collaborated to customize a playlist of songs to suit each individual. Songs from the playlist were then played to the residents, but included several totally unfamiliar songs. Reactions to known songs were compared to unfamiliar songs. The second phase explored the degree to which the same residents could independently learn how to operate simple controls (volume, mute, skip). The final phase was to observe the social dynamics around the use of the chair in a common area over a multi-day period. **Results:** The analysis of direct observations, oral feedback from the residents participating in the study and comments from care staff on duty are presented. The discussion addresses issues of usability by people with different levels of cognitive status and the impact of the music player on family interaction in creating the playlists and during consequent visits. **Conclusions:** The research suggests that the music player has the potential to enhance the well-being of residents in care homes.

O3-08-06 THE COACH: A REAL-WORLD EFFICACY STUDY

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Background: Globally the number of people living with Alzheimer's disease (AD) is expected to continue to rise. AD and other forms of dementia negatively affect quality of life; particularly when activities of daily living (ADL) become challenging or even impossible to complete. Intelligent assistive technologies (AT) pose one possible solution to ease the burden associated with ADL support, but few AT ever undergo real-world trials leading to low user acceptance and adoption. The COACH is an intelligent computer-based AT that has been shown in supervised clinical trials to support older adults with dementia through the ADL of hand washing by emulating caregiver guidance. An overhead camera tracks the user and communicates assistance - using audio and video prompts - when needed. This study presents the results of an efficacy study of the COACH in a real-world, community-based deployment. **Methods:** The COACH has been installed in a washroom at the Toronto Memory Program, a multidisciplinary, community based, medical facility in Toronto, Canada, specializing in the diagnosis and treatment of Alzheimer's disease and related disorders. The COACH is running in an unsupervised state, interacting with users when the task is not progressing. Video, currently being collected from the overhead camera, will be manually annotated to determine the system's efficacy. Data will be collected from approximately 300 study participants over a six month period from December 2011 to May 2012. **Results:** The efficacy of the COACH will be presented within four categories: 1) tracking accuracy -the system's ability to track multiple users without user-specific calibration; 2) decision-making - how well the system makes decisions under sensor uncertainty; 3) prompt effectiveness - the system's ability to stimulate users to resume progress in the task after stopping; and 4) technical system challenges - potential hardware and software failures. Based on preliminary data anticipated results suggest that methods of tracking multiple users will need further development and decision making policies need to be more robust. **Conclusions:** Findings will be discussed toward the translation of the COACH beyond a device shown effective in clinical trials into an intelligent assistive technology that supports older adults with dementia in their homes.

ORAL SESSIONS: O3-09 CELLULAR AND MOLECULAR MECHANISMS: NEUROPATHOLOGY

O3-09-01 ALZHEIMER'S DISEASE PATHOLOGY BURDEN ASSOCIATED WITH CLINICAL DEMENTIA DECREASES WITH AGE

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Background: Age is the number one risk factor for dementia, specifically Alzheimer's disease (AD). Previous studies have suggested that AD pathological burden is a less salient etiological factor for dementia in older individuals. Few have objectively examined tissue markers of AD pathology in relation to age of dementia onset (DO). **Methods:** 285 volunteers evaluated through the Oregon Alzheimer's Disease Center underwent brain autopsy with CERAD plaque and Braak neurofibrillary tangle staging, and had frozen brain tissue available for histochemical analysis. 104 volunteers had DO at age 60 or older, with Alzheimer's pathology as a likely contributor to their dementia by Braak staging (III or greater). Brain was serially extracted in detergent solutions and residual detergent-insoluble protein was evaluated by ELISA to determine beta-amyloid and tau. Vascular disease presence was determined through tissue microscopic examination. Multiple regressions were examined to determine relationships between DO age and pathological measures, adjusting for dementia duration, vascular disease, and brain weight. **Results:** The mean age at death was 84.8± 9.1. Vascular pathology was present in 64%, and was associated with increased age of DO ($p = 0.008$). In separate multiple regression analyses, older age at DO was associated with decreased total tau ($p = 0.0007$), lower Braak stage ($p = 0.02$), lower abeta-42 ($p < 0.09$), and lower CERAD score ($p = 0.02$). Vascular disease was associated with older DO in all models. In a final model including both tau protein levels and CERAD score, decreased tau levels, lower brain weight, and the presence of vascular disease were associated with increased age of DO, while CERAD scores were only weakly related. **Conclusions:** The degree of AD pathology burden in those with clinical dementia decreases with advanced age, a finding not fully accounted for by brain atrophy and the presence of vascular disease. These results suggest that the aging brain may be more susceptible to the effects of abnormalities in tau than those in beta-amyloid pathology, and that biochemical determinations of tau may reveal this susceptibility better than scoring measures. Further studies investigating tissue markers accounting for dementia risk are needed.

