Neurobiology of addiction: cocaine

Carme Ripoll Fiol – BSc Biotechnology – Universitat Autònoma de Barcelona – Bellaterra, 2015

INTRODUCTION

It is hereby discussed how drugs can change the brain to foster compulsive drug use. **Addiction is considered a disease** that affects both the brain and behavior of the person involved. This addiction has **biological** and **environmental** factors related to it, but it is true that **genetic variations** can contribute the development and the progression of the disease.

Drug addiction, also known as Substance Dependence, is a chronically relapsing disorder that is characterized by compulsion to seek and take the drug, loss of control in limiting intake, and emergence of a negative emotional state (e.g., dysphoria, anxiety or irritability) when access to the drug is prevented.

Addiction cause **physical changes in areas of the brain** that are critical to judgment, decision making, learning and memory, and behavior control. Scientists believe that these changes alter the way the brain works and may help explaining the compulsive and destructive behaviors of addiction.

MAIN AIMS

- To study which parts of the brain are involved in addiction.
- To understand how neural processes are affected by drugs.
- To study the molecular mechanisms of drugs of abuse, concretely cocaine.

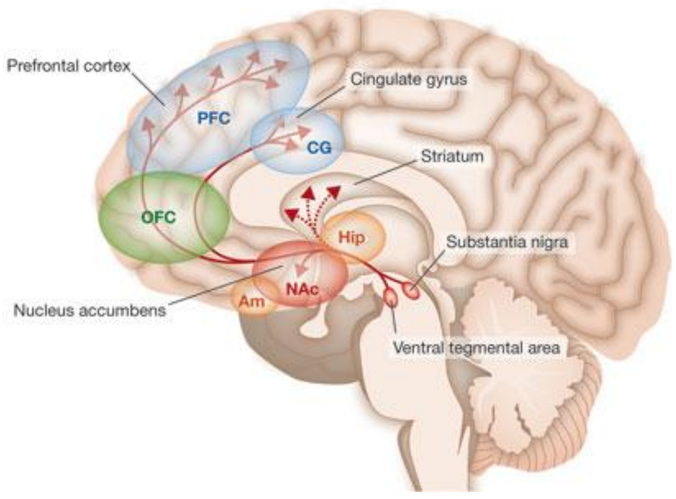
METHODOLOGY

Acquisition of a background on the field searching on websites with general information. Later, deeper readings about drug consumption on actualized papers and reviews.

Key words: synapses, dopamine, mesocorticolimbic system, LTP/LTD, AMPAR, NMDAR, GABA, glutamate, cocaine.

NEUROBIOLOGY OF THE BRAIN IN ADDICTION

Neural substrates of drug consumption

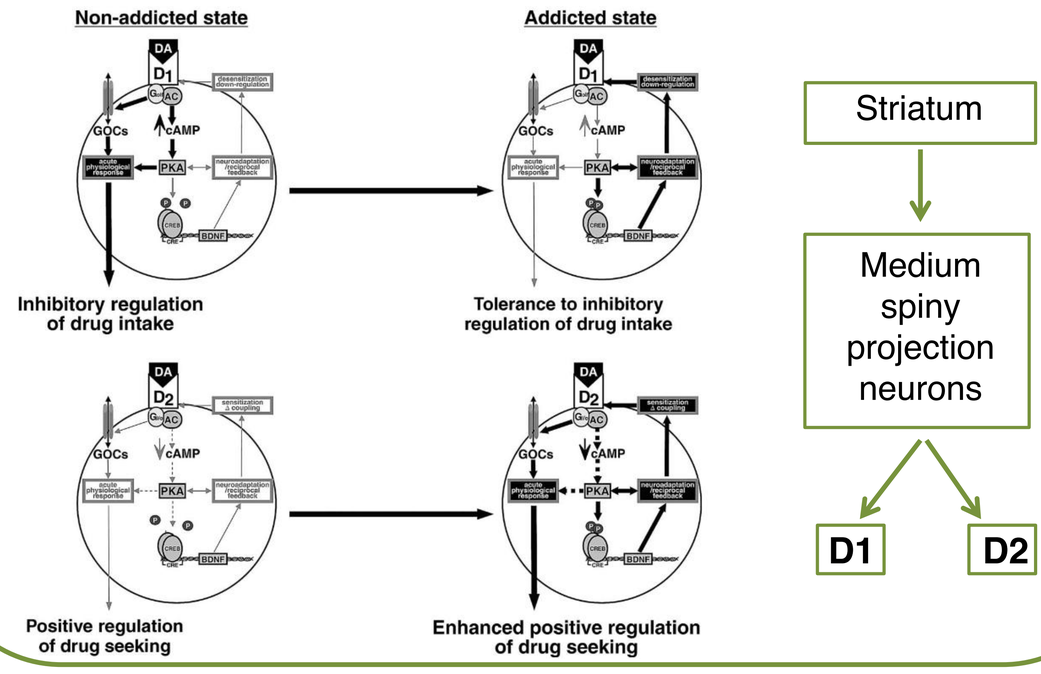


Addictive drugs act on brain **reward systems**, although the brain evolved to respond not to drugs but to natural rewards.

All addictive drugs **increase dopamine concentrations** in projection areas of the brain. Drugs can release 2 to 10 times the amount of dopamine that natural rewards do.

