Episodic-like Memory: Effects of Aging, Behavioral Interventions, and Cholinergic Activity

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Introduction

- Episodic memory involves the recollection of a specific event, and is comprised of three substituents: object discrimination (what), timing (when), and spatial navigation (where).[1]
- Episodic memory is often the first type of memory to decline in natural aging processes and dementia.[2]
- Cholinergic activity in the hippocampus has been implicated in episodic memory function.[3]
- Episodic memory is susceptible to proactive interference (PI), which occurs when previously stored memories conflict with retrieval of new memories.[4]
- This study aimed to assess and compare the episodic-like memory performance of aged and young rats through the use of a food discrimination intervention targeted toward the "what" substituent. Memory performance was compared to cholinergic function assessed via immunohistochemistry.
- An understanding of the components of episodic-like memory and their relationship to cholinergic function may provide insight toward combating episodic memory decline.

Methods

Subjects

24 male Sprague Dawley rats

- Young group ~ 7 months old (n=12)
- Aged group ~ 23 months old (n=12)

(The human equivalent of 18 and 55 years)

Baseline

- Subjects tested in an open field task where they searched for target locations of food reward.
- Eight sessions per day, each session consisted of two different trials:

  Encoding trial: subjects learned the location of two targets.

  Test trial: subjects utilized their episodic-like memory to find the target locations.

Intervention

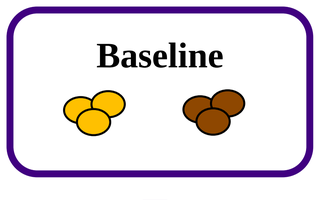
Food Discrimination: experiment-grade food pellets were replaced with more unique food rewards.

Immunohistochemistry

- Choline acetyltransferase (ChAT) synthesizes acetylcholine (Ach)[4].
- The optical density of ChAT in the CA1, CA3, and DG was measured using ImageJ to assess hippocampal cholinergic function via Ach.

Analysis

- Recorded correct choices of the target location for the *current* trial.
- Recorded proactive interference (PI) errors where the choice made was a target location from a *previous* trial.
- Analysis via generalized mixed effects modeling.



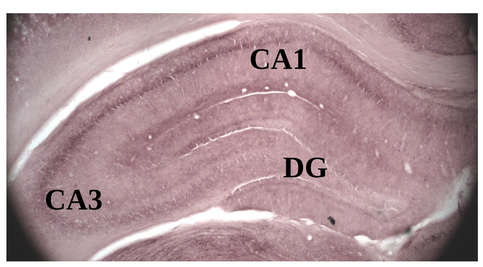


Figure 1. Image of brain tissue stained with the hippocampal ChAT assay. The CA1, CA3, and DG regions were used for the optical density measurements.

Results

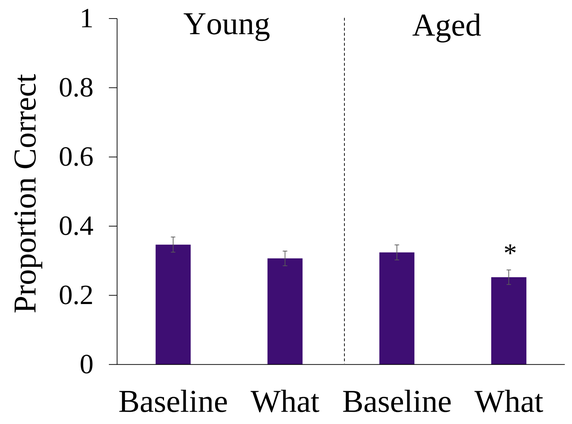


Figure 2. The mean proportion of correct choices made by the aged and young groups in each task. The food discrimination (What) intervention significantly worsened the aged rats' performance, while there was no significant difference in the young rats' performance.

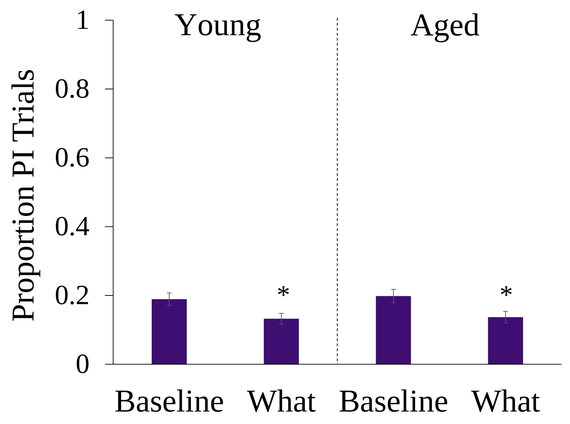


Figure 3. The mean proportion of trials in which proactive interference (PI) errors were exhibited by the young and aged groups in each task. Both groups experienced significantly less PI during the food discrimination (What) intervention compared to the baseline task.

Aged Discrimination

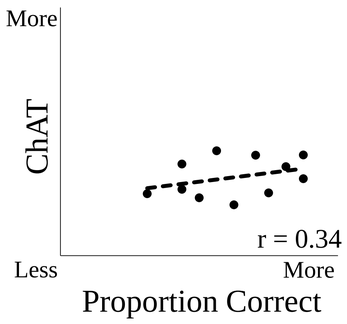


Figure 4. In the aged rats, a higher level of hippocampal ChAT was related to more correct choices in the food discrimination task.

Young Discrimination

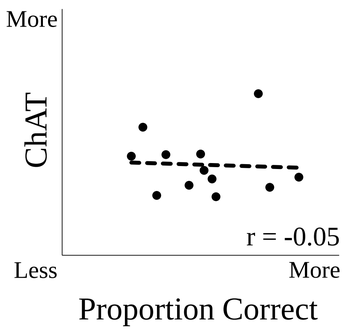


Figure 5. The young rats showed no correlation between ChAT levels and the proportion of correct choices in the food discrimination task.

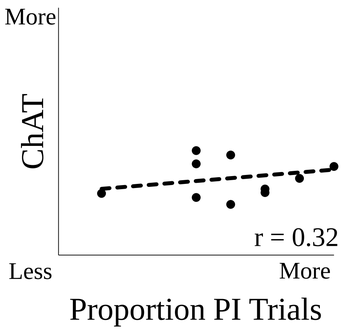


Figure 6. In the aged rats, a higher level of hippocampal ChAT was related to the amount of PI errors during the food discrimination task.

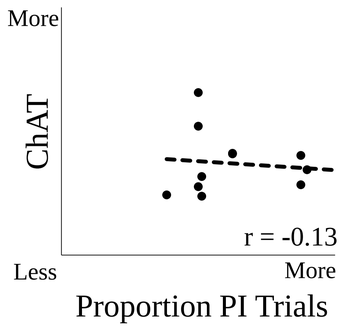


Figure 7. The young rats showed no correlation between ChAT levels and the proportion of PI errors in the food discrimination task.

Discussion

- While the food discrimination intervention was designed to support the "what" component of episodic-like memory, the task resulted in the aged rats making significantly fewer correct choices and had no effect on the young rats.
- However, both groups experienced fewer proactive interference (PI) errors during the intervention, suggesting that the task was successful in that it may have reduced previous trial interference.
- The aged rats show a positive relationship between ChAT and correct choices, which implies that higher hippocampal ChAT levels increase memory performance.
- However, the aged group also exhibited a positive relationship between ChAT levels and proactive inference errors, suggesting that higher ChAT levels could reduce memory decay rate and thus increase previous trial interference.
- Other behavioral and neurologic mechanisms (e.g. GABA) may contribute to task performance, as there was no relationship between ChAT and task performance in the young rats.

References

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