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Background: A couple of population studies demonstrated that elderly with depression have lower plasma amyloid-β 42 (Aβ42) than those without depression, and so called "amyloid depression hypothesis" (i.e., the hypothesis that cerebral amyloid deposition is related to late-life depression) was proposed. This study aimed to investigate the relationship between global cerebral Aβ burden and depressive symptoms in elderly individuals with normal cognition (NC), amnestic mild cognitive impairment (MCI) and Alzheimer's disease dementia (AD). **Methods:** Twenty-six NC, 23 MCI and 27 AD individuals were recruited. Subjects with history of major depressive episode or stroke were excluded. All subjects received three-dimensional volumetric 3T MRI, Pittsburgh Compound B (PiB)-positron emission tomography (PET) and comprehensive clinical evaluation including vascular burden assessment. Depressive symptoms were measured using Geriatric Depression Scale (GDS) and Hamilton Depression Rating Scale (HAM-D). **Results:** There were significant group differences of GDS and HAM-D scores among diagnostic groups, and post-hoc tests showed that AD had significantly higher GDS and HAM-D scores than NC (see Table). However, multiple linear regression analysis controlling for age, gender, diagnostic group, and vascular burden did not reveal that global cerebral Aβ burden measured by PiB-PET was associated with GDS or HAM-D scores. In subgroup analyses for each diagnostic group, we did not find any significant associations between global cerebral Aβ burden and GDS or HAM-D scores after controlling age, gender and vascular burden. **Conclusions:** Our results did not support "amyloid depression hypothesis", while the relationship between diagnostic group and depression scores implied that late-life depression might be associated with overall brain degeneration.

IC-P-018 CRITICAL APPRAISAL OF THE APPROPRIATE USE CRITERIA: EFFECT ON DIAGNOSIS AND PATIENT CARE

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Background: In 2013 the Amyloid Imaging Task Force developed the Appropriate Use Criteria (Auc) for clinical use of amyloid PET imaging. The AUC utility remains to be empirically tested. **Methods:** Fifty-three patients underwent F^{18}-Florbetapir scanning at UCLA as part of their individualized diagnostic work up. 50 were evaluated by dementia experts. 3 presented with lobar hemorrhages suggestive of cerebral amyloid angiopathy and were evaluated by stroke experts. Clinical amyloid PET interpretations were performed, and F^{18}-Florbetapir data were further subjected to automated quantitative analysis. Mean standardized uptake volume ratios (SUVR's) were obtained using the Clark method with whole cerebellum as reference. Images were dichotomized as positive or negative using the recently proposed cut-off of SUVR=1.17. Analyses (T-test and Chi square statistics) were first done in the full sample and then in the dementia-expert sample only. **Results:** Subjects were classified based on age of onset (cut-off=65 years) as early onset (EO, N=23) and late onset (LO, N=30), and as Auc-congruent (Auc+, N=39) and incongruent (Auc-, N=14). Compared to Auc- subjects, Auc+ were significantly younger (67 vs. 76 years, p<0.0001). There were no differences in sex, education or disease duration between Auc+ and Auc- or EO and LO. Compared to LO, EO were more likely to be amyloid positive (91% vs. 60%, p=0.01) but showed comparable mean SUVR (1.45 vs. 1.33, p=0.12). Auc+ were as likely to be amyloid positive (74% vs. 71%, p=0.83) and had similar mean SUVR (1.39 vs. 1.36, p=0.43) as Auc-. There was no significant difference in rate of diagnostic (21% vs. 33%, p=0.41) or treatment change (66% vs. 77%, p=0.38) between Auc+ and Auc-. We observed significantly greater rate of diagnostic change in LO compared to EO (43% vs. 13%, p=0.017) but no difference in treatment change (62% vs. 78%, p=0.21). These results remained unchanged in the dementia-expert sample only. **Conclusions:** In our preliminary retrospective series we no difference in pre/post-scan diagnosis in Auc- vs. Auc+ and treatment changes in both comparisons. Changes in diagnosis were significantly more common in LO relative to EO suggesting that greater emphasis on scanning LO might be appropriate.

IC-P-019 BRAIN AMYLOIDOSIS IS ASSOCIATED WITH WORSE COGNITIVE PERFORMANCE IN BOTH THE COGNITIVELY NORMAL AND IMPAIRED STAGES: A [^{18}F]FLUTEMETAMOL PET STUDY

