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The food- finding test without deprivation delays the ethogram but preserves the olfactory signatures in female mice with normal and AD-pathological aging with minor effects of social isolation

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INTRODUCTION

Olfactory loss is regarded as an early indicator in the neurodegenerative processes associated with Alzheimer's and Parkinson's disease. Additionally, in some people with modest cognitive impairment, this loss has been seen during the period when normal aging and dementia are transitioning into one another. Olfactory impairment or deficit may be a sign that patients with mild cognitive impairment are more likely to acquire dementia, according to earlier research (Invitto et al., 2018). The study of the roles played by biological, psychological, and social factors, their functional interactions, and their effects on the crosstalk of homeostatic networks in health and disease throughout the life cycle can be done using the male and female sexes as two exceptional natural scenarios. (Giménez-Llort et al., 2014).

In the present translational work, a new food finding test (FFT) olfactory paradigm (Marin-Pardo et al., 2021) without food deprivation was used to investigate olfaction in old animals. In this case food deprivation was not carried out since it has been determined that n the triple-transgenic mouse (3xTgAD mice) model of AD, dietary energy restriction can prevent cognitive decline by delaying the aging processes in the brain, which is the main risk factor for AD (Halagappa et al., 2017).

The effects of social isolation in 16-months-old female 3xTg-AD mice, a genetic model of AD, and their age-matched non-transgenic counterparts, the gold-standard C57BL/6 mice were also studied.

AIMS

- To study **olfactory ethograms** in normal and advanced AD-related pathological aging using female Non-transgenic mice and the **3xTg-AD mice**
- Short forced isolation (3 months) was observed male and female mice 3xTg-AD and wildtype who were separated their cage mates after 10 months of living in a standard social environment.
- To study the effects of isolation in 16-month-old female mice 3xTg-AD and wildtype and how it affects or influences their olfaction-related behaviors.

MATERIALS AND METHODS

Female 3xTg-AD	10	ISO Female 3xTg- AD	7
Female NTg	7	ISO Female NTg	8

An olfactory paradigm, was used to investigate in 16 month-old females with normal (WT mice) and AD-pathological (3xTg-AD mice) aging the ethological patterns shown in the olfactory inspection of a new cage with beddings and the posterior detection, finding and consumption of food pellets hidden in this new anxiogenic environment.

RESULTS

Table 1. Effects of forced social isolation of female NTg and 3xTg-AD mice in food-finding test and the time delay between actions.

	Female 3xTg-AD (n=10)		ISO Female 3xTg-AD (n=7)		Female NTg (n=7)		ISO Female NTg (n=8)	
	Mean	± SEM	Mean	± SEM	Mean	± SEM	Mean	± SEM
A)Food finding test	Lat Sniffing:*** Genotype; Lat FF:*Genotype, * ISO; LatEat: **Genotype							
Lat of sniffing (s)	558.6	± 66.6	599.7	± 13.6	471.7	± 71.2	496.5	± 70.6
Lat of finding food (s)	607.3	± 84.5	800.1	± 149.5	541.7	± 120.9	993.8	± 172.1
Lat of eating (s)	1662.6	± 170.2	2497.1	± 366.5	2098.3	± 112.4	2247.6	± 160.5
B) Time (s) delay								
Sniffing - Finding	48.7	± 42.2	200.4	± 152.7	70,0	± 35.2	498.8	± 183.4
Finding - Eating	1055.3	± 233.9	1697.0	± 319.9	1556.6	± 289.6	1253.1	± 255.2
Sniffing - Eating	1104.0	± 241.1	1897.4	± 358.9	1626.6	± 292.5	1751.9	± 198.2

Results are expressed as mean ± SEM. A) Food-finding test: Latencies in the food finding test: Lat of Sniffing, latency to smell the hidden pellet; Lat of Finding Food, latency to find the hidden pellet; Lat of Eating, latency to eat the pellet. B) Time (s) between actions: Sniffing and Finding food; Finding food and Eating it; Sniffing and Eating it. Statistics: * $p < 0.05$, **$p < 0.01$, ***$p < 0.001$,
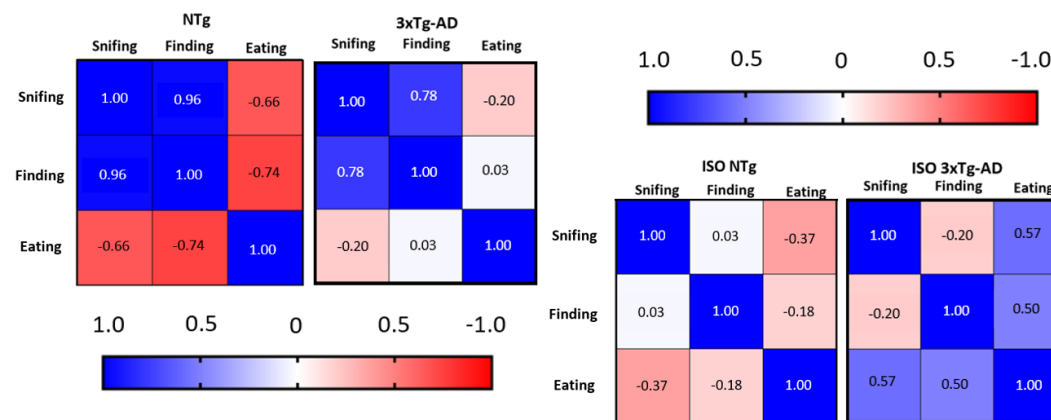

Figure 1. Olfactory signatures in mice with normal and AD-pathological aging in the food-finding test. Meaningful correlation analysis in food finding test. Graphical representation of the significant Pearson r correlations between the three olfactory actions. All of them were positive. Graphical representation of the significant Pearson r correlations between the three olfactory actions.

DISCUSSION AND CONCLUSIONS

The present results on the olfactory signatures in female 3xTg-AD mice compared to C57BL/6 non-transgenic mice show the following:

- The FFT paradigm without food deprivation elicited longer ethograms than previously reported with the standard overnight food deprivation protocol. However, it identified the genotype-dependent olfactory signatures in normal and AD-pathological aging.
- Social isolation slightly increased the latencies, but the olfactory signatures were preserved. However, a functional derangement was detected since the internal correlation among the three goal-directed behaviors was lost under isolation.
- **In conclusion, the new paradigm without overnight deprivation was sensitive to genotype and isolation changes in the ethogram and function and can be used to study old animals.**

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