RISE RESEARCH INNOVATION SCHOLARSHIP ENTREPRENEURSHIP

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Palmitoylethanolamide Causes Dose-Dependent Changes in Brain Function and the Brain/Plasma Lipidome

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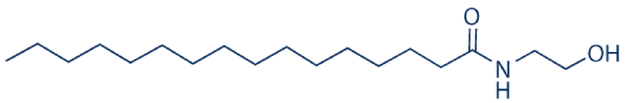
EKAM
THE IMAGE OF DRUG DISCOVERY

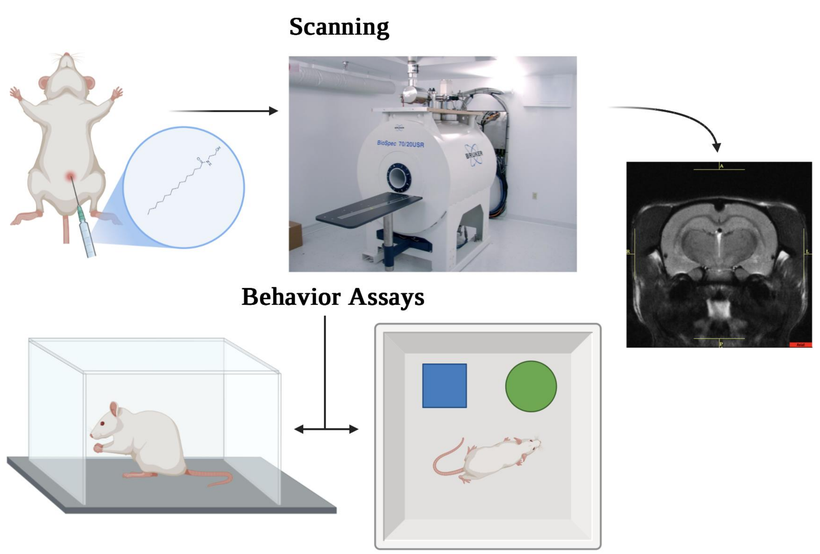
Background, Motivation, and Goals

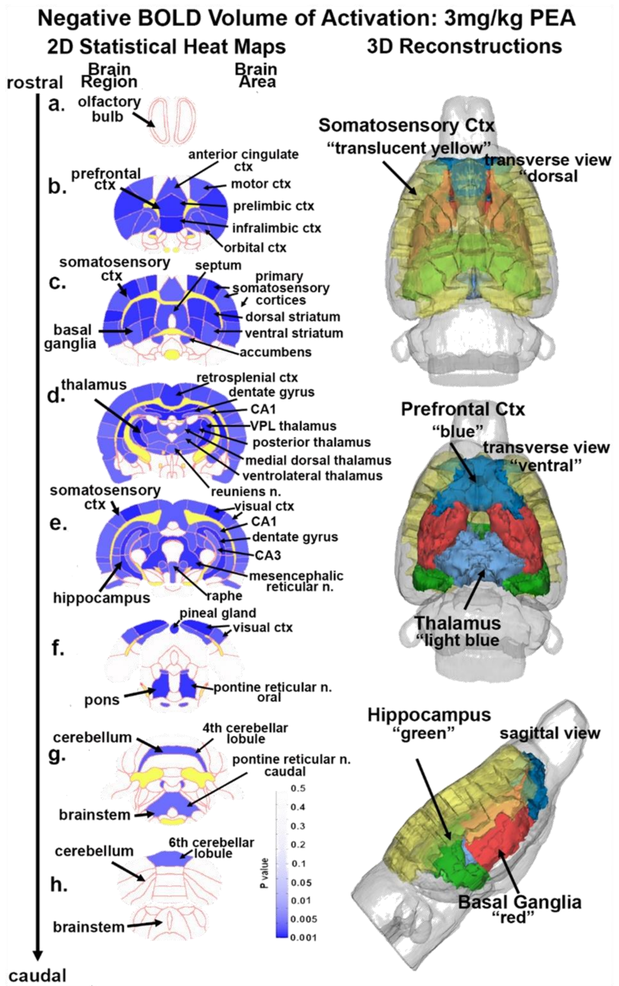
- Palmitoylethanolamide (PEA) is a naturally occurring endocannabinoid that indirectly targets CB1 receptors in the brain.
  - Anti-convulsive, neuroprotective and anti-nociceptive properties.
  - Mechanisms include inhibiting FAAH (hydrolyzes anandamide).
- Main Goal: Examine effects of PEA on awake rat brains using BOLD fMRI imaging, behavioral assays, and brain/blood lipidomics.



