

2016 Annual NIH Pain Consortium Symposium

NICOTINE DEPRIVATION INCREASES PAIN SENSITIVITY, NEUROGENIC INFLAMMATION, AND SECONDARY HYPERALGESIA AMONG DAILY TOBACCO SMOKERS

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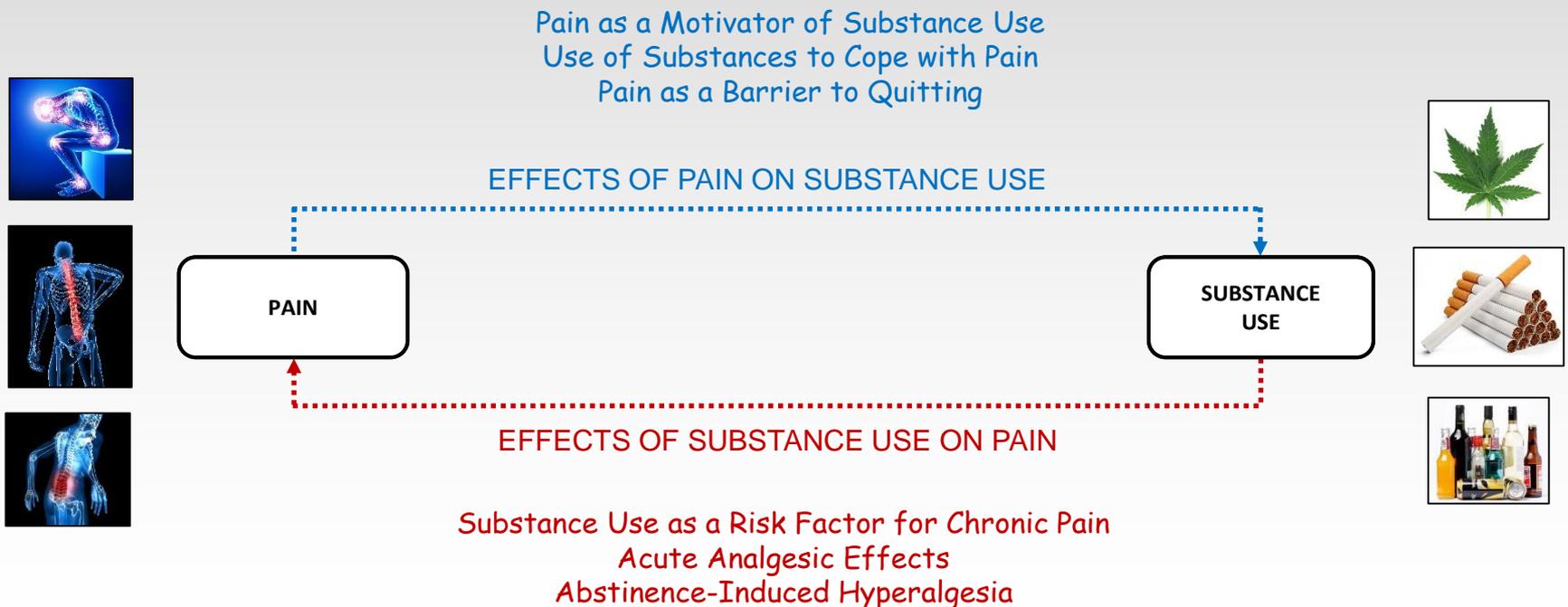
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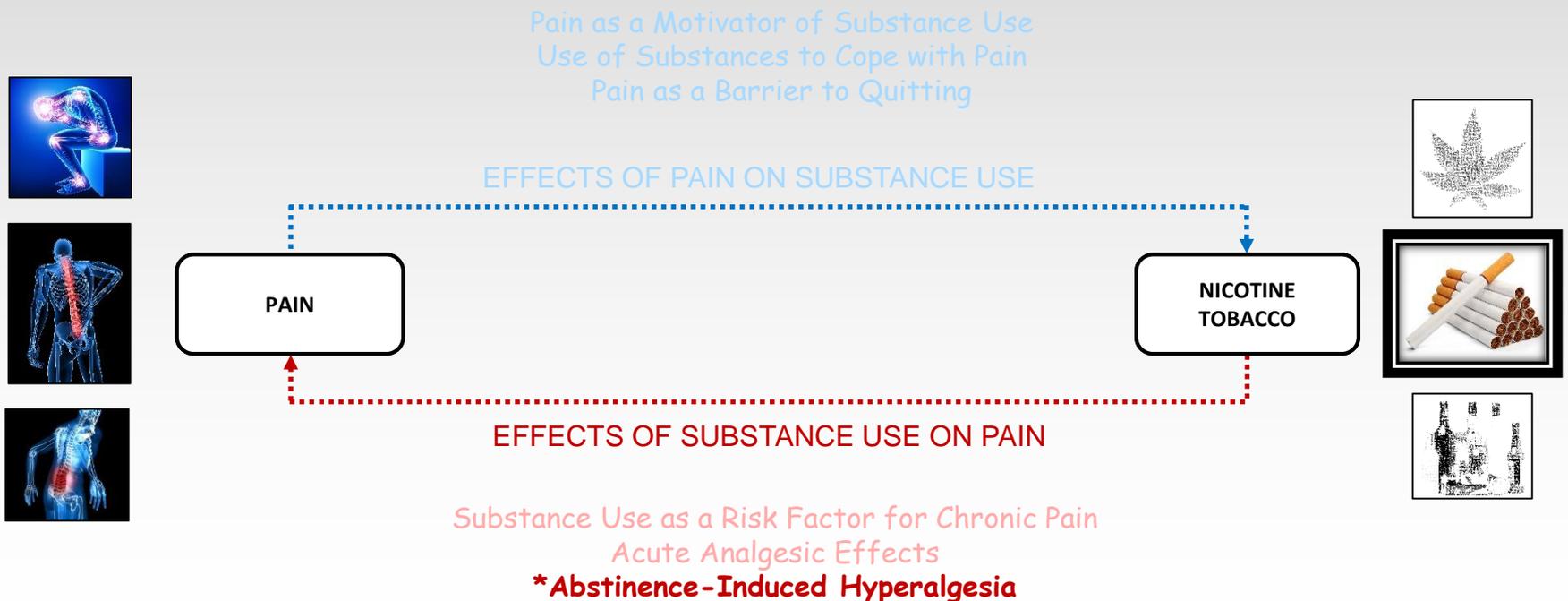
Overview

