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FLOW CYTOMETRIC MEASUREMENT OF MICROPARTICLES IN HUMAN CEREBROSPINAL FLUID OF NEURODEGENERATIVE DISORDERS

Yue Yang¹, Elaine R. Peskind², Eiron Cudaback³, Angela M. Wilson³, Thomas J. Montine⁴, C. Dirk Keene⁵, ¹University of Washington, Seattle, Washington, United States; ²VA Puget Sound Health Care System, Seattle, Washington, United States; ³University of Washington, Seattle, Washington, United States; ⁴University of Washington, Seattle, Washington, United States; ⁵University of Washington, Seattle, Washington, United States.
Contact e-mail: yangyue@uw.edu

Background: Cerebrospinal fluid (CSF) lipoprotein particles and cell derived microparticles have been shown to be associated with pathological conditions. Acknowledgment of their roles both as markers and pathogenic effectors in neurodegenerative disease has increased the interest of their measurement in clinical practice. However, assessment of their clinical use is impeded by technological issues. **Methods:** Here, we have described a quantitative flow cytometric assay by which annexin V + microparticles, apolipoprotein (apo)-E, -AI, -J containing lipoprotein particles, and A β 42 containing particles can be measured for concentration and size distribution in human CSF. We applied this technique to CSF from 126 research volunteers, and analyzed our results with respect to age, APOE genotype, and Alzheimer's disease (AD) or Parkinson's disease (PD) status. **Results:** APOE4/4 subjects with mild cognitive impairment (MCI) or AD dementia had apoE + particles that were larger but less concentrated on average than in APOE3/3 or APOE3/4. In vitro studies using mice with targeted replacement of mouse apoE gene with human apoE3 (E3 +/+) or apoE4 (E4 +/+) demonstrated that E4 +/+ mice had significantly lower apoE + particle levels than E3 +/+ mice in astrocyte conditioned medium, and E4 +/+ mice has significantly greater % of larger apoE + particles than E3 +/+ mice in microglia conditioned medium. Our data suggest that the effects of APOE genotype on the size and concentration of apoE containing particles in human CSF can be reproduced, at least in part, by primary cultures of mouse glial cells with no influence by processes of disease. We also observed that A β 42 was co-labeled with both apoE + and apoJ + particles in human CSF. Interestingly, the concentration of A β 42 containing particles was not significantly associated with the concentration of CSF A β 42 as determined by luminex. Both apoA-I + and annexin V + particle levels were significantly lower in human CSF of AD dementia than in older controls. Exploratory analysis for correlations among CSF particles demonstrated annexin V + and apoA-I + particle levels were positively correlated with each other, suggesting a potential biological interaction. **Conclusions:** Our results suggest annexin V and perhaps apoA-I particles in CSF might be diagnostically helpful addition to existing biomarkers for AD patients.

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SALIVARY BIOMARKER MODELING FOR ALZHEIMER'S DISEASE

Balwant Rai, KSI, Bluffton, South Carolina, United States.
Contact e-mail: raibalwant29@gmail.com

Background: Alzheimer's disease (AD) is a gradually progressing disorder in which pathophysiological abnormalities, detectable in vivo by biomarkers from cerebrospinal fluid, blood and saliva, lead to the appearance of clinical symptoms for many years. Biomarkers of amyloid- β plaques, tau-related neurodegeneration and inflammatory pathways are currently the main diagnostic tools used to confirm AD. Salivary biomarkers, if available, have the capability to offer multiple advantages over more invasive forms of testing including blood serum, or cerebrospinal fluid [CSF]. These include lower cost, minimal training requirements and ease of use. In addition the opportunity to provide an option which is pain-free for the patient is non-infectious and is easy to transport is compelling. The aim of this study was to find out the diagnostic value of salivary of bio-markers in AD patients **Methods:** Ten AD patients and ten [10] non-demented controls were selected for this study. Unstimulated saliva samples were taken from subjects in each group using the

simple "passive" drooling technique. The following panel of salivary biomarkers: IL-1 β , alpha amylase, A β (A β -40, A β -42) IGF-I, IGF-II and TNF- alpha, was used (1) **Results:** In this study, salivary IL-1 β , alpha amylase, A β (A β -40, A β -42), IGF-I, IGF-II and TNF-alpha have been shown to be significantly different in AD patients in comparison to normal healthy individuals **Conclusions:** In our opinion, we believe these salivary biomarkers can act as highly useful diagnostic tool for the detection of Alzheimer's disease.

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A 6-WEEK RANDOMIZED CONTROLLED TRIAL TO INCREASE SOCIAL INTERACTIONS USING HOME-BASED TECHNOLOGIES IMPROVED LANGUAGE-BASED EXECUTIVE FUNCTION

Hiroko H. Dodge¹, Molly Bowman¹, Jian Zhou², Nora Matteck¹, Katherine Wild³, Jeffrey Kaye¹, ¹Oregon Health & Science University, Portland, Oregon, United States; ²University of Michigan, Ann Arbor, Michigan, United States; ³OHSU, Portland, Oregon, United States.
Contact e-mail: dodgeh@ohsu.edu

Background: Past epidemiological studies have demonstrated that larger social networks or more frequent social interactions may have protective effects on the incidence of Alzheimer's Disease. This accumulating evidence suggests that increasing social interaction could be a promising intervention for improving the cognitive well-being of the elderly. We developed a randomized controlled behavioral clinical trial to examine whether conversation-based cognitive stimulation as delivered through the use of personal computers, webcams, and a user-friendly interactive Internet interface using a touch screen has high adherence and a positive effect on general and domain-specific cognitive functions among older adults with either normal cognition or mild cognitive impairment (MCI). The study presented here is the first report of this trial's results. **Methods:** Daily (except on weekends) 30 minute face-to-face communications were conducted over a six week trial period. Cognitive status of normal and MCI subjects was operationally defined as Clinical Dementia Rating (CDR) = 0 and 0.5, respectively. Age, sex, education and CDR score were used as balancing factors. Study subjects were recruited using mass-mailing invitations targeted to selected retirement communities. **Results:** 83 subjects who met the study inclusion criteria participated. The mean (sd) age was 80.5 (6.8) years old with 76% women. Adherence to the protocol among the experimental group was high; there was no dropout and mean % of days completed out of the targeted 30-day trial was 89% (range: 77%-100%). Among the normal cognition group, at the post-trial assessment, the experimental group improved on the semantic fluency test (category fluency) (p=0.003) and at the 6-week assessment conducted to assess retention effects, on the phonemic fluency test (letter fluency) (p=0.004), in comparison with the control group. **Conclusions:** Social engagement interventions (daily conversations) using user-friendly Internet communication programs demonstrated high adherence among octogenarians. The experimental group showed significantly greater improvement in neuropsychological test scores that tap language-based executive functions, despite the short duration of the trial period. Increasing daily social contacts through communication technologies could offer cost-effective execution of home-based prevention trials. Larger trials are warranted to examine their translational effects on everyday living.

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TAILORING NAVIGATION SUPPORT TO THE NEEDS AND CAPABILITIES OF PERSONS WITH MCI AND EARLY AD

Philipp Koldrack¹, Stefan J. Teipel², Thomas Kirste³, ¹German Center for Neurodegenerative Diseases (DZNE), Rostock, Germany; ²University Medicine Rostock and DZNE Rostock, Rostock, Germany; ³University of Rostock, Rostock, Germany. Contact e-mail: philipp.koldrack@dzne.de

Background: Social activities usually require leaving home. Spatial disorientation caused by cognitive decline due to Alzheimer's disease (AD)