# **Beyond the Brain:** Interactions between drugs and society

### Carl L. Hart, Ph.D.

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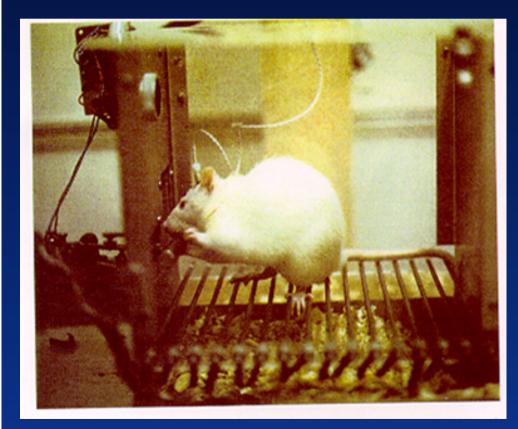
Department of Psychiatry, College of Physicians & Surgeons of Columbia University,

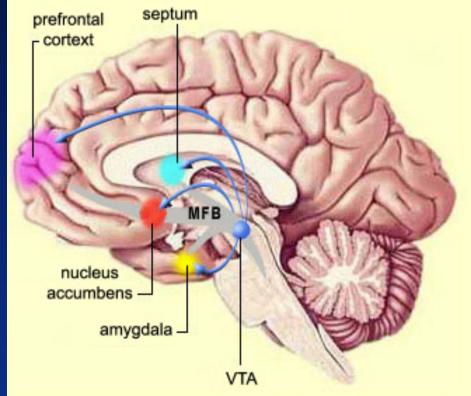
and

Institute for Research in African-American Studies, Columbia University

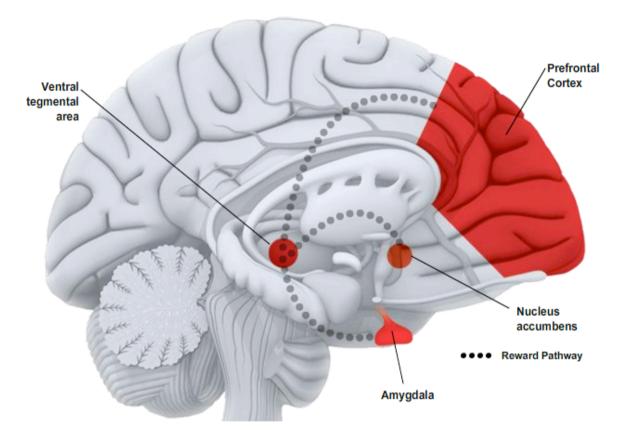
# Positive reinforcement produced by electrical stimulation of the septal area and other regions of rat brain

### James Olds and Peter Milner (1954)





# All of the drugs of abuse increase DA activity in the nucleus accumbens





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# Smoked Cocaine Self-Administration is Decreased by Modafinil

#### Carl L Hart\*<sup>1,2</sup>, Margaret Haney<sup>1</sup>, Suzanne K Vosburg<sup>1</sup>, Eric Rubin<sup>1</sup> and Richard W Foltin<sup>1</sup>

<sup>1</sup>Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, NY, USA; <sup>2</sup>Department of Psychology, Columbia University, New York, NY, USA



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# Smoked Cocaine Self-Administration is Decreased by Modafinil

