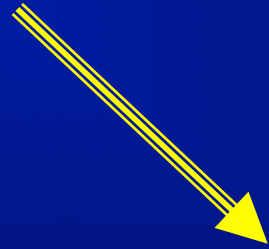


USAGE



ABUS



DEPENDANCE

USAGE

DA

ABUS

NA / 5-HT

DEPENDANCE





ACh

GABA

GLY

NE

DA

5-HT

Sub-P

GLU

TRF

SRIF

ENK

END

LRF

NTSN

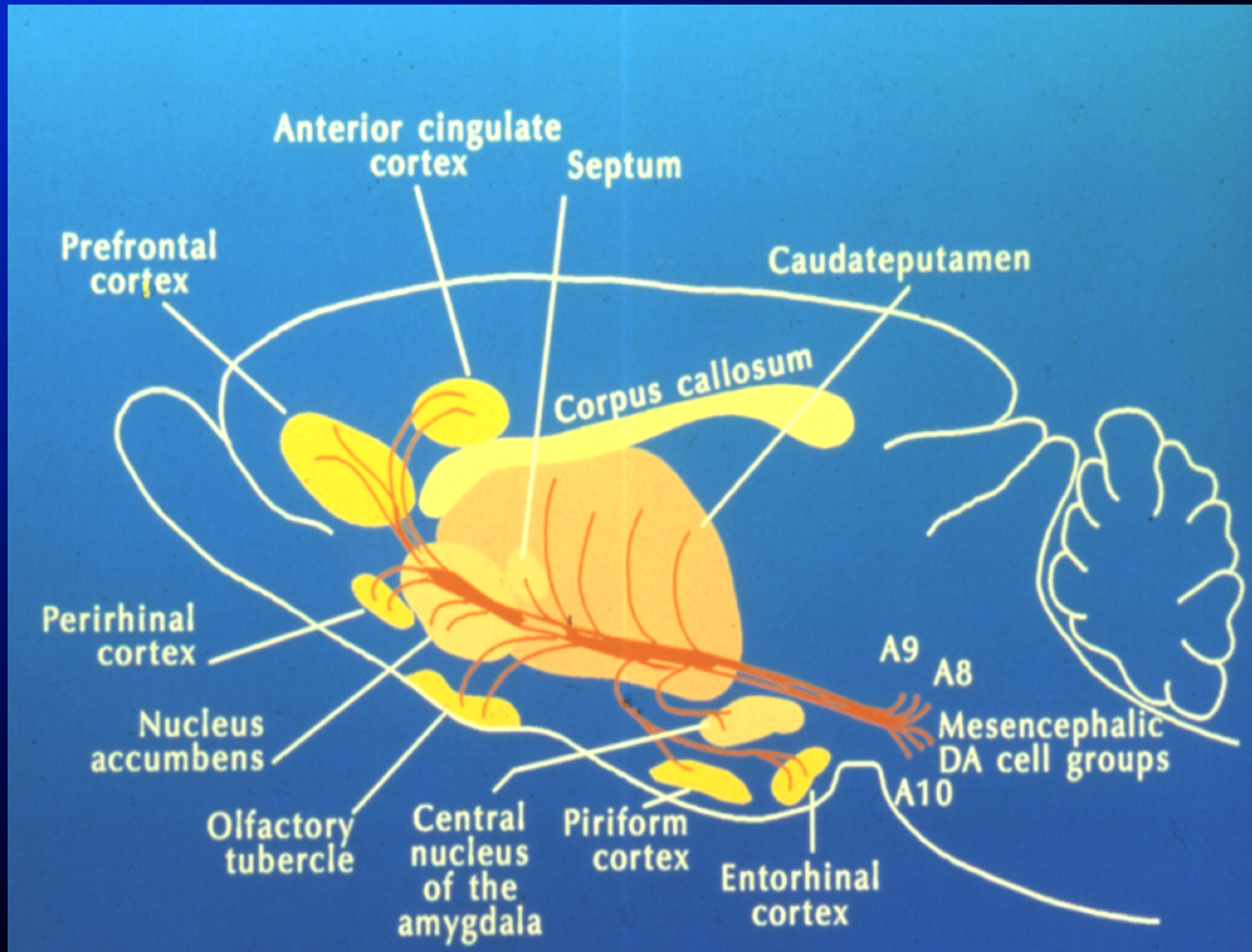
ANG-II

GAST

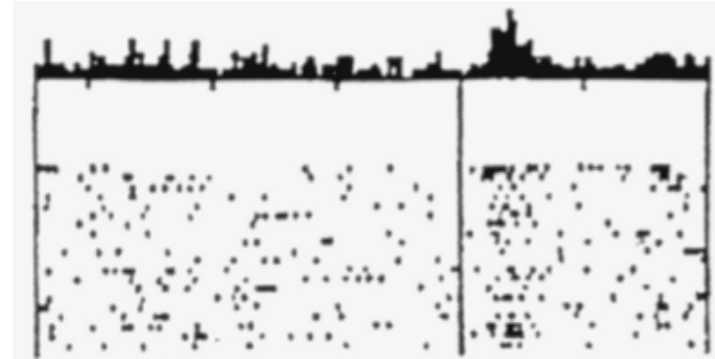
VASOP

OXY

Simon



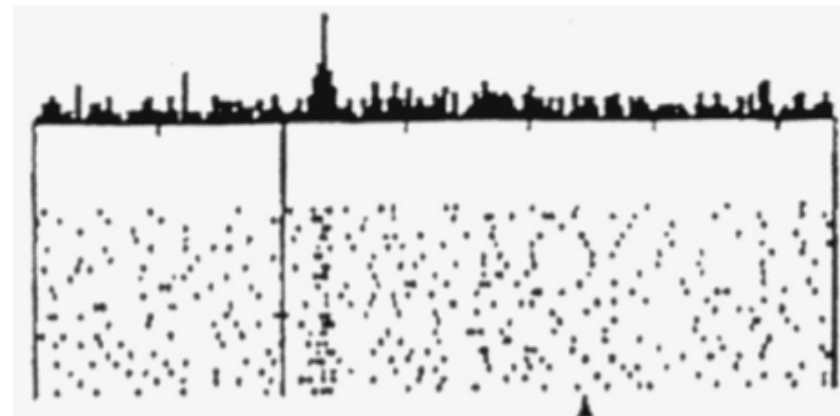
No prediction
Reward occurs



(No CS)

R

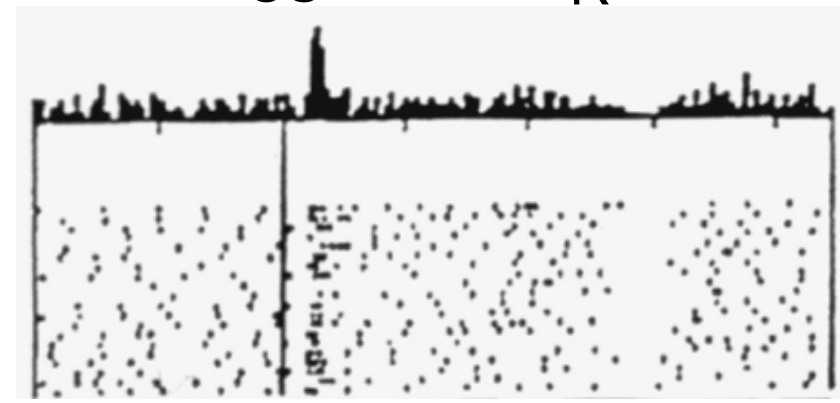
Reward predicted
Reward occurs



CS

R

Reward predicted
No reward occurs



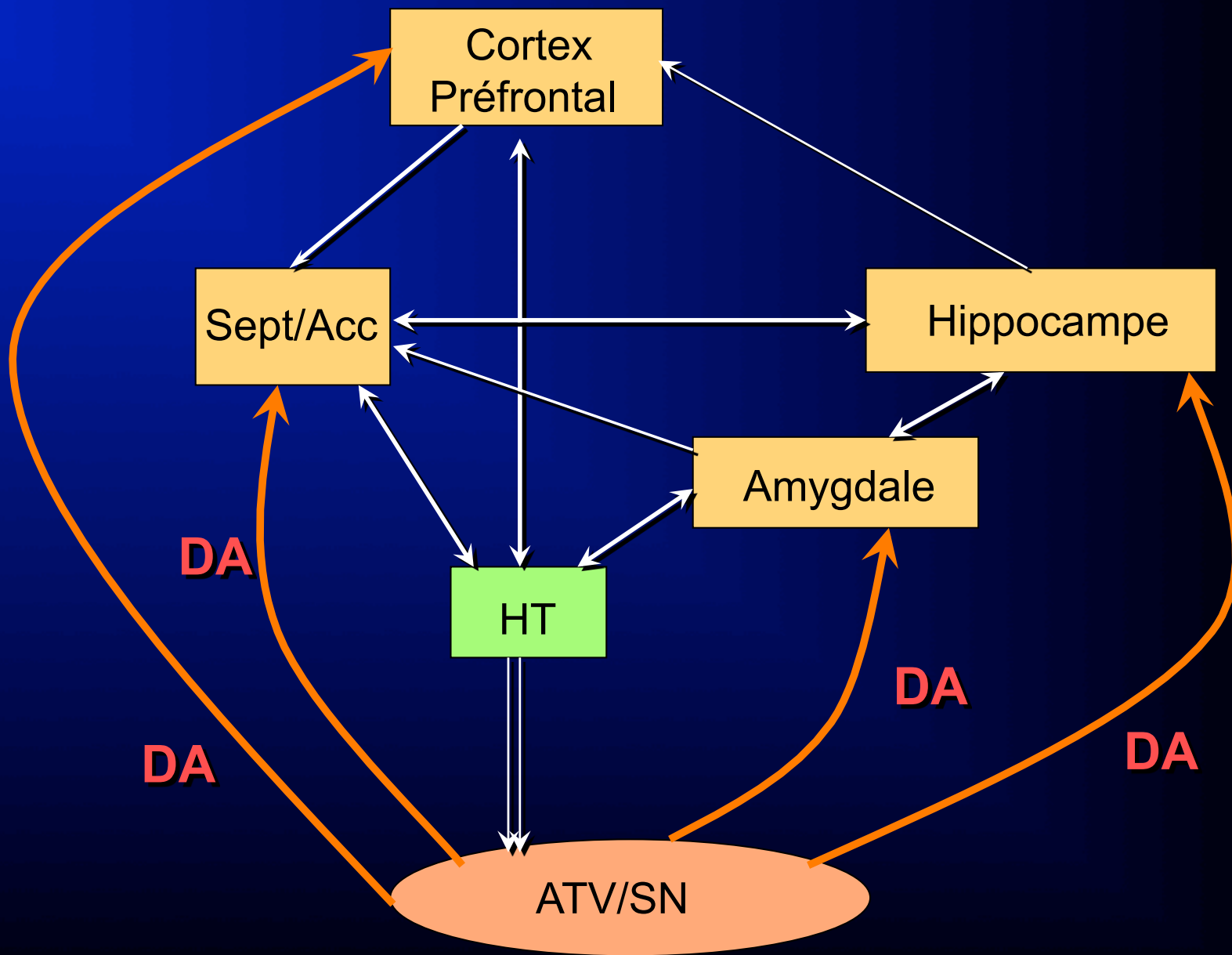
-1

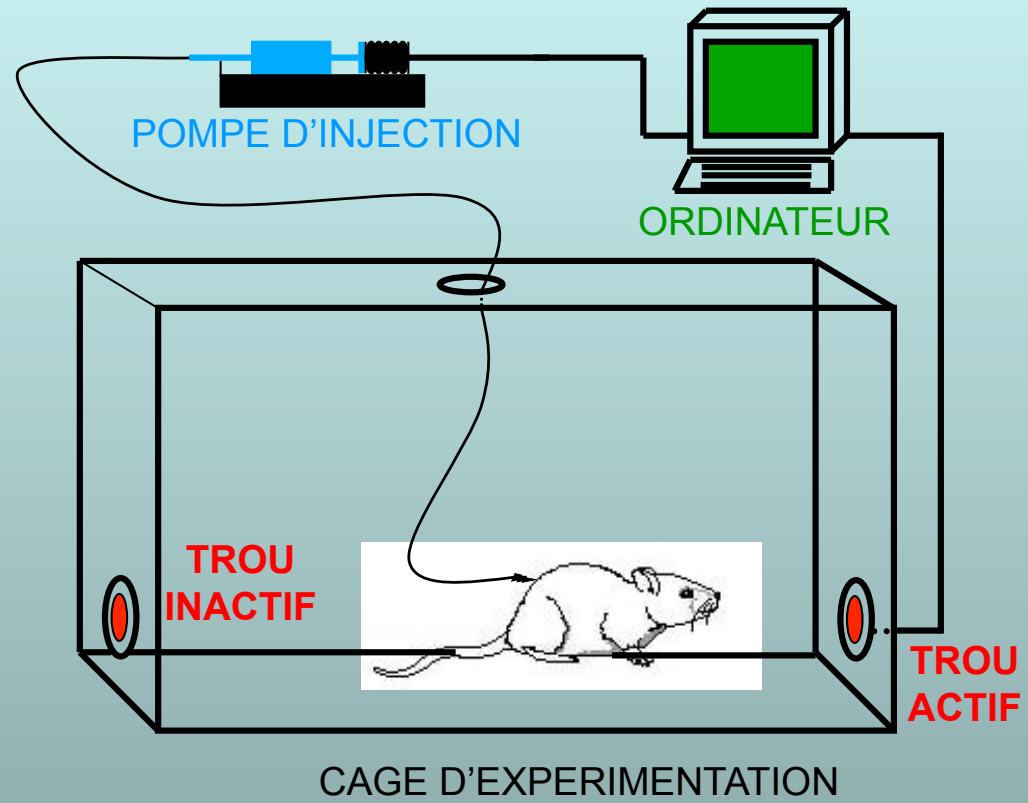
CS

1

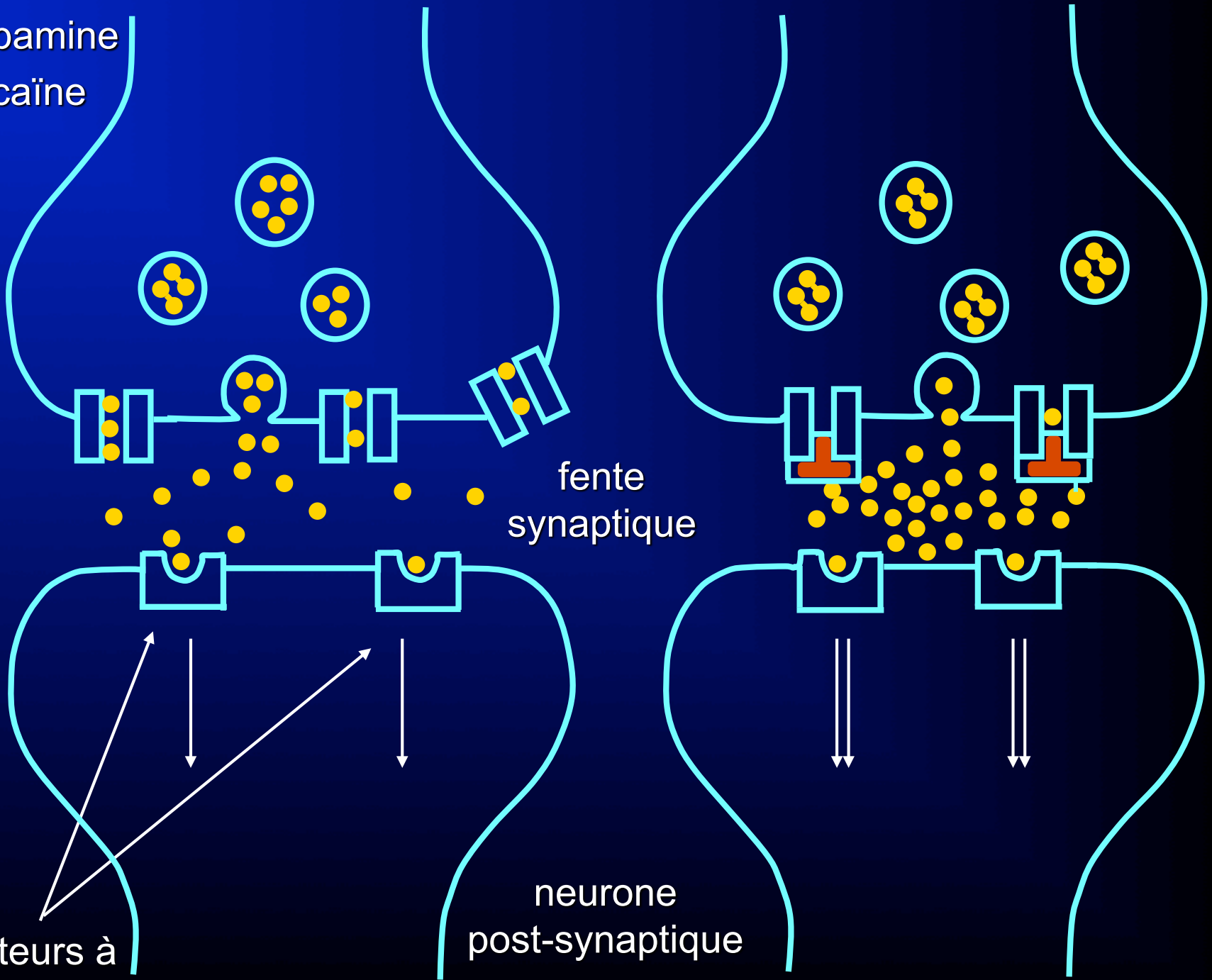
2s

(No R)





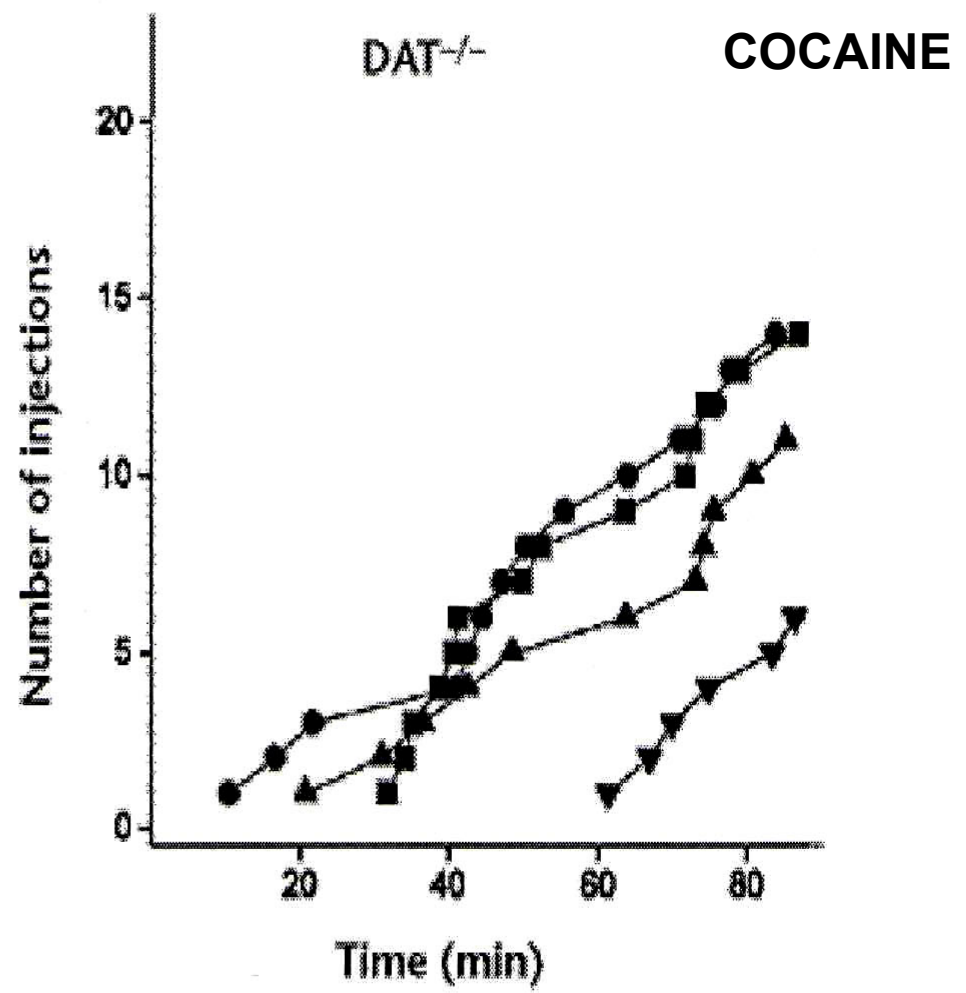
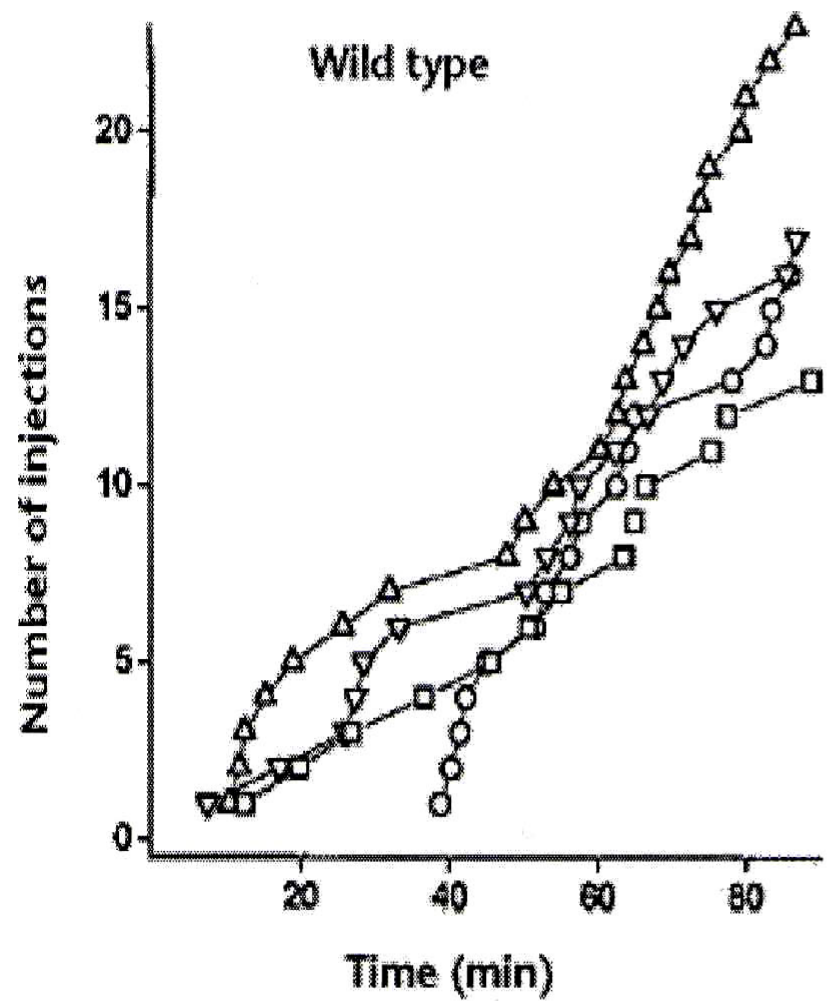
● Dopamine
⊥ Cocaïne

