IMPLICIT LEARNING SYSTEMS: APOE GENOTYPE AND HEALTHY AGING

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Abstract

The relations of APOE genotype to implicit learning systems in healthy older adults are unknown. The present study investigated two forms of implicit learning – contextual cueing and sequence learning – and examined the sensitivity of these implicit systems to APOE status. 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 responses to predictable than unpredictable stimuli. 24 healthy older adults completed both tasks, where 11 were APOE-e4 carriers, while 13 were non-carriers. Results revealed a dissociation: healthy older adults carrying the APOE-e4 allele showed contextual cueing deficits compared to those who did not carry the APOE-e4 allele. Sequence learning, by contrast, was not influenced by APOE genotype. To our knowledge, this is the first study to show that implicit learning of spatial contexts could be influenced by APOE genotype, and suggests that the contextual cueing paradigm could be sensitive at detecting group differences based on APOE genotype even in healthy individuals who do not have cognitive impairment.

Method

Participants:

- **11 Healthy APOE-e4 carriers**
  – mean age: 78.5 (*SD*: 5.2); mean education level: 13.6 (*SD*: 2.7)
- **13 Healthy APOE-e4 non-carriers**
  – mean age: 74.5 (*SD*: 4.5); mean education level: 13.8 (*SD*: 2.4)
- **24 MCI Patients**
  – mean age: 77.1 (*SD*: 6.0); mean education level: 13.8 (*SD*: 3.2)

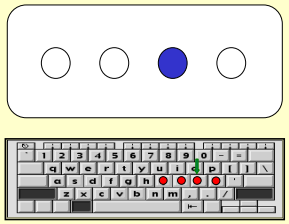
Tasks:

- Serial Reaction Time (SRT) & Contextual Cueing tasks
- Recognition tests at the end of each task

Measures of Learning:

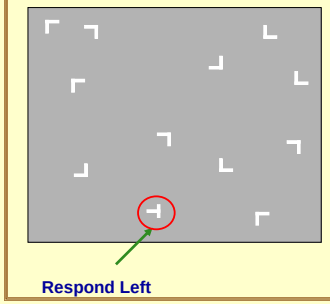
- ***Implicit:*** Difference in performance between predictable and unpredictable trials *(trial-type effect).*
- ***Explicit***: Verbal reports and Recognition tests

SRT Task



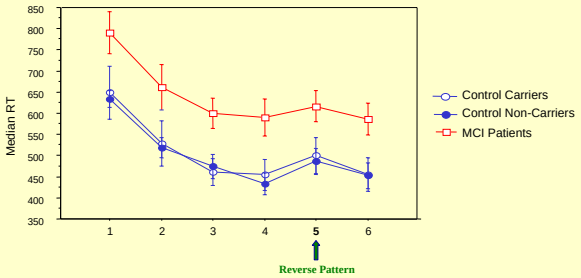
- Spatially arranged locations
- On each trial, one of the circles fills in
- Predetermined 8-element pattern:
  – **1-3-4-1-2-4-3-2**
- 10 repetitions of 8-element pattern/block
- 6 blocks: **P- P- P- P- *R* - P** ***(P = Pattern, R = Reverse)***

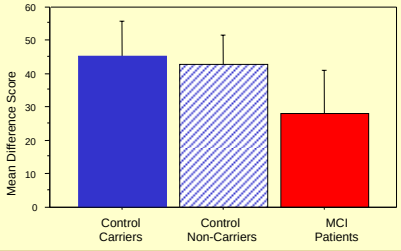
Contextual Cueing Task



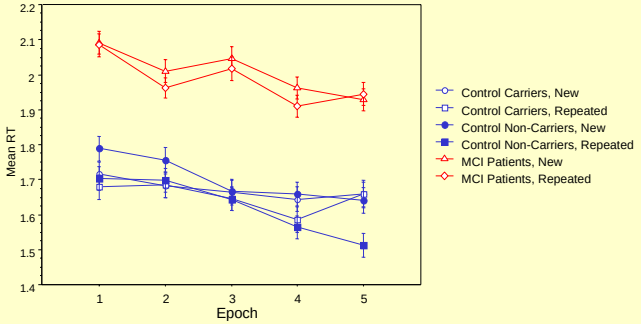
- Visual array of 12 items
  - 11 distractors (L's--orientation varies)
  - 1 target **(horizontal T)**
- 1 block = 24 trials
  - 12 **repeated** configurations
  - 12 **new** configurations
- On repeated trials
  - Configuration predicts **location** of T
  - NOT direction of T
- 10 blocks; 5 epochs (2 blocks/epoch)

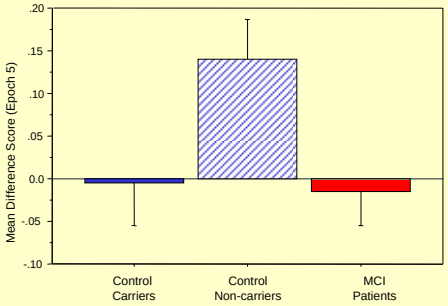
Results #1: Sequence learning





Results #2: Contextual Cueing





Conclusions

- Neither healthy individuals carrying the APOE-e4 allele nor the MCI group revealed contextual cueing.
- Sequence learning, by contrast, was uninfluenced by either MCI or by APOE genotype in healthy controls.
  - Results implicate the influence of APOE genotype on implicit learning of spatial contexts in healthy older individuals without cognitive impairment.
  - Healthy APOE-e4 carriers show a pattern of spared and impaired implicit learning similar to that in MCI patients.
  - These findings support existing evidence that these tasks rely on different brain systems.

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