- There is growing empirical and clinical interest in bidirectional associations between pain and the onset/maintenance of addictive behaviors



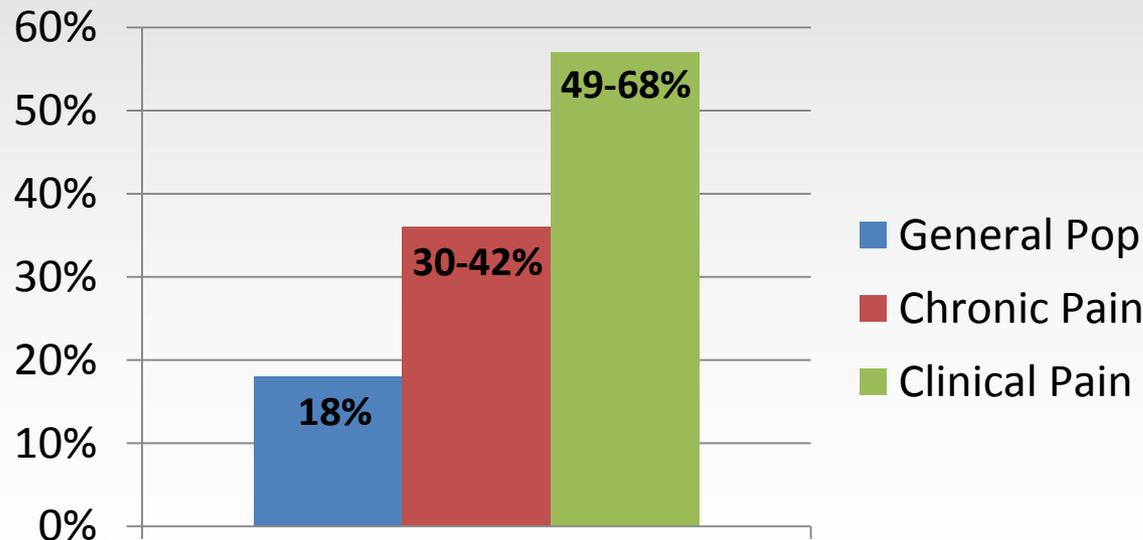
Overview

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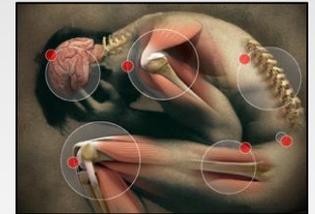


