Novel Intervention Targets for Adolescent Smoking Prevention

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About 443,000 U.S. Deaths Attributable Each Year to Cigarette Smoking*

- Lung Cancer: 128,900 (29%)
- Ischemic Heart Disease: 126,000 (28%)
- Chronic Obstructive Pulmonary Disease: 92,900 (21%)
- Other Diagnoses: 44,000 (10%)
- Stroke: 15,900 (4%)
- Other Cancers: 35,300 (8%)

* Average annual number of deaths 2000–2004; Source: CDC SAMMEC, MMWR 2008;57(45):1226–1228.
Adolescent Smoking Problem

- 1,000 adolescents start smoking regularly every day in US.
- Almost 20% of adolescents currently smoke.
- 80% of adults who have regularly smoked cigarettes tried their 1st cigarette before age 18 and half became regular smokers by age 18 years old.
Adolescent Cigarette Smoking

*smoking one or more cigarettes in the last 30 days; Source: Youth Risk Behavior Survey, 2012
Rationale & Objective

• Identifying factors that decrease the risk for or protect adolescents from smoking adoption is critical to inform smoking prevention and intervention efforts.

• Risk and protective factors for smoking uptake may be identified best through comprehensive, prospective longitudinal studies.

• Early identification of adolescents at risk for smoking, highlight variables to target for intervention, may aid the understanding of the bio-behavioral basis of adolescent smoking.
GATOR Participants and Procedures

- Adolescents (n=1,123) taking part in a longitudinal study (54% female, 68% White) of the predictors of adolescent smoking adoption
  - 14 years at baseline and followed for 4 years (age 14-18 years old)
  - Annual 30-minute school-based survey
  - $10 gift card after each survey
  - < 10% smoking regularly at baseline
ALOHA Participants and Procedures

• Adolescents (n=1,123) who took part in GATOR where invited to participate in longitudinal study of the predictors of smoking adoption and escalation

• 18-19 years at baseline and followed for 4 years (age 22-23 years old)

• Annual 30-minute telephone survey

• $20 gift card after each survey

• Raffle entry for each survey completed
**PATH Participants and Procedures**

- Adolescents (n=1,429) taking part in a longitudinal study (54% female, 68% White) of the relationship between PA and smoking
- 14 years at baseline and followed for 4 years
- Bi-annual 40-minute school-based survey
- $10 - $25 after each survey
- ~99% participation at baseline, ~80% retained 4 years later
- ~10% smoke regularly at baseline; Average hours MVPA/week = 8.72, SD = 8.42)
Smoking Progression

• What factors are responsible for this growth in smoking across time?

• Behavioral Economic Theory suggests that the choice to smoke depends on substitute reinforcers for smoking (e.g., clubs, PA, academics) and complementary reinforcers to smoking (e.g., etoh, MJ, peer smoking).

• There may also be individual differences in delay discounting or the value of a reinforcer depending on the length of delay to delivery.
Behavioral Economics & Smoking Progression

Implications for Intervention

Adolescents who smoke have fewer reinforcers that protect against smoking and more reinforcers that promote smoking. *Is physical activity a key SR?*

Interventions to prevent smoking initiation and progression should focus on helping adolescents identify and engage in SRs and discourage involvement in CRs. *Does physical activity prevent smoking? Does depression influence SR?*

Discounting of future rewards impacts smoking via reinforcer type, thus interventions may need to help adolescents identify and value rewards that are not immediate. *What affects reward valuation?*

Adolescent Physical Activity

- > 60% of adolescents do not engage in 60 minutes of PA of ≥ 5 days each week

- only 18% achieve the recommended 60 minutes of PA every day

- PA declines during adolescence and physical inactivity tracks into adulthood
Measures

**Smoking Progression** 5 ordered categories based on standard epi smoking questions (never, puffer, experimenter, current, frequent)

**Physical Activity** 4 items from the YRBS measuring past 7 days vigorous, moderate and strength training, and # of team sports played in past 12 months

**Covariates** gender, race, depression, PE

> 30% progressed in smoking, PA significantly declined with individual differences in baseline PA and rate of change.
Higher PA reduced odds of smoking progression by 50%.

Team Sport Participation & Smoking

Low (n=433), Decreasing (n=144), Erratic (n=74), High (n=447)

Physical Activity, Team Sport & Smoking

• PA and team sport appear to protect against adolescent smoking uptake and may be an important youth smoking prevention target.

