Category Learning Brain Potentials as Neurocognitive Markers for Pathologic Aging

Robert G. Morrison[1], Krishna Bharani[1], Dietta Chihade[1], Kevin Nuechterlein[1], Arie Zakaryan[1], Sandra Weintraub[2], Paul J. Reber[2], & Ken A. Paller[2]

Loyola University Chicago[1] Northwestern University[2]

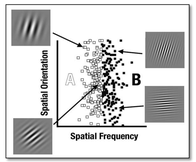
Introduction

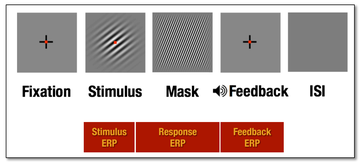
- A central challenge for translational cognitive neuroscience is to develop neurocognitive markers for normal and pathological aging.
- Previous fMRI studies have demonstrated the importance of prefrontal cortex and medial temporal lobe (Ashby & Maddox, 2005; Nomura et al., 2007), two areas implicated in pathological aging including Alzheimer's disease (AD), as important for explicit rule-based category learning.
- Previous event-related potential (ERP) studies involving an incidental learning paradigm suggest that memory ERPs can predict the conversion of amnestic mild cognitive impairment (aMCI) to a probable AD diagnosis (Olichney et al., 2008).
- Neuropsychological studies have found that aMCI patients are at increased risk for developing probable AD if their executive functions are compromised at the time of aMCI diagnosis (Albert et al., 2007).
- Thus, rule-based category learning may be sensitive to factors predicting subsequent pathology.

Methods

Task

- We adapted a rule-based category learning based on the methods of Maddox et al., (2003) and Normura et al., (2007) for use with scalp electroencephalography (EEG; Morrison et al., 2009)
- Participants categorized Gabor patches (320 trials) that varied in spatial frequency (i.e. how many stripes) and orientation (i.e. the angle of the lines in the patch).
- Two categories (A or B) were predetermined based on spatial frequency.
- Participants received feedback on each trial.
- Participants also completed a second task after initial learning to ensure they could see the differences between the category boundary and category exemplars to test possible vision deficits.





EEG

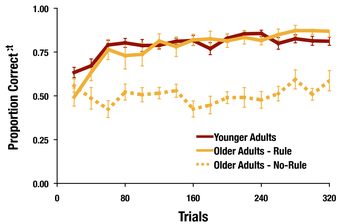
- EEG data was collected using a 38-channel Biosemi Active2 EEG system including two mastoid electrodes for digital re-referencing and four electrodes for monitoring eye movements.
- Data were filtered offline using a 0.01Hz high-pass filter and a 59-61Hz band-stop filter in EMSE (Source Signal Imaging) and all channels were corrected for occular artifacts using EMSE's PCA-based algorithm. Epochs with greater than ±100µV deflections were rejected.
- Stimulus-, Response-, and Feedback-locked ERPs were calculated for correct and incorrect trials.

Participants

- We tested 21 younger adults (M = 20.8 , SD = 2.7) and 20 older adults (M = 70.9 , SD = 3) recruited from the Northwestern Alzheimer's Disease Center Core (NADCC).
- NADCC older adults included in the study were within ±1.5 SD of their age-based norms on neuropsychological tests of memory, language, visuospatial ability, and executive function and did not meet diagnostic criteria for Mild Cognitive Impairment.

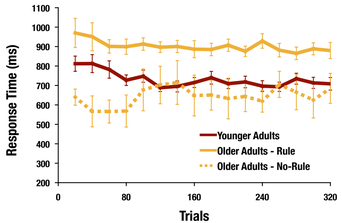
Behavioral Results

Accuracy



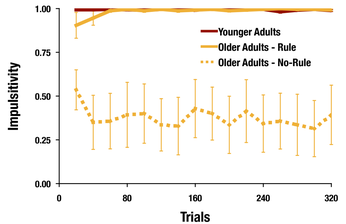
- Overall older adults showed lower accuracy than younger adults, but there were two distinct subgroups based on patterns of accuracy.
- The Rule subgroup (n=13; mean age M=71.5, SD = 3.9) learned slightly more slowly during the beginning of the first block of trials than younger adults, but showed equivalent asymptotic accuracy. The No-Rule subgroup (n=7; mean age M=70.5, SD = 2.3) did not learn and showed near chance performance throughout the task.
- Mean accuracy across the older adults was correlated with MMSE score (r=.69) and Backward Digit Span (r=.38).

