P1-467 TAU PATHOLOGY BURDEN ASSOCIATED WITH LEVEL OF COGNITIVE RESERVE IN ALZHEIMER'S DISEASE

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Background: PET studies have demonstrated that higher educated patients with Alzheimer's disease (AD) display greater levels of beta amyloid pathology than lower educated patients with equal symptom severity, supporting the concept of cognitive reserve. Whether similar associations exist for *in vivo* tau pathology remains elusive, although closer relations between tau-deposition and cognitive decline have been reported. Therefore, this study examined differences in tau pathology load and spread in higher versus lower educated AD patients using [^{18}F]AV-1451-PET imaging. **Methods:** 24 patients with typical AD were grouped into a higher (HEAD) and lower educated (LEAD) group. The two groups were matched for age and cognition measured by the Mini Mental State Examination. Additionally, a group of 14 age-matched healthy controls was included. [^{18}F]AV-1451-PET scans were acquired to assess cerebral tau-burden. Regional tau ratios (reference region: cerebellum) were determined in a set of regions of interest (ROIs) which were defined according to the pathological disease stages by Braak & Braak. The obtained tau ratios were then compared between the groups. Furthermore, whole brain voxel-wise comparisons were conducted using Statistical Parametric Mapping to determine differences in tau-distribution between each AD-group and the healthy controls, respectively, as well as between the two AD-groups. **Results:** The ROI analysis yielded tau pathology in regions corresponding to more advanced Braak stages exclusively in the HEAD group, whereas tau pathology in the LEAD group was still confined to lower Braak stages. These results were confirmed by voxel-wise comparisons revealing higher tau levels in dorsomedial fronto-parietal cortical areas in the HEAD group when compared to the LEAD group. **Conclusions:** Highly educated AD patients seem to be able to tolerate more tau tangle pathology than lower educated patients with comparable cognitive impairment in support of the cognitive reserve hypothesis. These cognitive reserve-related differences in disease manifestation have crucial implications for early detection of AD, prognosis and assessment of disease progression and the monitoring of drug treatments.

P1-468 NETWORKS OF TAU DISTRIBUTION IN ALZHEIMER'S DISEASE

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Background: A stereotypical anatomical propagation of tau-pathology has been described in Alzheimer's disease (AD). According to recent concepts (network degeneration hypothesis), this is thought to be indicative of misfolded tau proteins possibly spreading along functionally connected networks. We examined whether independent coherent components could be identified in the distribution pattern of *in vivo* AD-related tau-pathology and if these components coincide with specific functional connectivity networks. **Methods:** 22 [^{18}F]AV-1451 PET scans of patients with amnestic AD were spatially normalized, intensity standardized to the cerebellum and z-transformed using the mean and deviation image of a healthy control sample to assess AD-related tau-pathology patterns. First, to detect distinct tau-pathology networks (TPNs), the deviation maps were submitted to an independent component analysis. Second, to investigate if regions of high tau-burden are associated via functionally connected networks, we extracted the region with the maximum z-value in each of the generated TPNs and adopted them as seeds in the following resting state functional MRI analysis. The seed-based analysis was conducted in a group of healthy adults who were part of the 1000 Functional Connectome Project. Third, to examine if tau-pathology co-localizes with functionally connected networks, we quantified the spatial overlap between the seed-based networks and the corresponding TPNs by calculating the dice similarity coefficient. Finally, we assessed if the tau-dependent seed-based networks corresponded with commonly known functional resting state networks, previously published by the FIND lab of Stanford University (Shirer et al. 2012). **Results:** We identified 10 distinct and independent TPNs with the majority showing a symmetrical bi-hemispheric expansion. The tau maxima of the respective TPNs coincided with highly functionally connected regions such as the precuneus and hippocampus. The topographical patterns of the tau-dependent seed-based networks resembled known resting state networks, predominantly the default mode network. **Conclusions:** A set of independently coherent networks of tau-pathology could be identified in AD, coinciding partly with functional networks previously reported to be disrupted in AD. This supports the idea that the temporal coherence of tau-pathology observed in specific brain regions may be induced by a transneuronal spread within specific functional networks.

P1-469 RACE AND AMNESTIC MCI SUBTYPE PERFORMANCE IN COMPARISON TO HEALTHY OLDER CONTROLS ON THE NIH TOOLBOX-COGNITIVE

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Background: As the older adult population increases, medical conditions will become more prevalent, including neurodegenerative diseases. Measures for early detection of cognitive change that are low-cost, readily accepted, and can be used in a community setting are increasingly necessary for preventative and treatment approaches. One such option, computerized testing, also is increasingly in use in clinical trials. While computerized tests have shown promise in identifying at the mild cognitive impairment (MCI) level, it is still unclear how race may affect such measures. We

