mutual complaint evidenced more diffuse amyloid plaques (OR=6.8, p=0.01), a trend for a higher BRAAK stage (OR=3.0, p=0.086), and a trend to meet NIA/Reagan (OR=3.2, p=0.068) and CERAD criteria (OR=3.7, p=0.09). In a secondary analysis, logistic regression related the combination of AD and vascular pathology (using 'vascular pathology only' as the referent) to the presence of any complaint prior to death (self, informant, and mutual), yielding a significant observation (OR=7.2, p=0.006). **Conclusions:** MCI individuals with a mutual (both self- and informant-) complaint are more likely to have AD pathology at death than their peers with no-complaint. This finding is consistent with research suggesting mutual complaint is most predictive of cognitive trajectory and conversion. Additionally, MCI individuals with concomitant vascular and AD pathology are more likely to have some type of cognitive complaint than their peers with only vascular pathology. Funding: R01-HL11516, R01-AG034962, K12-HG043483, NIRG-13-283276, K24-AG046373, U01-AG016976.

P1-305 CORTICAL BURDEN OF AMYLOID BETA AND PHF TAU IN DEMENTED AND NON-DEMENTED INDIVIDUALS

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Background: Amyloid beta (Aβ) and paired helical filament (PHF) tau are pathological hallmarks of Alzheimer's disease (AD). Relationships between amounts of these proteins in different brain regions and clinical AD severity is complex, and their levels are not routinely measured. Quantifying the amount of Aβ and PHFÏ' in people with and without dementia may provide insights into pathophysiology. **Methods:** We applied a novel technique, Histelide, to quantify the amount of Aβ 42 and PHF tau in formalin-fixed paraffin embedded (FFPE) brain tissue from frontal, temporal and parietal cortex of 337 individuals (161 with and 176 without the diagnosis of dementia). All subjects were participants in the Adult Changes in Thought study. As a secondary analysis, we compared levels of Aβ 42 in different cortical regions among those with one or more APOE ε4 alleles to those with none. **Results:** Among those with dementia cohort, levels of PHF tau in all three regions were significantly higher in the individuals with high level of AD-related pathology (Braak stag e V-VI, CERAD score "frequent"), compared to the individuals with low or intermediate level of AD pathology. Similar results were observed for Aβ 42. Also, levels of Aβ 42 and PHF tau were significantly correlated with each other in all cortical regions in the dementia group. Among those without dementia, levels of PHFÏ, in the temporal cortex and Aβ 42 in all three regions were significantly higher in individuals with Braak stage V-VI compared to Braak stage None-II. Individuals with CERAD score of "frequent" had significantly higher levels of Aβ 42 in the temporal and frontal cortex compared to the CERAD "absent" or "sparse".Also, APOE ε4 carriers without significant AD-related pathology (Braak stage None-IV), with or without dementia, showed significantly higher levels of Aβ 42 in all three cortical regions, compared to non-carriers. **Conclusions:** Levels of Aβ 4 and PHF tau among people with dementia reflect disease burden assessed by standard neuropathological criteria. Among people without dementia, the relationship is more complex. We conclude that Histelide, a method for measuring levels of pathological proteins in FFPE tissue, can be a valuable tool for assessing disease burden in neurodegenerative diseases.

