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Alcohol and Nicotine Dependence: Shared Mechanisms

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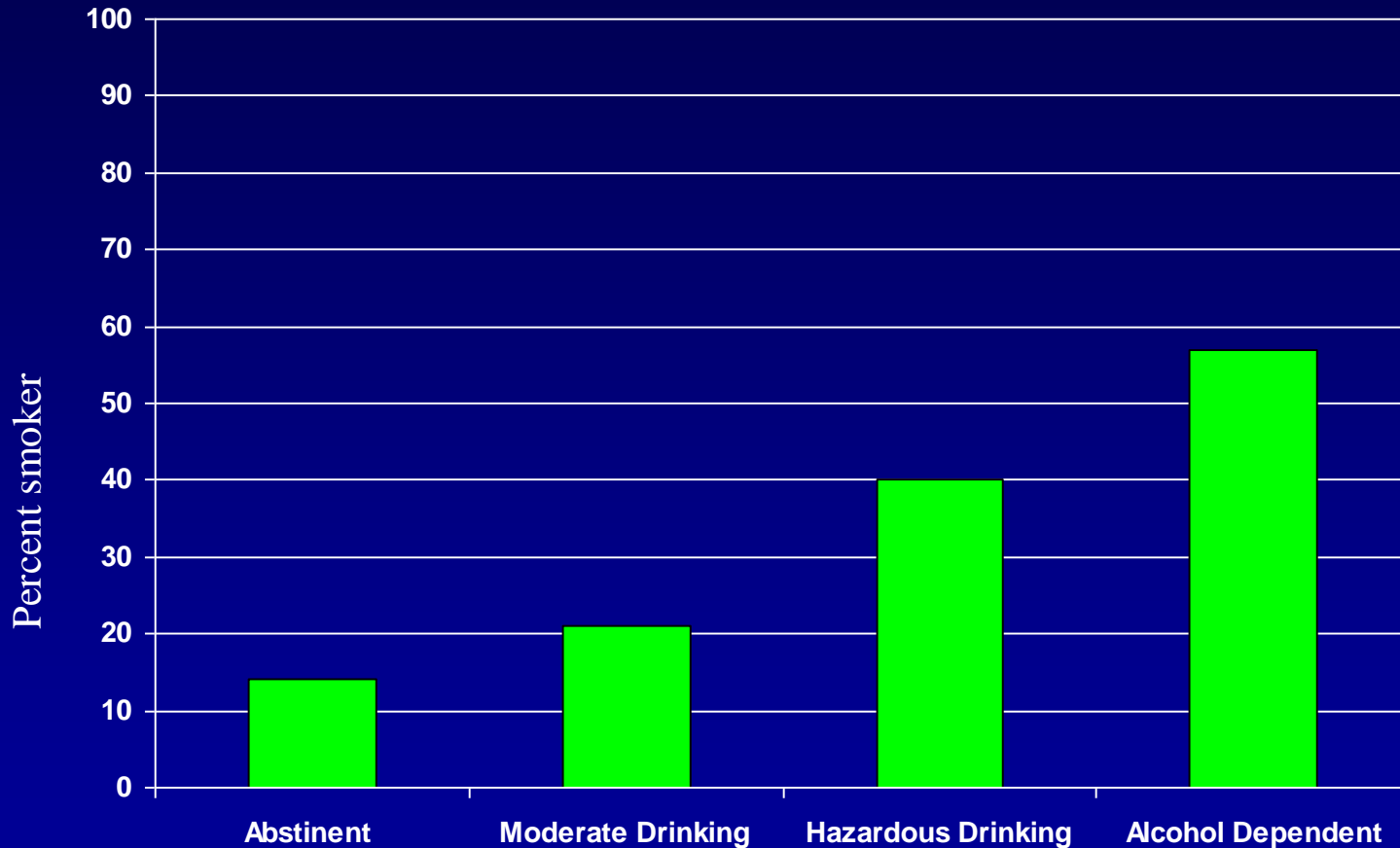
Overview

- Epidemiological evidence of this association
- Overview of Potential Shared Mechanisms
- Focus on functional effects of concurrent use
- Highlights of studies investigating mechanisms for the association between alcohol and tobacco and relapse

Prevalence of Co-Occurring Diagnoses of Alcohol Use Disorders and Nicotine Dependence (Grant et al., 2001)

| Nicotine Dependence (12.8%) | Alcohol Diagnosis if Nicotine Dependent | Nicotine Dependence if Alcohol Diagnosis |
|-----------------------------|---|--|
| Alcohol Abuse (4.7%) | 9.3% | 25.5% |
| Alcohol Dependence (3.8%) | 13.5% | 45.4% |