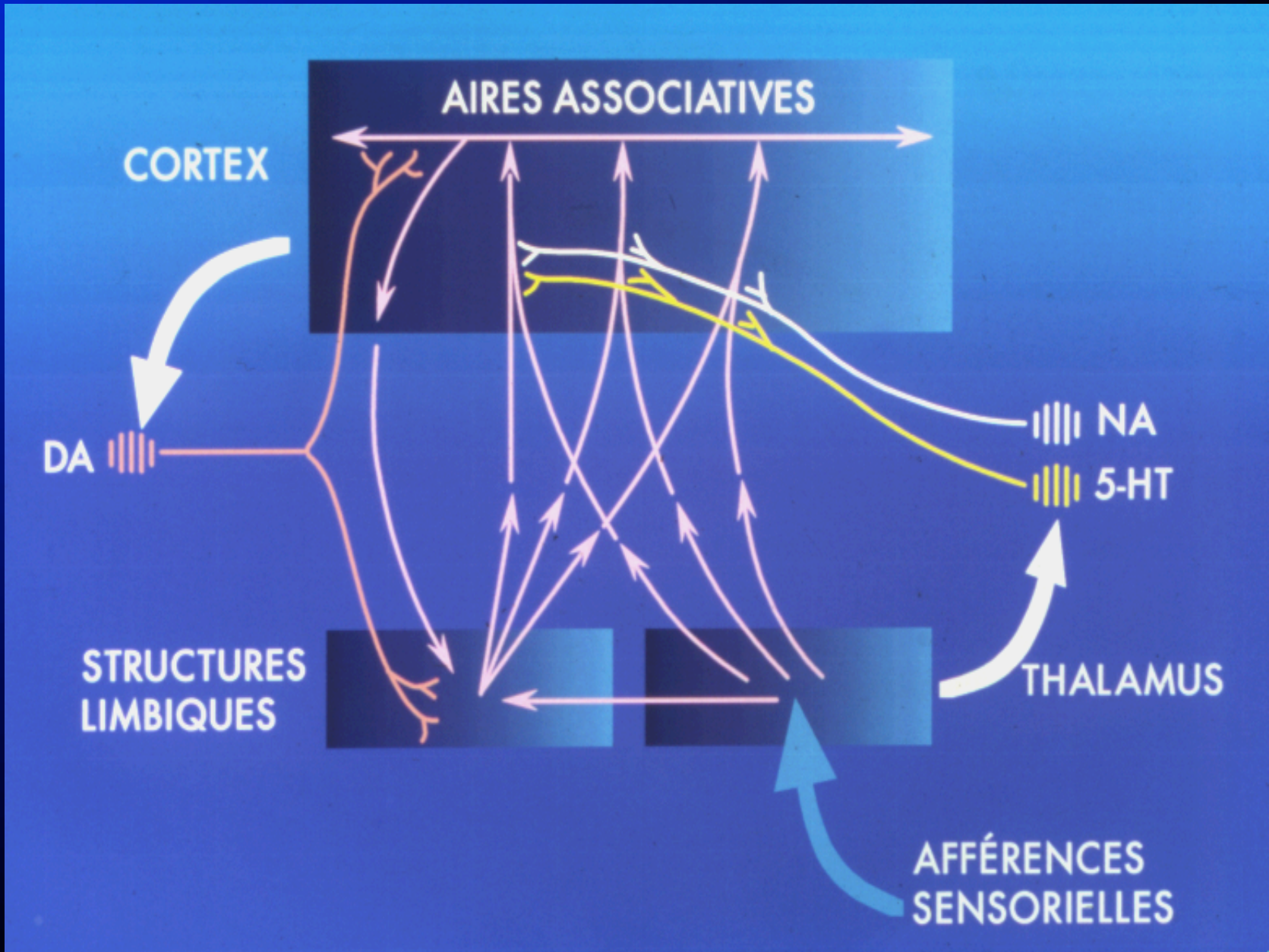


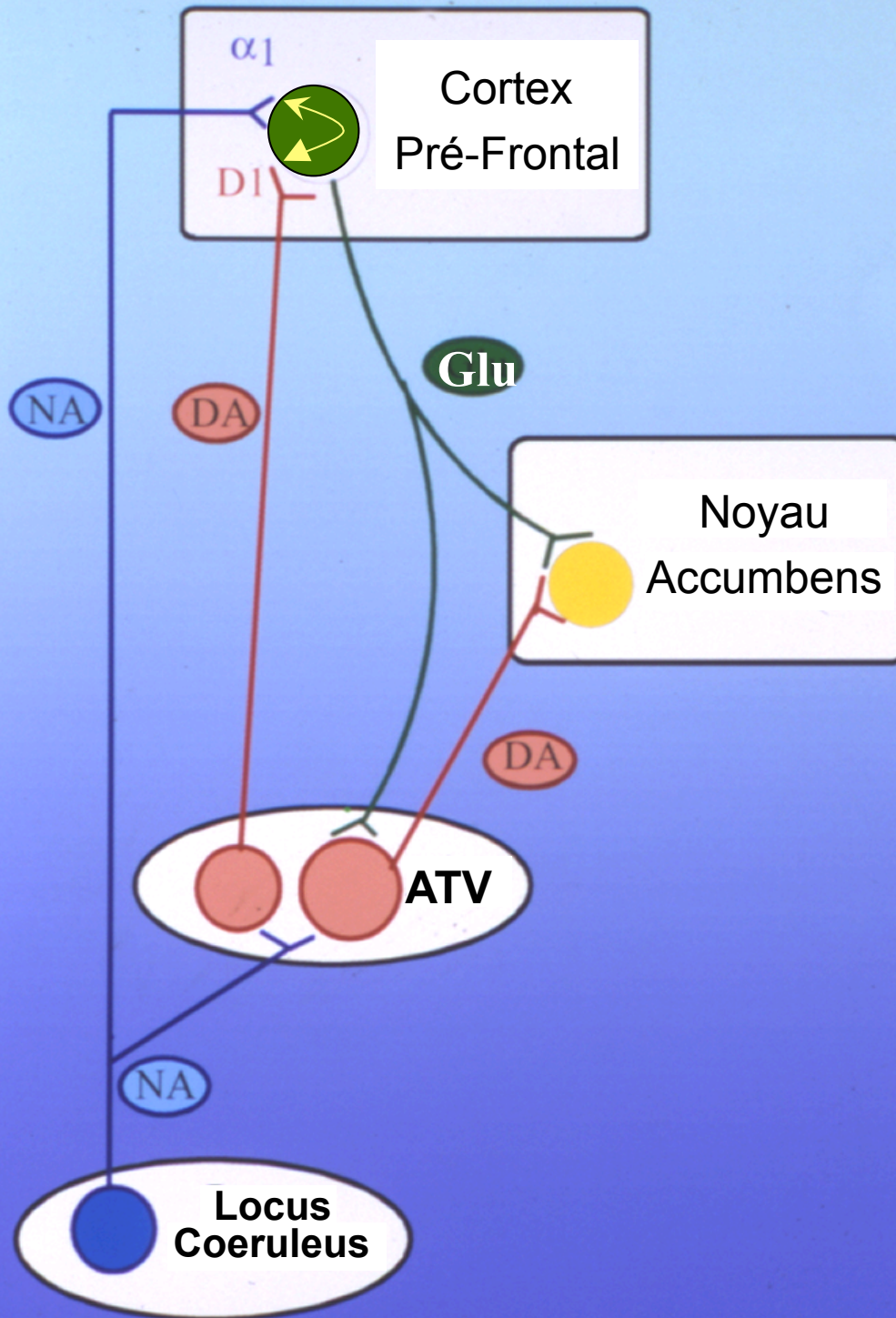
fente
synaptique

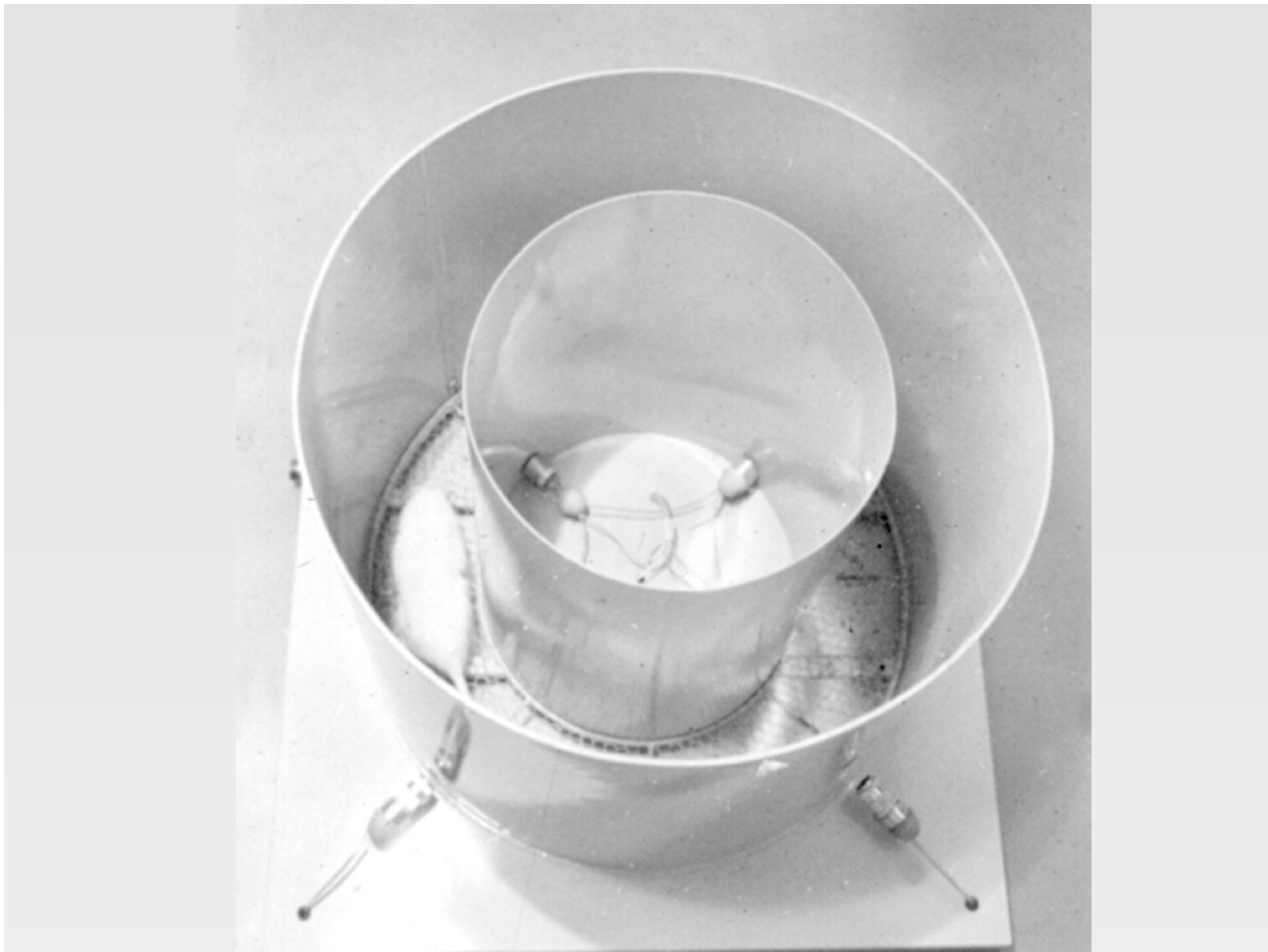
neurone
post-synaptique

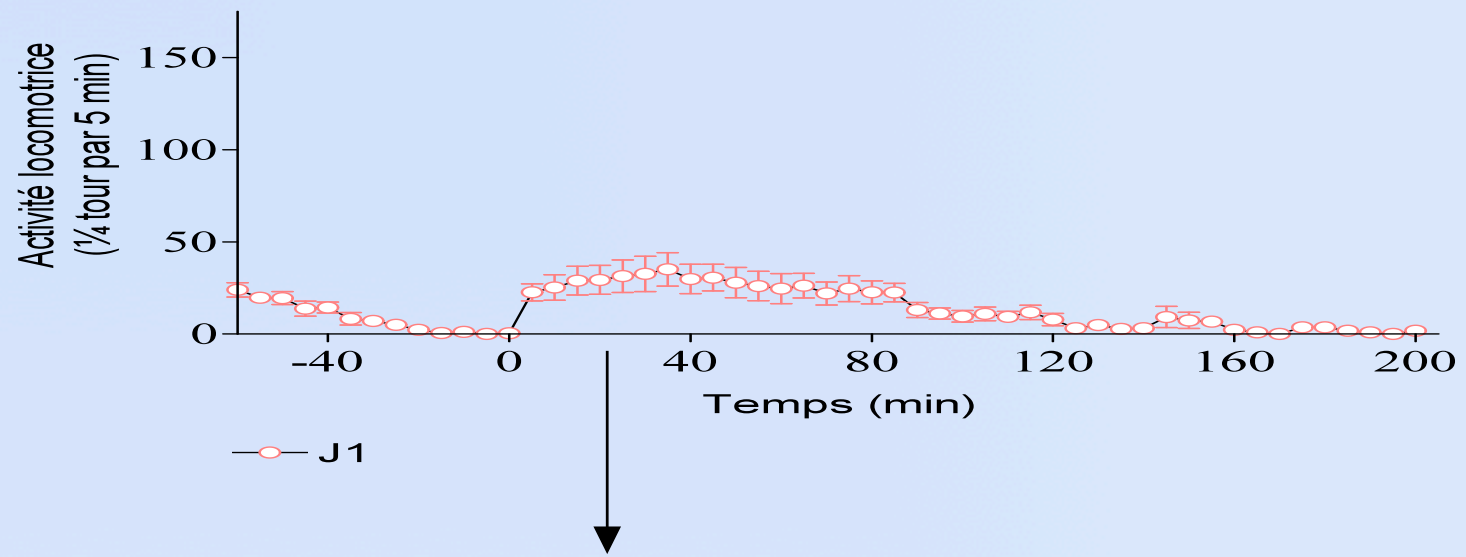
récepteurs à
la dopamine

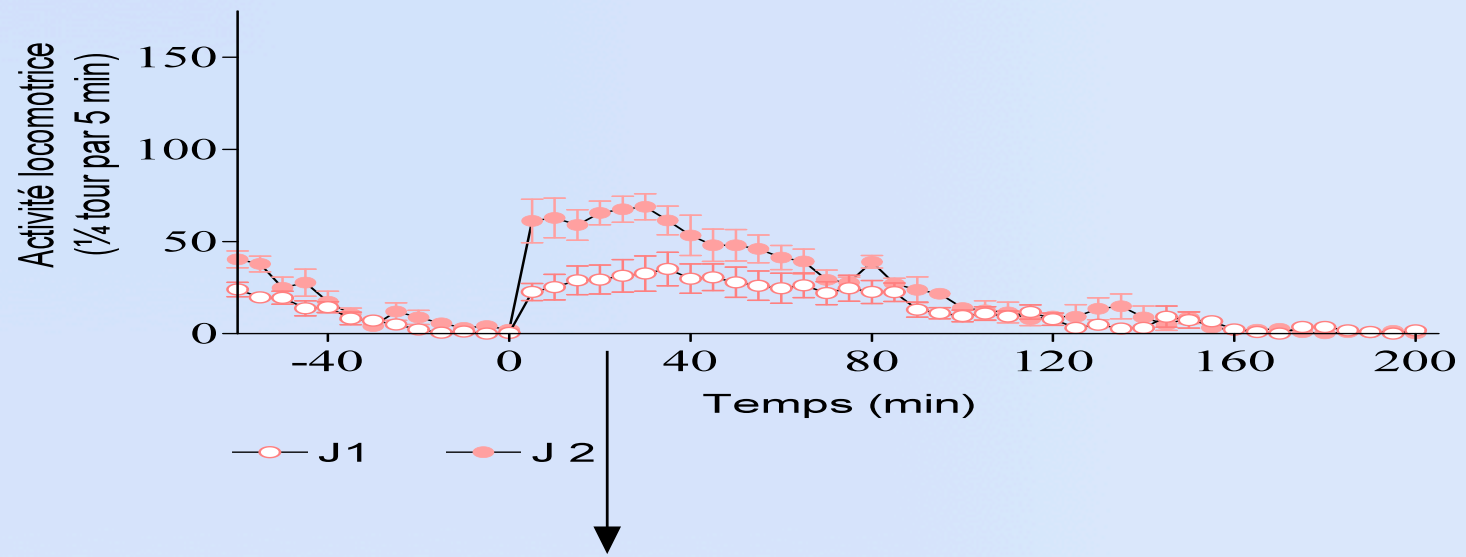


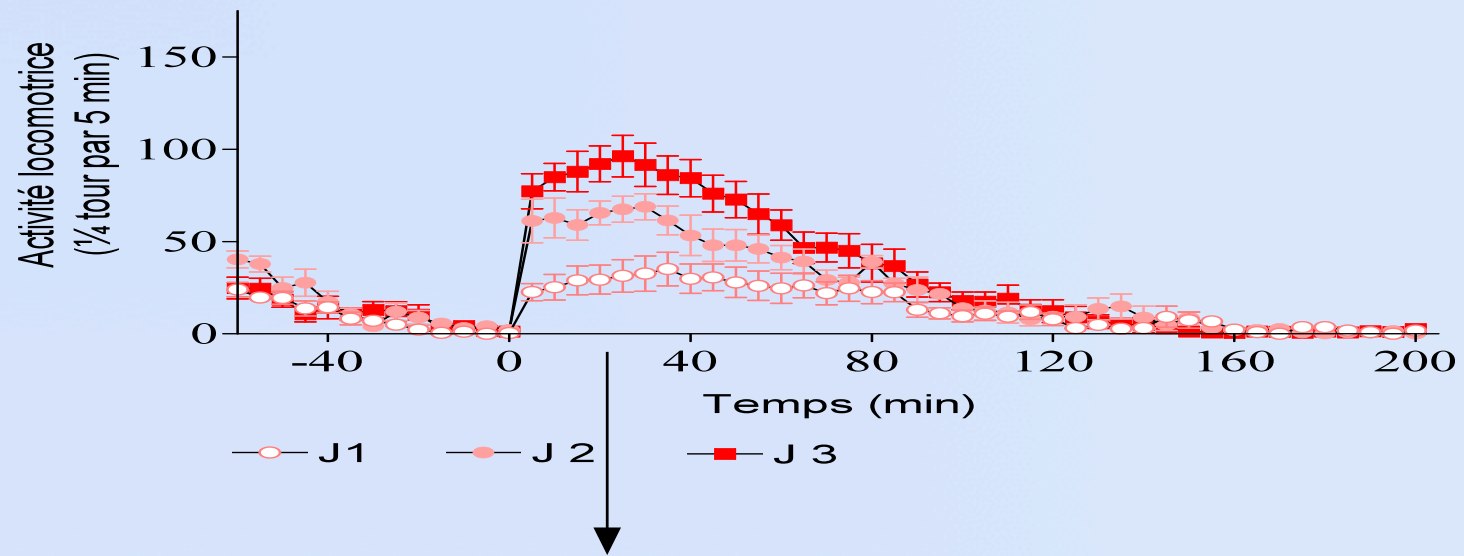


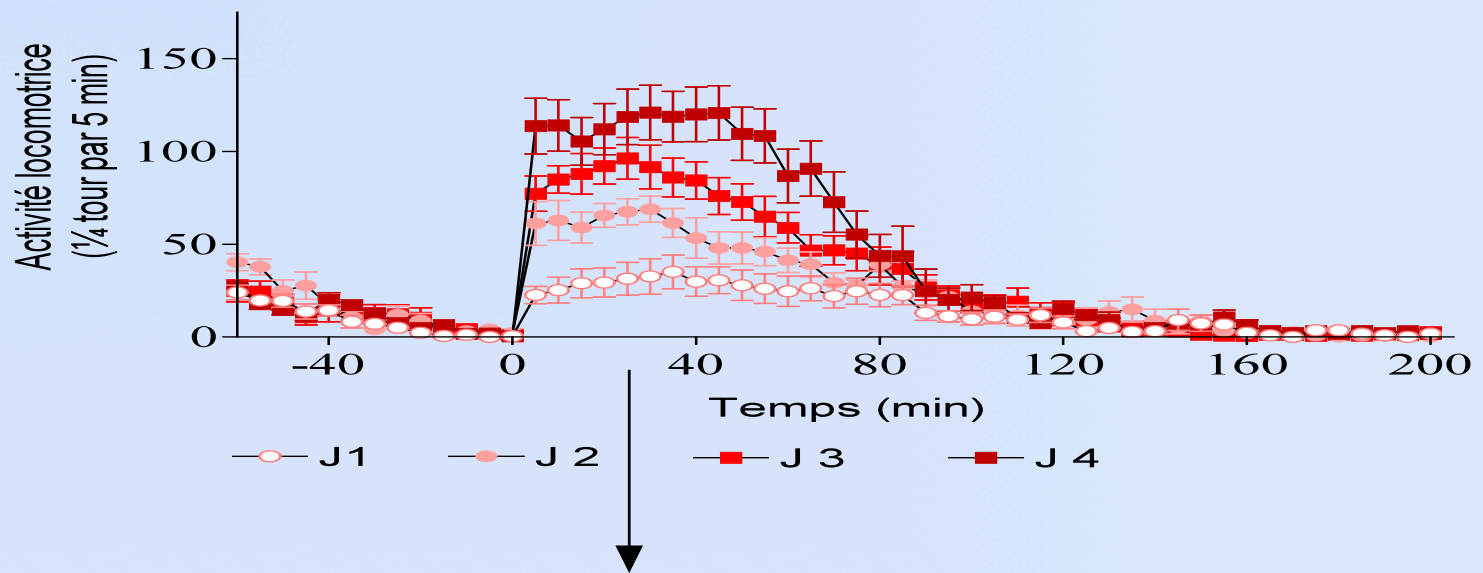




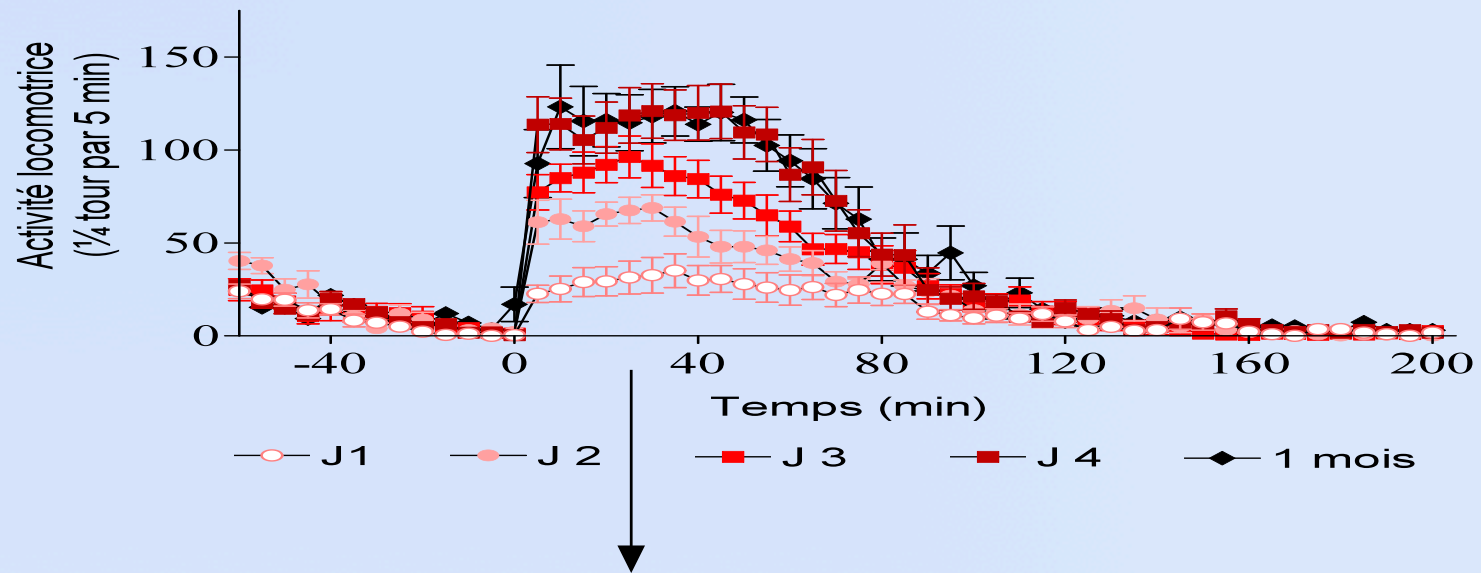




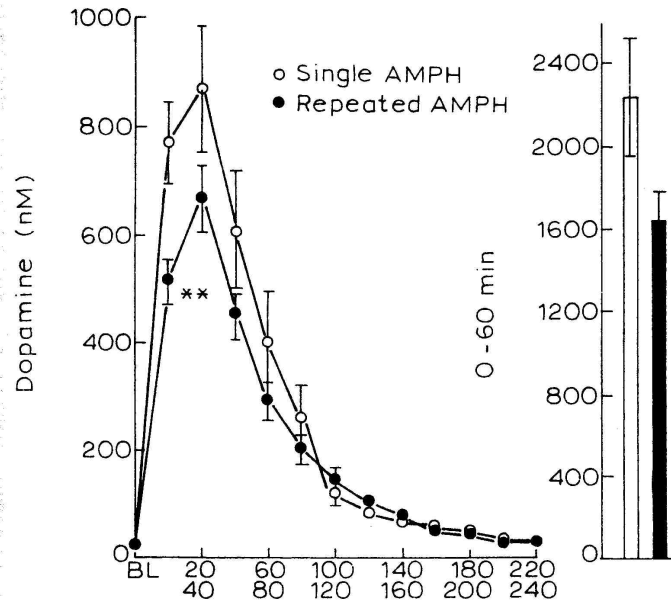




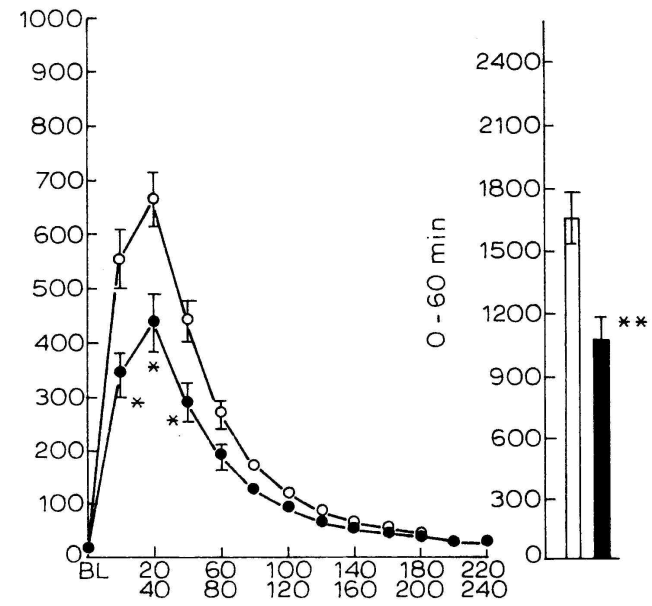
Sensibilisation comportementale



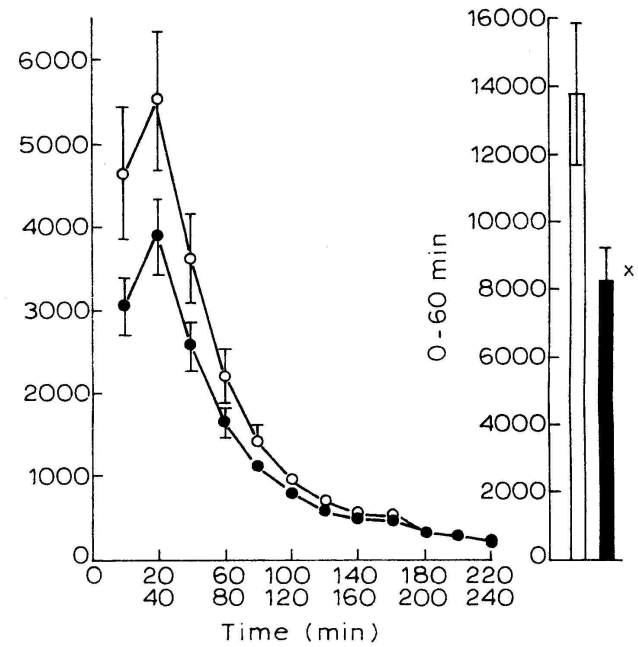
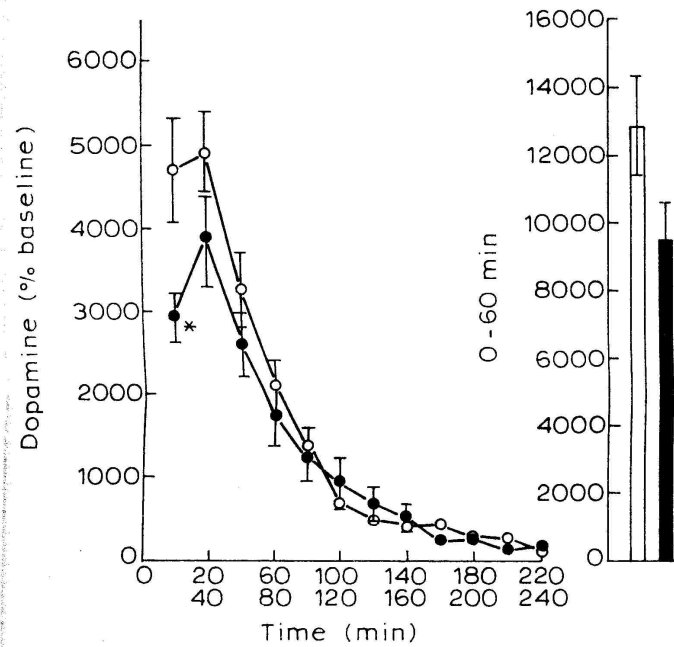
A Caudate

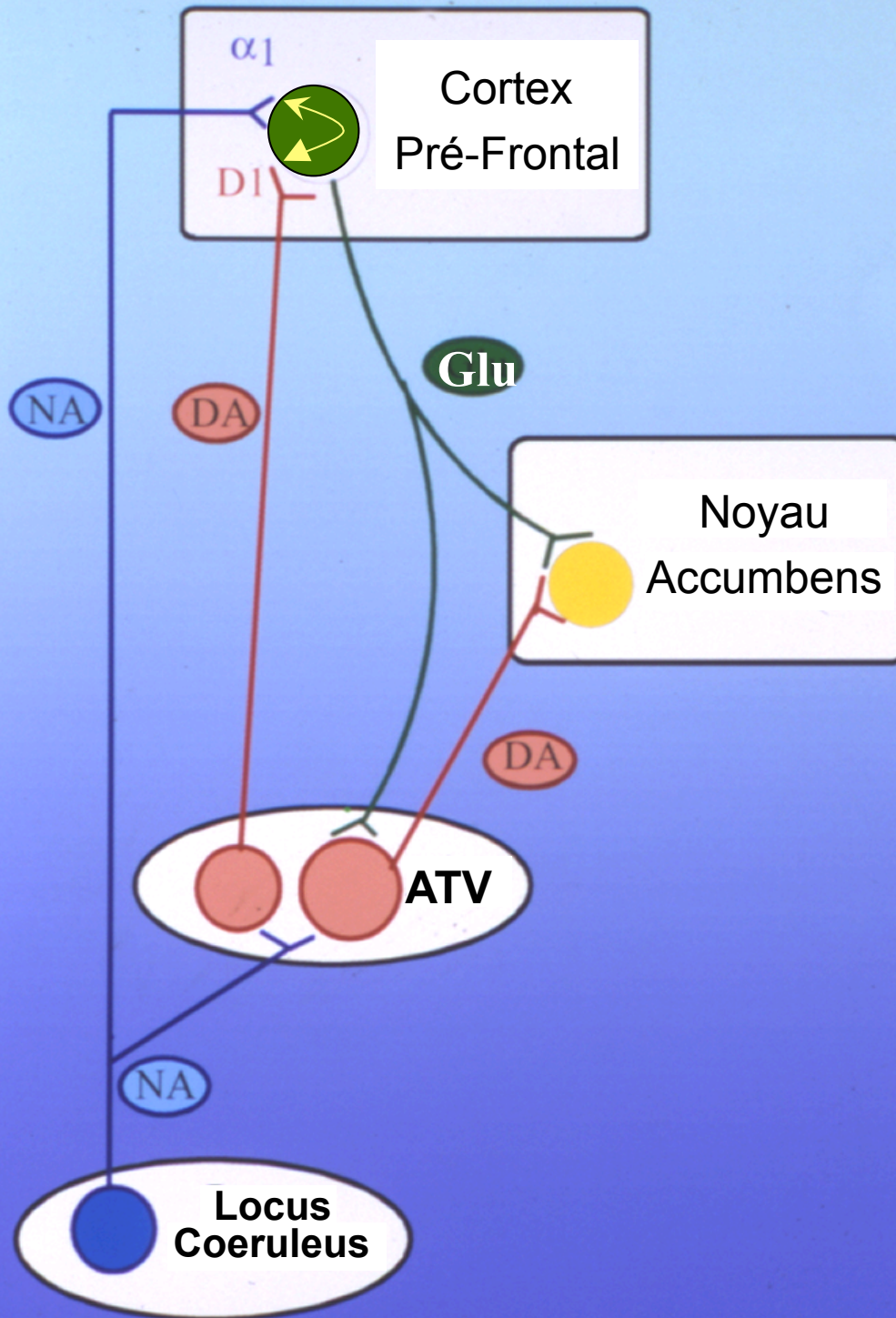


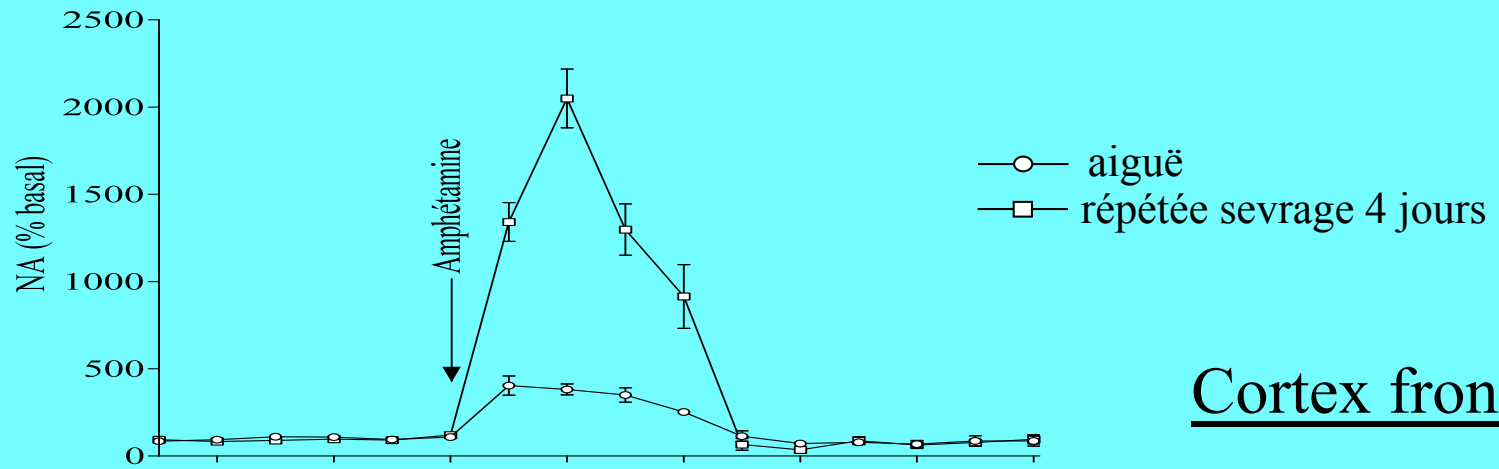
B Nucleus accumbens



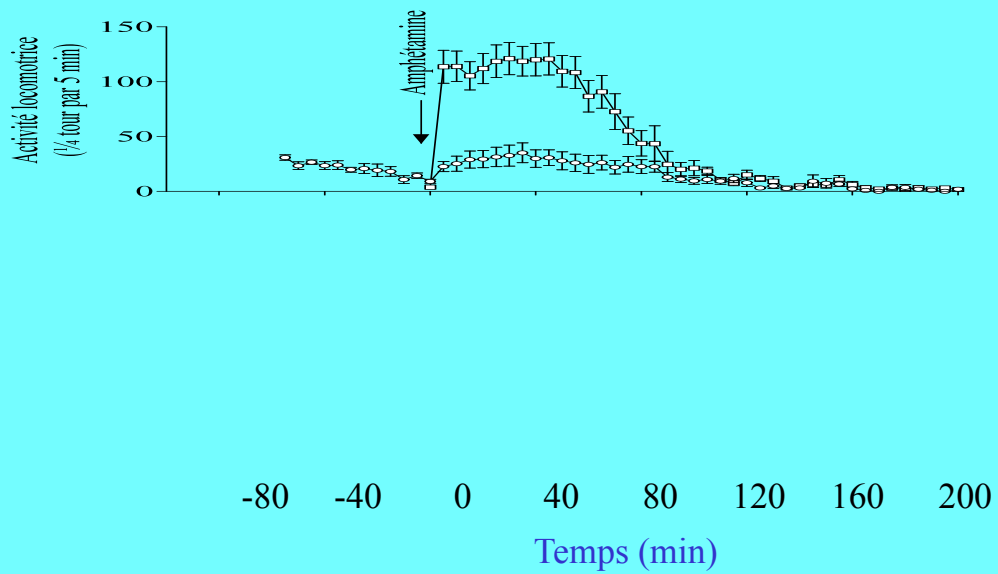
C

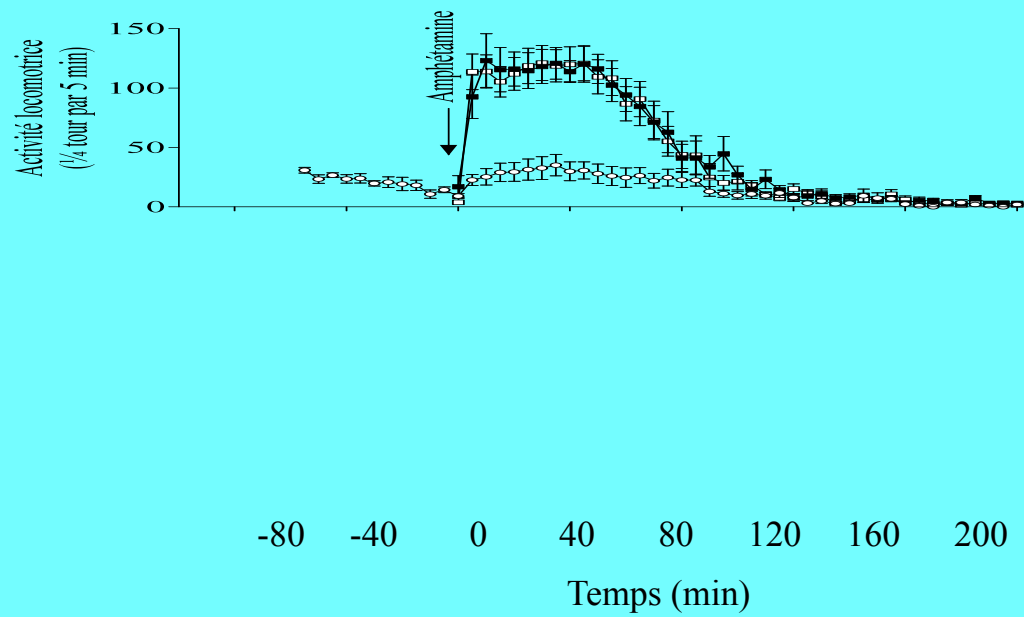
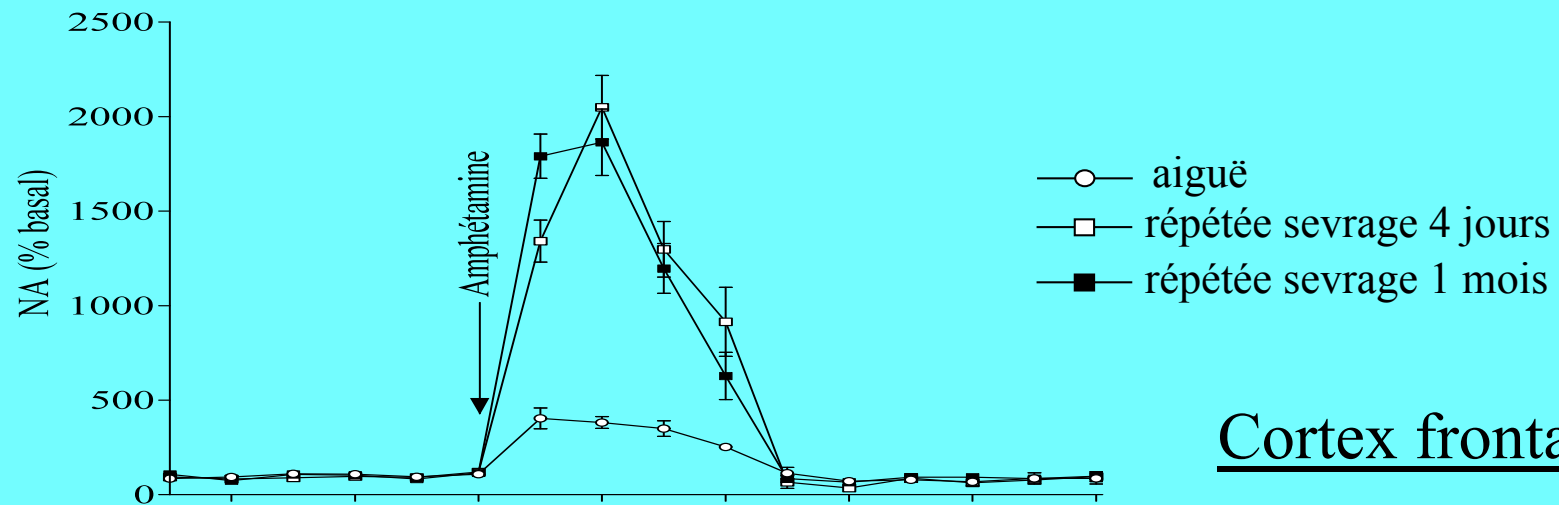


