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17<sup>th</sup> UFAA *Distinguished Professor*  
Professor, Dizney Distinguished Professor,, *Eminent Scholar, Emeritus Eminent Scholar (1990-2015)*
- Professor (Adjunct )Keck Medical School at USC
- Professor-in-Residence & Professor, Washington University School of Medicine, St. Louis, Missouri

My Career in Dual Disorder-Related  
Addiction Research : Dual Disorders-  
Chicken or Egg or Both

Missouri - 2017

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[www.drmarkgold.com](http://www.drmarkgold.com)
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# Research You Can Use

<http://www.addictionresearchnow.com>



Summaries of the latest addiction research provided by [Mark Gold, MD](#) -

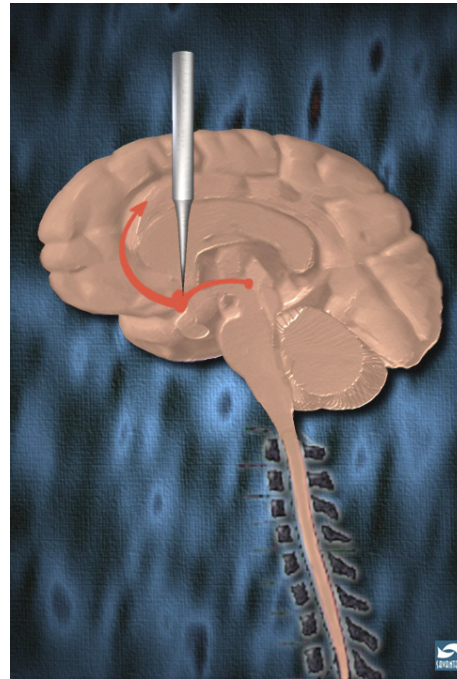
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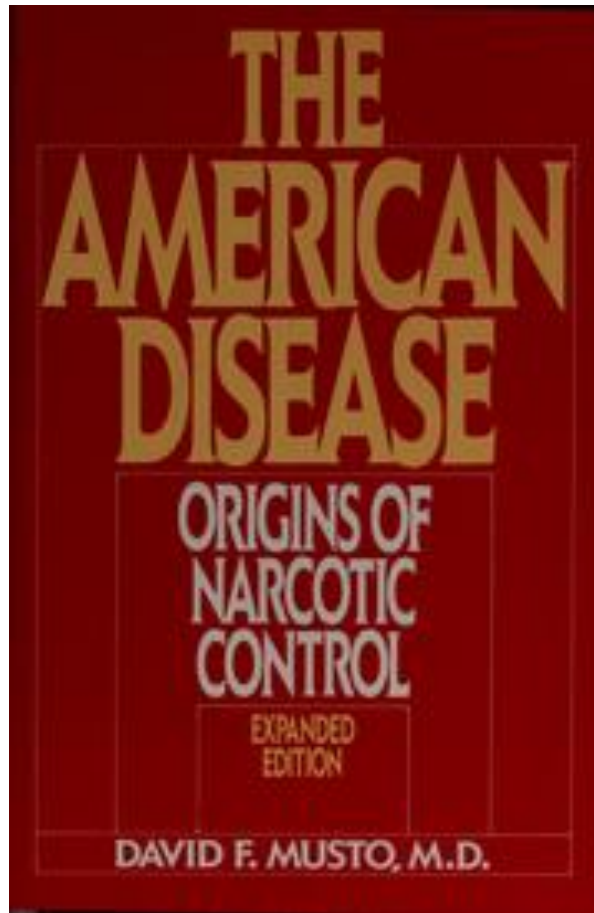
1969- Present