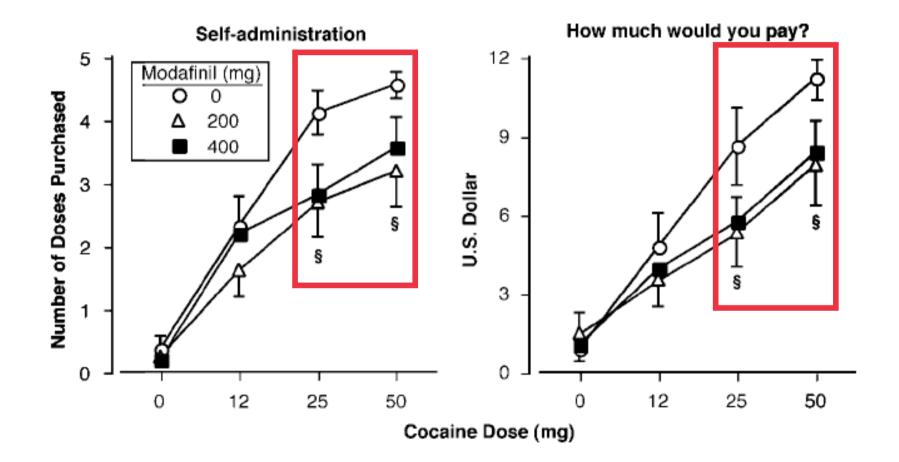
**Carl L Hart**\*\*<sup>1,2</sup>, **Margaret Haney**<sup>1</sup>, **Suzanne K Vosburg**<sup>1</sup>, **Eric Rubin**<sup>1</sup> and **Richard W Foltin**<sup>1</sup> <sup>1</sup>Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, NY, USA; <sup>2</sup>Department of Psychology, Columbia University, New York, NY, USA

## Modafinil (Provigil®)

-Approved to treat excessive daytime sleepiness

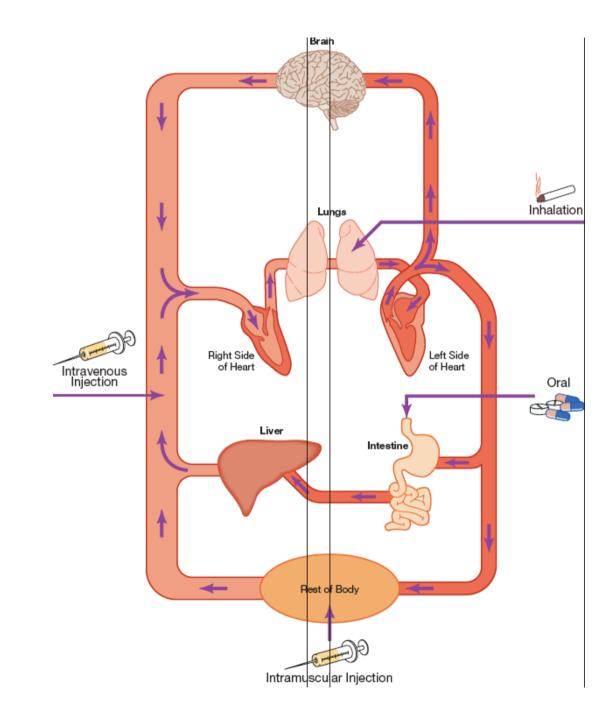
Mechanism of action remains unclear, but

- -Hypothesized: increase catecholaminergic activity
- -Also increase glutamatergic and histaminergic transmission and decrease GABAergic transmission