O3-09-02 CAUCASIANS AND AFRICANS HAVE DIFFERENT SUSCEPTIBILITY TO NEURITIC PLAQUES: A POPULATION-BASED CLINICOPATHOLOGICAL STUDY USING GENETIC ANCESTRY-INFORMATIVE MARKERS

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Background: Epidemiological studies suggest that Africans have a higher risk to develop Alzheimer's disease (AD) than Caucasians, suggesting ethnic-based differential susceptibility to AD. However, this is still a controversial matter that required clarification from studies using large admixed populations, preferentially exposed to the same environmental factors, in which the ethnicity is reliably determined and with postmortem assessment validation. In a study with a series showing the characteristics described above (n=202), we demonstrated that Africans have a lower risk of showing neuritic plaques, even after adjustment for several factors. These results in principle disagree with the epidemiological studies. Here, we aimed to determine if ethnicity impacts AD clinical threshold. **Methods:** Brain samples of subjects older than 50 years (n=268) from the Brazilian Aging Brain Study Group, collected from 2004-2009, were studied. Seventy-nine cases were excluded because the presence of non-AD dementia-related changes. Study samples do not significantly deviate from census data for demographics. Knowledgeable informants were interviewed by trained nurses. The questionnaires included cognitive evaluation Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) and CDR. The multivariate linear regression model used IQCODE as outcome; ancestry and semi-quantitative AD neuropathological measures as independent variables and was adjusted for demographics, ApoE and head circumference. Ancestry was determined through ancestry-informative markers. **Results:** Out of the 181 subjects (mean age; 72.1±11.6; 56%F), 52.5% had significant African ancestry. There were no differences in demographics between the groups. The Africans showed worse cognition scores, when compared to Caucasians having similar neuritic plaque burden ($p<0.03$) after all adjustments.

Conclusions: Despite a lower susceptibility to show neuritic plaques, once this process is established, neuritic plaques are more deleterious to cognition in Africans than in Caucasians. Considering that the studied population share similar demographics and dwells in an acculturated city, we hypothesize that these differences are product of genetics. Several gene variations related to the amyloid cascade have been identified in GWAS. To determine if these variations impact varies according to ethnicity may lead to a better understanding about protective and risk factors to AD and suggest the need of ethnic-based therapeutic schemes.

O3-09-03 LONGITUDINAL REDUCTION IN BLOOD PRESSURE IN HYPERTENSIVE INDIVIDUALS IS ASSOCIATED WITH INCREASED LEVELS OF BIOMARKERS FOR ALZHEIMER'S DISEASE

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Background: In hypertension (HTN), cerebral blood flow (CBF) regulation limits are changed and the blood pressure (BP) threshold at which CBF is safely maintained is higher. This shift may increase the brain's vulnerability to hypoperfusion at lower BP. Despite growing recognition of the link between hypoperfusion and neurodegeneration little is known about whether blood pressure reductions can induce deficient perfusion and promote expression of cerebrospinal fluid (CSF) biomarkers of amyloid and neurofibrillary pathology. We investigated the relationship between longitudinal changes in mean arterial pressure (MAP) and CSF biomarkers of Alzheimer's disease in a group of cognitively healthy elderly with and without HTN. **Methods:** Longitudinal assessments of blood pressure (MAP), CSF p-tau181 (phosphorylated tau), total tau, amyloid ß 1-42 (Aß42), cognition and whole brain volume were conducted on average 2.0±0.6 years apart in a group of 77 cognitively healthy elderly (age 63.4±9.4, range 44-86 years; education 16.9±2.1, range 10-22 years; 60% women). MAP was calculated as: 1/3 systolic blood pressure + 2/3 of diastolic blood pressure. **Results:** At baseline HTN was found in 23 individuals (30%). When longitudinal change (†) in p-tau181 was predicted with the †MAP, HTN, and the HTNx†MAP interaction, both the total model (F 3,73=3.9, p=.01), and the interaction term (p=.01) were significant. These data indicate that the relationship between †MAP and †p-tau181 was strongly dependent on the presence or absence of HTN. Only in the HTN group was a decrease in MAP from baseline to follow-up related to an increase in p-tau181 (r=-0.5, p=.01). In addition, only among subjects with HTN, was a reduction in MAP related to the worsening of verbal episodic memory (r=0.46, p=.03). Finally in the entire group the increase in p-tau181 was associated with reduction in the verbal episodic memory score (ß=-.223, p=.048). No relationship was observed between changes in MAP and whole brain volume. **Conclusions:** In subjects with HTN, MAP reduction is associated with increased CSF p-tau181 and deterioration of episodic memory, possibly resulting from suboptimal perfusion and subsequent accumulation of neurofibrillary tangles. Prior experimental work has demonstrated a relationship between perfusion, energetic reductions and tauopathy.