Career In Addiction Research Started In  
Psychiatry– Feighner, Guze, Robbins

# Brain Reward Threshold Changes With Drug Use . Does it change back?



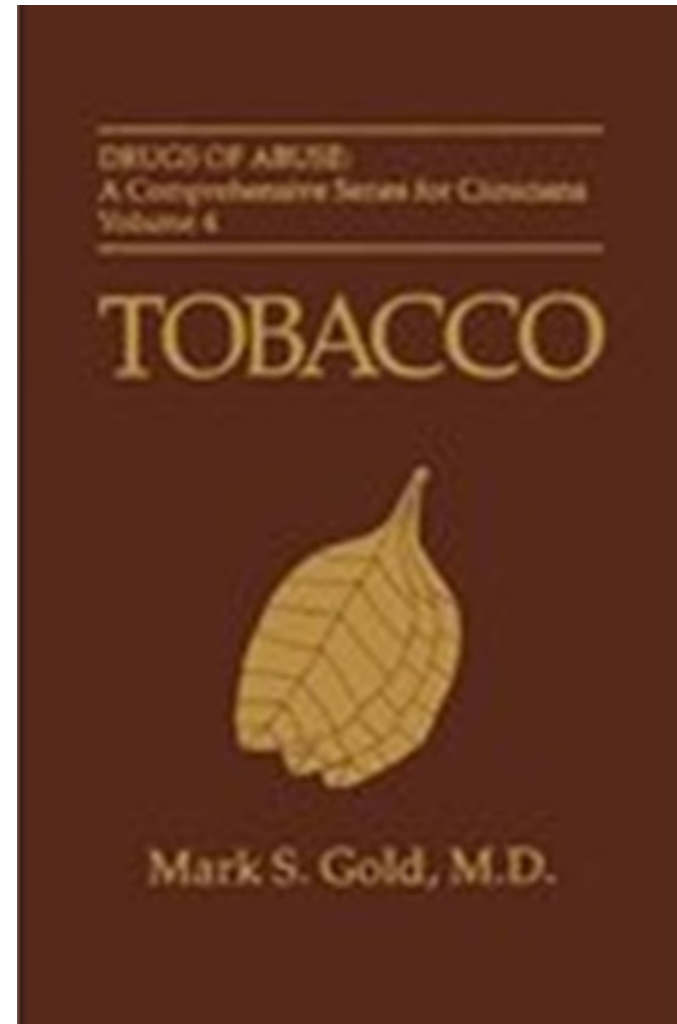


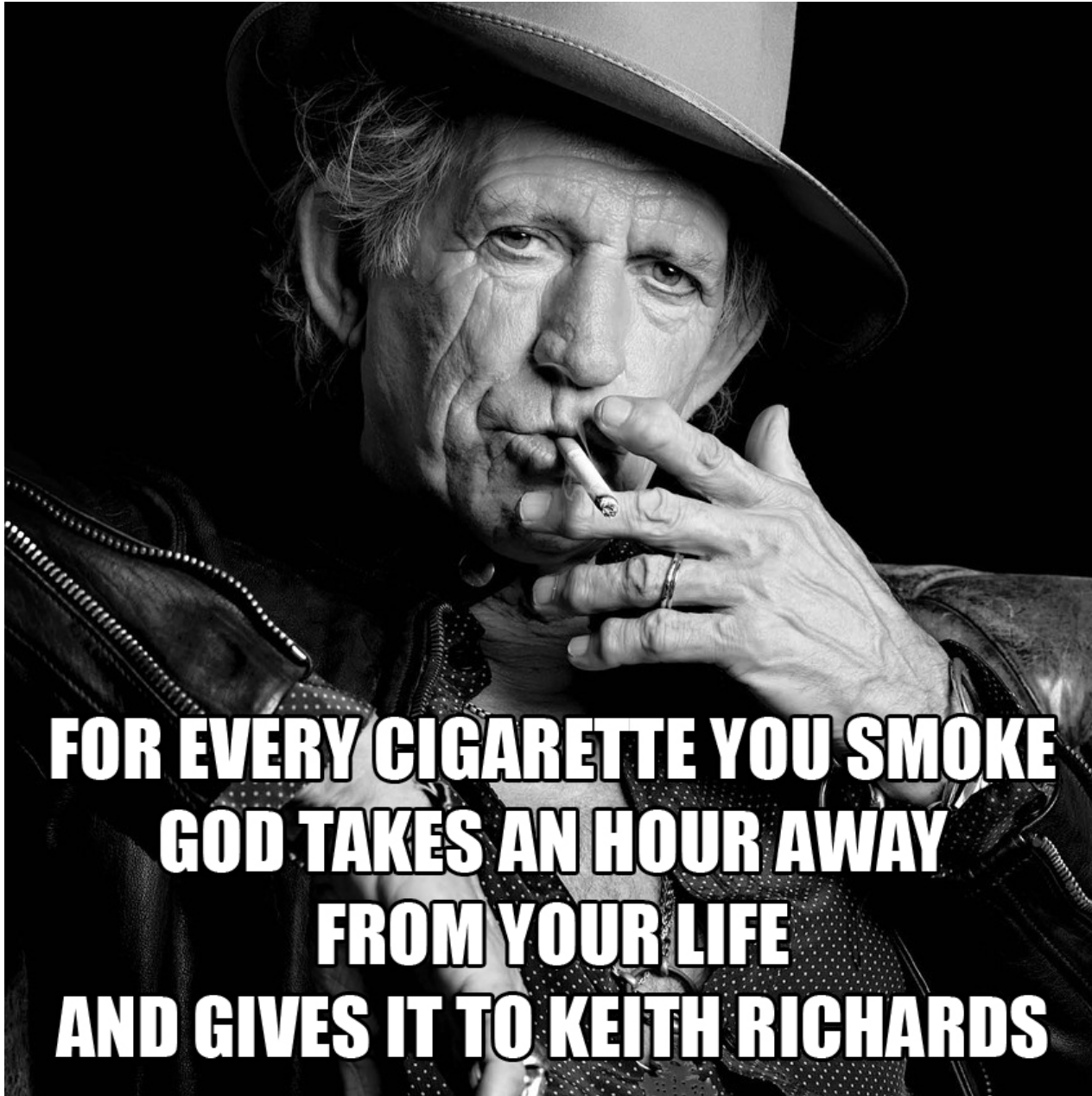
The American Disease  
Oxford University Press

## Review

'Mark S. Gold, MD, the most prolific and brilliant of the addiction experts writing today, has devoted the fourth volume of his impressive books in the Drugs of Abuse series to tobacco. Here, in one small, comprehensive, and readable book is an authoritative treatment of topics ranging from the history of tobacco in the US economy to the effects of tobacco use on the mind and the body....This book provides valuable information that every physician can use.'

