Age-related changes in performance on the frontal cortex-dependent temporal order memory task

Evelyn F. McKnight Brain Institute

Olivia Guswiler[1], Salma Khattab[1], Kimberly Bohne[1], Carol A. Barnes[1,2]

[1]Evelyn F. McKnight Brain Institute; [2]Departments of Psychology, Neurology and Neuroscience, University of Arizona, Tucson, AZ 85724

The University of Arizona

Background

It is known that cognitive performance declines with normative aging in several domains, but few studies have attempted to tease apart the specific regions that may be more susceptible to or robust against age-related changes over time. The temporal ordering memory (TOR) task is a simple and efficient test used to assess recognition memory, specifically the ability to recall *when* an object or event was committed to memory. In aging humans, prefrontal cortex-dependent memory exhibits some of the most dramatic and early changes relative to other brain functions[1]. Previous work has shown that lesions to the medial prefrontal cortex (mPFC) significantly disrupt performance on this task in young rats[2,3]. Although the TOR task has been utilized in many studies, there has been little to no research on the effect of age on performance.

Methods

Subjects: Male Fisher 344 (F344) rats, 11 old (22-23mo) and 14 young (8-9mo).
Apparatus: The behavior arena consists of a 50 x 50 x 30cm (L x W x H) wooden box, painted black. Objects for exploration are made from nonporous materials and are affixed to the floor using re-closable fasteners. The room is lit by several overhead red lights.
Procedure: Food restriction is used prior to and throughout the duration of this task to encourage exploratory behavior. Days 1 and 2, the animals are habituated to the empty apparatus for a 10min period. Days 3 and 4, each rat undergoes a trial consisting of three phases: two exploration phases and one test phase. During the 1st exploration phase, the rat is given 4min to explore a pair of identical objects. Following a 1hr delay period, the same procedure is followed for the 2nd exploration phase, except that a different pair of identical objects is used. After a 2hr retention period, the test phase is administered using the same procedure as the exploration phases, except one object from both previous pairs is presented. Different objects were used between days 3 and 4 and test phase object position was counterbalanced so that each rat experienced both potential configurations.

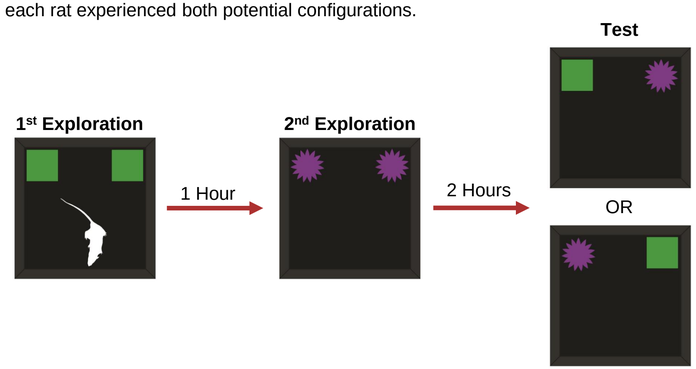

Figure 1. Schematic of the TOR task.

Analysis and Results

Video recordings were scored for time spent exploring each object by an individual blind to the conditions. Rats were excluded if they did not explore each object ≥2s during the exploration phases or if their total exploration time during the test phase was not ≥4s. From the test phase scores, a discrimination ratio was calculated for each rat by taking the difference in time spent exploring the object presented last by the time spent exploring the object presented first, divided by the total time spent exploring both objects:

$$\frac{t_{first\ object} - t_{last\ object}}{t_{total}} = \textit{Discrimination Ratio}$$

		Indicates preference for…
>	0	*First presented object*
=	0	*No preference*
<	0	*Last presented object*

Several rats from both age groups were excluded due to insufficient exploration, with most exclusions occurring on day 4. Final group numbers were as follows: day 3, old, n = 9 and young, n = 13; day 4, old, n = 3 and young, n = 5. From days 3 and 4, discrimination ratios and object exploration times from the test phase were analyzed using a mixed-effects model and post hoc analysis was completed using Šídák's multiple comparisons test, $p < 0.05$.

