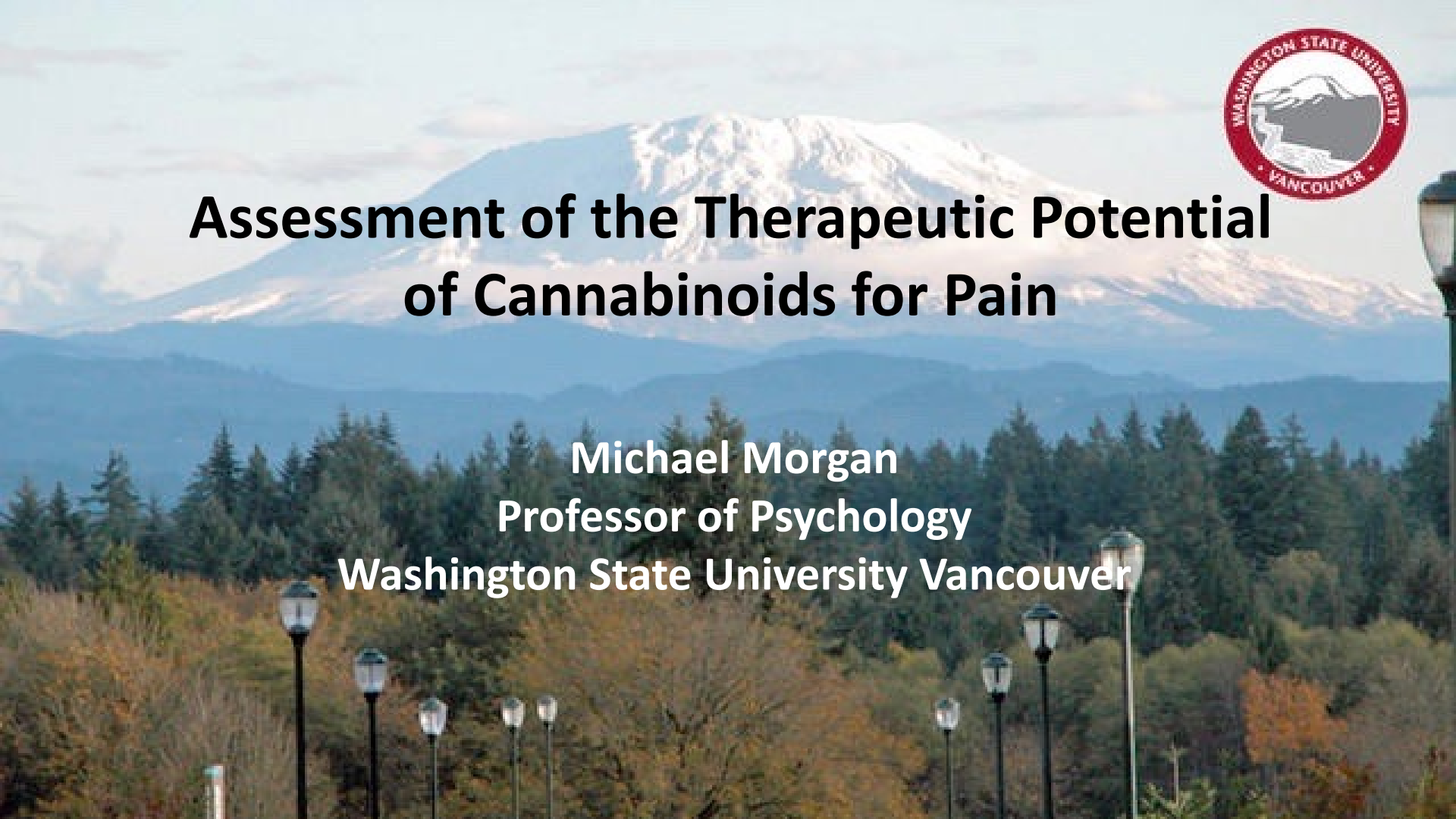


Assessment of the Therapeutic Potential of Cannabinoids for Pain

Michael Morgan
Professor of Psychology
Washington State University Vancouver

Opioids are the most effective treatment for pain, but …

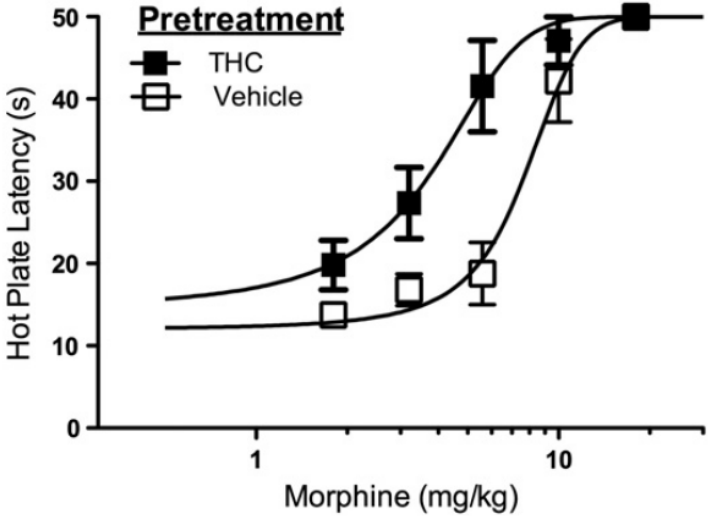
Opioids

- Morphine
- Fentanyl
- Oxycodone

Problems

- Side effects
- Tolerance
- Dependence

Pretreatment with THC enhances morphine analgesia



Wilson-Poe, A. R., Pocius, E., Herschbach, M., & Morgan, M. M. (2013). The periaqueductal gray contributes to bidirectional enhancement of antinociception between morphine and cannabinoids. Pharmacology, Biochemistry & Behavior, 103:444-449. PMID: 23063785