Background

- Chronic pain and tobacco smoking are both highly prevalent and co-occurring conditions
 - Together account for >\$800 billion in annual health care and lost productivity costs



Prevalence of Tobacco Smoking among Persons with Pain



Background

- Smokers with co-occurring pain:
 - Smoke more cigarettes per day
 - Report experiencing more severe nicotine withdrawal and greater difficulty quitting
- Animal research
 - Reliably demonstrated hyperalgesic responding following nicotine deprivation
 - Pain has been shown to reinstate drug seeking following extinction



Current Study

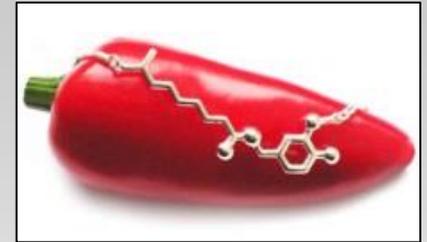
- Objective:
 - Develop a human laboratory model of pain and smoking, and conduct first test of experimental pain reactivity following a nicotine deprivation manipulation
- Primary Hypothesis:
 - Smokers randomized to overnight smoking abstinence (vs. continued smoking) would evince greater capsaicin-induced sensitivity to pain, neurogenic inflammation, and secondary hyperalgesia

Method

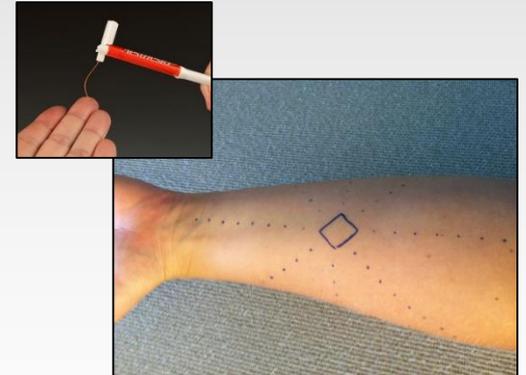
- Participants
 - 165 daily smokers (M CPD = 22; 43% Female)
- Deprivation Manipulation
 - **Nicotine Deprivation**: Abstain 12-24 hours (n = 74)
 - Minimal Deprivation: Abstain 2 hours (n = 28)
 - **Continued Smoking**: Smoke as usual (n = 63)

Method

- Capsaicin Pain Model
 - Vanilloid receptor agonist (derived from chili peppers) that provides longer lasting stimulus to approximate key features of neuropathic and inflammatory pain