**JAMA**



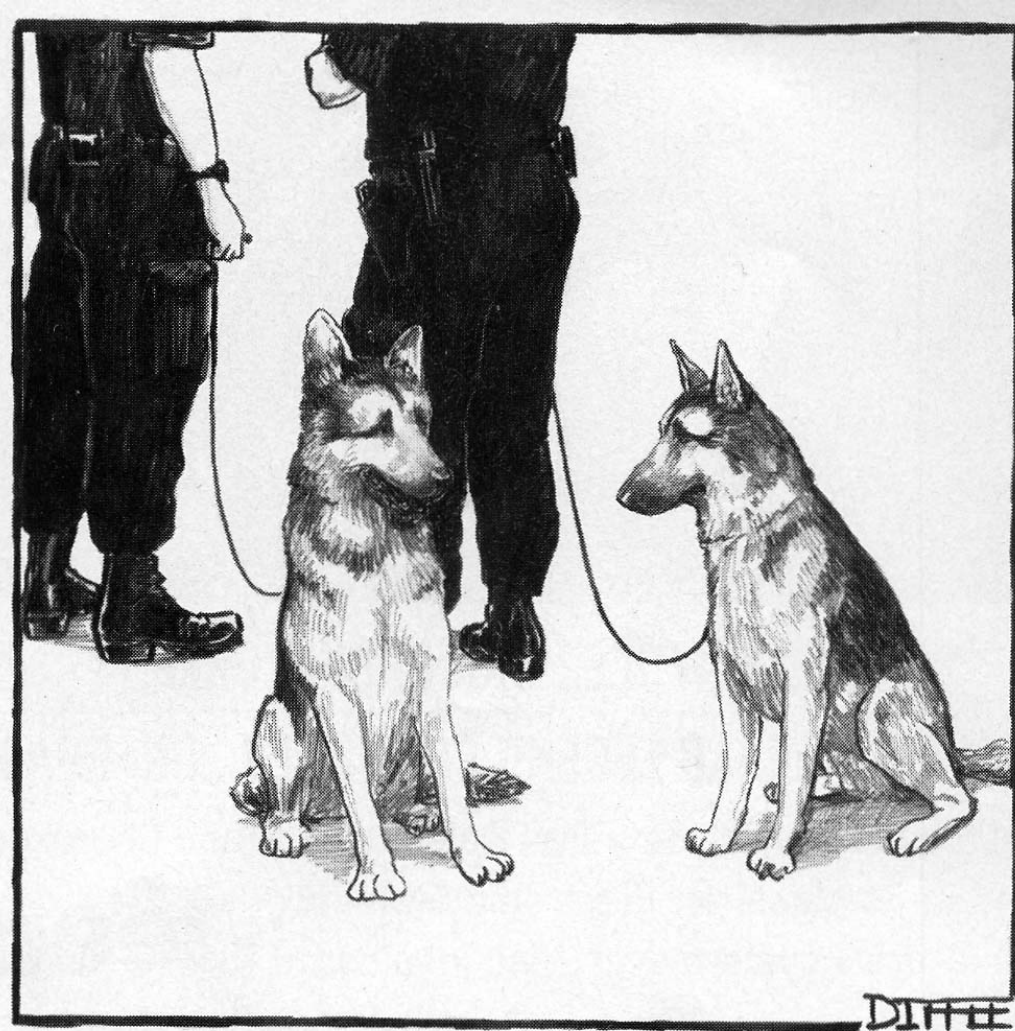


**FOR EVERY CIGARETTE YOU SMOKE  
GOD TAKES AN HOUR AWAY  
FROM YOUR LIFE  
AND GIVES IT TO KEITH RICHARDS**

# Drug Rewards Sensed by Animal Brains

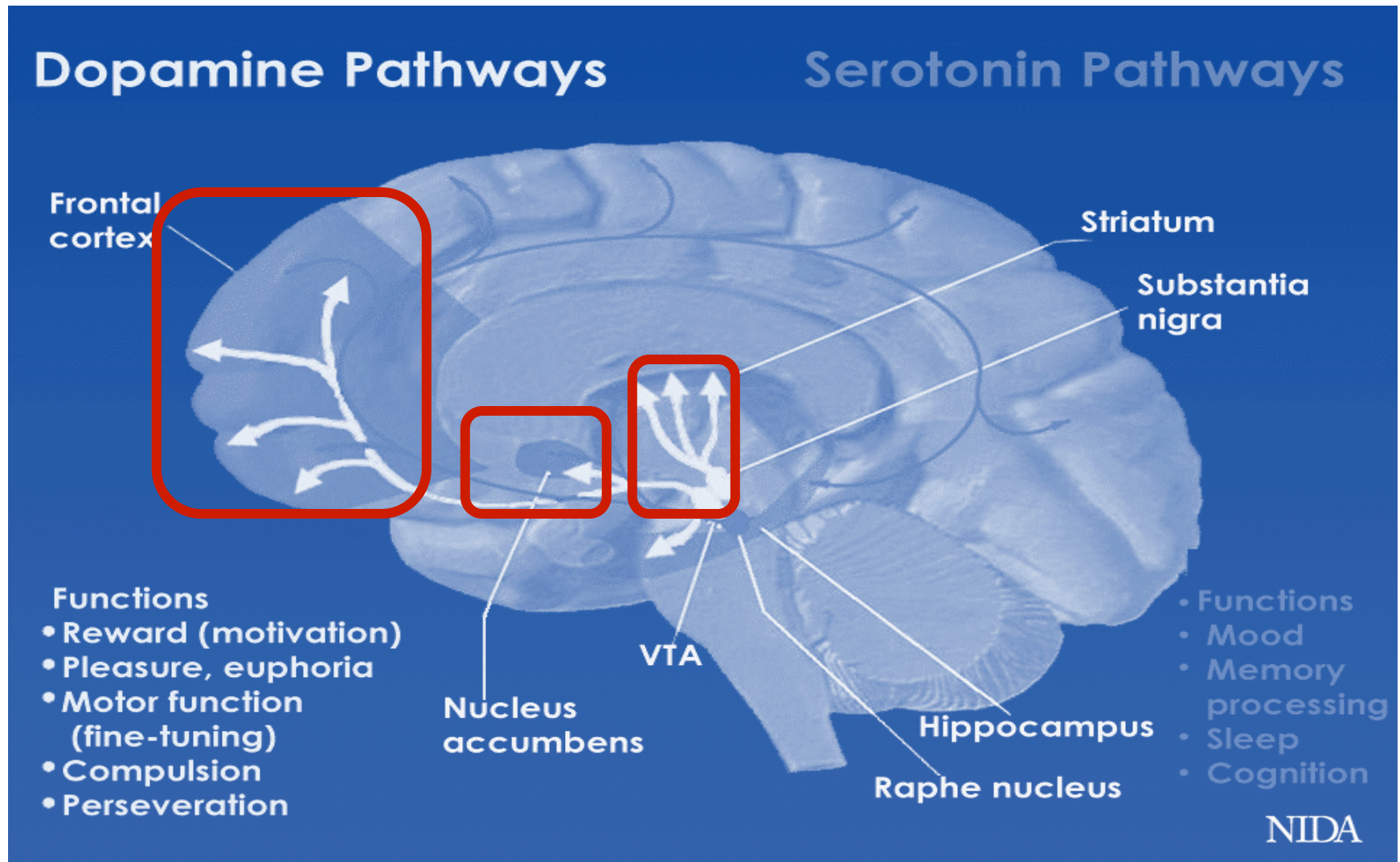
DRUG	HUMAN	ANIMAL
<b>Caffeine</b>	Yes	Yes
<b>Alcohol</b>	Yes	Yes
<b>Nicotine</b>	Yes	Yes
<b>Marijuana</b>	Yes	Yes
<b>Cocaine</b>	Yes	Yes
<b>Heroin</b>	Yes	Yes
<b>Hallucinogens</b>	Yes	Some
<b>Inhalants</b>	Yes	?
<b>Benzodiazepines</b>	Yes	Yes





*"I'm starting to really like the smell of cocaine."*

# What Drugs do Have in Common They Affect Dopamine Signaling in Brain



## Cocaine Addiction & Hypofrontality

Cocaine-addicted patients have reduced frontal metabolism, diminished gray matter & poor performance on neuropsychological tests of frontal function

PET O-15 Hypoactivity



Reduced Gray Matter



# Charlie Sheen---before & after



**Table 1**

**Processes associated with the prefrontal cortex that are disrupted in addiction**

Process	Possible disruption in addiction	Probable PFC region
Self-control and behavioral monitoring: response inhibition, behavioral coordination, conflict and error prediction, detection and resolution	Impulsivity, compulsivity, risk taking and impaired self-monitoring (habitual, automatic, stimulus-driven, and inflexible behavioral patterns)	DLPFC, dACC, IFG, and vIPFC
Emotion regulation: cognitive and affective suppression of emotion	Enhanced stress reactivity and inability to suppress emotional intensity (for example, anxiety and negative affect)	mOFC, vmPFC, and subgenual ACC
Motivation: drive, initiative, persistence, and effort towards the pursuit of goals	Enhanced motivation to procure drugs but decreased motivation for other goals, and compromised purposefulness and effort	OFC, ACC, vmPFC, and DLPFC