Response Time (Correct Trials)



- Overall younger and older adults showed similar RT for correct trials, but once again the older adults divided into two distinct subgroups.
- The No-Rule subgroup (M = 602 ms) and the young adults (M = 738 ms) had faster RTs that were lower than the Rule subgroup (M = 841 ms) throughout the task.
- Mean RT across the older adults was correlated with MMSE score (r=.42) and Backward Digit Span (r=.43). Thus, older adults with better span were slower at categorization on correct trials.

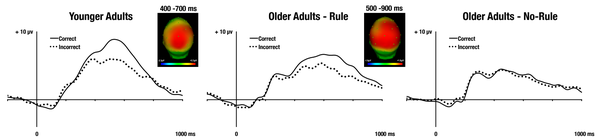
Impulse Control



- Impulse control was determined by calculating the proportion of trials that participants answered more than once for a single stimulus (only the first response was used to determine accuracy).
- The No-Rule subgroup showed poor impulse control compared to the Rule-subgroup.
- Mean Impulse Control across the older adults was correlated with RT (r=.66), Backward Digit Span (r=.49), and negatively correlated with errors in the Trails B task (r=-.35) suggesting a deficit in executive control may be important in understanding their task deficit.

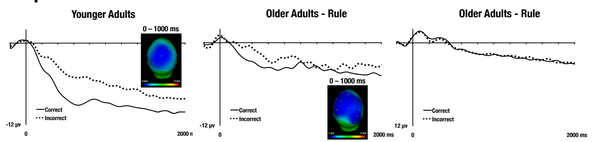
Neuroimaging Results

Stimulus-Locked ERPs



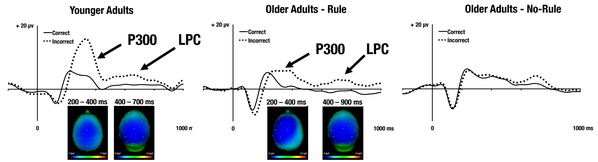
- The Late Positive Complex (LPC), a metric of memory updating, was measured from 400 to 700ms for younger adults and from 500 to 900ms for rule-learning older adults.
- Correct/Incorrect LPC ERP subtractions of mean amplitude measured at electrode Pz showed a reliable difference for younger and rule-learning older adults as in Morrison et al. (2009), but not for nonrule-learning older adults.
- Younger and older adults showed similar Correct/Incorrect LPC ERP topographies.

Response-Locked ERPs



- The Continuous Negative Variation (CNV), a metric of short-term memory, was measured during the delay between response and feedback (0 to 1000 ms post-response).
- Correct/Incorrect CNV ERP subtractions of mean amplitude measured at electrode Pz showed a reliable difference for younger and rule-learning older adults, but not for nonrule-learning older adults.
- Older adults showed a slightly broader Correct/Incorrect CNV ERP topography than younger adults.

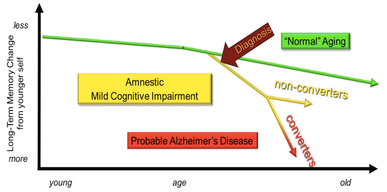
Feedback-Locked ERPs



- The feedback P300, a metric of violation of expectancy, was measured from 200 to 400 ms; while the feedback LPC, a metric of memory updating in response to feedback, was measured from 400 -700 ms in younger adults and from 400 - 900 ms in older adults who learned the rule.
- Correct/Incorrect P300 and LPC ERP subtractions of mean amplitude measured at electrode Pz showed a reliable difference for younger and rule-learning older adults, but not for nonrule-learning older adults.
- Older adults showed a slightly more left lateralized Correct/Incorrect P300 ERP topography than younger adults while the LPC topographies appeared to be identical.

Discussion

- In this study we identified two subgroups both from a sample of neuropsychologically normal older adults who differed in their ability to learn simple visual categories based on trial-by-trial feedback.
- The rule-learning older adult subgroup performed similarly in accuracy to younger adults but showed slower RTs. The nonrule-learning older adult subgroup showed chance performance with much quicker RTs similar to those exhibited by younger adults.
- Older adults who learned the categorization rule generally showed correct/incorrect subtraction ERPs of similar mean amplitude to those for younger adults, but with slightly later onset.
- Two exceptions to the above statement include older adults reduced response-locked CNV, which dissipated in the face of distraction approximately 1 s after the response, and older adults' feedback-locked P300 to incorrect trial, which was dramatically reduced compared to younger adults suggesting older adults were less confident in their learning in spite of equivalent accuracy.
- RT and Impulse Control results in older adults showing pronounced category learning deficits (No-Rule Subgroup) suggests that this group shows insufficient executive control to modify their behavior to adapt to their declining short and long-term memory function, a hallmark of successful aging.
- Our results suggest that with additional modifications, rule-based category learning with ERP analysis may be an excellent means to screen older adults for increased risk for pathological aging.



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