ß-Amyloid isoforms (Aβ(1-38), Aβ(1-40), Aβ(1-42)). The presented results demonstrate that these kits are suitable for large-scale automated measurement (specific, precise, accurate) in EDTA plasma, and are potential tools in the (pre-) clinical stages of drug development.

P3-189 PLASMA METABOLIC ALTERATION IN MCI AND ALZHEIMER'S DISEASE SUBJECTS

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Background: Effective therapies in Alzheimer's disease (AD) are associated with the identification of early biomarkers that anticipate the clinical diagnosis of the disease. The accumulation of β-amyloid and the cerebral alterations associated to AD started 10-15 years before the clinical onset. In this lag time the biological events responsible of the disease progress could be monitored The clinical phase usually starts with "mild cognitive impairment" (MCI), during which subjects have measurable cognitive deficits with no influence on the life activities, even though the clinical progression may then fulfill criteria for different types dementias. Biomarkers are needed to improve the diagnostic sensitivity and specificity and to monitor the disease progression from MCI to AD. Until accurate preclinical indicators are defined and validated, the promise of disease-modifying therapeutic strategies for AD will remain elusive. **Methods:** We analyzed 129 plasma samples from 23 normal cognitive controls (NC), 68 MCI and 38 AD patients using a targeted quantitative liquid chromatography-mass spectrometry (LC-MS) platform (AbsoluteIDQ 180 kit, Biocrates) allowing the simultaneous quantification of amino acids, biogenic amines, acylcarnitines, glycerophospholipids, sphingomyelins. **Results:** Multivariable logistic regressions highlighted 21 metabolites whose abundance changed significantly among the study populations. There was a general upward trend from NC to AD of low-saturated long-chain sphingomyelins (SM), lysophophatidylcholines (LPC), diacyl and acyl-alkyl phosphatidylcholins (PC-aa and PC-ae) and octadecanoylcarnitine. On the contrary, lysine was the only metabolite whose concentration was higher in NC than in MCI and AD. None of the metabolites was significantly association with clinical biochemical features, APOE genotype and neurocognitive scores. The analyses identified a combination of four metabolites [SM-C20:2+PC-ae-C34:0+LPC-C28:0+Lys] that together with BMI discriminated NC from AD with 96% accuracy (AUC 0.96), while [PCaa-C28:1+Lys+BMI] were able to differentiate NC from MCI with an AUC of 88%. **Conclusions:** Our findings are in accordance with prior studies reporting variations of circulating lipids profile as early predictors of memory impairment, probably reflecting the breakdown of neural cell membrane. Moreover, lysine perturbation would call for an early derangement in mitochondrial energy production. Establishment of the pathogenic relevance of our findings are on-going in a follow-up study aimed at monitoring the conversion from MCI to AD status.

P3-190 RELATIONSHIP BETWEEN SERUM PESTICIDE LEVELS AND COGNITIVE FUNCTION IN ELDERLY INDIVIDUALS IN THE UNITED STATES: RACE/ETHNICITY DIFFERENCES

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Background: Alzheimer's disease (AD) risk is reported to be higher among Mexican-Americans and African-Americans compared to Non-Hispanic Whites. Although the reasons for these disparities are not known, differences in genetics, medical conditions and socioeconomic factors are thought to contribute. Previously, we reported that higher serum levels of the organochlorine pesticide metabolite p,p'-DDE were associated with increased risk of AD and reduced cognitive function, among Non-Hispanic Whites (Richardson et al., 2014). Here, we sought to determine whether serum pesticide levels were associated with race/ethnicity differences in cognitive function of elderly individuals using data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative health survey of the resident US population. **Methods:** Data were merged from the 1999-2000 and 2001-2002 NHANES cycles in which oversampling was conducted among persons of Mexican-American and Non-Hispanic Black race/ethnicity, and persons 70 years of age and older. Cognitive function was assessed in a total of 776 individuals aged 60-84 using the Wechsler Adult Intelligence Scale, and the Digital Symbol Substitution Test (DSST). Serum p,p'-DDE and its parent compound p,p'-DDT were measured at the Centers for Disease Control and Prevention using gas chromatography/mass spectrometry. Exposure-response relationships between DDT, DDE and DSST scores were determined using regression models. **Results:** Of the 776 individuals, 667 completed the DSST task including 396 Non-Hispanic Whites, 142 Mexican-Americans and 87 Non-Hispanic Blacks. The lowest scores on the DSST were observed in the highest category of DDT and DDE. Single metabolite models were adjusted for serum lipids and other potential confounders, including poverty index ratio, education, sex, age and BMI. We observed a significant inverse relationship between low cognitive function and high serum concentrations of DDT (-2.2, $p = 0.019$). When stratified by race/ethnicity, the inverse relationship between DDT and DSST was statistically significant only among Mexican Americans (-3.3, p=0.02). A similar effect was observed with DDE (-1.9, p=0.04). **Conclusions:** Environmental factors such as pesticide exposure may contribute to the reported increased risk of AD in Mexican-Americans (O'Bryant et al., 2014, 2015).

