Prenatal Nicotine and THC Exposure via E-Cigarettes in Rats Alters Select Maternal Factors

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Background

Nicotine and cannabis are two of the most commonly consumed drugs among pregnant women, with prevalence rates of 16% and 10% in the United States, respectively. These numbers are consistently increasing, partially due to the rise in popularity of electronic cigarettes (e-cigarettes). Consumption of drugs via e-cigarettes is assumed to be safer than traditional smoking routes, including among pregnant women. However, the longitudinal effects of prenatal e-cigarette use with either nicotine or cannabis constituents are not well understood. Moreover, the effects of combined use of these drugs has not yet been examined, particularly when consumed via e-cigarettes. This is the case even though nicotine and cannabis are more often consumed together than separately, a practice made easier with the tanks used for e-cigarettes. Unfortunately, data from prospective longitudinal studies examining this public health concern will not be completed for years to come.

Purpose and Objectives

- **To develop a clinically relevant co-exposure model of prenatal nicotine and THC exposure in pregnant rats via e-cigarette vapor inhalation.**
- **Confirm physiological effects of each drug in pregnant rats while avoiding potential nutritional confounds.**

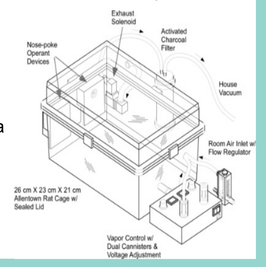
This paradigm was designed for use in future studies examining the long-term effects of prenatal nicotine and THC exposure on offspring brain and behavioral development.

Methodology

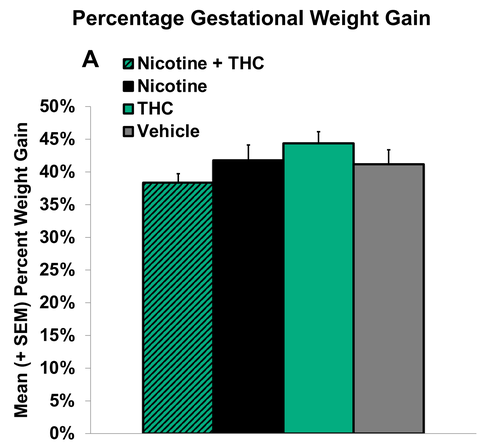
In rats, gestational days (GD) 5-20 mimics the first and second trimesters in humans. Beginning on GD 5, pregnant Sprague-Dawley rats were exposed to either nicotine (36 mg/mL), THC (100 mg/mL), the combination, or the vehicle (propylene glycol) via commercially available e-cigarettes (SMOK V8 X-Baby Q2). Dams were placed in the vapor inhalation chamber (La Jolla Alcohol Research Inc) for 30 min daily; e-cigarette drug administration was delivered through airflow (2 L/min) in individual 6-sec puffs every 5 min during the 30 min session (7 puffs total). Pregnant dams remained in the chamber for an additional 10 min with only airflow in order to clear any residual vapor before removal.

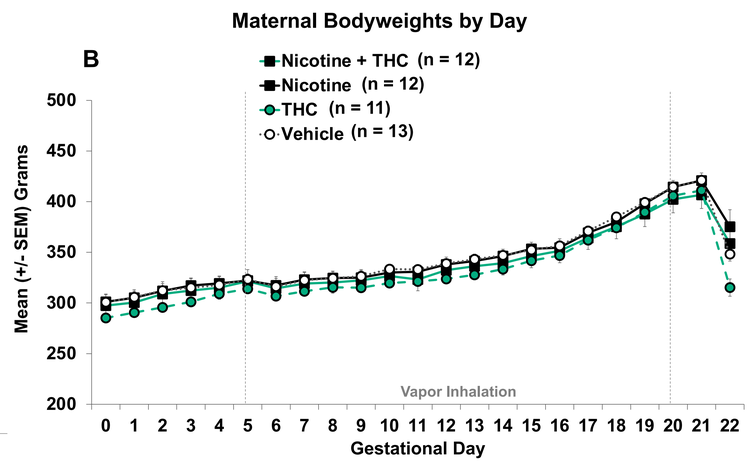
Throughout pregnancy, subjects' body weights, food intake, and water intake were measured daily. Core body temperatures were recorded before and after each exposure session, as THC via e-cigarettes is known to decrease temperature.

Plasma drug levels and litter outcomes were also recorded and are presented in a separate poster.