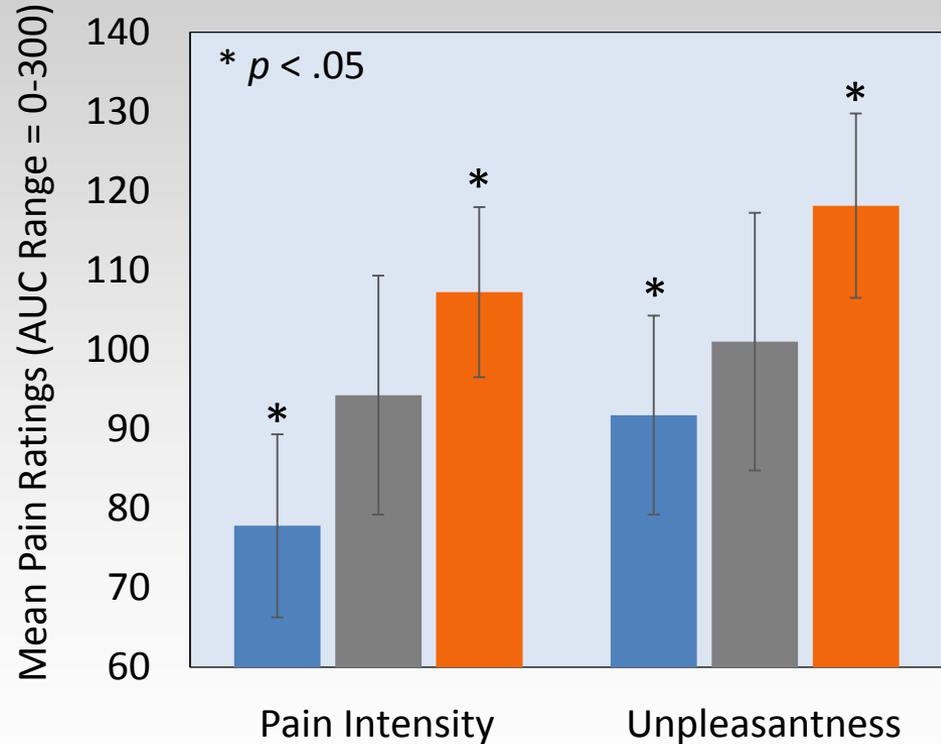
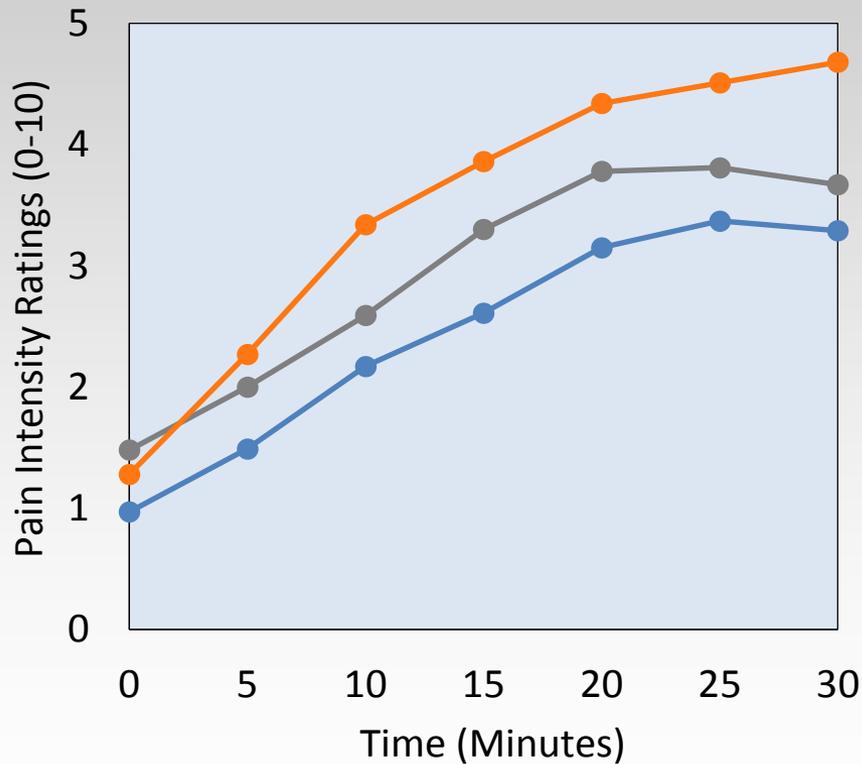


- Pain Assessment
 - Pain Intensity/Unpleasantness
 - Numerically rated (0-10) at 5-min intervals
 - Neurogenic Inflammation
 - Measured as area of visible flare
 - Secondary Hyperalgesia
 - Assessed via tactile stimulation at every 5mm point along eight linear paths from the center of application site