• Adolescents who decrease or who have irregular participation (20% of sample) in team sport were > likely to become regular smokers.

• Limit sports attrition (focus on skill development, individual goal mastery, and enjoyment vs. competition).

• Increase accessibility for females and non-white adolescents.

• Social and possibly biological mechanisms.
Why is physical activity protective against smoking uptake?

The mechanisms by which PA protects adolescents from smoking have yet to be formally evaluated.

Researchers have speculated that there may be individual, environmental and biological reasons.

PA reward or the hedonic value derived from engaging in PA is one possible mechanism that may help explain the link.

Participation in PA is associated with > PA reward. ¹

¹ Dishman et al., 2005; Deforche et al., 2006; Davidson et al., 2007; Garcia Bengoechea et al., 2010
Physical Activity Reward

If an adolescent derives pleasure from PA, they may be less likely to seek alternative sources of reward, such as smoking.

PA may create neuro-adaptations that lessen the likelihood that an adolescent will find smoking rewarding and escalate in use.

Accumulating evidence indicates that PA influences many of the same neurotransmitters, intracellular signaling molecules & neuroanatomical structures that mediate the positive reinforcing effects of drugs.¹

¹ Smith & Lynch, 2012; Audrain-McGovern et al., Arch Gen Psychiatry, 2006
Physical Activity Reward

Goal – provide initial evidence for PA reward as a potential mechanism underlying the relationship between PA and smoking

Hypothesis - > levels of PA will be associated with > PA reward, which in turn, will decrease the odds of adolescent smoking uptake (reciprocal too)

Importance - Identifying evidence-based tx targets will be important to inform smoking prevention and intervention efforts that incorporate PA as a tx component.
Measures

**Smoking progression** ordered categories based on standard smoking questions (never, experimenter, monthly, weekly, daily)

**Physical Activity Recall** measured minutes of MVPA over the past 7 days

**Physical Activity Reward** 16-item PACES, measured enjoyment derived from PA

**Covariates** gender, race, parental edu, peer & household smoking, PA access, impulsivity

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1Sallis et al., 1985; Sallis et al., 1997; Sallis & Owen, 1999; Sallis et al., 1999; Sallis et al., 1993; 2 Motl et al 2001; Heesch et al., 2006
Adolescents who derive greater reward from PA are less likely to become smokers.
Implications

• Interventions that promote PA and target PA enjoyment may have an important impact on adolescent smoking initiation and progression

• Insufficient attention to strategies that foster adolescents enjoyment of PA

• Help adolescents identify and engage in the types of PA that are most rewarding

• Differences in subjective reward & reinforcing value of PA may reflect biologically-based individual differences in the response to PA

Audrain-McGovern et al., Initial insight into why physical activity may help prevent adolescent smoking uptake Drug and Alcohol Dependence, 2013.
Physical Activity & Tobacco Use Uptake

• Our research has documented the importance of maintaining regular PA to lessen the odds of smoking, but little is known about when the relationship between PA and smoking begins to unfold.

• Examination of the variation in timing, rate and magnitude of PA decline could highlight PA trajectories that are linked to a likelihood of smoking.

• Hypotheses
Measures

Regular smoking smoking in past 30 days

Physical Activity 6-month physical activity recall, hours of weekly MVPA calculated ¹

Covariates gender, race, parental education

¹Aaron et al., 1993; Aaron & Kriska, 1995
Adolescent PA Patterns

- Stable Higher (n=299)
- Decreased (n=170)
- Stable Regular (n=213)
- Curvilinear (n=77)
- Stable Low (n=670)

Hours of MVPA per week vs. Wave

Wave: 1 2 3 4 5 6 7 8
Intervention Implications

• Adolescents who average 90 minutes of PA a day are least likely to smoke (3%) at age 18.

• Smoking prevention efforts need to occur before and during high school.

• Types of PA as well as the sharp decline in PA levels may be more predictive of tobacco use than the amount of PA per week; 27% of Decreased smoking at age 18.

• Public health messages are aimed at increasing overall PA, so identifying smoking associated PA is important to prevent involvement in PA linked to tobacco use.