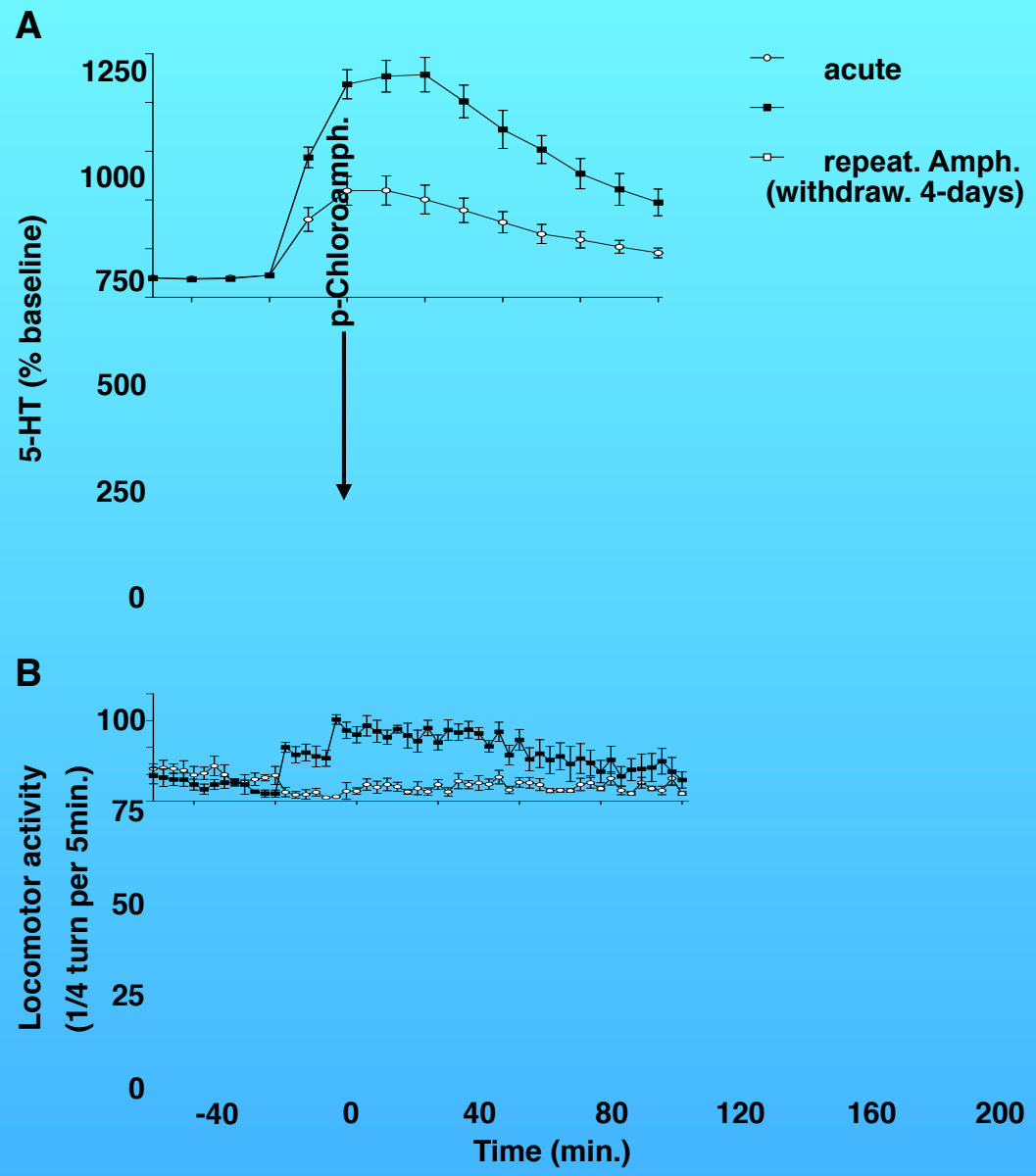




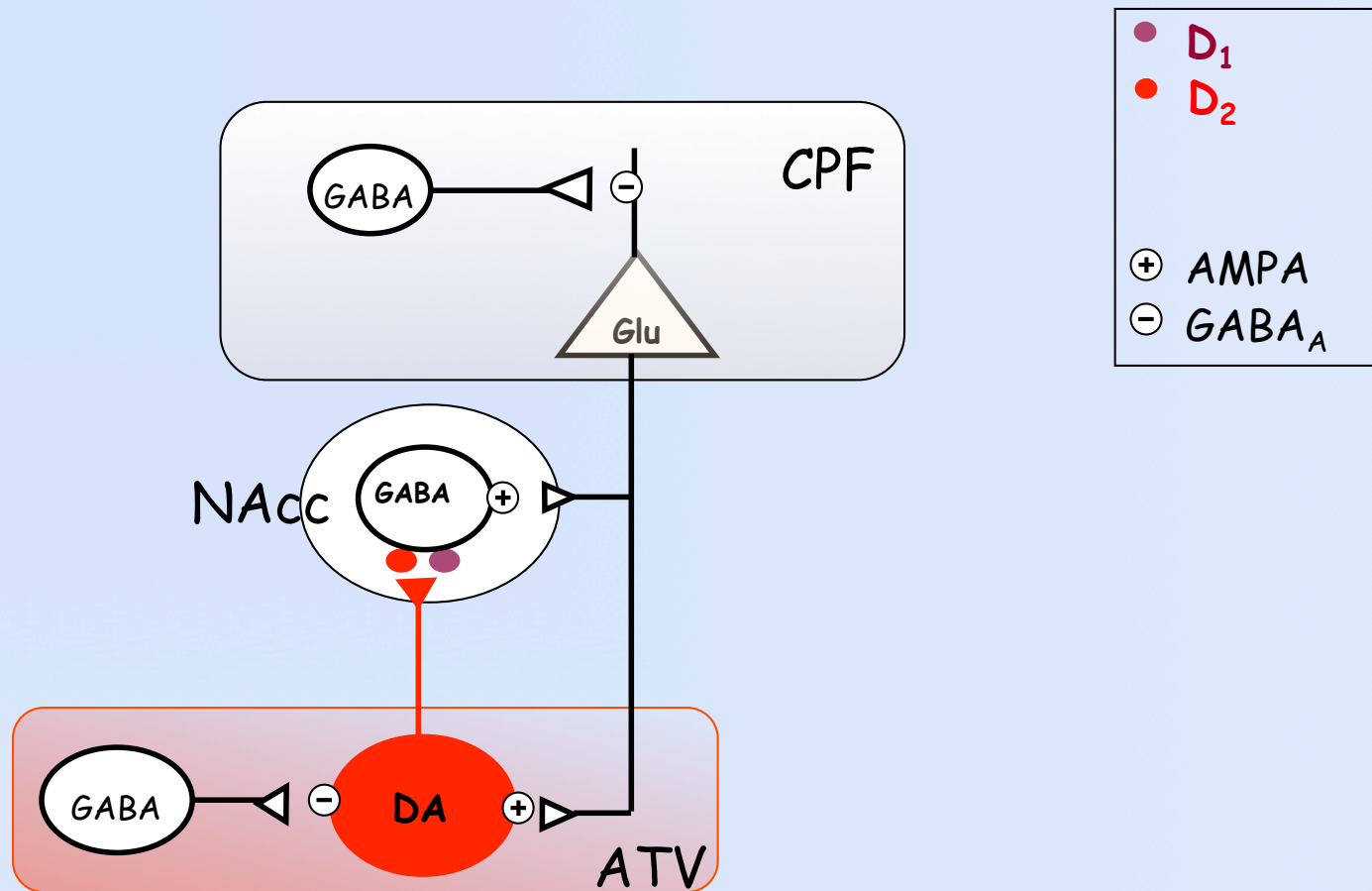
Cortex frontal

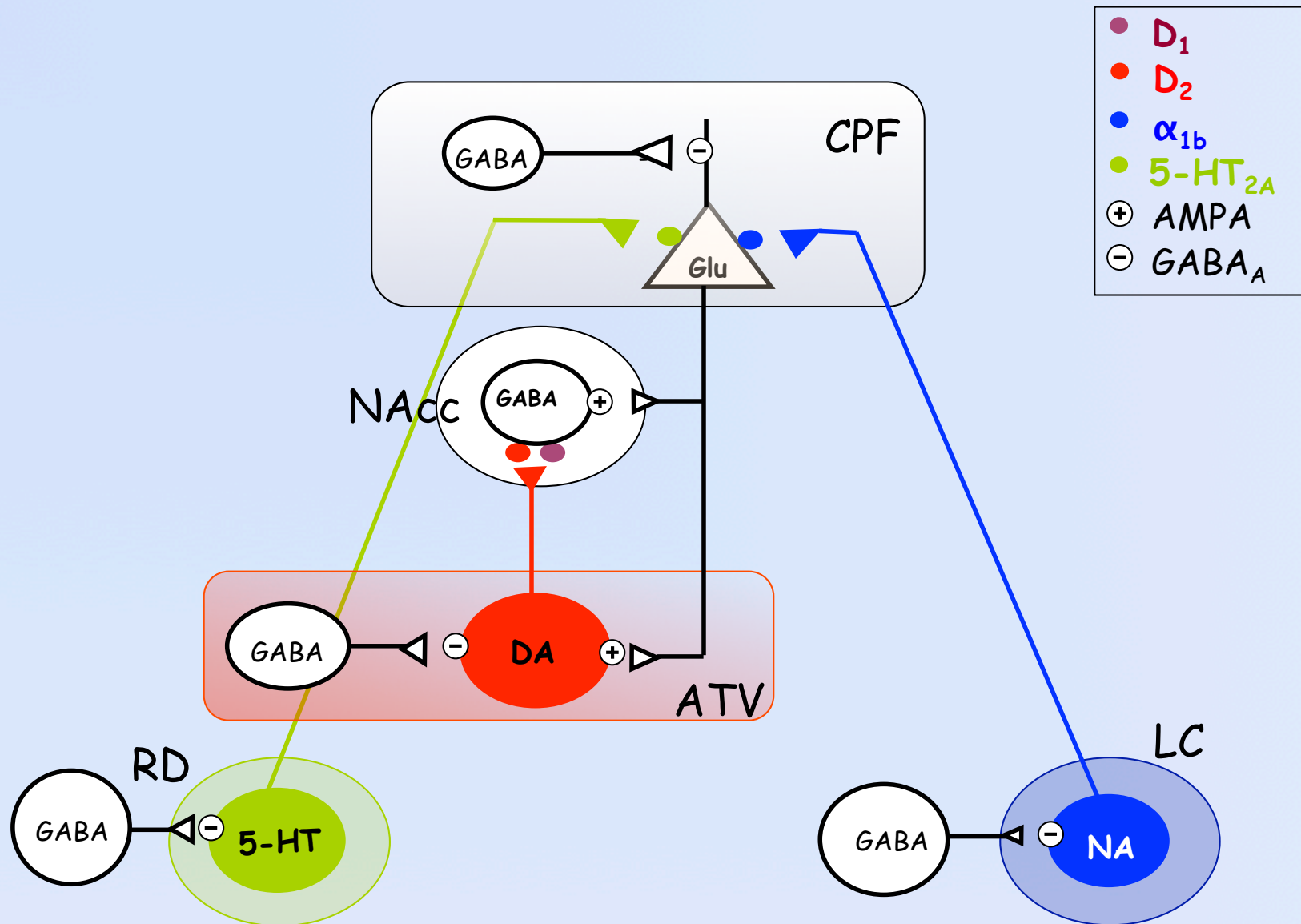


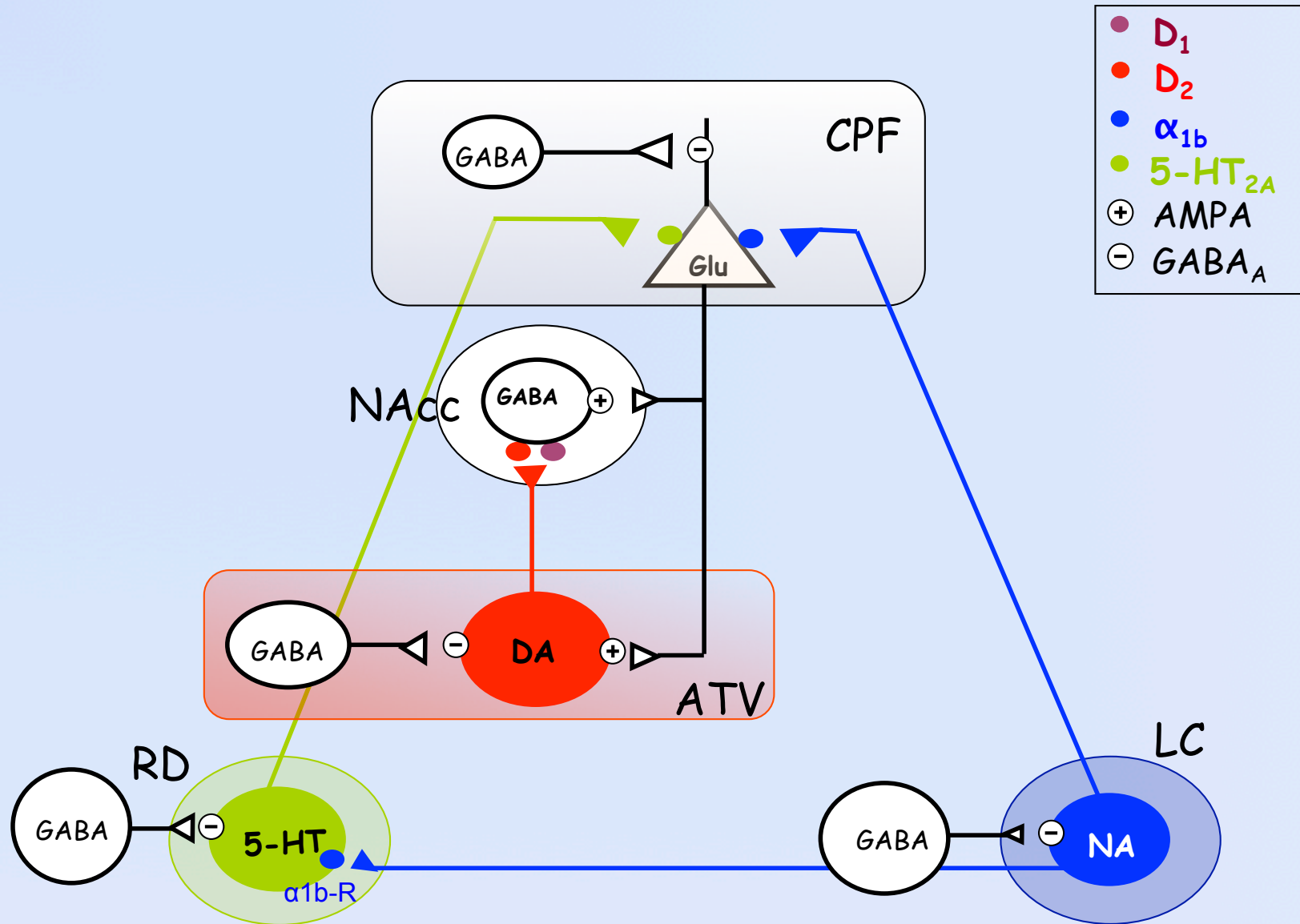


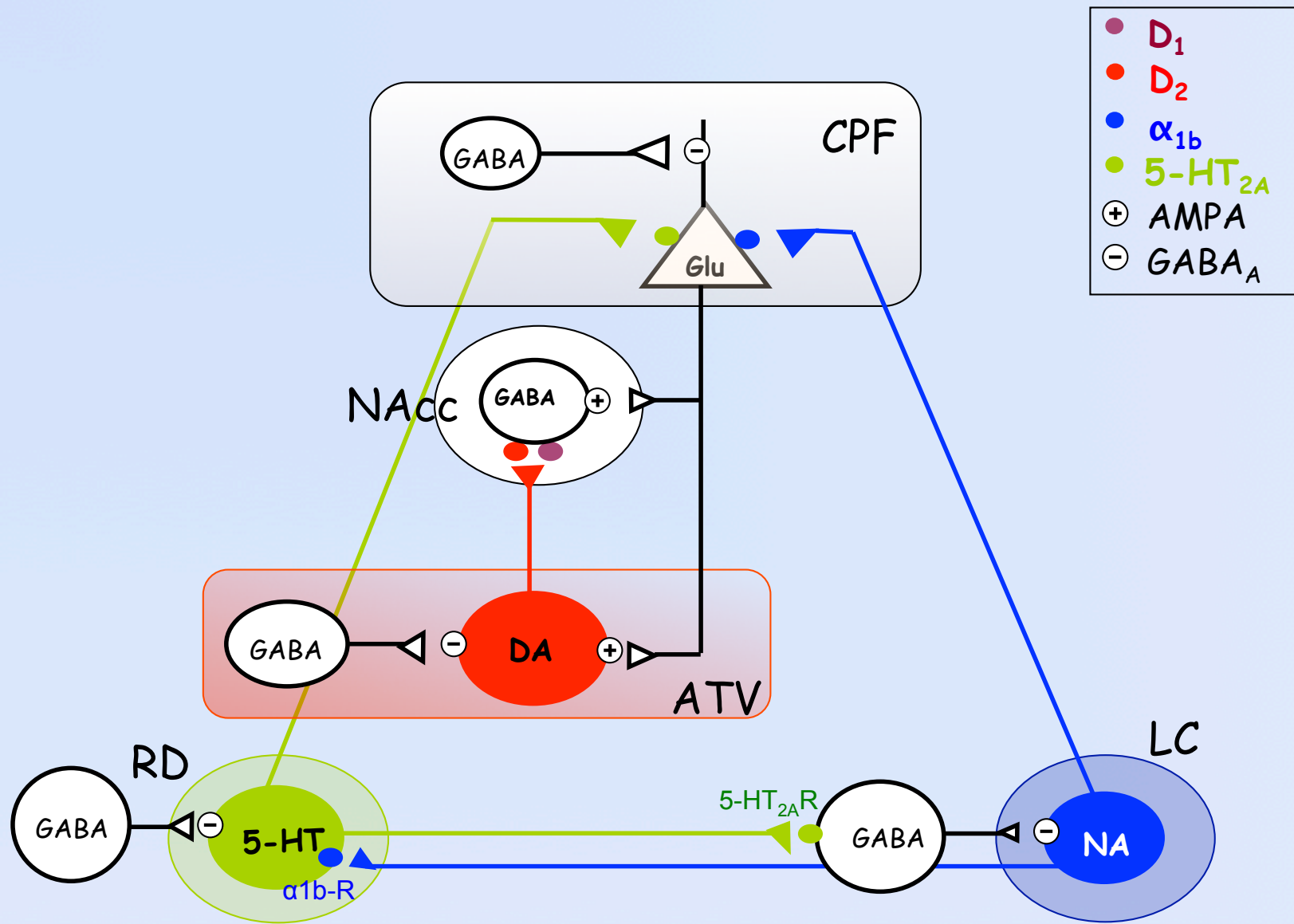


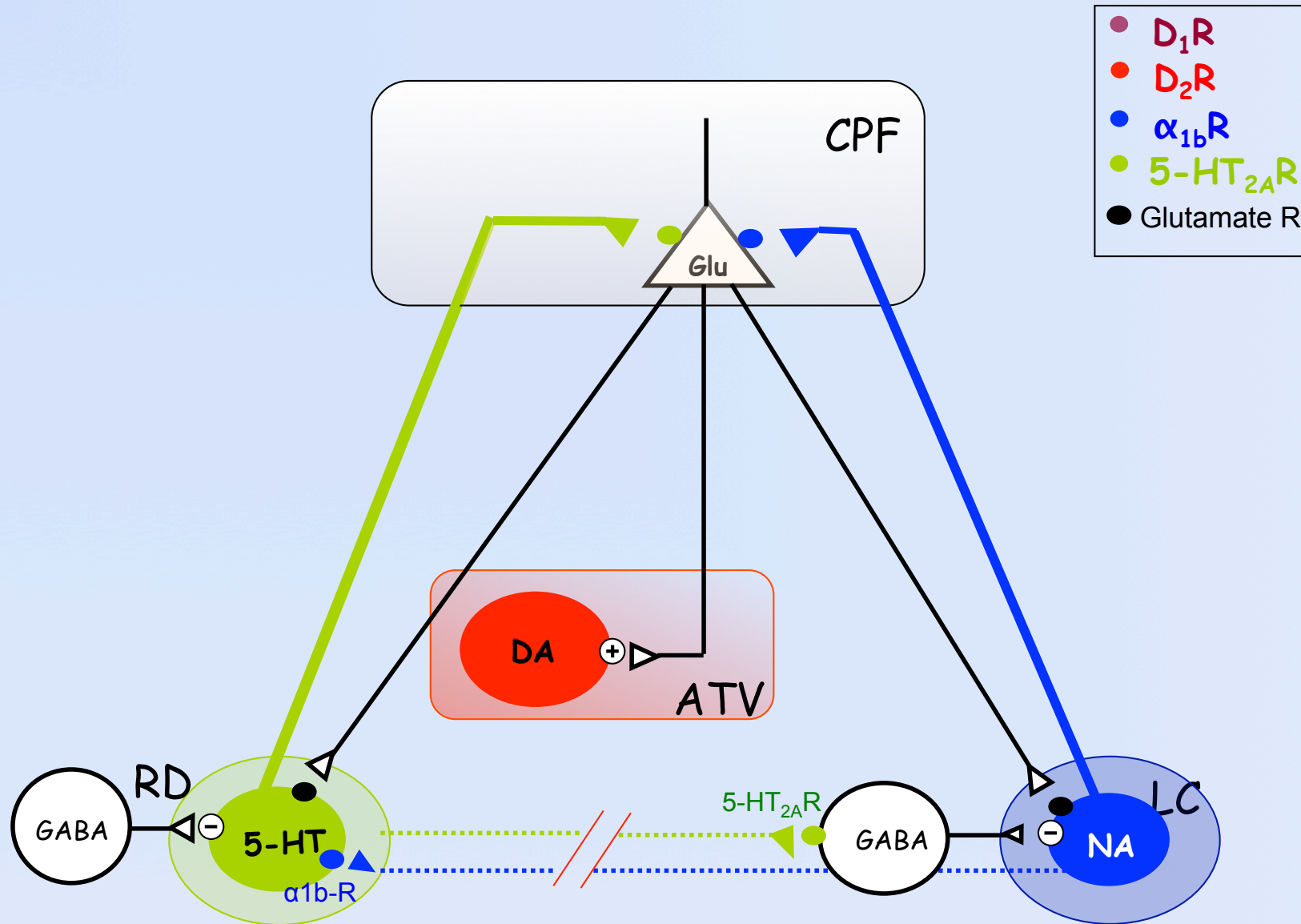
Frontal cortex

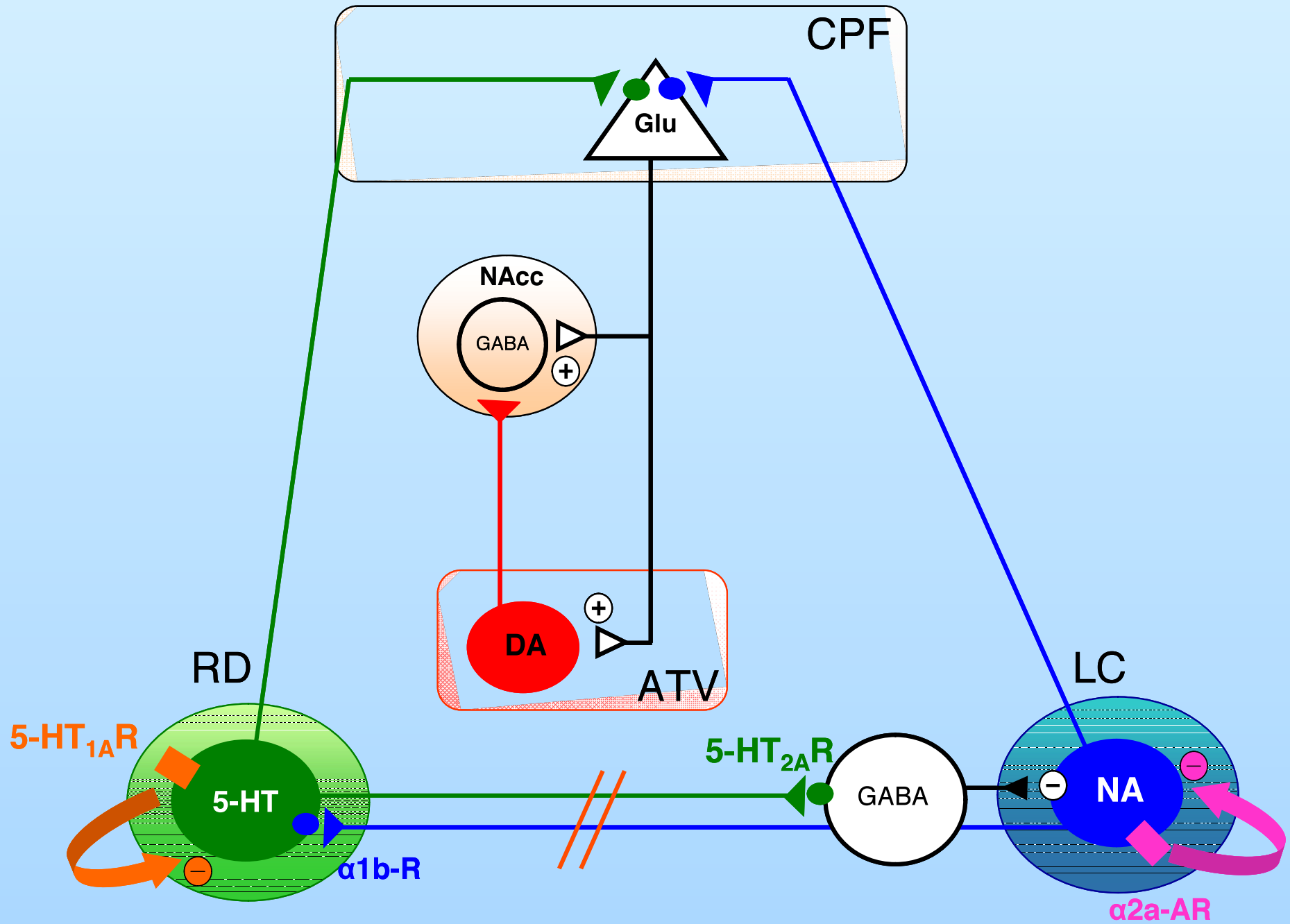










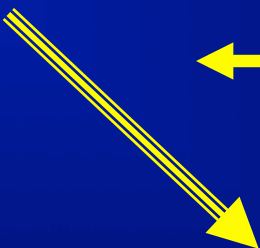


USAGE

Jus de pomme



DA



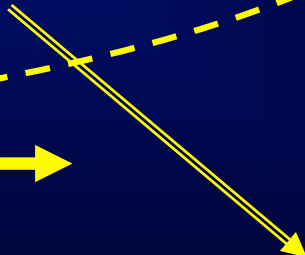
ABUS



NA / 5-HT



Drogues d'abus



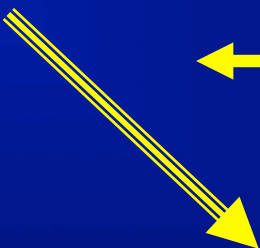
DEPENDANCE

USAGE

Jus de pomme



DA



ABUS



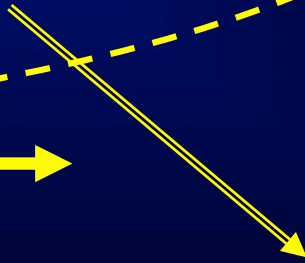
NA / 5-HT



Drogues d'abus

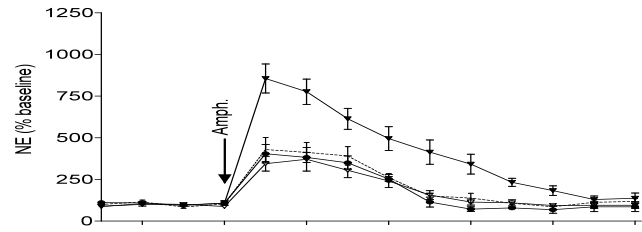


Jeu

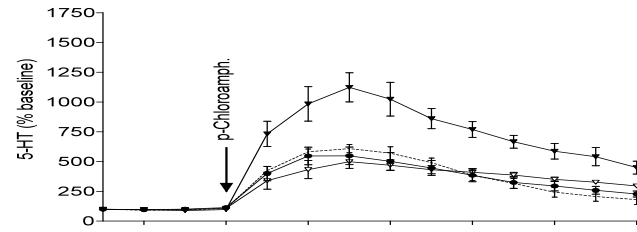


DEPENDANCE

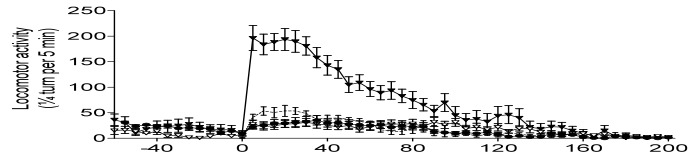
Cocaine



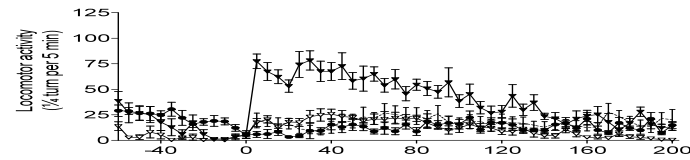
A



C



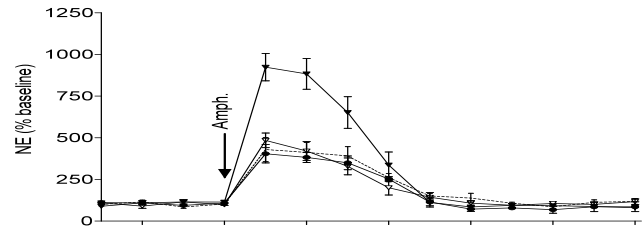
B



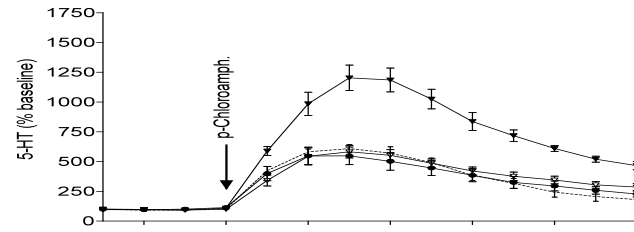
D

● acute repeated saline ▲ repeated cocaine ▽ repeated SR/Pz + cocaine

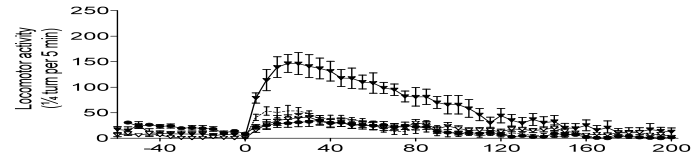
Morphine



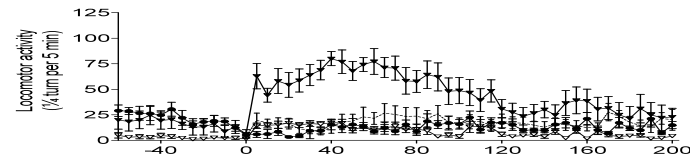
A



C



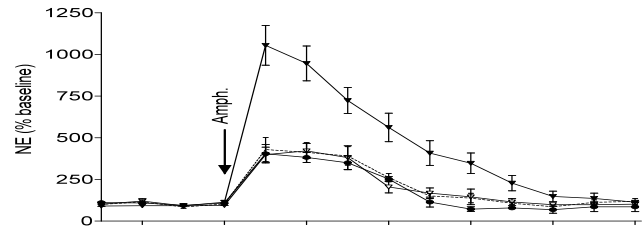
B



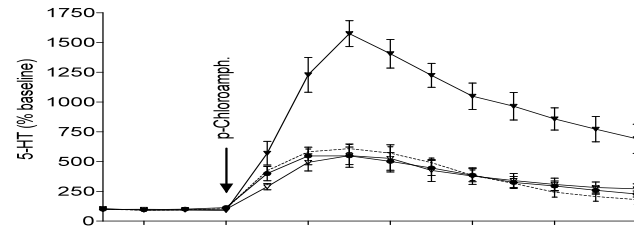
D

● acute repeated saline ▲ repeated morphine ▽ repeated SR/Pz + morphine

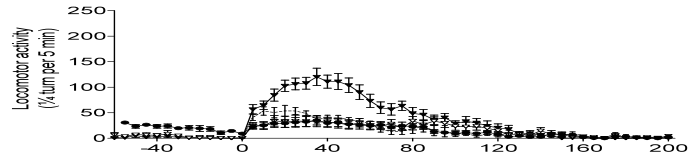
Ethanol



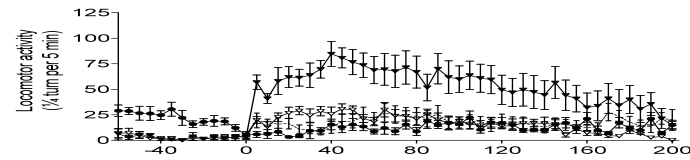
A



C



B



D