Percent Reporting Smoking Past Year by Current Alcohol Use Pattern



Abstinent

Moderate Drinking

Hazardous Drinking

Alcohol Dependent

28.8%

40.9%

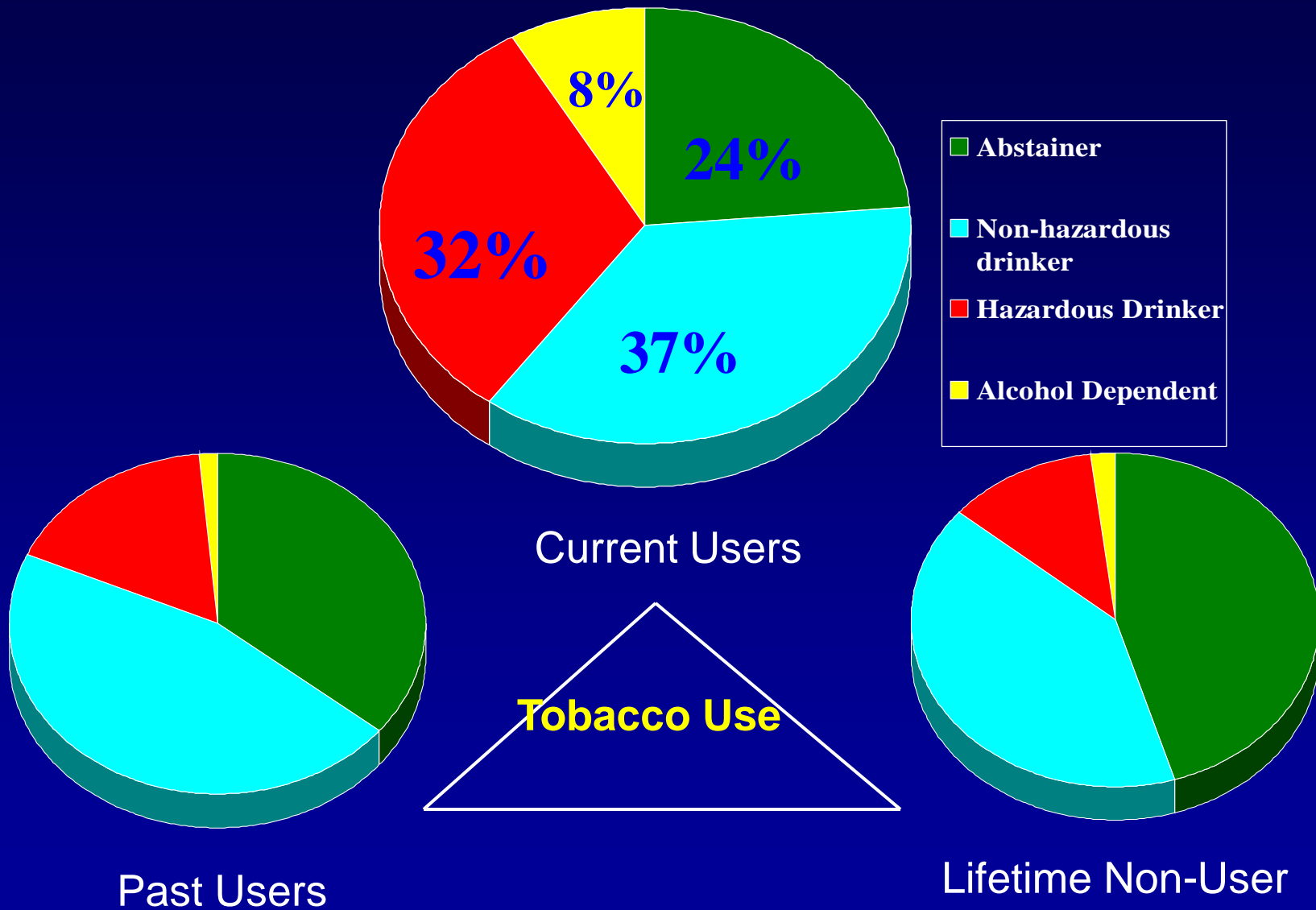
24.9%

5.4%

Percent of U.S.
Population

McKee, unpublished data NESARC

Current Alcohol Use as a Function of Tobacco Use



Shared Mechanisms

- Shared Risk Factors
 - Genetics
 - Psychiatric risk factors
- Shared environmental factors
 - Inadequate parental monitoring
 - Increased availability
 - Stressful life events
- Pharmacological Interactions
 - Altered reinforcement
 - Cross tolerance
 - Conditioning

Alcohol Tobacco Interactions

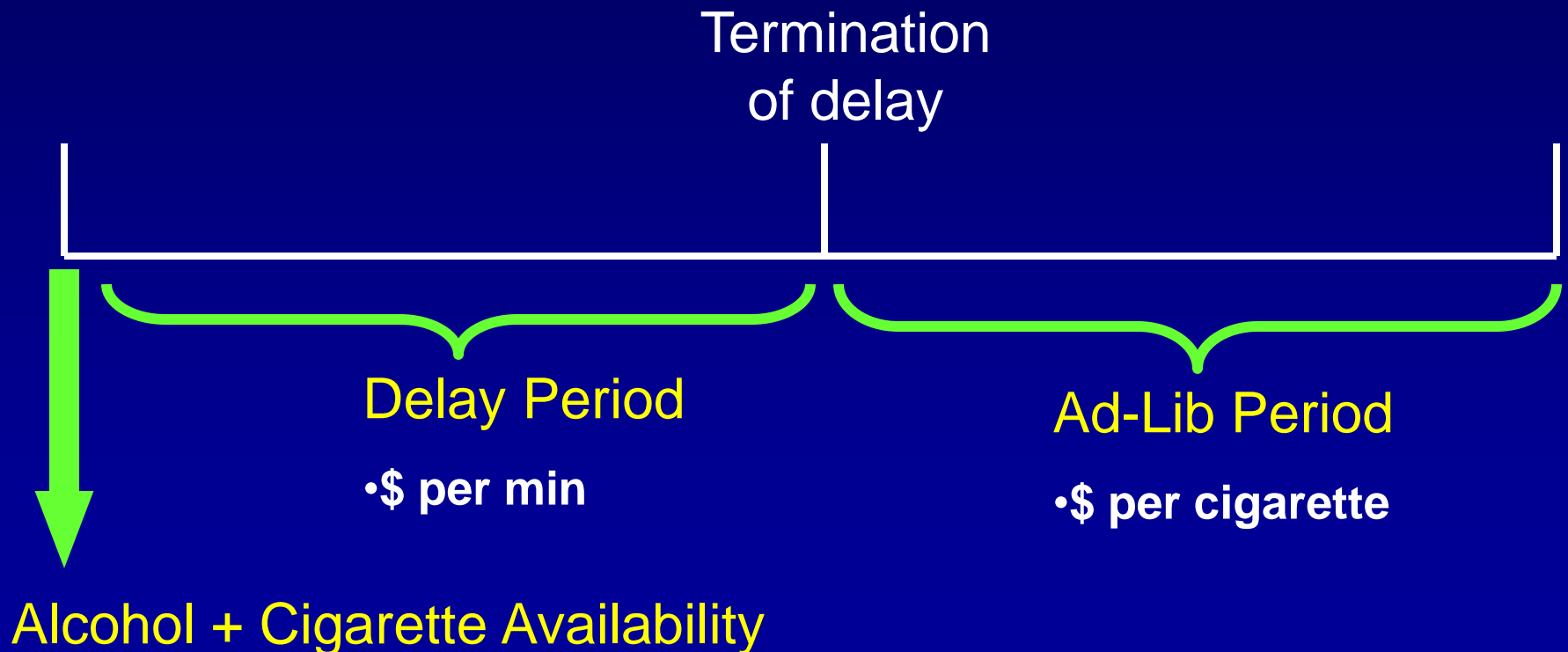
Does alcohol consumption increase urge to smoke and inhibit ability to resist?

Does smoking promote urge to drink and drinking?

What are the subjective effects of alcohol, nicotine and their combined use?

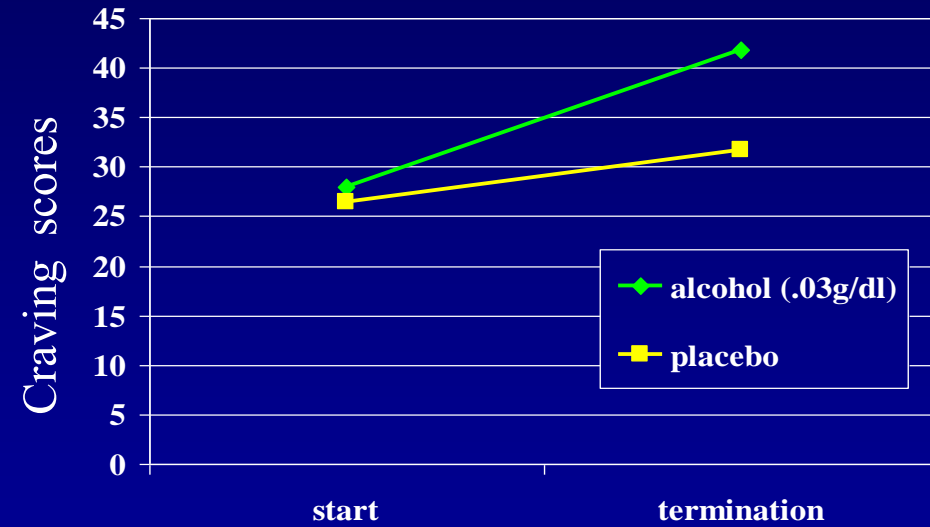
Modeling the ability to resist the first cigarette (McKee, 2004)

