

Bizarre behaviors limit exploratory activity and impair spontaneous gait performance in aged mice with AD pathology

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INTRODUCTION

Age-related behavioral changes in older mice develop similarly to older people, but their shorter life spans provide an exceptional experimental gerontology scenario. In 6 month-old 3xTg-AD mice model for Alzheimer's disease (AD), compared to C57BL/6 wildtype, we previously described increased bizarre (disruptive) behaviors related to psychiatric and neurological disorders when confronting new and unfamiliar environments.

AIMS

The present work aimed to identify distinctive patterns of bizarre behaviors related to impairments and functional limitations of spontaneous gait and exploratory activity in 16-month-old male 3xTg-AD mice in an advanced stage of AD and their counterparts with normal aging.

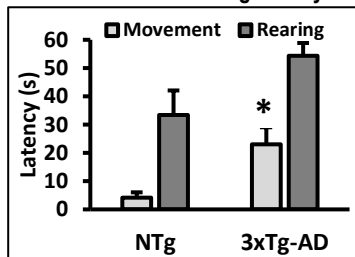
METHODS

Mice's behavior was evaluated in a transparent test box during the neophobia response. The latency to start the movement, the number of visited corners, the latency, and the rearings were recorded. Bizarre behaviors were identified during the gait and exploratory activity execution.

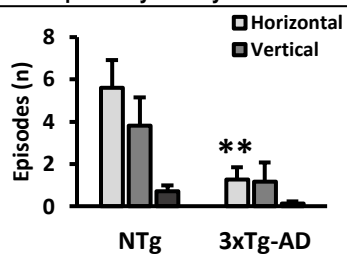
RESULTS

1. Exploratory activity

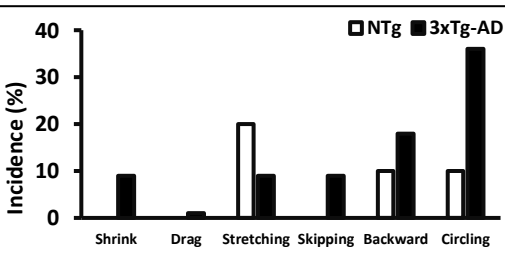
A. Movement and rearing latency



B. Exploratory activity

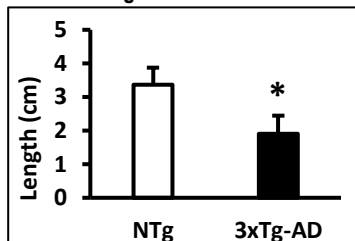


C. Bizarre behaviors incidence



2. Quantitative parameters of gait

D. Stride length



E. Speed

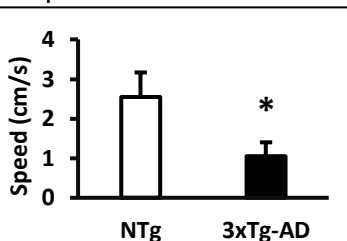
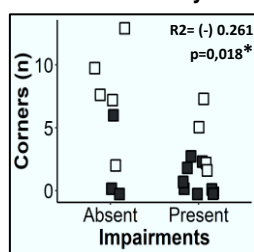


Figure 1. Exploratory activity: movement and rearing latency (panel A), exploratory activity (panel B), and bizarre behaviors incidence (panel C). **Figure 2.** Qualitative parameters of gait: stride length (panel D), and speed (panel E). Data expressed by mean of episodes, latency and time. Statistics: T-Student's test, U-Mann Whitney, and χ^2 . * $p < .05$, ** $p < .01$, *** $p < .001$.

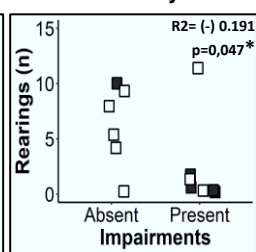
Figure 3. Correlation analysis between indicators of spontaneous gait limitation, exploratory activity, and quantitative parameters of gait. Horizontal activity (panel F), vertical activity (panel G), rearing latency (panel H), stride length (panel I), and speed (panel J). Meaningful, significant Pearson r correlations. Statistics: Pearson r2, * $p < .05$, ** $p < .01$ and *** $p < .001$.

3. Correlations analysis

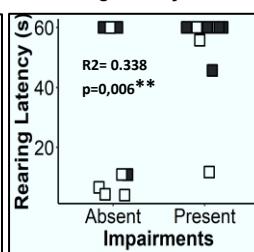
F. Horizontal activity



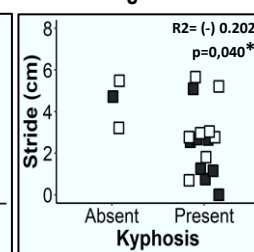
G. Vertical activity



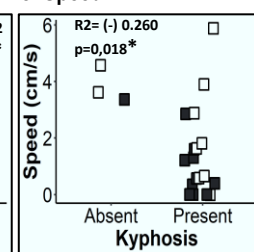
H. Rearing latency



I. Stride length



J. Speed



DISCUSSION / CONCLUSIONS

Similar to those that occur in humans, the frailty markers may be related to a progressive loss of locomotor performance, along with functional limitations in exploratory activity. This way, the results corroborate that in the face of novelty and recognition of places, old 3xTg-AD mice exhibit increased bizarre behaviors than mice with normal aging. (1) Bizarre circling and backward movement delayed the elicitation of horizontal and vertical locomotion and exploratory activities. (2) Kyphosis (differentiated into flexible and rigid) stood out as more characteristic of 3xTg-AD mice than C57BL/6, with a higher incidence and a possible limitation in spontaneous gait and vertical activity performances. We have previously reported on bizarre circling behavior in MWM and its consequences on aquatic performance. Thus, The study of co-occurrence of psychomotor impairments and anxiety-like behaviors is helpful for understanding and managing the progressive functional deterioration in patients with AD.

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