P1-306 APOE4 NON-CARRIERS WITH THE CLINICAL DIAGNOSIS OF ALZHEIMER'S DEMENTIA AND MINIMAL AMYLOID HISTOPATHOLOGY

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Background: While amyloid- b (A b) plaques are considered a cardinal neuropathological feature of Alzheimer's disease (AD), over a third of apolipoprotein E e 4 (APOE4) non-carriers with the clinical diagnosis of mild-to-moderate Alzheimer's dementia may not meet positron emission tomography (PET) criteria for significant A b plaques. This study sought to clarify the percentage of APOE4 non-carriers with the primary clinical diagnosis of mild-to-moderate Alzheimer's dementia near the end of life and minimal A b plaques at autopsy–and the extent to which these cases are associated with appreciable tau pathology (i.e., higher Braak scores) or a primary neuropathological diagnosis other than AD. **Methods:** Subjects for this study were National Institute on Aging (NIA)-sponsored AD Center research participants who were assessed with the National Alzheimer's Coordinating Center Uniform Data Set (NACC UDS) and met our selection criteria. Exactly 100 APOE4 non-carriers and exactly 100 carriers had the primary clinical diagnosis of mild-to-moderate Alzheimer's dementia at their last visit, died within the ensuing 24 months, and had standardized neuropathological assessments. **Results:** 37% of the APOE4 non-carriers with the primary clinical diagnosis of mild-to-moderate Alzheimer's dementia had non-existent or sparse neuritic A b plaques and 28% had non-existent or sparse neuritic and diffuse plaques. By comparison, 13% of the APOE4 carriers had non-existent or sparse plaques and only 4% had non-existent or sparse neuritic and diffuse plaques. Of the 37 APOE4 non-carriers with minimal neuritic plaques, 16 (43%) had Braak Stage III-VI ratings, and 15 of the others met neuropathological criteria for other dementia-related diseases. Of the 13 APOE4 carriers with minimal neuritic plaques, 6 (46%) had Braak Stage III-VI ratings and 4 met neuropathological criteria for other dementia-related diseases. **Conclusions:** Over a third of APOE4 non-carriers (and a much smaller proportion of carriers) with the primary clinical diagnosis of mild-to-moderate Alzheimer's dementia had minimal amyloid- b pathology and many had appreciable tau pathology. Additional research is needed to further characterize the clinical , biomarker and neurochemical features of the disease, clarify pathogenic mechanisms and risk factors, and develop suitable treatment and prevention strategies for what may be a relatively common non-amyloidogenic variant of clinical Alzheimer's dementia.

P1-307 CENTRAL OBESITY AND DEMENTIA: A CROSS-SECTIONAL STUDY WITH DIRECT MEASURES OF VISCERAL FAT

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Background: The association between central obesity and cognitive impairment has been investigated using imaging methods to measure visceral adiposity. However, these methods can provide an indirect estimate of the amount of total visceral fat. We investigated the association between direct measures of visceral fat and dementia using postmortem material. **Methods:** 190 individuals aged 50 years and older who died from non-traumatic causes were included. The next-of-kin answered a clinical interview about past health status and cognitive function. Clinical Dementia Rating (CDR) and Informant Questionnaire on Cognitive

Decline in the Elderly (IQCODE) scales were used for dementia classification. Dementia was the dependent variable and assigned when participants had CDR $\geq$ 1 and IQCODE $\geq$ 3.4. Perirenal, omentum, mesocolonic and mesenteric fats were weighted in a high precision electronic scale and the total visceral fat was used as the independent variable. Multivariate logistic regression adjusted for age, sex, race, schooling, marital status, smoking, alcohol use, physical activity, hypertension, diabetes, dyslipidemia, coronary artery disease, heart disease, and stroke was applied. **Results:** Participants had mean age of 71.2±13.3 years, 57.4% were male, and 61.6% were White. Dementia prevalence was 20.0%. Mean total visceral fat was 1915±1240g. Each one unit increase in total visceral fat was associated with a 1% decrease in the odds of dementia (OR=0.998, 95% CI 0.998-0.999; p<0.0001). **Conclusions:** Total visceral fat was inversely associated with the dementia frequency in our clinicopathological study. Malnutrition related to dementia may be the underlying pathophysiological explanation for our findings.

P1-308 COLLAGENOSIS OF THE DEEP MEDULLARY VEINS CORRELATES WITH PERIVENTRICULAR WHITE MATTER CHANGES IN ALZHEIMER'S DISEASE

