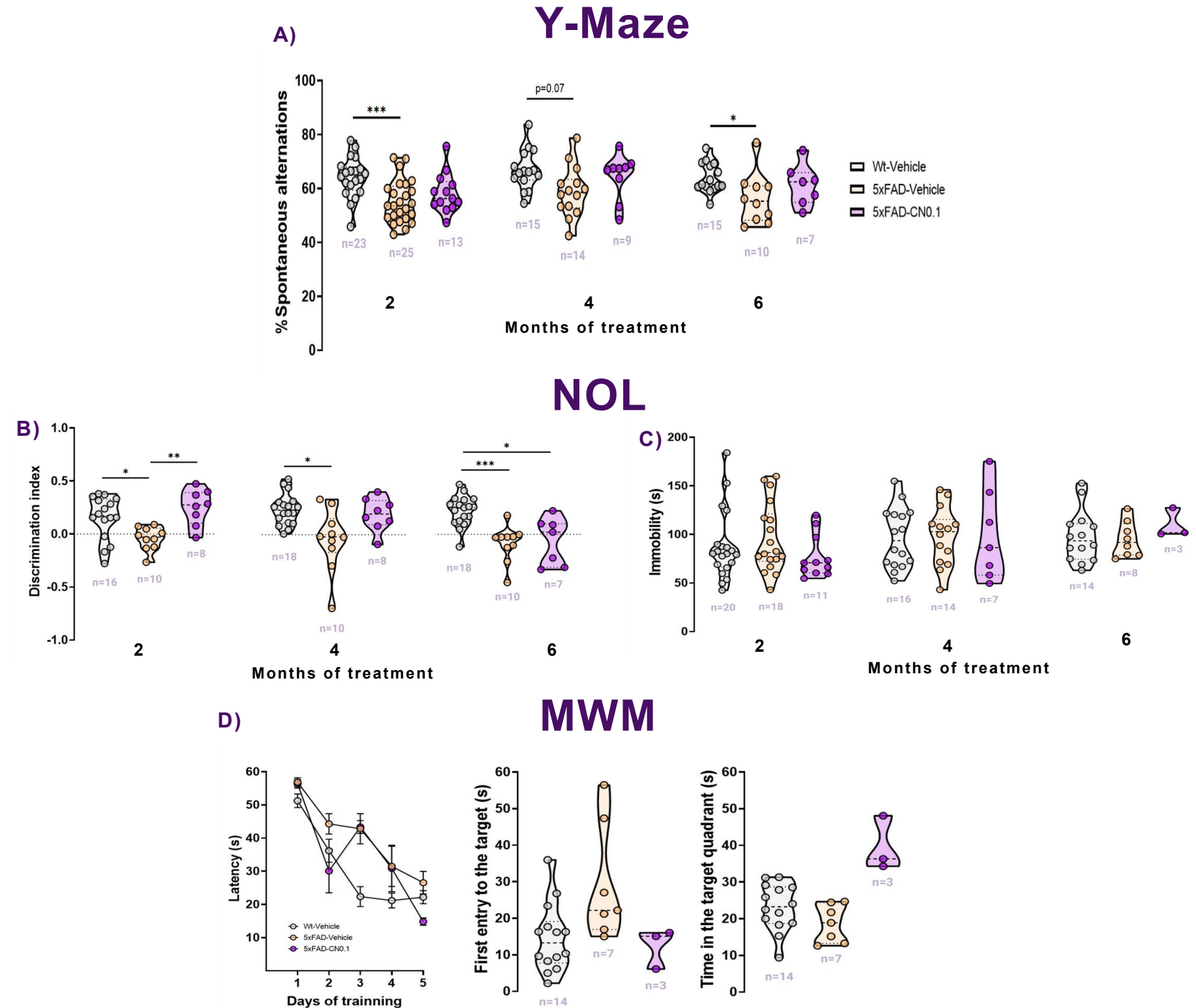
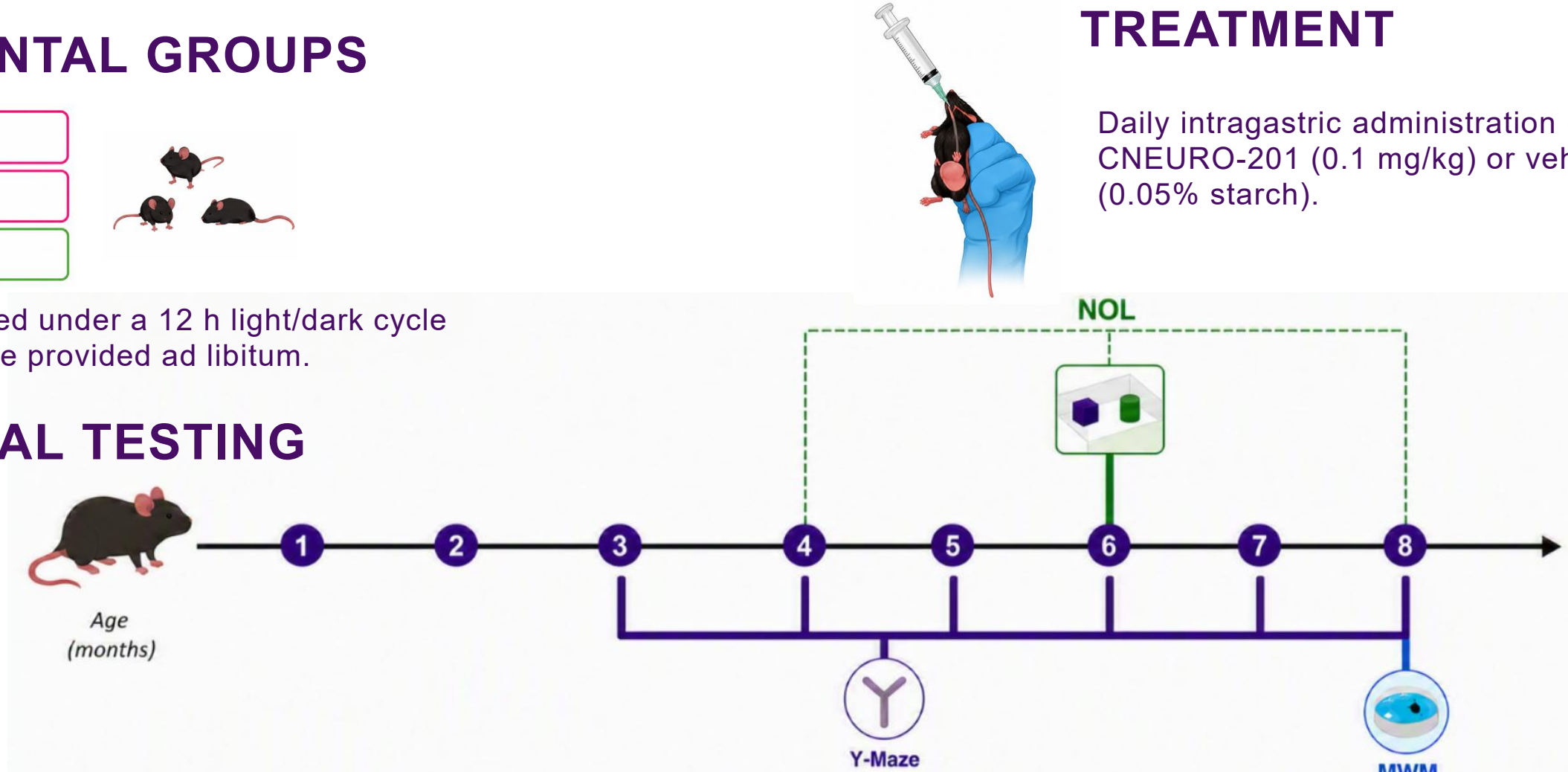


Behavioral Phenotypes Associated With Alzheimer’s Disease Progression And Pharmacological Intervention In 5xFAD Mice.

