

*Activité physique  
intense et  
Alcoolodépendance*

→ ~ 1990

## Classical Neurotransmitters

- DA
- NA
- 5-HT
- Ach

Alcohol → specific brain neurotransmitter(s)

1990



today

## AMINO ACIDS

### INHIBITORY

GABA

Taurine

Glycine

$\beta$ -alanine

### EXCITATORY

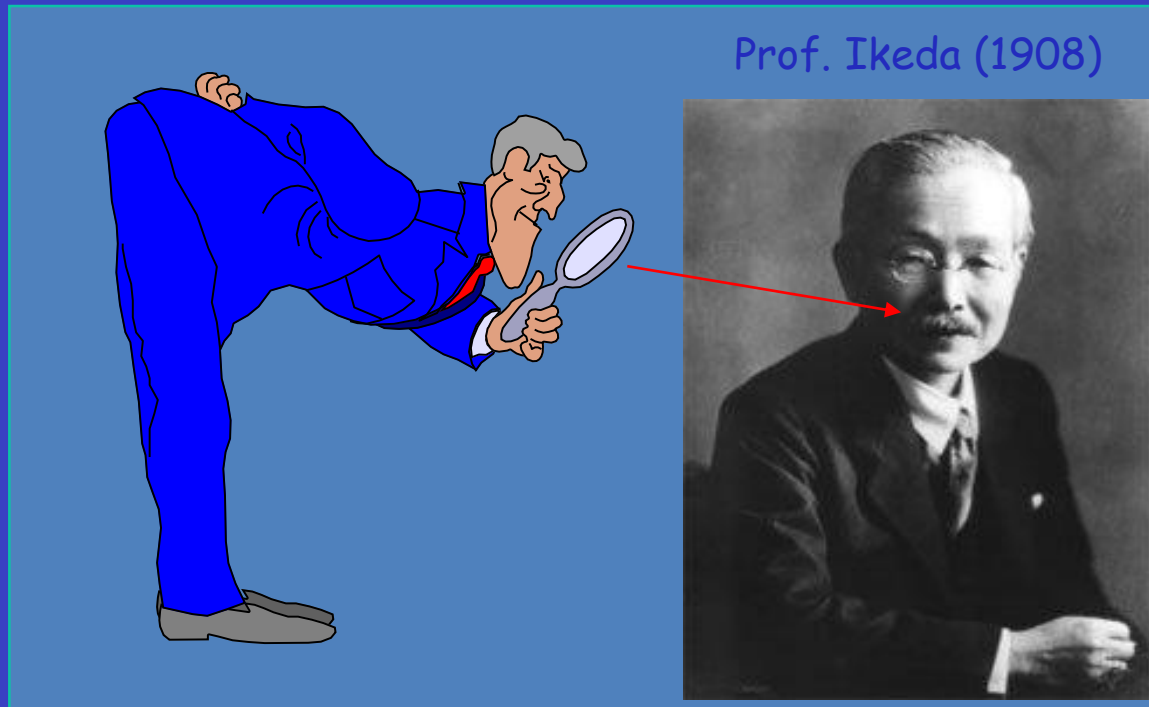
Glutamate

Aspartate

Cysteine

Homocysteine

# GLUTAMATE



Glutamate



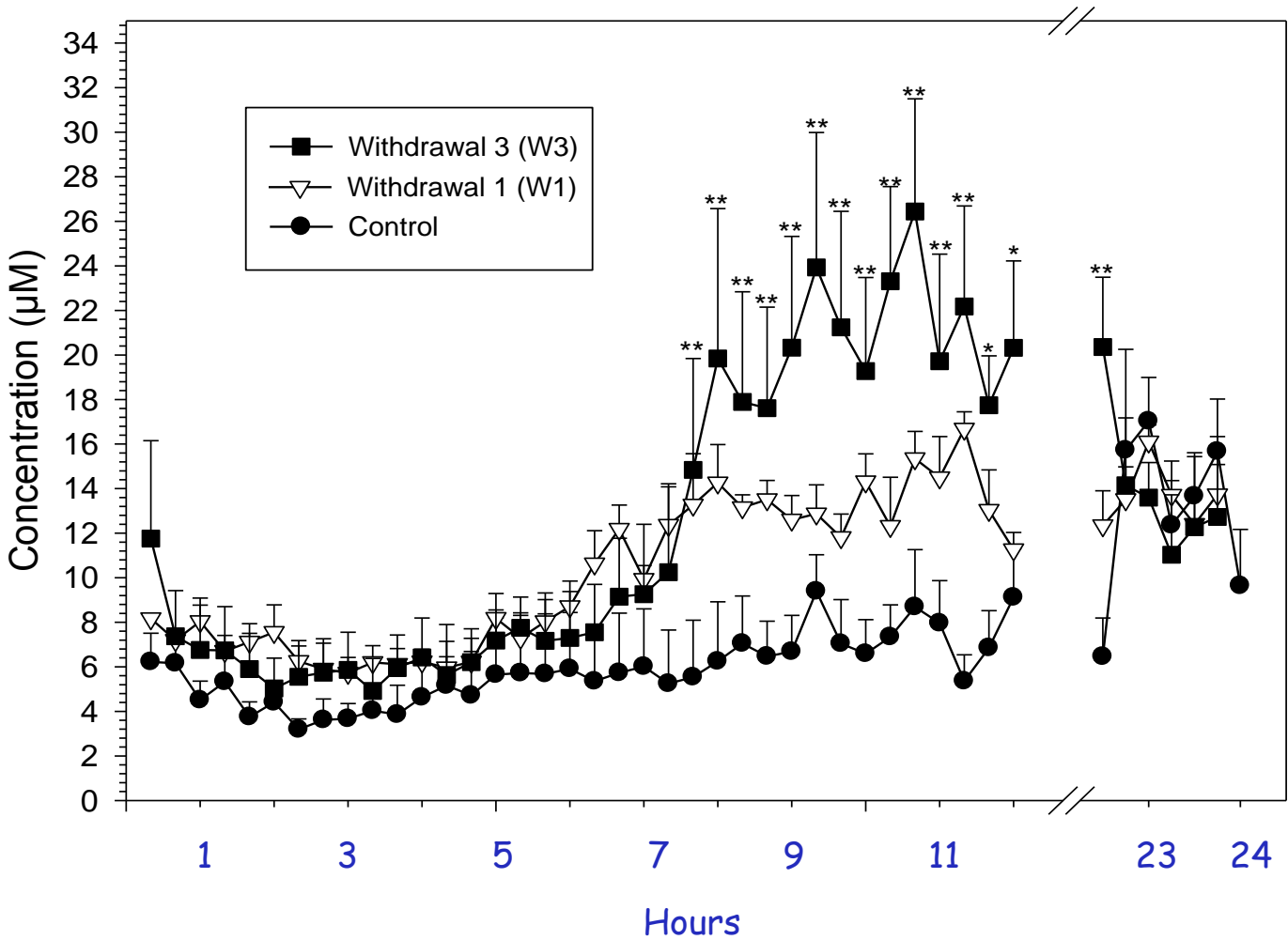
GAD

GABA



GABA-T

# GLUTAMATE

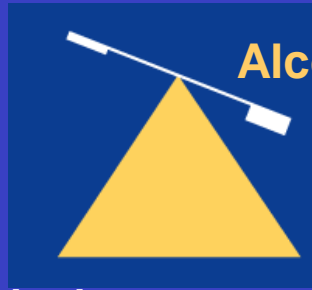


## Equilibrium



Excitation      Inhibition

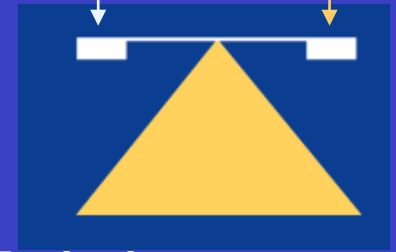