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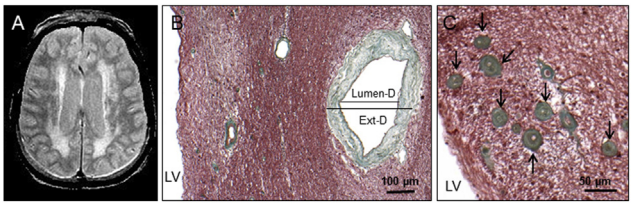
Background: Non-specific white matter hyperintensities (WMH), commonly seen in Alzheimer's disease (AD), are usually attributed to occlusive ischemic arteriolar disease. However, periventricular venous collagenosis (VC) is also seen as a pathological correlate. We investigated relationships of WMH on brain imaging with VC involving venules of different sizes, arteriolosclerosis and other white matter pathologies. **Methods:** 14 AD (age=62-81 years; Braak/Braak stage IV-VI; no strokes) were included from a longitudinal dementia study. 13 age-matched non-AD were also included as controls. Using archived autopsy tissue, 3 coronal sections of periventricular WM (frontal, middle and posterior) were examined by a neuropathologist blinded to imaging. For each region (total=81), VC of small-size (<20um) (sVC) and medium-size (50-150um) (mVC) venules were rated 0-to-3 based on severity of wall-thickening and stenosis on Masson trichrome staining; three largest vein (>200um) lumen and external diameters were also measured to calculate percent stenosis (laVS). (Fig1) Degree of arteriolosclerosis, amyloid angiopathy, myelin loss, clasmatodendrosis, and granular ependymitis were also rated. WMH on proton density MRI or WM hypodensity on CT at the regions corresponding to the pathology were rated 0-to-3 using the Fazekas scale blinded to histopathology. **Results:** Of the 42 regions in AD, median score (range) of WMH=2 (0-3), sVC=2 (0-3) and mVC=1 (0-2), and arteriolosclerosis=1 (0-1). Mean laVS was 21.5%+/-14%.These measures did not differ from non-AD subjects except for sVC, which was greater in AD than non-AD cases (p=0.03). laVS was significantly correlated with WMH scores (Spearman's r=0.410, p<0.005) and predicted WMH scores (R=0.39, R^2 =0.15, p=0.01) in linear regression with vascular and WM pathologies included as independent variables. When AD and non-AD cases were combined in an overall group, sVC, mVC and laVS all significantly correlated with WMH scores (Spearman r=0.30-0.36, p=0.002-0.009), and in linear regression, laVS predicted WMH in the overall group (R=0.34, R^2 =0.12, p=0.003). **Conclusions:** Periventricular large-vein VC best associates with WMH in AD. VC could increase venous resistance, plasma leakage, obstruct perivenous lymphatic drainage along perivenular spaces, leading to interstitial fluid stagnation and impaired amyloid clearance. The hypothesis that VC, especially in the larger deep medullary veins, is implicated in clearance of beta-amyloid in AD, warrants further investigation.



P1-309 AGREEMENT, SENSITIVITY, AND SPECIFICITY BETWEEN THE NEUROPATHOLOGICAL AND CLINICAL DIAGNOSES OF ALZHEIMER'S DISEASE (AD) DEMENTIA: A MULTICENTER LONGITUDINAL STUDY

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Background: The definite diagnosis of AD dementia relies on neuropathology. The literature reports an agreement of 83-93% between clinical and neuropathological diagnosis. In vivo markers could improve the diagnosis accuracy.Objectives: To analyze the agreement between the clinical and the neuropathological diagnosis & to establish the sensitivity and specificity of diagnostic markers. **Methods:** A cohort of 604 patients is being followed ("cohort FRA") annually with clinical follow-up including neuropsychological standardized evaluation, MRI and molecular imaging. So far 76 patients deceased, of which 39 accepted the postmortem brain neuropathological exam. We reviewed their pre-mortem and the neuropathological data. The agreement for the clinical and neuropathological diagnosis was subsequently established and the agreement between each exam (neuropsychological evaluation, CSF biomarkers, MRI, SPECT/PET) and the clinical and neuropathological diagnosis. The sensitivity and specificity of each marker was also calculated. **Results:** The mean age was 60,0 ±10,2 years at dementia onset. They died at a mean age of 69,5±10,3 years. The prevalence of AD pathology was (31/39) 79,5%. AD patients had at least another pathological finding among which the two more frequent were amyloid angiopathy (65 %) and Lewy body accumulation (45 %, half diffuse). The agreement between clinical and neuropathological diagnosis was 93,3% with a sensitivity and specificity of 100% for the diagnosis of AD dementia and the agreement between neuropsychological evaluation and both clinical and neuropathological diagnosis was 96% notwithstanding associated pathology (Lewy pathology was clinically underestimated). For CSF biomarkers assay, the agreement with both clinical and neuropathological diagnosis was 100%. For the patients who underwent functional imaging (SPECT/PET), the exam had an agreement of 90,0% for the clinical diagnosis and of 82,6% for the neuropathological diagnosis. MRI in this sample was unhelpful in 40-50% of the cases. **Conclusions:** The agreement, sensitivity and specificity between clinical and neuropathological diagnoses in this sample were high even though the cohort was multicentric and the mixed pathology prevalence elevated. The exams that have proven more useful were the extensive and early neuropsychological evaluation and the biomarkers assay in CSF.

P1-310 TDP 43 IS NOT ASSOCIATED WITH NEUROPSYCHIATRIC ALTERATIONS IN COGNITIVELY NORMAL ELDERLY

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