

# Neurobiology of drug addiction, a brain disease

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The drug addiction is a cluster of cognitive, behavioral and physiological symptoms that reveal the compulsive use of the drug despite the adverse effects related to the drug. This disorder shows a higher relapse rate, particularly the first 12 months of abstinence following dependence.

## Hypotheses to explain the compulsive drug seeking

The establishment of an automatic stimulus-response habit (Tiffany ST, 1990; Everitt BJ, 2001)

Drug-induced loss of impulse control (Jentsch JD, 1999)

Disruption of hedonic homeostasis (Koobs y Le Moal, 1997)

The sensitization to the incentive motivational effects of drugs (“wanting”) (Robinson y Berridge, 1993)

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# SCIENCE

## Self-Stimulation of the Brain

Its Use To Study Local Effects of  
Hunger, Sex, and Drugs

James Olds

This article reviews experiments which have led to the discovery and analysis of localized systems in the brain where electric stimulation has positive and negative motivational effects (1). Basically, the experimental animal in these studies is rewarded or punished by a brain shock. The site of electric stimulation determines the motivational effect.

The studies are important primarily as a beginning step toward filling the large gap which has existed between neurophysiological techniques and an understanding of complex psychological processes. Among other things, they carry the enterprise of brain mapping

peated more frequently than would be expected by chance; punished ones are repeated with less frequency. This is obvious.

Less self-evident is the thesis of the classical theory of reward, according to which reward is interpreted as being the falling phase of the same massive stimulation which at high levels constitutes punishment. This thesis is greatly weakened by the work outlined in this article; however, it has held sway for such a long time in psychology and conditions so many basic attitudes that it will certainly form a foundation stone for the new theories which replace it.

been determined by prior learning. More specifically, a group of cues actually selects the response which was previously followed by drive reduction in their presence. The drive reduction, on previous occasions, caused a rewarding or positive reinforcing effect which somehow increased the causal connection between these stimuli and this particular response.

The hedonistic view that behavior is pulled forward by pleasure as well as pushed forward by pain is rejected in this classical theory for the more parsimonious notion that pain supplies the push and that learning based on pain reduction supplies the direction.

The work reported in this article clearly shows one implication of the drive-reduction theory to be incorrect, for massive inputs to certain parts of the central nervous system are shown to have rewarding effects. Further, by showing that there are anatomically separate mechanisms for reward and punishment in the brain, it points directly to a physiological basis for the motivational dualism suggested in the hedonistic theory.

In fact, it appears that the area producing rewarding effects, upon electric stimulation, is far larger than the area producing punishment. In one early ex-

Dr. Olds, former member of the staff of the department of anatomy at the School of Medicine, University of California at Los Angeles, is now with the department of psychology at the University of Michigan, Ann Arbor.

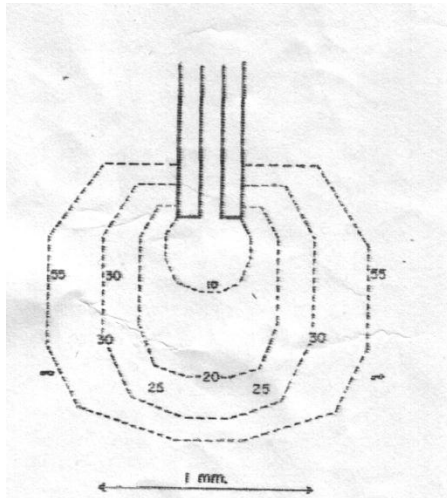
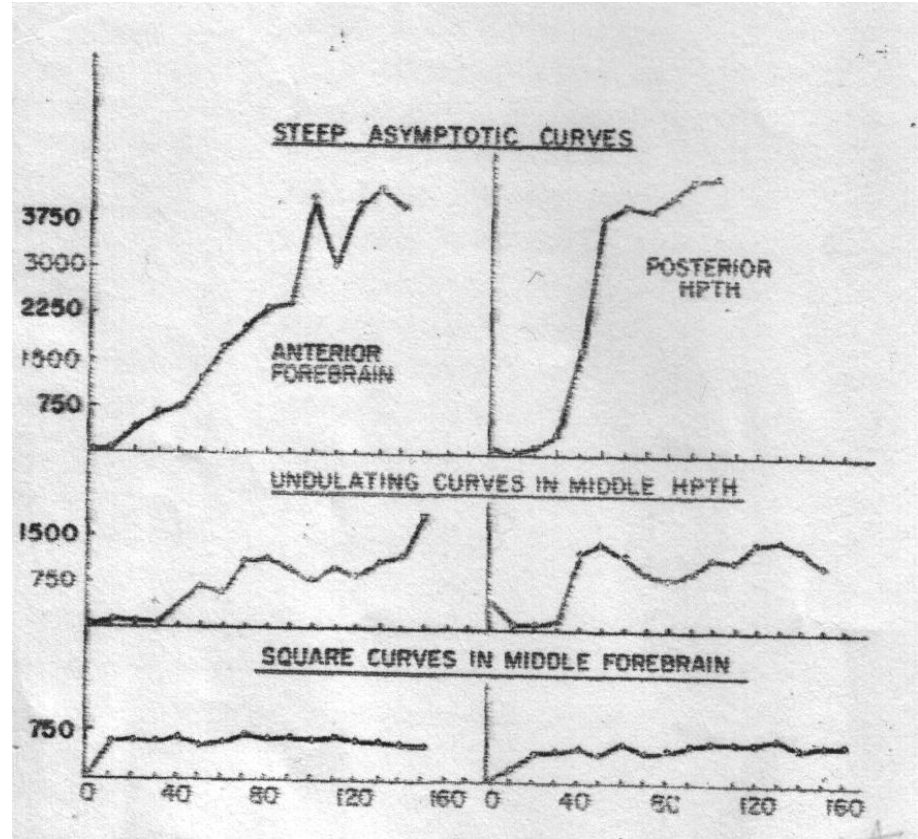


