Investigating DHA Levels in Rat Brain Tissues in Relation to Maternal THC Exposure Using MALDI-IMS

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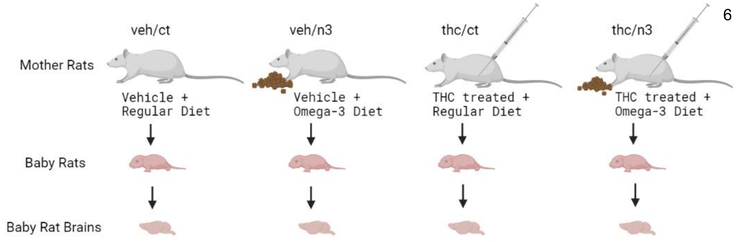
Background

Some pregnant women use cannabis for nausea, depression and anxiety. However, exposure to THC (Δ9-tetrahydrocannabinol) has been found to increase the risk of developing various psychiatric diseases including schizophrenia[1]. Our research team's current focus is to study if fetal development is affected by maternal exposure to THC. Specifically, we obtained compelling preliminary data that omega-3 fatty acids levels, including docosahexaenoic acid (DHA), significantly decreased in rat offspring after maternal exposure to THC. This is dangerous as omega-3 fatty acids are essential for brain health, development, and healthy aging, and insufficient amounts have been shown to correlate with a decrease in cognitive function and promoting psychiatric diseases such as Alzheimer's disease[2] and schizophrenia[3]. DHA is also important for proper fetal development as the concentration of omega-3 in the fetus is positively correlated to the quantity of omega-3 absorbed by the mother[4,5]. Our hypothesis is that an omega-3 supplemented diet may offset some for deleterious effects of THC.

Objective

This research focuses on comparing DHA levels in offspring rat brains from four groups of maternal rats, vehicle rats with a controlled diet (veh/ct), vehicle rats with an omega-3 rich diet (veh/n3), THC treated rats with a controlled diet (thc/ct), and THC treated rats with an omega-3 rich diet (thc/n3) to study if THC is responsible for lowering DHA levels, and if an omega-3 rich diet is able to suppress a THC caused deficiency.



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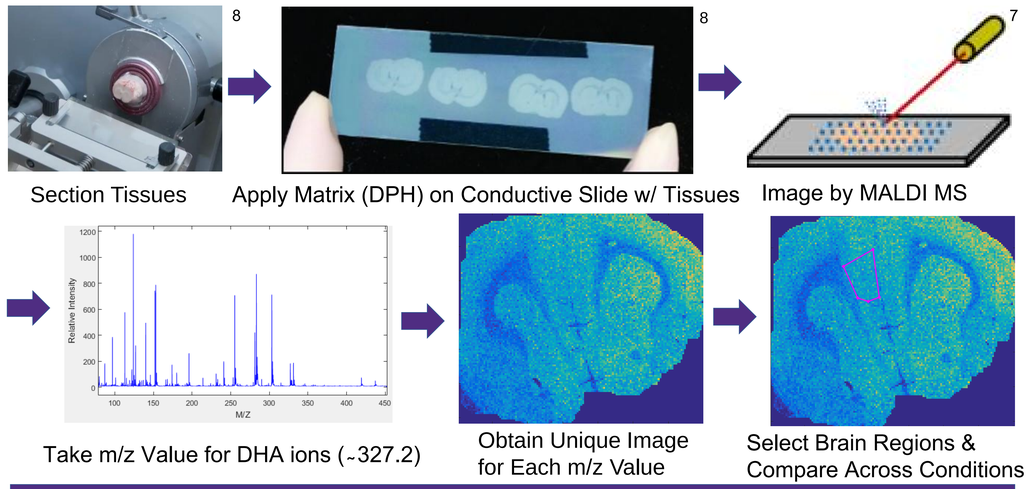
Methods

MALDI-IMS (Matrix Assisted Laser Desorption/Ionization Imaging Mass Spectrometry) is used to detect and quantify various analytes such as fatty acids in tissue samples.

In MALDI-IMS, sample tissues are coated with a UV absorbing matrix that allows for the ionization of non-UV absorbing analytes when laser energy is applied.

This method generates a mass spectrum of the ion masses at each "pixel" (the individual area hit by the laser beam) and shows the spatial distributions and identities of the various compounds present in the sample from a mass-to-charge ratio (m/z)[7].