Results

- Pain Intensity and Unpleasantness Ratings



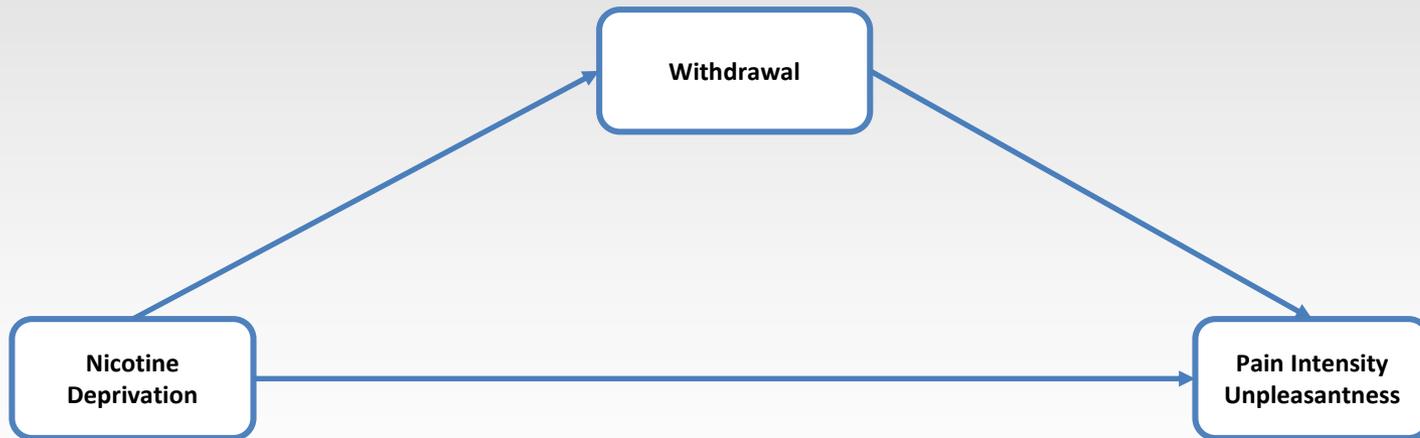
■ Continued Smoking

■ Minimal Deprivation

■ Nicotine Deprivation

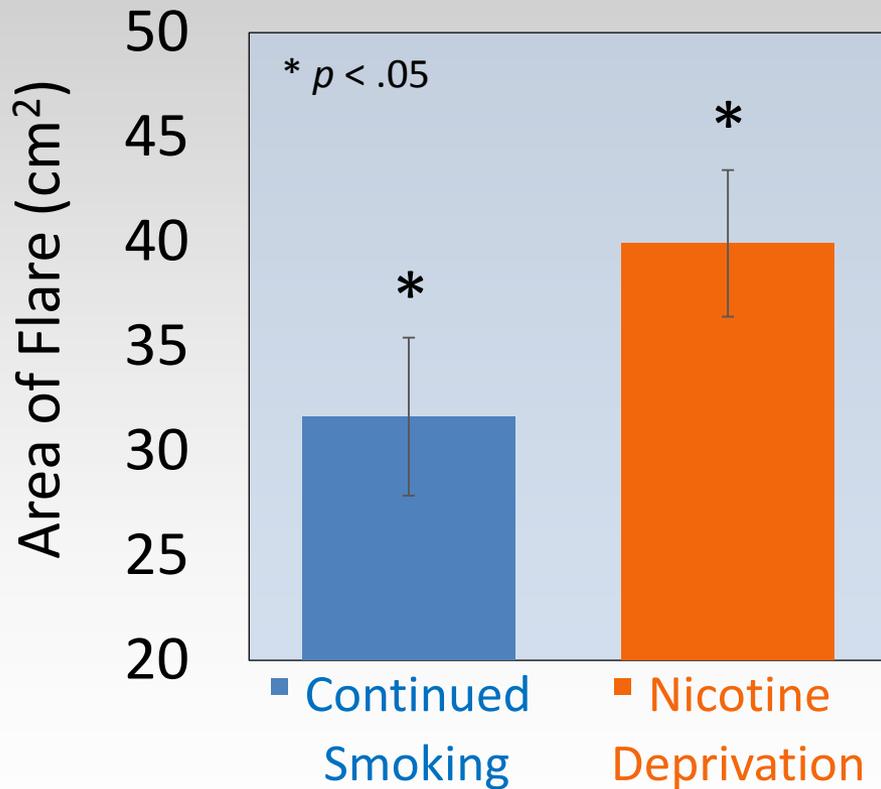
Results

- Indirect Effects of Nicotine Withdrawal
 - Nicotine deprivation increased withdrawal severity, which in turn was associated with greater pain intensity/unpleasantness ratings ($ps < .05$).



