old compared to 23.1% of the old ($p < 0.001$). Both AD and mixed pathologies independently increased the odds of dementia in both the old and oldest old (all p-values <0.001). There was no difference in the relationship of AD or mixed pathologies to dementia in the oldest old compared to the younger old ($p>0.2$ for all interactions). **Conclusions:** The frequency of mixed pathologies increase with age. AD pathology, LB and infarcts all individually and in combination increase the odds of dementia in both younger and older elders. AD pathology has the same effect on clinical dementia in the old and oldest old when accounting for other pathologies.

O2-07-05 CEREBRAL ARTERY ATHEROSCLEROSIS IS ASSOCIATED WITH VASCULAR DEMENTIA, BUT NOT WITH ALZHEIMER'S DISEASE: A POPULATION-BASED POSTMORTEM SERIES

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Background: Previous neuropathological studies have shown atherosclerosis of Circle of Willis (CW) arteries to be associated with Alzheimer's disease (AD). However, most of them used convenience samples based on very-old institutionalized individuals with advanced dementia. Considering that aging is a risk factor both for dementia and atherosclerosis, results should be confirmed in population-based samples. Aim: To verify the relationship between pathologically-proven CW atherosclerosis, AD and vascular dementia (VaD) in a clinicopathological population-based study. **Methods:** 183 subjects older than 50 years of age, sourced from the Brain Bank of the Brazilian Aging Brain Study Group, were submitted to neuropathological examination using immunohistochemistry. The diagnoses were AD ($n = 31$), VaD ($n = 28$) and controls ($n = 124$). Quantitatively measures of stenosis of CW arteries and the number of arteries with atheroma per CW were compared among groups. **Results:** Mean percentage of CW arterial stenosis was higher in VaD group compared to controls ($p = 0.001$). Moreover, the extent of atherosclerotic disease, measured by the number of arteries with atheroma per CW, was also higher in VaD subjects than in controls ($p = 0.001$). Both associations remained significant after multivariate linear regression analysis, adjusting for confounding factors as age, gender and years of education. Percentage of CW arterial stenosis was similar between AD and control group ($p = 0.09$). The number of arteries with atheroma per CW was initially higher in AD compared to controls ($p = 0.02$). However, after multivariate analysis, this association disappeared ($p = 0.20$). AD subjects were older than the control group (80.1 ± 7.6 vs. 70.3 ± 11.5; $p < 0.001$) and this difference was the most important confounding factor in the association detected between AD and the extent of CW atherosclerotic disease in the univariate analysis. **Conclusions:** Cerebral artery atherosclerosis was associated with neuropathological-proven VaD, but not with AD in this population-based autopsy study, after adjusting the results for confounding, particularly age. Our results highlight the influence of aging as a important risk factor for dementia and atherosclerosis. However due to our small sample size, further population studies are needed to verify if the association between AD and CW atherosclerosis found in convenience sample studies are reproducible.

O2-07-06 ALTERATION IN STRUCTURAL PROTEINS IN WHITE MATTER INJURY IS ASSOCIATED WITH VASCULAR BRAIN INJURY

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Background: Three neuropathologic indices (Braak stage, microinfarctcount and cortical Lewy bodies) account for the majority of dementia in the Adult Changes in Thought study, a longitudinal community-based study of brain imaging. White matter injury (WMI) is an accepted contributor to cognitive impairment, but the pathology is poorly understood. Histopathologic measures of WMI are semi-quantitative and inconsistent. Biochemical analyses offer a less biased evaluation of white matter that might offer mechanistic insight. Structural components of white matter include astrocytes, axons and myelin, which can be interrogated through measurement of glial fibrillary acidic (GFAP), neurofilament 2f11 (NF) and myelin basic protein (MBP). **Methods:** Proteins were extracted from parietal white matter from 59ACT decedents. Protein extract underwent ELISA against GFAP, NF and MBP. The concentrations of GFAP, NF and MBP were analyzed in a regression model with Braak stage, micro infarct count and cortical Lewy bodies as covariates. Our *a priori* hypothesis was that protein concentration were related to these indices. **Results:** GFAP concentration was not related to Braak stage, micro infarct count or cortical Lewy bodies. NF and MBP concentrations were negatively associated with microinfarctcount ($p<.005$ and $p<.05$), and were not associated with Braak stage or cortical Lewy bodies. NF concentration was associated with micro infarcts in the basal ganglia ($p < 0.05$) and internal capsule ($p<.003$) but not with cortex and lobar white matter. NF and MBP concentration was associated with lobar white matter micro infarcts ($p < .05$) but not with basal ganglia or thalamic micro infarcts. **Conclusions:** Microinfarct number is associated with damage both to NF and myelin. Vascular injury may impact ischemia sensitive axons and oligodendrocytes. There does not appear to be a strong signal for pure demyelination from these findings. NF and MBP were more strongly associated with white matter microinfarcts suggesting either direct effects or shared microvascular pathology within the vascular beds specific to white matter.

O2-07-07 OXIDATIVE STRESS-INDUCED MITOCHONDRIAL DNA OVERPROLIFERATION AND DELETION, CELLULAR HYPOPERFUSION AND BRAIN HYPOMETABOLISM IN THE CONTEXT OF ALZHEIMER'S DISEASE: PAST, PRESENT AND FUTURE

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Background: It's widely accepted that during neuronal energy crisis, cerebral hypometabolism and cellular hypoperfusion are major and potentially treatable contributors to the loss of function in patients with stroke as well as AD. The mounting evidence indicates that targeting mitochondria with antioxidants and metabolites is a powerful treatment capable of restoring cell integrity and eliminating damage in the brain, resulting in significantly restored cognitive function and spatial memory. **Methods:** We have determined the pathology of mitochondria in brain vascular wall cells and neurons from human AD brain biopsies, human short postmortem brain tissues, aged rats, rat model of 2 vessel occlusion (2-VO), yeast artificial chromosome (YAC), and C57B6/SJL transgenic positive (Tg+) mice overexpressing amyloid beta precursor protein (AßPP) and ApoE4 mice. In situ hybridization, using mitochondrial DNA (mtDNA) probes for human wild type, 5kb deleted and mouse mtDNA, was performed in conjunction with immunocytochemistry. We have also measured age-dependent effects of the human ApoE-e4 on cerebral blood flow (CBF) using ApoE-e4 transgenic mice compared to age-matched wild-type (WT) mice by use of [14-C] iodoantipyrene autoradiography. Spatial memory and temporal memory tests were also employed to determine the potential protective effects of ALCAR+LA as a selective mitochondrial antioxidants treatment. **Results:** A significantly higher degree of mitochondrial structural alterations coexist with mitochondrial DNA overproliferation and/or deletion in all brain cellular compartments in AD and in animal models used when compared to age-matched controls and non-treated subjects. ApoE-e4 associated factors reduced the CBF gradually and created brain hypoperfusion when compared to the WT, and the differences in CBF were greatest as animals aged from 6 weeks to 12 months. The aged rats and ApoE-e4 mice that received ALCAR+LA treatment showed an absence of any visible damage in brain cellular compartments and improvement of cognitive function. **Conclusions:** Our conclusion is that for the first time we were able to demonstrate the potential pharmacologic modulation of brain hypometabolism and therefore the cognitive improvements by using a combination of selective mitochondrial antioxidants/ metabolites.