- 16 smokers with moderate to heavy drinking patterns
- Tested with alcohol or masked placebo beverage cues



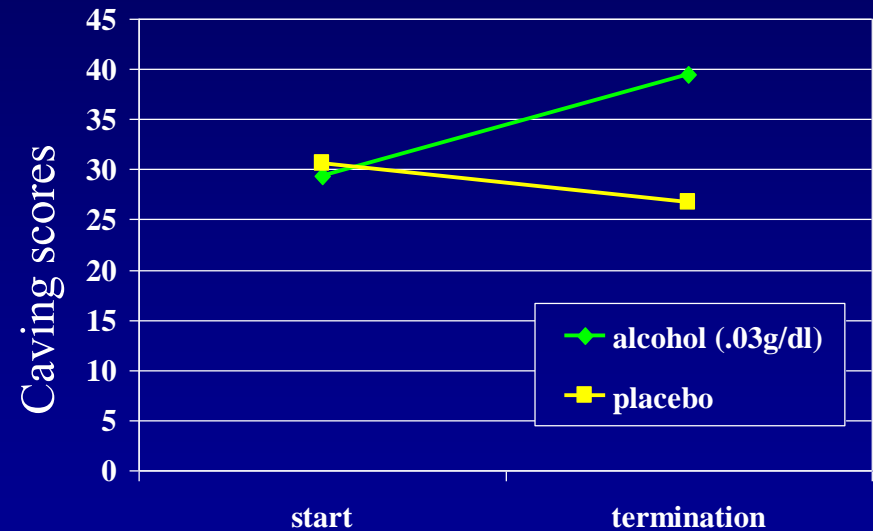
Alcohol increases tobacco and alcohol craving

Tobacco



$F(1, 15) = 6.88, p = .02$ (time x session)

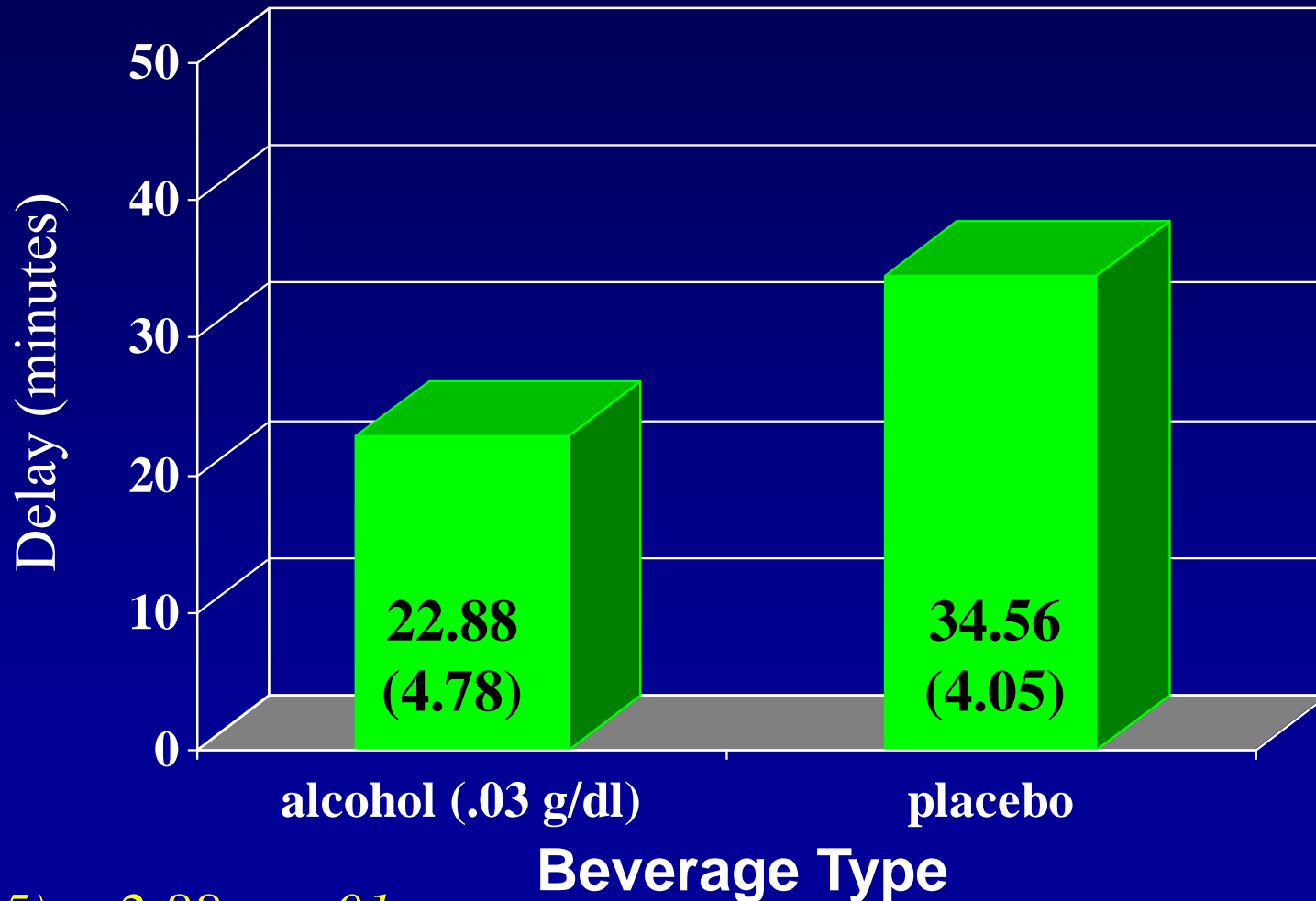
Alcohol



$F(1, 15) = 3.52, p = .08$ (time x session)

