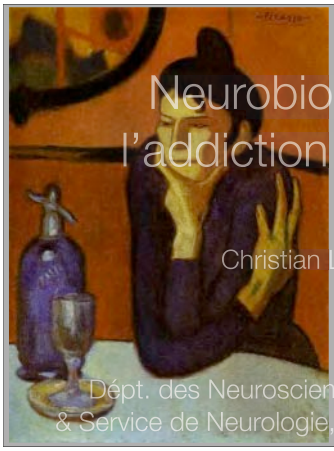

Neurobiologie de l'addiction à l'alcool

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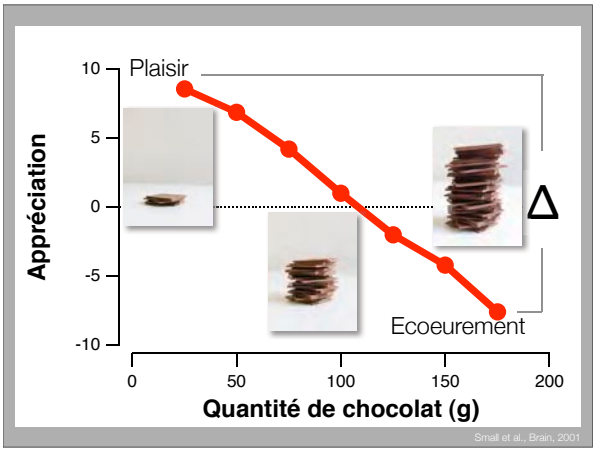
La consommation d'alcool peut induire l'addiction

L'addiction se distingue de la dépendance

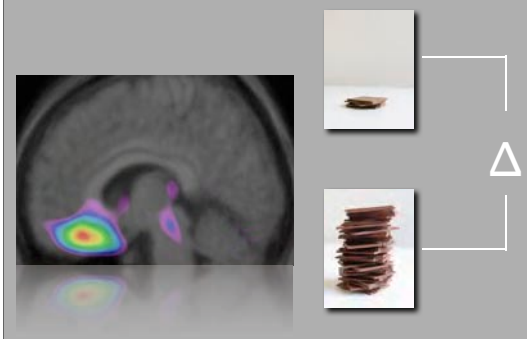
Les substances euphorisantes stimulent le système du cerveau responsable de la perception de la récompense peut induire l'addiction

L'activation de ce système altère la communication entre cellules nerveuses

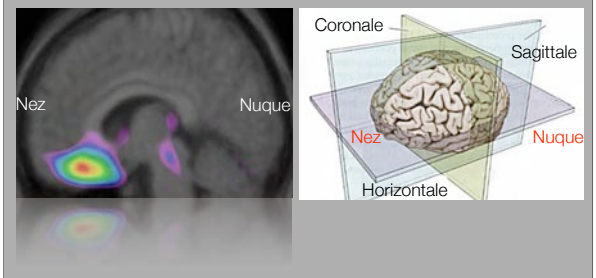
L'addiction est donc un maladie de l'apprentissage & de la mémoire