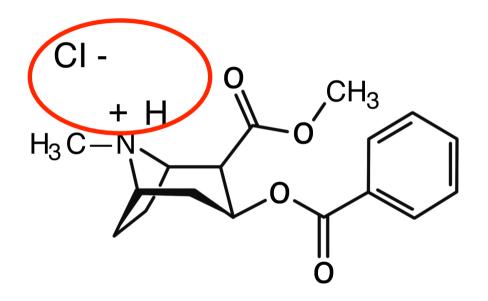


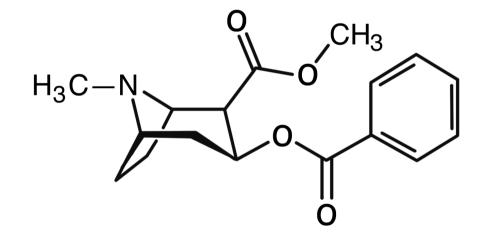
- Dose
- Route of administration



#### **Powder Cocaine**

#### **Crack Cocaine**

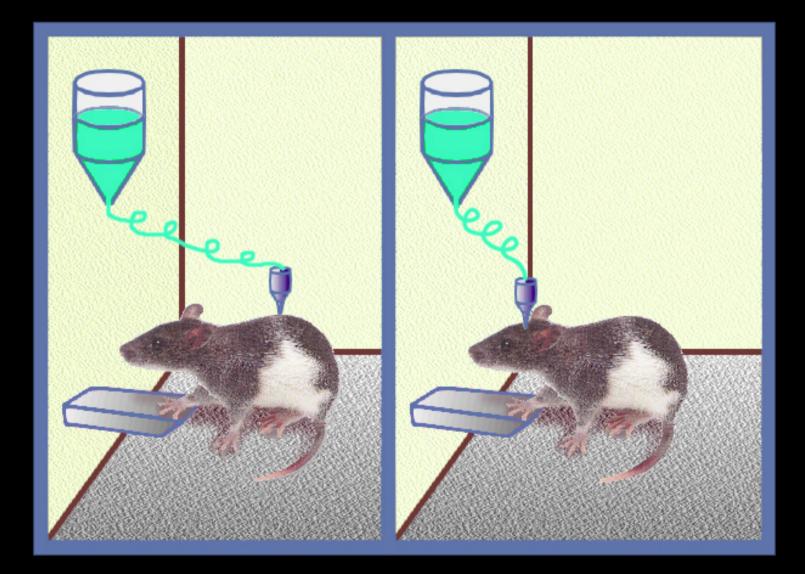






- Dose
- Route of administration
- User's experience (set)
- Environment (setting)

# **Drug Self-administration**





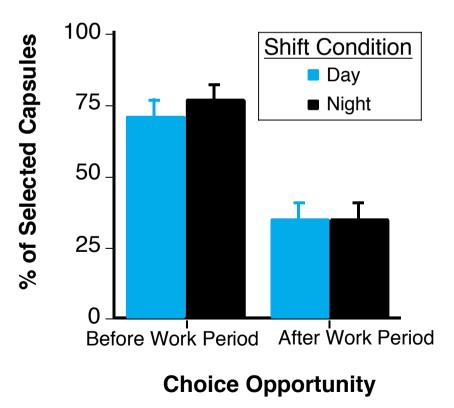
ORIGINAL INVESTIGATION

## Methamphetamine self-administration by humans subjected to abrupt shift and sleep schedule changes

Matthew G. Kirkpatrick • Margaret Haney • Suzanne K. Vosburg • Sandra D. Comer • Richard W. Foltin • Carl L. Hart ORIGINAL INVESTIGATION

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#### FINDINGS

# The Rational Choices of Crack Addicts

By JOHN TIERNEY Published: September 16, 2013

Long before he brought people into his laboratory at Columbia University to smoke crack cocaine, Carl Hart saw its effects firsthand. Growing up in poverty, he watched relatives become crack addicts, living in squalor and stealing from their mothers. Childhood friends ended up in prisons and morgues.

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Béatrice de Géa for The New York Times Carl Hart an accordiate professor of

Those addicts seemed enslaved by crack, like the laboratory rats that

couldn't stop pressing the lever for cocaine even as they were starving to death. The cocaine was providing such powerful dopamine stimulation to the brain's reward center that the addicts couldn't resist taking another hit.

GET TICKETS At least, that was how it looked to Dr.

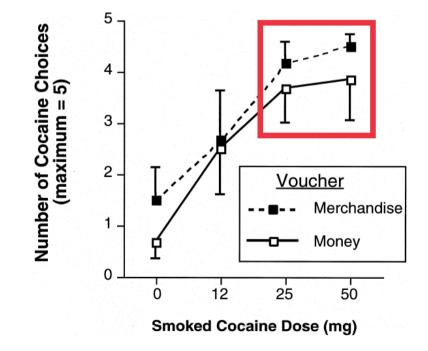
Hart when he started his research career in the 1990s. Like other scientists, he hoped to find a neurological cure to addiction, some mechanism for blocking that dopamine activity in the brain so that people wouldn't succumb to the otherwise irresistible craving for cocaine, heroin and other powerfully addictive drugs.