• Certain motives for engaging in PA are linked to smoking

Intervention Implications

• Low PA trajectory comprised about half of the sample, 17% smoking at age 18, more females than any other trajectory.

• These adolescents may lack features important to PA (e.g., PA enjoyment, PA support) and have risk factors for smoking.

• Research has shown that persistent inactivity in adolescence predicts adult smoking, even after familial factors are taken into account. ¹

• May benefit from an intervention that targets PA promotion & smoking prevention

Is all PA created equal?

PA linked with smoking = “negative PA” - wrestling, dancing, skating, walking for exercise or transportation, biking, bowling, chores

PA negatively correlated with smoking “positive PA” - baseball, basketball, dance, cheer, gymnastics, hockey, running, calisthenics, soccer, track & field, volleyball, swim, lifting, yoga, frisbee
All PA does not protect against smoking uptake

For every 30” increase in negative PA per week at age 14, there was a **4-fold** increase in the odds of smoking progression.

For every 30” increase in positive PA per week at age 14, there was a **51% decrease** in the odds of smoking progression.
Summary & Integration

• Many, but not all PA are protective against smoking progression.

• > 60 minutes of PA every day - - type of PA

• Adolescents with declining PA are at > risk for smoking and alternative tobacco uptake.

• Deriving enjoyment from PA is an important mechanism underlying the relationship.

• As PA and smoking influence each other, adolescent health behavior interventions should consider the maintenance of PA and the prevention of tobacco use.
Adolescent onset

Smoking is a rewarding behavior - prevalence doubles from mid to late adolescence \(^1\)

Depression has been conceptualized as a disorder of disrupted reward processing \(^2\)

25% experience elevated symptoms during this developmental period and ~ 20% one MD episode by 18 y.o. \(^3\)

1. CDC, 2010; Johnston et al., 2010; 2. Forbes, 2009; 3. Fergusson et al., 2005; Georgiades et al., 2006; Lewinsohn et al., 2004; SAMHSA, 2005
Depression is linked to smoking

• Depression, clinical episodes and subclinical symptoms, appears to be an important risk factor for adolescent and young adult smoking.

• History of depression predicts the onset of daily smoking and progression to nicotine dependence\(^1\).

• Elevated depression symptoms in late adolescence predicts the transition from nonsmoking to regular smoking in emerging adulthood\(^2\).

1. Breslau et al., 1993; 1998
2. Wang et al., 1999
Depression is associated with fewer alternative reinforcers

- Less interest in pleasant or reinforcing activities
- Difficulties making decisions about activities
- Less pleasure derived from activities

Fewer alternative reinforcers predict smoking

- Adolescent smoking uptake
- Young adult smoking status
- Smoking may be an easy way to increase the level of pleasurable experiences
- Abstinence from other substances of abuse

Hypothesis

• we sought to determine if depression contributes to a decline in alternative reinforcers, which in turn, increases the likelihood of smoking uptake.

• ~ 26% of young adults smoke cigarettes\(^1\)

• Young adulthood represents a period of continued smoking uptake and the establishment of regular and long-term smoking practices\(^2\)

1. CDC, 2006; 2. Chassin et al., 2000; Tercyak et al., 2007; Choi et al., 2003; 3. Perkins et al., 2000
Measures

**Smoking** # of cigarettes smoking in past 30 days

**Depression symptoms** Center for Epidemiological Studies Depression (CES-D)

**Substitute alternative reinforcers** Modified Pleasant Events Schedule, 78 items rated once in terms of frequency (0=none to 2=often) and once in terms of enjoyability (0=none to 2=very) over the past 30 days, cross-product provides a measure of the activity’s reinforcement

**Covariates** gender, race, household & peer smoking, marijuana use, alcohol use, stress
Declining substitute reinforcers link depression to young adult smoking

\[ X^2(101,834) = 222.74, \text{ p}<.0001, \text{ CFI}=0.97, \text{ RMSEA}=0.04, \text{ 90% CI}=.03-.05; \text{ prob. RMSEA} \leq .05=1.00; \text{ SRMR} = .04. \]
Clinical Implications

- promoting greater SRs or mitigating declines in SRs may prevent smoking uptake and further increases in smoking rate in young adults with elevated depression symptoms.

- ~50% of the sample had elevated depression, so the effects of an intervention could have an important impact on smoking.

- Smoking may compensate for fewer reinforcers, but does it alter depression?