The intersection of science and politics

- Tom Coburn (R, Oklahoma)
  - #68 on list of “Wasteful Stimulus Projects”
- Darrell Issa (R, CA 49th district)
  - Introduces Bill to terminate funding for my grant
- Dino Rossi (Republican candidate for WA Governor)
  - “It’s always 420 at WSU”

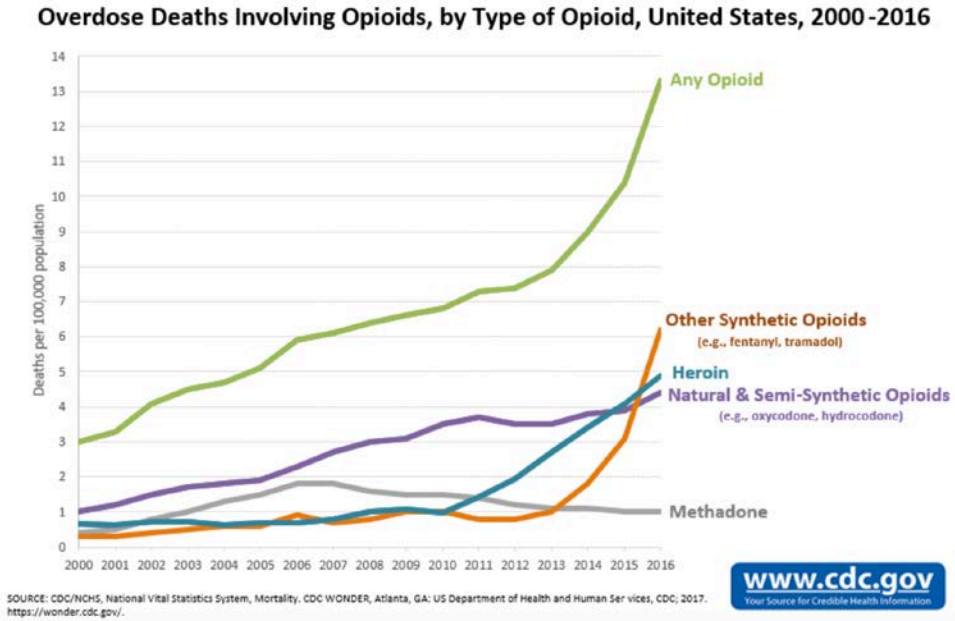
The cost of pain is very high

- Suffering
  - 100 million Americans

- Financial (Health care & worker productivity)
  - $635 billion
    - Heart disease: $309 billion
    - Cancer: $243 billion