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A SLAVE

# Alternative reinforcers differentially modify cocaine self-administration by humans

C.L. Hart, M. Haney, R.W. Foltin and M.W. Fischman

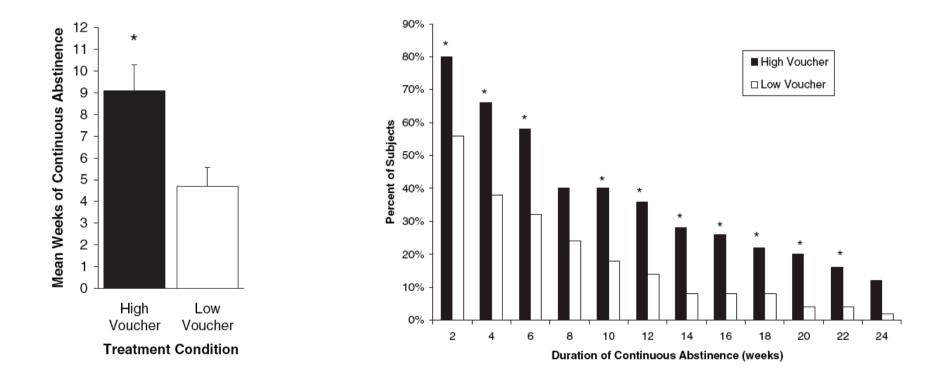


# Alternative Reinforcers: Clinical Data

#### Effects of varying the monetary value of voucher-based incentives on abstinence achieved during and following treatment among cocaine-dependent outpatients

Stephen T. Higgins<sup>1,2</sup>, Sarah H. Heil<sup>1,3</sup>, Robert Dantona<sup>1</sup>, Robert Donham<sup>1</sup>, Martha Matthews<sup>1</sup> & Gary J. Badger<sup>3</sup>

Departments of Psychiatry<sup>1</sup>, Psychology<sup>2</sup> and Medical Biostatistics<sup>3</sup>, University of Vermont, Burlington, VT, USA

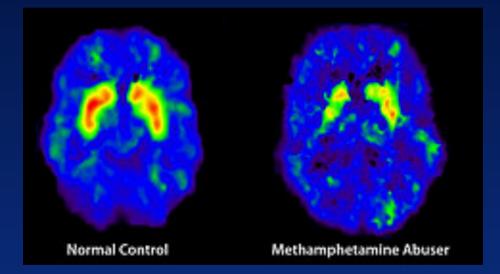


### A Reinforcement-Based Therapeutic Workplace for the Treatment of Drug Abuse: Three-Year Abstinence Outcomes

Kenneth Silverman, Dace Svikis, Conrad J. Wong, Jacqueline Hampton, Maxine L. Stitzer, and George E. Bigelow Johns Hopkins University School of Medicine

- Integrates abstinence reinforcement contingencies in an employment setting
- Participants' salary used to reinforce drug abstinence

# Methamphetamine causes brain damage





### Review Is Cognitive Functioning Impaired in Methamphetamine Users? A Critical Review

#### Carl L Hart\*<sup>1,2,3</sup>, Caroline B Marvin<sup>1</sup>, Rae Silver<sup>1,4,5</sup> and Edward E Smith<sup>1,6</sup>

<sup>1</sup>Department of Psychology, Columbia University, New York, NY, USA; <sup>2</sup>Division on Substance Abuse, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, NY, USA; <sup>3</sup>Institute for Research in African-American Studies, Columbia University, New York, NY, USA; <sup>4</sup>Department of Psychology, Barnard College of Columbia University, New York, NY, USA; <sup>5</sup>Department of Anatomy and Cell Biology, Columbia University, New York, NY, USA; <sup>6</sup>Division of Cognitive Neuroscience, New York State Psychiatric Institute and Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY, USA