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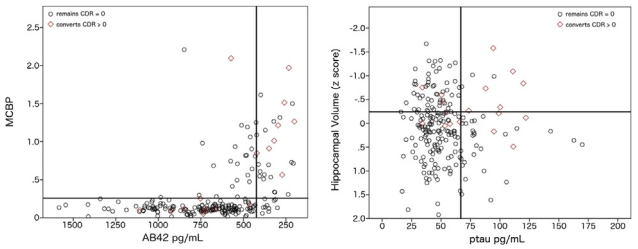
Background: Alzheimer's pathology develops gradually over time and the latent stages of the disease often go undetected. The Mini Mental State Examination (MMSE) is generally thought to be insensitive in meaningfully capturing cognitive decline during the presymptomatic stages. **Objective:** To explore the relationship between [^{18}F]Flutemetamol binding and MMSE in cognitively normal and cognitively impaired individuals. **Methods:** MMSE and [^{18}F]Flutemetamol PET were administered to 34 and 64 cognitively normal elderly at UCLA (UCLA-NC) and University of Leuven (Leuven-NC), respectively. [^{18}F]Flutemetamol mean standard uptake volume ratios (SUVR) (Clark method), as well as mean lobar and basal ganglia (BG) SUVR measurements were obtained. We used linear regression to study the association between MMSE and SUVR measures. We repeated the analyses after the inclusion of 19 MCI and 12 dementia UCLA subjects. All regression analyses were adjusted for age, education and ApoE4 genotype. **Results:** Compared to Leuven-NC, UCLA-NC were on average older (75.8 vs. 65.3 years, p<0.0001) and more educated (16.5 vs. 13.6 years, p=0.001). There were no differences in gender, ApoE4 genotype distribution, MMSE, mean or lobar SUVR. Leuven-NC had significantly higher BG SUVR (1.5 vs. 1.3, p=0.0002). Parietal SUVR was the single amyloid measure that predicted MMSE (beta coefficient =1.2, p=0.045). Mixed effect linear regression with random subject and fixed MMSE effects showed that for each unit decline in MMSE parietal and posterior cingulate SUVR increased by 0.04 (p=0.047) and 0.05 (p=0.02), respectively. In the combined analyses one unit decline in MMSE was associated with significant increase in cingulate SUVR in all three

diagnostic categories (UCLA/Leuven-NC ΔSUVR=0.06, p=0.01; MCI ΔSUVR=0.13, p<0.0001; dementia ΔSUVR=0.04, p=0.0007). An effect was also seen for parietal SUVR in MCI (ΔSUVR=0.1, p=0.0004) and UCLA/Leuven-NC (ΔSUVR=0.05, p=0.04) as well as in frontal (ΔSUVR=0.09, p=0.0006) temporal (ΔSUVR=0.08, p=0.005), occipital (ΔSUVR=0.1, p=0.0004) and basal ganglia (ΔSUVR=0.08, p=0.0016) SUVR in MCI only. **Conclusions:** Higher SUVR is associated with worse cognitive performance in both the cognitively normal and impaired stages. Most significant SUVR increases per unit MMSE were seen in MCI, followed by NC and finally demented subjects in agreement with the sigmoid curve of increasing amyloid deposition.



IC-P-020 COMPARISON OF NIA-AA PRECLINICAL ALZHEIMER'S DISEASE STAGING WITH CSF AND NEUROIMAGING BIOMARKERS

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Background: Using the recently proposed National Institute of Aging and Alzheimer's Association (NIA-AA) criterion, cognitively normal individuals can be classified into preclinical stages using cerebrospinal fluid (CSF) and neuroimaging biomarkers: abnormal amyloid markers (stage 1), abnormal amyloid and neuronal injury markers (stage 2), and abnormal amyloid and neuronal injury markers and subtle cognitive changes (stage 3). Prior work has utilized either CSF or neuroimaging biomarkers for operationalization, but no analyses have taken an integrated approach. Here we directly compare CSF and imaging biomarkers, use both approaches to assign individuals to preclinical stages, and examine the longitudinal cognitive outcomes of individuals in each stage. **Methods:** We included 212 cognitively normal individuals (mean age 66. 8, females=132), with a clinical dementia rating (CDR) of 0. All participants had clinical data and a measurement of hippocampal volume on MRI, abeta1-42 and tau in CSF and amyloid binding on ^{11}[C]Pittsburgh Compound B (PiB) PET, all within one year. Cutoffs to denote abnormality were determined using ROC analysis comparing cognitively normal individuals to those with very mild dementia (CDR=0.5) and a clinical AD diagnosis. Subtle cognitive impairment was defined using a composite of three neuropsychological tests. Using CSF biomarkers alone, neuroimaging markers alone, and using an integrated approach the cohort was classified into Stages 1-3, Suspected Non-Alzheimer

Table 1

N=212	CSF Biomarkers	Imaging Markers	CSF or Imaging
Stage 0	118 (56%]	107 (51%)	74 (35%)
Stage 1	23 (11%)	32 (15%)	29 (14%)
Stage 2	12 (6%)	9 (4%)	30 (14%)
Stage 3	7 (3%)	2 (1%)	11 (5%)
SNAP	40 (19%)	45 (21%)	62 (29%)
Unclassified	12 (6%)	17 (8%)	6 (3%)