Gaskin & Richard, 2012. The Economic Costs of Pain in the United States. J. Pain.

The cost of using opioids to treat pain is also high: 60,000 overdose deaths in the U.S. in2016



Elvis Presley

Prince

Tom Petty

Survey data suggest cannabinoids are a reasonable treatment for pain

Citation:	Schnelle 1999	Swift 2005	Walsh 2005	Sexton 2016
Sample:	Recreational N = 170	Medical N = 128	Medical N = 628	Medical N = 1429
Location:	Germany	Australia	Canada	Washington St.
#1 condition:	Multiple sclerosis	Pain	Sleep	Pain
#2 condition:	HIV	Depression	Pain	Anxiety
#3 condition:	Migraine	Arthritis	Anxiety	Depression
#4 condition:	Asthma	Nausea	Depression	Headache
#5 condition:	Back pain	Appetite	Appetite	Nausea

Randomized controlled trials show mild cannabinoid analgesia for neuropathic pain

Citation	Sample	Result
Wilsey et al., 2013	39 crossover	1.3% THC reduced VAS in 57% vs. 26%
Ware et al., 2010	23 crossover	THC= 5.4 vs. 6.1 on 11 point pain scale
Ellis et al., 2009	34 crossover	Pain reduced in 46% CB patients vs. 18%
Wilsey et al., 2008	38 crossover	Decrease in pain VAS with 3.5% & 7% THC
Abrams et al., 2007	28 CB/27 control	Pain reduced in 52% of CB patients vs. 24%
Rog et al., 2005	34 CB/30 control	2.7 vs. 1.4 drop (11 pt scale) in MS patients
Wade et al., 2004	77 CB/ 77 control	Greater MS pain reduction in placebo vs. CB

Side effects: Sedation, disorientation confusion, dizziness, anxiety, nausea

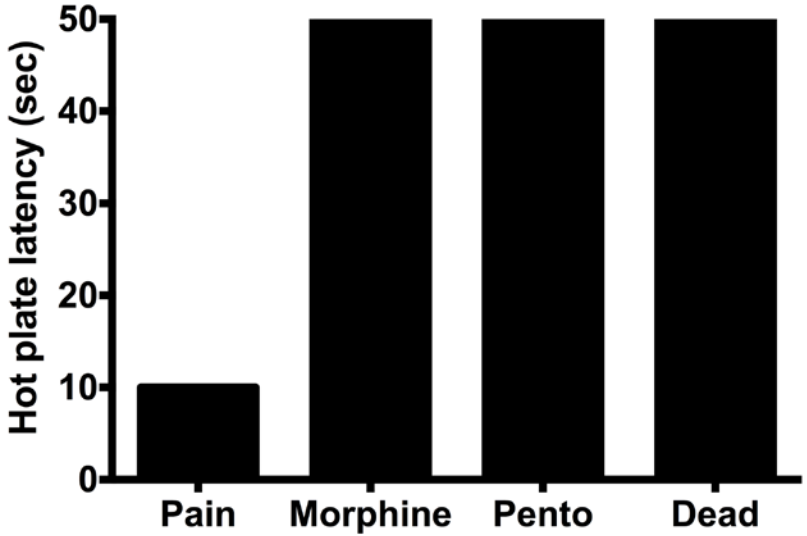
Animal studies show consistent “analgesic” effects

