

Introduction

CBD use is rising among adolescents, driven by widespread availability and the perception that it is a "safe," non-intoxicating wellness product. Adolescence is a critical window for synaptic pruning and circuit refinement. Previous research shows that exposure to cannabinoids (like THC) during this period can induce aberrant pruning and lasting prefrontal dysfunction [1]. Despite this risk, the long-term effects of *pure* CBD on the maturation of social circuits and dendritic architecture remain largely unknown.

Methods

Design

128 Sprague-Dawley rats (Equal sex ratio).

Exposure (PND 23–33):

CBD (50 mg/kg) or Vehicle (Sesame Oil) i.p. every other day

Behavior (PND 41–68)

- *Light-Dark Box* (PND 41): Assessed avoidance of illumination.
- *Elevated Plus Maze & Open Field* (PND 56–62): Assessed generalized anxiety and locomotion.
- *3-Chamber Interaction* (PND 46): Measured sociability and social novelty preference.
- *Resident-Intruder* (PND 68): Evaluated aggression and hierarchical submission.

Neuroanatomy (PND 71)

Golgi-Cox Staining: Medial Prefrontal Cortex (mPFC), BNST, and Hippocampal CA2.

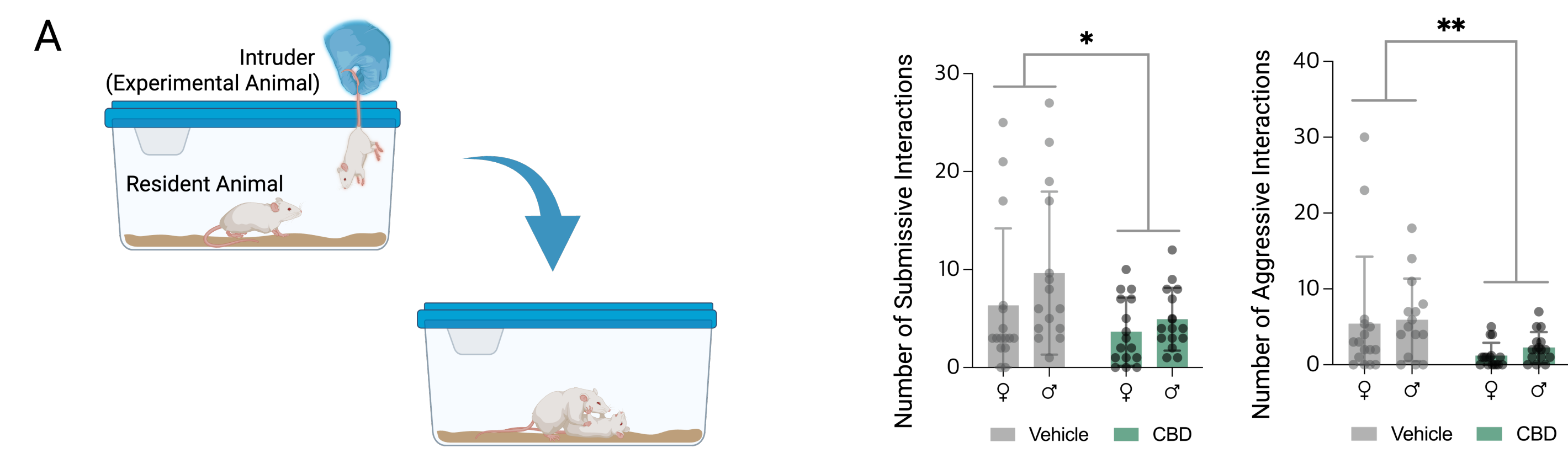
Analysis: 3D neuronal reconstruction for Sholl analysis (branching) and dendritic spine density.

