Impact of prenatal exposure to THC on brain anatomy and behavior in adolescent and adult mice

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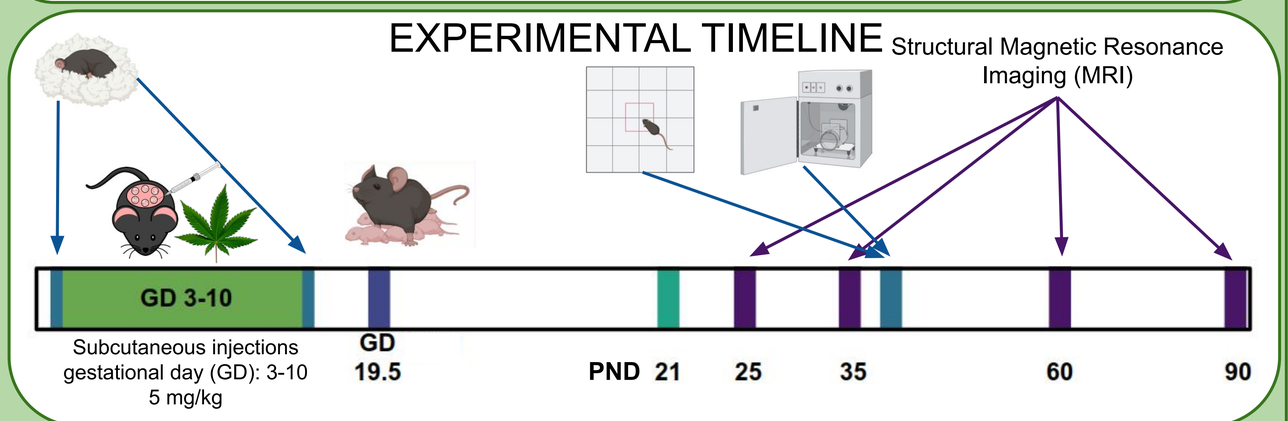
INTRODUCTION

- Increasing rates of cannabis use during pregnancy, before knowledge of pregnancy, or to manage morning sickness
- Cannabis products contain **increasing rates** of the psychoactive component, delta-9-tetrahydrocannabinol (**THC**)
- Few studies investigate long-term impact of prenatal cannabis exposure (**PCE**)

EXPERIMENTAL TIMELINE



SAMPLE SIZE

Reduced sample size in later timepoints

	Males	Females	Litters
Sal	12	12	6
THC	9	11	5

METHODS

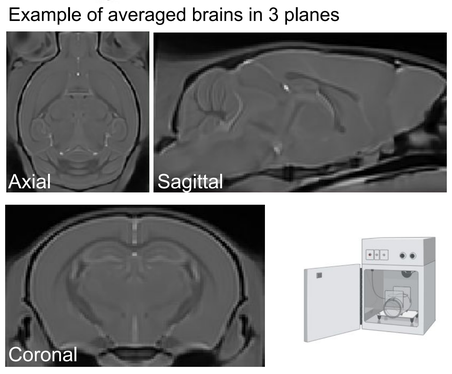
Acquisition

- Nest quality assessed in pregnant dams pre- and post-injections
- 3g material given overnight 19:00-9:00

- Pups weaned at PND 21
- Up to 2 males and 2 females used per litter

- Structural scans acquired on Bruker Biospec 7T small animal scanner
- T1w Fast Low Angle Shot (FLASH), 100 um isotropic

Example of averaged brains in 3 planes



- Open Field Test (OFT) for locomotion and anxiety assessed 2 days after scan 2
- Acquired for 15 minutes
- Processed with Ethovision software

- Prepulse inhibition (PPI) for sensorimotor gating assessed 2 days after OFT
- %PPI calculated where reduced %PPI indicates impaired sensorimotor gating

Statistical analyses: behavior

Linear mixed effects models (LMERs) used for repeated measures

- Outcome: Logged quality ratings
- **Nest quality model:** Main effect - **treatment**; random effects - **ID**

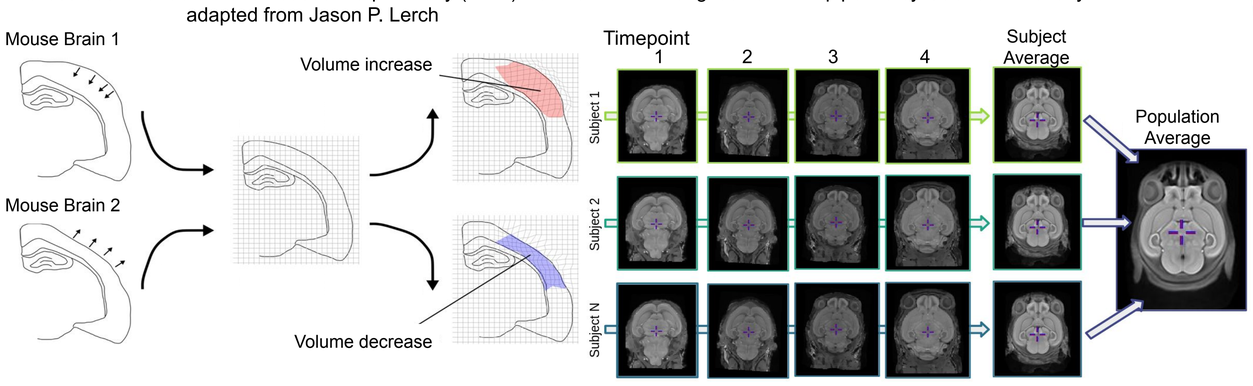
- Outcome: Time in center, distance moved
- **Nest quality model:** Interaction - **treatment*sex**; random effects - **Litter**

