in 175 patients (prevalence rate: 4.8%); 77.7% being an ADWA (136 patients, prevalence rate: 3.7%), 5.1% an AD with depressive mood and 14.9% a mixed AD. Prevalence rate of ADWA was 4.8% and 3.5% among the patients included respectively by psychiatrists or GPs($p = 0.13$). The main life stressor events involved in ADWA development were: serious personal illness or health problem (29.4%), illness of a family member (20.6%), familial conflict (12.5%), problems with children (as child leaving the family, divorce…)(7.4%), and work-related problems (7.4%). On Sheehan disability scale, at least moderate discomfort was observed in 82% of patients and a severe discomfort in 48.2%. **Conclusions:** The ADWA is frequent in aged patients with a prevalence rate of 3.7%. This underlines the importance of the phenomenology and suggests to study the link between anxiety and possible occurrence of dementia.

P2-188 CIRCADIAN ACTIVITY RHYTHMS AND RISK OF INCIDENT DEMENTIA AND MILD COGNITIVE IMPAIRMENT IN OLDER WOMEN

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Background: Previous cross-sectional studies have observed alterations in activity rhythms in patients with dementia but the direction of causation is unclear. We determined whether circadian activity rhythms measured in community-dwelling older women are prospectively associated with risk of incident dementia or mild cognitive impairment (MCI). **Methods:** A prospective cohort study of healthy older women (mean age 83 years) from three US clinic sites was performed among 1,282 community-dwelling women from the Study of Osteoporotic Fractures cohort. Circadian activity rhythm data were collected in 2002-2004 with wrist actigraphy for a minimum of three 24-hour periods. Parameters of interest included time of peak activity (acrophase), height of activity peak (amplitude), mean activity level (mesor), and strength of activity rhythm (robustness). Each participant also completed a neuropsychological test battery and had clinical cognitive status (dementia, MCI or normal) adjudicated by an expert panel approximately 5 years later. All analyses were adjusted for demographics, BMI, exercise, functional status, depression, medications, alcohol, caffeine, smoking, self-reported health status, and co-morbidities. **Results:** After 4.9 years of follow-up, 195 (15%) women had developed dementia and 302 (24%) had developed MCI. When compared to women with average timing of peak activity (1:34PM-3:51PM), those whose timing of peak activity occurred later in the day (after 3:51PM) had an increased risk of developing dementia (Odds Ratio [OR] = 1.67, 95% Confidence Intervals [CI], 1.07-2.61) or MCI (OR = 1.73, 95% CI, 1.15-2.61). Compared with women in the highest quartiles of amplitude or rhythm robustness, those in the lowest quartiles had a higher likelihood of developing dementia or MCI (Amplitude, OR = 1.54, 95% CI, 1.07-2.21; robustness OR = 1.55, 95% CI, 1.08-2.22). **Conclusions:** Among older women without cognitive impairment at baseline, those with weak and late-shifted circadian activity rhythms have increased odds of developing dementia and MCI. If confirmed in other prospective cohorts, studies will be needed to test whether interventions (e.g. physical activity, bright light exposure) that influence circadian activity rhythms will reduce the risk of cognitive decline in the elderly.

P2-189 RISK FACTORS FOR PRIMARY BRAIN ATROPHY, A COMMON CAUSE OF DEMENTIA

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Background: Prior reports from the Honolulu-Asia Aging Study (HAAS) and other large community-based autopsy projects have demonstrated associations of dementia with several specific brain lesions, including Alzheimer lesions, microvascular infarcts, cortical Lewy bodies, and hippocampal sclerosis. Generalized brain atrophy is often observed with AD lesions and/or with microvascular infarcts, and increases the likelihood of dementia. When atrophy occurs with negligible levels of all recognized dementia-related lesions, it is referred to as primary brain atrophy (PBA). **Methods:** The HAAS is a longitudinal study of 3734 Japanese-American men born 1900-1920. Among 442 autopsied HAAS decedents aged 73-97 at death, severe brain atrophy occurred in 96, including 19 with PBA. Approximately 60 candidate factors defined prospectively in middle and late life were examined as possible predictors of PBA. Analyses were conducted using linear and logistic modeling, with the non-PBA comparison group defined in several alternative ways (with and without other lesion types), controlling for age at death, education, and other variables. **Results:** Among autopsied decedents with severe brain atrophy, dementia or definite cognitive impairment had occurred in 69% with AD lesions, 65% with microvascular infarcts, 84% with mixed lesions, 10% without recognized neuropathologic lesions, and in 50% with PBA. All of the PBA cases who had been demented had received a diagnosis of AD during life. Only midlife systolic hypertension and short height were significantly and consistently associated with PBA. **Conclusions:** Although severe primary brain atrophy appears to be an important "cause" of dementia distinct from AD, vascular dementia, and other diagnoses, its pathogenesis is not understood. Dementia in PBA was incorrectly diagnosed as AD. A search for middle and late life predictors of PBA identified only midlife systolic hypertension and short height.

