Time Dependency of Craving and Response Inhibition during Nicotine Abstinence

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Why do we care about nicotine and smoking?
Why do we care about nicotine and smoking still?

[Danaei, et al., 2009]
Withdrawal Symptoms
Withdrawal Symptoms

- Physiologic
  - Weight gain
  - Fatigue
  - Heart rate
Withdrawal Symptoms

• Physiologic
  – Weight gain
  – Fatigue
  – Heart rate

• Behavioral
  – Craving
  – Irritability
  – Restlessness
  – Affect
Withdrawal Symptoms

- Physiologic
  - Weight gain
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  - Craving
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- Cognitive
  - Response inhibition
  - Sustained attention
  - Working memory
Withdrawal Symptoms

• Physiologic
  – Weight gain
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• Behavioral
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  – Irritability
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• Cognitive
  – Response inhibition
  – Sustained attention
  – Working memory

[Powell et al., 2010]
Craving

• Strong desire for something
• Self-report measure obtained through questionnaires
• Post-quit craving is associated with success of long term abstinence

[Doherty, 1995; Swan 1996; Killen, 1997; Cappelleri, 2007; Powel, 2010]
Response Inhibition

• Ability to suppress an inappropriate action that interferes with a goal-driven behavior

• Measured by computer tasks such as the “Stop Signal Task”

• Response inhibition deficits seen during abstinence
  – Predictive of long term quit rates

(Ashare and Hawk, 2012; Harrison, 2009)
(Powel, 2010)
Study Design

Phone Screen

Intake/Baseline

24 hours abstinent

72 hours abstinent
Participants

Criteria

Demographics
Participants

Criteria

• >10 cigarettes/day
  – Verified by breath carbon monoxide (CO)
## Participants

### Criteria

- >10 cigarettes/day  
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- Non-treatment seeking smokers

### Demographics
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• >10 cigarettes/day
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• Non-treatment seeking smokers
• No use of recreational or psychoactive drugs
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• Able to perform cognitive tasks
  – Shipley Institute of Living Scale (Zachary, 2000)

Demographics

Introduction
Methods
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Discussion
Participants

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Demographics (n=21)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Age</td>
<td>34.7</td>
</tr>
<tr>
<td>Age started smoking</td>
<td>19.0</td>
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<tr>
<td>Sex (female:male)</td>
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<td>Cigarettes per day</td>
<td>15.9</td>
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<td>Shipley institute of living scale</td>
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<td>Carbon monoxide (ppm) Initial</td>
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<td></td>
<td>3.1</td>
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<td></td>
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<td>24hr abstinence</td>
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</tr>
<tr>
<td>72hr abstinence</td>
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Measure of Craving
Questionnaire on Smoking Urges (QSU-brief)

• 10 statements on a 1-7 scale
• Two factors with 5 questions each:
Measure of Craving
Questionnaire on Smoking Urges (QSU-brief)

• 10 statements on a 1-7 scale
• Two factors with 5 questions each:

Factor 1 (positive craving):
Anticipation of Improved Positive Affect

  – “I have a desire for a cigarette now”
  – “I have an urge for a cigarette”
  – “A cigarette would taste good right now”
Measure of Craving
Questionnaire on Smoking Urges (QSU-brief)

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- Two factors with 5 questions each:

Factor 1 (positive craving):
Anticipation of Improved Positive Affect
- “I have a desire for a cigarette now”
- “I have an urge for a cigarette”
- “A cigarette would taste good right now”

Factor 2 (negative craving):
Anticipated Relief from Negative Affect
- “I could control things better now if I could smoke”
- “Smoking would make me less depressed”
Measure of Response Inhibition
Stop Signal Task

- Ability to suppress an inappropriate action that interferes with a goal-driven behavior
  - Goal-driven behavior: pressing the correct arrow key seen on a screen (prepotent response)
  - Inappropriate action: pressing an arrow key after hearing an audible signal
  - Measure: stop signal reaction time (SSRT)
Relationship between Response Inhibition and Craving

• Response inhibition is one of the facets of impulsivity

• There is conflicting data regarding the connection between impulsivity and craving
Data Analysis

- Craving and response inhibition analyzed using generalized linear regression models
- Within-subject variable
  - Length of abstinence
    - Baseline vs. 24hrs vs. 72 hrs
- Between-subjects variables (covariates):
  - sex, nicotine dependence, age, Shipley IQ score
- Relationship between craving and response inhibition – Pearson correlations
Craving over Time