Rewarding → **Reinforcing** → **Tolerance** → **Sensitization**

Regulation of drug-seeking behavior



Striatum → Medium spiny projection neurons → **D1** / **D2**

Neuroplasticity

Drug-induced synaptic plasticity in the Nac and dorsal striatum contribute to addiction by consolidating **drug-wanting, drug-seeking and drug-taking behaviors**.

Synapses in the striatum and related basal ganglia exhibit various forms of long-term synaptic plasticity which appear to be aberrantly engaged by exposure to addictive drugs: **LTP** and **LTD**.

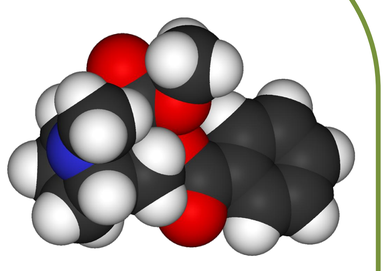
To monitor changes in excitatory synapses strength:

AMPAR/NMDAR ratio

NEUROBIOLOGY OF ADDICTION TO COCAINE

Cocaine properties

Cocaine is an **ester alkaloid** with a rigid structure, present in the leaves of two different species of shrubs: *Erytroxylum coca lam* and *Erytroxylum novogranatense Hieron*.

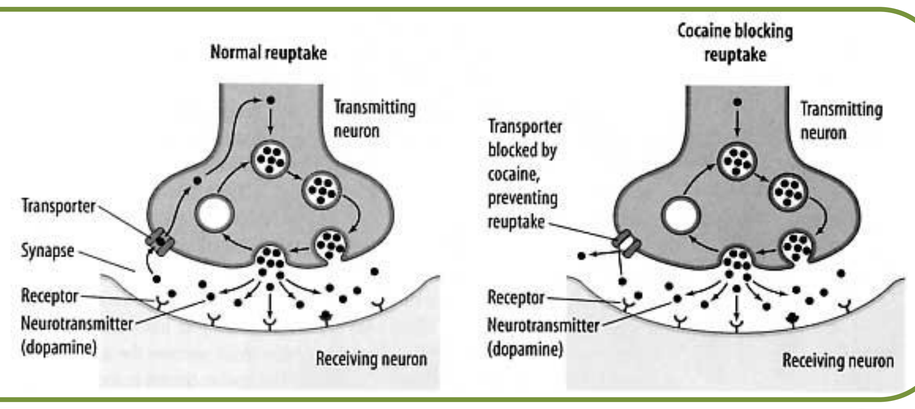


ROUTE	ONSET OF ACTION	PEAK EFFECT	DURATION
Inhalation	8 s	2-5 min	10-20 min
Intranasal	2-5 min	5-10 min	30 min
Intravenous	Seconds	10-20 min	60-90 min
Oral	30-60 min	60-90 min	Unknown
"Skin popping"	Unknown	Unknown	Unknown

Cocaine
Amphetamine
MDMA → **Sympathomimetic drugs**

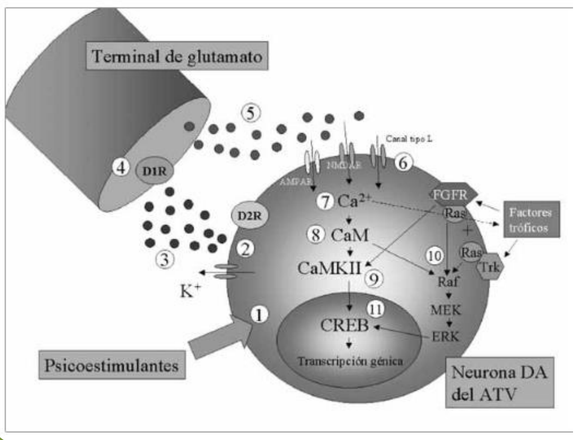
The effects of this consumption can be observed shortly after consuming it, yet changes in molecular and cellular mechanisms are **long-lasting** so the effects persist in time.

Dopamine
Serotonin
Norepinephrine
↓
Reuptake inhibited



Behaviorlal sensitization

-The induction stage



-The expression stage

It takes place in the striatum. It requires the activation of the **glutamate projections** from the prefrontal dorsal cortex to the core of the nucleus accumbens.

Continuous cocaine use produces **changes in the striatum**, such as the increase in the number of dendritic spines, new dendrites appear or the establishment of *gap junctions*.

CONCLUDING REMARKS

- Drug-evoked synaptic plasticity in the mesocorticolimbic DA system is common to all addictive drugs.
- The neurochemical systems implicated in the acute reinforcing effects of drugs of abuse include key elements of the basal forebrain linked by the mesocorticolimbic DA system.
- LTP/LTD processes are affected by drug consumption, as well as the AMPAR/NMDAR ratio.
- Cocaine increase extracellular dopamine levels by interacting with dopamine transporters.

RELEVANT LITERATURE

- Lee NM, Carter A, Owen N, Hall WD. The neurobiology of overeating. *EMBO reports* 2012;*13:* 785-790.
- Self DW. Regulation of drug-taking and –seeking behaviors by neuroadaptations in the mesolimbic dopamine system. *Neuropharm* 2004;47:242-255.
- Abadinsky H. Drugs: An Introduction. 5th edition. Wadsworth; 2004.
- Fernandez-Espejo E. Neurobiología de la adicción a psicoestimulantes. *Rev Neurol* 2006;43:147-154.