P2-190 USE OF AN FDG-PET DERIVED HYPOMETABOLIC CONVERGENCE INDEX ENRICHMENT STRATEGY TO REDUCE SAMPLE SIZES IN ALZHEIMER'S DISEASE CLINICAL TRIALS: FINDINGS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI)

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Background: While the Alzheimer's disease Assessment Scale-Cognitive Subscale (ADAS-Cog) is commonly used to measure cognitive decline in probable Alzheimer's disease (pAD) and mild cognitive impairment (MCI) patients, rates of decline vary. We previously introduced a single index, Hypometabolic Convergence Index (HCI), to characterize the extent to which the pattern and magnitude of cerebral hypometabolism in a person's fluorodeoxyglucose-positron emission tomography (FDG-PET) image corresponds to that in pAD patients. Here, we used data from ADNI to examine the extent to which 1) a person's baseline HCI predicts cognitive decline using the ADAS-Cog, Mini-Mental State Exam (MMSE), Clinical Dementia Rating-sum of boxes (CDR-SB) and Auditory-Verbal Learning Test (AVLT-Total), and 2) the HCI could be used to enrich clinical trials for clinical decline and reduce the number of patients needed to detect a treatment's clinical effects. **Methods:** Baseline HCIs were computed for 120 MCI and 54 mild AD patients who had up to 24-month data. We first characterized the extent to which HCIs correlated with 12-month and 24-month clinical declines. We then estimated the sample sizes needed to detect an AD-slowing treatment's effects on ADAS-Cog before/after enrichment for those patients with HCIs greater than the predetermined threshold of 13.82 for pAD and 8.19 for MCI (Chen et al., 2011, Neuroimage) with 80% power, 0.05 type-I error and a 25% treatment effect. **Results:** In pAD, HCIs correlated ($p <= 0.05$) with subsequent ADAS-Cog, MMSE, CDR-SB and AVLT-Total 12-month(24-month) decline ($r = 0.42(0.47)$, -0.35(-0.55), 0.28(0.29), -0.40(-0.43), respectively). In MCI, HCI also correlated with subsequent decline at 12-month(24-month) ($r = 0.33(0.32)$, -0.43(-0.50), 0.29(0.37), -0.17(-0.32), respectively). HCI enrichment is estimated to reduce the number of pAD patients needed per treatment arm to detect an AD-slowing treatment's effect on ADAS-Cog from 406 to 243 in a 12-month trial and from 168 to 137 in a 24-month trial. Similarly, it is estimated to reduce the number of MCI patients from 1,718 to 749 in a 12-month trial and from 926 to 374 in a 24-month trial. **Conclusions:** Baseline HCIs could be used to predict subsequent clinical declines in pAD and MCI patients and to reduce the number of patients needed to detect an AD-slowing treatment's effects in randomized clinical trials.

