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

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Overview

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

Pain as a Motivator of Substance Use
Use of Substances to Cope with Pain
Pain as a Barrier to Quitting

EFFECTS OF PAIN ON SUBSTANCE USE

EFFECTS OF SUBSTANCE USE ON PAIN

Substance Use as a Risk Factor for Chronic Pain
Acute Analgesic Effects
Abstinence-Induced Hyperalgesia
Overview

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

![Graph showing pain intensity and unpleasantness ratings over time]

- Continued Smoking
- Minimal Deprivation
- Nicotine Deprivation

* $p < .05$
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

![Graph showing AUC Von Frey Ratings for Continued Smoking and Nicotine Deprivation](image)

* $p < .05$
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
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