Thigmotaxis helps to differentiate normal and pathological aging processes in a mice model for Alzheimer's Disease

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INTRODUCTION

- Differentiating impairments in spatial orientation in the early stages of Alzheimer's Disease (AD) from a normal aging process is a challenge due to a similar magnitude of affectation in both entities.[1].
- In the preclinical field, the Morris Water Maze (MWM) test evaluates spatial learning in mice; nonetheless, a more thorough analysis is required to better understand the cognitive impairments associated with AD [2,3].
- REFERENCES:

1. Moffat SD (2009) Aging and spatial navigation: What do we know and where do we go? Neuropsychol Rev 19:478–4892.
2. Garthe A, Kempermann G (2013) An old test for new neurons: Refining the morris water maze to study the functional relevance of adult hippocampal neurogenesis. Front Neurosci 7:1-11.
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AIMS

To determine the sensitivity of a swimming strategies approach for detecting differences in the spatial learning and reference memory of a group of experienced 3xTg-AD mice and their age-matched non-transgenic (NTg) counterpart in the MWM test.

METHODS

Fifteen NTg (C57BL/6J) and 22 3xTg-AD mice were evaluated at two-times point (12 and 16-months of age) in the MWM test, using a modified 5-day protocol. Quantitative analysis was further followed by a manual multiple swim pattern identification within a single trial using the video tracking software ANY-MAZE version 6.33.

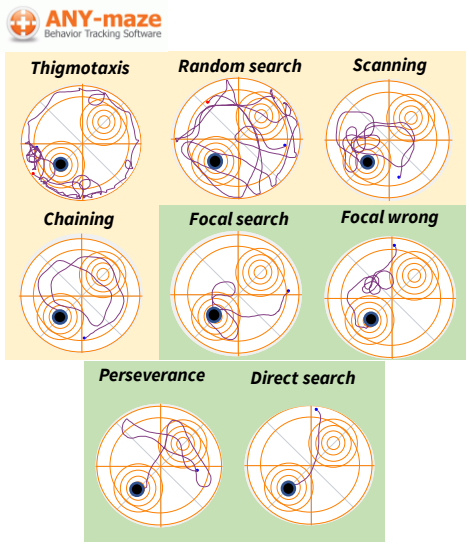

Figure 1. The sequence of swimming strategies. Patterns were classified into eight different swimming strategies [3]. Time spent on each (quantitative) and the number of episodes (qualitative) were analyzed. Furthermore, a distinction between non-hippocampus (yellow) and hippocampus-dependent search was considered.

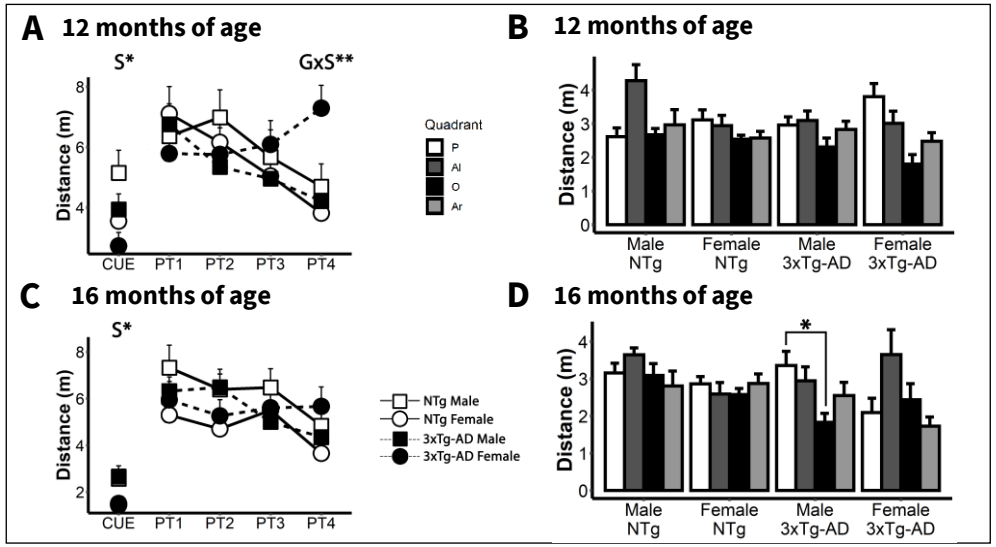

Figure 2. A and C, cue test (CUE) and place task (PT) phases of MWM in 12-and 16-month-old mice. B and D, Probe trial phase of MWM at 12-and 16-months of age, respectively. Data are expressed by mean ± sem. Mixed ANOVA 2x2x4. S, sex effect; GxS, genotype per sex interaction;* p<0.05; ** p< 0.01.

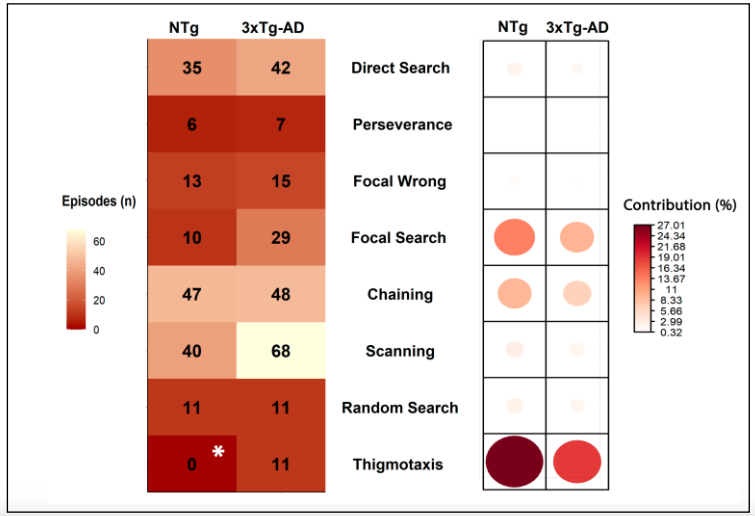

Figure 3. Frequency of episodes of each strategy during the four days of place task (PT) phase of the MWM (left) and relative contribution of each strategy to the total chi-square test (right). *p<0.05 Fisher's exact test.

RESULTS

Classical parameters showed that all animals learned the basic principles of the test more rapidly with age (Fig.2.A,C).

Contrary to expected, the 16-month-old 3xTg-AD male mice performed better when short-term memory was evaluated. However, a "by chance" preference of the previous platform location cannot be dismissed(Fig.2D).

Persistence in thigmotaxis episodes, a non-hippocampus-associated search strategy, was found in the pathological AD-like model at 16 months of age but not in the NTg group (Fig.3)).

CONCLUSIONS

Considering these preliminary results, a qualitative multiple strategies analysis of the MWM test shows that thigmotaxis episodes is a cue factor for differentiating the learning process between a group of aged and pathological mice submitted twice to the test.

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