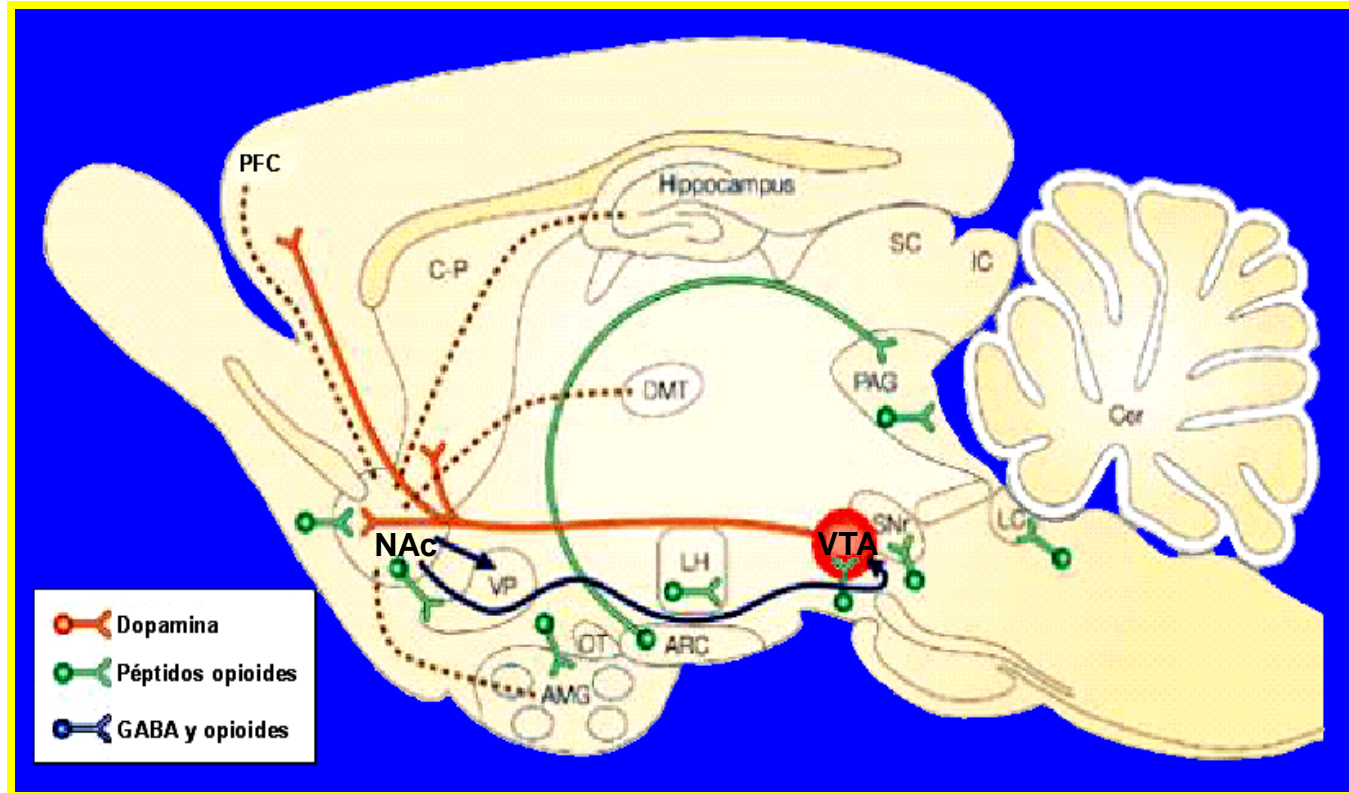
Fig. 14. Electric fields for different levels

Self-stimulation rate

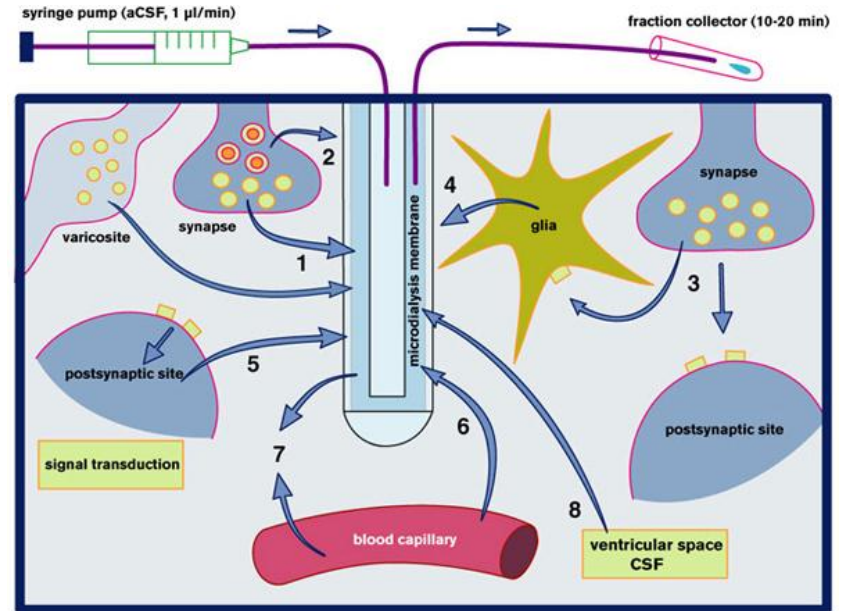


Current ( $\mu A$ )