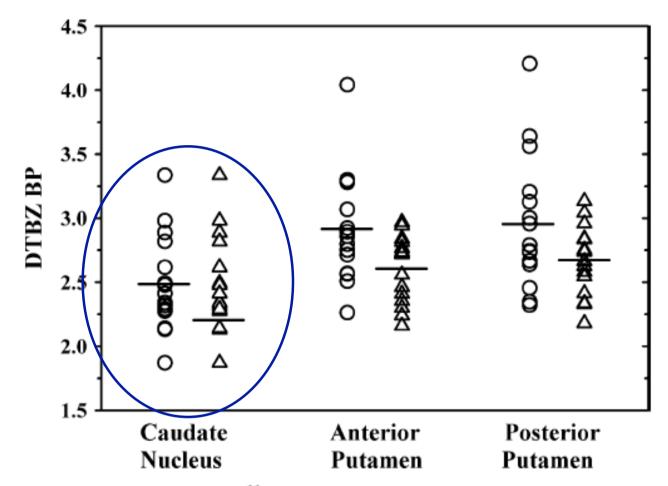


Fig. 1 Scatter plot of  $[^{11}C]DTBZ$  binding potential in the caudate nucleus and anterior and posterior putamen. The *open circles* represent individuals in the control group (n=16) and *triangles* represent individuals in the methamphetamine group (n=15)

Johanson et al. 2006, Psychopharmacology 85, 327-38

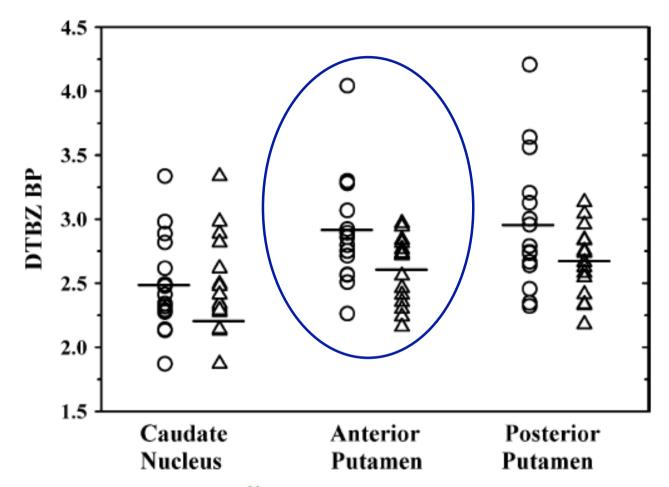


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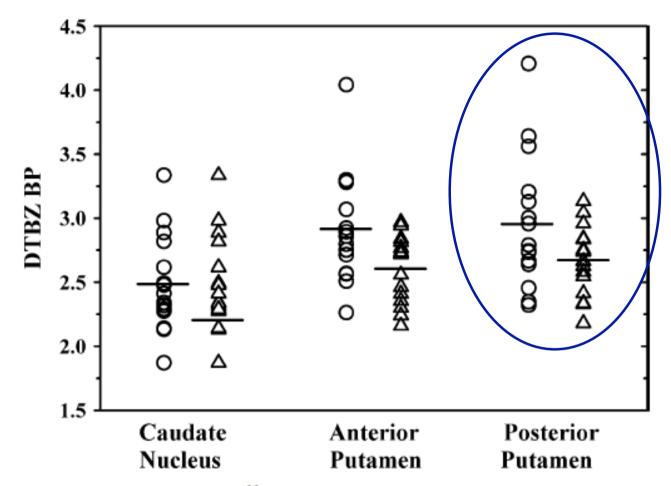