Alcohol reduces the ability to resist the first cigarette

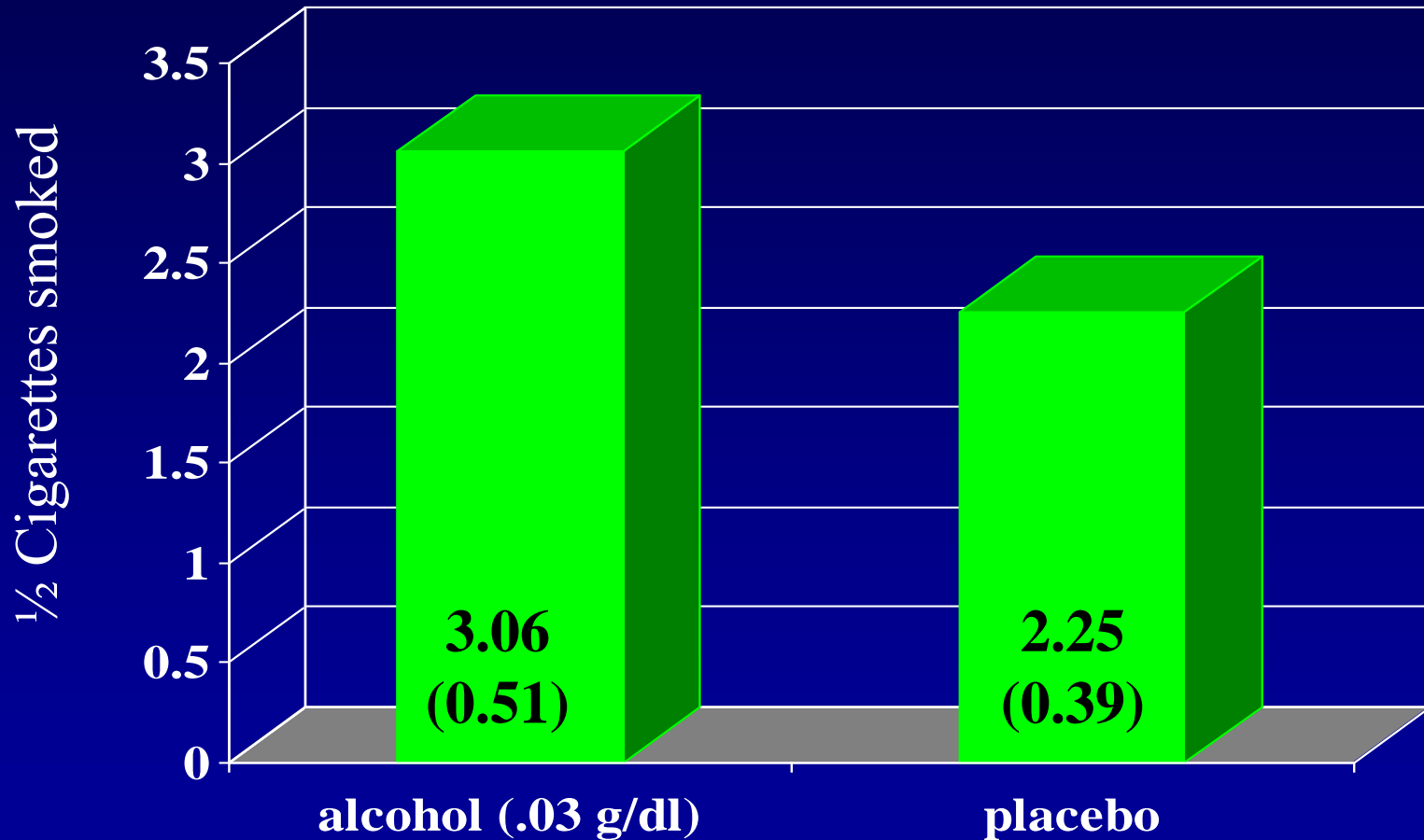
Mean length of delay after consuming alcohol or placebo



$t(15) = 2.88, p = .01$

Alcohol increases subsequent smoking

Mean ½ cigarettes smoked during ad-lib period



$t(15) = 1.98, p = .06$

Beverage Type

Does Smoking Elicit Urge to Drink and Drinking Behavior?

- Smoking in combination with alcohol, but not smoking abstinence, increased responding for an alcohol reward (Perkins et al, 2000).
- Using EMA technology in alcoholics quitting smoking and drinking Cooney (SRNT, 2005):
 - Alcohol urge increased immediately after cigarette smoking.

Summary

- Alcohol can increase craving for cigarettes and undermine the ability to resist smoking
- Provides support for advice to avoid alcohol during a quit attempt
- Smoking in combination with alcohol increases alcohol consumption
- Modest increase in urge to drink in abstinent alcoholics