investigated the use of the NIH-Toolbox-Cognition computerized neuropsychological battery in the identification of amnestic MCI (aMCI) compared to healthy older adults in a sample of African-American and Caucasian seniors. **Methods:** Ninety-three African American and 75 white older adults were recruited from the University of Michigan Alzheimer's Disease Center (MADC) and the Wayne State University Institute of Gerontology's Healthy Black Elders Center (WSU-HBEC). All were enrolled in the longitudinal cohort of the MADC and underwent complete NACC Uniform Data Set (UDS) assessment, being diagnosed via consensus conference as aMCI (n = 47, 72.54 ± 7.4 years) or cognitively healthy older adults (n = 121, 70.59 ± 7.4 years). Computerized tests were not used for consensus. All Toolbox subscales were evaluated through Diagnosis by Race ANOVAs, adjusted for age and education, using each of the Toolbox available scores (unadjusted, age-adjusted, percentile, fully-adjusted). After evaluation of those results, ROC Area under curve (AUC) analyses were conducted to determine discriminatory ability of each Toolbox composite and subtest measure. **Results:** ANOVAs revealed a number of significant main effects and interactions across both Fluid and Crystalized Toolbox measures when using all but the fully-adjusted scores, so those scores were used for AUC analyses. Total (0.846) and Fluid Composites (0.815) had the highest or "good classification" AUC values, with five other subtests (Pattern Comparison, Picture Sequence Memory, Crystalized Composite, Picture Vocabulary, Dimensional Card Sort) between 0.75-0.720 ("fair"). The fully-adjusted subtests with significant race main effects or interactions (Oral Reading, List Sort, Flanker) had AUC values below 0.70. **Conclusions:** Fully-adjusted Toolbox-Cognitive scores appear least sensitive to race effects. In terms of discriminating aMCI cases from controls, the Total and Fluid Composites appeared strongest.

P1-470 THE FEASIBILITY OF USING A TEST GENERATOR TO AMELIORATE LEARNING EFFECTS IN REPEAT COGNITIVE TESTING

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Background: The accurate and valid measurement of cognitive change is important for providing dementia trials outcomes, describing cognitive trajectory in population studies, and for detecting early impairment. Repeating traditional tests has shown clear learning effects, in both laboratory (Salthouse et al, 2004) and epidemiological studies (Gallacher et al, 2008). A major determinant of learning effect is familiarity with the test items. Using fluid intelligence as the cognitive domain, and Raven's Standard Progressive Matrices (SPM) as the test paradigm, a test generator that enabled item familiarity to be manipulated is demonstrated as an option for use in pharmacologic and epidemiologic studies. **Methods:** Corvus, a Raven's-like test generator was designed and built. Item familiarity can be manipulated using varying similarity between element attributes, layouts, rules and answer sets. To investigate the impact of item familiarity data were collected from 25 individuals who were randomised to complete either tests generated by Corvus or SPM on 5 occasions over a 14 day period. **Results:** There were two indices of performance, test duration and test score. Test duration reduced over the five occasions for both Corvus (Figure 1) and SPM (Figure 2). However SPM showed a significantly greater reduction in test duration. Additionally participants taking Corvus sped up at a relatively constant rate throughout the test, while participants taking SPM sped up to a greater degree on harder questions and begin to approach a constant time per item regardless of difficulty. For test score there was only marginal change for both tests. **Conclusions:** The use of item generators to produce parallel test versions has advantages over the use of parallel test items. Data presented here shows that a test generator (Corvus) can be used to assess fluid intelligence and ameliorates item familiarity effects. References: 1. Gallacher, J. et al, Prevalence and Pattern of Cognitive Impairment in a Community Cohort of Men in South Wales: Methodology and Findings from the Caerphilly Prospective Study, Neuroepidemiology, 30(1), 25-33. 2. Salthouse, T., Ferrer, E. & Schroeder, D. (2004), Estimating Retest Effects in Longitudinal Assessments of Cognitive Functioning in Adults Between 18 and 60 Years of Age, Developmental Psychology, 40(5), 813-822.

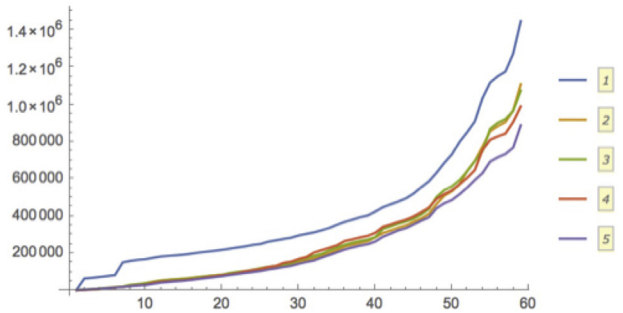

Figure 1. Average cumulative time taken per test item for each of the five sessions for the tests generated by Corvus.

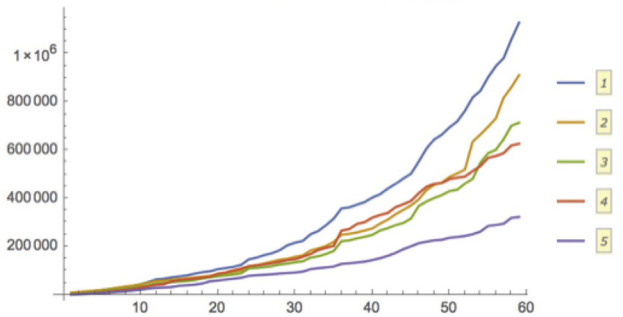

Figure 2. Average cumulative time taken per test item for each of the five sessions for the online version of Raven's Standard Progressive Matrices.

P1-471 EFFECT OF ALZHEIMER'S DISEASE ON SPATIAL PATTERN SEPARATION

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Background: Alzheimer's disease (AD) is characterized by early hippocampal changes leading to episodic memory and spatial navigation deficits. Hippocampal subregions – dentate gyrus and CA3 play a critical role in pattern separation, a process of creating and maintaining distinct non-overlapping representations for similar