QSU Estimated Marginal Means Relative to Baseline

<table>
<thead>
<tr>
<th>Session</th>
<th>QSU Factor 1 (positive)</th>
<th>QSU Factor 2 (negative)</th>
<th>p</th>
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<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>24hr</td>
<td></td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>72hr</td>
<td></td>
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<td>0.08</td>
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</table>

Introduction | Methods | Results | Discussion
Response Inhibition over Time

SSRT Estimated Marginal Means Relative to Baseline

- Baseline
- 24hr Session: p = 0.315
- 72hr: p = 0.056

Introduction | Methods | Results | Discussion
Relationship between Craving and Response Inhibition

- No relationship between either positive or negative craving and stop signal reaction time at any time point

<table>
<thead>
<tr>
<th>Session</th>
<th>Factor 1 (positive)</th>
<th>Factor 2 (negative)</th>
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<tbody>
<tr>
<td></td>
<td>R²</td>
<td>p</td>
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<td>Baseline</td>
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<td>0.1949</td>
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<tr>
<td>24 hours</td>
<td>-0.0940</td>
<td>0.9360</td>
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<tr>
<td>72 hours</td>
<td>-0.1621</td>
<td>0.5074</td>
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Why do we care?

• Majority of quit attempts fail during the first week of abstinence [Garvey et al., 1992; Hughes, 2004]

• Withdrawal symptoms are associated with ability to maintain abstinence
  – Craving [Killan & Fortmann, 1997]
  – Response inhibition [Krishnan-Sarin et al., 2007; Powel, 2010]
Craving

• Our results agree with previous work that craving increases soon after abstinence, then decreases

• We specifically see increases in negative craving
  – Craving early on in a period of abstinence acts through negative reinforcement
Craving

• Other study shows that positive craving changes more over 7 weeks abstinence
• Craving during long term abstinence acts through positive reinforcement
• During abstinence, craving may shift from a negatively reinforced phenomenon to a positively reinforced phenomenon

Cappelleri, 2007

Introduction	Methods	Results	Discussion
Craving

- Shift in reinforcement may be related to the pattern of other withdrawal symptoms
- Supports the bidimensional model of drug addiction, integrating both positive and negative reinforcement
Response Inhibition

• Other studies have shown an abstinence effect on response inhibition at 24 hours
• May have been due to practice effects of testing

[Ashare and Hawk, 2012; Dawkins, 2006; Harrison, 2009]
Response Inhibition
Change over time

• Small effect seen at 72 hours
• Harrison (2009) also had time dependent changes in response inhibition
• Partial support for hypothesis that deficits in response inhibition increase over the length of abstinence
Relationship between Craving and Response Inhibition

• Impulsivity
  – Trait
  – Behavioral (response inhibition)
  – Neurobiological

• Trait impulsivity and craving
  – Mixed results

• Behavioral impulsivity and craving
  – Mixed results
Relationship between Craving and Response Inhibition

Reasons for Heterogeneity

• Different measures of behavioral impulsivity
  – Stop signal task vs. delayed discounting task

• Supports the multifactorial construct of impulsivity [Whiteside & Lynam, 2001]
Limitation of Study Design

- Sample size
- Gender imbalance
  - Craving [Xu et al., 2008, Saladin, 2012; Knott et al., 2008]
  - Response inhibition [Li, 2006; Rubia, 2013]
- Learning effects
- Treatment seeking vs. non-treatment seeking smokers
Conclusions

Time course of withdrawal symptoms

• Importance of treating craving early on
  – Nicotine replacement [Water, 2004]

• Importance of extended treatment of cognitive deficits such as response inhibition
  – Varenicline [Patterson et al, 2009]
  – Galantamine [Wilkinson, 2011]
Conclusions

Individualized Treatment

- Lack of relationship shows that smokers form a heterogeneous group
- May benefit from individualized treatment
- Future work in identifying different clusters of smokers and develop specified treatments
Questions?
Participants

• 135 phone screened, 66 eligible
• 44 attended screening, 26 eligible
• 25 enrolled
• 3 missed mandatory sessions
• 1 tested positive for drug
• Total (n) = 25-3-1 = 21
Learning Effects of Neurocognitive Tasks

• Participants become more and more proficient at tasks
• Observed deficits may be masked by learning effect
Comparative Withdrawal Effects

SSRT and QSU Estimated Marginal Means Relative to Baseline

- SSRT
- QSU Factor 1
- QSU Factor 2

Session
- Baseline
- 24hr
- 72hr

Introduction | Methods | Results | Discussion
References