Independent and Combined Effects

Alcohol Effects

Ascending limb
Stimulation

Descending Limb
Sedation, fatigue
Impairment

Nicotine Effects

Increased alertness
Increased tension and arousal
Decreased fatigue

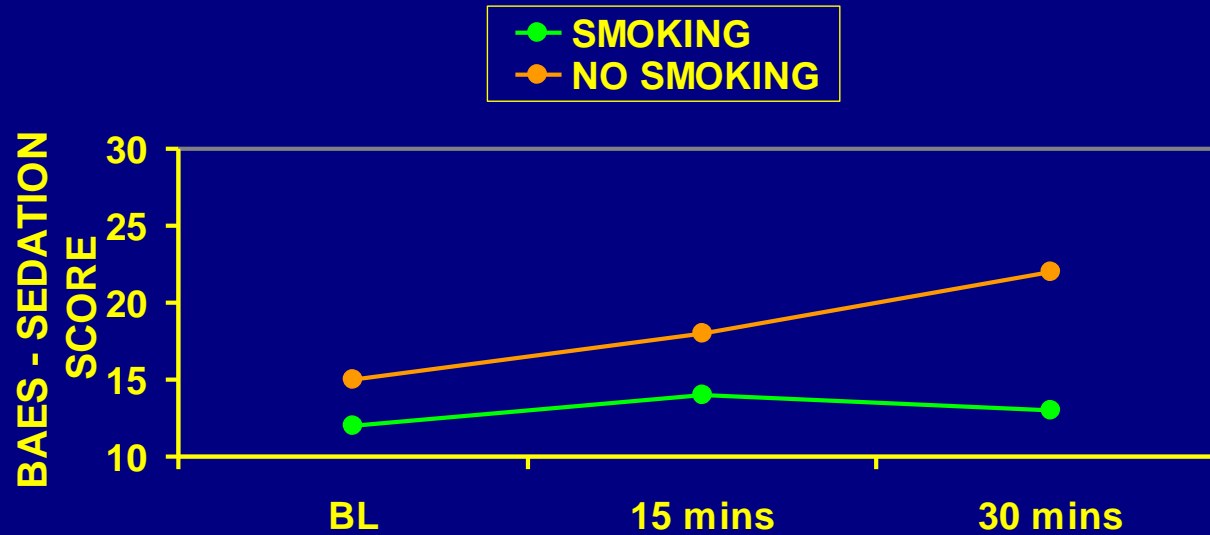
Combined Effects

Decreased intoxication
Decreased sedation

Perkins et al., 1997, 1999,
2000

Zacny, 1990

Smoking reduces sedation from alcohol measured with the BAES

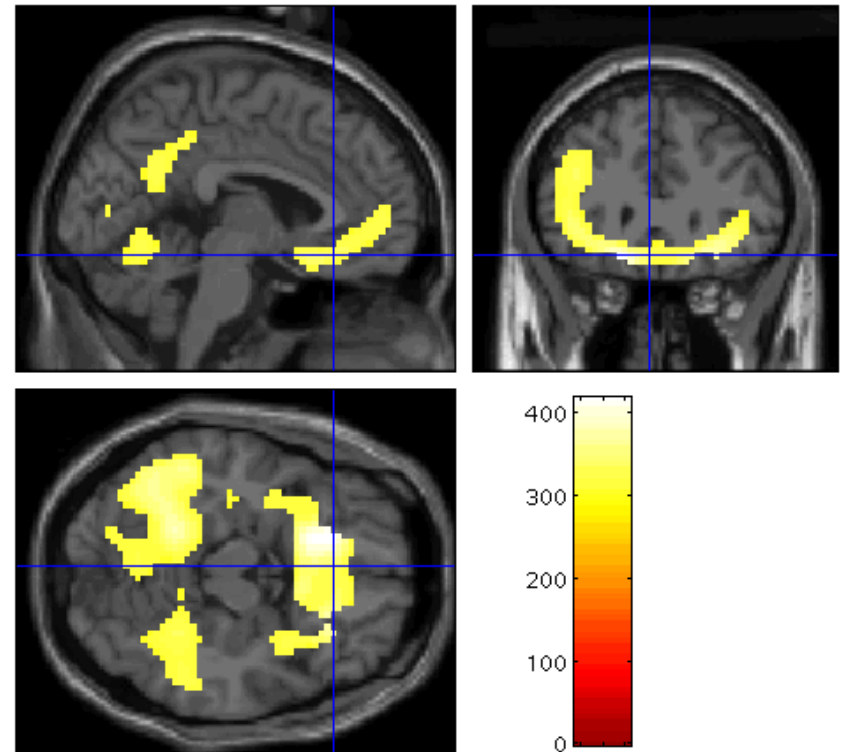
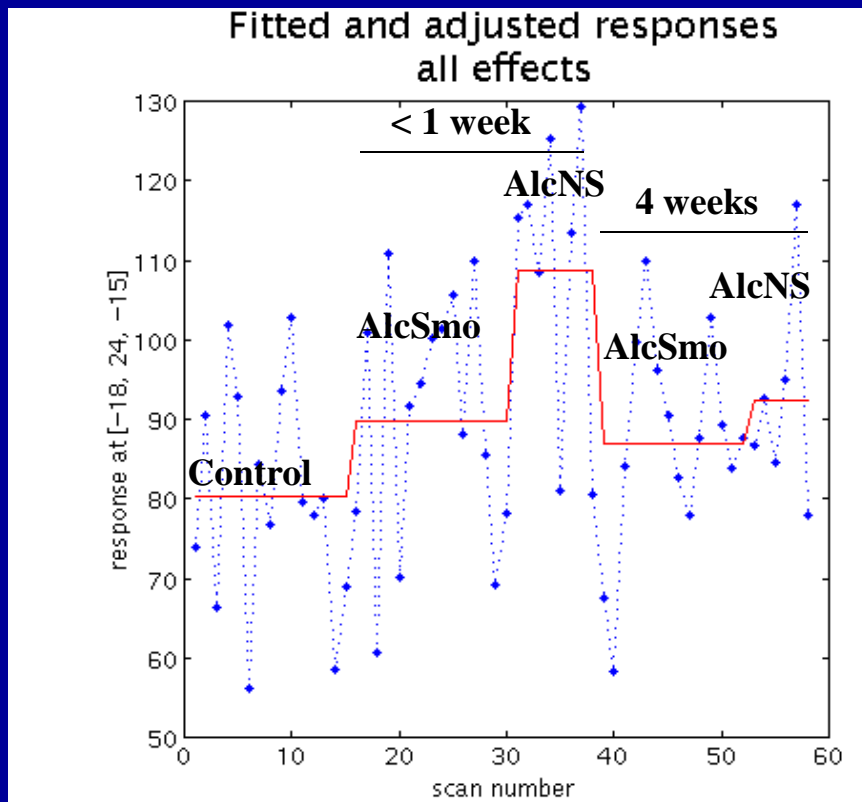


Perkins, *Addiction Biology*, 1997, 2: 255-267

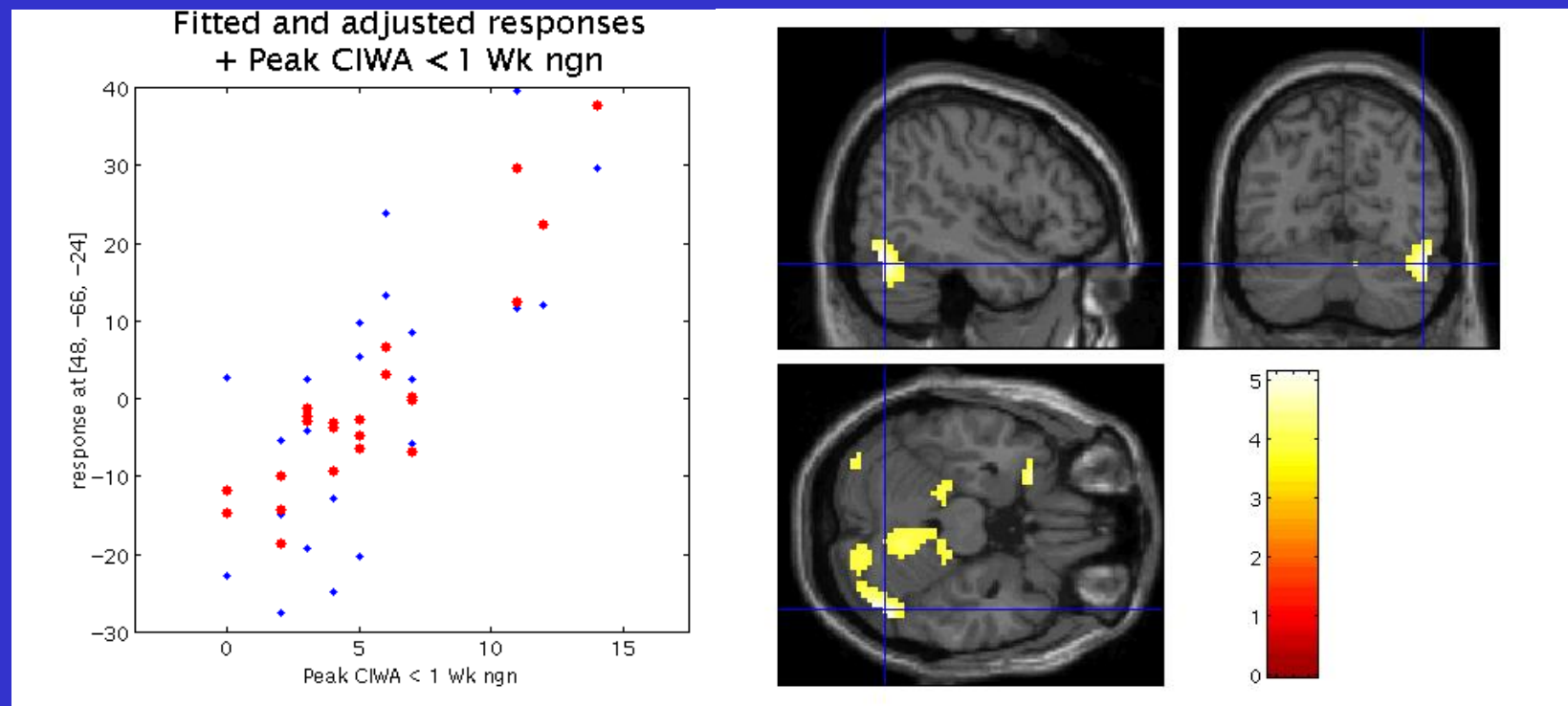
Functional Significance

- Nicotine antagonism of acute alcohol induced sedation or intoxication:
 - Allow additional drinking
 - Reinforce smoking through negative reinforcement
 - Enhance positive effects of smoking
- What about possibility that smoking could counteract aversive effects of chronic alcohol consumption?