Awareness and interoception: feeling one's own bodily and subjective state, insight	Reduced satiety, 'denial' of illness or need for treatment, and externally oriented thinking	rACC and dACC, mPFC, OFC, and vIPFC
Attention and flexibility: set formation and maintenance versus set-shifting, and task switching	Attention bias towards drug-related stimuli and away from other stimuli and reinforcers, and inflexibility in goals to procure the drug	DLPFC, ACC, IFG, and vIPFC
Working memory: short-term memory enabling the construction of representations and guidance of action	Formation of memory that is biased toward drug-related stimuli and away from alternatives	DLPFC
Learning and memory: stimulus-response associative learning, reversal learning, extinction, reward devaluation, latent inhibition (suppression of information), and long-term memory	Drug conditioning and disrupted ability to update the reward value of non-drug reinforcers	DLPFC, OFC, and ACC
Decision making: valuation (coding reinforcers) versus choice, expected outcome, probability estimation, planning, and goal formation	Drug-related anticipation, choice of immediate reward over delayed gratification, discounting of future consequences, and inaccurate predictions or action planning	IOFC, mOFC, vmPFC, and DLPFC
Saliency attribution: affective value appraisal, incentive salience, and subjective utility (alternative outcomes)	Drugs and drug cues have a sensitized value, non-drug reinforcers are devalued and gradients are not perceived, and negative prediction error (actual experience worse than expected)	mOFC and vmPFC