## Motivation circuit



# Microdialysis technique



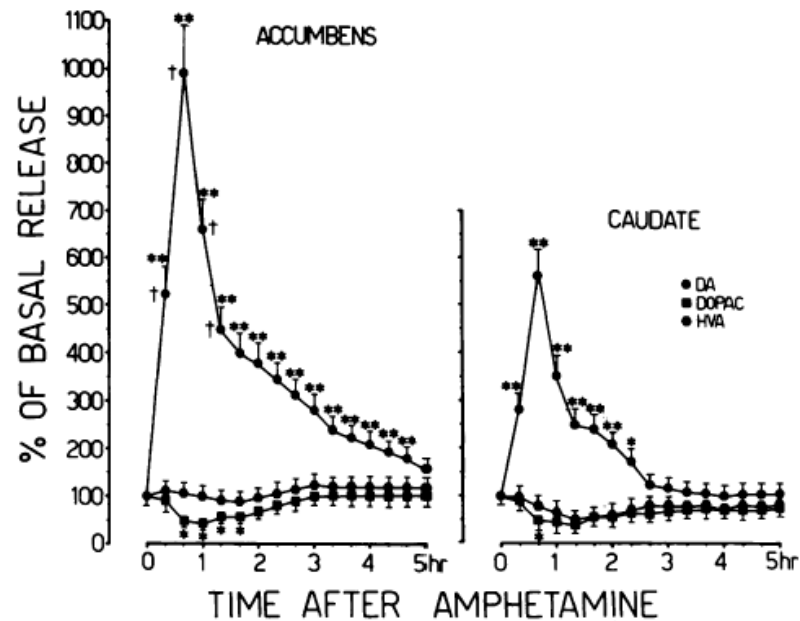
## The Dopamine history!

*Proc. Natl. Acad. Sci. USA*  
Vol. 85, pp. 5274-5278, July 1988  
Neurobiology

### Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats

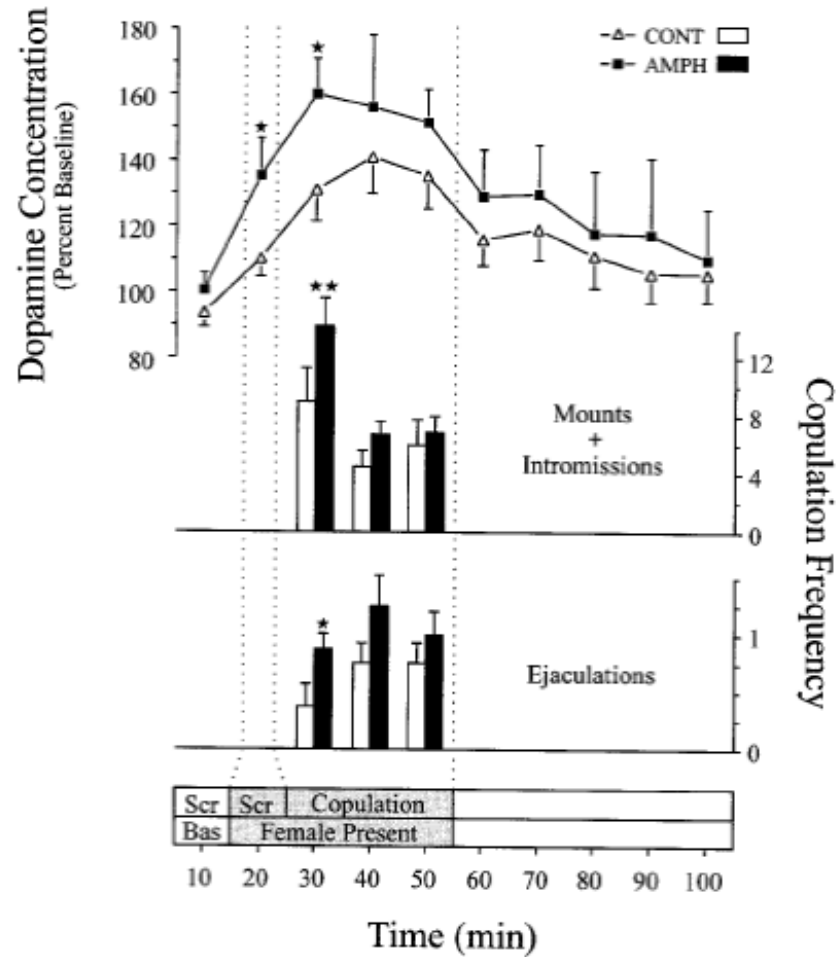
(amphetamine/cocaine/ethanol/nicotine/opiates)