GABA_A-Benzodiazepine receptors are higher in Alcoholic Nonsmokers, but not in Alcoholic Smokers during first week of abstinence



Severity of Alcohol Withdrawal Correlates with GABA_A-BZ Receptors in Alcoholics Abstinent < 7 days



Dependence and Withdrawal: Tolerance and Cross Tolerance

- Tolerance develops to one drug may transfer to the other drug.
 - This could promote more rapid development of dependence on each substance
- Hypothesis: Tobacco tolerance may contribute more in the progression of alcohol dependence due to cross tolerance
 - Smoking progresses more rapidly to dependence
 - Can smoke 18 hours a day
 - Alcohol use is limited by intoxicating effects

Alcohol Tobacco Interactions:

Role of Drug Associated Cues

Drug/Alcohol Associated Cues

Cues associated with drug use can become rewarding on their own and motivate behavior, including drug relapse.

people, places, sight or smell of the drug, moods

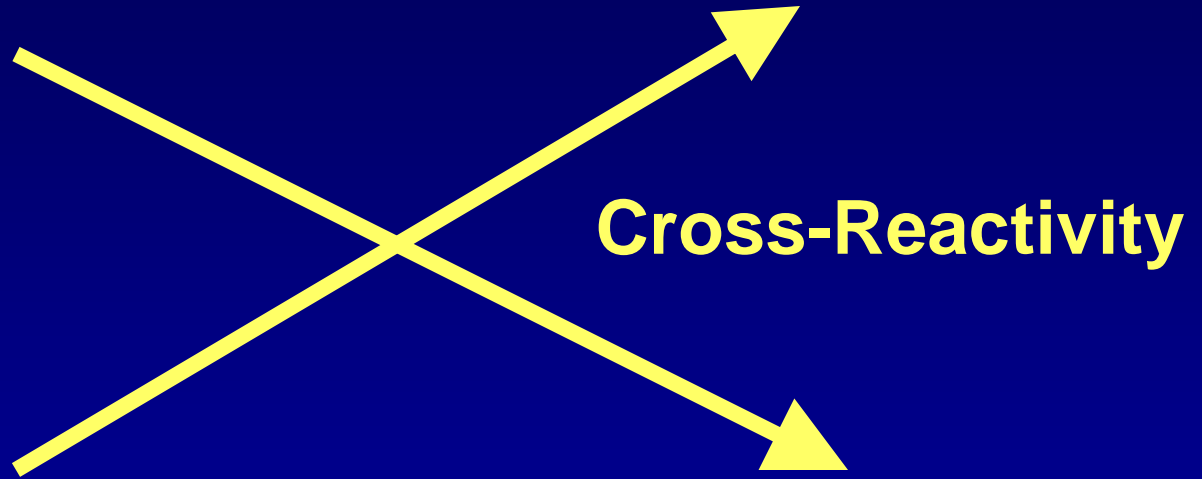


These cues can:

- *activate brain systems associated with addiction/alcoholism*
- *elicit craving and drug/alcohol-seeking behavior*
- *elicit withdrawal and drug/alcohol-taking behavior*