Pharmacokinetics

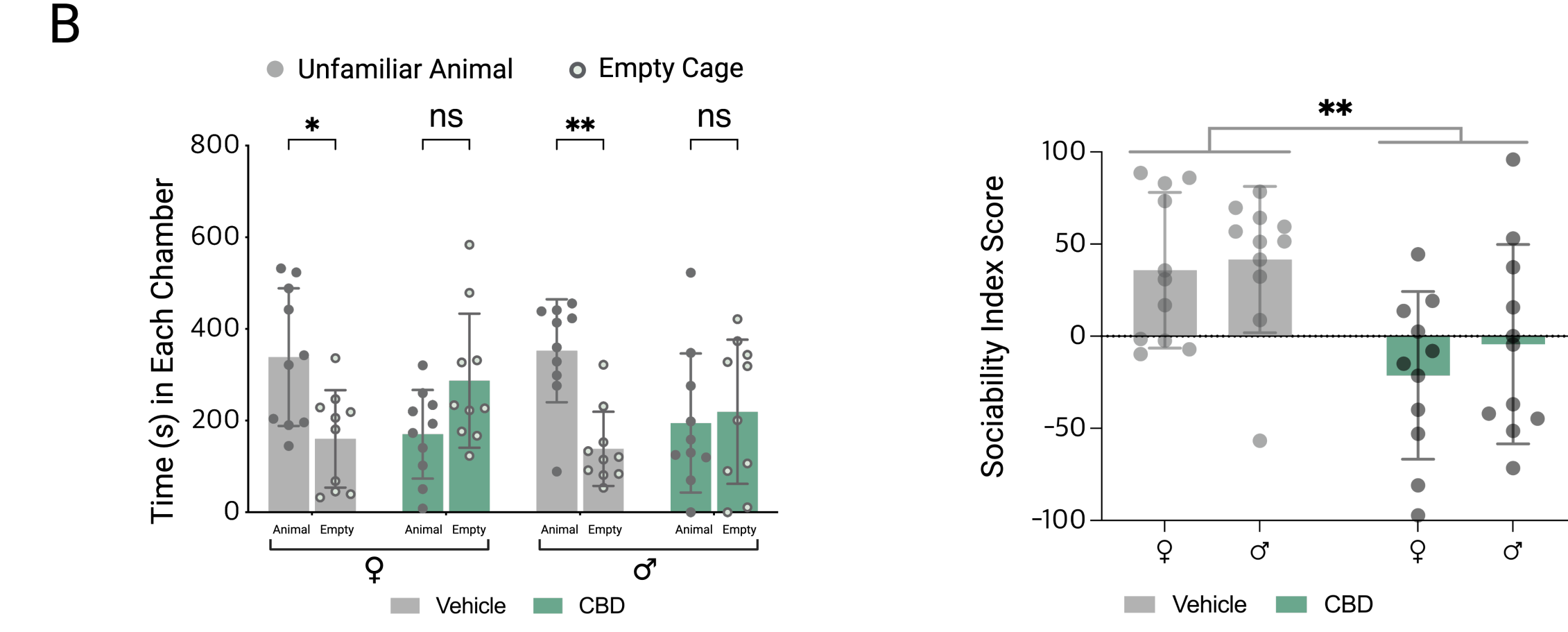
Plasma CBD levels analyzed via LC-MS/MS.

Behavioral Outcome (Fig. 1)