GAETANO DI CHIARA AND ASSUNTA IMPERATO

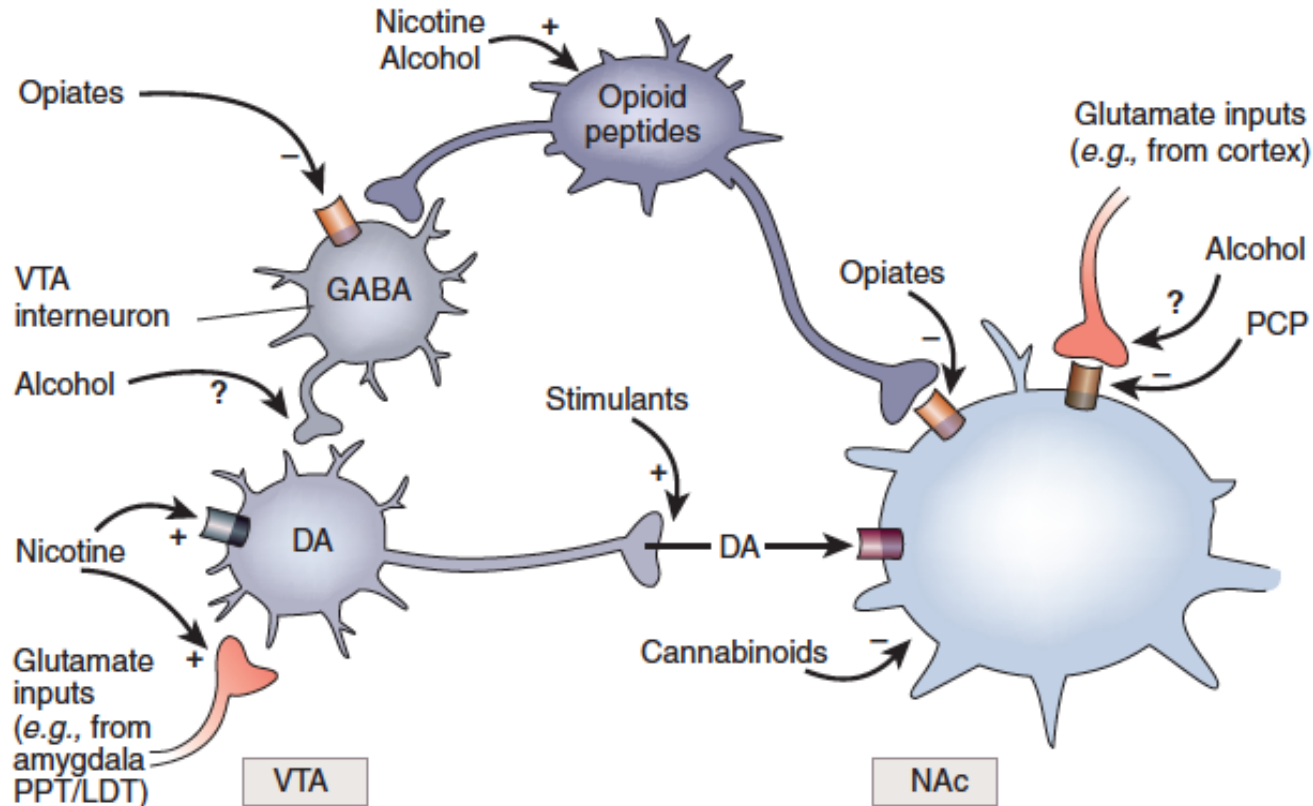




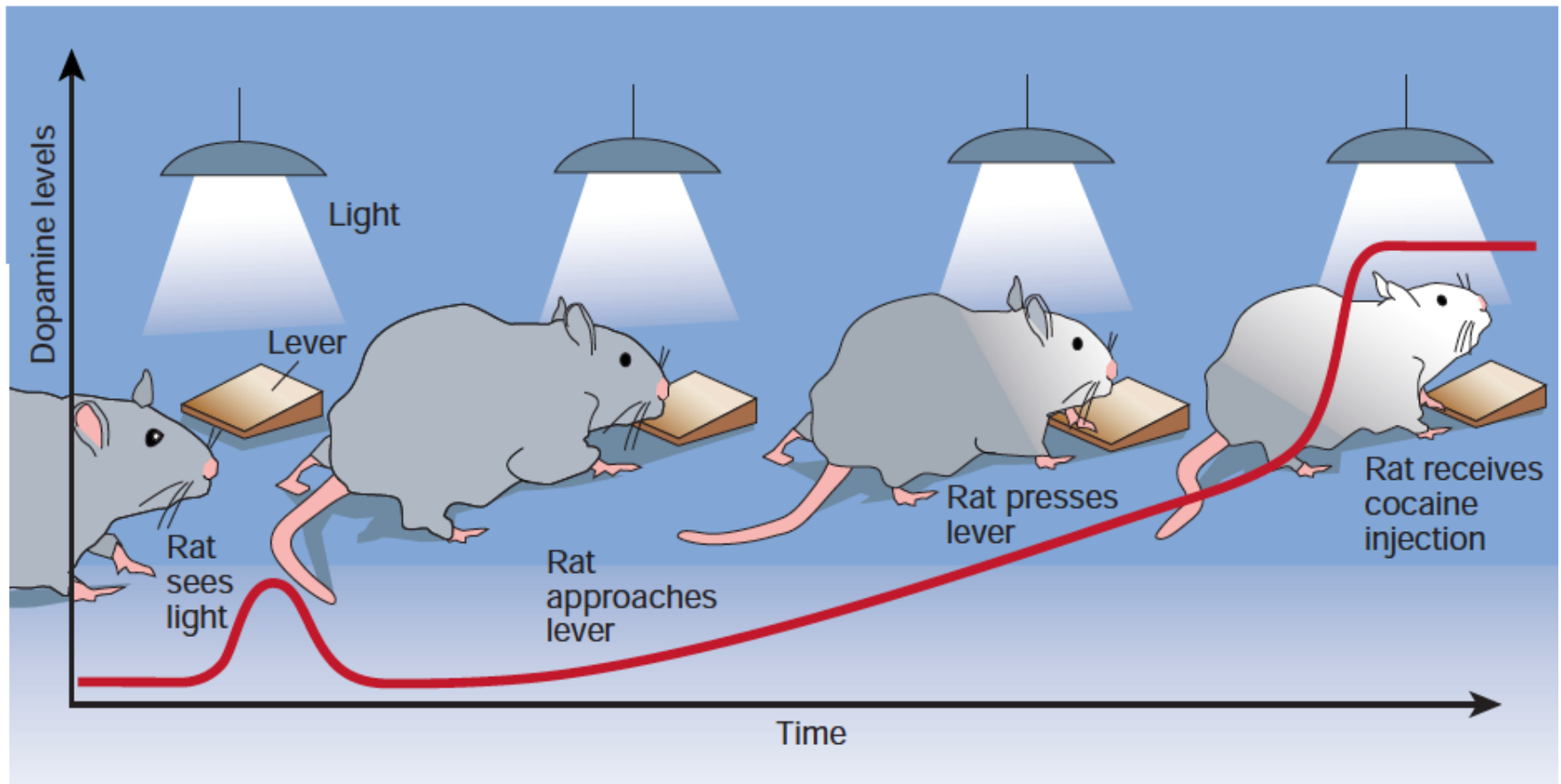
## Dopamine and natural reward



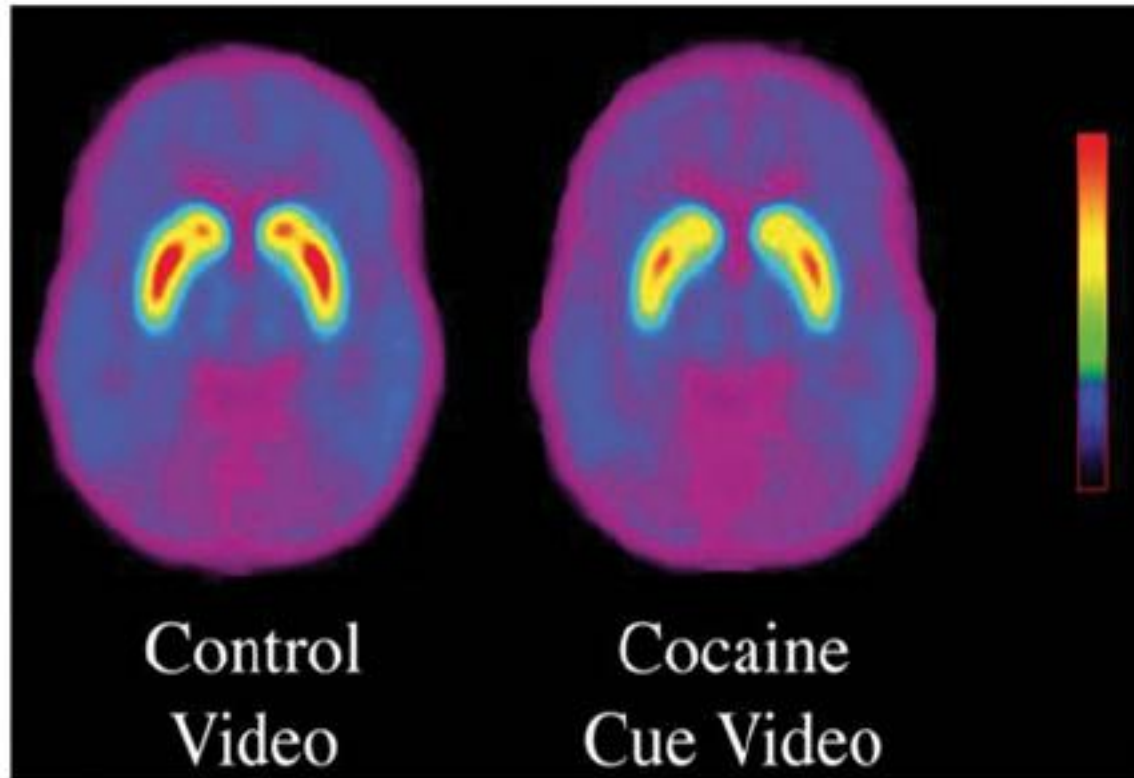