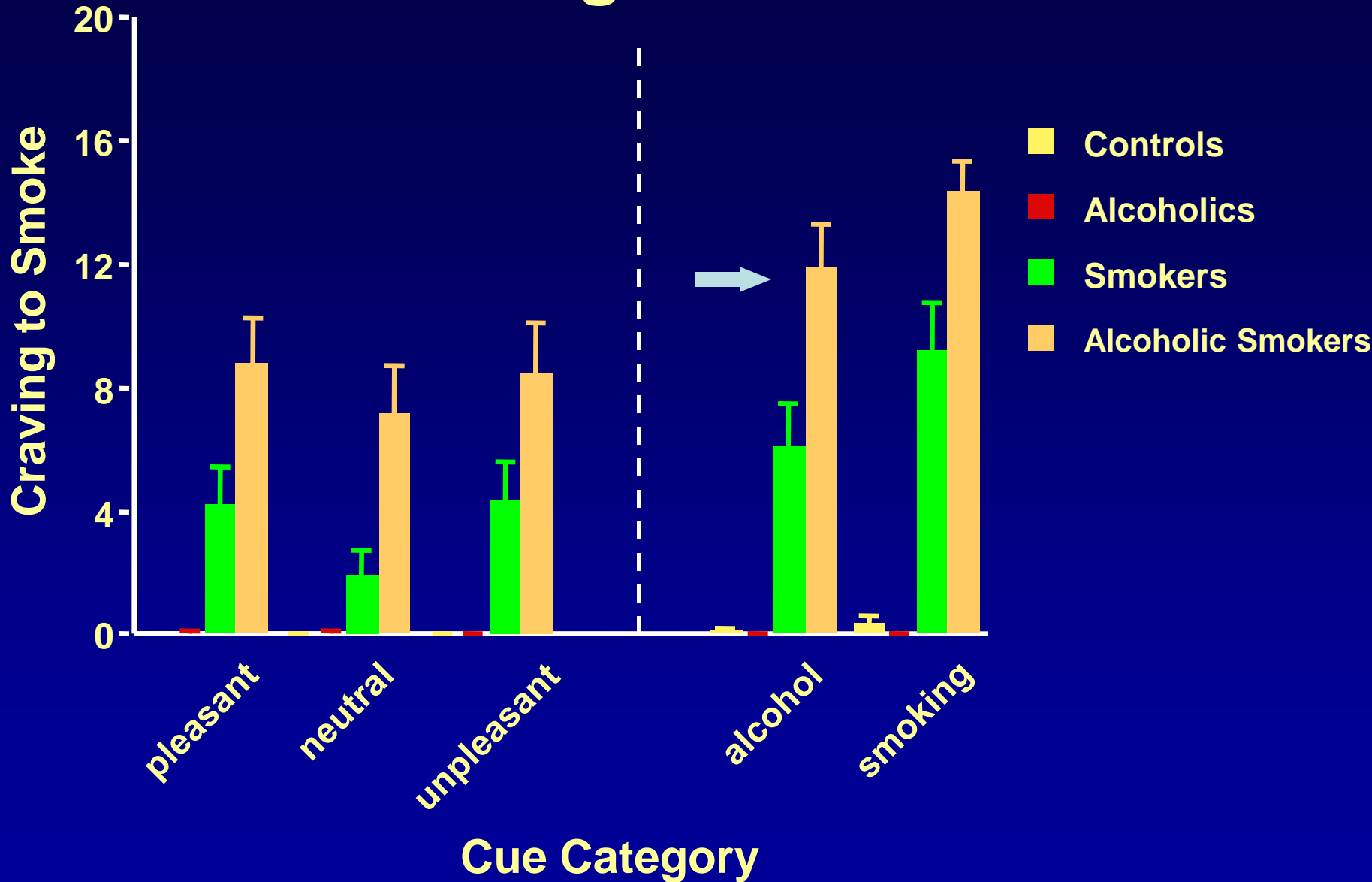


→ **“I want to smoke”**

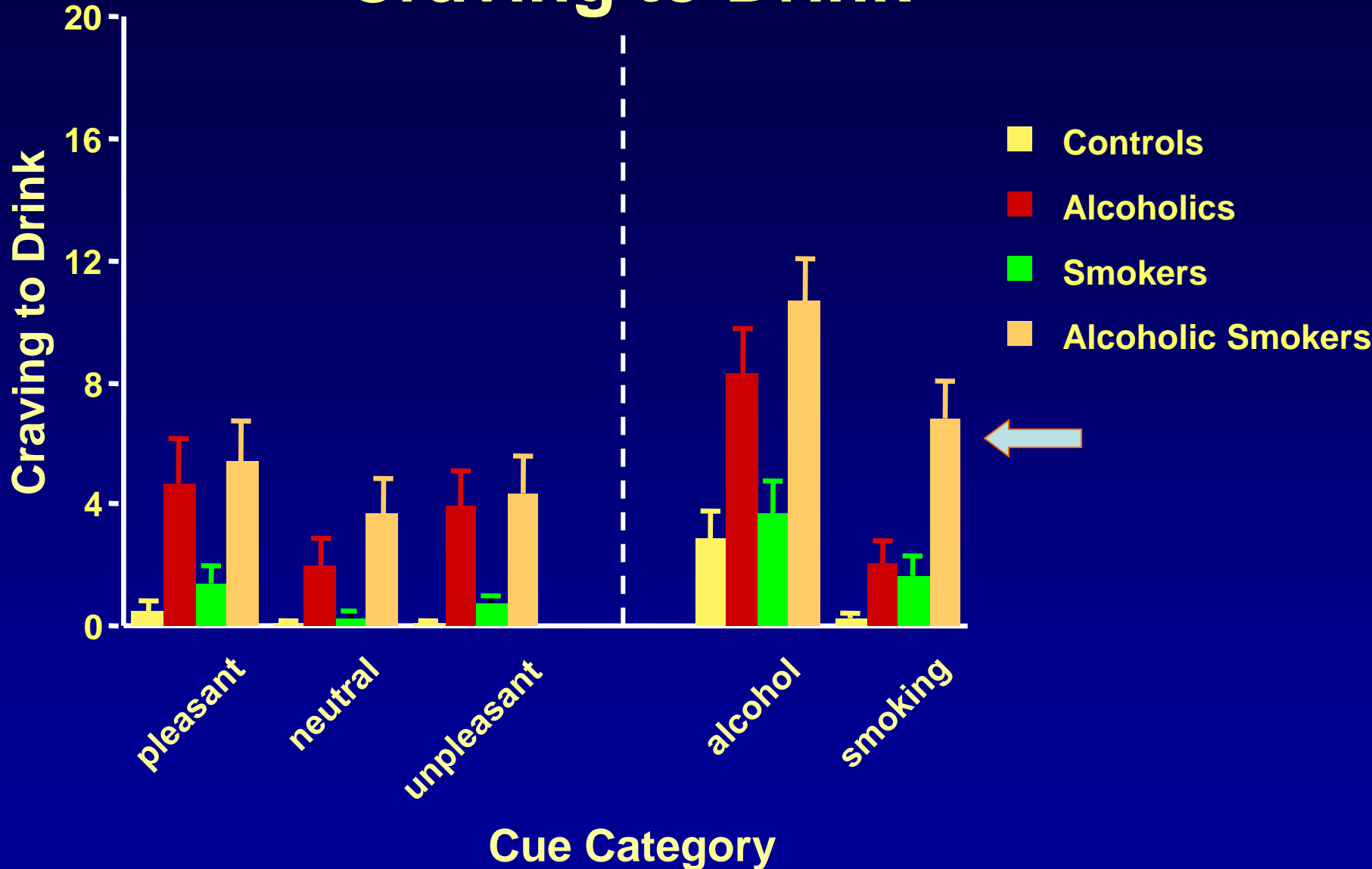


→ **“I want to drink”**

Craving to Smoke



Craving to Drink



Summary

- **Alcoholic smokers report stronger cue-elicited cravings than single addict groups.**
- **Substantial “cross-cue reactivity” between smoking and alcohol cues in alcoholic smokers.**

Animal - Translational Studies

Understand the role of nicotine receptors in the neurobiology of cue-induced craving:

Can nicotine enhance the behavioral effects of cues ?

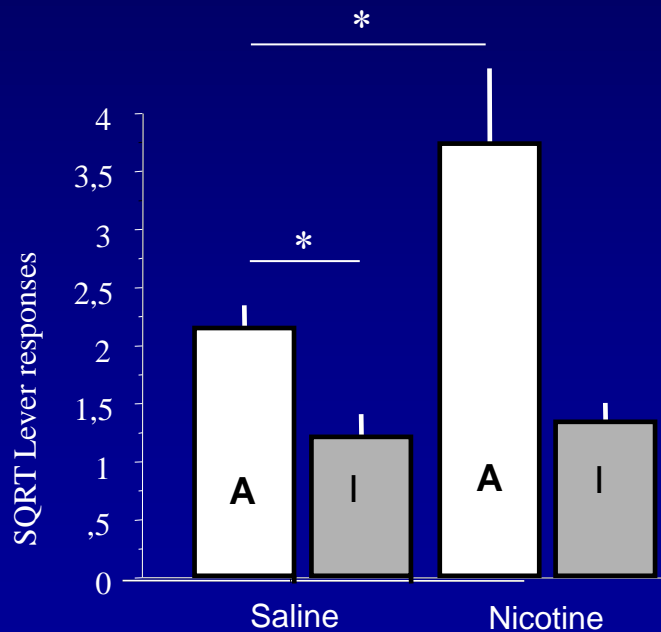
Can a medication that blocks nicotinic receptors (**Mecamylamine**) block the behavioral effects of alcohol associated cues?



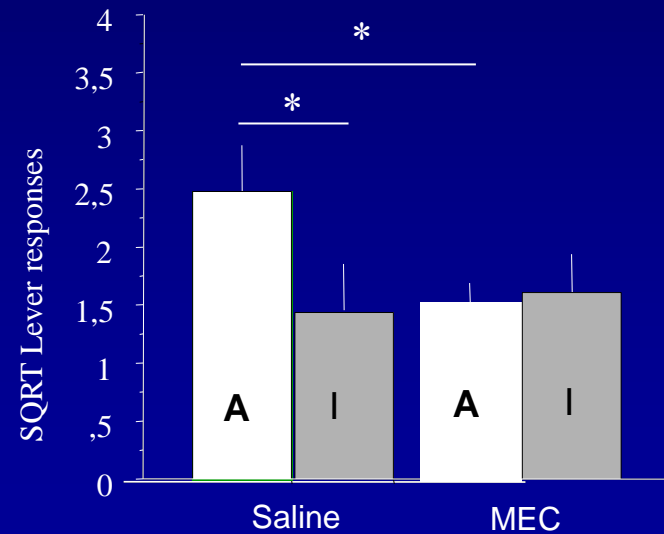
Behavior motivated by cues

- Rats learn to associate cues (light + tone) with reinforcer (“conditioning”)
- Tested the ability of cues (conditioned stimuli) to “motivate” behavior

Nicotine enhances responding for water cues



Mecamylamine blocks responding for alcohol cues



Summary and Implications

- Nicotinic receptors can modulate the ability of alcohol associated cues to “motivate” behavior
 - Enhanced with nicotine/smoking
 - Reduced with nicotine receptor antagonists
- Potential Implications:
 - Nicotine/smoking may enhance cue-induced craving for alcohol and promote continued smoking and drinking behavior
 - Mecamylamine may help prevent cue-induced craving for alcohol

Alcohol Tobacco Interactions

Will public policy interventions to reduce tobacco use also reduce alcohol drinking?