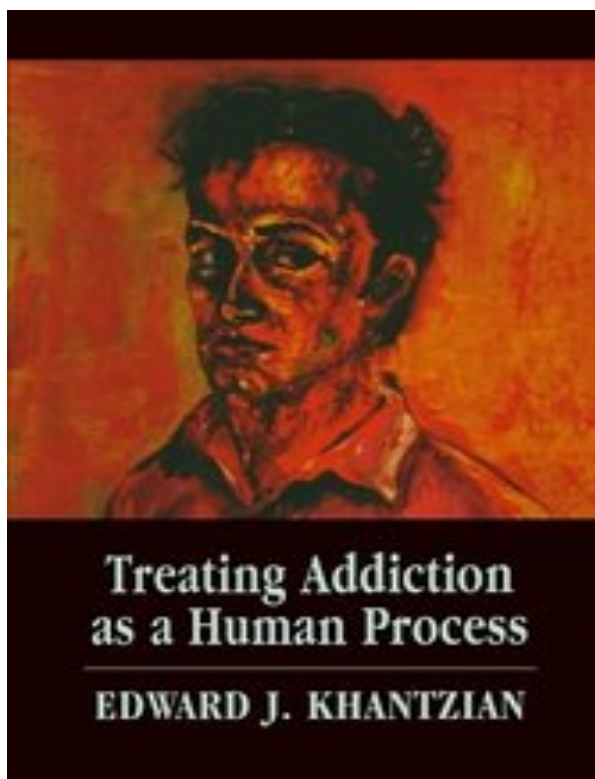
Reprinted with permission [13].

Orbitofrontal cortex (OFC) includes Brodmann area (BA) 10–14 and 47, and inferior and subgenual regions of anterior cingulate cortex (ACC) (BA 24, 25 and 32) in the ventromedial prefrontal cortex (vmPFC); ACC includes rostral ACC (rACC) and dorsal ACC (dACC) (BA 24 and 32, respectively), which are included within the medial PFC (mPFC). The mPFC also includes BA 6, 8, 9 and 10; dorsolateral PFC (DLPFC) includes BA 6, 8, 9 and 46; and the inferior frontal gyrus (IFG) and ventrolateral PFC (vIPFC) includes inferior portions of BA 8, 44 and 45. These various processes and regions participate to a different degree in craving, intoxication, bingeing and withdrawal. IOFC, lateral OFC; mOFC, medial OFC; PFC, prefrontal cortex.