O3-09-04 CLINICAL PATHOLOGICAL CORRELATIONS OF DEMENTIA IN THE OLDEST-OLD: THE EFFECT OF MULTIPLE PATHOLOGIES

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Background: The presence of individual dementing neuropathologies is not strongly related to dementia in the oldest-old. Here, we explore whether the number of neuropathologies contributes to the expression of dementia in the very elderly. **Methods:** The study included 149 participants from The 90+ Autopsy Study, a population-based epidemiological study of aging and dementia in the oldest-old. Dementia diagnoses (DSM-IV) were assigned post-mortem during a consensus conference using all available clinical information including neurological exam, neuropsychological testing, medication use, and medical records. Neuropathological evaluations were done blinded to clinical diagnoses. Pathological Alzheimer's disease (AD) was defined as an index score > 3, created by adding Braak tangle score (0=I/II, 1=III/IV, 2=V/VI) and CERAD neuritic plaque score (0=none/rare, 1=moderate, 2=frequent). Pathological vascular disease (VaD) was defined as an index score > 4, created by adding the scores of 6 vascular pathological markers: atherosclerosis (0=none, 1=mild/moderate, 2=severe), arteriolarsclerosis (0=normal, 1=other, 2=white matter gliosis), microinfarcts, lacunes, large infarcts, and amyloid angiopathy (0=none, 1=single, 2=multiple). Other pathologies included Lewy body disease (LBD), hippocampal sclerosis (HS), and corticobasal degeneration. **Results:** Participants ranged in age at death from 90 to 108 years, 72% were women, and 54% had dementia. The prevalence of each pathological abnormality was as follows: AD (36%), VaD (26%), LBD (5%), HS (14%), and corticobasal degeneration (.7%). The percentage of people with dementia increased with increasing number of pathologies (table). After adjusting for age and gender, odds of dementia increased with the number of pathological abnormalities (table). For example, the odds ratio was 2.6 for people with one pathology and 12.2 for people with 2 pathologies compared to people with none. Furthermore, the number of pathological abnormalities was strongly related to severity of dementia, as indicated by mini-mental score (Figure). **Conclusions:** A variety of pathological diagnoses, alone or in combination, were found in this oldest-old cohort. The presence of more than one neuropathology greatly increased the odds and severity of dementia. Whether the effect of multiple pathological abnormalities are additive or synergistic should be the topic of future research. Strategies to prevent dementia in the oldest-old may need to be broadened to include multiple pathologies.

Odds of Dementia In Relation to the Number of Neuropathological Abnormalities

Number of Pathologies	Percent with Dementia	OR (95% CI)	*P*-value
0	34	1.0 (reference)	–
1	58	2.6 (1.2 - 5.4)	0.01
2	87	12.2 (3.2 - 46.2)	<0.001
3	100	>99 (undefined)	–

Abbreviations: OR=odds ratio; CI=confidence interval

Footnote: Pathologies included Alzheimer's disease pathology index ≥ 3, vascular disease pathology index ≥ 4, Lewy body disease, hippocampal sclerosis, and corticobasal degeneration;

Odds ratios and 95% confidence intervals obtained from logistic regression models adjusted for sex and age at death

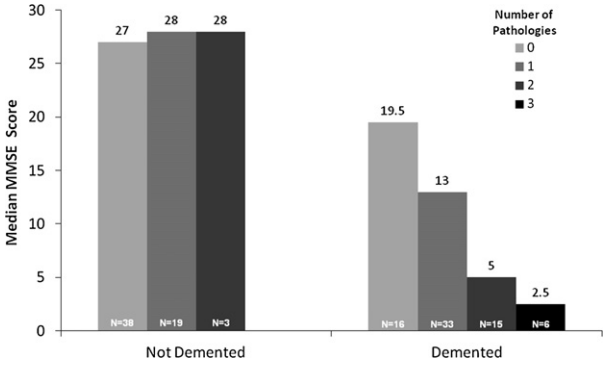

Figure 1. MMSE Score by Number of Pathological Abnormalities in Demented and non-Demented Participants of *The 90+ Study*

Pathological abnormalities included: Alzheimer's disease pathology index ≥ 3, vascular disease pathology index ≥ 4, Lewy body disease, hippocampal sclerosis, and corticobasal degeneration

MMSE=mini-mental state exam