Size indices (ES; Cohen's *d* for repeated measures) were also computed. We analyzed the seven dementia experts who both filled out the questionnaire at all time points and enrolled a minimum of 15 patients. **Results:** 'Belief' did not affect the probability of diagnostic change in different scenarios and over time (p=0.655). The probability of diagnostic change did not change significantly throughout the study for all scenarios (p=0.970). Due to the very small sample size, we considered ES greater than 0.20 ('small'). These were consistent with: i) a trend in increase in the belief on a causal role of AB in AD and ii) a growth of the positive predictive value of the amyloid-PET in 'NonAD-positive' over the whole study (Table). **Conclusions:** Beliefs on the pathogenic role of amyloid-B do not affect the intended clinical use of amyloid-PET in the course of a naturalistic study using amyloid-PET. ES suggested an increase of the belief in a causal role of AB in AD pathogenesis over the study. Moreover, an increased use of the positive predictive value of amyloid-PET emerged after practical usage of amyloid-PET. These results will be compared with the actual use of amyloid-PET by the same physicians.

IC-P-006 REGIONAL BETA-AMYLOID PET COMPARISON ACROSS ATYPICAL AND TYPICAL VARIANTS OF ALZHEIMER'S DISEASE

Alissa M. Butts, Mary M. Machulda, Joseph R. Duffy, Scott A. Przybelski, Ronald C. Petersen, Clifford R. Jack, Jr, Val J. Lowe, Keith A. Josephs, Jennifer L. Whitwell, *Mayo Clinic, Rochester, MN, USA.*
Contact e-mail: butts.alissa@mayo.edu

Background: Typical dementia of the Alzheimer's type (DAT) presents as a primary amnestic syndrome, and three "atypical" variants are now recognized. Two of these atypical variants include posterior cortical atrophy (PCA), which presents with visual deficits and the logopenic variant of primary progressive aphasia (lvPPA), which presents with primary language disruption, both of which are commonly due to Alzheimer's disease pathology. Here, we compare these Alzheimer's disease variants on the pattern of beta-amyloid deposition on PiB PET, as well as cognitive measures. **Methods:** We matched 27 PCA, 50 LPA, and 77 DAT patients on age, gender, and disease duration as best as possible. Only subjects with positive beta-amyloid deposition on PiB PET, defined using a standardized uptake value ratio (SUVR) of $\geq$ 1.5, were included. All voxels in the PiB-PET images were divided by median uptake in cerebellum and transformed into template space. Partial volume correction (PVC) was performed. Voxel-level comparisons were performed across groups both with and without PVC using SPM5. **Results:** were assessed after correction for multiple comparisons using family-wise error at p<0.05.Subjects also completed memory, language, and visuospatial tests that may have been used to augment DAT and PCA diagnosis, but was not used in diagnosis of LPA. Results: Cognitively, DAT subjects had poorer memory than lvPPA and PCA subjects, lvPPA subjects had poorer language scores than DAT and PCA subjects, and PCA had poorer visuospatial scores that lvPPA and DAT subjects. The groups did not differ on global SUVR. Regional distribution of PiB-PET was similarly widespread in each of the three groups, although PCA showed greater uptake in bilateral occipital lobe compared to DAT, and greater uptake in right occipital lobe compared to lvPPA. These findings were observed both with and without PVC. No other regional PiB-PET differences were observed across groups. **Conclusions:** These findings suggest that while beta-amyloid deposition is typically diffuse in Alzheimer's disease variants, regional differences exist as compared to DAT, although this DAT group may represent those with an earlier onset. The occipital lobe is particularly vulnerable to beta-amyloid deposition, as well as neurodegeneration, in PCA.