Acute Pain Tests	Dose	Effect
Sofia et al., 1973	8 mg/kg	Inhibit paw pressure
Lichtman & Martin, 1991	10 mg/kg	TF inhibition & immobility
Smith et al., 1998	5 mg/kg	Inhibit paw pressure
Tseng & Craft, 2001	3-10 mg/kg	Inhibit tail, paw, & locomotion
Kwilasz & Negus, 2012	3.2-10 mg/kg	Inhibit acetic acid-induced writhing
Britch et al., 2017	1.8-10 mg/kg	Inhibit tail, paw & locomotion

Hindpaw Inflammation	Dose	Effect
Sofia et al., 1973	0.9 mg/kg	Inhibited mechanical hyperalgesia
Craft et al., 2013	1-3.2 mg/kg	Inhibited thermal and mechanical hyperalgesia

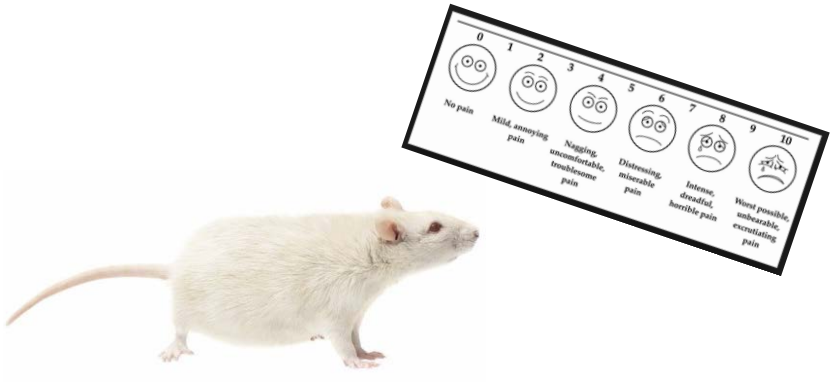
Side effects: Sedation, Immobility