● acute repeated saline ▼ repeated ethanol ▽ repeated SR/Pz + ethanol

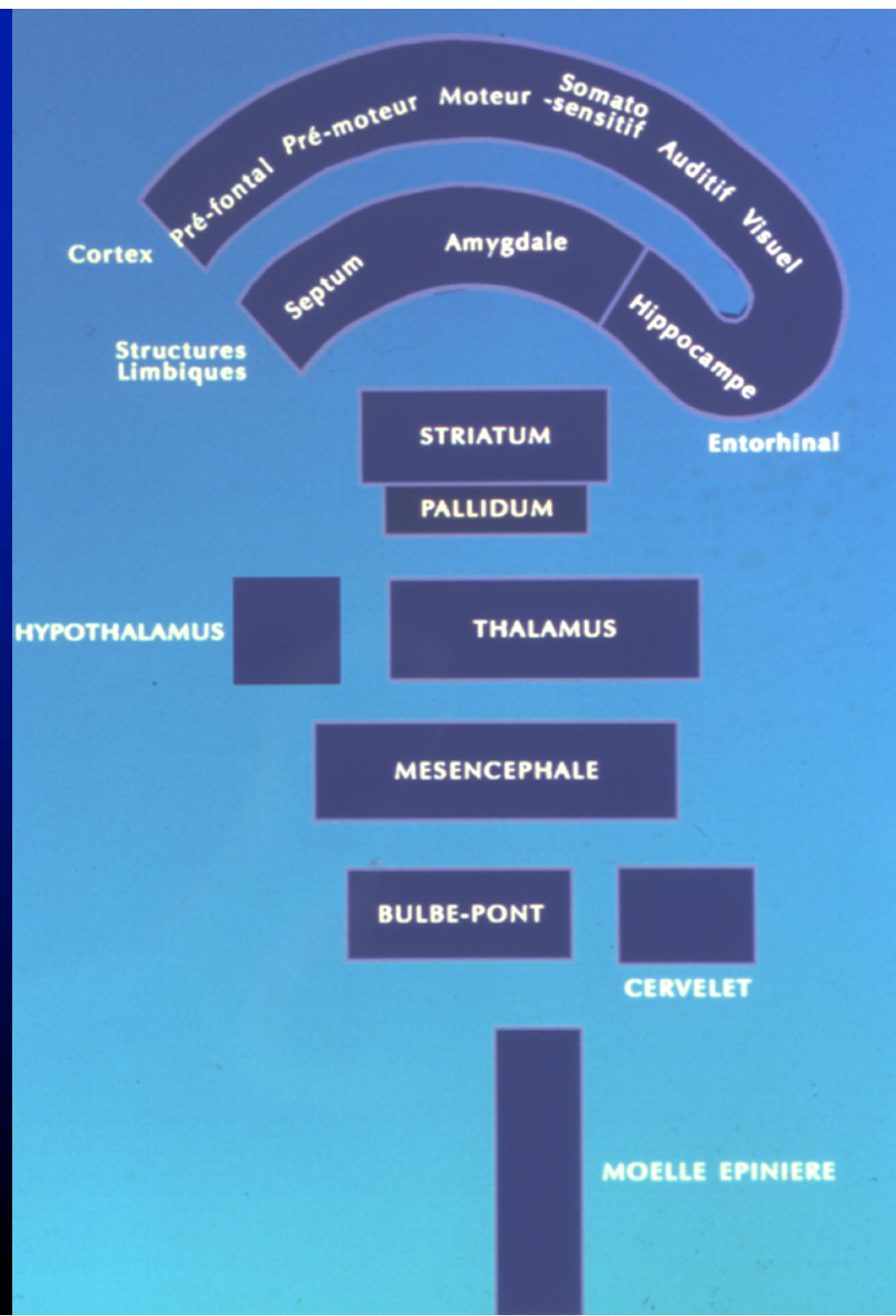
5-HT NA **DA**

GABA
ACIDE GLUTAMIQUE
NEUROPEPTIDES

1% — NEURONES — 99%

ÉMETTEUR DIFFUS (modèle radiophonique) ← INFORMATION → POINT à POINT (modèle téléphonique)

MODULATEURS → RÉSEAUX



CORTEX
CÉRÉBRAL

STRUCTURES
LIMBIQUES

HYPOTHALAMUS

MÉSENCÉPHALE

BULBE/PONT

STRIATUM/
PALLIDUM

THALAMUS

ŒIL

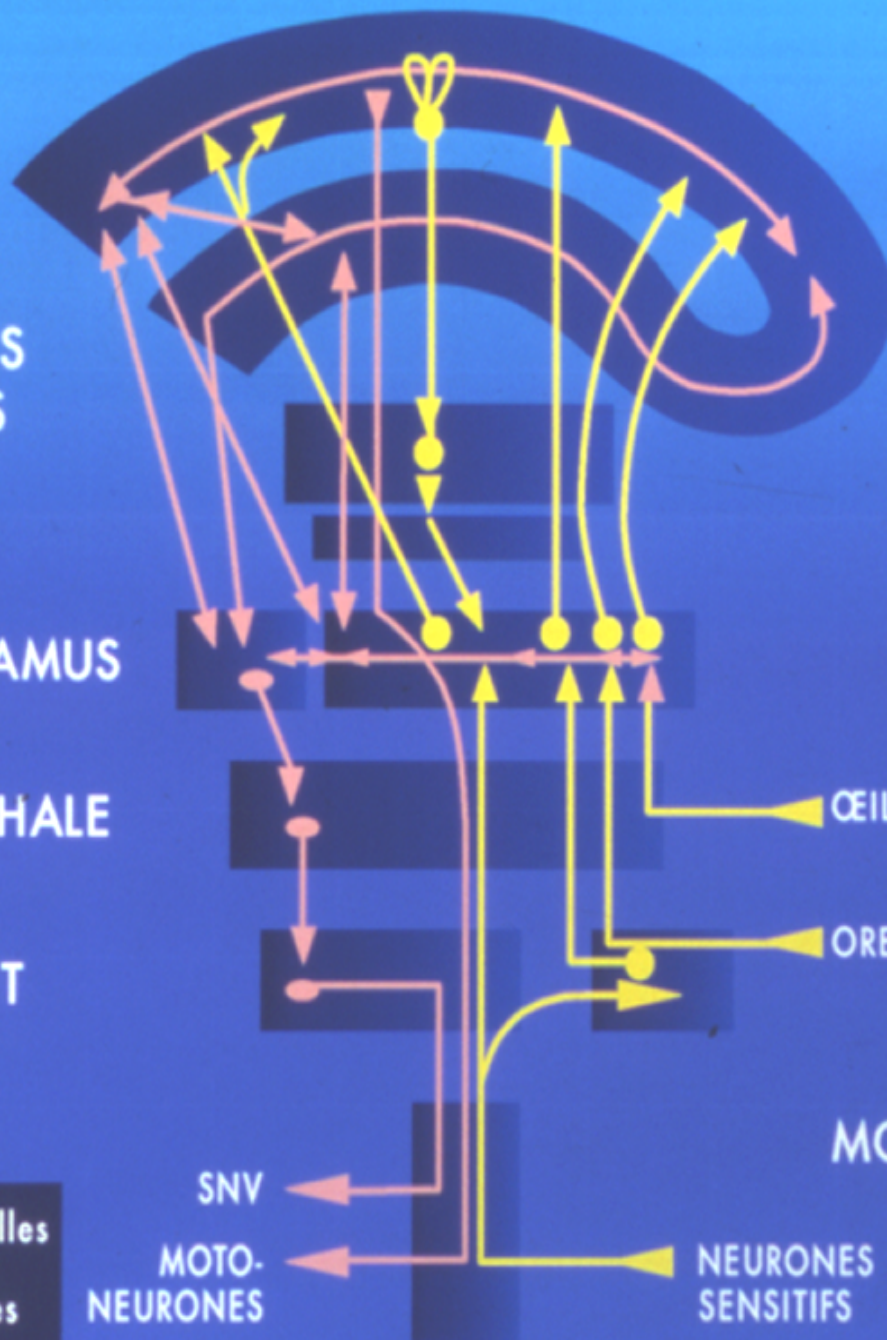
OREILLE

MOELLE ÉPINIÈRE

— Voies somato-sensorielles
— Voies neuro-végétatives
et affectives

SNV
MOTO-
NEURONES

NEURONES
SENSITIFS



CORTEX
CÉRÉBRAL

STRUCTURES
LIMBIQUES

HYPOTHALAMUS

MÉSENCÉPHALE

BULBE/PONT

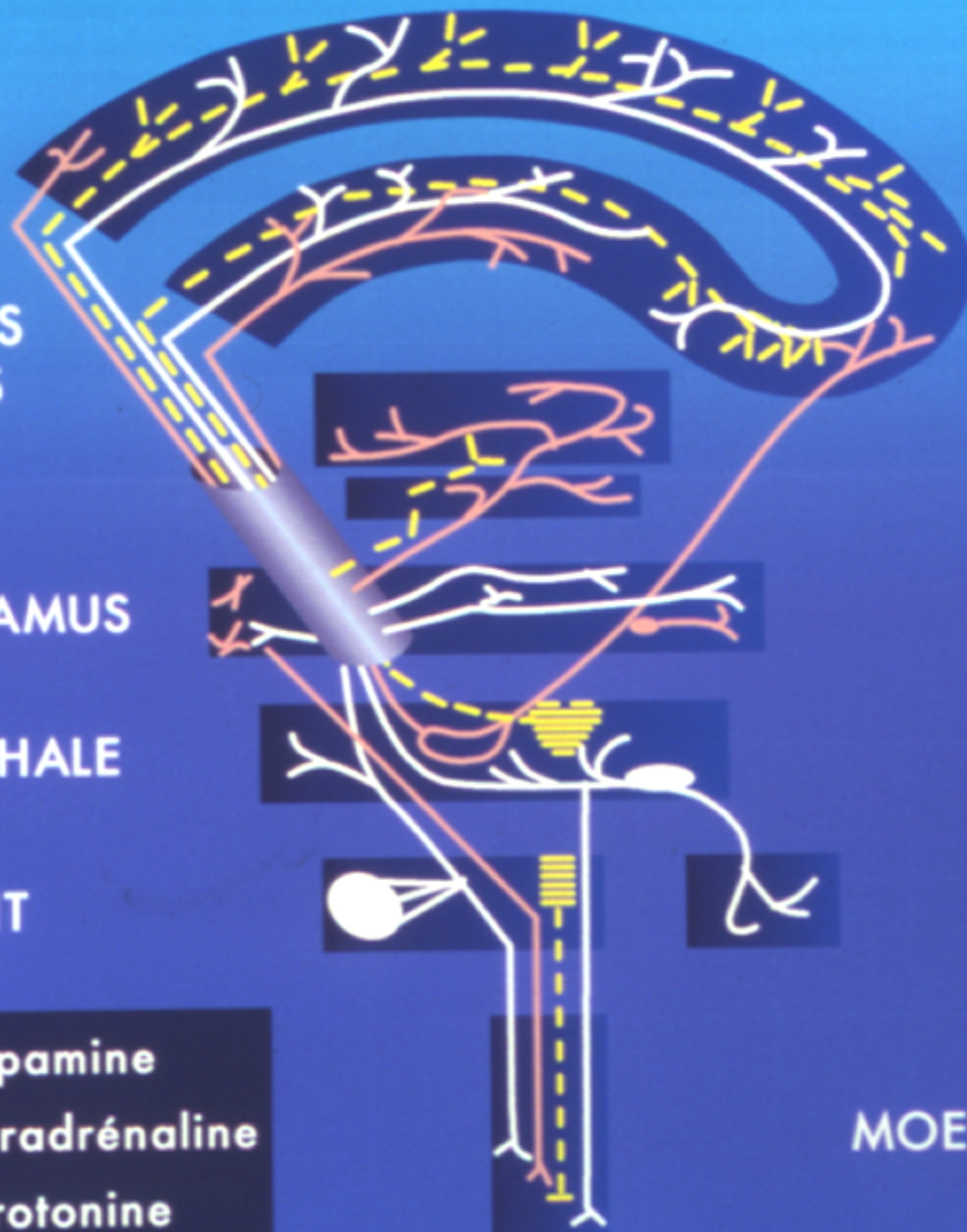
○ — Dopamine
○ — Noradrénaline
||| — Sérotonine

STRIATUM/
PALLIDUM

THALAMUS

CERVELET

MOELLE ÉPINIÈRE



**LES NEURONES MONOAMINERGIQUES
PRESENTENT
DES DIFFERENCES FONCTIONNELLES**

**Neurones
noradrénergiques**



**Sélection et
amplification
des informations externes**

**Neurones
sérotoninergiques**



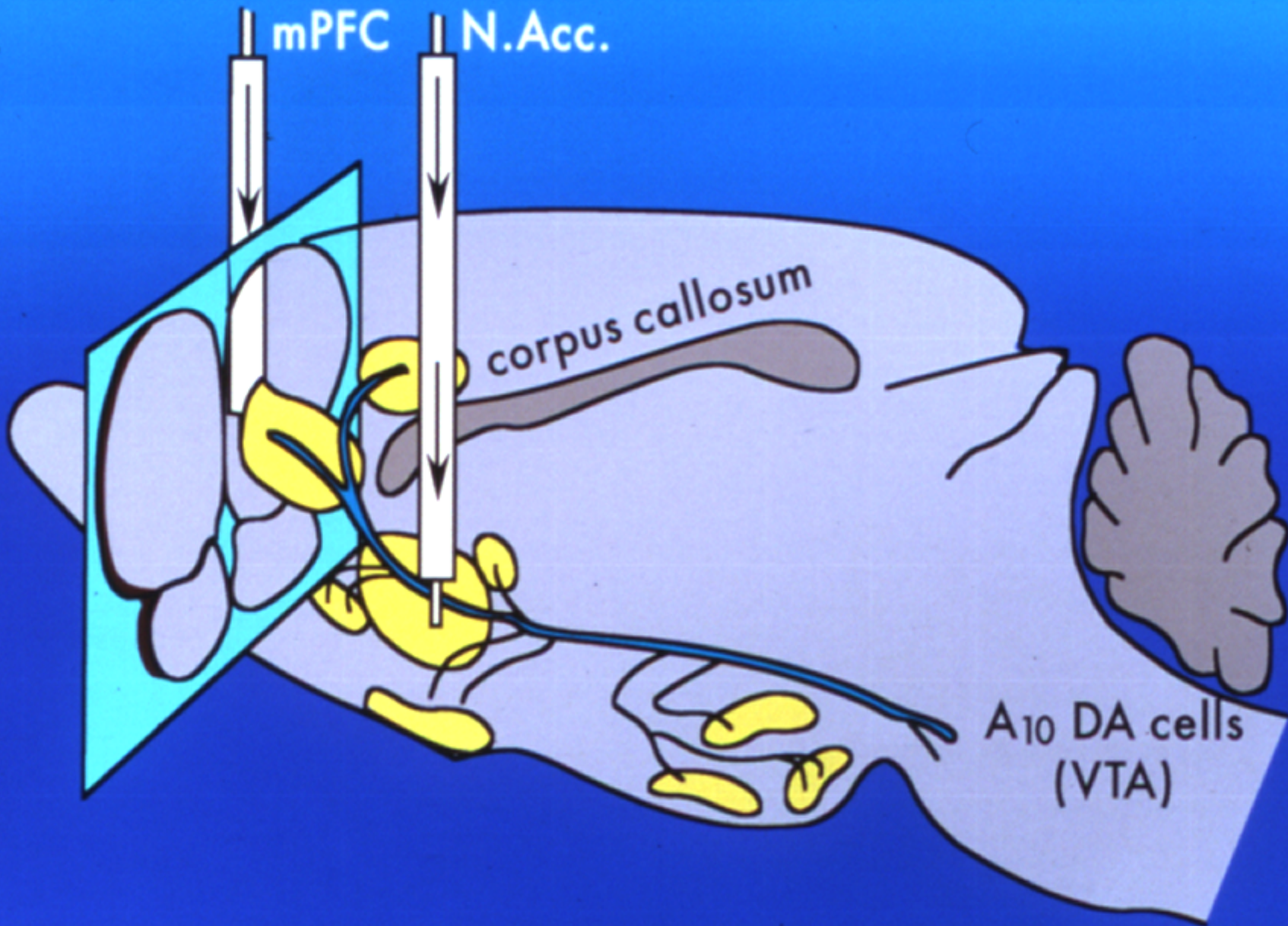
**Maintien
du traitement
des informations internes**

**Neurones
dopaminergiques**

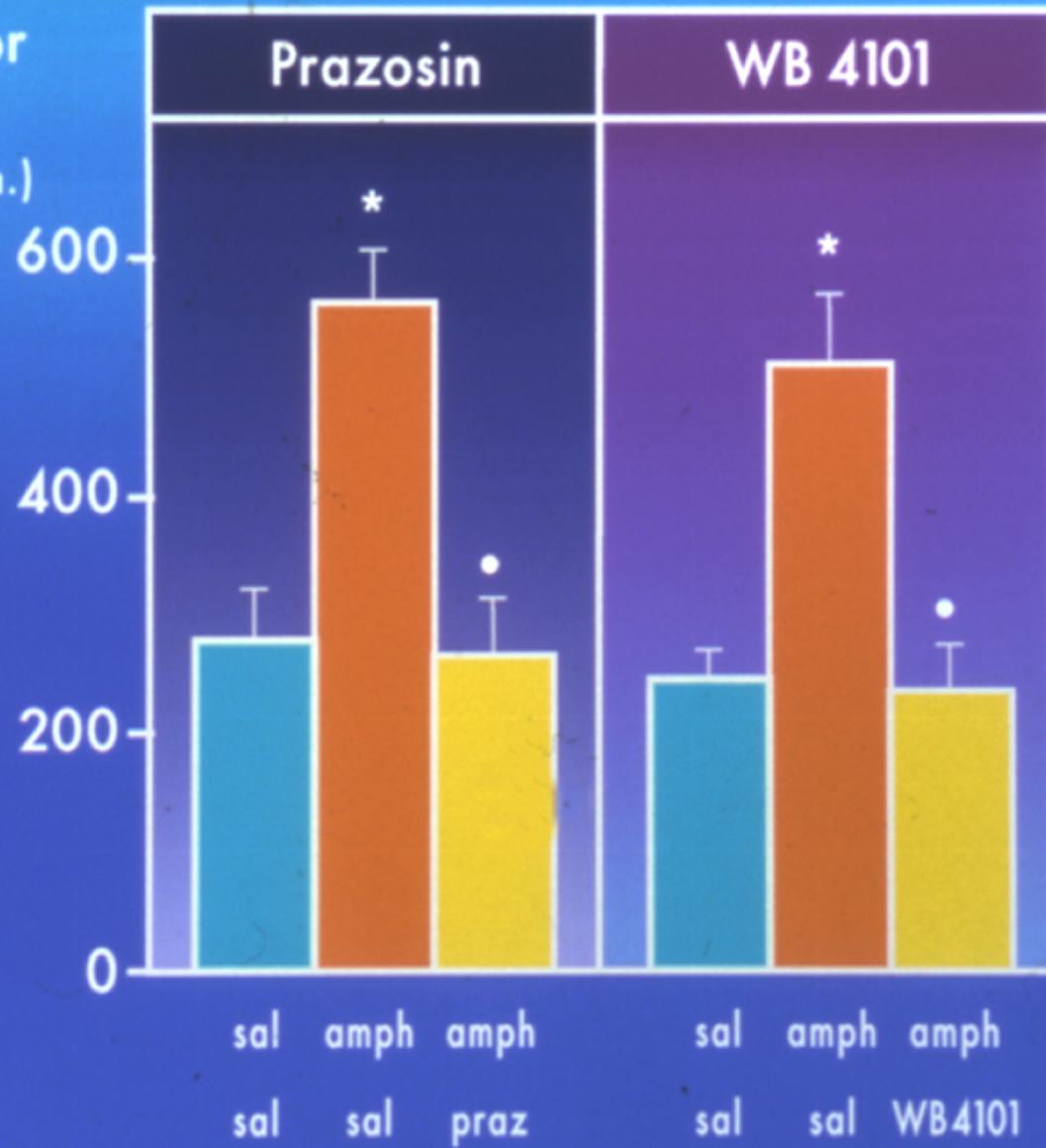


**Décodage
de la signification
des informations
externes et internes**

INJECTIONS



Locomotor activity
(counts/30 min.)

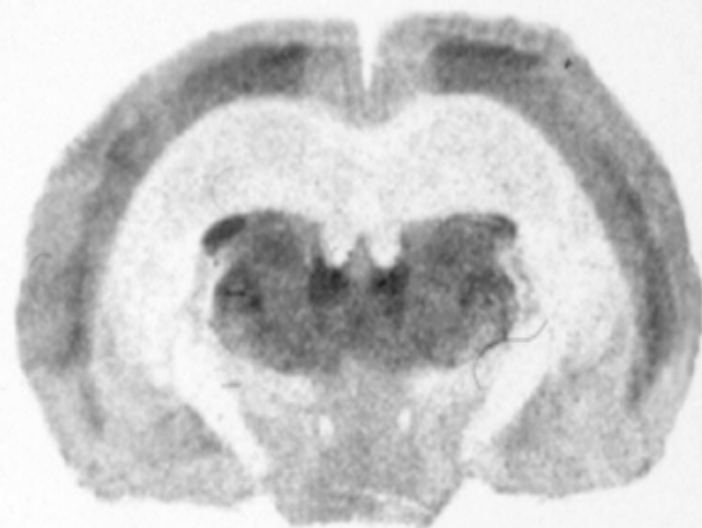
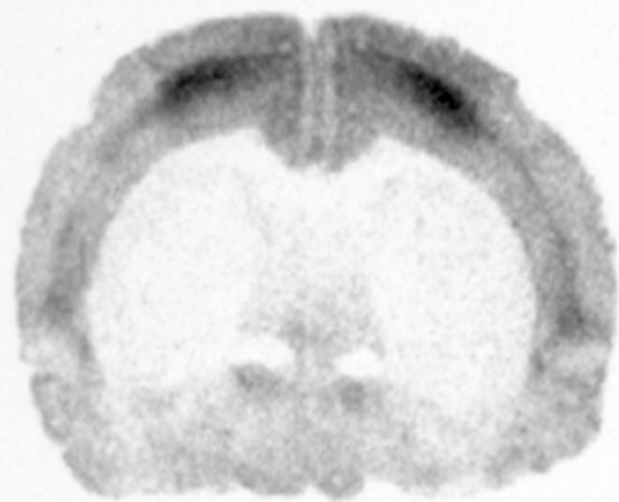
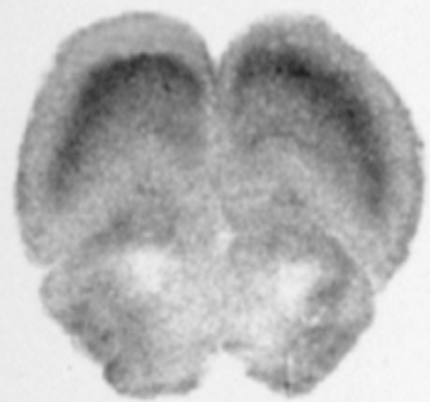


N.Acc.