- Outcome: %PPI
- **Nest quality model:** Interaction - **treatment*PPLevel*Sex**; random effects - **Litter, ID, Chamber**

IMAGE PROCESSING & ANALYSIS

Cross-sectional deformation based morphometry (DBM) workflow adapted from Jason P. Lerch

Longitudinal DBM pipeline by Gabriel A. Devenyi



- Voxelwise volume differences (logged absolute Jacobians) measured with LMERs
- **MRI model:** Interaction-**treatment***quadratic(**age**)***sex**; random effects-**litter** & **ID**
- **FDR** corrected for multiple comparisons

REFERENCES & ACKNOWLEDGEMENTS

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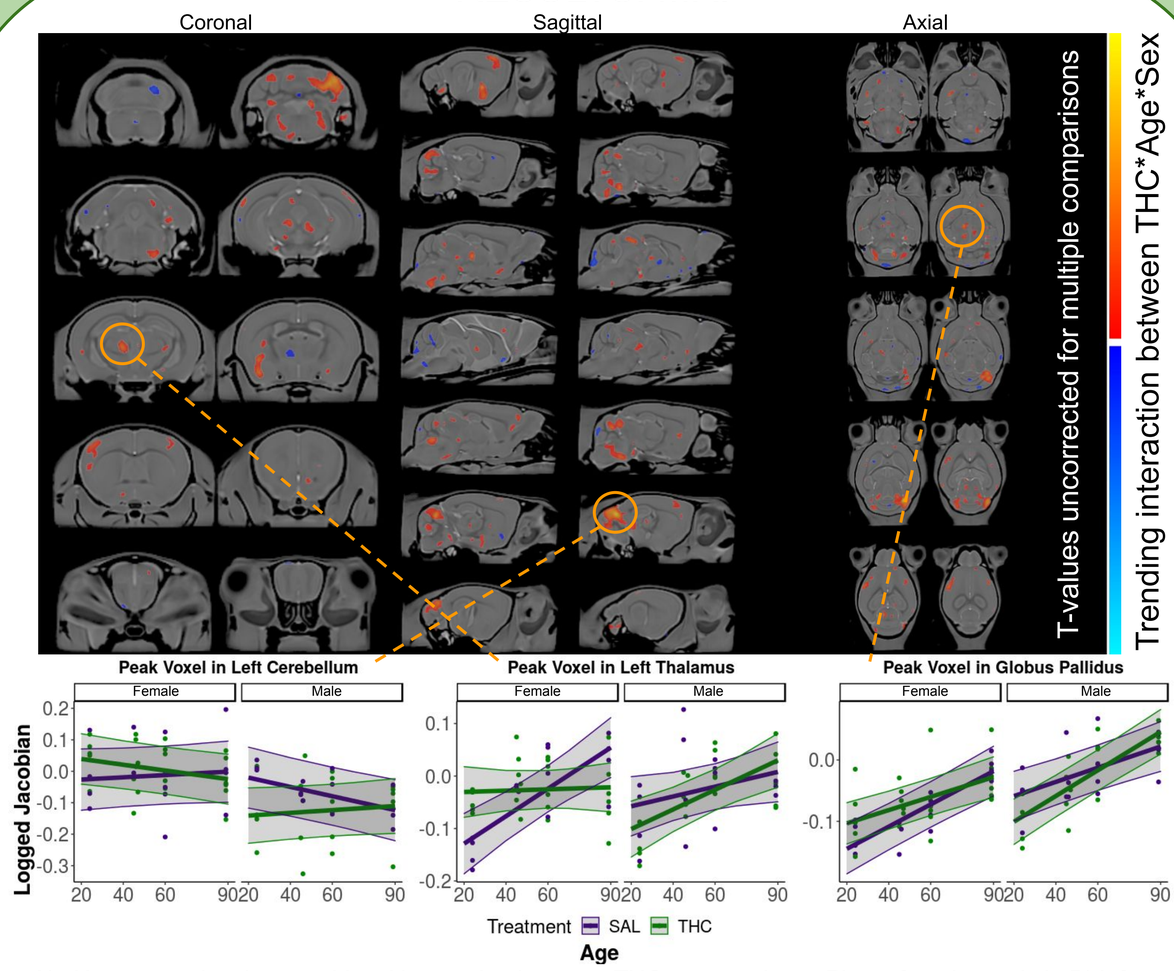
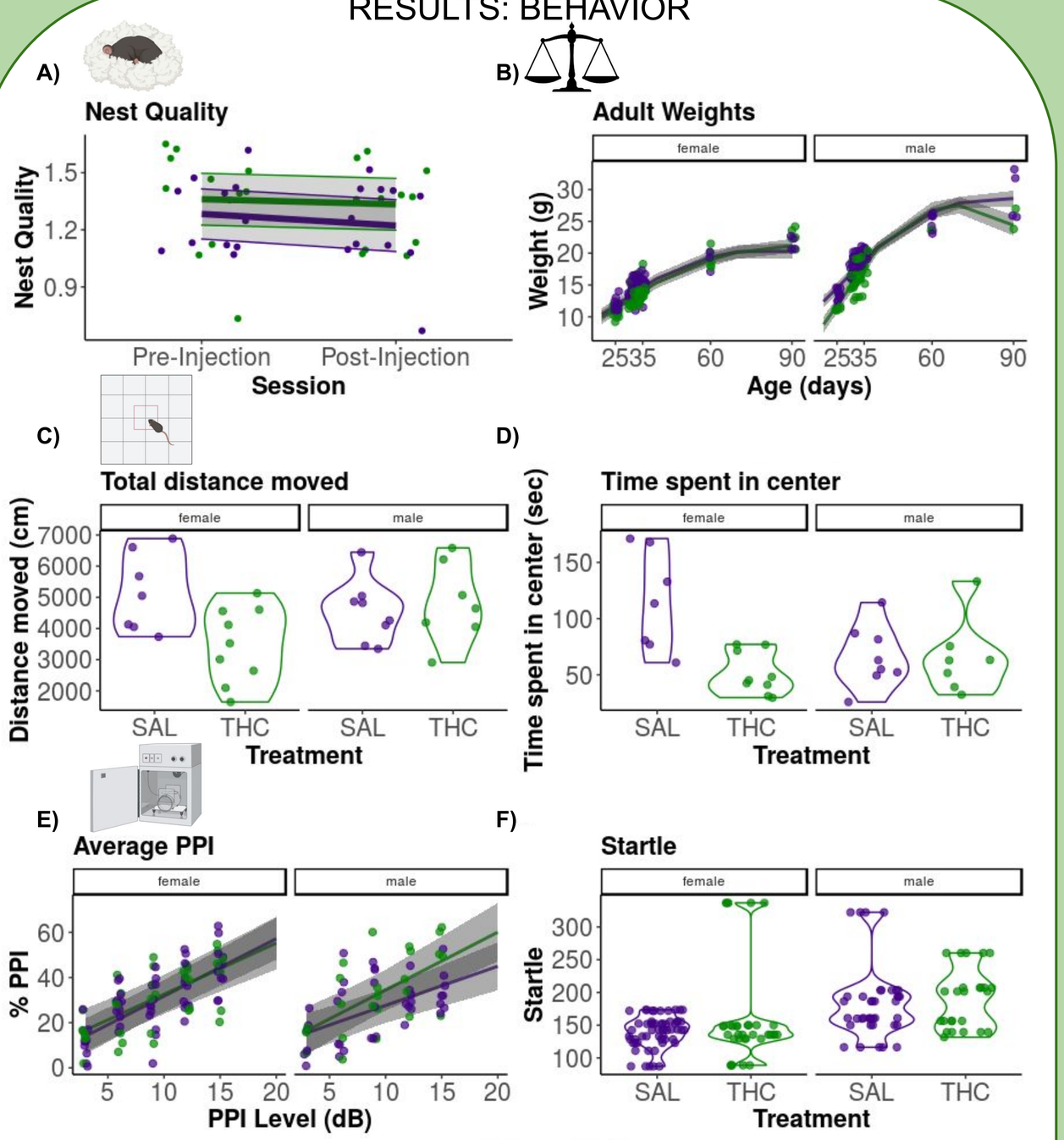
CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada
bio RENDER

RESULTS: MRI



A) Heatmaps showing trend-level interaction between THC, age, and sex. Plots of peak voxels in B) left cerebellum, C) left thalamus, and D) globus pallidus showing in females, PCE tends to decrease volume relative to controls, while it increases it in males. Treatment*age N.S. at 20% FDR.

RESULTS: BEHAVIOR



Results from behavioral analyses: **A)** Neither THC (condition), nor injections (pre-or-post) impacted quality of nests; **B)** Preliminary data suggest PCE may reduce weights in adult male mice ($p < 0.001$). **C)** In females only, PCE reduced total distance moved ($p < 0.05$) and **D)** time spent in center of OFT ($p < 0.05$); **E)** Trending interaction between sex and PPI Level, suggesting increased sensorimotor gating in males ($p = 0.07$); **F)** Trending interaction between sex and PCE ($p = 0.09$), suggesting THC increases startle in females only. Main effect of chamber, suggesting acoustic startle may differ across chambers ($p < 0.001$).

CONCLUSIONS

- PCE alters trajectories of development differently in males and females
- PCE does not impact maternal behavior, but has a sex-dependent impact on adolescent behaviors
- Full sample required to validate the preliminary results
- Future directions include examining the impact of PCE on resting state brain function