Side effects confound assessment of analgesia

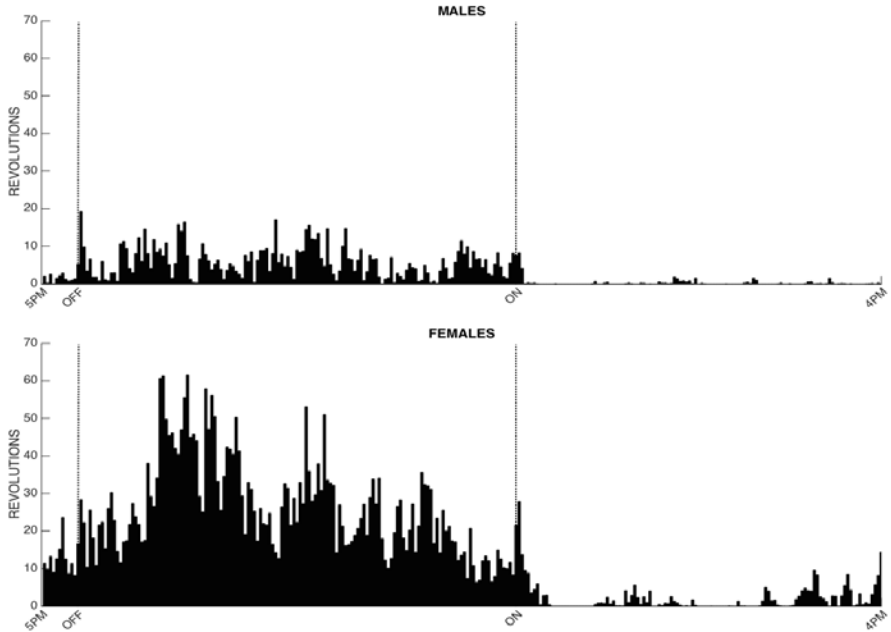


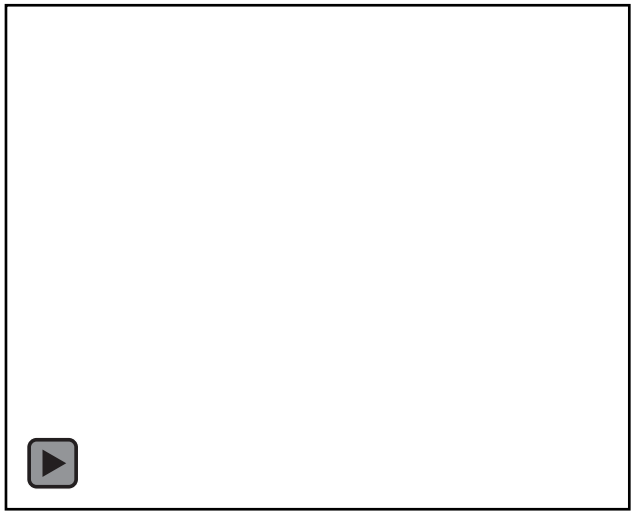
Two Research Goals

- More Randomized Controlled Trials
- More clinically relevant animal research



Home cage wheel running is a reliable and clinically relevant method to assess pain

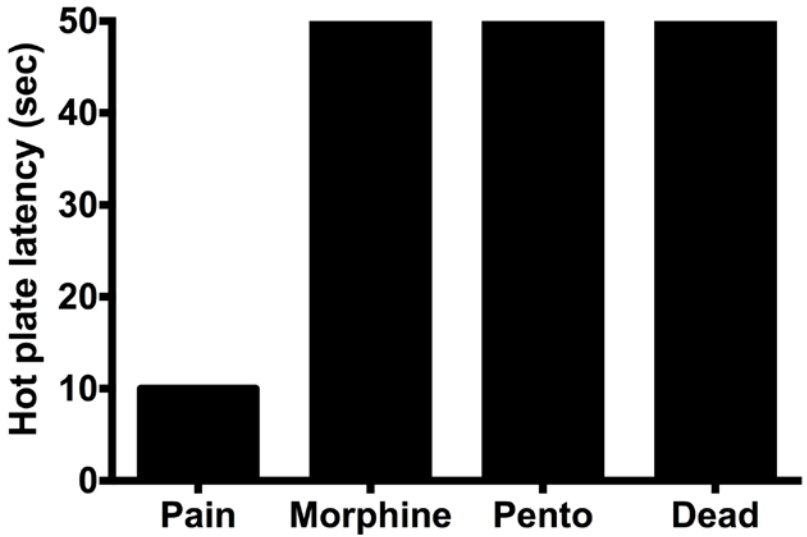




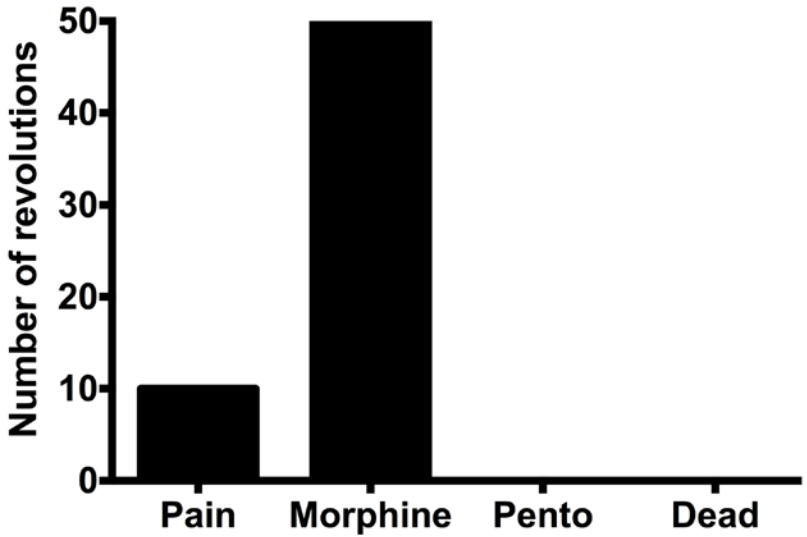
Kandasamy, R., Calsbeek, J. J., & Morgan, M. M. (2016). Home cage wheel running is an objective and clinically relevant method to assess inflammatory pain in male and female rats. *J. Neurosci. Methods*, *263*, 115-122.

