30 AD patients and 30 non-demented controls (NDC). The AD subjects were diagnosed according to NINCDS-ADRDA and DSM-IV criteria. We measured the glycosylation of serum glycproteins using lectin blot analysis and improved lectin enzyme-linked immunosorbent assay. The study was approved by the Tottori University Ethical Committee and informed consent was obtained from each patient or their relatives prior to inclusion in the study. The study was performed in accordance with the Helsinki Declaration. **Results:** We identified several kinds of sugar chain in some serum glycoproteins were altered in AD patients compared with NDC groups. And these changes were observed in early stage of AD. **Conclusions:** These data implicate glycosylation changes in AD patients are potential biological markers to diagnose with serum. Moreover, the aberrations are prospective to detect the initial phase of AD.

P3-192 CONFORMATIONALLY ALTERED P53 AS A PERIPHERAL MARKER FOR MILD ALZHEIMER'S DISEASE

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Background: The identification of biological markers of mild Alzheimer's disease (AD) can be extremely useful to improve diagnostic accuracy and/or to monitor the efficacy of putative therapies. In this regard, peripheral cells may be of great importance because of their easy accessibility. Previous studies suggest conformationally altered p53 may be overexpressed in mononuclear cells from AD patients. **Methods:** We measured the mononuclear cells expresion of a conformationally altered p53 in 50 patients with mild Alzheimer's disease, 50 patients with mild cognitive impairment and age-matched 60 controls. Two independent methods to evaluate the differential expression of a conformational mutant p53 were developed. Mononuclear cells were analyzed by immunoprecipitation or by flow cytometric analysis, following incubation with a conformation-specific p53 antibody, which discriminates unfolded p53 tertiary structure. Patients with mild cognitive impairment were followed for 1 year. **Results:** Mononuclear cells from mild AD patients express a statistically significantly higher amount of mutant-like p53 compared to mononuclear cells from controls. Mononuclear cells from MCI patients who converted to AD also tended to express a higher (not statistically significant) amount of mutant-like p53 compared to patients with MCI who did not convert. **Conclusions:** This study support the possibility of using the conformational mutant p53 as a new putative marker in the early diagnosis of Alzheimer's disease.

P3-193 THE PLASMA Aβ42/Aβ40 RATIO: A PROMISING BIOMARKER FOR COGNITIVE DECLINE

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Background: Although some studies have found lower plasma levels of Amyloid-β (Aβ) 42 and Aβ42/Aβ40 plasma ratio associated with incident dementia, findings have been mixed. This study investigates the association between the Aβ42/Aβ40 plasma ratio and cognitive decline over nine years in a biracial cohort of adults aged 70-79. We also evaluate the association in selected subgroups. **Methods:** We studied 997 participants in the Health ABC study. Cognitive function was measured serially with the Modified Mini-Mental State Exam (3MS) and Digit Symbol Substitution Test (DSST). The Aβ42/Aβ40 ratio (measured with Innogenetics INNO-BIA assays at Mayo Clinic, Jacksonville, FL) was categorized into ''low'' ''medium'' and ''high'' tertile. We used mixed effects repeated measures models to determine the association between tertile and nine-year decline in cognitive function. We stratified models by race, sex, education and APOEe4 and tested for interactions. **Results:** At baseline, average age was 74.0 years, 55.2% were female, and 54.0% were Black. After adjustment for age, race, sex, education, and diabetes, lower Aβ42/Aβ40 was associated with greater 9-year cognitive decline, on the 3MS (Low -6.58 $\pm$ 0.63 points, Medium -6.32 $\pm$ 0.60, High -3.58 $\pm$ 0.62, $p = 0.01$) and on the DSST (-6.57 $\pm$ 0.68 points, -6.81 $\pm$ 0.66, -4.41 $\pm$ 0.67, $p = 0.02$). In stratified adjusted models, the association between the Aβ42/Aβ40 ratio and decline over 9 years was stronger in blacks compared to whites (3MS: inter-tertile difference [low-high] -3.23 points for blacks vs. -1.84 points for whites, p for interaction <0.001; DSST: -3.43 vs. -1.34, $p < 0.001$), and in those with less education (3MS: -3.55 for $<$HS vs. -2.36 for $\geq$HS, $p < 0.001$; DSST: -2.69 vs. -1.95, $p < 0.001$). There was no significant interaction between Aβ42/Aβ40, cognitive decline and APOE e4 or sex. **Conclusions:** Lower plasma Aβ42/Aβ40 predicts greater cognitive decline over 9 years, and this association was stronger in blacks and those with less education. As plasma levels can be obtained easily, Aβ42/Aβ40 may be a promising biomarker of cognitive impairment, especially in certain groups.

P3-194 REGIONAL DIFFERENCES IN AMYLOID LOAD AND CORTICAL CHOLINERGIC PLASTICITY DURING THE PROGRESSION OF ALZHEIMER'S DISEASE

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Background: Cholinergic activity is up-regulated in the superior frontal cortex (SFC) but remains stable in other cortical regions in mild cognitive impairment (MCI). The relation between cortical cholinergic activity and amyloid pathology across clinical stages of Alzheimer's disease (AD) remains unclear; this is clinically relevant given the diagnostic potential of amyloid imaging and the established role of cholinergic neurotransmission dysfunction in AD. **Methods:** SFC and posterior medial parietal cortex (precuneus) were harvested postmortem from subjects with clinical diagnoses of MCI, no cognitive impairment (NCI), or mild-moderate AD (mAD). Samples were evaluated for choline acetyltransferase (ChAT) activity, and for amyloid load by a [H-3]PiB (Pittsburgh Compound-B) binding assay. **Results:** Precuneus [H-3]PiB binding distinguished clinical groups (NCI$<$MCI$<$mAD), while SFC [H-3]PiB binding was significantly increased only in the mAD group. Precuneus ChAT activity levels were significantly reduced in mAD ((NCI, MCI)$>$mAD)), while SFC ChAT activity was significantly increased in the MCI group relative to both NCI and mAD (NCI$<$MCI$>$mAD). In the precuneus, [H-3]PiB binding correlated inversely with regional ChAT activity ($r = -0.65$, $p < 0.0001$); MMSE scores correlated inversely with [H-3]PiB binding ($r = -0.86$, $p < 0.0001$) and directly with ChAT activity levels ($r = 0.61$, $p < 0.001$). In the SFC, there was a weak inverse correlation of [H-3]PiB binding with ChAT activity ($r = -0.37$; $p < 0.05$). MMSE scores correlated weakly with ChAT activity ($r = 0.36$; $p < 0.05$) and strongly with [H-3]PiB binding in the SFC ($r = -0.70$; $p < 0.0001$). **Conclusions:** PiB binding in the SFC differentiates mAD, but not MCI, from NCI subjects. SFC ChAT activity is increased in MCI, while in mAD it is comparable to control levels. In contrast, PiB binding in the precuneus differentiates the three clinical groups. Despite the significantly increased precuneus PiB binding in MCI, precuneus ChAT activity was stable, and decreased only when PiB binding reached levels seen in mAD. The present observations of up-regulated SFC ChAT activity before PiB binding reaches levels seen in mAD, and of stable precuneus ChAT activity despite high levels of PiB binding in MCI, suggest that amyloid may not be a necessary precondition of cholinergic enzyme changes in prodromal AD.