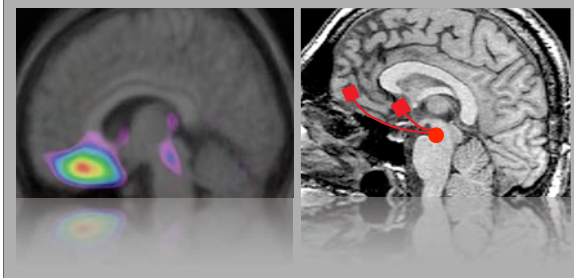
Small et al., Brain, 2001



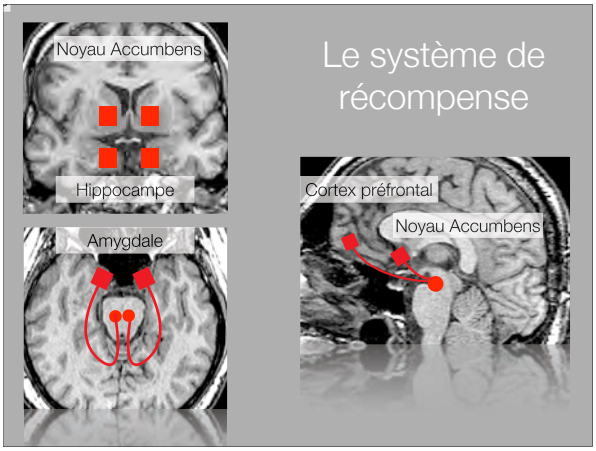
Small et al., Brain, 2001

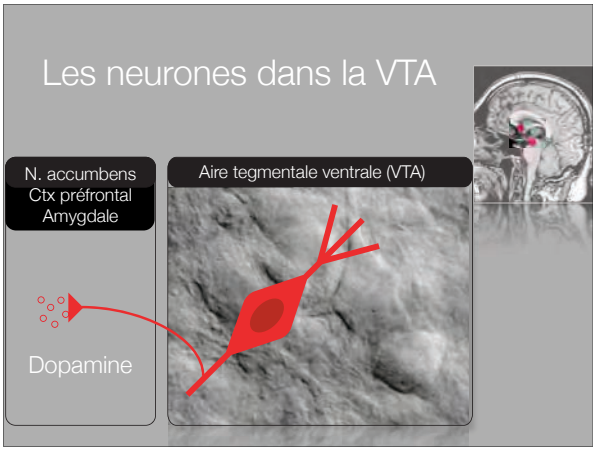


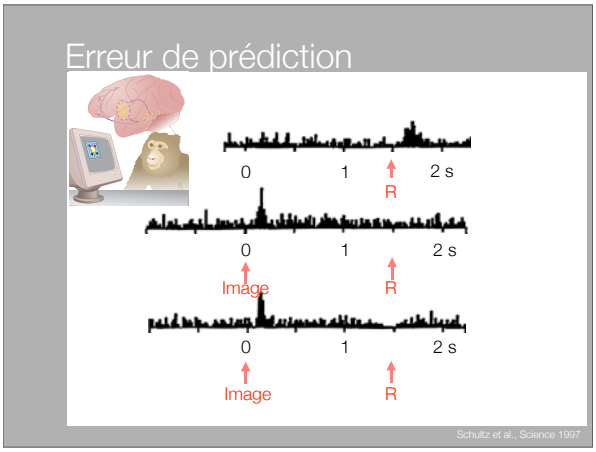
Small et al., Brain, 2001

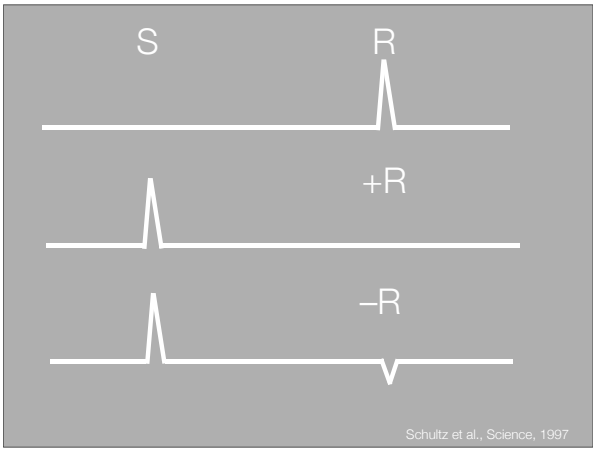


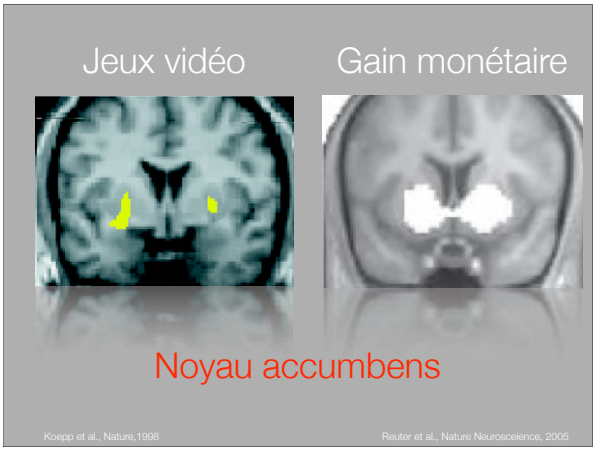
Small et al., Brain, 2001

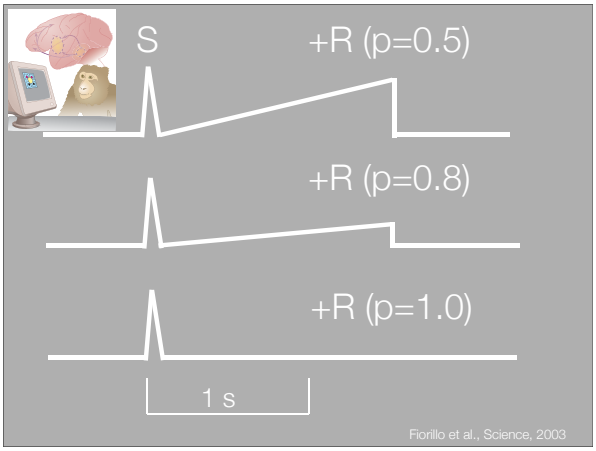

Noyau Accumbens
Hippocampe
Amygdale
Le système de récompense
Cortex préfrontal
Noyau Accumbens