## All drugs of abuse increase Dopamine release in the Nucleus Accumbens



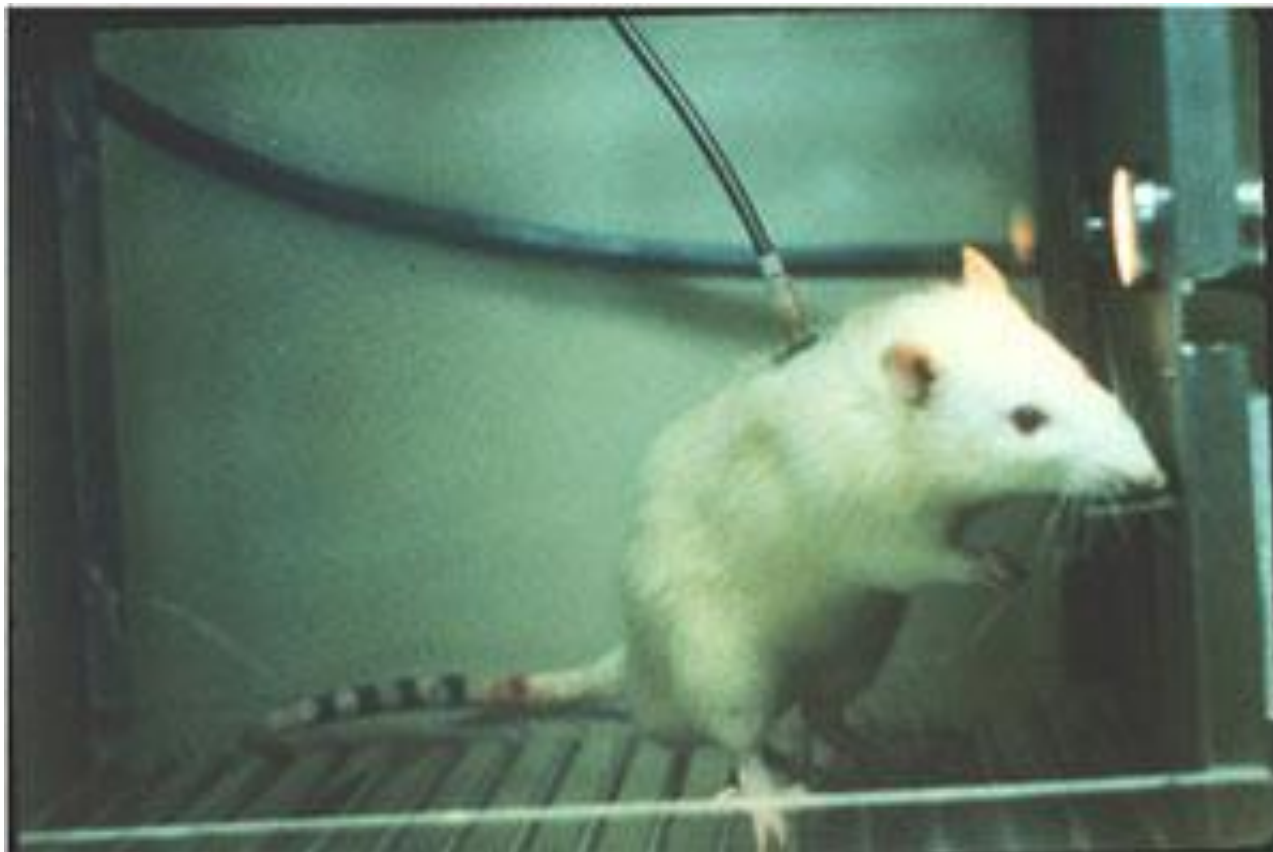
Dopamine both motivates reward-seeking behaviour and signals the receipt of a reward



