

Effects of Tetrahydrocannabinol on Prenatal Skeletal Development

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INTRODUCTION: The rapid expansion of legalized marijuana has been accompanied by an increase in the number of people using this drug. Tetrahydrocannabinol (THC) is the primary psychoactive component in marijuana and can cross the placental barrier, potentially affecting fetal development. Currently, there are no data on the effects of prenatal THC exposure on skeletal development. Therefore, we conducted a study in which rats were prenatally exposed to THC.

METHODS: Rat dams were exposed to THC (0.8 mg/kg) via inhalation or normal air daily from 3 days prior to pairing for breeding until they gave birth. This dose results in peak THC blood plasma levels of 71.6 +/- 10.9 ng/mL which is similar to the clinical levels detectable after smoking marijuana in humans. The pups were then euthanized on postnatal day 60, corresponding to the end of adolescence in humans. All researcher participating were initially blinded. Digital caliper measurements were taken to ascertain tibial and femoral length. The mid-diaphyseal diameter on the anterior-posterior (AP) and medial lateral axes (ML) were taken as well. All measurements were taken with a "Manostat" Caliper. Biomechanical analyses were performed by subjecting femora to a 3-point bending test to determine energy to failure, stiffness, ultimate force, failure force, and yield force. Results were compared between THC and normal air (control) within the male and female cohorts. Sample sizes were 8 for each group. Significance was determined by a two-way ANOVA with Tukey's multiple comparisons tests.

RESULTS SECTION: For the caliper measurements, significant differences were found between the control group and the group exposed to THC for tibial ML diameter in both males and females. Specifically, tibial ML diameter was 57% wider in male controls compared to THC exposed and 29% wider in the female controls compared to THC. We also found that femoral length in females was 4% longer in controls compared to THC. Biomechanically, only male femoral yield force differed significantly, with THC exposure resulting in a 28% increase compared to control.

DISCUSSION: Ongoing analyses include safranin O/fast green staining to assess tibial growth plates and tibial microCT to measure bone density and microstructure. The current data suggests that the effects of prenatal exposure to THC on skeletal development are relatively minor. The completion of these studies will provide us with a better understanding of the effects of prenatal THC exposure on skeletal development.

SIGNIFICANCE/CLINICAL RELEVANCE: Clinical studies have reported that users of marijuana have an increased incidence of skeletal fractures and decreased bone mineral density. Other studies have shown that 2-5% of woman use marijuana regularly during their pregnancies.

REFERENCES: 1. Casey M. O'Connor, et. al. Cannabinoid Use in Musculoskeletal Illness: a Review of the Current Evidence. 2. Committee on Obstetric Practice. Marijuana Use During Pregnancy and Lactation. 3. Joel Ehrenkranz, et. al. Bones and Joints: The Effects of Cannabinoids on the Skeleton.

IMAGES AND TABLES:

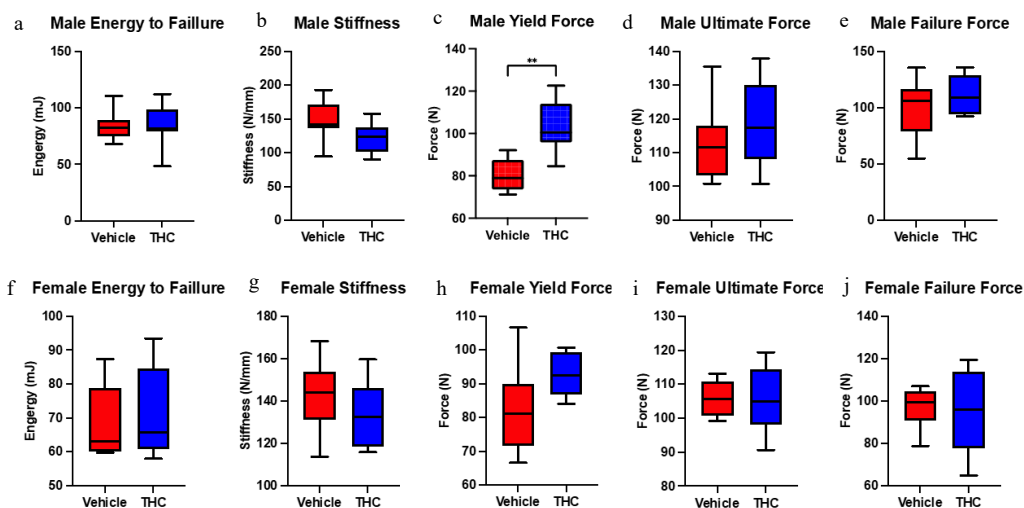


Figure 1. Mechanical integrity of male (a-e) and female (f-j) rat pup femora. Femora were tested for (a,f) energy to failure [mJ], (b,g) stiffness [N/mm], (c,h) yield force [N], (d,i) ultimate force [N], and (e,j) failure force [N]. *p<0.05, **p<0.01