Wheel running assesses ability of a treatment (e.g., cannabis) to restore activity

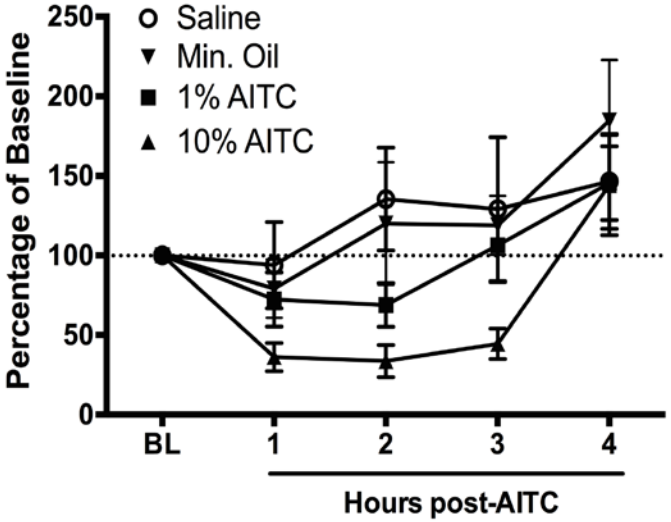
Pain-evoked test

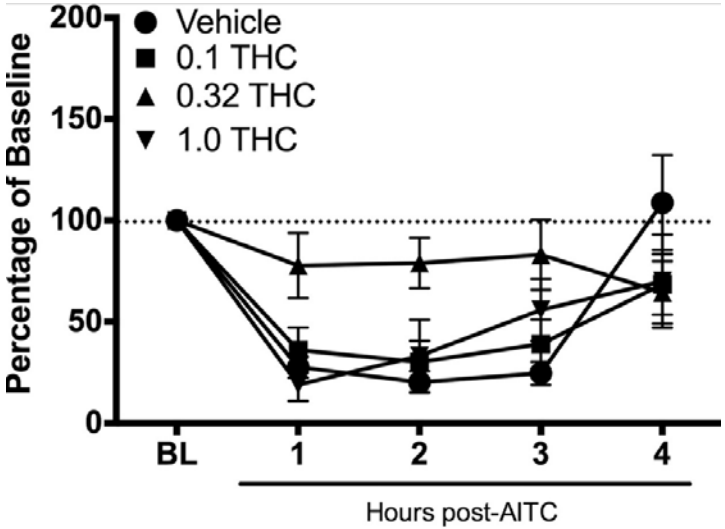


Wheel running test



THC restores wheel running depressed by migraine-like pain

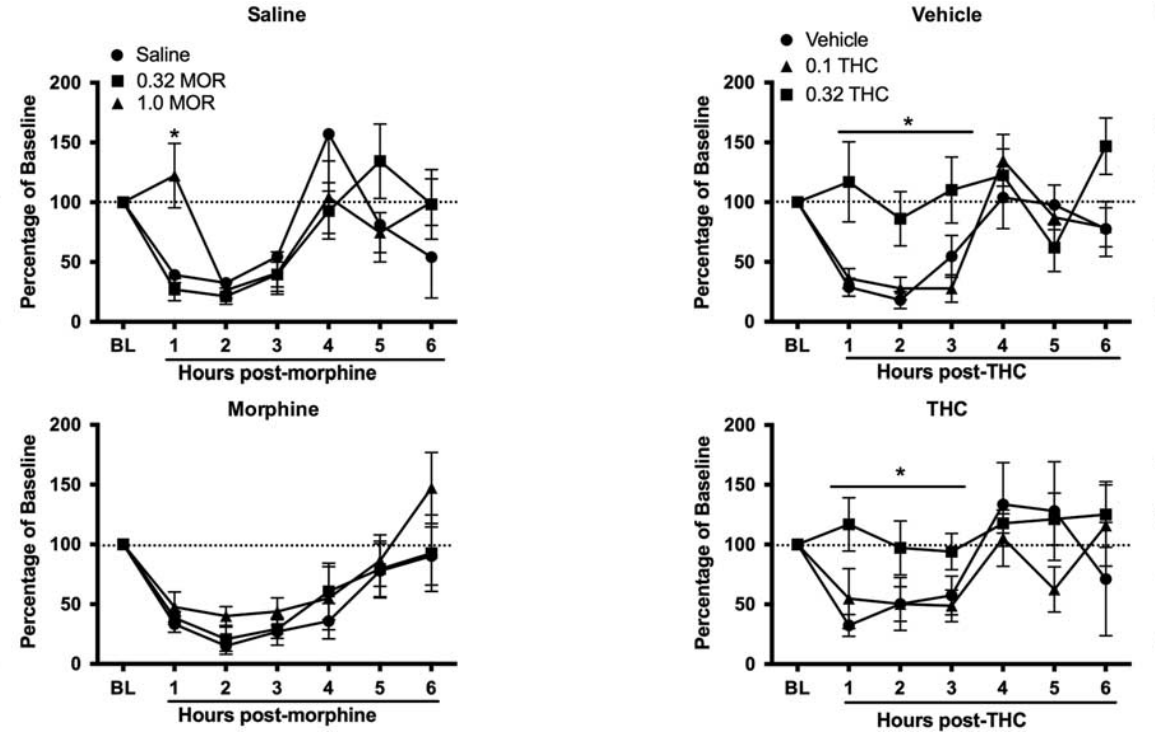




Kandasamy, R., Lee, A. T., & Morgan, M. M. (2017). Depression of home cage wheel running: A reliable and clinically relevant method to assess migraine pain in rats. The Journal of Headache and Pain, 18(1): 5 . PMID 28091820

Kandasamy, R., Dawson, C.T., & Morgan, M.M. (2018). Anti-migraine effect of Δ^9-tetrahydrocannabinol in the female rat. European Journal of Pharmacology, 818:271-277. PMID 29111112.

Tolerance develops to repeated morphine, but not THC administration



Kandasamy, R., Dawson, C.T., Hilgendorf, T.N., & Morgan, M.M. (2018). Medication overuse headache following repeated morphine, but not THC administration in the female rat. Behavioral Pharmacology. PMID: 29462111.

Repeated morphine administration prolongs migraine-induced depression of running

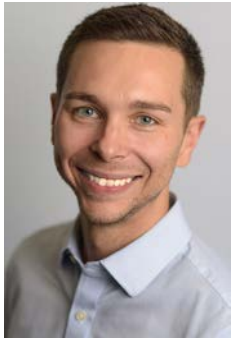
Medication overuse headache?

Kandasamy, R., Dawson, C.T., Hilgendorf, T.N., & Morgan, M.M. (2018). Medication overuse headache following repeated morphine, but not THC administration in the female rat. Behavioral Pharmacology. PMID: 29462111.

Other clinically relevant animal research at WSU

- Dr. Rebecca Craft
  - Sex differences in response to cannabinoids

- Dr. Ryan McLaughlin
  - Vapor chambers for cannabinoid inhalation



Why this matters: Implications for public health

Cannabinoids vs. opioids

- Treatment for pain
- Dependence
- Side effects

Moving Forward

- Many Research Questions
  - Which cannabinoids and doses?
  - Which pain conditions?
  - Which ages?
- Barriers to Research
  - Research funding
  - Schedule 1 classification

Funding provided by:

National Institute of Neurological Disorders and Stroke

Washington State Initiative No. 171 & 502