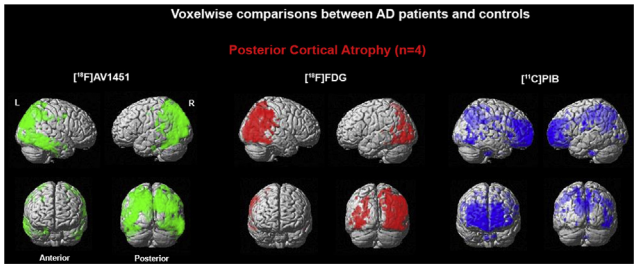

pathology) and [^{18}F]FDG (glucose metabolism) PET. **Methods:** PET scans were performed in 5 posterior cortical atrophy (PCA), 4 logopenic variant primary progressive aphasia (lvPPA), 1 early-onset AD and 2 (memory-predominant) late-onset AD patients (all PIB+) and in 19 cognitively normal controls (Table 1). We created SUVr images for [^{18}F]AV1451 (80-100 minutes, gray matter cerebellum as reference region) and [^{18}F]FDG (30-60 minutes, pons-normalized), and DVR images for [^{11}C]PIB (0-90 minutes, gray matter cerebellum as reference region). We visually assessed [^{18}F]AV1451, [^{11}C]PIB and [^{18}F]FDG uptake patterns in 3 distinct AD variants, and performed voxel-wise contrasts (in SPM) between PCA patients and controls. **Results:** Figure 1 shows asymmetric [^{18}F]AV1451 uptake in parietal, temporal and frontal regions (left>right) in a patient with lvPPA, a classical temporoparietal pattern in a patient with memory-predominant AD, and mainly occipitotemporal and occipitoparietal involvement in a PCA patient. [^{18}F]AV1451 and [^{18}F]FDG appeared strikingly as mirror images, with regions of high [^{18}F] AV1451 uptake corresponding to low [^{18}F]FDG uptake and vice versa, while [^{11}C]PIB binding was observed throughout the association neocortex. Voxelwise contrasts with [^{18}F] AV1451 and [^{18}F]FDG showed that PCA patients significantly differed from controls in clinically affected posterior brain regions, while [^{11}C]PIB binding was greater in both posterior regions and in clinically less affected anterior regions (Figure 2). **Conclusions:** [^{18}F]AV1451 was specifically retained in brain regions closely related to the clinical presentation across distinct AD variants and overlapped substantially with hypometabolic regions in PCA, while [^{11}C]PIB binding was more diffuse and showed less overlap with [^{18}F]FDG uptake. This provides preliminary *in-vivo* evidence that hypometabolism and symptomatology are more closely linked to tau than to Aβ pathology.

IC-02-03 HYPOMETABOLISM OF THE POSTERIOR CINGULATE CORTEX IS NOT RESTRICTED TO ALZHEIMER'S DISEASE

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Background: Hypometabolism of the posterior cingulate cortex (PCC) is associated with Alzheimer's disease (AD). PCC vulnerability, however, could also be present in other neurodegenerative diseases, such as behavioural variant of frontotemporal dementia (bvFTD), and normal aging. The aims of this study were to assess 1) the proportion of AD, bvFTD and cognitive normal subjects (CN) with PCC hypometabolism, and 2) the relationship between PCC metabolism and demographical, neuropsychological, and neurobiological characteristics in AD, bvFTD and CN. **Methods:** We included 33 probable bvFTD patients (Neary criteria, low likelihood of AD pathophysiology based on CSF amyloid-beta$_{1-42}$ >550ng/l), 82 probable AD patients (National Institute on Aging-Alzheimer's Association workgroups core criteria, high likelihood of AD pathophysiology based on CSF tau/amyloid-beta$_{1-42}$ >.52ng/l), and 26 CN (22 subjects with subjective memory complaints and 4 healthy controls, CSF amyloid-beta$_{1-42}$ >550ng/l). Glucose metabolism was assessed using [^{18}F]FDG-PET. Parametric images of standardized uptake value ratios (SUVr) using cerebellar grey matter as reference tissue were generated. First, we defined PCC hypometabolism based on the Receiver Operating Characteristic (ROC) separating AD from CN, to assess the relative prevalence of PCC hypometabolism in AD, bvFTD and CN. Second, we explored relationships between PCC metabolism and demographics (age, sex, and education), Mini-Mental State Examination (MMSE), neuropsychological tests, CSF biomarkers (amyloid-beta$_{1-42}$, tau and phosphorylated tau), and APOE genotype within diagnostic groups using linear regression analyses or ANOVA where appropriate. **Results:** Mean age was 63±7 (AD), 65±8 (bvFTD) and 61±8 (CN) years old. PCC [^{18}F]FDG SUVr was CN > bvFTD > AD. Based on optimal discrimination of AD and CN, the PCC [^{18}F]FDG SUVr cut-off was set at 1.052, resulting in PCC hypometabolism in 78% (AD), 33% (bvFTD), and 23% (CN). PCC [^{18}F]FDG SUVr was associated with age in CN (beta±SE: -.007±.002, p=.002) and bvFTD (beta±SE: -.007±.003, p=.011), not in AD. **Conclusions:** PCC hypometabolism was present in 33% of bvFTD and 23% of CN. PCC [^{18}F]FDG SUVr was associated with age in bvFTD and CN. In the context of diagnostic work-up of dementia, it is important to realize that PCC vulnerability is not restricted to AD, but could be present in bvFTD and normal aging.