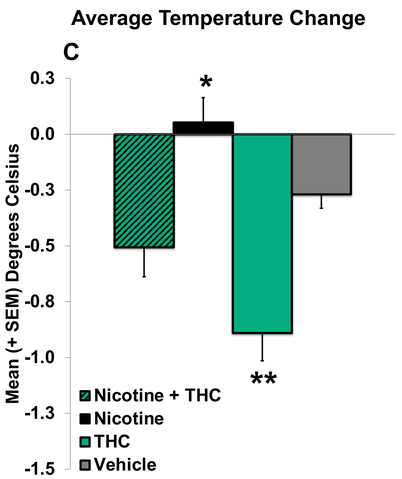


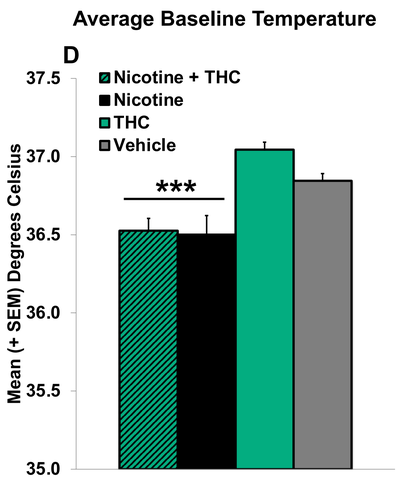
Results

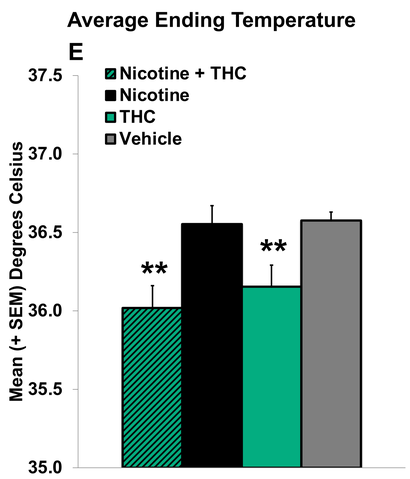




Exposure to nicotine, THC, or the combination via e-cigarettes did not alter the overall percentage of maternal weight gain during pregnancy (A), nor did it alter body weights on or across individual days (B). Similarly, prenatal exposure to either drug did not change the daily food or water intake (data not shown). Thus, this co-exposure model does not produce nutritional confounds in pregnant rats.





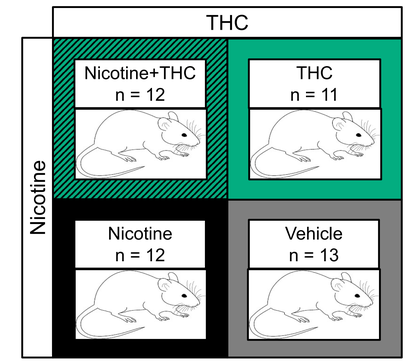


Pregnant rats exposed to THC alone showed significantly greater temperature changes than dams exposed to the Vehicle following intoxication. In contrast, dams exposed to Nicotine alone had significantly smaller temperature changes during intoxication compared to the Vehicle controls, while dams exposed to combined Nicotine+THC had an intermediate effect and did not differ from controls ($F[3,44] = 12.83$, $p < 0.001$, SNK p's < 0.05; C).

To better understand the magnitude of these temperature changes during intoxication, we also examined subjects' body temperatures before (baseline) and after (ending) vapor inhalation sessions. Overall, chronic nicotine exposure via e-cigarettes to pregnant rats decreased baseline core body temperatures ($F[1,44] = 29.06$, $p < 0.001$; D); this effect took place during the latter half of pregnancy (data not shown). Following drug exposure, dams exposed to THC had lower body temperatures, alone or in combination with nicotine ($F[1,44] = 17.19$, $p < 0.001$; E). Thus, the smaller temperature change in the combined exposure group may have been due to a lower baseline temperature.

* = Nicotine > all other groups, $p < 0.05$. ** = THC different from all other groups, p's < 0.05. *** = any Nicotine < no Nicotine, $p < 0.001$.

Subject Information



Conclusions

These data suggest that this prenatal co-exposure paradigm to nicotine and THC via e-cigarettes among pregnant rats:

- Avoids potential nutritional confounds
- Replicates expected physiological effects of THC intoxication
- Induces clear physiological effects of repeated nicotine intoxication

Taken together, use of this paradigm will:

- Provide a clinically relevant model of co-exposure to nicotine and THC via e-cigarettes for preclinical research
- Help inform both the public and public policy on e-cigarette use during pregnancy

Acknowledgements

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Data were analyzed and interpreted at WCUPA by the authors.