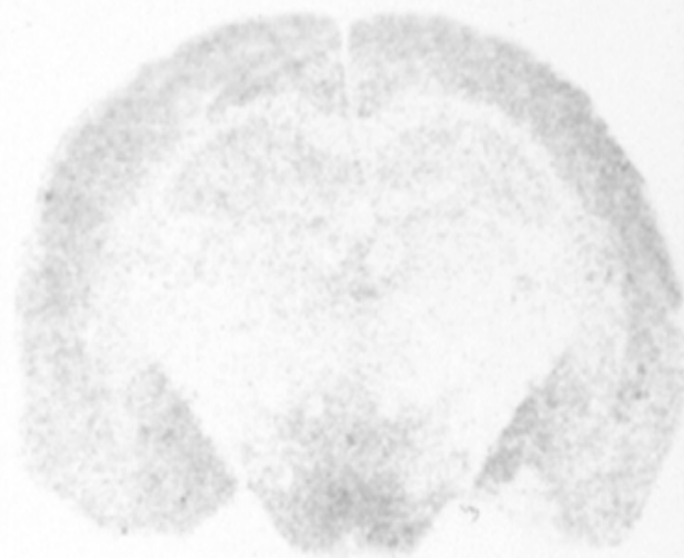
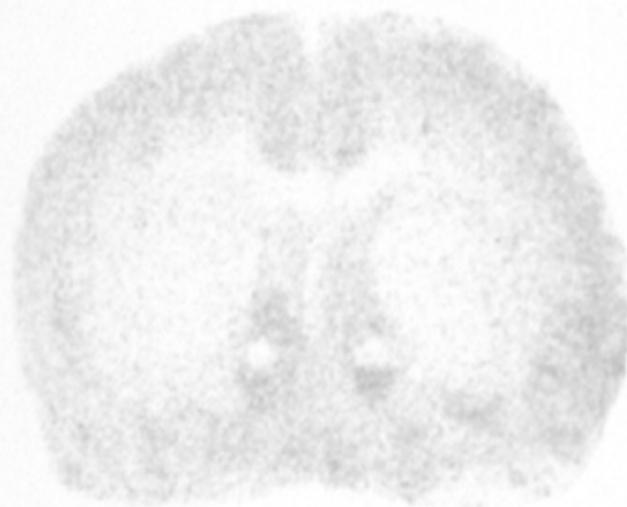
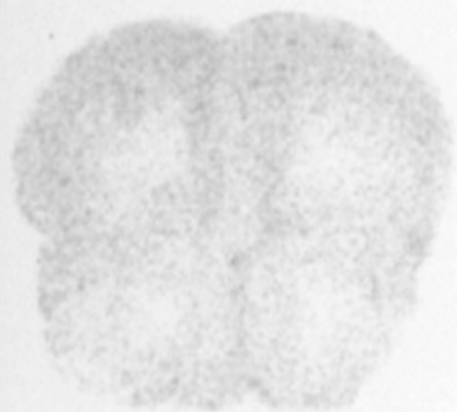
PFC

^3H -Prazosin

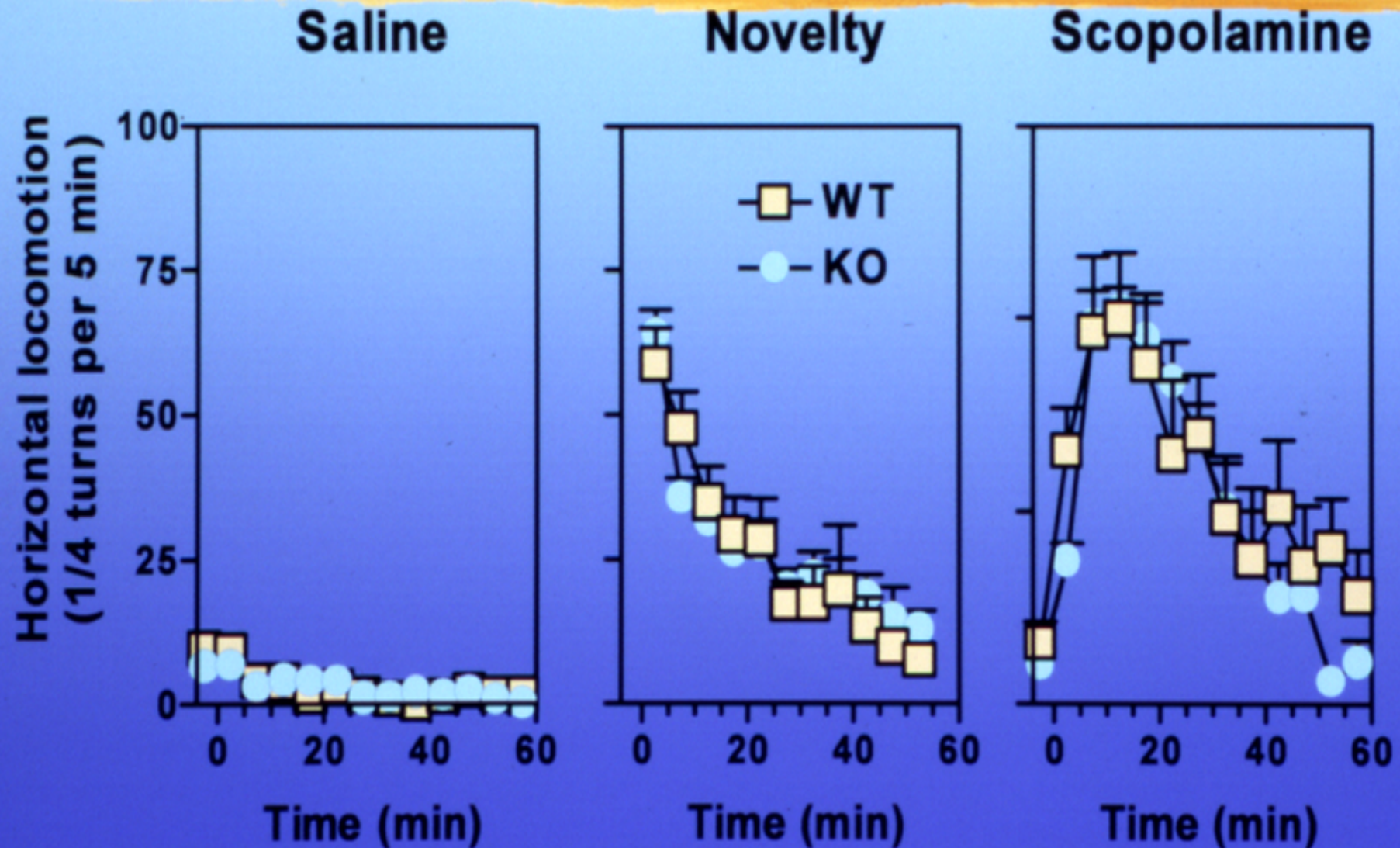
WT



KO



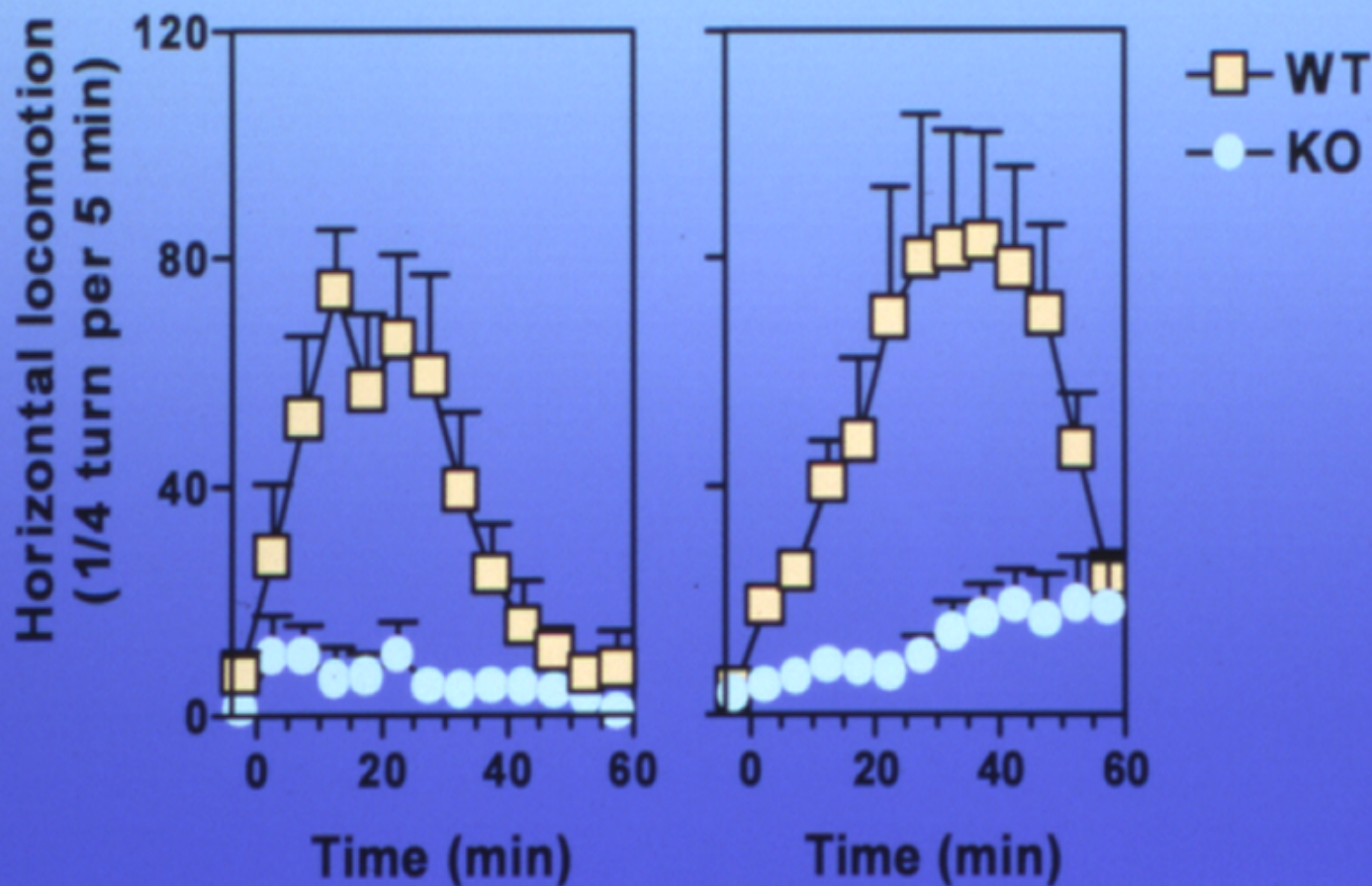
Locomotor responses to saline injection, novelty and scopolamine



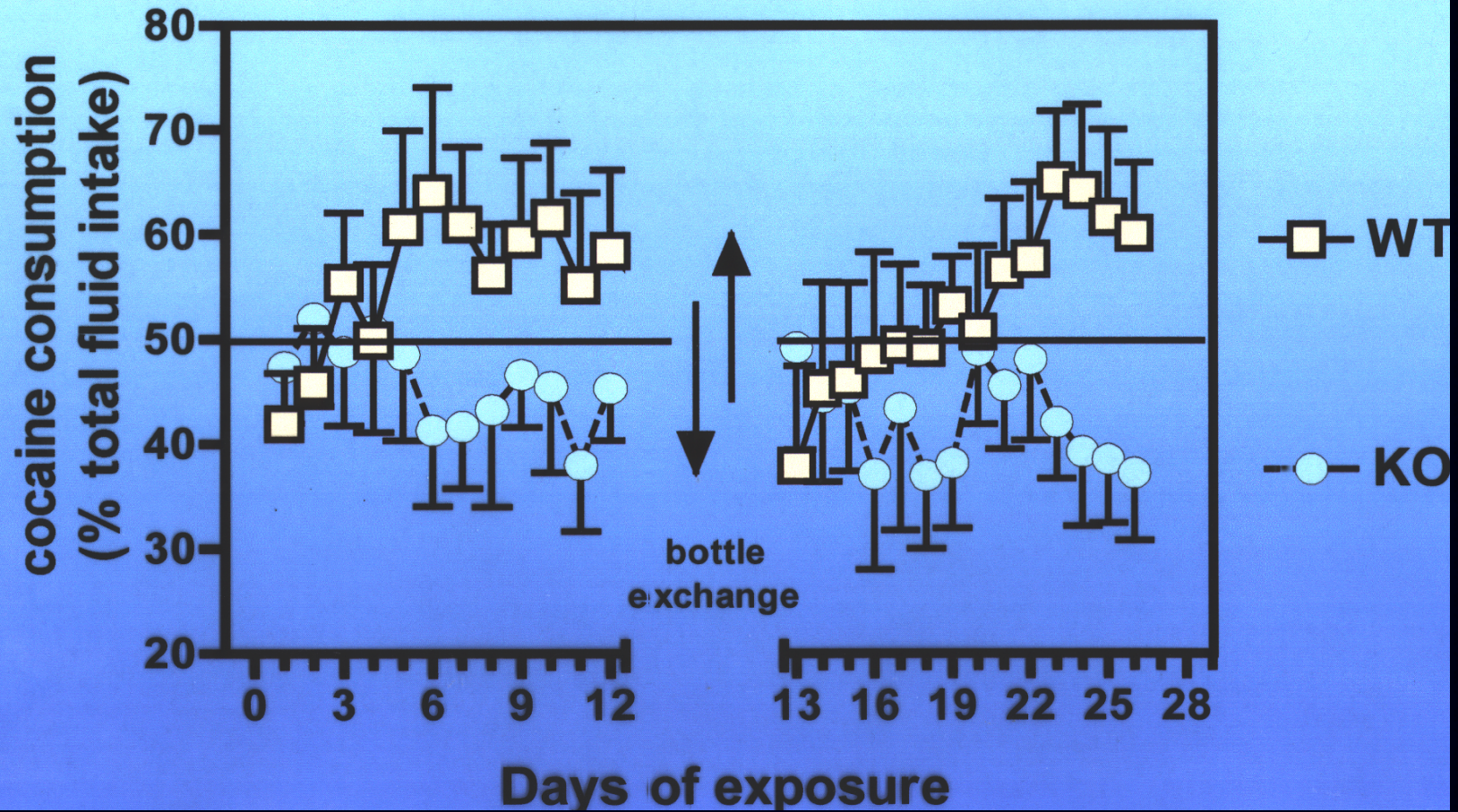
Alpha1b-adrenergic receptor knockout Response to psychostimulants

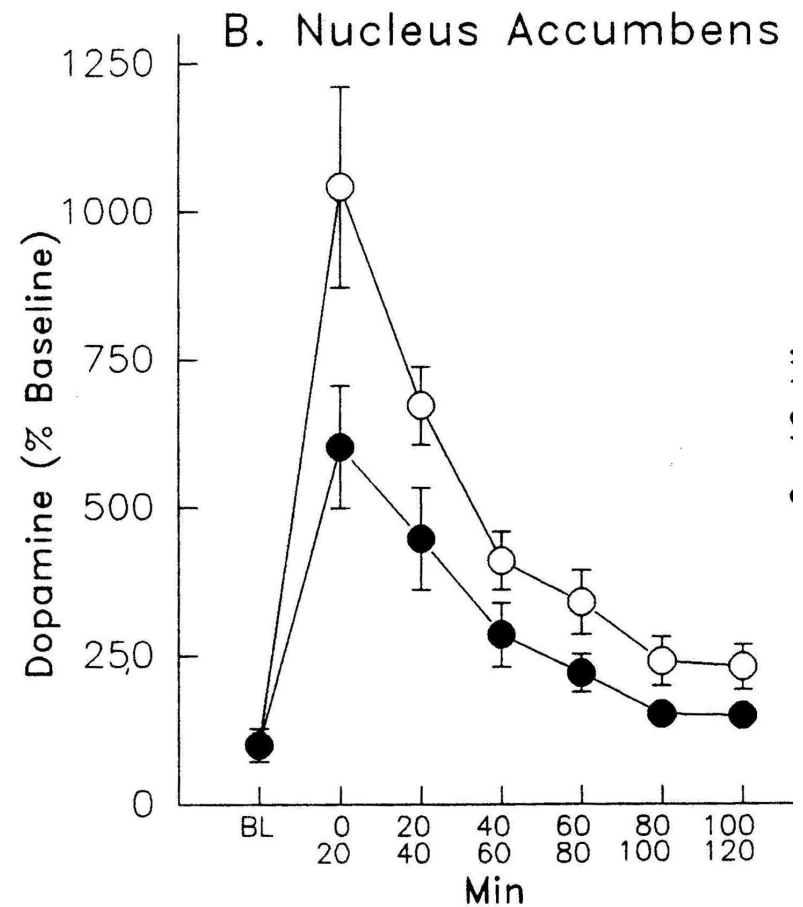
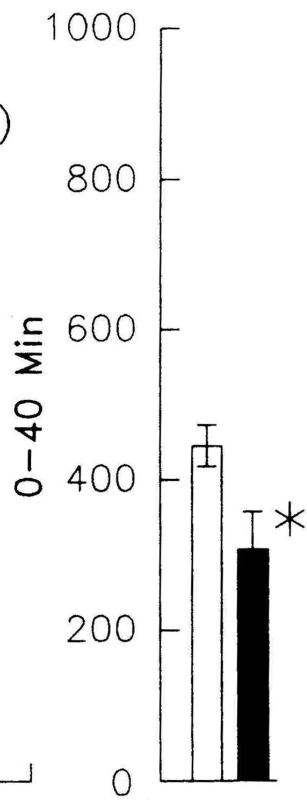
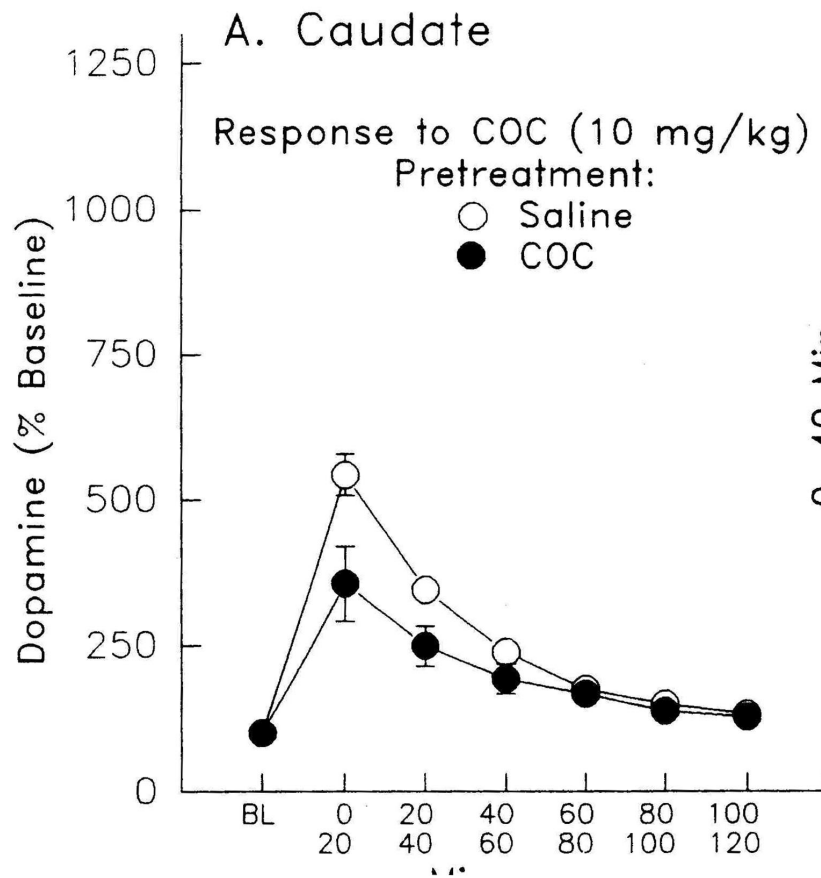
Cocaine
15 mg/kg

D-amph
2 mg/kg



Oral cocaine self-administration



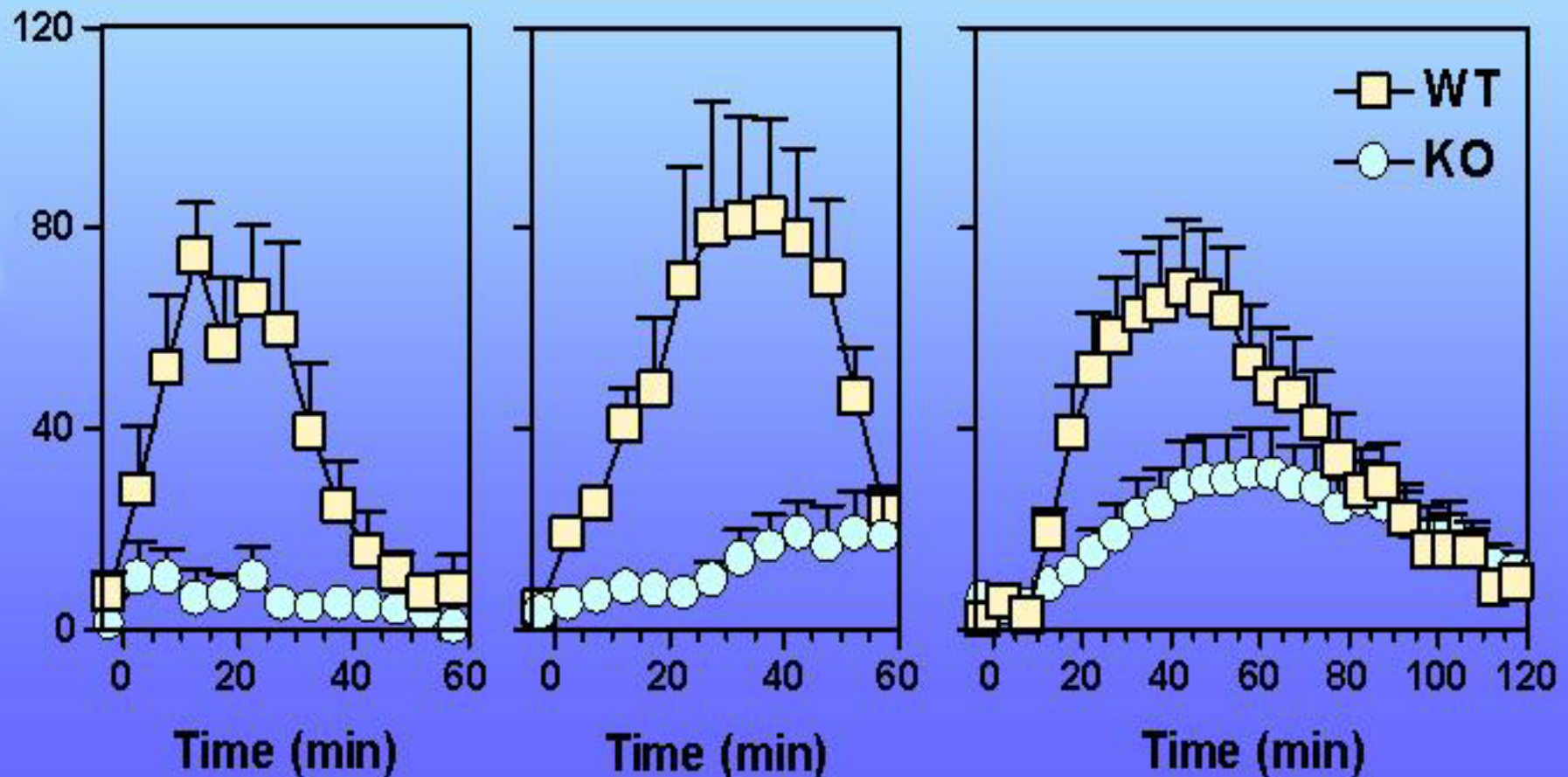


Alpha1b-adrenergic receptor knockout Response to drugs of abuse

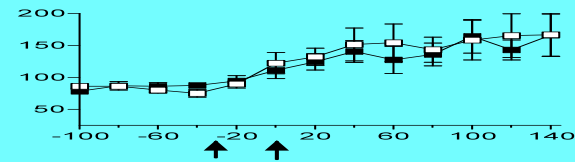
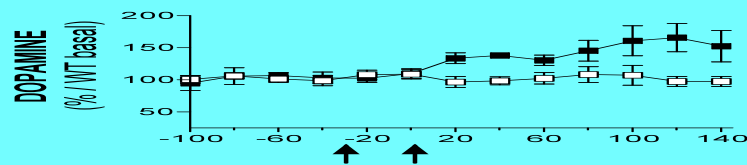
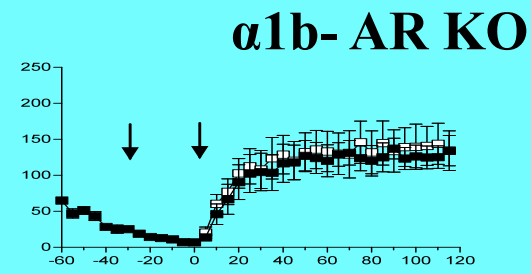
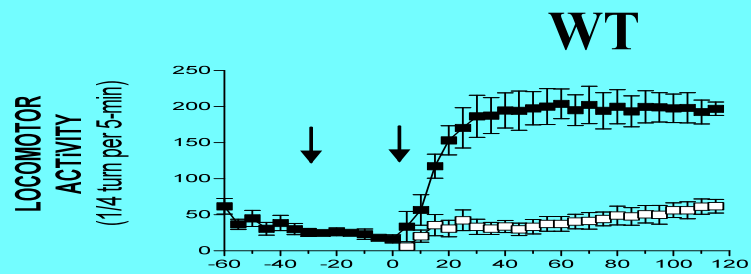
Cocaine
15 mg/kg

D-amph
2 mg/kg

Morphine
7.5 mg/kg

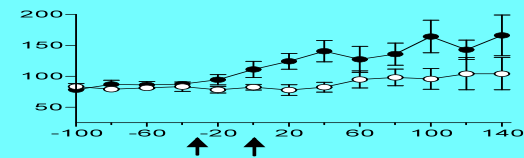
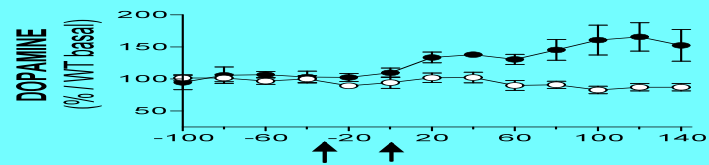
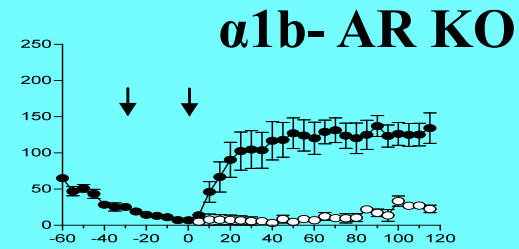
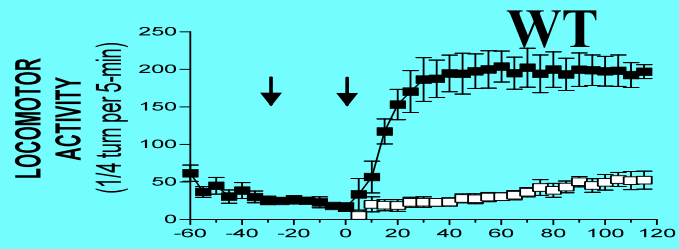


Injection AIGÜE Morphine / test Prazosine



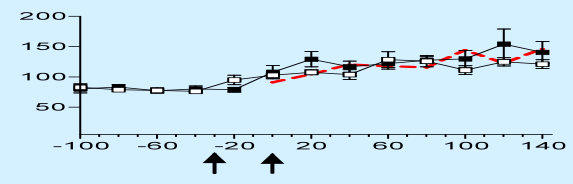
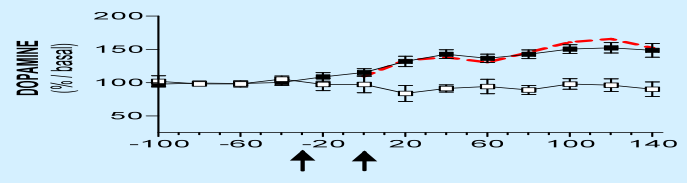
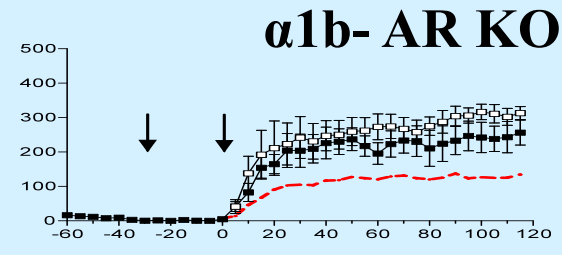
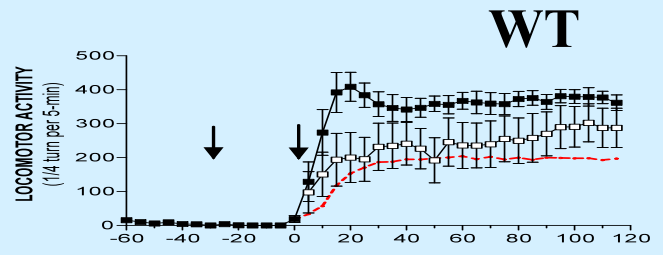
■ Saline – Morphine (20 mg/kg)
□ Prazosine - Morphine

Injection AIGUË Morphine / test SR46349B

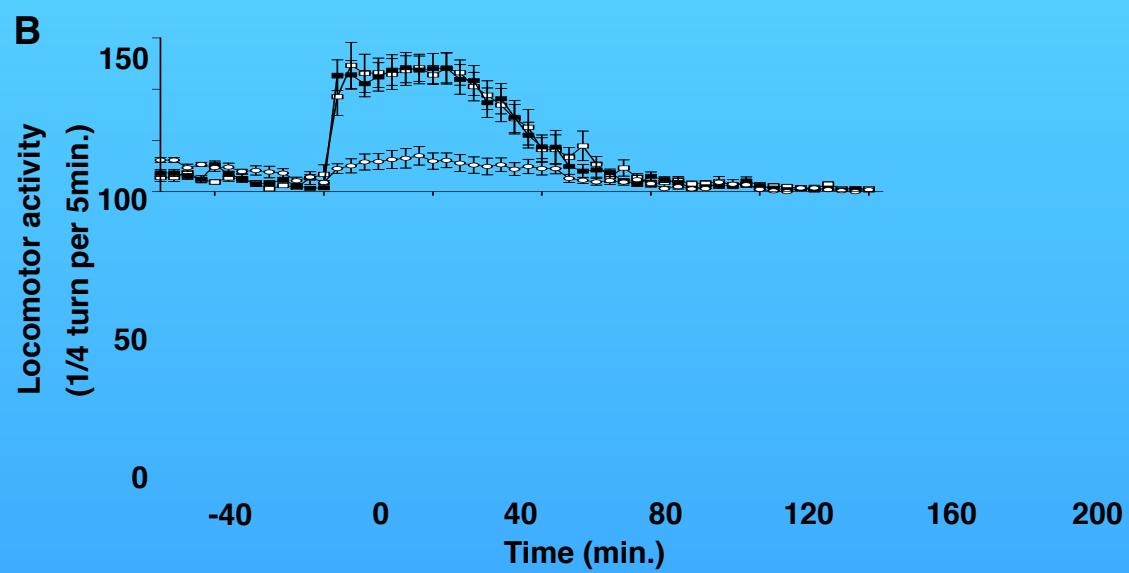
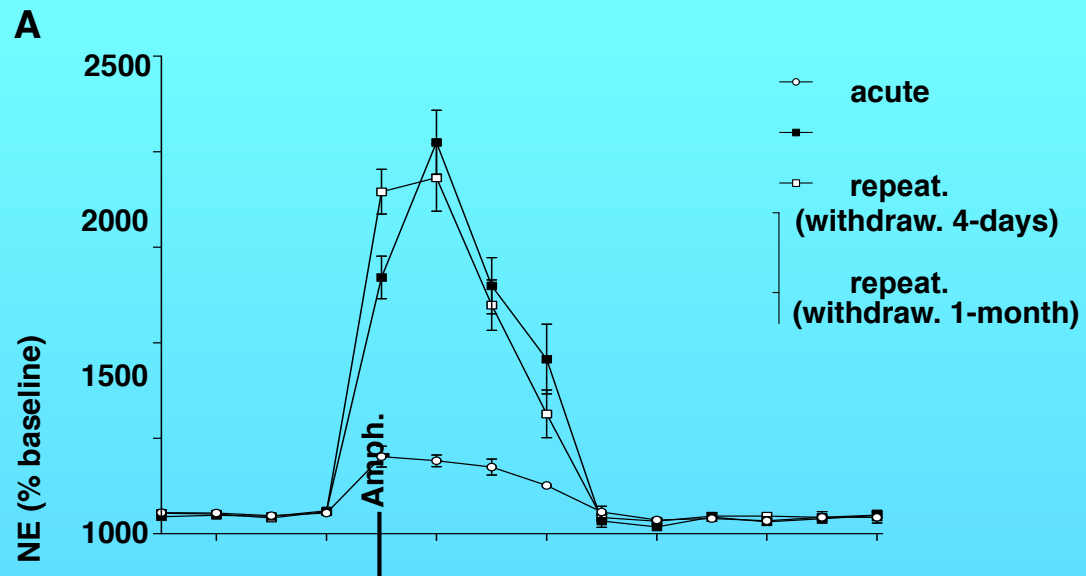