Does smoking alter depression?

Smoking mitigates depression

N = 1,093         14 to 18 y. o.  annual surveys

Do depressed youth expect smoking to be rewarding?

• Declines in involvement in, or pleasure derived from other reinforcers may lead to expectations that other activities, such as smoking confer reward.

• Expectations of smoking reward correlate with Hx+ of MD and smoking status. ¹

• Expectations that smoking reduces negative affect predicts smoking escalation. ²

1. McCharge et al., 2004; 2. Heinz et al., 2010
## Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>(N=1,393)</th>
<th>Survey every 6 months (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>14 - 17 years</td>
<td></td>
</tr>
<tr>
<td>Smoking past 30/days (n)</td>
<td>11% (150)</td>
<td></td>
</tr>
<tr>
<td>Smoking progression</td>
<td>6% vs 16%</td>
<td></td>
</tr>
<tr>
<td>CES-D</td>
<td>26% &gt; 22</td>
<td></td>
</tr>
<tr>
<td>Reward Expectations (sd)</td>
<td>10.2 (4.0)</td>
<td></td>
</tr>
<tr>
<td>Household smoking (yes)</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Peer smoking (0-9, sd)</td>
<td>1.6 (2.3)</td>
<td></td>
</tr>
<tr>
<td>Parental monitoring (sd)</td>
<td>12.3 (2.7)</td>
<td></td>
</tr>
</tbody>
</table>
Parallel processes latent growth curve model

$X^2(253, 1393) = 455, p<.0001$
$CFI=.99, RMSEA=.02,$
Expectations of smoking reward facilitate smoking uptake among depressed adolescents

- Initial glimpse of reward related processes that can occur early in the smoking acquisition process
- Highlights depressed adolescents who are vulnerable to smoking
- Expectations of reward are an important mechanism to target for smoking prevention
- Addressing alternative ways to meet the rewards (e.g., source of pleasure, something to do) expected of smoking

Audrain-McGovern et al., Drug & Alcohol Dependence, 2012
As nicotine can ameliorate the affective and reward processing deficits associated with depression, adolescents may learn that smoking is rewarding (experience validates expectations).

Depressed adolescents may find smoking more reinforcing (primary and secondary) than nondepressed adolescents.

Depression-prone smokers have greater smoking-induced dopamine release than smokers not prone to depression (Brody et al., 2009).
Hedonic Capacity

• heritable, stable dispositional ability to experience pleasure in response to stimuli that are typically rewarding

• Individual can experience pleasure deficits without concurrent depression symptoms

• Thought to reflect a disruption of neural pathways implicated in reward and motivation

2. Shafer, 2006; Watson, 2005  
3. Fawcett et al., 1983; Harvey et al., 2007; Meehl, 1975; 1987
Narrow Range

Low Capacity

Narrow Range

Diminished Responsiveness

High Capacity

Broad Range

High level of Responsiveness

> willingness to try cigarettes to stimulate an under-responsive reward system

less likely to smoke cigarettes
Hedonic Capacity

• overlooked as a risk factor for adolescent smoking uptake, even though the ability to derive pleasure from natural reinforcers seems like a salient trait to consider

• use smoking to stimulate an under responsive reward system?

• Reduced hedonic capacity may predispose adolescents to become regular smokers.
Maintenance of Smoking - adults

Lower hedonic capacity predicts

• greater cigarette craving within 24 hours of abstinence
  \(^1\)

• a tendency to place higher priority on smoking vs other reinforcers
  \(^2\)

• Shorter time to smoking relapse \(^3\)

Important to determine whether HC influences uptake as the adolescent brain may be particularly responsive to drugs such as nicotine that act on brain reward pathways to alter hedonic tone

1. Cook et al., 2004; Leventhal et al., 2009  
2. Leventhal et al, 2009  
3. Cook et al., 2010
Measures

**Smoking**  # of cigarettes smoking in past 30 days

**Hedonic Capacity**  Snaith-Hamilton Pleasure Scale (SHAPS), 14 items, *definitely agree = 3 to definitely disagree = 0*; range 0 - 42. alpha = .94
Not normally distributed, median split $> 34$ vs $\leq 34$

**Covariates**  gender, race, household & peer smoking, depression, parental monitoring and impulsivity
Analyses

• A two-part LGCM - permits the inclusion of two correlated latent growth curves, one for initiation of use (transition NS to S) and one for the change in the number of cigarettes among adolescents previously reporting smoking

• Binary with linear trend: $X^2_{(20, 1106)} = 24.91$, $p=.20$, CFI=1.00, RMSEA=.01; WRMR = .54.