P2-192 LEUKOENCEPHALOPATHY AND MICROHEMORRHAGES

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Background: Amyloid angiopathy is a common disease in elderly population and Alzheimer's disease (AD), due to ß-amyloid deposition in small and medium cerebral vessels. Frequently asymptomatic or related to lobar brain hemorrhage, more rare presentations include, sub acute encephalopathy, headache, epilepsy or focal signs, characterized by leukoencephalopathy and/or vasogenic edema. Immunosuppressive treatment results in clinical and imagiological recovery. **Methods:** We present a case report. **Results:** A seventy year-old female, caucasian, with mild previous cognitive deterioration, initiates confusion, severe headache and vomits. Arterial pressure values were normal. Neurological examination disclosed temporal-spatial disorientation, severe impairment of immediate verbal memory, executive dysfunction, visuo-construtive apraxia, acalculia, bilateral papilledema and hyperactive myotatic reflexes. MRI showed extensive subcortical and periventricular leukoencephalopathy. Lumbar puncture revealed high proteins, low ß-amyloid peptide 42 and high p-tau. Analytic evaluation was normal. The patient was treated with one week of endovenous corticotherapy, with total clinical recovery, and significant leukoencephalopathy reduction. One year after, new acute cognitive impairment with agitation and hallucinations. Neurological examination was similar with the previous. MRI disclosed a new left frontal leukoencephalopathy and disperses microhemorrhages. Cerebral angiography was normal. Treatment with oral corticotherapy was begun and maintained during 6 month with clinical and imagiological improvement. **Conclusions:** We present a case of AD with episodes of sub-acute encephalopathy and reversible leukoencephalopathy with corticotherapy. Clinical, imagiological and therapeutic response support the possibility of cerebral amyloid angiopathy related inflammation. This is an important diagnosis to consider because of its reversibility with correct treatment, and in AD cases, to avoid anti-amyloid therapeutic because of its potential risks.

P2-193 TREATMENT EFFECTS ON HIPPOCAMPAL DEGENERATION IN DEMENTIA OF THE ALZHEIMER TYPE

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Background: Treatment of patients with moderate-to-severe Alzheimer's Disease (AD) using the combination of donepezil, acholinesterase inhibitor, and memantine, an NMDA antagonist, is well tolerated and has been shown to provide cognitive and behavior benefits. Other recent research suggests that memantine may also provide similar benefits to patients with more mild disease. Previously, we showed that hippocampal surface deformities were present early in the course of illness in individuals with very mild dementia of the Alzheimer type (DAT) and were correlated with a poor response to donepezil treatment. However, treatment with donepezil did not slow the progression of hippocampal deformation in individuals with DAT as compared to untreated individuals. In this study, we compared rates of change in hippocampal volume and surface structure inpatients with very mild and mild DAT who were treated with the combination of memantine and donepezil, donepezil alone, or no drug treatment. Cognitively normal individuals were used as a reference group for all groups of DAT patients. **Methods:** Fifty-six (56) cognitively normal individuals, 14 very mild and mild DAT patients treated with the combination of memantine and donepezil, 18 very mild and mild DAT patients treated with donepezil alone, and 14 untreated DAT patients were recruited for this study. Drug treatment was selected by the patients' clinicians and followed published recommendations with target does of 10 mg/daydonepezil and 20 mg/day memantine, limited by tolerability. At each longitudinal assessment, the Alzheimer Disease Assessment Scale-cognitive subscale (ADAS-Cog) total score was used as the primary measure of dementia severity, and the Clinical Dementia Rating (CDR) scale was used as a secondary measure of dementia severity. MRI scans were collected using MPRAGE sequences approximately two years apart on 1.5-Tesla Siemens Vision MRI platform. Longitudinal, large-deformation diffeomorphic metric mapping (LDDMM) was applied to all scans to generate hippocampal surfaces and surface zones corresponding to the underlying CA1, subiculum and remainder (CA2-4, dentate gyrus) cellular subfields. Rates of change in total hippocampal volume and the degree of surface subfield displacement were computed, and compared across all groups. **Results:** At baseline, main group effects were significant for hippocampal volume and all subfield deformations. Between-group contrasts showed differences between all groups of DAT patients and the group of cognitively normal individuals. However, the three DAT groups (untreated, donepezil-treated and combination-treated) did not differ from each other on any of the hippocampal measures. There were no significant main group effects in the rates of change of hippocampal volume or any subfield deformation. Again, although all three groups of DAT patients differed from the group of cognitively normal individuals, the three groups of DAT patients did not differ from each other in rates of change of hippocampal volume or in the degree of CA1 or subiculum subfield deformation. We then