## Acute alcohol



Excitation      Inhibition

## Chronic alcohol

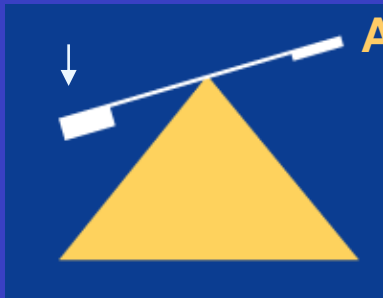
Neuroadaptation      Alcohol



Excitation      Inhibition

## Withdrawal

Neuroadaptation

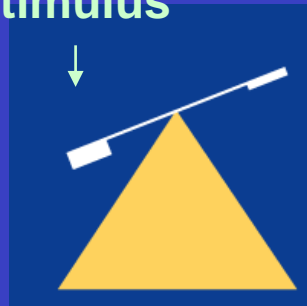


Excitation      Inhibition

~~Alcohol~~

## Pseudo-withdrawal

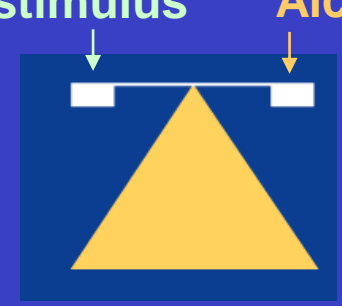
Conditioned stimulus



Excitation      Inhibition

## Conditioned tolerance

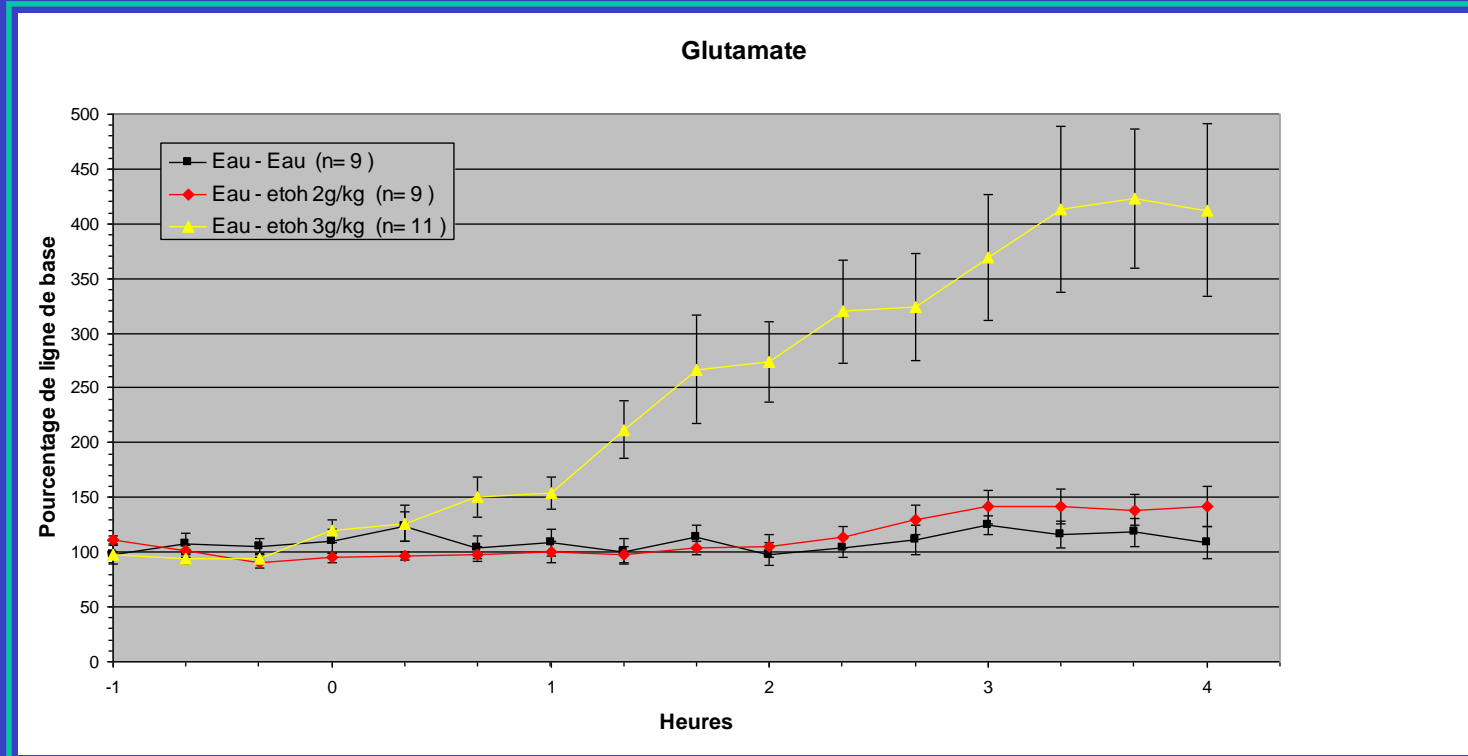
Conditioned stimulus



Excitation      Inhibition

Alcohol

# Binge Drinking



% of Glutamate baseline



# GLUTAMATE

Acute