Policy Research

Economic Analysis of Shared Mechanisms

Substitutes

- An increase in the price of one, leads to an increase in demand for the other
- E.g., if the cost of cigarettes increases, people smoke less but increase their use of alcohol as a substitute

Complements

- An increase in the price of one leads to a decrease in demand for the other
- Most studies support the idea of modest complementary relationship

Table 3: Differences in expenditure shares between smoking and non-smoking households, by income, adjusted for demographic characteristics, CES, 1995-2001

| | Expenditure Shares | | (1) | (2) | Percent Change |
|----------------|--------------------|-------------|-----|-----|----------------|
| | Non-Smokers (A) | Smokers (B) | | | |
| Full Sample | | | | | |
| Food | 16.60 % | 16.46 % | * | | -0.84% |
| Alcohol | 0.76 | 1.37 | *** | | 80.26 |
| Housing | 36.27 | 34.63 | *** | | -4.52 |
| Apparel | 4.41 | 4.23 | *** | | -4.08 |
| Transportation | 14.86 | 14.53 | ** | | -2.22 |
| Health Care | 4.29 | 4.11 | *** | | -4.20 |
| Miscellaneous | 22.80 | 21.50 | *** | | -5.70 |
| Tobacco | 0 | 3.74 | | | |
| Low Income | | | | | |
| | Non-Smokers (C) | Smokers (D) | | | |
| Food | 22.34 % | 21.70 % | *** | *** | -2.86 % |
| Alcohol | 0.51 | 1.07 | *** | | 109.8 |
| Housing | 40.41 | 37.31 | *** | *** | -7.67 |
| Apparel | 4.97 | 4.50 | *** | *** | -9.46 |
| Transportation | 13.64 | 13.19 | ** | | -3.30 |
| Health Care | 4.06 | 3.69 | *** | | -9.11 |
| Miscellaneous | 14.08 | 12.19 | *** | *** | -13.42 |
| Tobacco | 0 | 5.10 | | | |

Consumer Expenditure Survey

10% increase in taxes leads to a 7% reduction in tobacco use and a 2% increase in alcohol expenditures.

Susan Busch

In progress

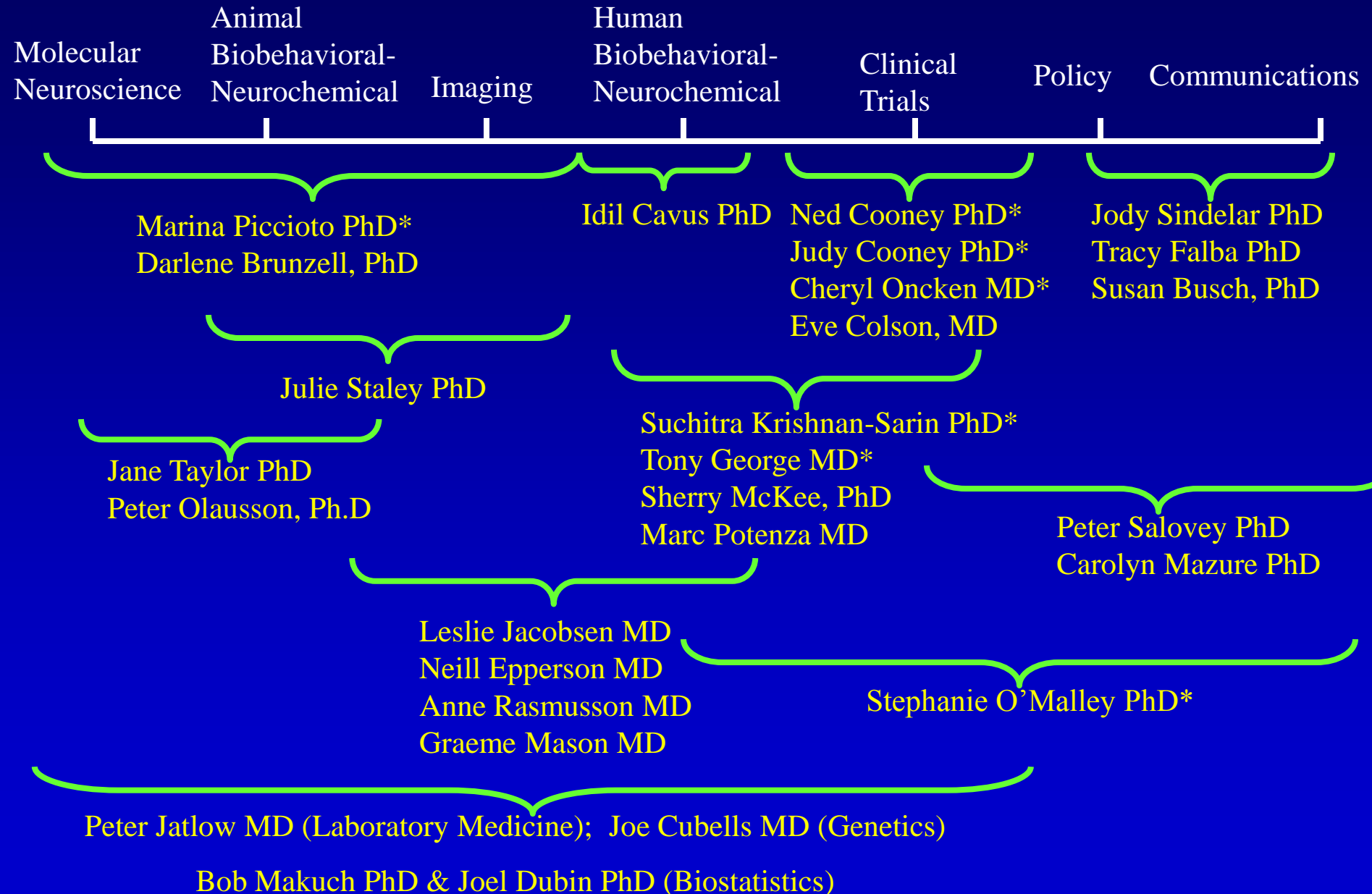
Summary

- **Enhanced reinforcement**
 - Similar positive effects may increase positive reinforcement
 - Opposing effects may also increase the reinforcing value of each drug
- **Cross tolerance**
 - Promote the more rapid development of dependence on each drug
- **Cue reactivity**
 - Cross reactivity between alcohol and tobacco cues
 - Nicotine itself may enhance the learning of the rewarding value of cues and their ability to elicit drug seeking

Summary

- We have preliminary evidence that may help explain in part the association between alcohol and tobacco dependence
- Integration of findings across different methods of analysis will be critical to this understanding and the development of more effective prevention and intervention.

CENTURY Researchers



Funders

National Institute on Alcohol Abuse and Alcoholism

National Institute on Drug Abuse

National Cancer Institute

Robert Wood Johnson Foundation