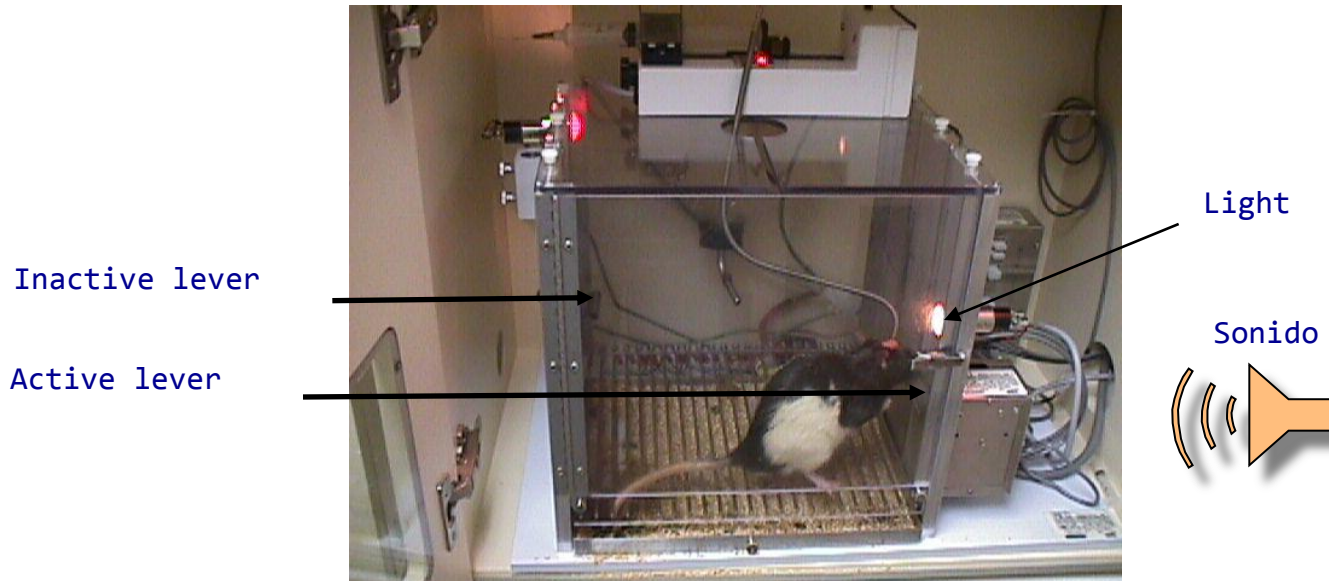
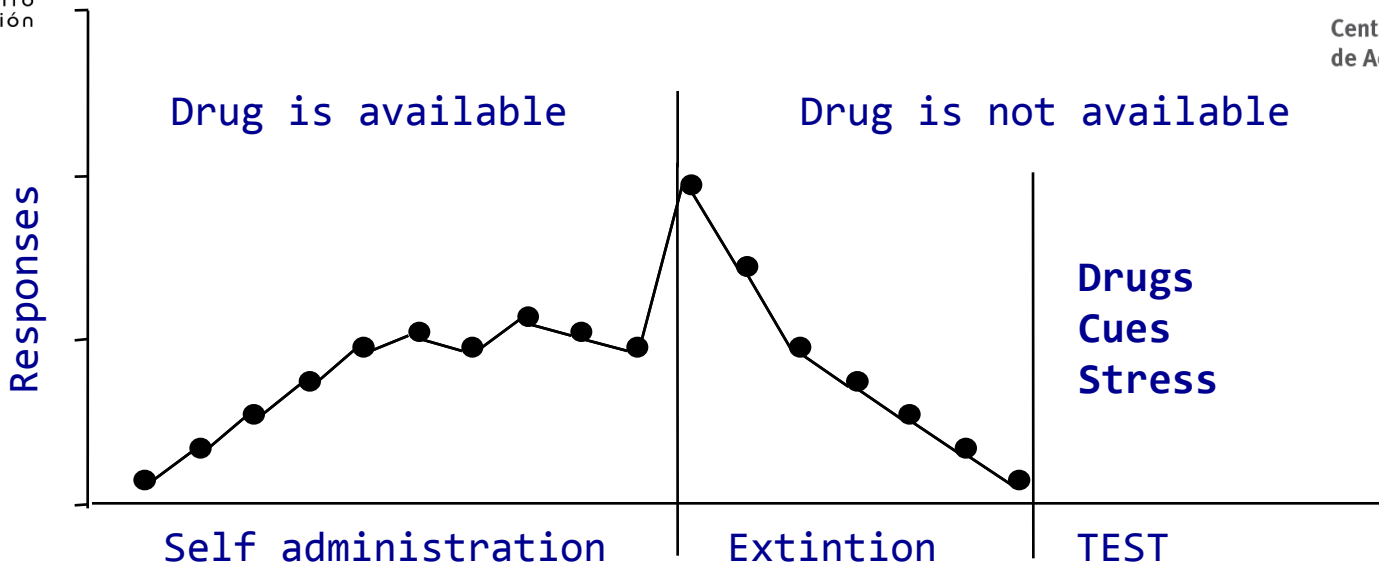
What happens with Dopamine in the human brain ??