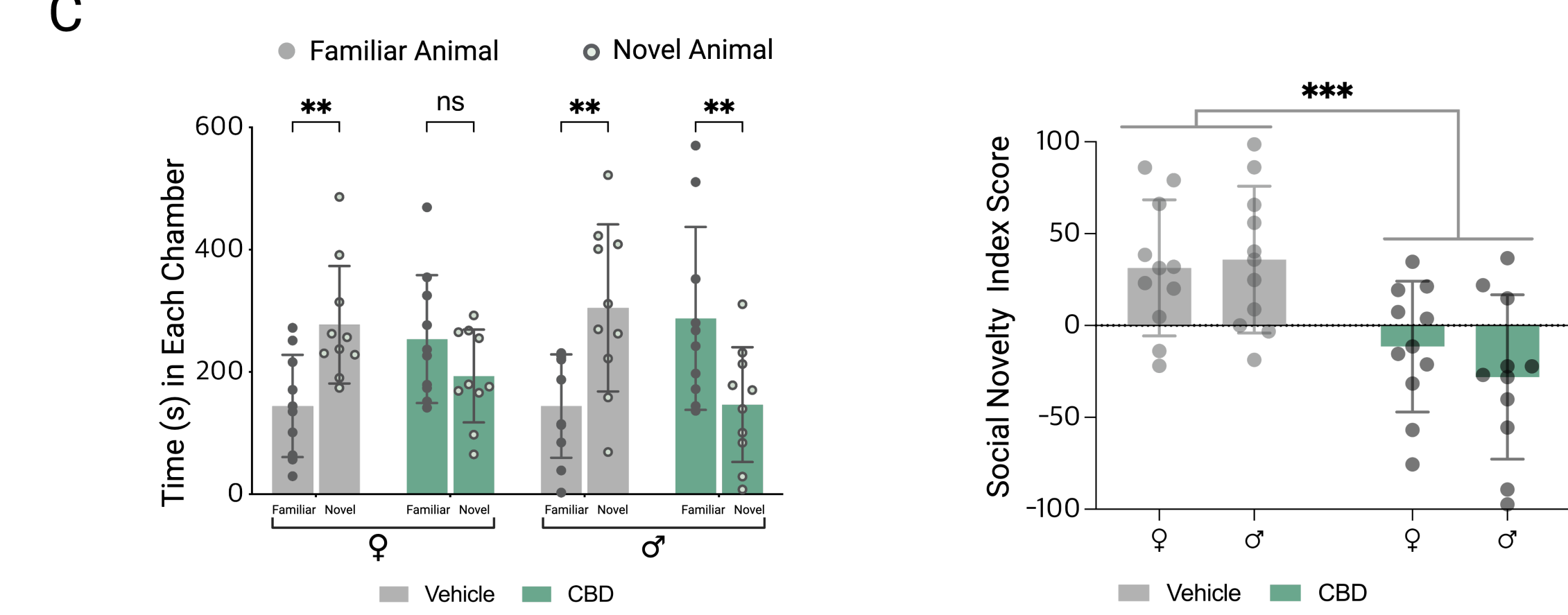
Social/Hierarchical



Three-Chamber Social Interaction: Sociability



Three-Chamber Social Interaction: Social Novelty

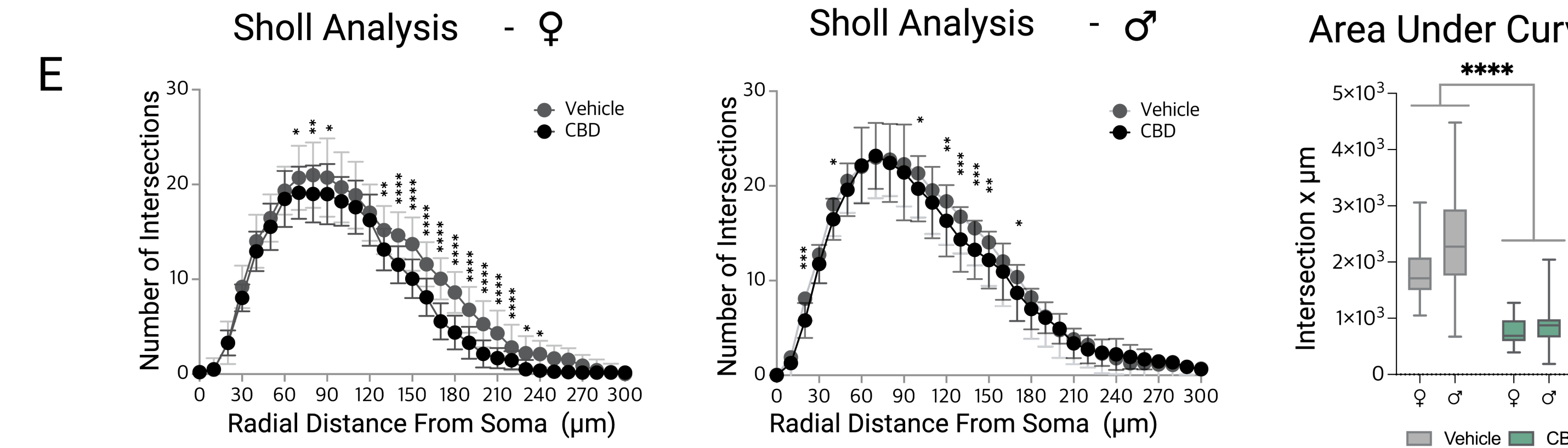
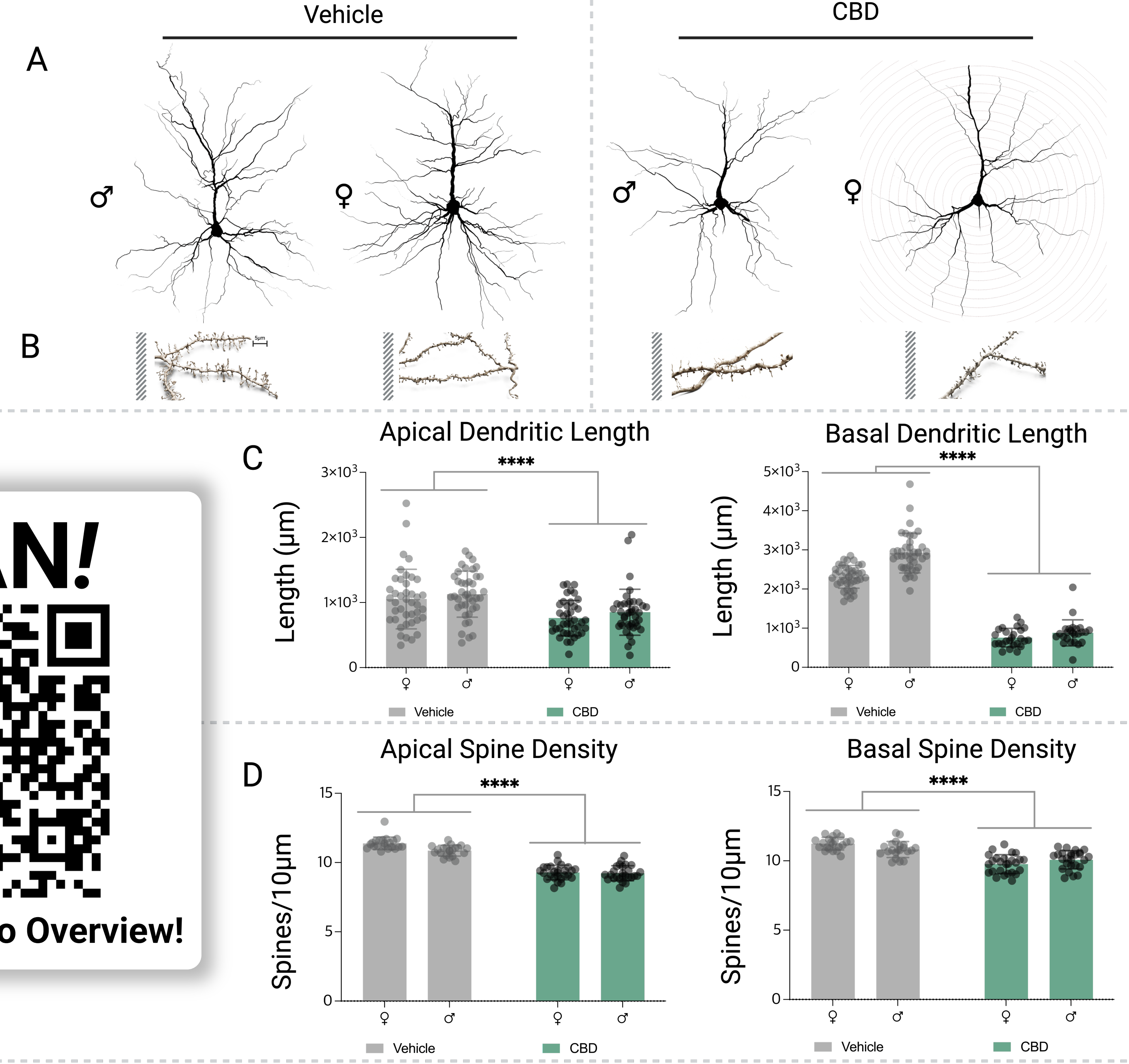