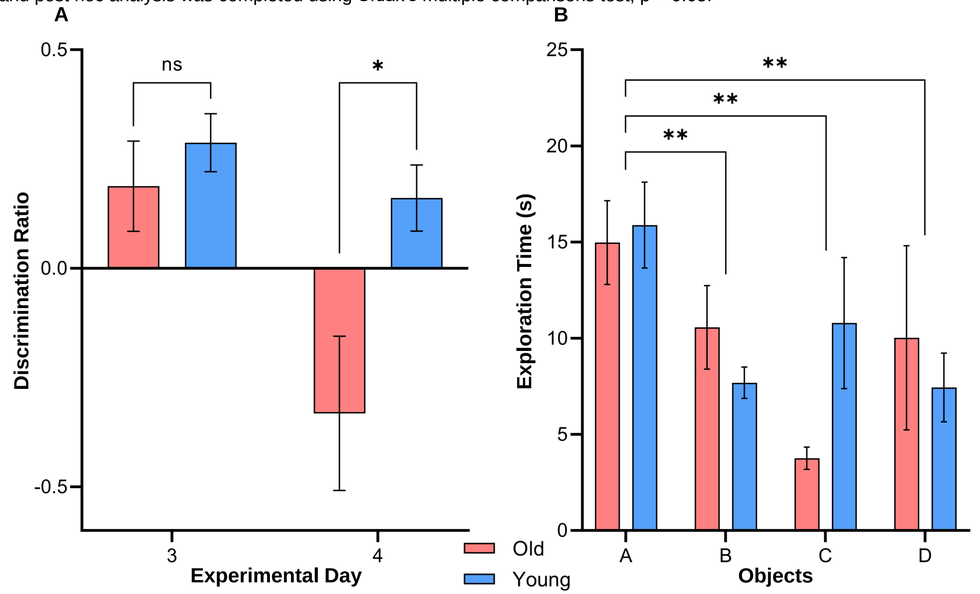

Figure 2. **A)** Performance of young and old F344 rats on the TOR task. Shown are the discrimination ratio mean (±SEM) *p < 0.05. **B)** Exploration times for each object used in the task. Objects A and B were presented on day 3, objects C and D presented on day 4. Shown are the exploration time mean (±SEM) **p < 0.01.

Discussion

Rats typically explore an object more, the more temporally remote the exposure to that object was. When the prefrontal cortex is damaged, this 'temporal bias' is eliminated. When object preference is taken into account, these results suggest that aged rats are impaired compared to the younger animals in the ability to recognize which object was most recently experienced. The lack of an age effect on Day 3 can be attributed to an object preference anomaly for object A (presented day 3) compared to any other object. When there was no significant object preference (such as for objects C and D, presented on day 4), a significant temporal discrimination deficit can be observed in the old rats. Two improvements to the procedures used in conducting this task are suggested by these data. The first is to conduct an experiment to determine the 'preference' that rats have for the objects that will be presented in this task. This will allow the appropriate matching on object interest in studies going forward. Additionally, the overall decrease in exploration observed between days 3 and 4 in both age groups could be a result of 'low interest' in particular objects. It may be ideal to only choose objects of high interest (e.g., eliciting more exploration) to use in the TOR task, in order to maximize exploration levels on subsequent testing days.
This simple temporal order memory task will be extremely useful for further exploration of the differences between young and aged animals, particularly in combination with high-density cell recordings in the mPFC and related structures.

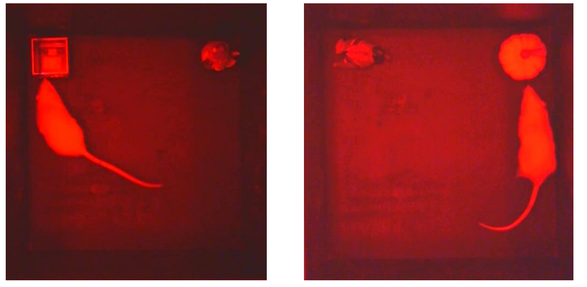

Figure 3. Screen captures from test phases of the TOR task.

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References

1. Park et al., Psychol. Aging, 2002, 17:299
2. Mitchell and Laiacona, Behav. Brain Res., 1998, 97:107
3. Barker et al., J. Neurosci., 2007, 27:2948