# All Drugs of Abuse Change the Brain

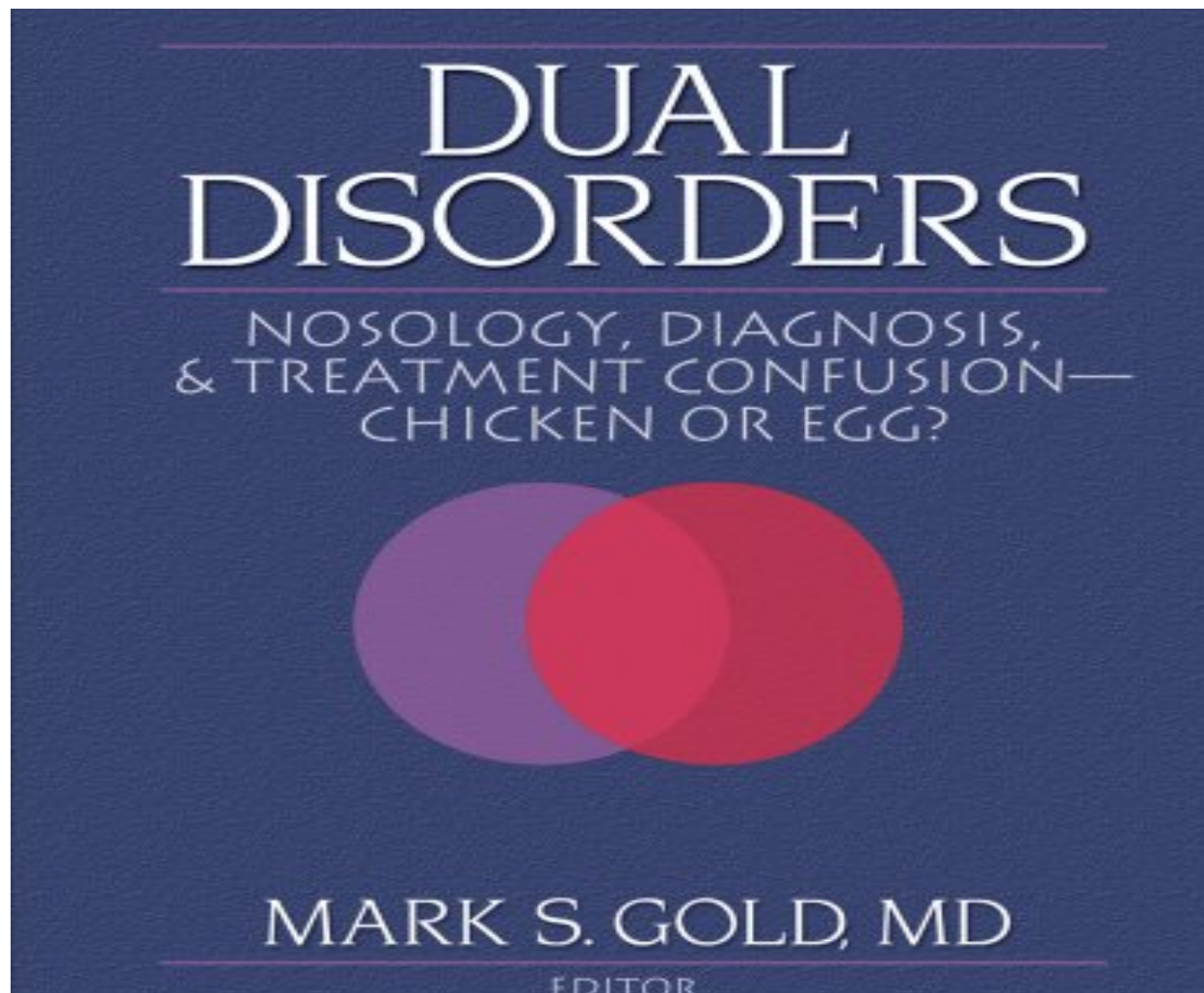


# Edward J. Khantzian, M.D.



Gold MS. (2008) Dual disorders: nosology, diagnosis & treatment confusion—chicken or egg? . J Addict Disease, 26(51), 1-4.

ASAM Tobacco,  
Alcohol, Other  
Drugs Commonly  
Associated With  
Psychiatric Illness  
*Co-morbidity Is  
The Rule*





# Psychopathology of Impaired Physicians

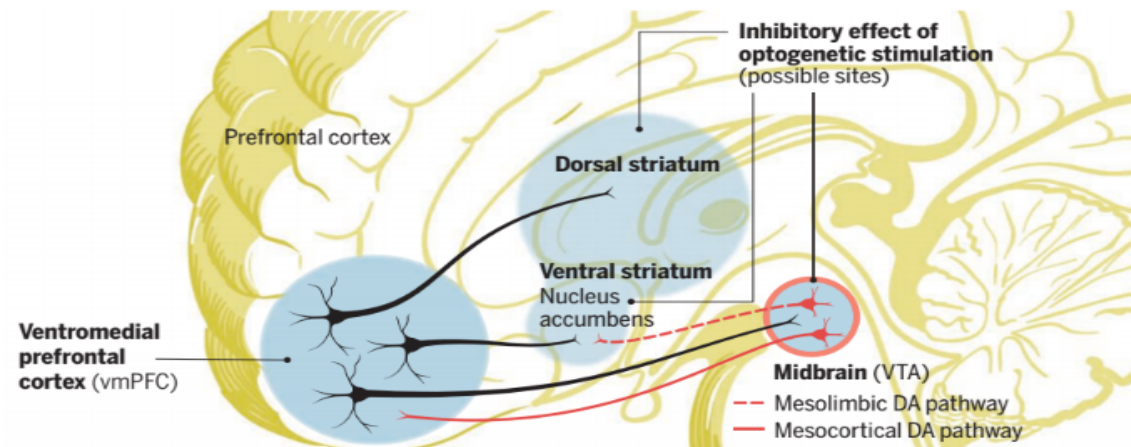


- Physicians referred to a PHP have significantly higher odds of abuse/dependence disorders for cannabinoids and cocaine/crack compared with a matched general population sample. Physicians had higher odds of abuse/dependence for opiates, sedatives and alcohol.
- Co-Morbidity with Anxiety and Affective disorders.

Cottler LB, Ajinkya S, Merlo LJ, Nixon SJ, Abdallah AB, Gold MS. Lifetime Psychiatric and Substance Use Disorders Among Impaired Physicians in a Physicians Health Program: Comparison to a General Treatment Population. J Addict Med 2013;7(2):108-112.