IC-P-007 BRAIN AMYLOIDOSIS AND COGNITIVE DECLINE IN MCI: 12-MONTH FOLLOW-UP

Daniele Altomare[1,2], Cristina Festari[1,2], Clarissa Ferrari[1], Cristina Muscio[1,3], Alessandro Padovani[2,4], Giovanni B. Frisoni[1,5], Marina Boccardi[1], INDIA-FBP working group, *[1]IRCCS Fatebenefratelli, Brescia, Italy; [2]University of Brescia, Brescia, Italy; [3]Fondazione IRCCS Istituto Neurologico, Milano, Italy; [4]Spedali Civili di Brescia, Brescia, Italy; [5]Universite de Geneve, Geneve, Switzerland.*
Contact e-mail: daltomare@fatebenefratelli.eu

Background: Two previous studies demonstrated greater cognitive decline in MCI patients with positive amyloid-PET compared to negative MCI, as assessed by several neuropsychological tests, over 18 (Doraiswamy et al., 2012) and 36 months (Doraiswamy et al., 2014) follow-up. Our aim is to evaluate whether positive amyloid-PET scans are predictive of greater cognitive decline than negative scans over a shorter 12 months period. **Methods:** A naturalistic series of seventy-six MCI patients underwent amyloid-PET with ^{18}F-Florbetapir (FBP-PET), and homogeneous clinical and neuropsychological multi-domain assessment before FBP-PET and after 12 months (12-FU). For each neuropsychological test we constructed a linear mixed model with scores as the dependent variable, and 'FBP-PET result' (positive or negative) and 'time' (baseline or 12-FU) as main factors. 'Age' and 'education' were included as covariates. Effect size indices (partial Eta-squared, η_p^2) were also computed (0.02, 0.13 and 0.26 referring respectively to small, medium and large Eta-squared). **Results:**

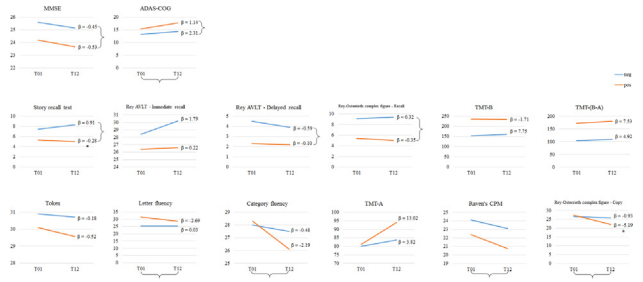

Figure. Cognitive decline in MCI patients over a 12-month follow-up. Horizontal parentheses indicate significant effect of the factor 'time', vertical parenthese indicate significant effect of the factor 'FBP-PET result' and '*' indicates significant interaction of these factors.

Patients with positive scan had overall worse performance on tests of global functioning (MMSE, p=0.005, η_p^2=0.11; ADAS-COG, p=0.007, η_p^2=0.10) and on tests involving memory (Story recall, p=0.002, η_p^2=0.13; Rey AVLT – Delayed recall, p=0.005, η_p^2=0.11; Rey-Osterrieth complex figure – Recall, p = 0.001, η_p^2=0.15). A significant worsening over 12 months was observed in ADAS-COG (p=0.003, η_p^2=0.12), Rey-Osterrieth complex figure – Copy (p<0.001, η_p^2=0.19), Raven's CPM (p=0.039, η_p^2=0.06), Letter (p=0.044, η_p^2=0.06) and Category fluency (p=0.021, η_p^2=0.08). Finally, positive patients showed a significantly greater cognitive decline over the time in the Story recall test (p=0.026, η_p^2=0.07) and the Rey-Osterrieth complex figure – Copy (p=0.018, η_p^2=0.08) (Figure). **Conclusions:** The cognitive performance of MCI patients positive to amyloid-PET is overall worse than in negative ones, but significantly greater deterioration over 12 months emerged in only a minority of tests. Longer time or more specific episodic memory tests may be useful for more sensitive monitoring of performance. Differences with previous studies may be due to different selection of tests or to our shorter follow-up. These data contribute information to define the proper time window for repeated testing for neuropsychology used as a biomarker for AD.

IC-P-008 MULTIMODAL IMAGING OF APOE2 EFFECTS IN THE AGED BRAIN: SPECIFICITY FOR REDUCED AMYLOID PATHOLOGY

Michel J. Grothe[1], Sylvia Villeneuve[2], Martin Dyrba[1], David Bartrés-Faz[3], Miranka Wirth[4], *[1]German Center for Neurodegenerative Diseases (DZNE), Rostock, Germany; [2]Douglas Mental Health University Institute and McGill University, Montreal, QC, Canada; [3]Department of Psychiatry and Clinical Psychobiology, Universitat de Barcelona and IDIBAPS, Barcelona, Spain; [4]NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Berlin, Germany. Contact e-mail: michel.grothe@dzne.de*

