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Episodic Memory Measures Complement Structural and Functional MRI for Predicting Cognitive Decline in Apolipoprotein E ε4 Carriers

John L. Woodard
Wayne State University

Michael Seidenberg
Rosalind Franklin University of Medicine and Science

Kristy A. Nielson
Marquette University, kristy.nielson@marquette.edu

Michael Sugarman
Wayne State University

J. Carson Smith
University of Maryland - College Park

See next page for additional authors

LONG-TERM MEMORY: Development & aging

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INTER-INDIVIDUAL VARIABILITY IN CRITERION SHIFTING ACROSS THE LIFESPAN Brian Lopez[1], Craig Bennett[1], Tyler Santander[1], Michael Miller[1]; [1]University of California, Santa Barbara – A critical aspect of recognition memory is the integration of available memory evidence and a decision criterion. Previous work has shown that a wide range of factors can affect the placement of a decision criterion, including cognitive and personality factors. In this study we attempted to quantify the impact of aging on criterion placement during episodic recognition. To that end, we used fMRI to examine recognition behavior and regional brain activity in 30 young adults (25-35 yrs) and 30 elderly subjects (60-75 yrs) during a task involving criterion shifting. Subjects were first asked to encode 150 words for later recognition. The words were then presented alongside new, unobserved words in conditions of high target probability (70% old, 30% new) and low target probability (30% old, 70% new). Subjects had to decide for each word whether it was a target old word or a non-target new word. The results demonstrated that target discrimination ability (d-prime) was lower in the elderly group, and that the elderly group showed increased variability in the degree of criterion shifting between the two probability conditions. We also found that the elderly group had significantly increased inter-individual variability in regional brain activity relative to the young adult group while performing the task. The results suggest that aging is associated with increased variability in criterion shifting and in the regional brain activity that accompanies such criterion shifts.

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THE CONTRIBUTION OF BLOOD SERUM BIOMARKERS TO THE PREDICTION OF COGNITIVE DECLINE BY FMRI AND APOLIPOPROTEIN-E IN HEALTHY OLDER ADULTS Kristy A. Nielson[1,2], Michael A. Sugarman[3], John L. Woodard[3], Michael Seidenberg[1], J. Carson Smith[5], Sally Durgerian[2], Stephen M. Rao[6]; [1]Marquette University, [2]Medical College of Wisconsin, [3]Wayne State University, [4]Rosalind Franklin University of Medicine and Science, [5]University of Maryland, [6]Cleveland Clinic – Biomarkers are a promising approach to the prediction and early intervention of Alzheimer's disease. We demonstrated that cortical functional MRI (fMRI) activation during a semantic memory task and apolipoprotein-E ?4 allele inheritance (APOE?4) effectively predicted cognitive decline after 18-months in healthy, asymptomatic elders. Hippocampal volume added modest prediction, while AD family history and demographics were ineffective. Previous studies have linked plasma homocysteine (tHcy), vitamin B12 and creatinine values to cognitive functioning, cortical atrophy, hippocampal atrophy and neuropathology, and vascular integrity. Here we incorporated total plasma homocysteine (tHcy), B12 and creatinine values into our previous predictive models. Of 78 healthy elders, 27 (34.6%) exhibited significant cognitive decline after 18-months. tHcy, but not B12 or creatinine, was marginally positively correlated with cortical semantic memory fMRI activation, particularly in stable participants. Logistic regression showed that tHcy, when added to APOE?4 and cortical fMRI, was a significant predictor of outcome and strengthened the already significant model ($p = .007$; $C = .80$ and $R2 = .37$). However, control for B12 and creatinine covariates diminished tHcy as a predictor ($p = .084$), though the model was still stronger than without this factor ($C = .78$ and $R2 = .31$). tHcy did not significantly interact with APOE?4, as has previously been reported. Neither B12 nor creatinine was similarly effective as a predictor. These results suggest that commonly investigated blood serum biomarkers are at best weakly associated with predicting age- and dementia-related cognitive decline in healthy, asymptomatic elders. fMRI and APOE?4 presently provide the best predictive model.