■ Saline – Morphine (20 mg/kg)
□ SR46349B - Morphine

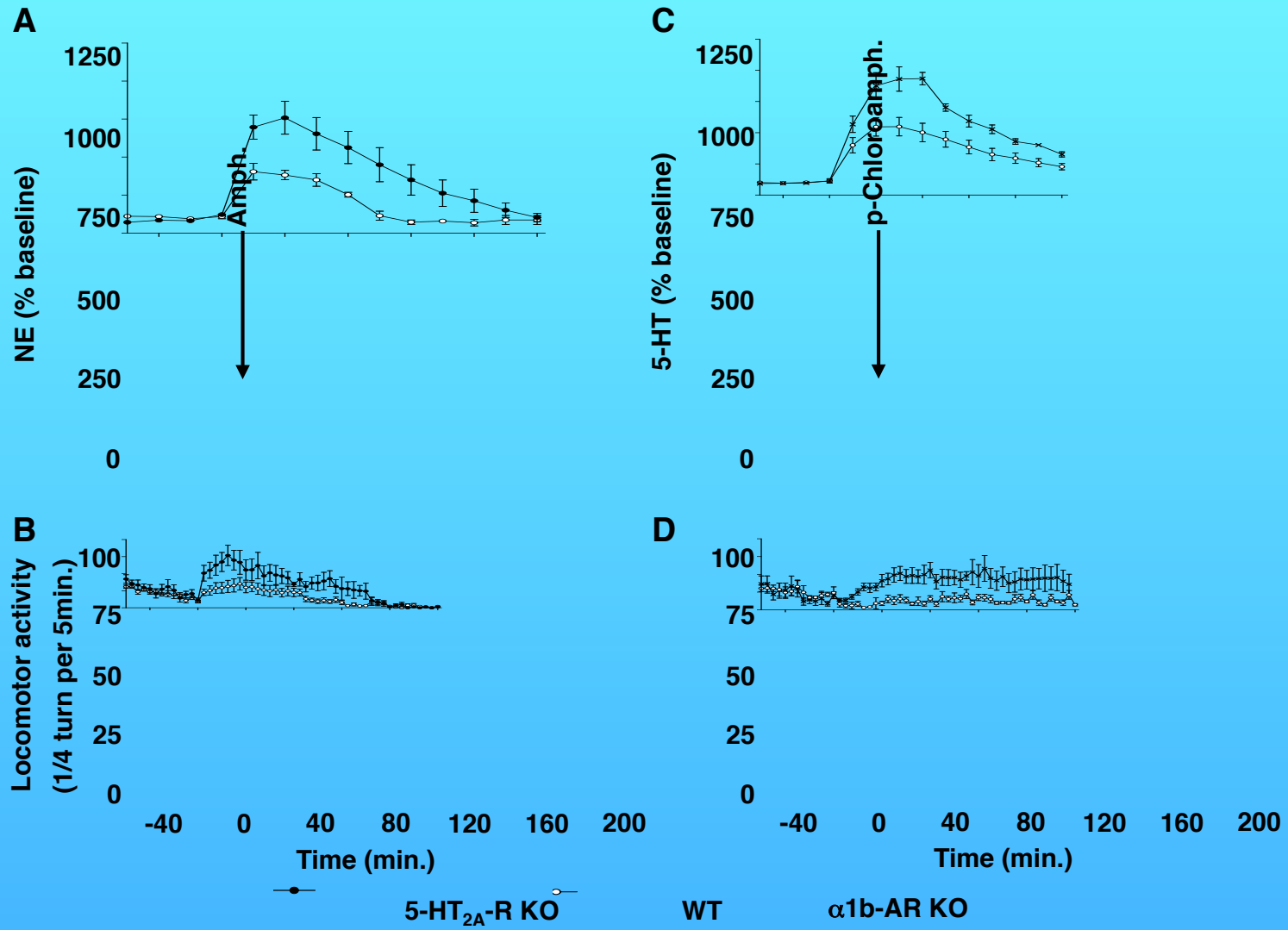
Injections REPETEES Morphine / test prazosine



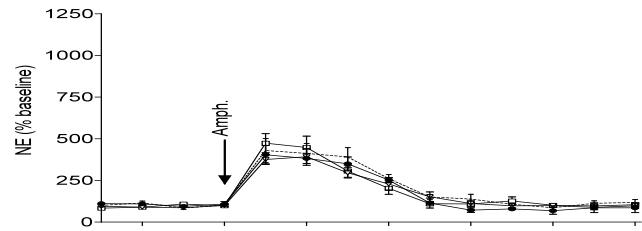
■ Saline – Morphine (20mg/kg)
□ Prazosine - Morphine



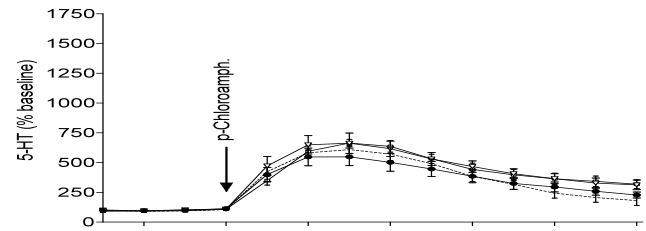
Frontal cortex



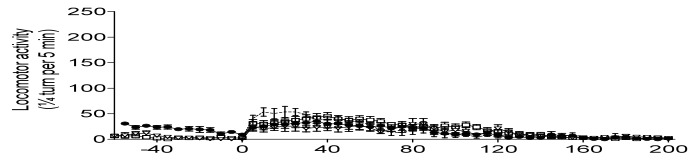
Venlafaxine/Clorimipramine



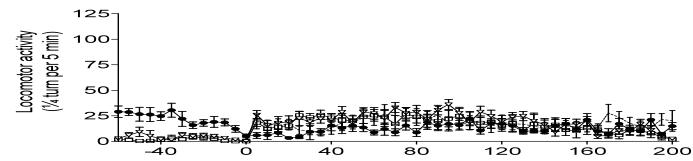
A



C



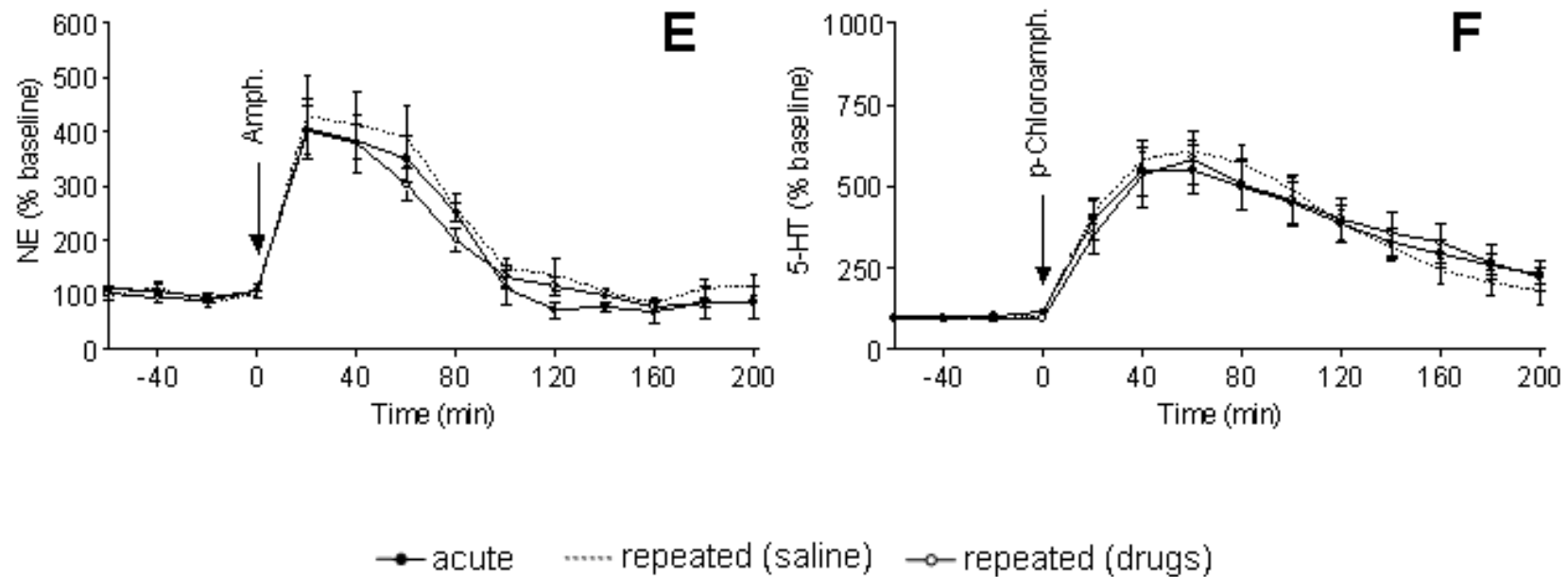
B



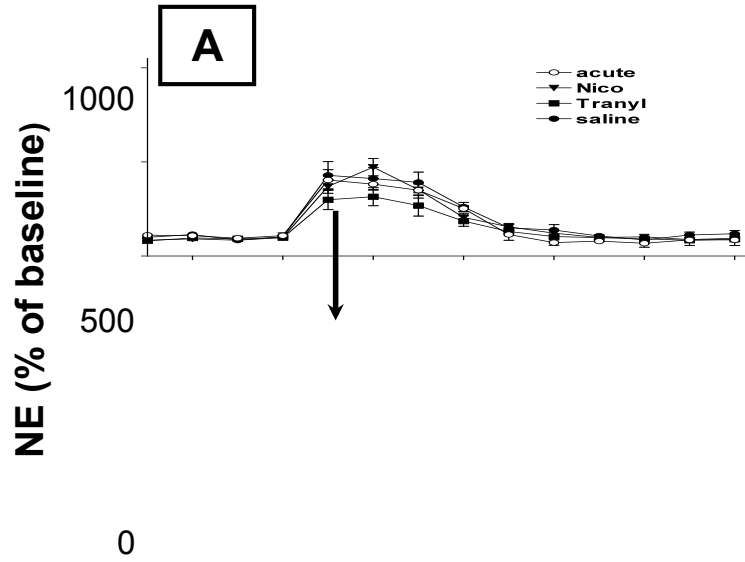
D

● acute repeated saline ▽ repeated venlafaxine □ repeated clorimipramine

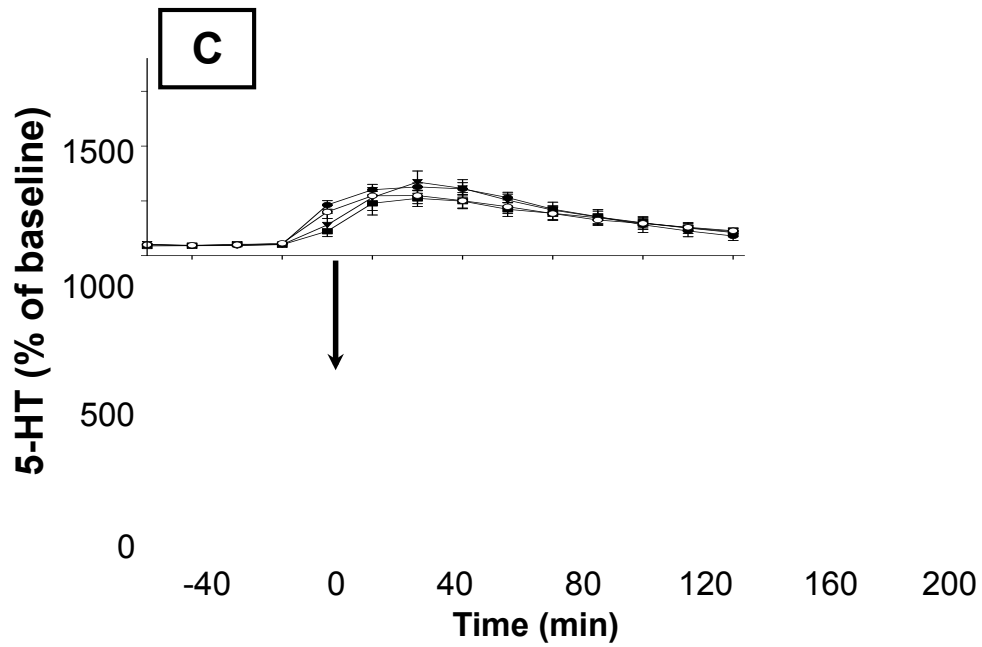
GBR 12783 (20 mg/kg)



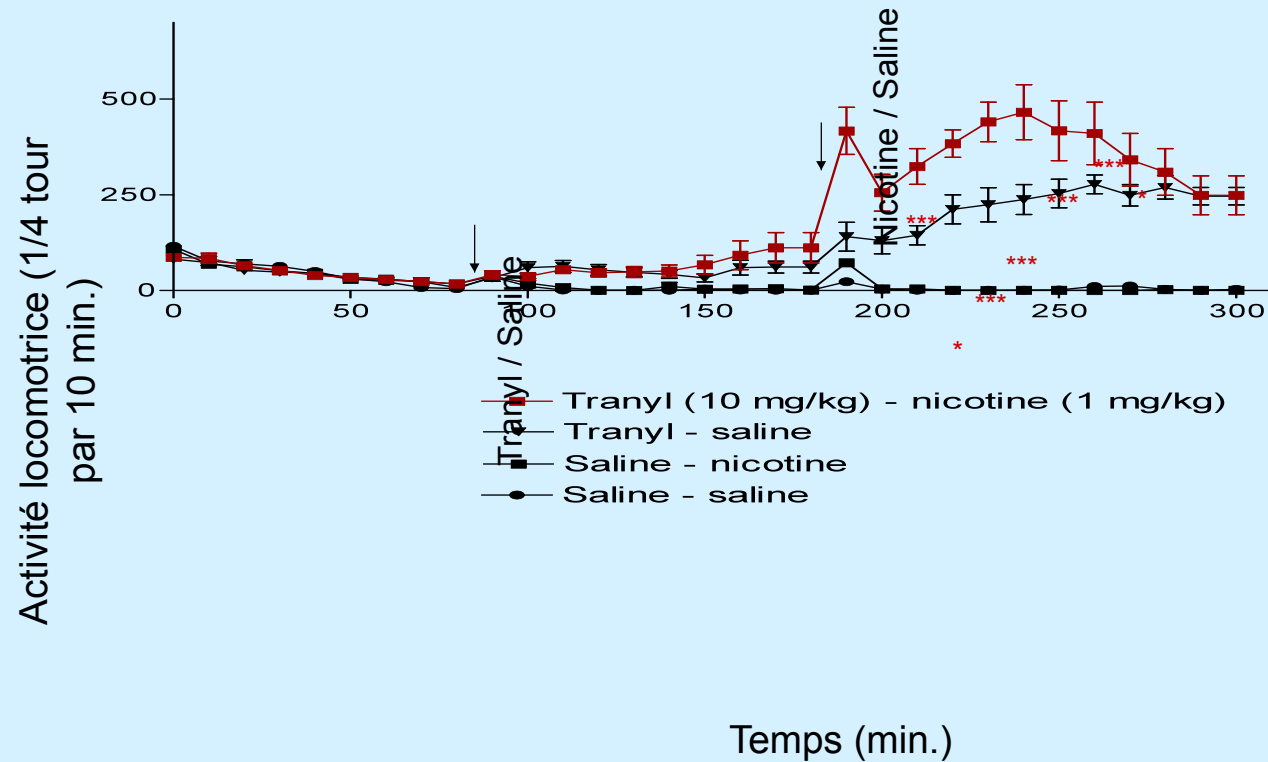
d-amphetamine



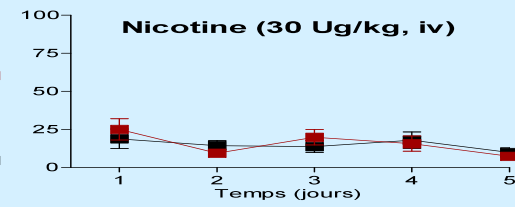
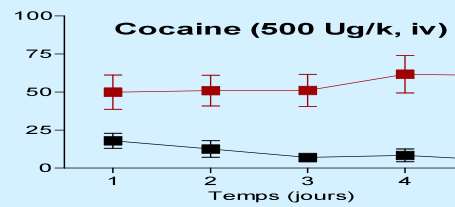
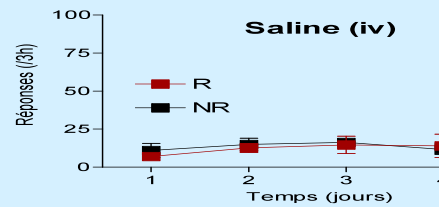
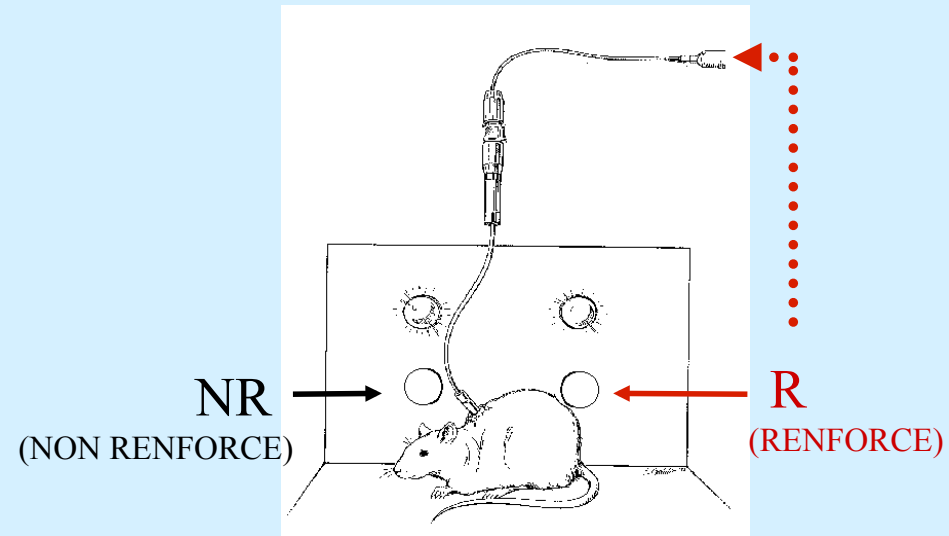
para-chloro-amphetamine



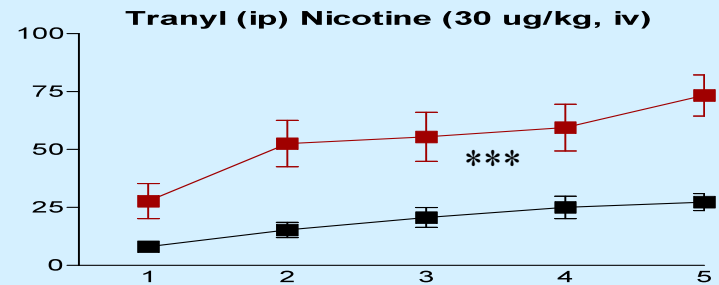
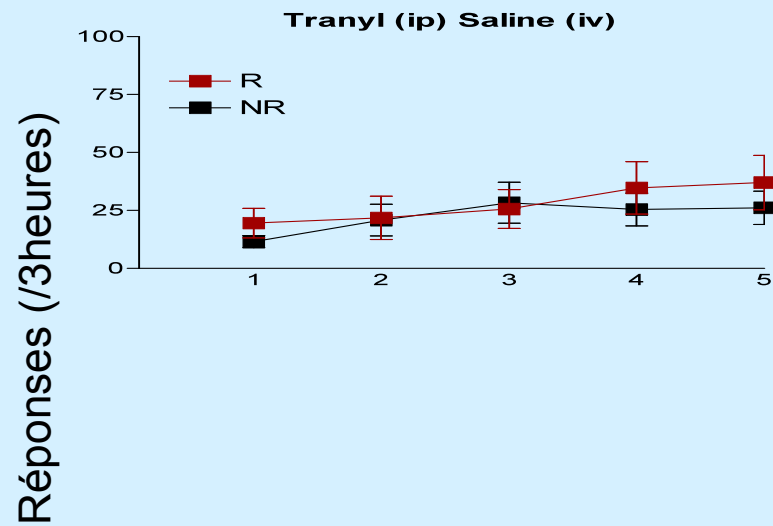
EFFET HYPERLOCOMOTEUR DE LA NICOTINE CHEZ LA SOURIS PRE-TRAITEE PAR LA TRANYLCPROMINE



AUTO-ADMINISTRATION

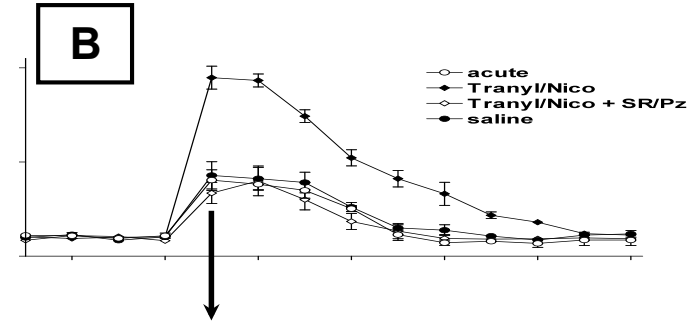
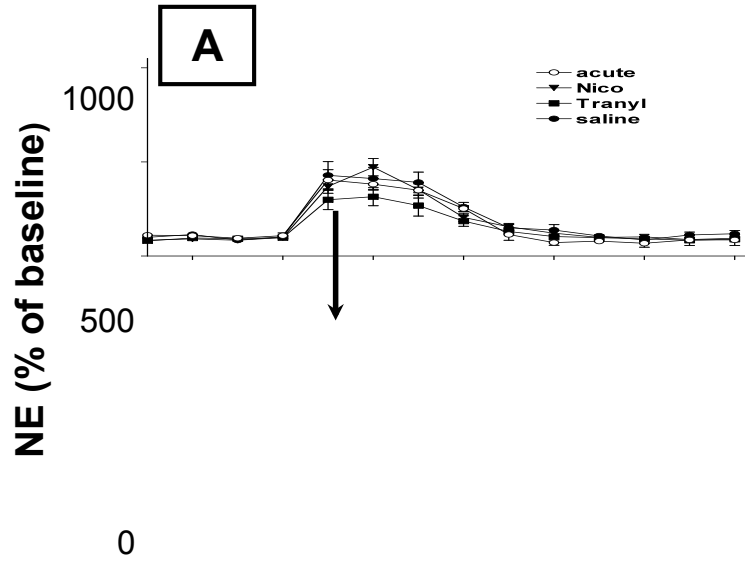


AUTO-ADMINISTRATION DE NICOTINE CHEZ LE RAT PRE-TRAITE PAR LA TRANYLCPROMINE

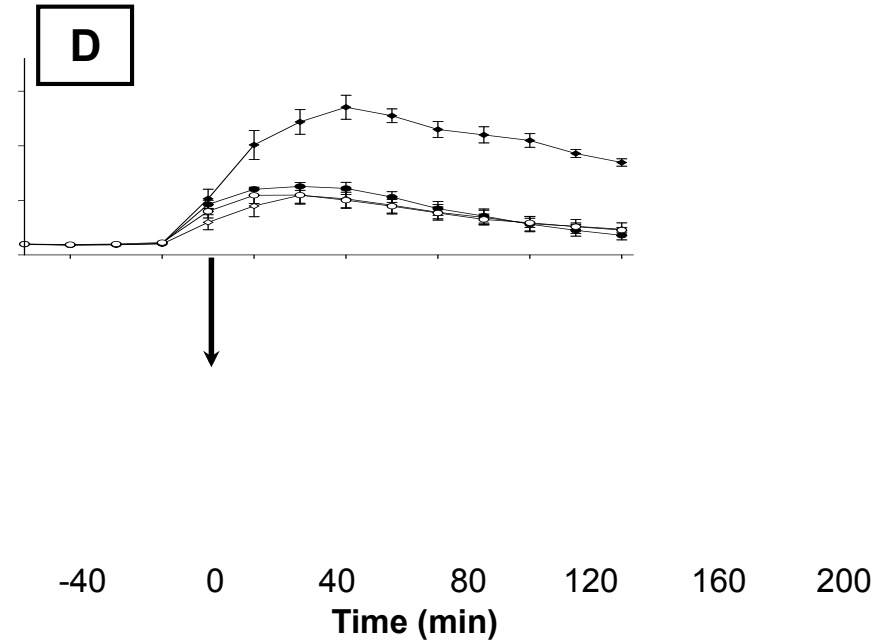
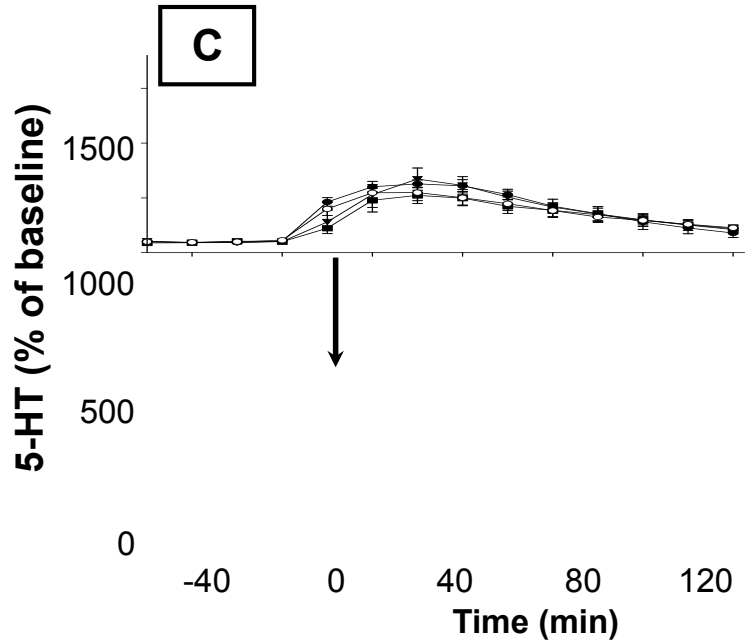


