

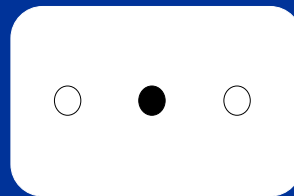
IMPLICIT LEARNING AND APOE GENOTYPE IN HEALTHY OLD-OLD ADULTS

Selam Negash¹, Lindsay E. Petersen¹, Yonas E. Geda¹, David S. Knopman¹, Bradley F. Boeve¹, Glenn E. Smith¹, Robert J. Ivnik¹, Darlene V. Howard², James H. Howard, Jr.^{2,3}, and Ronald C. Petersen¹
¹Mayo Clinic, Rochester, ²Georgetown University & ³The Catholic University of America

Abstract

The goals were to examine implicit learning systems in old-old (80 years and above) individuals, and to determine the extent to which such learning systems are influenced by APOE genotype in this age group. We investigated two forms of implicit learning - contextual cueing and sequence learning. In the contextual cueing paradigm, people learn to use repeated spatial configurations to facilitate search for a target, whereas in sequence learning, they learn to use subtle sequence regularities to respond more quickly and accurately to each of a series of events. The former implicates the medial temporal lobe system, and the latter fronto-striatal-cerebellar circuits. Learning on both tasks was inferred from faster and/or more accurate response to predictable than unpredictable stimuli. Earlier research had shown that in a young-old group, APOE-E4 carriers learned more on contextual cueing than non-carriers, while sequence learning was not related to APOE genotype (Negash, in press). In the present study, 24 healthy old-old adults completed both tasks, where 11 were APOE-E4 carriers, while 13 were non-carriers. Results revealed that, first, contextual cueing remained intact in the old-old, whereas sequence learning revealed impairments, consistent with findings that the fronto-striatal system continues to decline with age. Secondly, the old-old did not reveal differences based on APOE genotype, and on contextual cueing, in contrast to earlier findings with young-old, there was a trend towards APOE-e4 carriers performing better than non-carriers. These findings indicate that the effect of the APOE-e4 allele on cognition weakens after age 80, consistent with epidemiological evidence of no increased risk of Alzheimer's disease in this age group.

Alternating Serial Reaction Time Task (ASRTT)



Howard & Howard, 1997

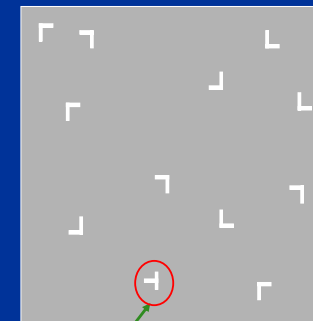


- Three spatially arranged locations
- On each trial, one of the circles fills in.
- Pattern trials alternate with random trials
 - e.g., 1-r-2-r-3-r
- 1 block = 70 trials (6-item sequence x 10) 10 random warm-up trials
- 20 blocks; 4 epochs (5 blocks/epoch)

Subjects:

- 11 APOE-e4 carriers; 6M/5F
 - Mean age: 83.9 (SD: 1.9)
 - Mean education level: 14.6 (SD: 1.9)
- 13 APOE-e4 non-carriers; 5M/8F
 - Mean age: 84.5 (SD: 1.9)
 - Mean education level: 14.3 (SD: 2.9)

Contextual Cueing Task



Chun & Phelps, 1998

Respond Left

Visual array of 12 items:
 ✦ 11 distractors (L's--orientation varies)
 ✦ 1 target (horizontal T)

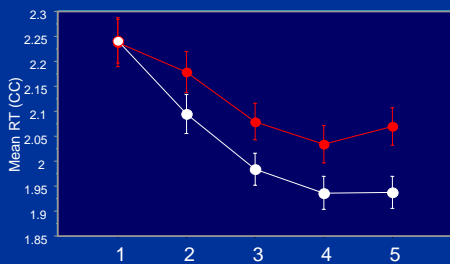
1 block = 24 trials:
 ✦ 12 repeated configurations
 ✦ 12 new configurations

On repeated trials:
 ✦ Configuration predicts location of T
 NOT direction of T

10 blocks; 5 epochs (2 blocks/epoch)

Results #1:

Implicit learning in old-old

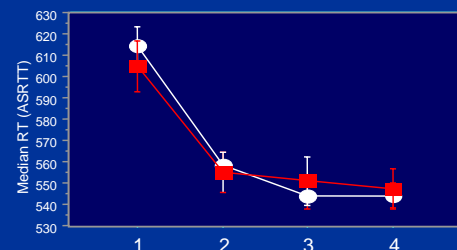
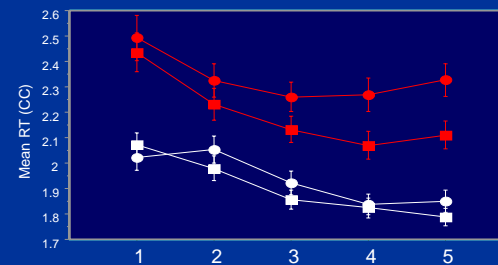


Contextual Cueing

● Repeated
 ● Novel

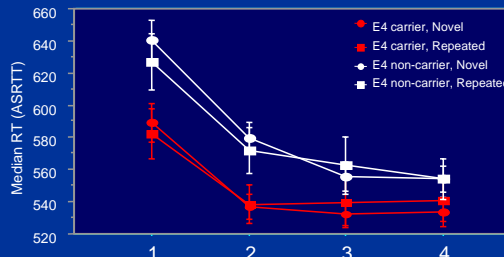
Results #2:

APOE Effect on implicit learning in old-old



ASRTT

● Consistent
 ● Inconsistent



Conclusions

- Sequence learning was impaired in old-old adults, while contextual cueing remained relatively intact.
 - Results are consistent with fronto-striatal dysfunction and relative integrity of the medial temporal lobe system with age
- On contextual cueing, APOE-e4 carriers were slower overall and showed a trend towards greater learning than non-carriers.
- On ASRTT, APOE-e4 carriers were faster overall and neither group showed learning.
 - These findings suggest that the effect of the APOE-e4 allele on cognition weakens after age 80, consistent with epidemiological evidence of no increased risk of Alzheimer's disease in this age group.

References

- Chun, M.M. and Phelps, E.A., Memory deficits for implicit contextual information in amnesic subjects with hippocampal damage. *Nature Neuroscience*, 2 (1999) 844-7.
- Howard, J. H., & Howard, D. V., (1997). Age differences in implicit learning of higher order dependencies in serial patterns. *Psychology and Aging*, 12(4), 634-656.
- Negash, S., Petersen, L.P., Geda, Y.E., Knopman, D.S., Boeve, B.F., Smith, G.E., Ivnik, R.J., Howard, D.V., Howard, J.H. Jr., & Petersen, R.C. (In press). Effects of ApoE Genotype and Mild Cognitive Impairment on Implicit Learning. *Neurobiology of Aging*.

Supported by the NIH Roadmap Multidisciplinary Clinical Research Career Development Award Grant K12 RR023263-03, NIA Grants P50 AG16574, U01 AG06786, R37 AG15450, and by the Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program of the Mayo Foundation

Society for Neuroscience, Atlanta, GA
 October 14-18, 2006