# *Illuminating anhedonia*

Optogenetics and fMRI reveal the brain circuitry of anhedonia



**Reward circuitry.** Shown are approximate anatomical relationships in the human brain between the midbrain dopamine (DA) pathways from the ventral tegmental area (VTA) to the nucleus accumbens (part of the ventral striatum) and the vmPFC, and reciprocal influences (mediated by glutamate) of the vmPFC. The vmPFC includes the medial orbitofrontal cortex and parts of the ventral cingulate cortex, including the subgenual cingulate cortex. Ferenzi *et al.* show that the rewarding effects of optogenetic stimulation of the VTA were counteracted by optogenetically-induced hyperexcitability of the vmPFC to mimic behavioral anhedonia-like symptoms in rats, presumably via descending pathways to the subcortical regions including the striatum and VTA.

# Annie Hall -- 1977

ALLEN'S ORIGINAL IDEA FOR THE MOVIE WAS ENTIRELY DIFFERENT.

Although Annie Hall is now heralded as one of the most influential and inventive romantic comedies of all time, director and co-writer Allen's original mission was not to make a relationship picture. Allen and his writing partner, Marshall Brickman, instead conceived of the story as a general exploration of the main character's life and psyche, which was to be filled with romantic, mysterious, and fantastical subplots in equal parts.

The project, reflecting protagonist Alvy Singer's persistent malaise, was first titled Anhedonia, a somewhat archaic psychiatric term referring to the inability to feel joy. The first cut of the movie ran about 140 minutes—almost 50 minutes longer than the final version.



# Self medication with social phobia and simply shy

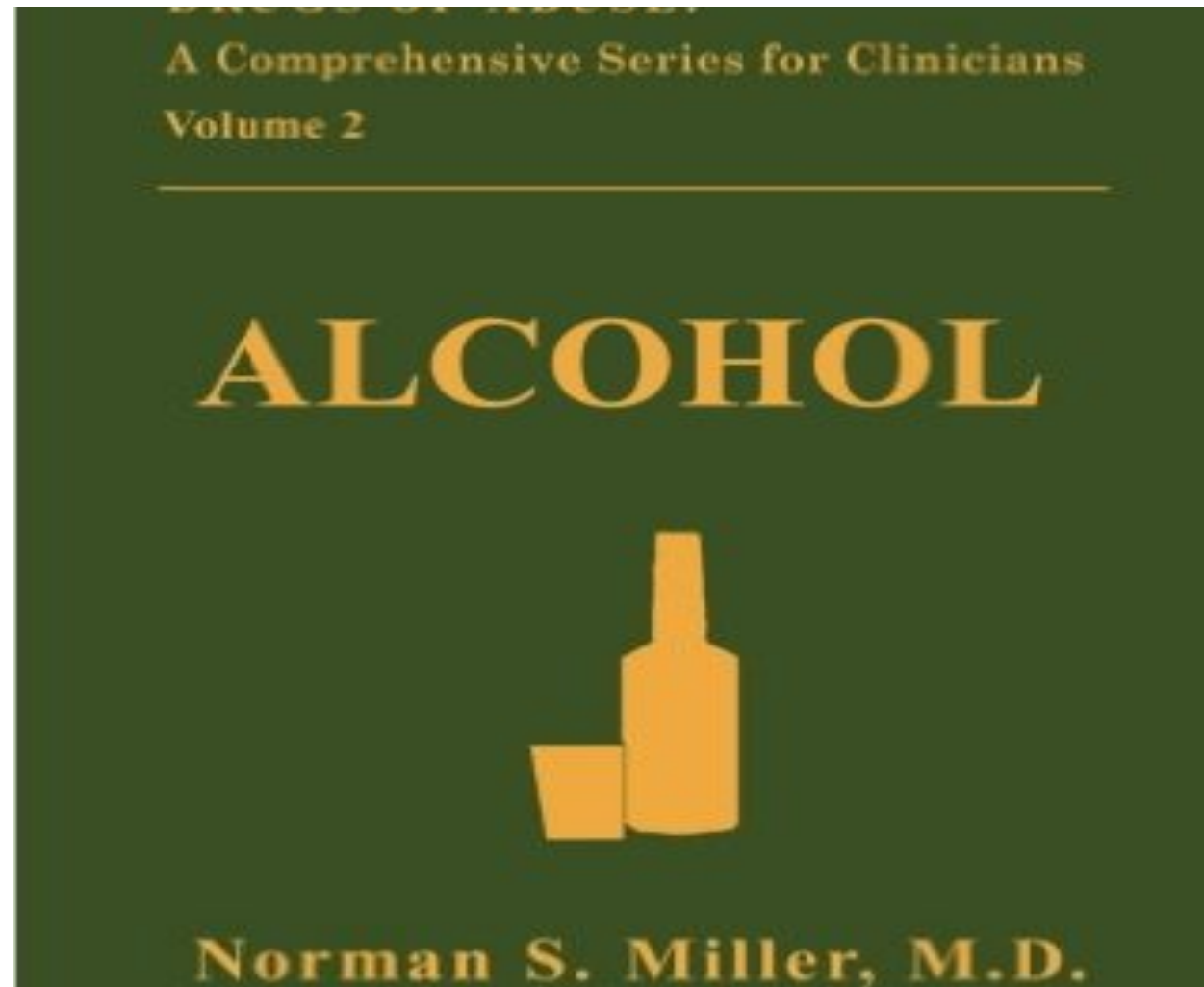
**Series:** Drugs of Abuse: A Comprehensive  
Series for Clinicians (Book 2)

