IC-P-057 AMYLOID IMAGING IN NONDEMENTED OLDEST OLD

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Background: PiB PET was used to assess amyloid load in a cohort of 190 older individuals [82-95 years of age (YOA)] from the Pittsburgh Ginkgo Evaluation of Memory Study (PGEMS) who were cognitively normal (NL) or had mild cognitive impairment (MCI). **Methods:** PiB PET imaging was performed in 152 PGEMS NL (MMSE = 28 ± 2; 85 ± 3 YOA) and 38 PGEMS MCI (MMSE = 25 ± 3; 86 ± 3 YOA). MRI defined the regions-of-interest (ROIs), and PiB images were sampled using MRI template ROIs including anterior and posterior cingulate, parietal, frontal, lateral temporal cortices and cerebellum (CER). PiB retention 50-70 min post-injection was measured using the standardized uptake value ratio for each ROI relative to CER. A comparative Pittsburgh (PITT) PiB PET data set (n = 123) consisted of 77 NL (MMSE = 29 ± 2; 71 ± 6 YOA) and 46 MCI (MMSE = 28 ± 2; 68 ± 7 YOA), whose age range was 54-79. Amyloid status (PiB + or PIB-) was determined using a statistical outlier method based on data quartiles over the five specified cortical regions. APOE status was available for 158 PGEMS subjects (126 NL, 32 MCI) who were classified as either E4 carrier or noncarrier. **Results:** Of the "oldest-old" PGEMS, PiB + prevalence in NL was 51% and 68% in MCI. PiB + prevalence in the (younger) PITT elderly cohort was 21% in NL and 46% in MCI. In PGEMS cases ≥ 90 YOA, 67% of 15 NL and 100% of 5 MCI were PiB +. While only 17% of PGEMS subjects were APOE4 carriers, PiB-positivity for E4 carriers was 84% (21 of 25) in the NL and 100% (7 of 7) in MCI. **Conclusions:** The presence of PiB-positivity in NL subjects increased from ∼20% in subjects 54-79 YOA to ∼50% in subjects ≥ 82 YOA. Prevalence of PiB-positivity in MCI increased from ∼50% in subjects 54-79 YOA to ∼70% in subjects ≥ 82 YOA. APOE4 carriers comprised a low percentage of oldest-old PiB + subjects, but those cases had very high prevalence of PiB-positivity. The presence of amyloid pathology as indexed by PiB-positivity increased progressively in the oldest-old, even with cognition in the normal range. These data are in agreement with the prevalence of amyloid-positivity in autopsy studies of people in this age range.