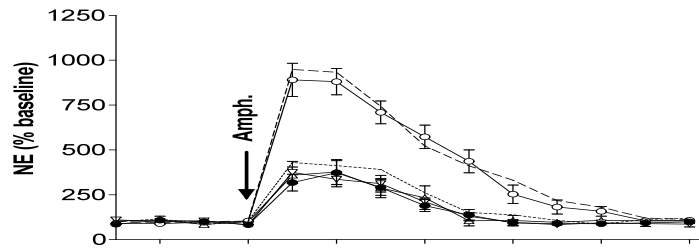
Temps (jours)

d-amphetamine

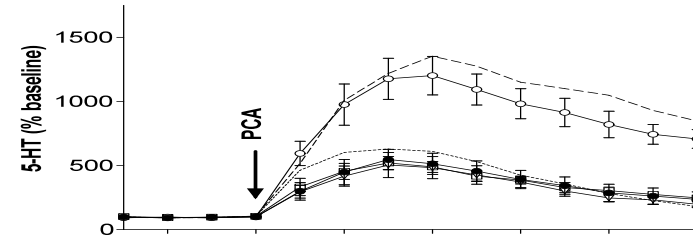


para-chloro-amphetamine

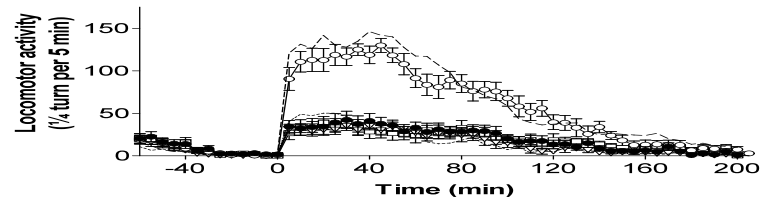




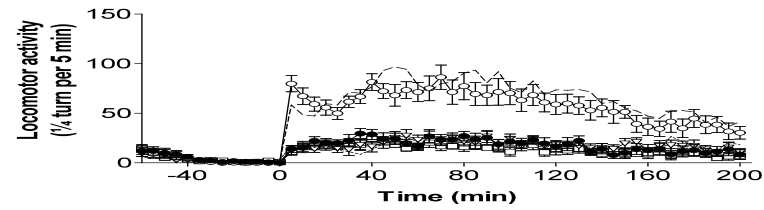
A



C



B

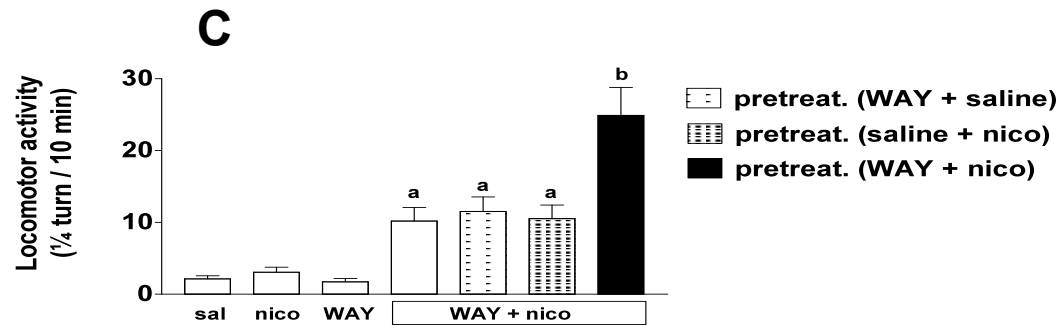
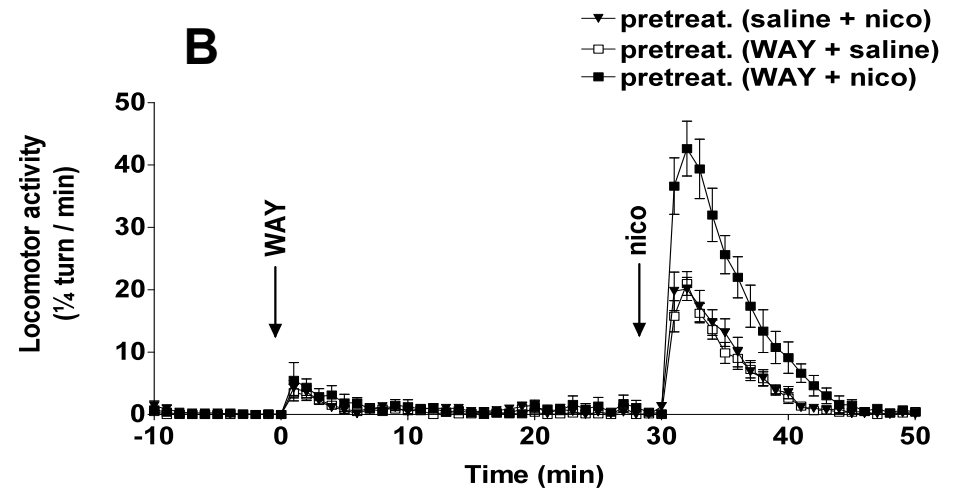
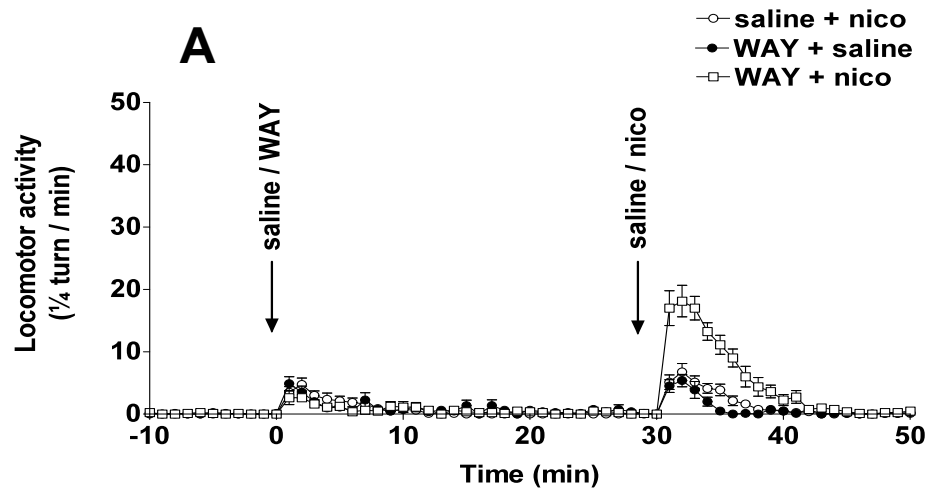


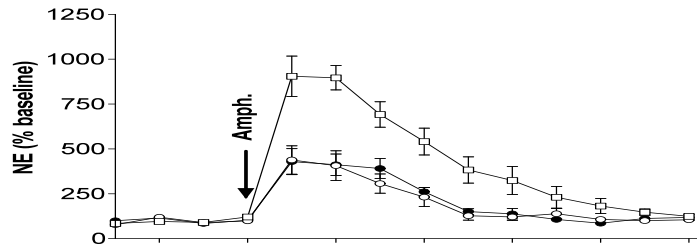
D

..... Repeated saline
 - - Repeated (tranyl/nico)

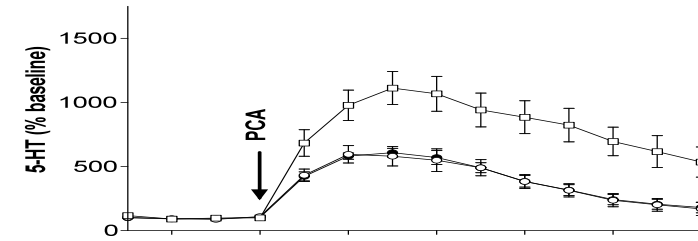
● Repeated (tranyl/nico + SR/Pz)
 ○ Repeated (tranyl/nico + SCH)

▽ Repeated (SR/Pz)
 □ Repeated (SCH)

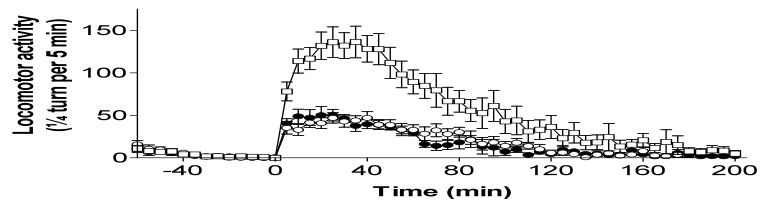




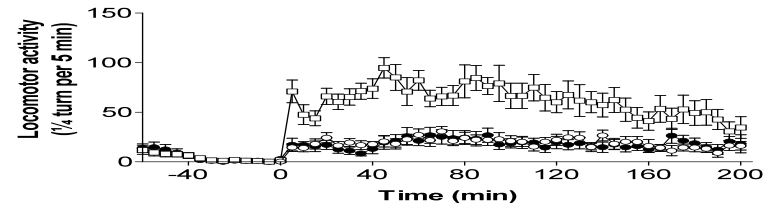
A



C

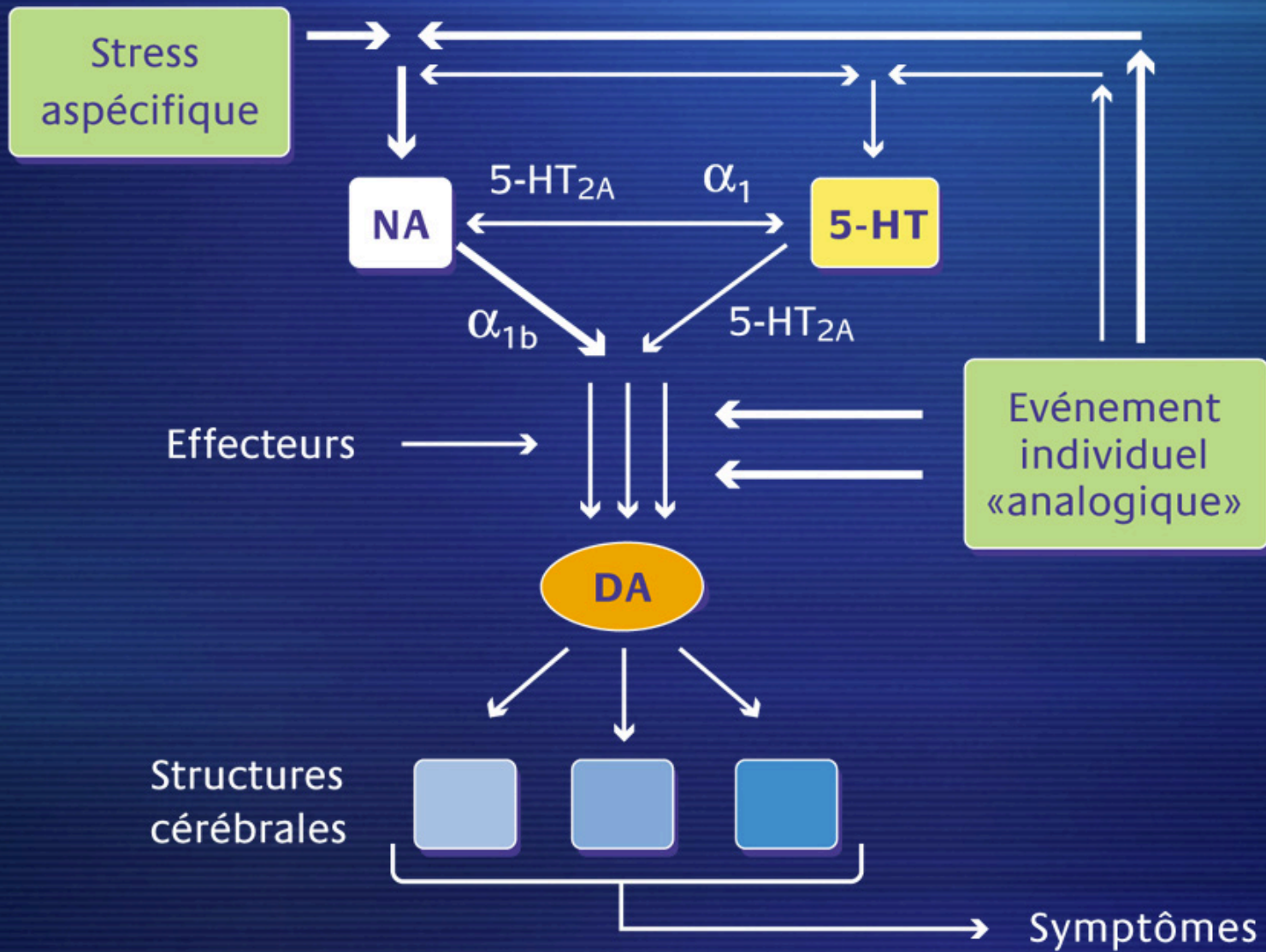


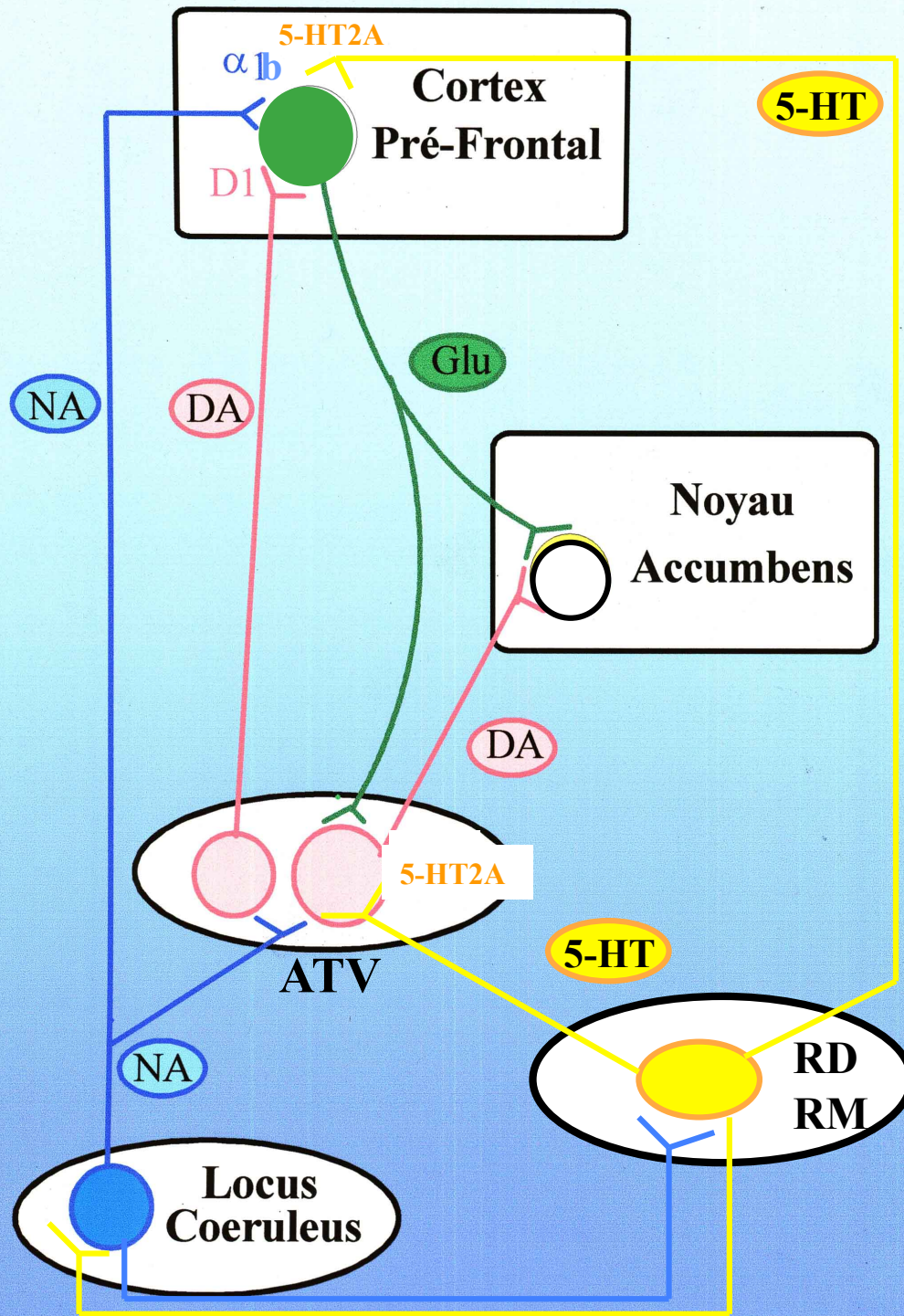
B



D

● Repeated saline ○ Repeated (WAY + saline) □ Repeated (WAY + Nico)





PROPOSITIONS ET OBSERVATIONS

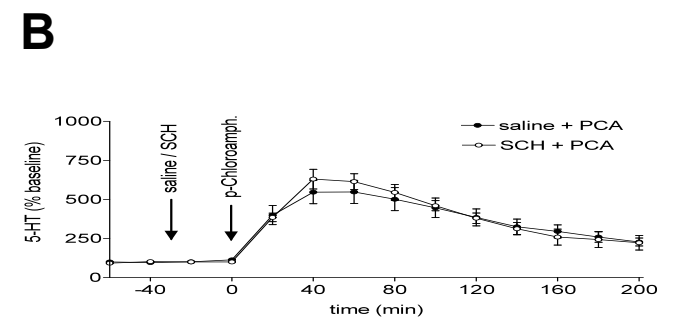
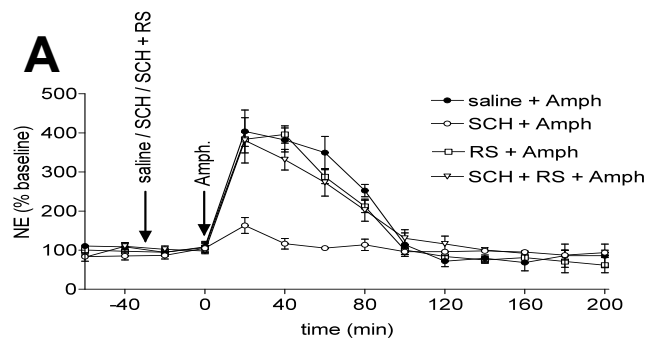
- L'addiction résulte d'un découplage des neurones NA et 5-HT.
- Ce découplage (obtenu avec l'amphétamine, la cocaïne, la morphine et l'alcool) est dû à la stimulation intense et répétée des récepteurs $\alpha 1b$ -adrénergiques et/ou 5-HT_{2A}.
- Le découplage n'est pas obtenu avec la nicotine seule.
- Le découplage est obtenu en présence de nicotine + IMAO ou de nicotine + un antagoniste des récepteurs 5-HT_{1A}.

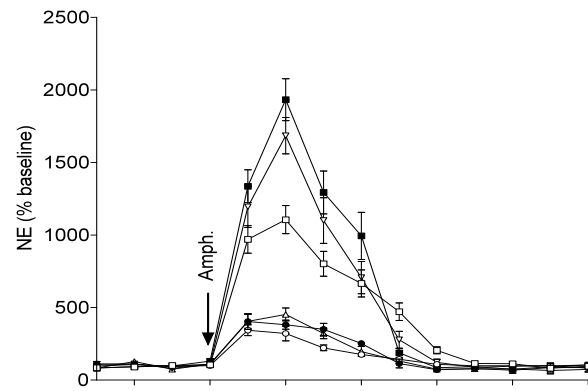
CONCLUSIONS

La nicotine n'est pas addictive par elle-même.

Elle le devient mélangée au tabac car les IMAOs qu'il contient désensibilisent les récepteurs 5-HT_{1A}.

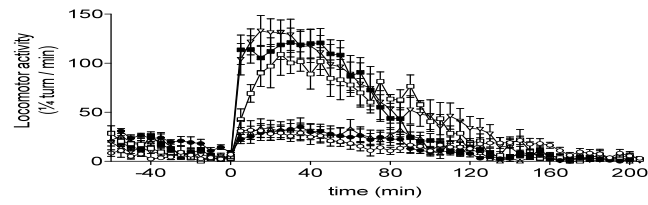
Anne-Sophie Villégier (Fondation G. Lagrue)/ *Lucas Salomon* (MRT)
/*Christophe Lanteri* (MILDT)





A

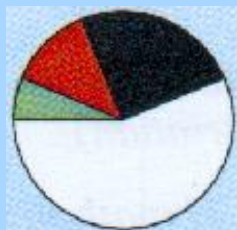
- repeated saline
- repeated amph
- repeated amph + SCH
- repeated amph + SCH + RS
- ▽ repeated RS + amph
- △ repeated RS



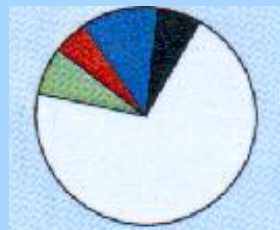
B

Dopaminergic antagonists

Antipsychotics



flupentixol



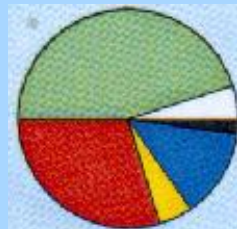
fluphénazine



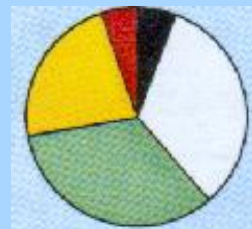
halopéridol



sulpiride



clozapine



olanzapine



rispéridone



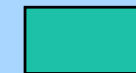
sertindole



D1



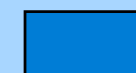
D2



5-HT2



α 1



H1

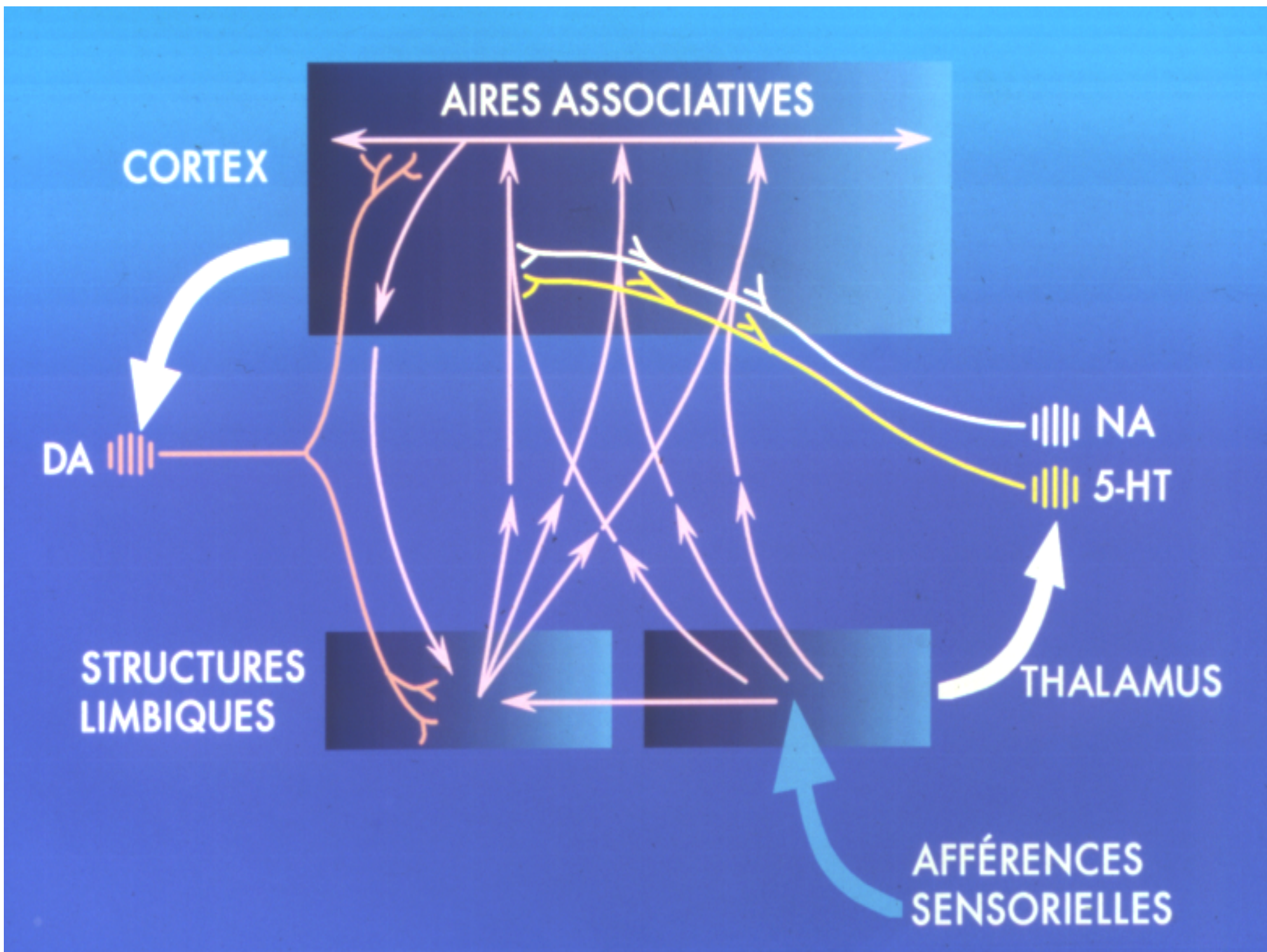


ACh

Receptor binding profile of antipsychotics

Receptor	olanzapine	risperidone	quetiapine	ziprasidone	clozapine	haloperidol
D ₁	31	430	455	525	85	210
D₂	11	4	160	5	126	0.7
D ₃	49	10		7	473	2
D ₄	27	9		32	35	3
5-HT _{1A}	>10000	210	2800	3	875	1100
5-HT_{2A}	4	0.5	295	0.4	16	45
5-HT _{2C}	23	25		1	16	>10000
α₁	19	0.7	7	11	7	6
H ₁	7	20	11	50	6	440
M ₁	1.9	>10000	120	>1000	1.9	>1500

^a Moore *et al.*, 1993; ^b Daniel *et al.*, 1999



**LES NEURONES MONOAMINERGIQUES
PRESENTENT
DES DIFFERENCES FONCTIONNELLES**

**Neurones
noradrénergiques**

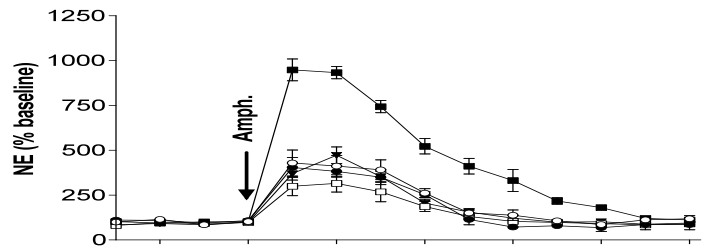
**Sélection et
amplification
des informations externes**

**Neurones
sérotoninergiques**

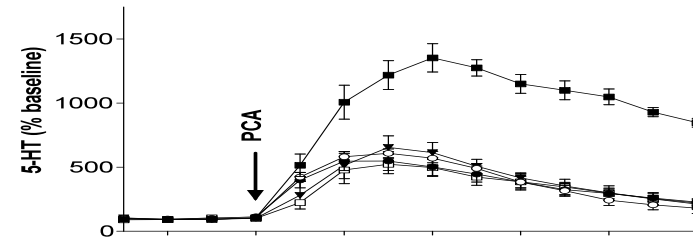
**Maintien
du traitement
des informations internes**

**Neurones
dopaminergiques**

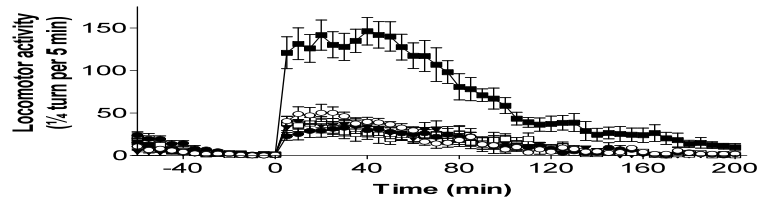
**Décodage
de la signification
des informations
externes et internes**



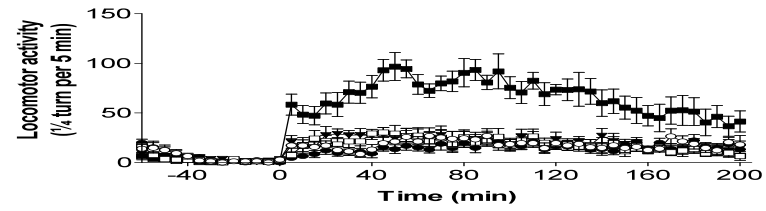
A



C



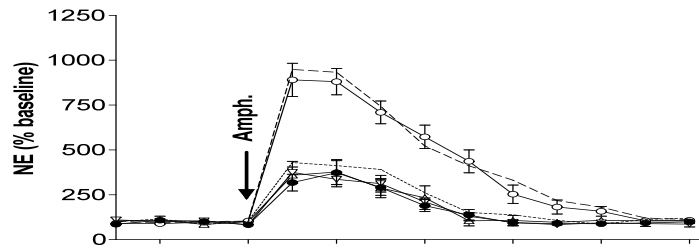
B



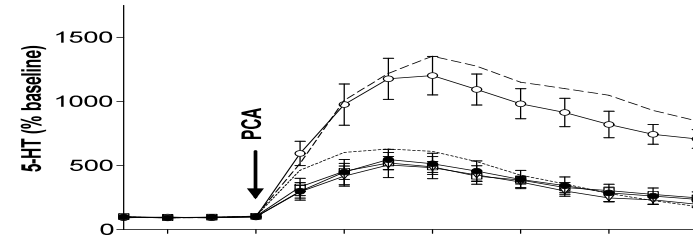
D

● Acute
○ Repeated saline

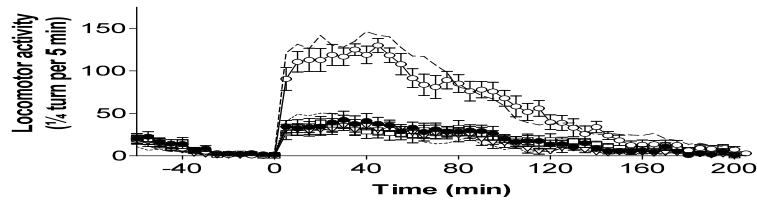
□ Repeated tranyl
▼ Repeated Nico
■ Repeated (tranyl + Nico)



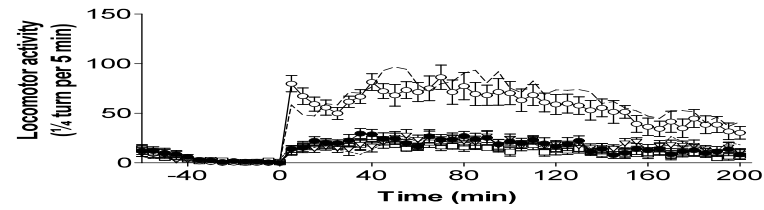
A



C



B

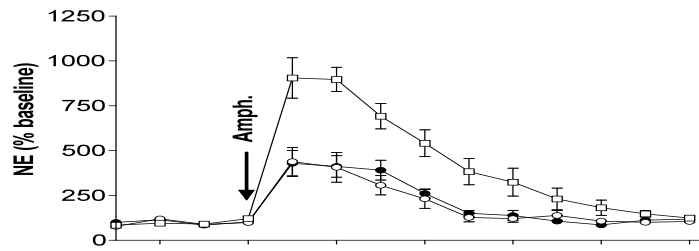


D

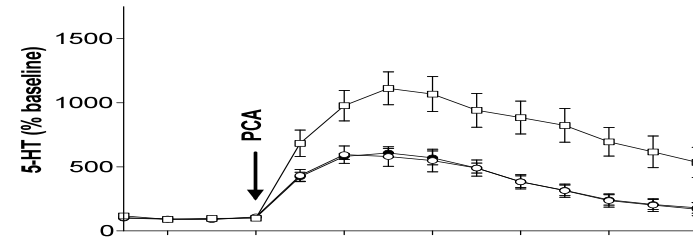
..... Repeated saline
 - - Repeated (tranyl/nico)

● Repeated (tranyl/nico + SR/Pz)
 ○ Repeated (tranyl/nico + SCH)

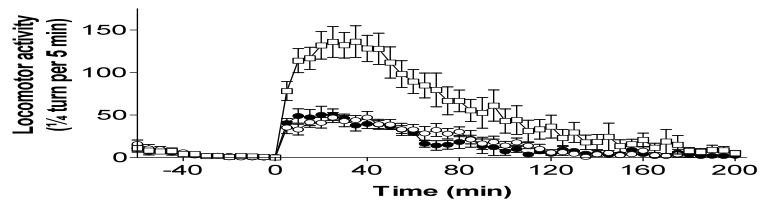
▽ Repeated (SR/Pz)
 □ Repeated (SCH)