Process and Methods

- PEA IP injected into Wistar Rats (250-300g) at concentrations of 3 (LD), 10 (MD), 30 (HD) mg/kg.
  - PEA Dissolved with Gum Arabic : 20 mg/kg
- Awake MRI Imaging (VEH: n=4, LD: n=6, MD: n=5, HD: n=6, equal sex split).
  - Bruker BioSpin 70/20 7T MRI
  - Awake functional MRI (fMRI) and Resting State Functional Connectivity (rsFC) scans
- Behavioral Assays: Open Field Test, Novel Object Recognition, Tail Immersion Assay
- Blood and Brain sample analysis: HPLC/MS/MS lipidomics, Blood Plasma PEA Concentrations

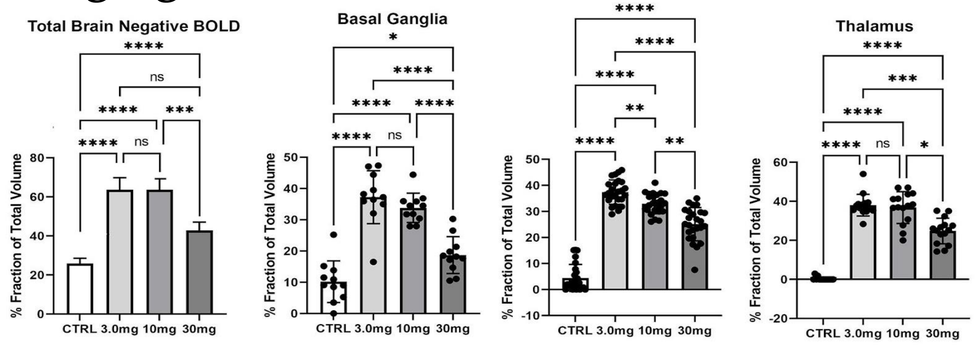


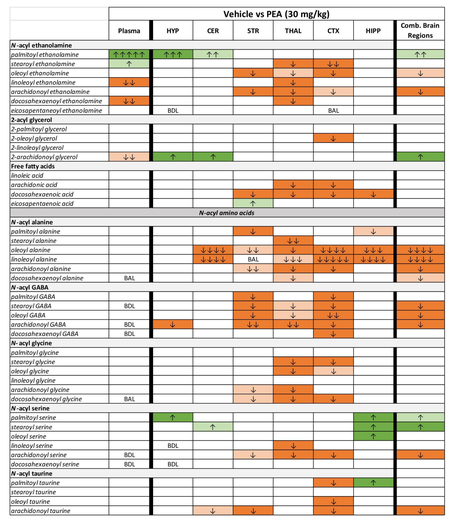


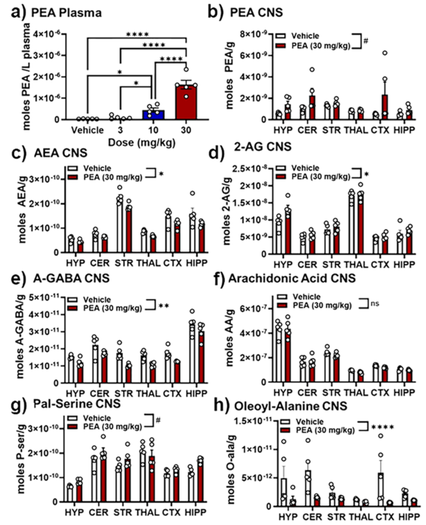
Findings

- Dose-dependent increase in functional connectivity within the prefrontal cortex, sensorimotor cortices, basal ganglia, and thalamus.
  - Inverse dose–response for negative blood-oxygen-level-dependent (BOLD) signals, suggesting a decrease in brain activity in these regions.
- Behavioral effects: reduced locomotion, but insignificant acute pain effects.
- Post-treatment analyses showed changes in plasma and central nervous system levels of PEA and over 80 endogenous lipids, suggesting that PEA influences lipid signaling pathways.

Imaging Results







Conclusion and Next Steps

- Implications: First study to look at effects of acute PEA on functional brain activity and connectivity.
- PEA, and possibly other endogenous endocannabinoid molecules, have widespread and variable effects on the brain's function and lipidome. More research is necessary to understand the nature of these interactions and the endocannabinoid system as a whole.
- Limitations:
  - Acute period: Long-term changes or adaptations were not evaluated. Effects on neuroplasticity or sustained lipidomic changes remain unknown.
  - U-shaped dose response: may limit the predictability of PEA's effects at different dosages.

Acknowledgements

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