IC-P-058 CATEGORY LEARNING BRAIN POTENTIALS AS NEUROCOGNITIVE MARKERS FOR PATHOLOGIC AGING

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Background: A central challenge for treating Alzheimer's disease is to develop neurocognitive markers to identify at-risk individuals before significant neural damage is done. Towards this aim our research program centers on measuring event-related potentials (ERPs) recorded during tasks requiring long-term memory and executive functions in younger adults and in older adults both with and without mild cognitive impairment or Alzheimer's diagnoses. Here we present behavioral and event-related potential results from younger and older adults on a rule-based category-learning task, as this may be an excellent task for predicting which older adults show Alzheimer's disease pathology later. Categories are central to our mental lives. Behavioral, neuropsychological, and neuroimaging methods have suggested that categories can be learned via either explicit (declarative) rule-based mechanisms or implicit (non-declarative) information-integration mechanisms. Patient and neuroimaging studies have further suggested that information-integration category learning is dependent on structures in the basal ganglia and sensory areas, whereas rule-based category learning depends on the medial temporal lobe and prefrontal cortex, two brain regions associated with mild cognitive impairment and Alzheimer's disease. It is likely that both mechanisms often operate together, and neuroimaging methods may thus be useful in dissociating them during behavioral performance and in identifying neural changes indicative of pathologic aging. Previous studies using event-related potentials to study changes in long-term memory have been effective in predicting which patients diagnosed with amnestic mild cognitive impairment go onto develop a diagnosis of probable Alzheimer's disease (e.g., Olichney et al., 2008). Likewise, neuropsychological studies have suggested that executive functioning at the time of diagnosis with mild cognitive impairment is the best predictor of which mild cognitive impairment patients go on to probable Alzheimer's disease (Albert et al., 2007). Rule-based category learning requires executive functions and long-term memory, both to test, update and maintain a rule as well as to learn, update, and maintain information about boundary conditions. Thus, we believe event-related potentials during this task hold promise for predicting the mild cognitive impairment to Alzheimer's disease progression and perhaps also for revealing changes even earlier in the aging progression. **Methods:** The rule-based category-learning task used in this study (Maddox et al., 2003) required participants to study visual gratings (Gabor patches) that varied in spatial frequency (i.e. how many stripes) and spatial orientation (i.e. the angle of the lines in the patch) and categorize each patch into one of two groups. In this rule-based version of the task we chose a particular spatial frequency as the decision threshold and randomly varied spatial orientation. Participants gradually learned the categories via auditory feedback on each trial. In the rule-based version of the task, participants can easily describe the rule they were using after learning. In a previous event-related potential study with younger adults we identified several event related-potentials that effectively dissociated explicit rule-based category learning from implicit information integration category learning (Morrison, Reber, & Paller, 2009). In the current study 18 healthy younger adults (m = 21 years) and 12 older adults (m = 71 years) performed 320 category-learning trials divided into four blocks. Older adults were within 1.5 standard deviations of their age norm on neuropsychological tests of long-term memory and had no sign of dementia.We recorded EEG using a Biosemi Active2 EEG system with 32 electrodes located at standard 10/20 system locations, two mastoid electrodes for subsequent digital re-referencing, and four electrodes to monitor eye movements for artifact correction and rejection. To ensure that participants could follow basic task directions and could see the differences between stimuli from the two categories, each participant completed a second control task after initial category learning. In this task each participant was given the category rule based on spatial frequency (members of category A have more, narrower stripes and members of category B have fewer, wider stripes;) and shown two Gabor patches on each trial. One patch represented the boundary condition while the other was sampled from the actual category distribution, with exemplars both near and far from the category boundary. Participants indicated via a button press whether the right patch had wider or narrower stripes. Like the learning stimuli, these stimuli also randomly varied in spatial orientation. **Results:** Older adults showed lower accuracy and longer RTs than did younger adults, but there were two distinct subgroups of older adults based on their categorization accuracy. The rule subgroup (n=6) learned slightly more slowly than younger adults, but showed equivalent asymptotic accuracy. The no-rule subgroup (n=6) did not learn the category rule and showed near chance performance throughout the task. Event related potentials were calculated for correct and incorrect trials across participant groups. We were particularly interested in a stimulus-locked late positive complex (LPC, 400-700ms), frequently

associated with long-term memory functioning and shown to be decreased in mild cognitive impairment patients subsequently diagnosed with probable Alzheimer's disease (Olichney et al., 2008), and a feedback-locked P300 which we believe is reflective of participants' confidence in their category learning. Younger adults showed similar patterns for the late positive complex and P300 event-related potentials as in our original study (Morrison, Reber, and Paller, 2009). Because of the previously described differences in accuracy between the rule and no-rule subgroups, we examined event-related potentials separately in these two subgroups. The rule subgroup showed a larger late positive complex for correct than incorrect trials, similar in magnitude to that observed for younger adults. The no-rule subgroup showed no late positive complex differences between correct and incorrect trials. The rule subgroup also showed a feedback P300 difference for correct/incorrect trials, but it was smaller than that in younger adults, suggesting decreased rule-learning confidence (despite similar accuracy across groups). The no-rule subgroup showed event-related potentials characteristic of chance performance, with no differences between correct and incorrect trials in the feedback-locked P300, paralleling the lack of an effect on the stimulus-locked late positive complex.There were no significant differences in the control task between younger and older adults. Rule and no-rule older adults also performed similarly showing performance approximately equal to the asymptotic categorization performance for the rule-subgroup during the primary task. This suggests that no-rule subgroup categorization performance was likely reflecting deficits in long-term memory or executive functions. **Conclusions:** Preliminary results in this study showed that a simple rule-based category-learning task elicited differential performance and event-related potential findings as a function of age. We focused on findings from a group of older adults known to have long-term memory within the normal range on standard neuropsychological tests. Yet, some members of this group were successful in learning to categorize stimuli and some were not. We thus identified two distinct subgroups of healthy older individuals, one subgroup with category learning similar to college students and the other with dramatic deficits. Event-related potentialss recorded during categorization confirmed this stratification. Specifically a stimulus-locked late positive complex believed to index long-term memory was preserved in older adults who learned to categorize, but not in the others. Secondly a feedback-locked P300 believed to reflect the degree to which the participant is confident in their category learning showed a graded decrement. P300 differences for feedback on correct versus incorrect trials were greatest in amplitude in younger adults, intermediate in rule-learning older adults, and smallest in those older adults who failed to learn to categorize. The current study suggests that rule-based category learning, a task utilizing long-term memory and executive functions, may be an effective means for identifying individuals at increased risk for mild cognitive impairment and probable Alzheimer's disease. Event-related potentials recorded during this task may provide a more sensitive measure of changes in cognition compared to simple neuropsychological tests by measuring neural function even when participants perform well, thus providing an objective measure of confidence in learning. Future work will be directed at testing patients with mild cognitive impairment and Alzheimer's disease using this paradigm.