Les neurones dans la VTA
N. accumbens
Ctx préfrontal
Amygdale
Aire tegmentale ventrale (VTA)
Dopamine

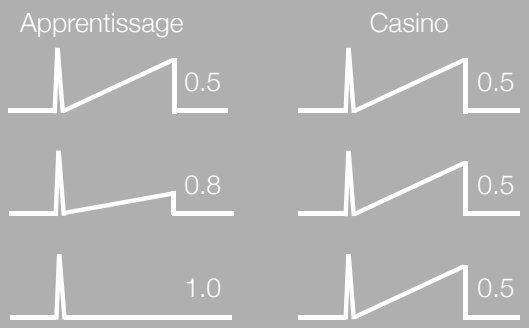

Erreur de prédiction
0
1
2 s
R
Image
Schultz et al., Science 1997


S
R
+R
–R
Schultz et al., Science, 1997

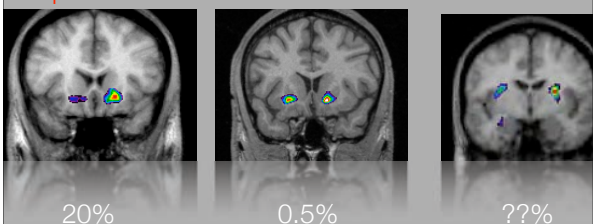

Jeux vidéo
Gain monétaire
Noyau accumbens
Koepp et al., Nature,1998
Reuter et al., Nature Neuroscience, 2005


S
+R (p=0.5)
+R (p=0.8)
+R (p=1.0)
1 s
Fiorillo et al., Science, 2003

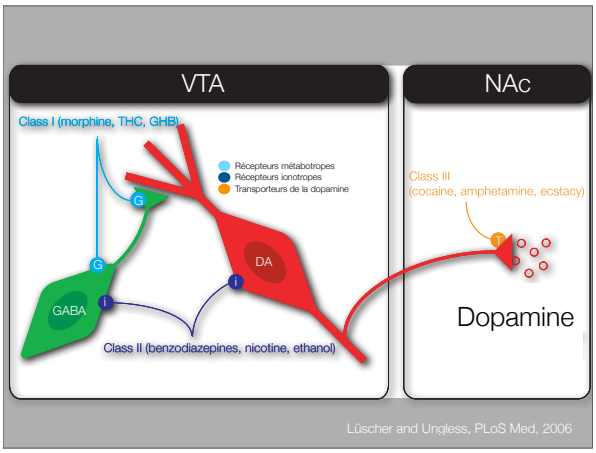
La dopamine est un signal d'apprentissage



L'activation excessive induit l'addiction chez certaines personnes



Leyton et al., 2002 — Boileau et al., 2003 — Small et al., 2003



Lüscher and Ungless, PLoS Med, 2006

Classification mécanistique

Class I: Drugs that activate G protein coupled receptors

Name	Main molecular target	Pharmacology	Effect on dopamine neurons	RR
Opioids	μ-OR (G_{io})	agonist	disinhibition	4
Cannabinoids	CB1R (G_{io})	agonist	disinhibition	2
γ-hydroxy butyric acid (GHB)	$GABA_BR$ (G_{io})	weak agonist	disinhibition	NA
LSD, Mescaline, Psilocybin	5-HT_{2A}R (G_q)	partial agonist		1

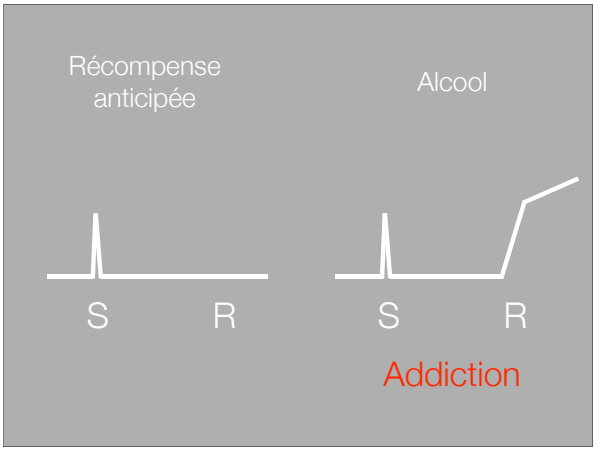
Class II: Drugs that bind to ionotropic receptors and ion channels