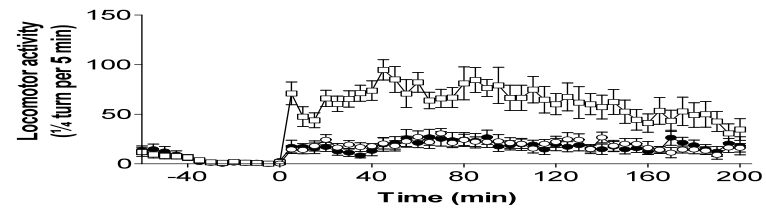
A



C

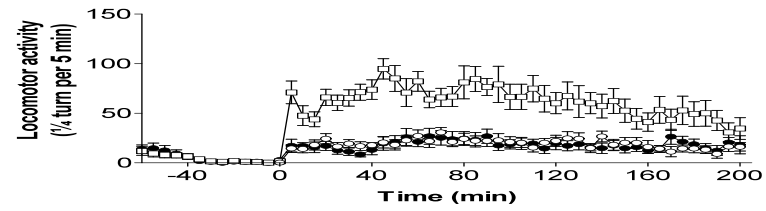
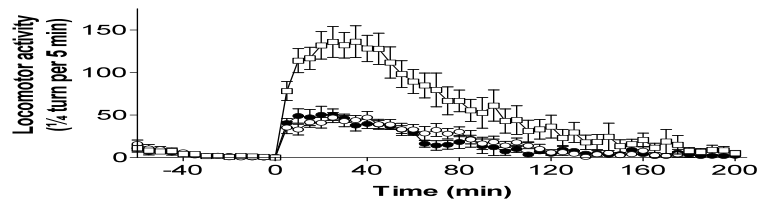
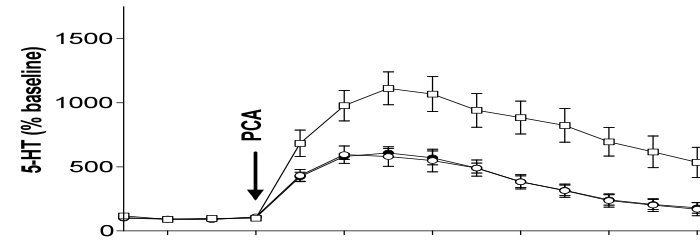
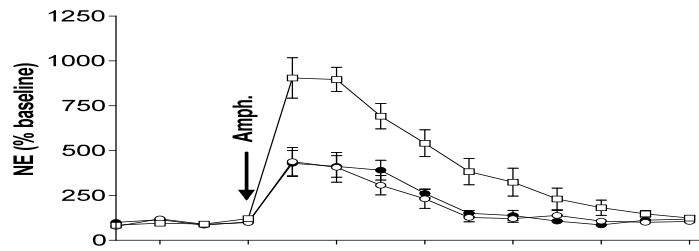


B

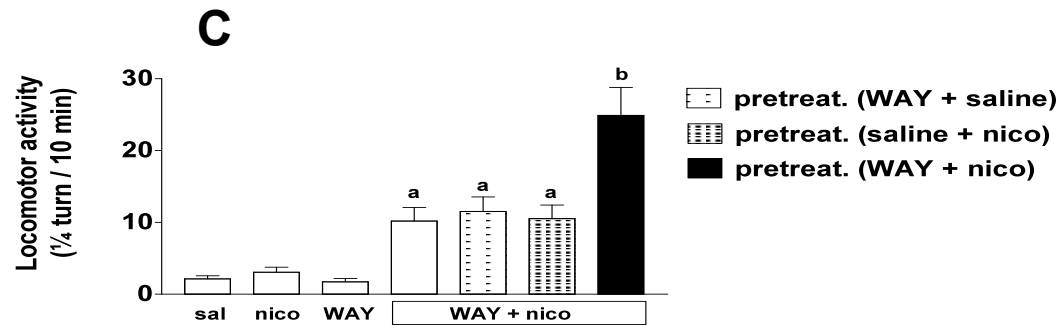
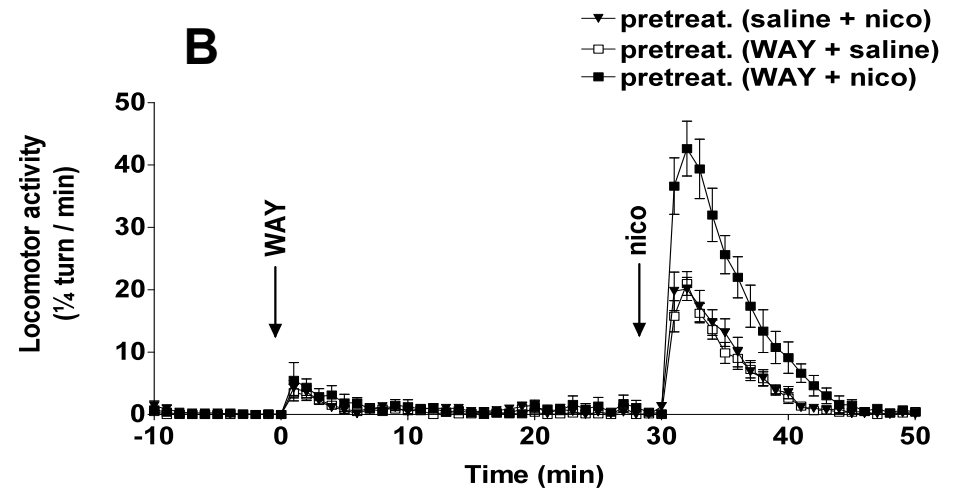
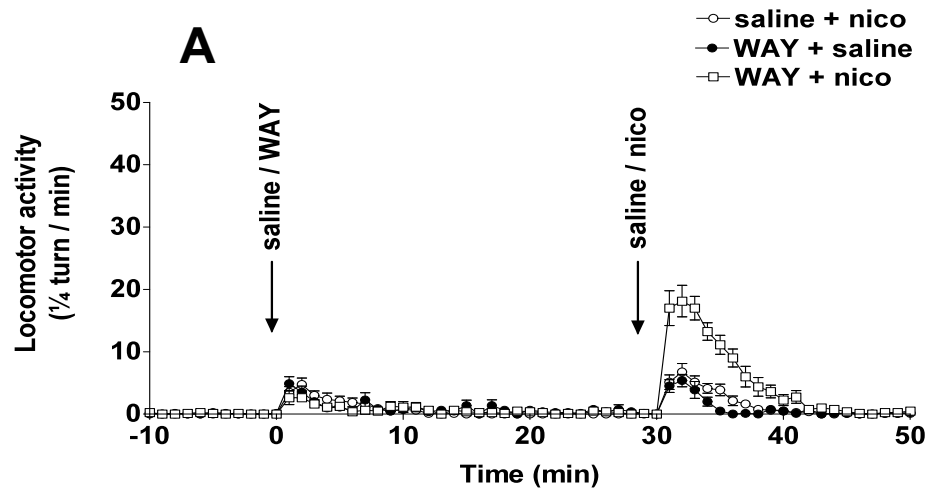


D

● Repeated saline ○ Repeated (WAY + saline) □ Repeated (WAY + Nico)

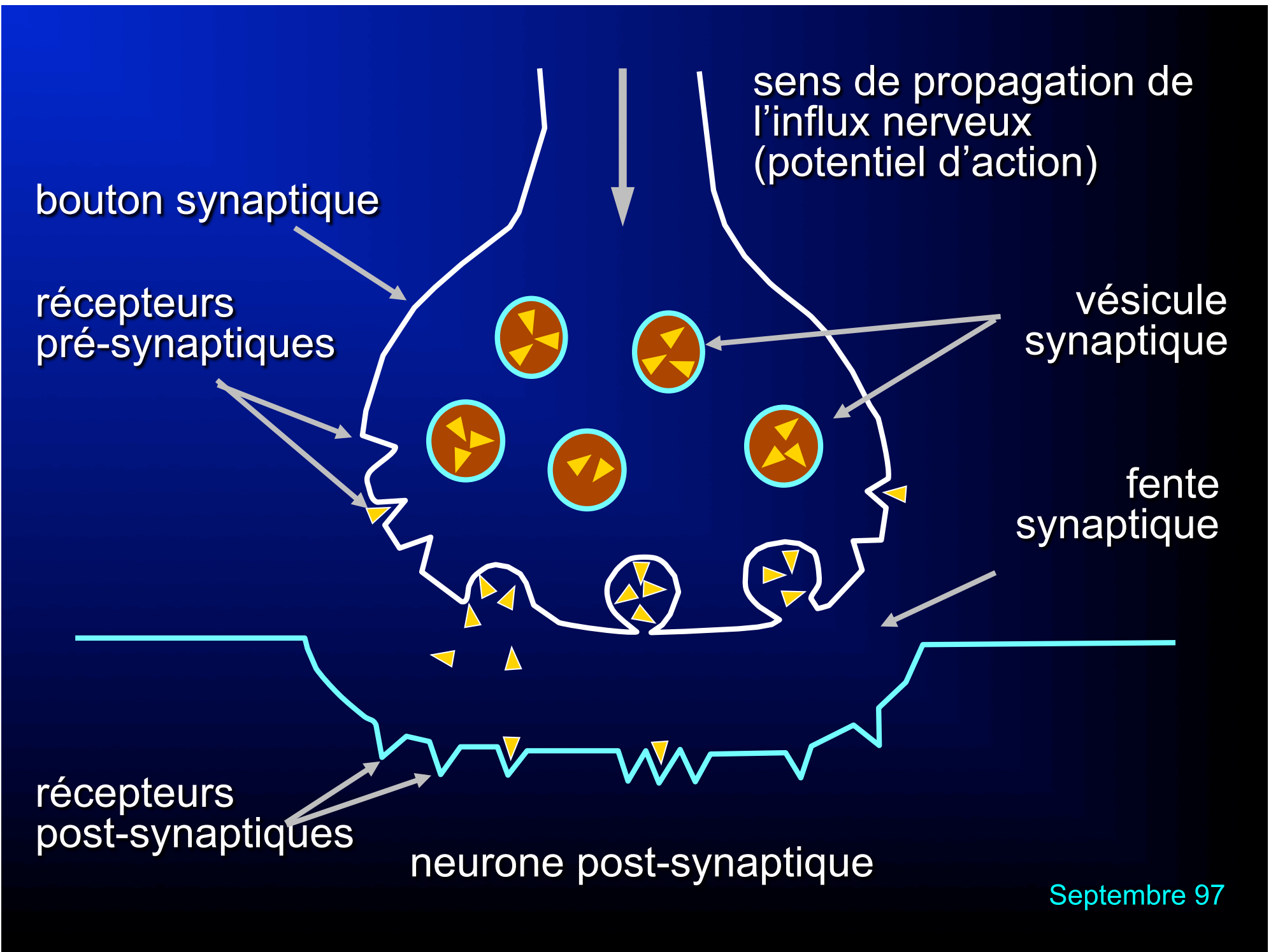


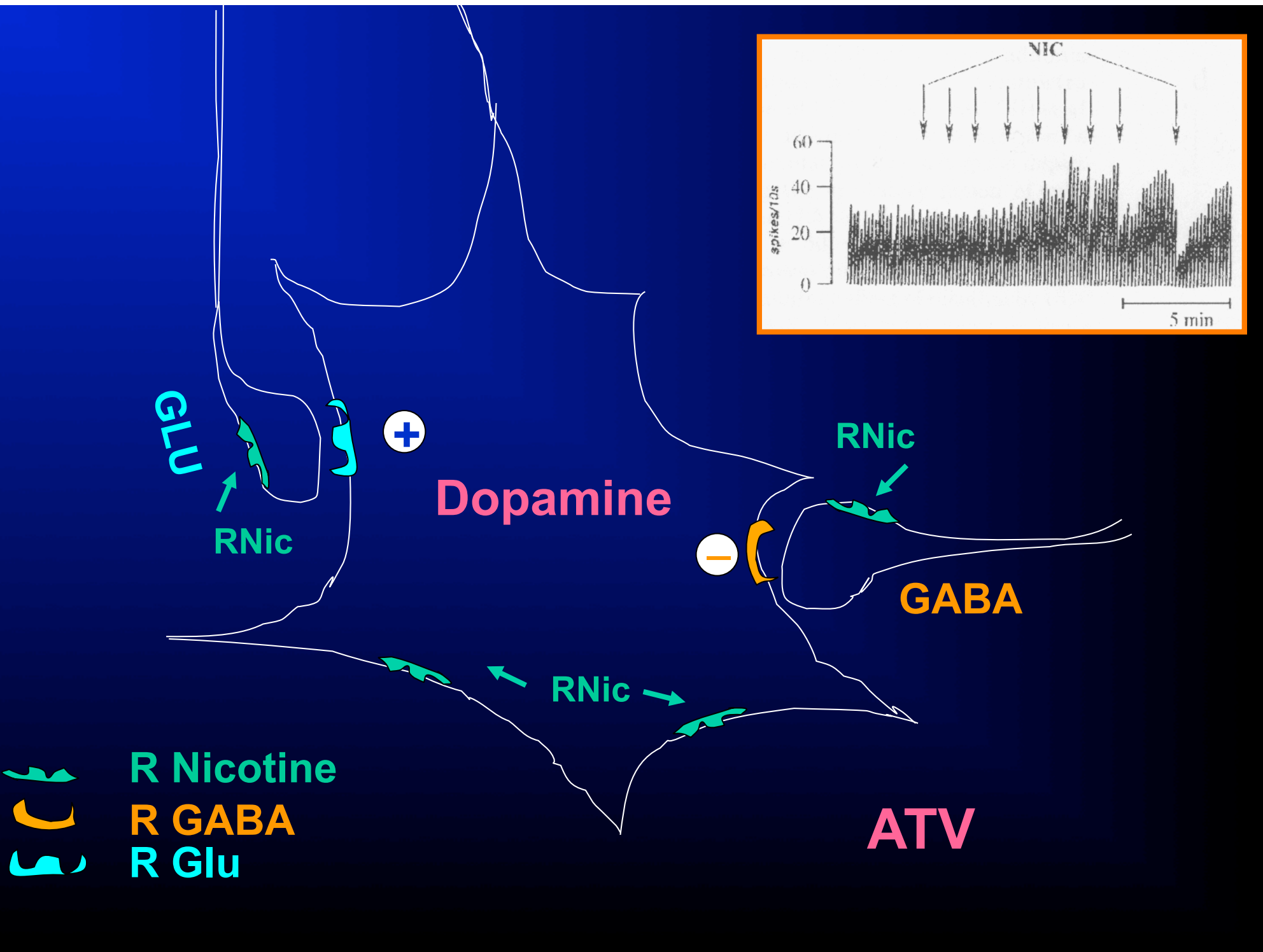
● Repeated saline ○ Repeated (WAY + saline) □ Repeated (WAY + Nico)



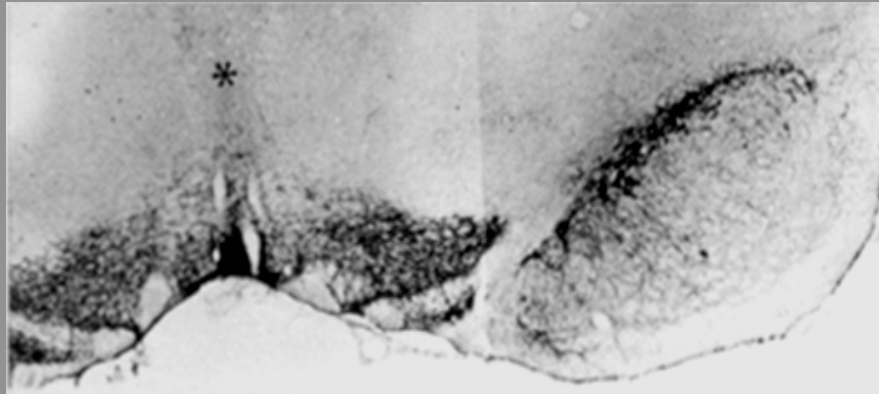
Le système de récompense

Jean-Pol TASSIN
Collège de France
Paris



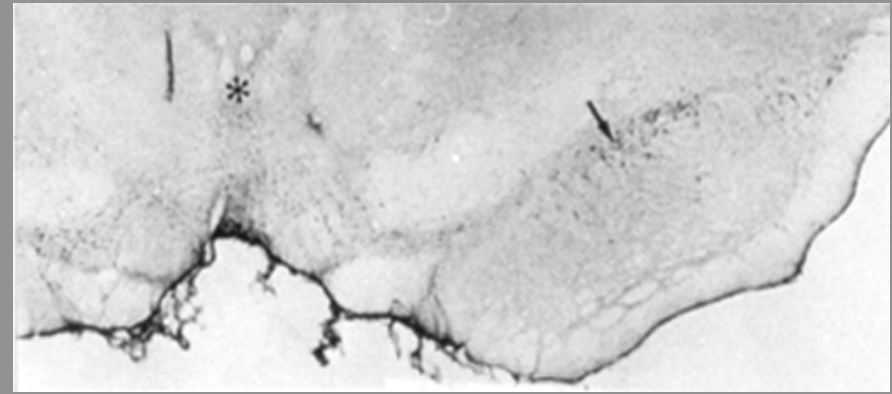


CONTROL

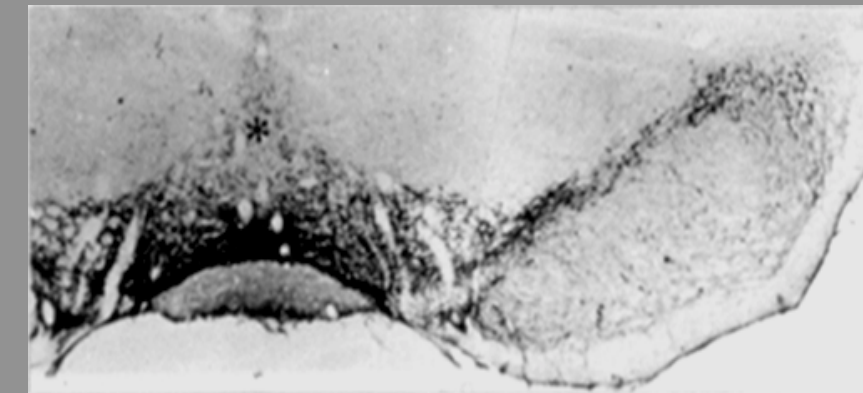


A

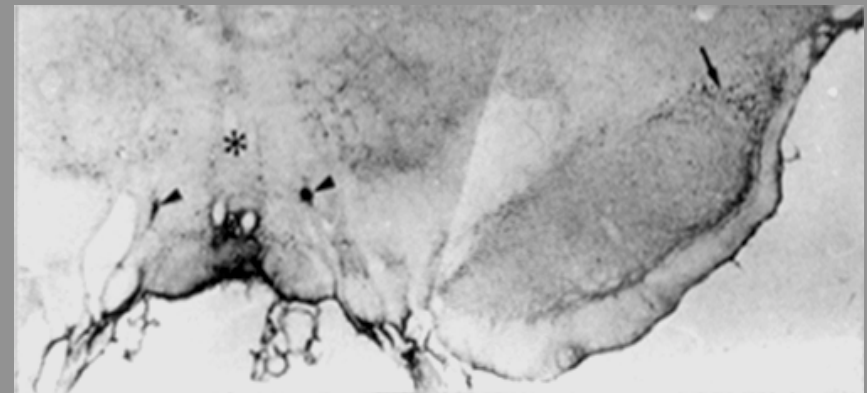
6-OHDA

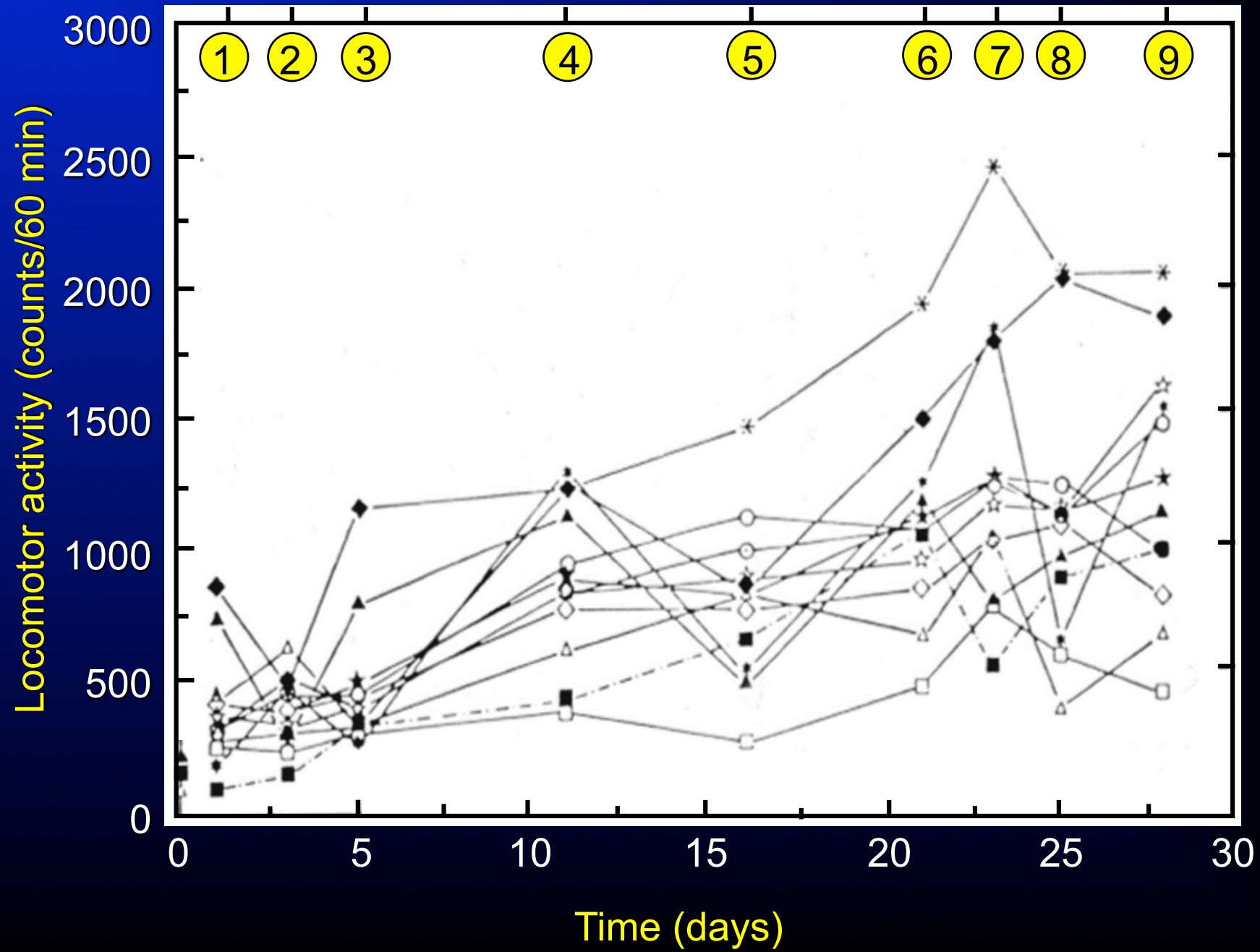


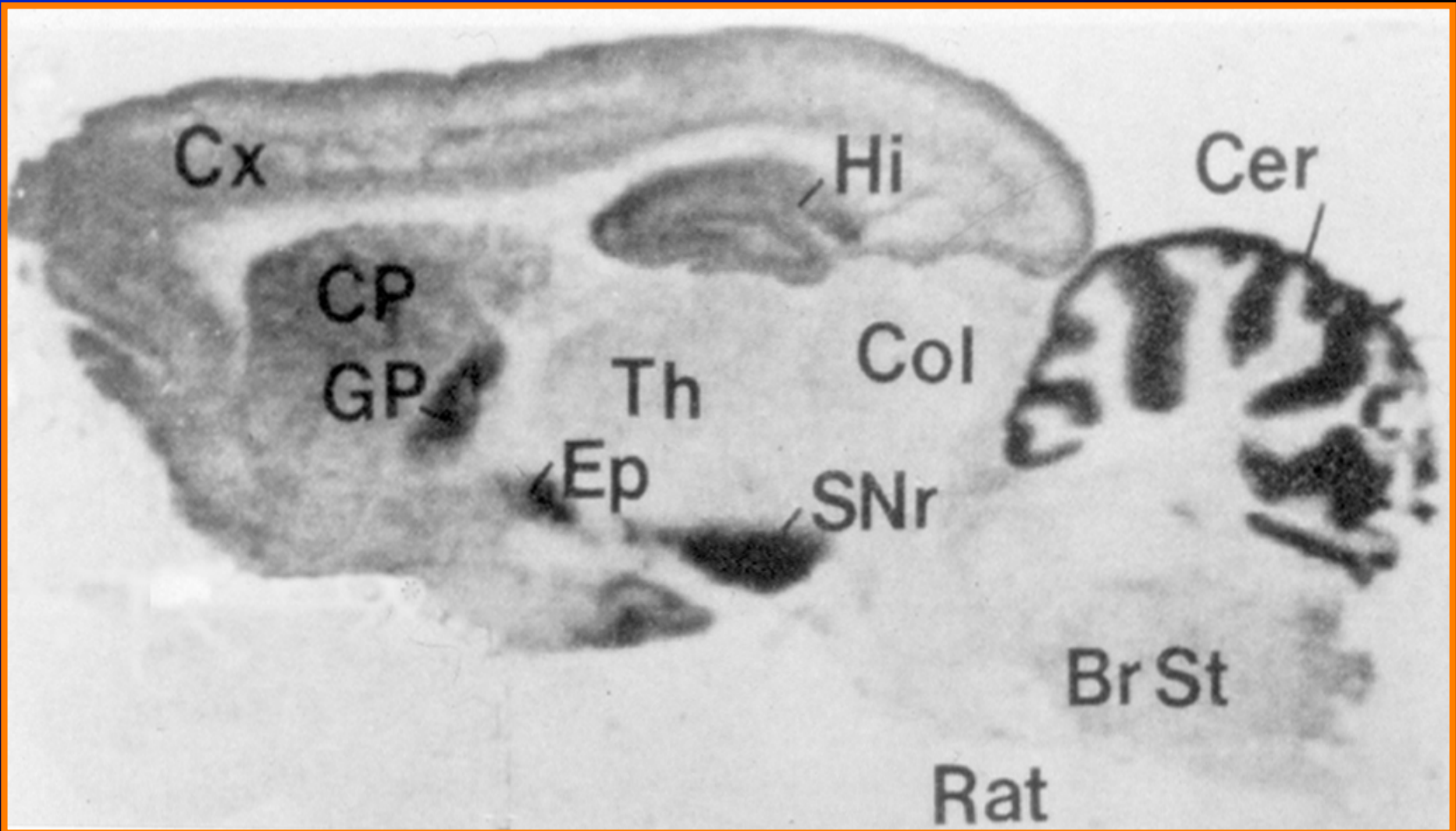
LESIONED

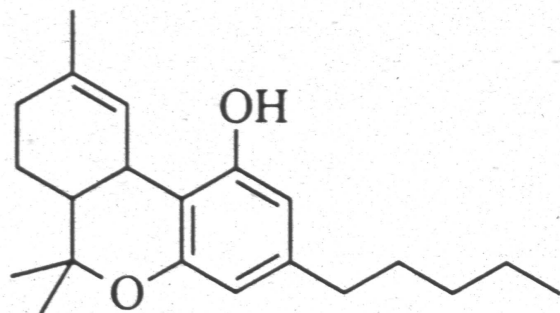


B

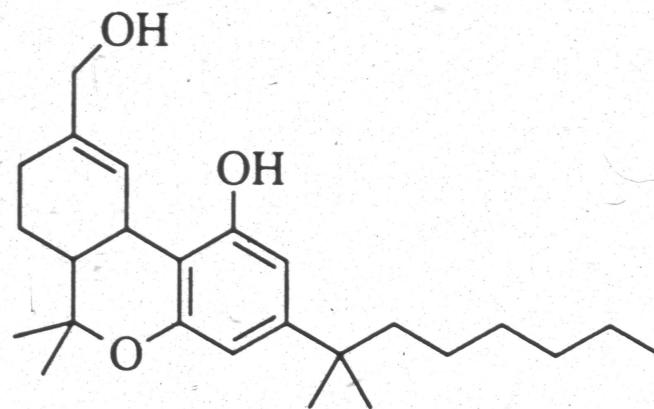




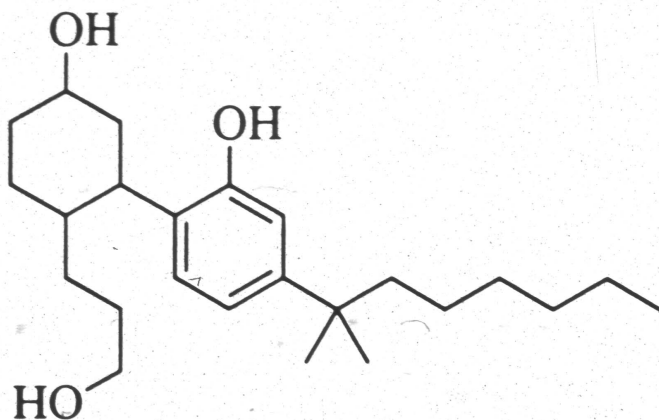




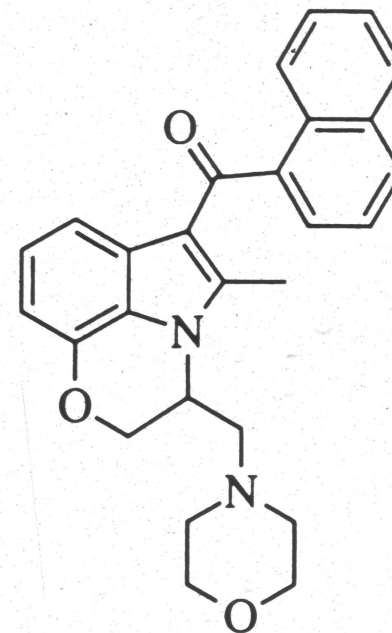
Δ^9 -THC



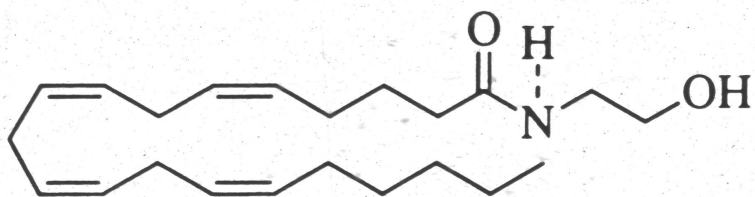
11-OH- Δ^9 -THC-dimethylheptyl



CP 55,940



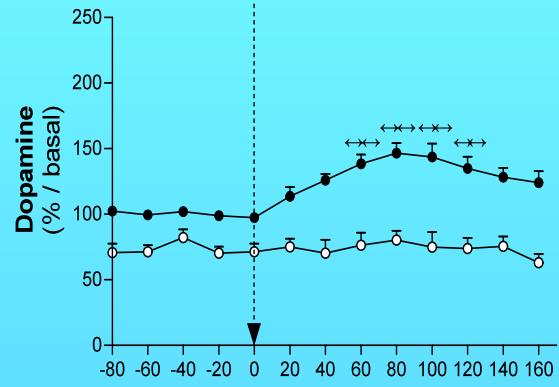
WIN 55,212-2



Anandamide

● $\alpha.1b^{+/+}$
○ $\alpha.1b^{-/-}$

D-Amph (3 mg/kg, ip)



D-Amph (6 mg/kg, ip)