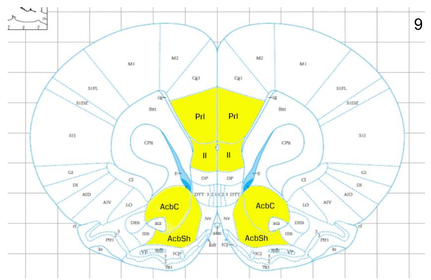
Workflow



Results

Regions of Interest

- Prl (Prefrontal Cortex)
- Il (Infralimbic Cortex)
- AcbC (Nucleus Accumbens Core)
- AcbSh (Nucleus Accumbens Shell)



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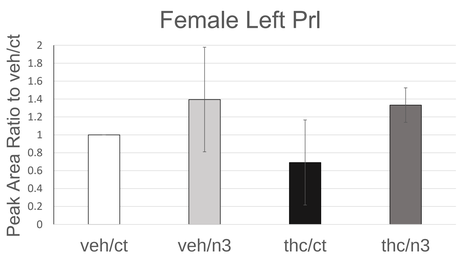
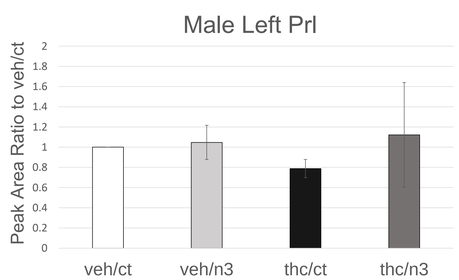
21-Day-Old Females (n=3)

	Average Peak Area Ratio to veh/ct ± SD		
Region	veh/n3	thc/ct	thc/n3
Left Prl	1.39 ± 0.58	0.69 ± 0.47	1.33 ± 0.19
Right Prl	1.36 ± 0.56	0.73 ± 0.47	1.30 ± 0.24
Left Il	1.45 ± 0.62	0.69 ± 0.47	1.41± 0.34
Right Il	1.35 ± 0.54	0.71 ± 0.50	1.42 ± 0.45
Left AcbC	0.99 ± 0.23	0.86 ± 0.51	1.24 ± 0.34
Right AcbC	1.20 ± 0.55	0.71 ± 0.51	1.21 ± 0.44
Left AcbSh	0.96 ± 0.19	0.82 ± 0.50	1.13 ± 0.48
Right AcbSh	1.22 ± 0.54	0.67 ± 0.52	1.26 ± 0.81



21-Day-Old Males (n=3)

	Average Peak Area Ratio to veh/ct ± SD		
Region	veh/n3	thc/ct	thc/n3
Left Prl	1.05 ± 0.17	0.79 ± 0.09	1.12 ± 0.52
Right Prl	1.02 ± 0.23	0.74 ± 0.09	1.01 ± 0.50
Left Il	1.07 ± 0.17	0.80 ± 0.10	1.09 ± 0.43
Right Il	1.06 ± 0.16	0.79 ± 0.10	1.06 ± 0.46
Left AcbC	1.14 ± 0.11	0.74 ± 0.08	1.04 ± 0.35
Right AcbC	1.00 ± 0.14	0.71 ± 0.11	0.90 ± 0.43
Left AcbSh	1.11 ± 0.25	0.79 ± 0.08	0.94 ± 0.35
Right AcbSh	0.96 ± 0.27	0.76 ± 0.18	0.88 ± 0.38



Conclusions

Preliminary results show that on average, THC is responsible for lowering DHA levels in 21-Day-Old rats, and DHA levels in thc/ct rats were found in lower amounts in all 4 regions.

Omega-3 rich diets were also found to be successful at increasing DHA levels, and DHA levels were higher in most regions in both veh/n3 and thc/n3 rats than veh/ct rats. Female rats on omega-3 rich diets also showed a greater increase in DHA levels than male rats.

Further Work

Further Work includes investigating 45-Day-Old rats & 120-Day-Old rats to study any changes in DHA levels with age. Further Work also includes studying estrogen as it is hypothesized that sex hormones are responsible for the differences in female and male DHA recoveries.

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Acknowledgements

I would like to express my gratitude to Dr. Ken Yeung, Kristina Jurcic, and Samantha Cousineau for their guidance, support, and patience while teaching and supervising me during my time in the USRI program.

Also, special thanks to the coordinators and funders of the USRI program which made my time in Dr.Yeung's lab possible.