Chronic

Withdrawal

Alcohol

=

=



Binge  
Drinking



# GLUTAMATE

IONOTROPIC    *(Channel opening)*

METABOTROPIC    *(Second messenger)*

# GLUTAMATE

IONOTROPIC

*(Channel opening)*

NMDA

→ NR1, NR2

AMPA

→ GluR 1-4

KA

→ GluR 5-7, KA1, KA2

METABOTROPIC

*(Second messenger)*

Class I

→ mGluRs 1,5

Class II

→ mGluRs 2,3

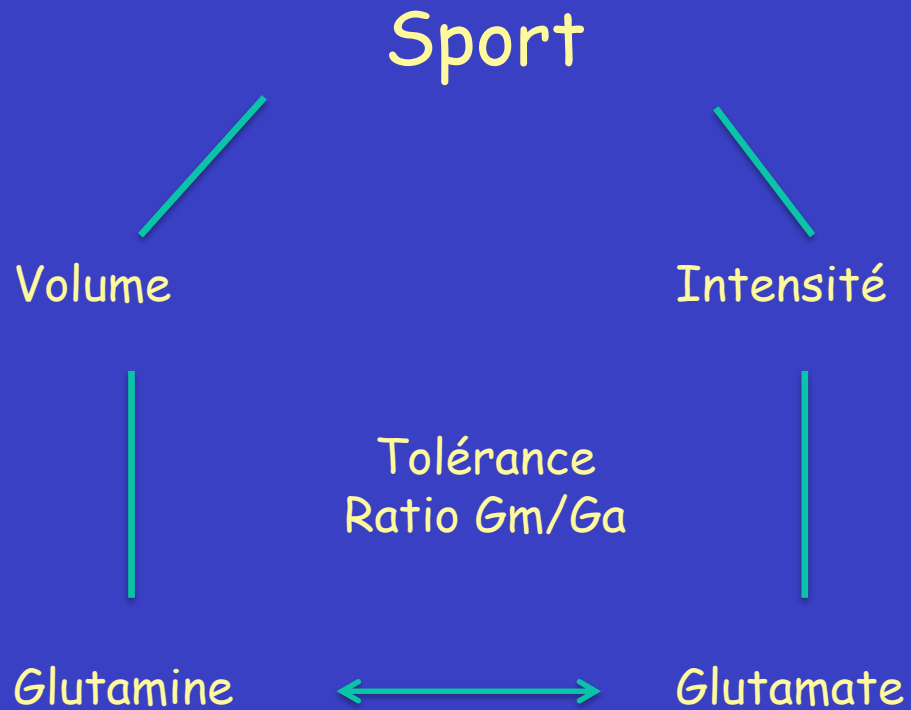
Class III

→ mGluRs 4,6,7,8

# GLUTAMATE

Dépolarisation de la membrane nerveuse ( $\text{Ca}^{++}$ )

- normale: excitation
- hyper-dépolarisation: hallucination
- supra-dépolarisation: excitotoxicité  
avec cascade glutamatergique de  
dommages cérébraux



Smith DJ, Norris SR. Changes in glutamine and glutamate concentrations for tracking training tolerance.  
*Med Sci Sports Exerc*, 2000, 32(3):684-689

# GLUTAMATE

Binge drinking **OU** Sport intense

- normale: excitation
- hyper-dépolarisation: déconnexion du monde réel (hallucination)
- supra-dépolarisation: excitotoxicité avec cascade glutamatergique de dommages cérébraux

Ketamine, PCP (angel dust) → Antagonistes glutamate (NMDA)

Les effets psychotropes comprennent des distorsions spatio-temporelles, des vécus de dépersonnalisation.