• Continuous with a quadratic trend: $X^2_{(14, 222)} = 8.69$, $p=.85$, CFI=1.00, RMSEA= 0.00, 95% CI=0 -.04; SRMR = .02.
Results

• Compared to adolescents with high HC, those with low HC were over 2 1/2 times more likely to have smoked in the past 30 days (OR = 2.64, 95% CI = 1.08 - 6.45) at age 15.

• Low HC was associated with a 90% increase in the rate of change in cigarettes smoked in the past 30 days across the following 18 months (β = .9, z=2.28, p=.02)

Audrain-McGovern et al., Drug Nicotine and Tobacco Research, 2012
Low HC is a risk factor for initiation & escalation

• Nicotine stimulates DA neurotransmission, which might increase hedonic tone and help anhedonic adolescents augment pleasure from nondrug stimuli\(^1\)

• Adolescents who begin smoking as a result of low HC may, after chronic nicotine exposure, further elevate their reward threshold \(^2\)

• Smoking to regulate reward deficits may lead to an even greater need to smoke

Positive Affect & Smoking Uptake

Baseline Positive Affect

Positive Affect linear trend

Baseline smoking

Smoking linear trend

Smoking quadratic trend

Negative Affect, W1

Negative Affect, W3

Path

p values < .05

Leventhal, Rodriguez & Audrain-McGovern, under review.
Results

• Less positive affect at age 14 was associated with higher rates of smoking escalation.

• Adolescents with higher levels of smoking at age 14 exhibited decreases in positive affect over time.

• Over time, increases in smoking are associated with increases in positive affect (reciprocally, decreases in positive affect are paralleled by decreases in smoking).

• Teens whose smoking escalation leveled off later tended to exhibit less change in positive affect over time.
These findings suggest...

- Deficient pleasure, not just increased displeasure is an important risk factor for adolescent smoking progression.

- Over time, increases in smoking are associated with increases in positive affect, but smoking to regulate reward deficits may lead to an even greater need to smoke.

- Earlier smoking onset may contribute to diminished happiness and enjoyment later in adolescence as chronic exposure to nicotine may further reduce reward functioning.
Summary

- Many depressed adolescents take up smoking
- Decreasing alt. reinforcers fosters smoking
- Smoking mitigates depression
- Depressed adolescents expect smoking to be rewarding
- Deficient positive affect, not just increased negative affect increases adolescent vulnerability to smoking
- Depression (positive & negative affect) is an important smoking prevention target
Characteristics of Depression, the Effects of Nicotine & Potential Tx Targets

<table>
<thead>
<tr>
<th>Depression</th>
<th>Smoking/Nicotine Effect</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fewer alternate reinforcers</td>
<td>Smoking is reinforcing and can compensate for limited reinforcers among smokers</td>
<td>Identification and involvement in alternative reinforcers</td>
</tr>
<tr>
<td>Less sensitive to or less pleasure derived from rewards</td>
<td>Nicotine increases reward sensitivity or ability to experience pleasure</td>
<td>Build skills to savor or amplify the pleasure derived from daily nonsmoking reinforcers</td>
</tr>
<tr>
<td>Less attention to potential rewards</td>
<td>Increases salience of rewards in the environment, and general attention</td>
<td>Increase attention to opportunities for reward (cognitive training, mindful meditation?)</td>
</tr>
<tr>
<td>Diminished Positive Mood</td>
<td>Increases Positive Mood</td>
<td>Goal is to Increase or Maintain Positive Mood</td>
</tr>
<tr>
<td>Heightened Negative Mood</td>
<td>Decreases Negative Mood</td>
<td>Skills to Decrease Negative Mood</td>
</tr>
</tbody>
</table>

Goal is to Increase or Maintain Positive Mood
Collaborators

- Daniel Rodriguez, Ph.D.
- Adam M. Leventhal, Ph.D.
- Jocelyn Cuevas, M.A.
- Kelli Rodgers, B.A.
- Joseph Sass, M.S.