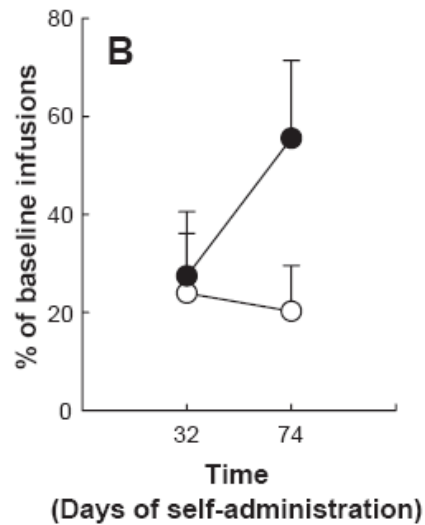
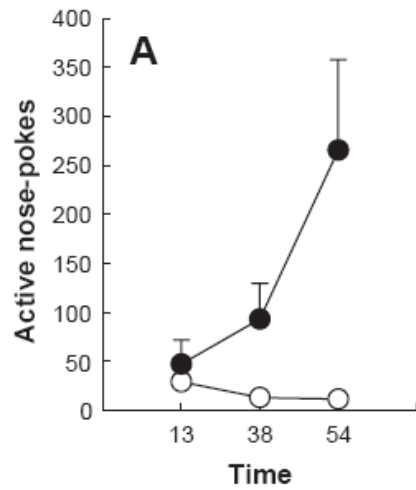
## The individual vulnerability



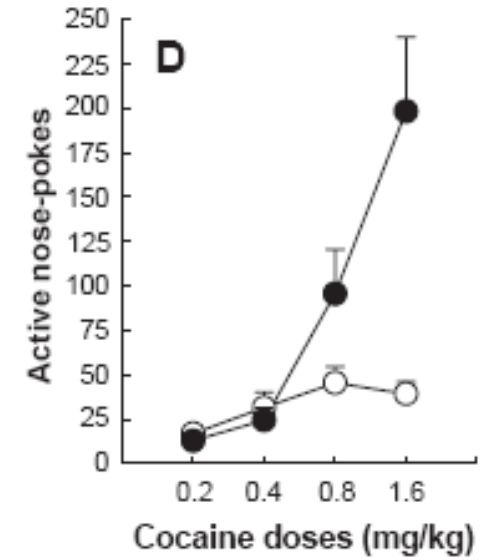
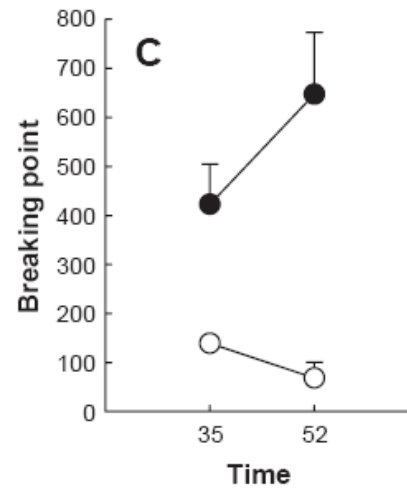
The self-administration paradigm