Background: The epsilon-2 allele of the APOE gene (APOE2) has been shown to reduce the risk for late-onset (sporadic) Alzheimer's disease (AD) dementia. Little is known about APOE2-related brain changes that may underlie this protective effect. **Methods:** We used multimodal neuroimaging data to comprehensively examine potential protective brain effects of the APOE2 genotype compared to the risk-neutral homozygous APOE3 genotype in a large sample of non-demented older individuals (cognitively normal subjects and those with mild cognitive impairment). Imaging data was obtained from a total of 572 APOE genotyped individuals enrolled in the ADNI study and included assessments of regional amyloid load using AV45-PET, glucose metabolism using FDG-PET, and gray matter volume using structural MRI. Group differences in imaging

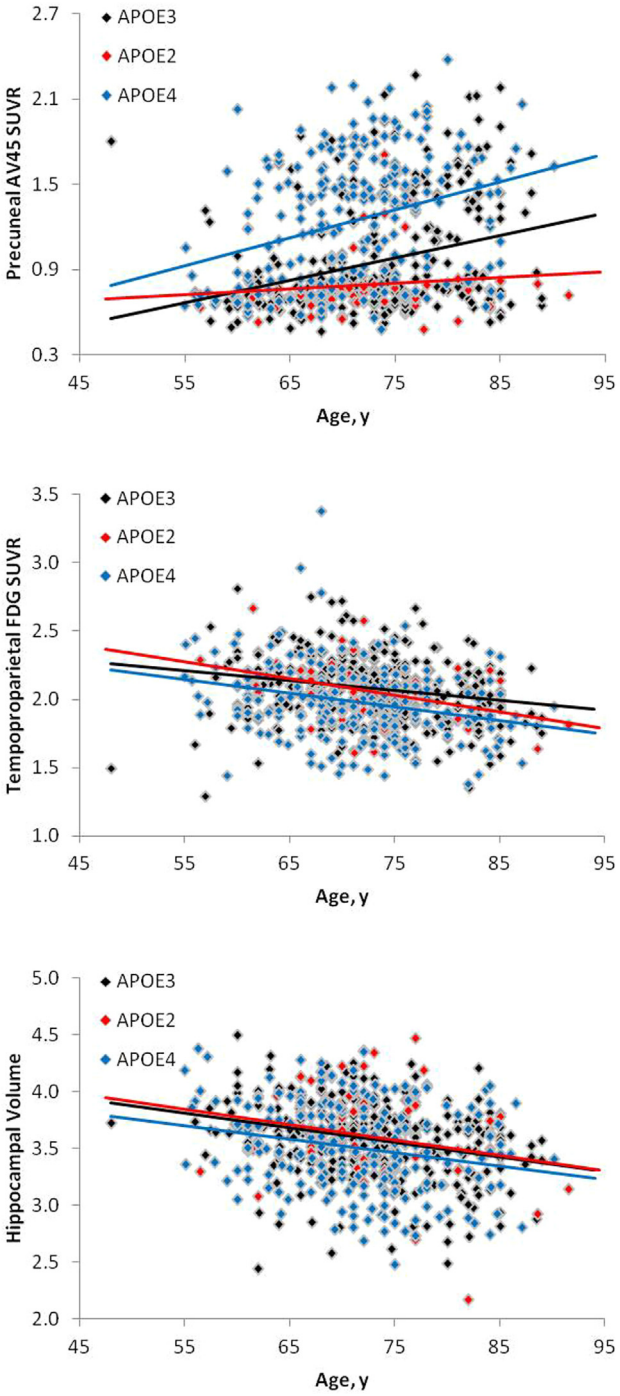

Figure 1. **Effects of age and APOE genotype on multimodal imaging markers**. Precuneal AV45-SUVR (top), temporoparietal FDG-SUVR (middle), and hippocampal volume (bottom) are plotted against age for APOE3 (black) and APOE2 (red) genotypic groups. APOE4 carriers (blue) are included for comparison. Separate linear regression lines are fitted for each group.

markers were assessed using region-of-interest (ROI) and voxel-based analyses, controlled for age, sex, education, and clinical diagnosis. Additional linear regression models examined genotype-specific effects of age on the distinct imaging markers. In secondary analyses, cerebrospinal fluid (CSF) markers of amyloid and tau