Results

- Neurogenic Inflammation

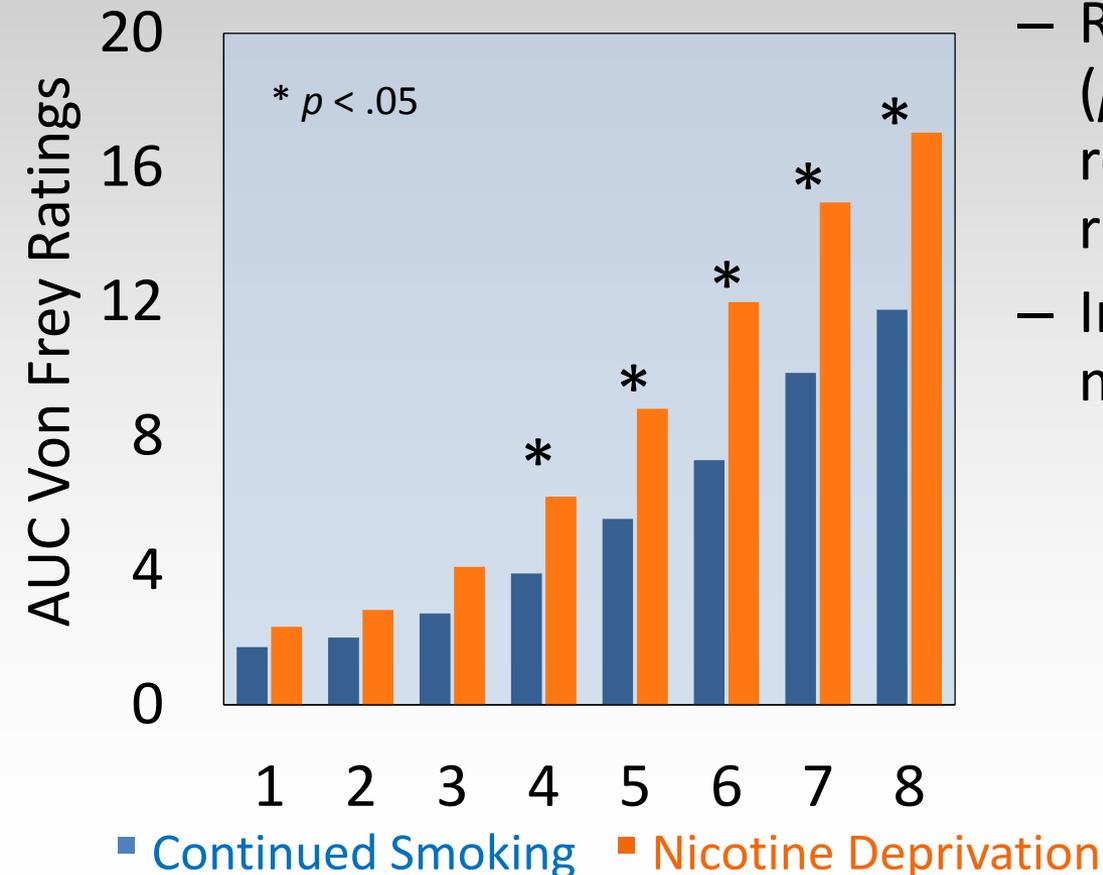


- ND evinced larger area of flare than CS
- Implicates peripheral mechanisms of action

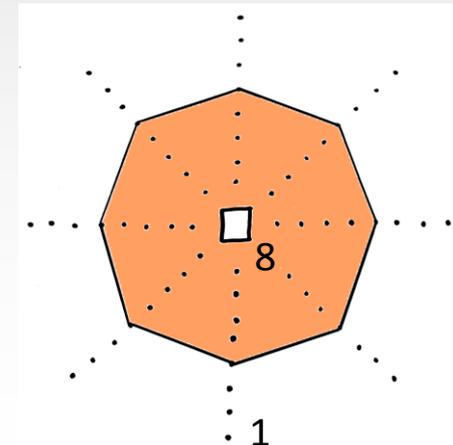


Results

- Secondary Hyperalgesia



- Ring X Condition interaction ($p < .05$), such that ND reported greater pain on rings 4 - 8 than CS
- Implicates central mechanisms of action



Discussion

- Nicotine deprivation increased spontaneous pain ratings, neurogenic inflammation, and secondary hyperalgesia
- Effects of deprivation on pain intensity and unpleasantness ratings were mediated by nicotine withdrawal severity

Discussion

- Findings may be consistent with an allostatic load model of pain and addiction (Koob & Le Moal, 1997, 2001; Egli, Koob, & Edwards, 2012)
 - Posits that repeated opponent process cycles of substance-induced analgesia and withdrawal-induced hyperalgesia may dysregulate overlapping neural substrates to engender a persistent imbalance favoring pain facilitation

Discussion

- Smokers with co-occurring pain may experience a variety of negative pain-related sequelae during early stages of a quit attempt
 - Increased pain may precipitate relapse
- Tailored cessation interventions should account for the antithetical influence of abstinence-induced amplification of pain



Thank you

- NIDA R21DA034285
 - Effects of Smoking Abstinence on Pain Reactivity: A Human Experimental Model
- NIH Pain Consortium
- Pain and Addiction Research (PAR) Lab
 - Syracuse University