Anxiety-Like Behaviors:

Light-Dark Box: Adolescent CBD exposure significantly increased avoidance of the light compartment (F (1,36) = 9.46, p = 0.0039).

While no significant differences were observed in the Elevated Plus Maze (F (1,55) = 0.22, p = 0.64) or the Open Field Test (F (1,55) = 1.30, p = 0.26)

Neuroanatomical Outcome (Fig. 2)



SCAN!



For a short Video Overview!

Conclusion

Repeated adolescent CBD exposure disrupted social circuit maturation. Adult rats exhibited blunted hierarchical responsiveness in the Resident-Intruder Test (Fig. 1A) and a significant loss of sociability and social novelty preference in the 3-Chamber Task (Fig. 1B, C).

These behavioral deficits were paralleled by significant structural regression in the mPFC. Reconstructed neurons (Fig. 2A) and representative spines (Fig. 3B) revealed profound reductions in dendritic length (Fig. 3C), spine density (Fig. 2D), and arborization complexity (Fig. 2E).

Plasma analysis confirmed that CBD was fully cleared from the system weeks prior to testing, consistent with established pharmacokinetic profiles [2]. This indicates that the observed deficits are the result of lasting developmental disruption rather than residual drug effects.

These structural alterations mirror neurotoxic effects previously seen with THC [15], challenging the prevailing view of CBD as a benign wellness product for youth.

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References

- Renard, Justine et al. "Adolescent THC Exposure Causes Enduring Prefrontal Cortical Disruption of GABAergic Inhibition and Dysregulation of Sub-Cortical Dopamine Function." Scientific reports vol. 7,1 11420. 12 Sep. 2017, doi:10.1038/s41598-017-11645-8
- Soni, Isha et al. "The Effect of Route of Administration and Vehicle on the Pharmacokinetics of THC and CBD in Adult, Neonate, and Breastfed Sprague-Dawley Rats." Cannabis and cannabinoid research vol. 9,5 (2024): e1443-e1451.
- Renard, Justine et al. "Adolescent THC Exposure Causes Enduring Prefrontal Cortical Disruption of GABAergic Inhibition and Dysregulation of Sub-Cortical Dopamine Function." Scientific reports vol. 7,1 11420. 12 Sep. 2017

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