IC-P-060 CONVERSION FROM MILD COGNITIVE IMPAIRMENT TO ALZHEIMER'S DISEASE OVER 12 MONTHS: PREDICTIVE VALUE OF Aβ IMAGING WITH 18F-FLORBETABEN

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Background: In-vivo amyloid imaging studies enable researchers to more clearly define the role of Aß deposition in the development of dementias where Aß may play a role. **Methods:** 45 subjects (72.7 ± 6.6 yo, MMSE 27.2 ± 1.8) with Mild Cognitive Impairment (MCI) underwent neuropsychological examination, MRI and 18F-Florbetaben PET at baseline and 12 months later. MCI was defined by a history of cognitive decline but largely intact normal activities and performance more than 1.5 standard deviation below normal on neuropsychological assessment. 41 were amnestic. Subjects were classified Aß-positive when Florbetaben cortical SUVR was greater than 1.4. **Results:** At baseline, 24 MCI subjects (53%) showed high Aß deposition, while 29/42 (69%) had hippocampal atrophy. By the 12-month follow-up 13 met criteria for dementia, 9 (20%) for probable AD, 3 for frontotemporal dementia and 1 for dementia with Lewy bodies. In a year, 33% of the Aß-positive MCI and one Aß-negative converted to AD, and 19% of Aß-negative subjects progressed to other dementias. While Aß-positive MCI were 7 times more likely to convert to AD in a year than Aß-negative, MCI with hippocampal atrophy were 1.3 times more likely to convert to AD. **Conclusions:** The presence of brain Aß deposits as measured by 18F-Florbetaben PET is a very strong predictor of progression from MCI to AD at one year. Follow-up is continuing to determine the longer-term predictive accuracy of 18F-Florbetaben PET for development of Alzheimer's disease.

IC-P-061 PERIVENTRICULAR WHITE MATTER LESIONS IN EARLY LEWY BODY DEMENTIA

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Background: White matter lesions (WML) are increased in AD, but the frequency and impact of WML in patients with dementia with Lewy bodies (DLB) are not known. The objective of this study was to explore the load of WML in patients with mild DLB and compare to patients with AD and healthy elderly normal controls (NC), using a semi-automatic method. We hypothesized that 1) patients with mild dementia have more WML than non-demented controls, and 2) DLB have similar degree of WML as AD and more than NC. **Methods:** The Dementia Study in Western Norway (DemWest) recruited outpatients with mild dementia. Diagnosis are made according to consensus criteria for AD, DLB and Parkinson's disease dementia (PDD) using standardised clinical instruments, blood tests and MRI. DLB and PDD were combined in a Lewy-body dementia (LBD) group. Cerebrospinal fluid and dopamine transporter scan were available in a subgroup. NC were recruited from friends and relatives of patients with Parkinson's disease in the same region. MRI scans of sufficient quality was available for 95 subjects. We segmented WML from T2-weighted FLAIR images and calculated the volume of WML in several regions of the brain using an atlas. We used non-parametric tests to compare groups. WML load was calculated as a ratio compared to total size of brain. **Results:** There were no significant difference in age or years of education between any of the groups, and no significant difference in MMSE between AD and LBD. The proportion with males was higher in LBD (82 %) than AD (24 %) and NC (38 %) ($p < 0.02$). There were significant differences in total periventricular WML between the groups (Kruskal Wallis, $p = 0.04$). Both LBD (Mann-Whitney test; $p = 0.045$) and AD ($p = 0.029$) had more WML than NC. There were no differences between AD and DLB ($p = 0.45$). **Conclusions:** LBD had more WML than elderly without brain disease, and the severity of WML in LBD was similar to that of AD. More studies are needed to explore the clinical impact of WML in LBD.