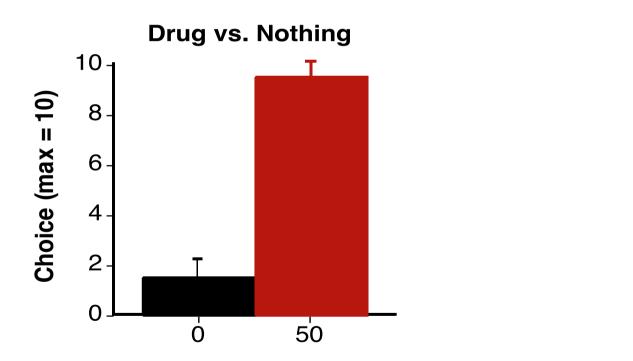
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# Summary of cognitive findings

Overwhelmingly impairment not demonstrated

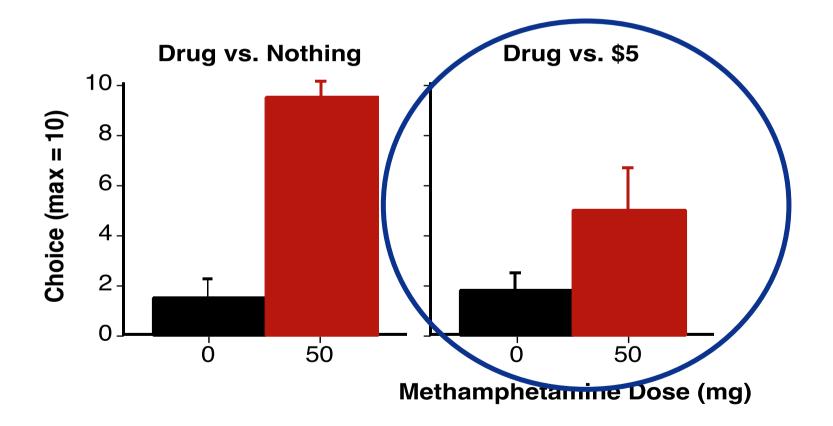
- Despite "brain changes" and exaggerated claims in the literature

## ... no alternative, they'll take drug every time

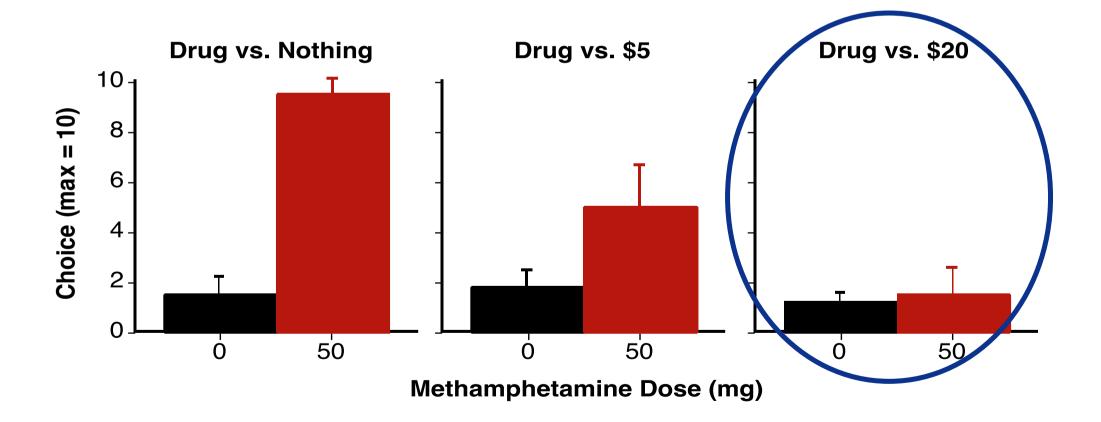


**Methamphetamine Dose (mg)** 

## ...drug-taking behavior become more malleable



## ...drug-taking behavior is abolished



# **Take-home Message**

- Neuroscience approaches useful in guiding medication development
  - But the promise may have been oversold
- Drug users behave rationally
  - Environmental manipulations effective at altering their behavior

## Findings underscore the importance of the basics

- Dose
- Route of administration
- User's experience (set)
- Environment (setting)