P2-02

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Behavioral assessment revealed an age-dependent cognitive decline in 5xFAD mice, characterized by impairments in working, recognition, and spatial memory. These findings support the use of the 5xFAD model as a robust preclinical platform for studying Alzheimer's disease progression and evaluating potential therapeutic interventions such as CNEURO-201.

INTRODUCTION		RESULTS		CONCLUSIONS	
Alzheimer's disease (AD) is a common neurodegenerative condition among the elderly, affecting millions of people worldwide. To date, there is no effective treatment to halt its progression. In this context, the development of multifunctional compounds represents a novel strategy for combating AD. A potential solution to this challenge may lie in the methodological approach used for the preclinical evaluation of new compounds. Specifically, multifunctional molecules with therapeutic potential for AD should demonstrate (in animal models) attributes such as the sustainability of long-term effects and the compound's anti-neurodegenerative capacity. A longitudinal study was designed to investigate these properties in CNEURO-201, an anti-amyloidogenic compound and $\sigma 1$ receptor agonist that has been shown to delay cognitive decline and the molecular alterations associated with AD. The ongoing protocol consists of a six-month intervention with a dose of 0.1 mg/kg of CNEURO-201 (treated group) or an equivalent volume of vehicle (control group) in 5xFAD transgenic mice (2 months), wild-type and heterozygous. In all animal groups, cognitive ability is assessed periodically using the Y-maze (monthly), the Novel Object Localization (NOL) (bimonthly), and the MWM (semesterly).		 Figure 1. Behavioral performance in WT-vehicle, 5xFAD-vehicle, and 5xFAD-CN201 mice across treatment duration. (A) Y-maze spontaneous alternations. (B) NOL discrimination index. (C) NOL immobility time. (D) Morris water maze performance. Data are shown as violin plots with individual values. Kruskal-Wallis test. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.		- Behavioral assessment revealed age-dependent cognitive deficits in 5xFAD mice, supporting its use as a robust preclinical model of Alzheimer's disease. - Preliminary analyses suggest that CNEURO-201 treatment may exert beneficial effects on selected behavioral parameters and could contribute to delaying aspects of cognitive decline. - Behavioral alterations observed across disease progression provide a valuable framework for evaluating therapeutic interventions in preclinical Alzheimer's disease models. - Further studies integrating behavioral and omics analyses are currently underway to elucidate the mechanisms underlying CNEURO-201-mediated effects.	
METHODS		REFERENCES		CONTACT	
EXPERIMENTAL GROUPS ♀ 5xFAD-CN 0.1 ♀ 5xFAD-VEH ♀ WT-VEH Mice were maintained under a 12 h light/dark cycle. Food and water were provided ad libitum. BEHAVIORAL TESTING  TREATMENT Daily intragastric administration of CNEURO-201 (0.1 mg/kg) or vehicle (0.05% starch).		- García-Pupo, L., et al. (2024). <i>Acta Pharmaceutica Sinica B</i>, 14(10), 4345-4359. https://doi.org/10.1016/j.apsb.2024.06.013 - Martínez-Orozco, H., et al. (2025). <i>International Journal of Molecular Sciences</i>, 26(3), 1301. https://doi.org/10.3390/ijms26031301 - Menéndez Soto del Valle, R., et al. (2026). <i>Journal of Psychopharmacology</i>. Advance online publication. https://doi.org/10.1177/02698811261458343 - Mercerón-Martínez, D., et al. (2024). <i>Brain Research</i>, 1831, 148848. https://doi.org/10.1016/j.brainres.2024.148848 - Oakley, H., et al. (2006). <i>The Journal of Neuroscience</i>, 26(40), 10129-10140. https://doi.org/10.1523/JNEUROSCI.1202-06.2006 - Rivera-Marrero, S., et al. (2020). <i>Bioorganic & Medicinal Chemistry</i>, 28(20), 115700. https://doi.org/10.1016/j.bmc.2020.115700		 ALZHEIMER'S ASSOCIATION AAIC 26	