Hypothalamic ghrelin signaling in cannabis induced feeding
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INTRODUCTION
Cannabis is one of the most widely cultivated and trafficked illicit drug worldwide. The recent partial legalization of cannabis is due to its high potential for use in medicine. Importantly, cannabis is widely acknowledged to stimulate appetite. Increasing appetite can be used therapeutically to help patients with cancer or AIDS who often suffer from anorexia. Data from our lab indicates that vapor cannabis exposure increases meal frequency while decreasing meal size. In addition, data also indicates an increase in plasma levels of the appetite-stimulating hormone, ghrelin. Ghrelin is a peptide that is released in the gastrointestinal (GI) tract, and increased levels of ghrelin indicate functional importance in feeding behavior. Once ghrelin is released from the GI tract, it acts on the ghrelin-1a receptor (GHSR-1a) in the CNS. Preliminary experiments from our lab indicate that blockade of ghrelin secretion, or blockade of GHSR-1a activity reduces cannabis induced feeding. Notably, ghrelin targets agouti related peptide (AgRP) neurons in the hypothalamus to stimulate appetite. Increasing appetite can be used potential for use in medicine. Importantly, cannabis is widely acknowledged to stimulate appetite. Increasing appetite can be used to create your presentation. Then send it to

METHODS
Male and female WT and AgRP-GHSR flx/flx mice are used as experimental subjects. Prior to experimental manipulation, mice are habituated to chambers for 5 consecutive days. Then, half of the mice in each group (n=12) are exposed to cannabis over a 5-minute period. Control mice are placed in an identical chamber that has the vaporizer turned on without cannabis. On test day, all mice go under a 6-hour fast prior to vapor cannabis exposure. Subsequently, we measured chow intake at 30 minutes, 1 hour, 2 hours, and 4 hours.

RESULTS
- Low doses of cannabis support appetite in mice relative to larger doses required in rats.
- AgRP-GHSR flx/flx mice display lower food intake after ghrelin injection relative to WT mice.
- WT mice display higher food intake after air exposure in comparison to AgRP-GHSR flx/flx mice.
- Following low doses of cannabis, AgRP-GHSR flx/flx mice display an increase in food intake in comparison to WT mice.

CONCLUSIONS
- Dose response data shows that inhalation of cannabis leads to increased food intake in mice.
- Because of the loss of function of GHSR-1a on AgRP neurons in AgRP-GHSR flx/flx mice, ghrelin-induced feeding is reduced in comparison to WT mice.
- After six hours fast, AgRP-GHSR flx/flx mice show attenuated re-feeding relative to WT mice, further implicating reduced ghrelin signaling.
- However, AgRP-GHSR flx/flx mice display a higher sensitivity to cannabis due high expression of AgRP, potentially due to increased AgRP mRNA expression.
- Collectively, this study validates that cannabis exposure increases feeding behavior in mice. AgRP-GHSR flx/flx mice display a higher sensitivity to cannabis indicating an association between cannabinoid receptors and AgRP neuronal activation in these mice.

VALIDATION OF GHERELIN RESPONSE IN AgRP-GHSR flx/flx MICE

Food Intake

REFERENCES