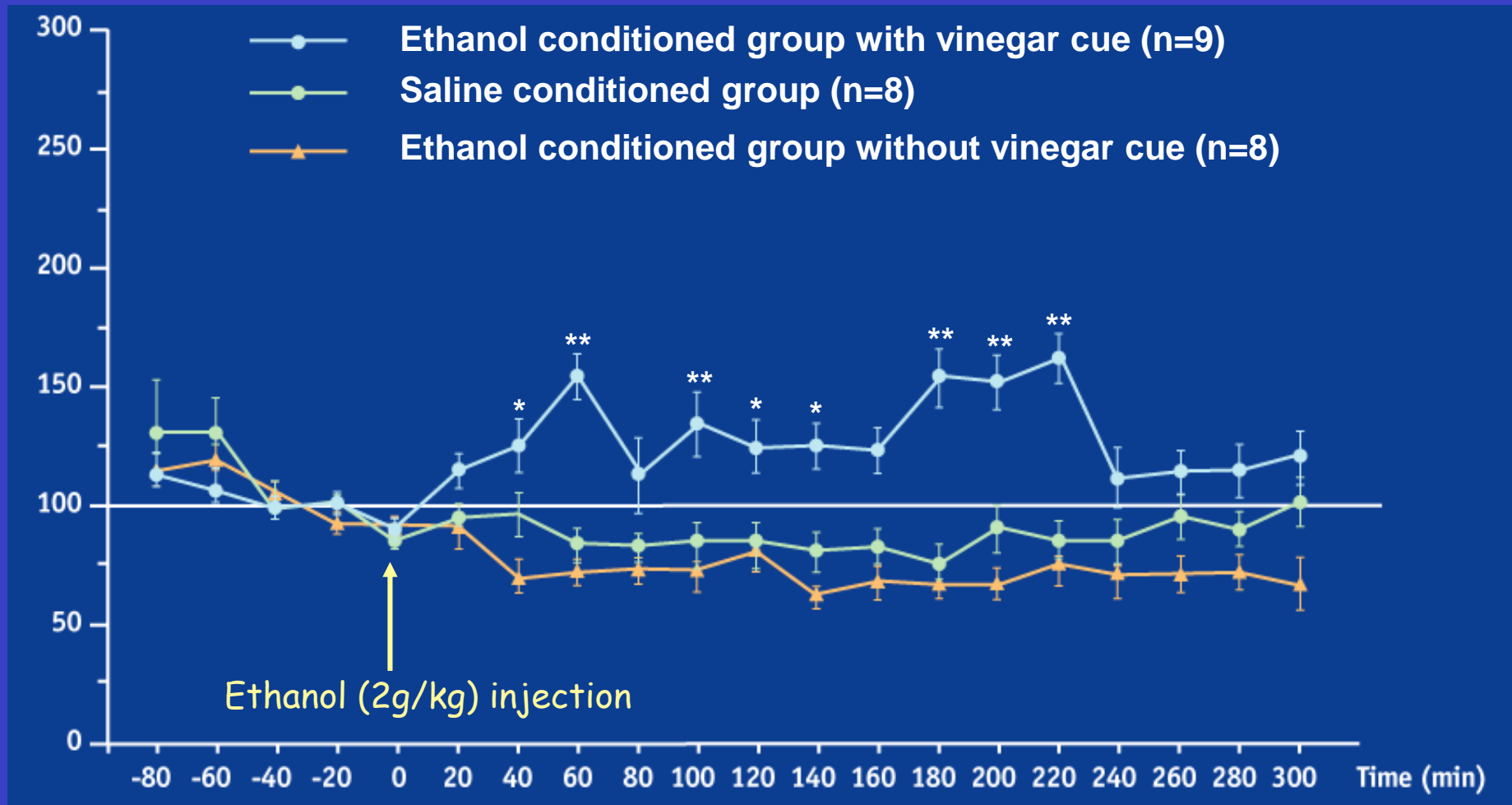
*Mauvaise nouvelle...*

*Et bonne nouvelle !*



# Effect of ethanol injections on amygdala glutamate content

% Baseline level



Quertemont E, de Neuille J, De Witte P. *Psychopharmacology*, 1998, 139:71-78

# Neuropharmacological basis of ethanol withdrawal

Acute effects of ethanol

Adaptation to chronic alcoholisation

Ethanol withdrawal

- Potentiation of Neuroinhibitory Receptors (Taurine, GABA)

Downregulation

- Inhibition of Neuroexcitatory Receptors (Glutamate, Aspartate)

Upregulation

Neuronal Hyperexcitability

↓ + ↑  
Glutamate Release