P3-191 RISK FACTORS ASSOCIATED WITH DECREASED CORTICAL THICKNESS IN DEMENTIA FREE OKINAWAN ELDERY

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Background: Cortical gray matter (GM) decline is a hallmark of neurodegenerative disease; however, its etiology and implication in dementia-free aging is unclear. The aims of this study were to: 1) investigate the impact of cortical thickness on cognition, and, 2) examine systemic inflammation and cerebrovascular disease (CVD) as potential risk factors for GM degeneration. **Methods:** 91 dementia-free Okinawan participants (mean age 83.6) from the Keys to Optimal Cognitive Aging (KOCOA) Project underwent MRI, cognitive, and physical evaluation. Mean cortical thickness (MCT) was derived using FreeSurfer. Serum markers of inflammation and CVD risk were obtained. CVD risk status was calculated based on >2 of the following: ever smoked, glycosylated hemoglobin >5.6, systolic blood pressure > 139, taking anti-hypertension medication, serum triglyceride >150, and high density lipoprotein < 40 in men, or < 50 in women. Inflammatory markers included: interleukin-6 (IL6) and high-sensitivity C-reactive protein (hsCRP). Subjects were surveyed regarding physical activities (PA), including walking and yoga. Multivariate analyses examined relationships between MCT and memory (mini mental word recall) and executive function (verbal fluency). Spearman's rank order correlation or t-tests examined the relationships between MCT and: age, PA, CVD risk, and inflammatory markers. Voxel based morphometry (VBM) examined relationships between regional GM density and factors significant in the previous univariate analysis. Exploratory analyses examined systemic inflammation in relation to PA. **Results:** After adjusting for age, gender, and %hippo volume, decreased MCT was associated with worse memory, but not executive function. In univariate analyses, decreased MCT was associated with increased IL6 (0.04), but not with age, PA, hsCRP or CVD risk. VBM analysis demonstrated greater IL6 to be associated with decreased cortical density in the inferior and middle temporal cortex, bilaterally. After adjusting for age and gender, greater yoga participation ($p = 0.02$), but not walking, was associated with lower IL6 levels. **Conclusions:** Decreased MCT is associated with worse memory performance in dementia free-Okinawans. Greater IL6 was related to decreased temporal lobe cortical thickness, and decreased PA. Low-impact stretch activities, such as yoga, should be further explored as potential ways to decrease systemic inflammation and prevent cortical thinning and memory loss in older individuals.

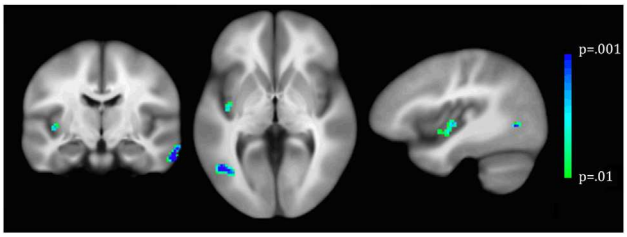

Figure 1. VBM analysis with threshold-free cluster enhancement and permutation testing to correct for multiple comparisons. Colored voxels indicate regions of decreased GM density significantly associated with higher IL6, age and gender adjusted.

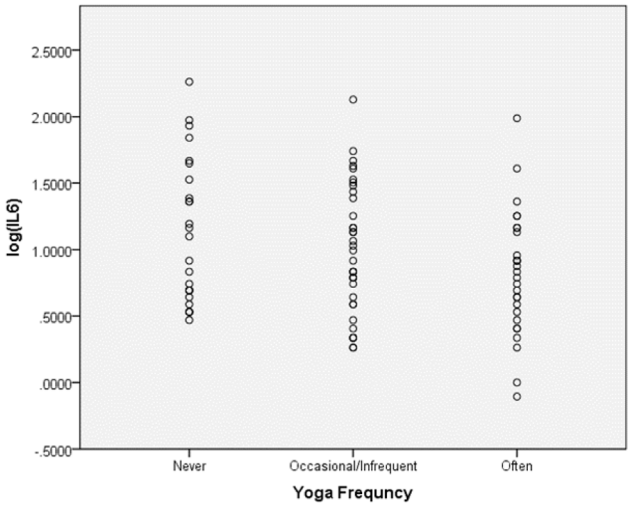

Figure 2. Serum IL6 in relation to yoga frequency ($p = 0.02$ in final model adjusted for age and gender).

Table 1
Regions in which VBM identified significantly reduced GM density in comparison with increased IL6 ($p<0.01$)

	Coordinates				Cluster size	
Talairach Region	side	X	Y	Z	Voxels	Volume (cm^3)
Inferior and Middle Temporal Gyrus*	L	61.8	13.9	-18.7	238	1.904
Inferior and Middle Temporal Gyrus	R	-42.8	61.2	-0.3	64	0.512
Superior Temporal Gyrus	R	-49.6	-7.8	-12.3	57	0.456
Insula and Claustrum	R	-38.6	5.2	-2.3	56	0.448

*remained significant after cluster thresholding