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EPISODIC MEMORY MEASURES COMPLEMENT STRUCTURAL AND FUNCTIONAL MRI FOR PREDICTING COGNITIVE DECLINE IN APOLIPOPROTEIN E ?4 CARRIERS John L. Woodard[1], Michael Seidenberg[2], Kristy A. Nielson[3,5], Michael A. Sugarman[1], J. Carson Smith[4], Sally Durgerian[5], Alissa M. Butts[3], Melissa A. Lancaster[2], Mary K. Foster[6], Nathan C. Hantke[3], Monica A. Matthews[2], Stephen M. Rao[6]; [1]Wayne State University, [2]Rosalind Franklin University, [3]Marquette University, [4]University of Maryland, [5]Medical College of Wisconsin, [6]The Cleveland Clinic – Apolipoprotein E (APOE) ?4 allele carriers demonstrate greater risk for cognitive decline and Alzheimer's disease than non-carriers. However, factors associated with risk of decline among APOE ?4 carriers are not well-known. In this longitudinal study, we investigated whether discrete aspects of baseline episodic memory performance and structural (sMRI) and functional (fMRI) magnetic resonance imaging were associated with cognitive decline in older APOE ?4 carriers and non-carriers. Seventy-eight healthy older adults underwent cognitive testing at baseline and after 18 months, baseline serum APOE genotyping, manually-traced hippocampal volume measurement from sMRI, and task-activated fMRI. Cognitive decline was defined as a one SD or greater reduction from baseline on at least one of three cognitive measures at follow-up (Rey Auditory Verbal Learning Test [AVLT] Delayed Recall and Trials 1-5 Sum, Mattis Dementia Rating Scale-2 Total Score). Declining APOE ?4 carriers ($n=14$) exhibited reduced hippocampal volume ($p<.009$) and fMRI semantic processing activity in cortical ($p<.04$) and hippocampal ($p<.05$) regions relative to stable carriers ($n=12$). On the AVLT, declining APOE ?4 carriers showed greater baseline susceptibility to retroactive interference ($p<.006$), intertrial forgetting (lost access; $p<.001$) and recognition false alarms ($p<.05$) compared to stable carriers. Stable ($n=39$) non-carriers showed slightly more susceptibility to proactive interference than declining ($n=13$) non-carriers ($p<.02$). Along with sMRI and fMRI, AVLT measures of rapid forgetting can help to identify APOE ?4 carriers with elevated risk for cognitive decline. These effects appear to be largely unique for APOE ?4 carriers, perhaps due to preclinical structural and functional alterations in structures subserving memory.

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ITEM AND ASSOCIATIVE MEMORY FOR NOVEL NATURALISTIC ACTIONS IN AMNESTIC MILD COGNITIVE IMPAIRMENT, OLDER ADULTS, AND YOUNGER ADULTS David A. Gold[1,3], Norman W. Park[3], Angela K. Troyer[2,3,4], Kelly J. Murphy[2,3,4]; [1]Joseph and Kathleen Bryan Alzheimer's Disease Research Center, Duke University Medical Center, [2]Baycrest Centre, [3]York University, [4]University of Toronto – Most research examining associative memory has focused on memory for non-naturalistic, laboratory-based stimuli. We extend current findings by exploring item and associative memory for novel naturalistic actions (NNA; e.g., how to make an arts-and-crafts style project such as a windspeed indicator). Based on previous research using laboratory tasks, a selective decline in memory for associative information (e.g., was this tool used with this object?) relative to item information (e.g., was this object presented?) was predicted in amnestic mild cognitive impairment (aMCI) and aging. Individuals with aMCI ($n = 24$), age-matched older adults ($n = 24$), and undergraduates ($n = 32$) viewed two 90 second NNA videos. Following a 90 second distractor task, participants completed forced-choice recognition memory tests of item and associative memory for the NNAs. A mixed ANOVA with the within-subjects factors of question type (item, associative) and response type (hits, false alarms), and the between-subjects factor of group (young, old, aMCI), revealed no significant interaction [$F(2, 77) = 0.870$, $p = .233$], contrary to previous findings with other stimuli that demonstrates older adults, and those with impaired memory, show selective decline in associative memory. A response type by group interaction confirmed the aMCI group had higher false alarms overall [$F(2, 77) = 20.797$, $p < .001$, $?p^2 = .351$], but no differences between younger and older adults. Further, the three groups did not differ in overall hit rate. The findings support protected encoding of within-domain associa-