IC-02-04 DIRECT COMPARISONS BETWEEN ATROPHY AND HYPOMETABOLISM IN SEMANTIC DEMENTIA AND ALZHEIMER'S DISEASE SUGGEST DISTINCT NEUROPATHOLOGICAL PROCESSES

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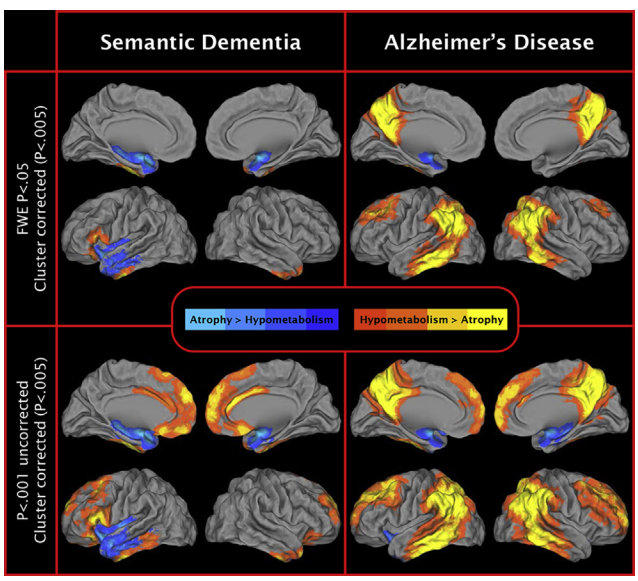
Background: Direct comparisons between atrophy and hypometabolism in Alzheimer's disease (AD) have allowed unraveling

topographic discrepancies that pointed to specific pathological processes. To date, this has never been assessed in semantic dementia (SD) although atrophy and hypometabolism appear more similar than in AD as they both concern the anterior temporal lobe. Therefore, the aim of the present study was to compare atrophy *versus* hypometabolism discrepancies in SD to that observed in AD in order to highlight similarities and differences in the pathological processes between both diseases. **Methods:** Sixteen patients with SD, 24 patients with AD and 39 healthy controls matched for age, sex and years of education underwent both structural MRI and 18F-fluorodeoxyglucose PET scans. Images were spatially normalized using dartel in SPM. Age-adjusted Z-score maps were then computed for each patient and each imaging modality using the healthy controls group as a reference. Direct between-modality voxel-wise comparisons were then performed within each patient group. **Results:** Between-modality analyses highlighted more atrophy than hypometabolism in the medial temporal lobe in both SD and AD (FWE p<.05). By contrast, more hypometabolism than atrophy was found in extended medial and lateral parietal regions, temporo-parietal and frontal areas in AD, and in much more restricted brain regions in SD, i.e. mainly in the prefrontal regions when using a more liberal threshold (p<.001 uncorrected). **Conclusions:** Interestingly, both neurodegenerative disorders were found to be characterized by stronger atrophy than hypometabolism in the medial temporal lobe. However, unlike in AD, the pattern of hypometabolism only slightly differed from the pattern of atrophy in SD. This likely reflects distinct neuropathological processes in both diseases with much less distant effect of neuronal damage in the hippocampal formation in SD. Yet, the excessive prefrontal hypometabolism in SD might as well reflect diaschisis, or the higher sensitivity of 18F-fluorodeoxyglucose PET than structural MRI to detect the underlying neuropathology. Altogether, these findings suggest that the pathological mechanisms affecting the brain might be more homogeneous in SD than in AD.



IC-02-05 **HIPPOCAMPAL VOLUMES PREDICT RISK OF DEMENTIA WITH LEWY BODIES IN MILD COGNITIVE IMPAIRMENT**

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Background: Amnestic mild cognitive impairment (MCI) has been established on clinical grounds in order to identify individuals with prodromal Alzheimer's disease (AD) dementia. However, patients with MCI, who have impairments non-amnestic cognitive domains, may be at an increased risk of dementia with Lewy bodies (DLB). We investigated whether the risk of AD dementia versus DLB can be predicted by hippocampal volume (HV) in patients with MCI, broadly defined with impairments in amnestic and/or non-amnestic cognitive domains. **Methods:** Consecutive patients with MCI (n=108) from the Mayo Clinic Alzheimer's Disease Research Center, who participated in the MRI study during years 2005 through 2013 were included and followed with approximately annual clinical evaluations. Patients with neurologic diseases other than cognitive impairment were excluded. MRIs were performed at 3Tesla and 3D MPRAGE scans were acquired at baseline. HVs were analyzed using FreeSurfer (5.3), and adjusted for TIV. Hippocampal atrophy was determined from the 10th percentile of the measurement distributions in clinically diagnosed AD patients in a previous study. The hazard ratios for progression to AD dementia versus DLB were estimated by taking into account the competing risks. **Results:** After a median (range) follow-up of 1.97 (0.78-8.10) years, 18 (16%) patients with MCI progressed to probable DLB and 34 (32%) progressed to AD dementia. Taking into account the competing risks, the estimated hazard ratio (95% confidence interval) for hippocampal atrophy (relative to normal HV) for progression to AD dementia was 4.58 (2.28-9.19) (p<0.001). The estimated hazard ratio for hippocampal atrophy (relative to normal HV) for progression to DLB was 0.213 (0.050-0.912), corresponding to an estimated hazard ratio for normal HV (relative to hippocampal atrophy) for progression to DLB of 4.71 (1.1-20.2) (p=0.037). (Figure) **Conclusions:** Patients with MCI who progress to DLB tend to have normal HV. Whereas hippocampal atrophy increases the risk of progression to AD demen-