Name	Main molecular target	Pharmacology	Effect on dopamine neurons	RR
Nicotine	nAChR ($\alpha4\beta2$)	agonist	excitation, disinhibition, modulates release	4
Alcohol	$GABA_AR$, 5-HT_3R, nAChR, , NMDAR, $K_2$3 channels		excitation	3
Benzodiazepines	$GABA_AR$	positive modulator	disinhibition	3
Phencyclidine, Ketamine	NMDAR	antagonist	disinhibition (?)	1

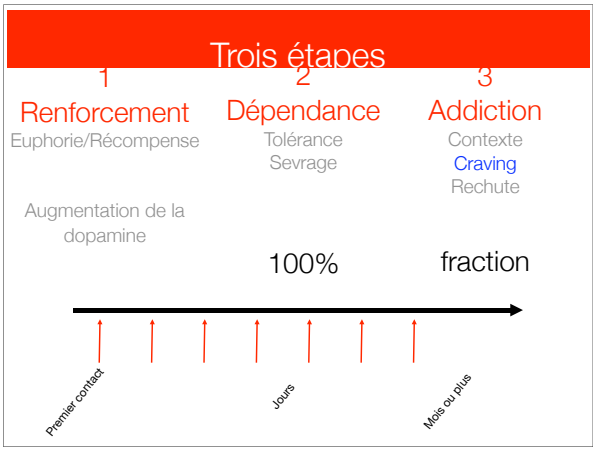
Class III: Drugs that bind to transporters of biogenic amines

Name	Main molecular target	Pharmacology	Effect on dopamine neurons	RR
Cocaine	DAT, SERT and NET	inhibitor	blocks DA uptake	5
Amphetamine	DAT, NET and SERT, VMAT	reverses transport	blocks DA uptake, synaptic depletion, excitation	5
Ecstasy	SERT > DAT, NET	reverses transport	blocks DA uptake, synaptic depletion	NA

Lüscher and Ungless, PLoS Med, 2006



Trois étapes

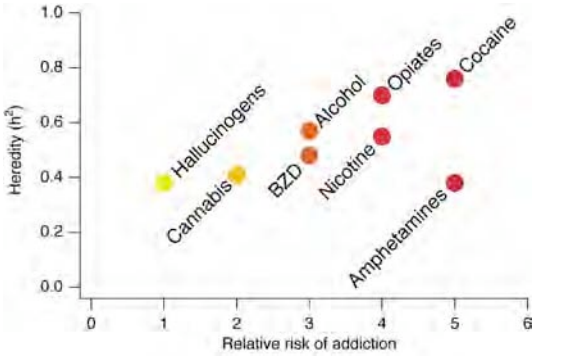


Risque relatif d'addiction

Goldstein & Kalant, Science 1990

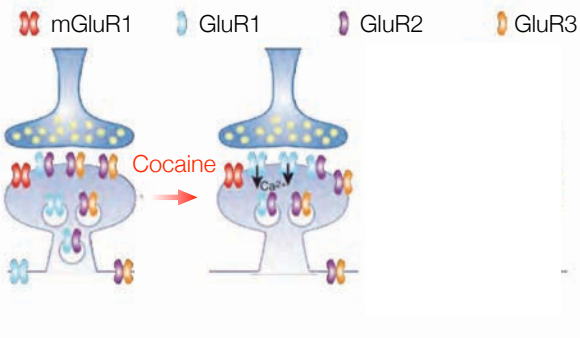
Hallucinogènes (LSD)	1
Cannabis (THC)	2
Benzodiazépines (BDZ)	2
Alcool	3
Nicotine	3
Opiacés (Morphine, Héroïne)	4
Amphétamines	5
Cocaïne	5

Hérédité versus risque d'addiction



Goldman et al. Nat Rev Genet. 2005

Plasticité synaptique



Cocaïne Nicotine Jeu Chocolat

↓

Libération inappropriée de dopamine

↓

Communication neuronale

↓

Apprentissage maladif

↓

Consommation compulsive

Désir sans plaisir

"Addiction: a disease of learning & memory"

Stephen E. Hyman, Am J Psychiatry. 2005

Maladies du cerveau en Europe

	Cas en millions	Coût en Mia€
Dépression	21	**104**
Addiction (sans nicotine)	9	**57**
Démence	5	**55**
Troubles anxieux	41	**41**
Schizophrénie	3.5	**35**
Accident vasculaires	1	**22**
Epilepsie	3	**15**
Parkinson	1.2	**11**

Addiction: une maladie du cerveau

- Nouvelles possibilités thérapeutiques
  - contrôler et anticiper les propriétés addictives de molécules pharmacologiques
  - inhiber l'activation excessive du système dopaminergique
  - corriger la plasticité synaptique pathologique
- Stigmatisation sociale (déculpabilisation, responsabilité personnelle)
- Prise en charge (accès aux soins)
- Politique de la drogue (législation, répression)