RISE RESEARCH INNOVATION SCHOLARSHIP ENTREPRENEURSHIP

Submission ID: 200
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Palmitoylethanolamide Causes Dose-Dependent Changes in Behavior, Brain Activity and N-Acetyl Ethanolamine Chemistry

EKAM THE IMAGE OF DRUG DISCOVERY

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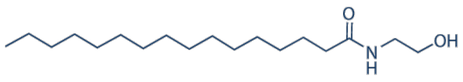
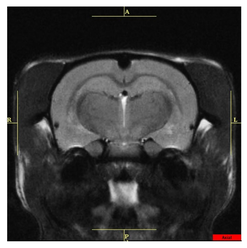
Background, Motivation, and Goals

- Endocannabinoid System
  - Control of motor functions, nociception, appetite
- Palmitoylethanolamide (PEA) is a naturally occurring endocannabinoid that indirectly targets CB1 receptors in the brain
  - Anti-convulsive, neuroprotective and anti-nociceptive effects
  - Mechanisms include inhibiting FAAH (hydrolyzes anandamide)
- Main Goal: Examine effect of PEA on awake rat brain using BOLD MRI Imaging techniques, behavioral assays, and brain/blood lipidomics



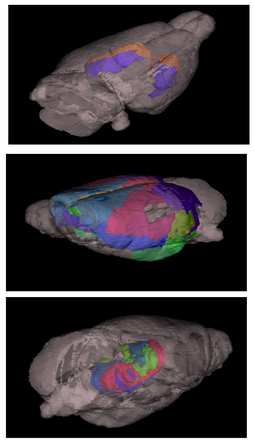


Process and Methods

- PEA Injected into Wistar Rats (250-300g) at concentrations of 3 (LD), 10 (MD), 30 (HD) mg/kg
  - IP Injection
  - PEA Dissolved with Gum Arabic as Vehicle: 20 mg/kg (VEH)
- Awake MRI Imaging (VEH: n=4, LD: n=6, MD: n=5, HD: n=6)
  - Bruker BioSpin 7T MRI
  - Awake Functional MRI (fMRI) and Resting State Functional Connectivity (rsFC) scans
- Open Field Test, Novel Object Recognition, Tail Immersion Assay
- Blood and Brain sample analysis

Findings

- fMRI: Expected Regions Targeted
  - Neg. BOLD response: Thalamus, Striatum, Cerebrum
  - Greater Response with Lower Dose
- Changes in connectivity
- Behavioral effects: reduced locomotion, but insignificant acute pain effects
- Effects on various lipid signaling molecules in blood samples for MD and HD groups



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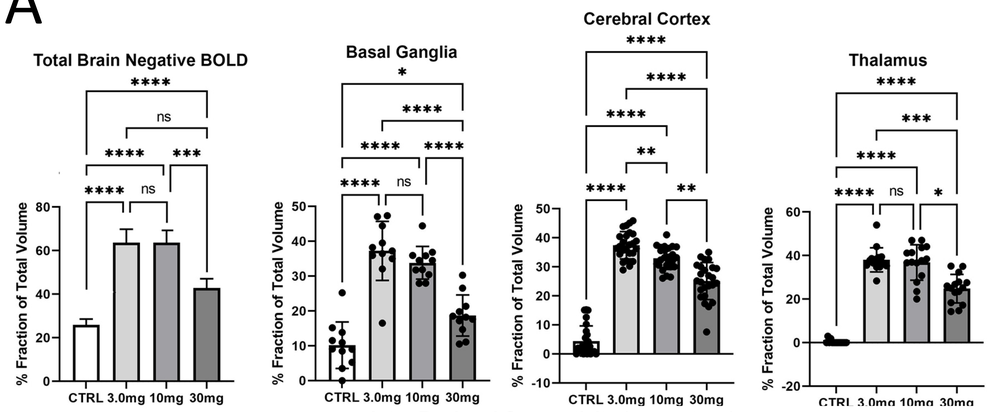

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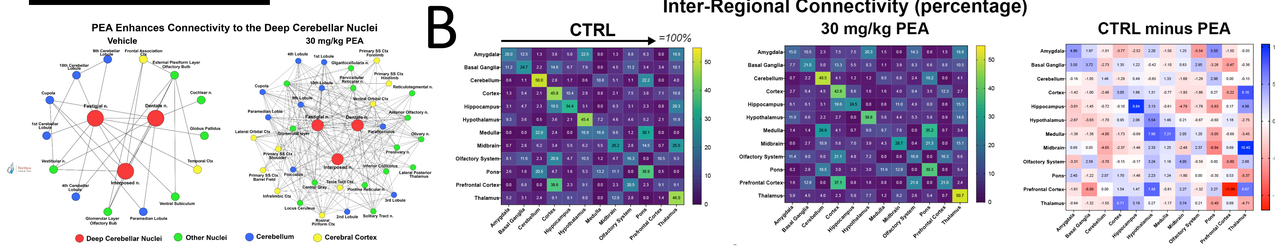

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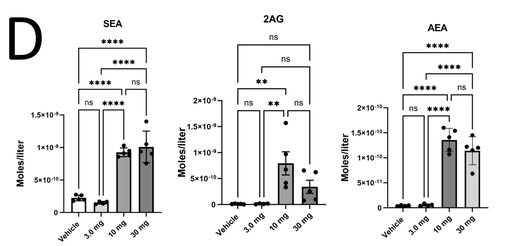

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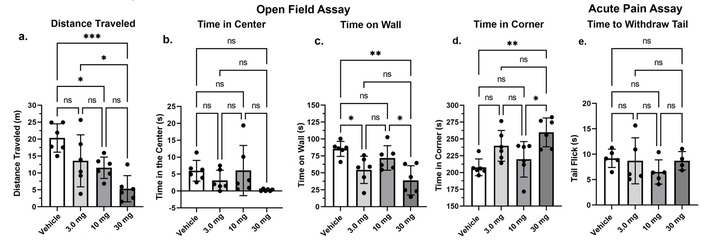

Conclusion and Next Steps

- PEA has a dose-inverse response in thalamus, striatum, and cortex, especially in areas related to pain and movement
- No effect on acute pain, but other behavioral effects; reduced locomotion in open field and novel object assay
- Blood/Brain Extraction
  - Extraction and Analysis of blood and brain sample by collaborators at Indiana University for VEH and LD groups

Acknowledgements

I would like to thank Dr. Craig Ferris and Dr. Praveen Kulkarni in helping me with all aspects of the study, including teaching me how to use the MRI and helping me with the data analysis. I would like to thank Ashley Ghaw and Nishit Singh for help with the blood and brain extractions. I would also like to thank Dr. Heather Bradshaw and all of our collaborators at Indiana University for their work on the blood and brain analysis of the rats.