## “Persistence”



## “Motivation”

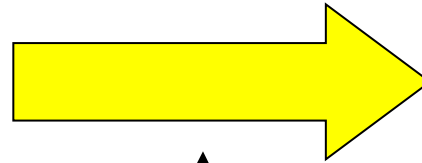


## “Resistance to Punishment”

## “Relapse”



**Controlled  
Intake**



**Addiction  
(Loss of control)**

Genetic Vulnerability



Environmental factors

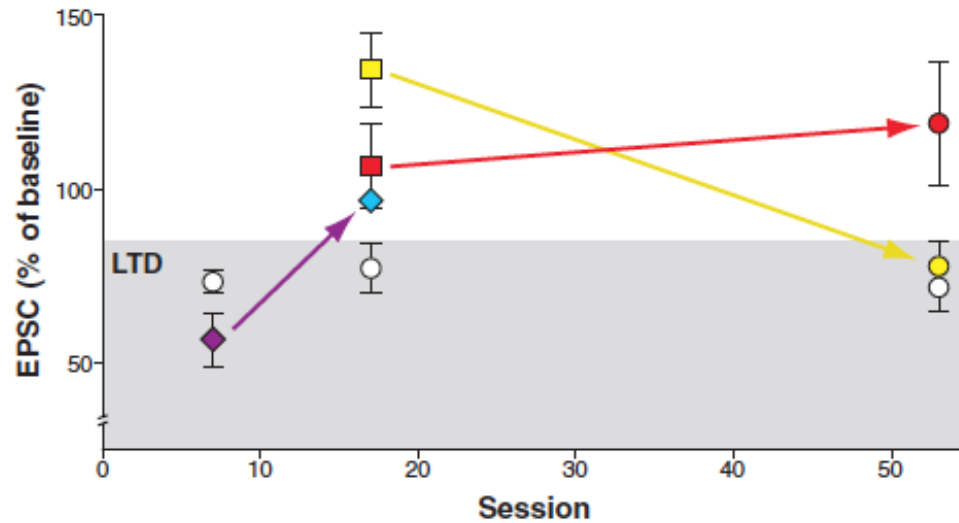
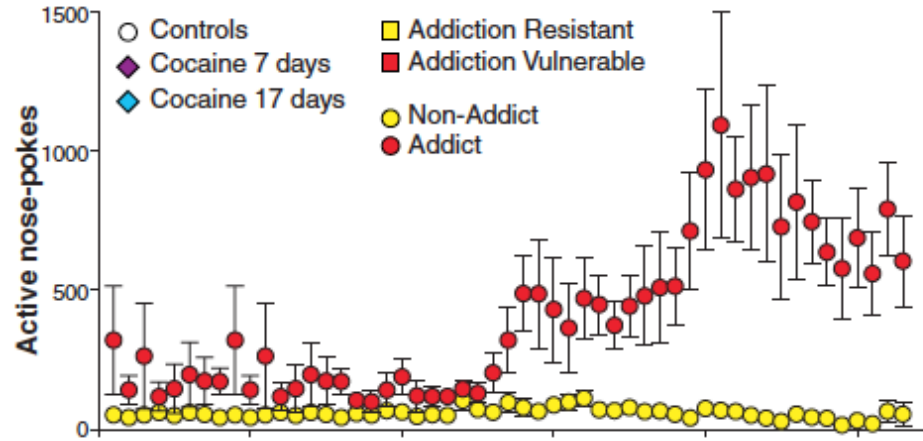
Neuroplasticity



# Transition to Addiction Is Associated with a Persistent Impairment in Synaptic Plasticity

Fernando Kasanetz,<sup>1,2\*</sup> Véronique Deroche-Gamonet,<sup>1,2\*</sup> Nadège Berson,<sup>1,2</sup> Eric Balado,<sup>1,2</sup> Mathieu Lafourcade,<sup>1,2</sup> Olivier Manzoni,<sup>1,2</sup>†‡ Pier Vincenzo Piazza<sup>1,2</sup>†‡

The anaplasticity : The incapacity of addicts to counteract initial drug-induced impairments



Persistent impairment in LTD is associated with transition to cocaine addiction

## Conclusions:

The stimulation of some brain nuclei positive motivational effects (also negative!)

Drugs of abuse increase dopamine release in the Nucleus Accumbens

Dopamine is necessary for '**wanting**' incentives

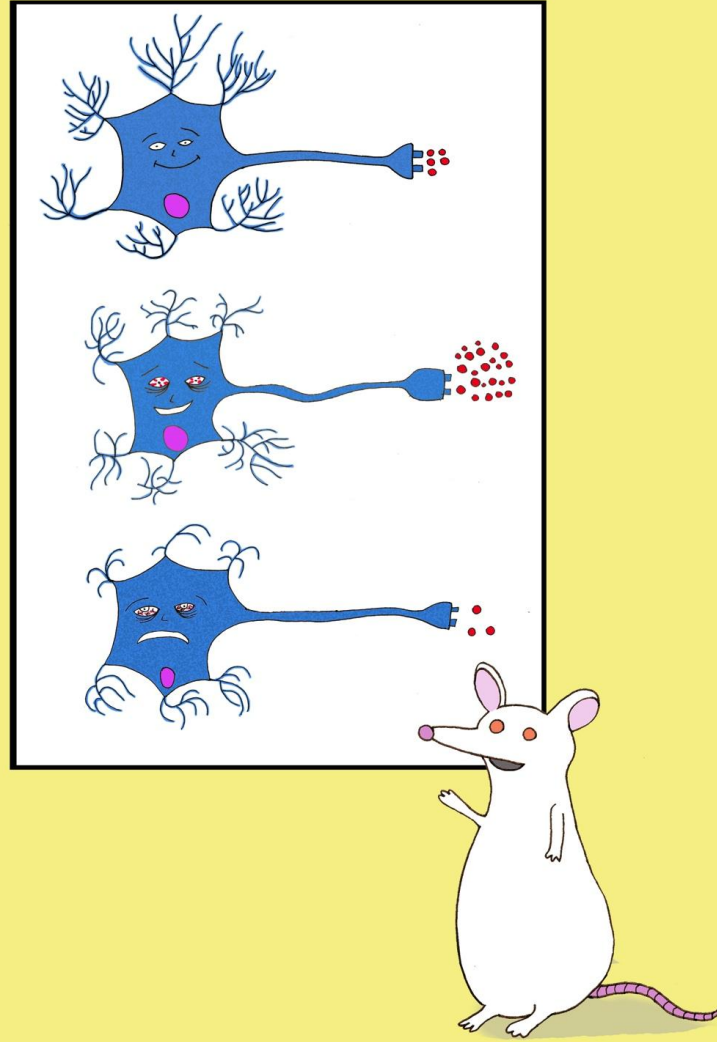
Not all subjects who use drugs of abuse become addicted

The development of addiction is associated with an inability to counteract the changes caused by drugs of abuse

“Despite the obstacles to developing effective therapies to treat the addiction, there are now unprecedented opportunities on both the short- and mid-term horizons for translating the many promising approaches identified by basic research into therapies for addiction”

Skolnick and Volkow, 2012

## Los tres estados de la dopamina y su relación con la motivación



Thank you!

