medical sciences forum

MDPI

Abstract

Thigmotaxis Helps Differentiate Normal and Pathological Ageing Processes in a Mouse model of Alzheimer's Disease †

Daniel Alveal-Mellado and Lydia Giménez-Llort *

Department of Psychiatry and Forensic Medicine, School of Medicine, Universitat Autònoma de Barcelona, 08193 Barcelona, Spain; daniel.alveal@e-campus.uab.cat

* Correspondence: lidia.gimenez@uab.cat

† Presented at the 2nd International Electronic Conference on Brain Sciences, 15–30 July 2021; Available online: https://sciforum.net/event/IECBS2021.

Abstract: A decline in learning and remembering a spatial route often accompanies the normal ageing process. Impairments in spatial orientation manifest from the early stages of disabling cognitive diseases such as Alzheimer's Disease (AD). In the preclinical field, detecting behavioural signs that help differentiate both entities improve understanding of the AD instauration process and promotes advances in novel treatments to ameliorate its impact. Here, the performance of 3xTg-AD mice of both sexes and their non-transgenic (NTg) (C57BL/6J) counterpart was evaluated at two time points (12 and 16-months of age) in the Morris water maze test, using a modified 5-day protocol for the assessment of cognitive and non-cognitive symptoms of dementia, followed by a multiple swim pattern identification within a single trial in the test. In the CUE stage, when a visible flag was available, the classical parameter of mean distance travelled until finding the platform showed that all animals learned the basic principles of the test more rapidly with a second experience (at 16 months of age). After switching the platform location in the Place task (PT) stage, mild variations in reference memory were detected along days at 12 months but not at 16 months of age. Later, in the removal (RMV) stage, where no platform was available, the 16-month-old 3xTg-AD male mice showed better results in short-term memory performance. However, when the swim pattern was visually analysed (qualitative analysis), persistence in Thigmotaxis episodes, a non-hippocampus-associated search strategy, was found in the pathological AD-like model but not in the NTg group, pointing out this pattern as a valuable differentiating trait. Finally, the multiple strategies approach seems valuable for differentiating both mice strains, despite a similar performance when quantitative parameters were analysed.

Keywords: ageing; Morris water maze; Alzheimer's disease; 3xTg-AD mice

Citation: Alveal-Mellado, D.; Giménez-Llort, L. Thigmotaxis Helps Differentiate Normal and Pathological Ageing Processes in a Mouse model of Alzheimer's Disease. *Med. Sci. Forum* **2022**, *8*, 2. https://doi.org/10.3390/IECBS2021-10669

Academic Editor: Stephen D. Meriney

Published: 14 July 2021

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/IECBS2021-10669/s1. References [1–6] are cited in the supplementary materials.

Author Contributions: L.G.-L., conceptualization and supervision; D.A.-M., writing and formal analysis. Both authors revised and approved the final manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: The colonies are currently sustained by Fet-Open ArrestAD European Union's Horizon 2020 research and innovation program under grant agreement No. 737390 to L.G.-L.; D.A.-M. is recipient of a CONICYT-ANID/73200493 grant from the Chilean government.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Departament de Medi Ambient i Habitatge, Generalitat de Catalunya (CEEAH 3588/DMAH 9452) the 8 March 2019.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are not publicly available due to ongoing analyses for future publications.

Acknowledgments: We thank Frank M. LaFerla Institute for Memory Impairments and Neurological Disorders, Department of Neurobiology and Behavior, University of California, Irvine, USA, for kindly providing the progenitors of the Spanish colonies of 3xTg-AD and NTg mice.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Moffat, S.D. Aging and spatial navigation: What do we know and where do we go? *Neuropsychol. Rev.* **2009**, *19*, 478–489. [CrossRef]
2. Garthe, A.; Kempermann, G. An old test for new neurons: Refining the morris water maze to study the functional relevance of adult hippocampal neurogenesis. *Front. Neurosci.* **2013**, *7*, 63. [CrossRef] [PubMed]
3. Gehring, T.V.; Luksys, G.; Sandi, C.; Vasilaki, E. Detailed classification of swimming paths in the Morris Water Maze: Multiple strategies within one trial. *Sci. Rep.* **2015**, *5*, 14562. [CrossRef] [PubMed]
4. Morris, R. Developments of a water-maze procedure for studying spatial learning in the rat. *J. Neurosci. Methods* **1984**, *11*, 47–60. [CrossRef]
5. Giménez-Llort, L.; Blázquez, G.; Cañete, T.; Johansson, B.; Oddo, S.; Tobeña, A.; LaFerla, F.M.; Fernández-Teruel, A. Modeling behavioral and neuronal symptoms of Alzheimer's disease in mice: A role for intraneuronal amyloid. *Neurosci. Biobehav. Rev.* **2007**, *31*, 125–147. [CrossRef] [PubMed]
6. Baeta-Corral, R.; Giménez-Llort, L. Persistent hyperactivity and distinctive strategy features in the Morris water maze in 3xTg-AD mice at advanced stages of disease. *Behav. Neurosci.* **2015**, *129*, 129–137. [CrossRef] [PubMed]