**Paperback:** 276 pages

**Publisher:** Springer; Softcover reprint of the  
original 1st ed. 1991 edition (September 12,  
2014)

**Language:** English

**ISBN-10:** 1489935525



# Kitty Dukakis, a Beneficiary of Electroshock Therapy, Emerges as Its Evangelist

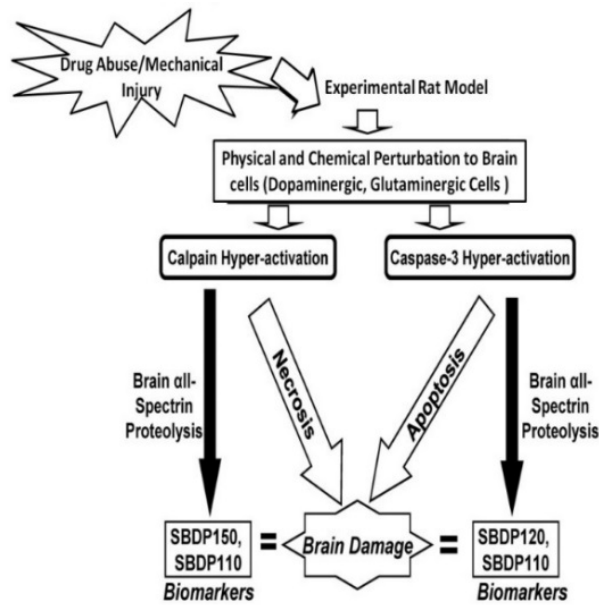
"An alcoholic can contain himself for only so long," Mrs. Dukakis would later write.



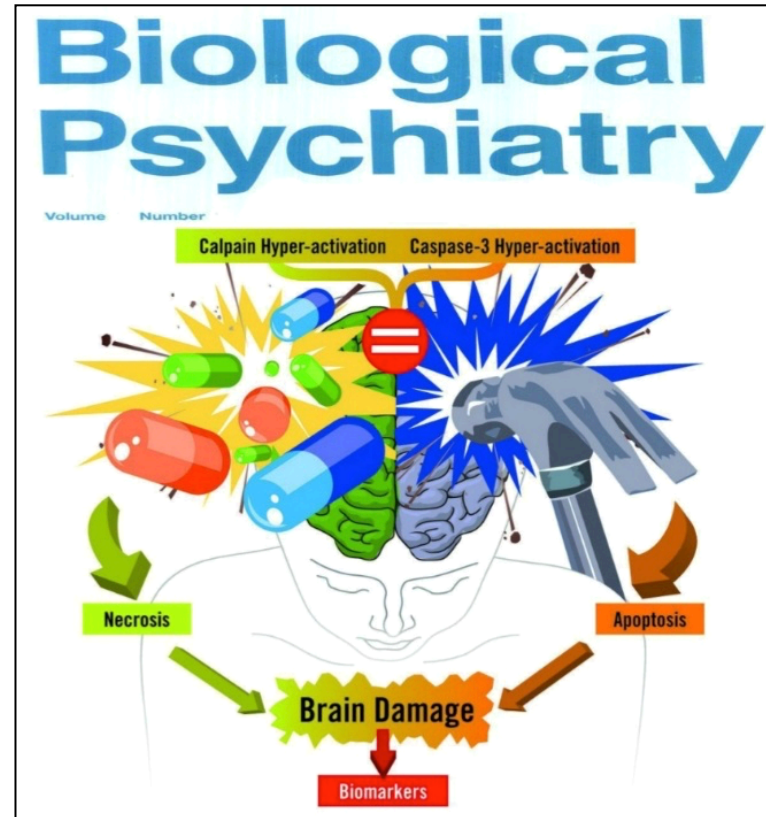
Mrs. Dukakis receives her maintenance therapy at McLean Hospital in suburban Boston, one of the world's largest and most renowned psychiatric hospitals. McLean does about 10,000 such treatments a year, up from 2,500 treatments in 1999

Chicken or Egg---Drugs may cause changes that are quite irreversible and cause the abstinent patient to appear as if they have a psychiatric disease

ARTICLE IN PRESS  
 BIOL PSYCHIATRY 2009;xxxxx M. S. Gold *et al.*  
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**Methamphetamine- and Trauma-Induced Brain Injuries: Comparative Cellular and Molecular Neurobiological Substrates**  
 Mark S. Gold, Firas H. Kobeissy, Kevin K.W. Wang, Lisa J. Merlo, Adriaan W. Buijnzee, Irina N. Krasnova, and Jean Lud Cadet



SBDP: Spectrin Break Down Product





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TIGER AND RACE  
THE G.O.P.'S CHINA CONNECTION  
ARMY RECRUITERS AND SEXUAL HARASSMENT

- ▶ SEX
- ▶ DRUGS
- ▶ DRINKING
- ▶ SMOKING

Scientists are discovering the chemical secret to

# HOW WE GET ADDICTED

... and how we might get cured

