

A photograph of a red mushroom with white spots, likely a fly agaric, growing on a bed of pine needles. The mushroom is the central focus, with its bright red cap and white spots contrasting against the dry, brownish-green needles. The text 'Adrenergic Transmission' is overlaid in yellow on the mushroom's cap.

# Adrenergic Transmission

A photograph of a red mushroom with white spots, likely a fly agaric, growing on a bed of pine needles. The mushroom is the central focus, with its bright red cap and white spots contrasting against the dry, brownish-green needles. The background is a dense layer of these needles, creating a textured, natural setting.

**by the end of this lecture**

- **you should be able to formulate a treatment strategy for an animal with vasodilatation**

**What would you do?**



# downer cow



- given dexamethasone 10 mins earlier to induce calving
- now gone down
- some swelling around perineum
- shaking / muscle twitching
- grunting respiration

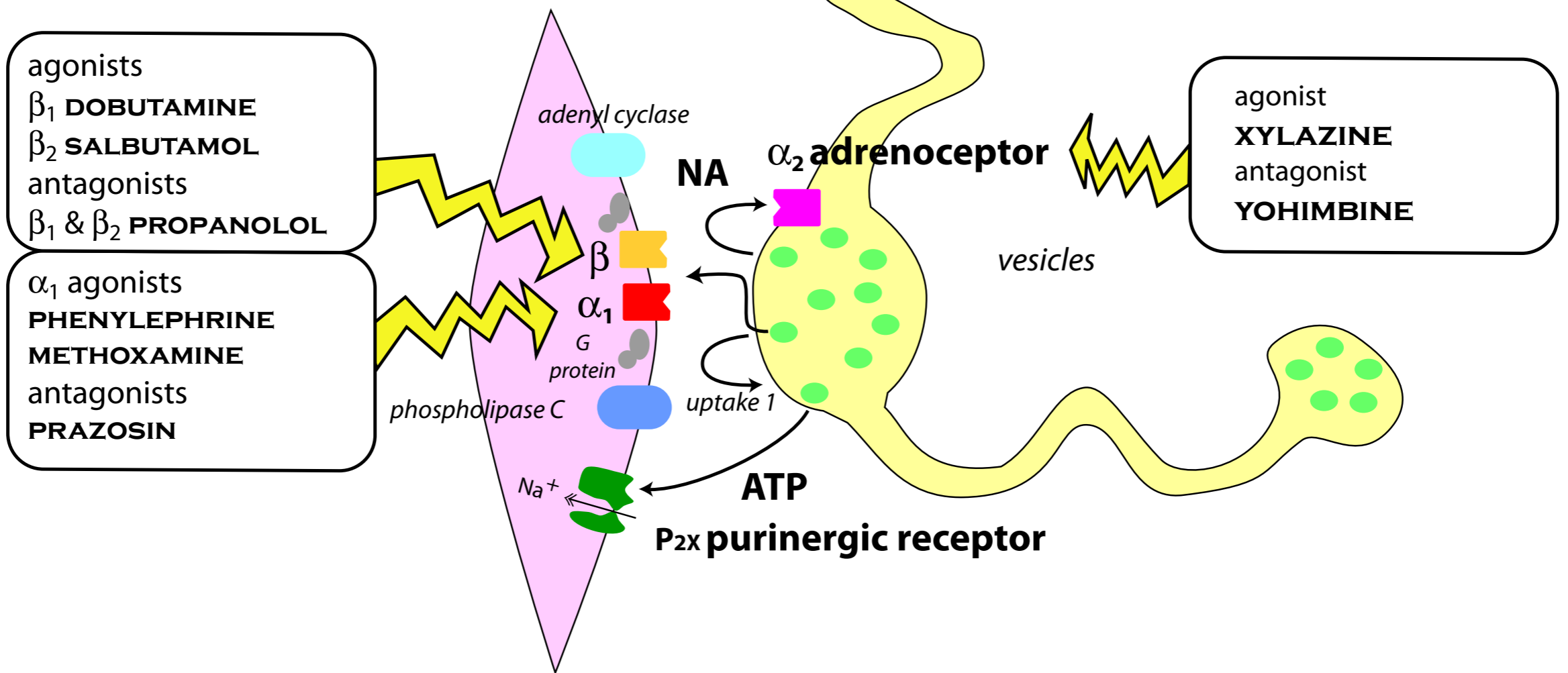
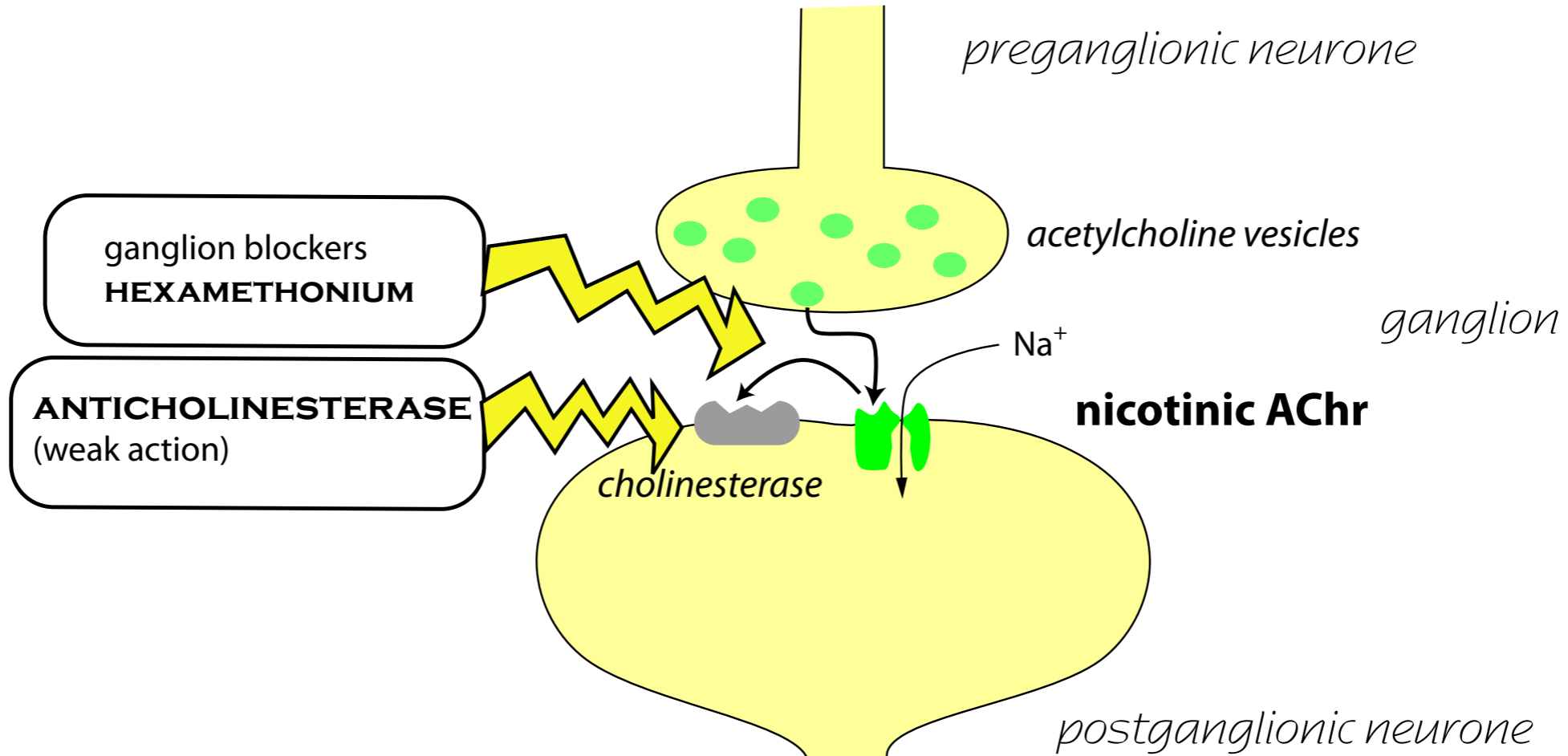
# adrenergic transmission

- **noradrenaline (norepinephrine USAN)**
  - from sympathetic nerve endings
- **adrenaline (epinephrine USAN)**
  - from adrenal glands
- **(dopamine)**
  - mainly in CNS
  - but also gut & visceral blood vessels

# sites of drug action

A large, red, mushroom-like structure with white spots, possibly a biological specimen, set against a background of dry grass. The structure is roughly circular and has a textured surface. The background is a dense field of dry, brownish-yellow grass.

- **synthesis**
- **storage**
- **release**
- **receptor binding**
- **uptake**

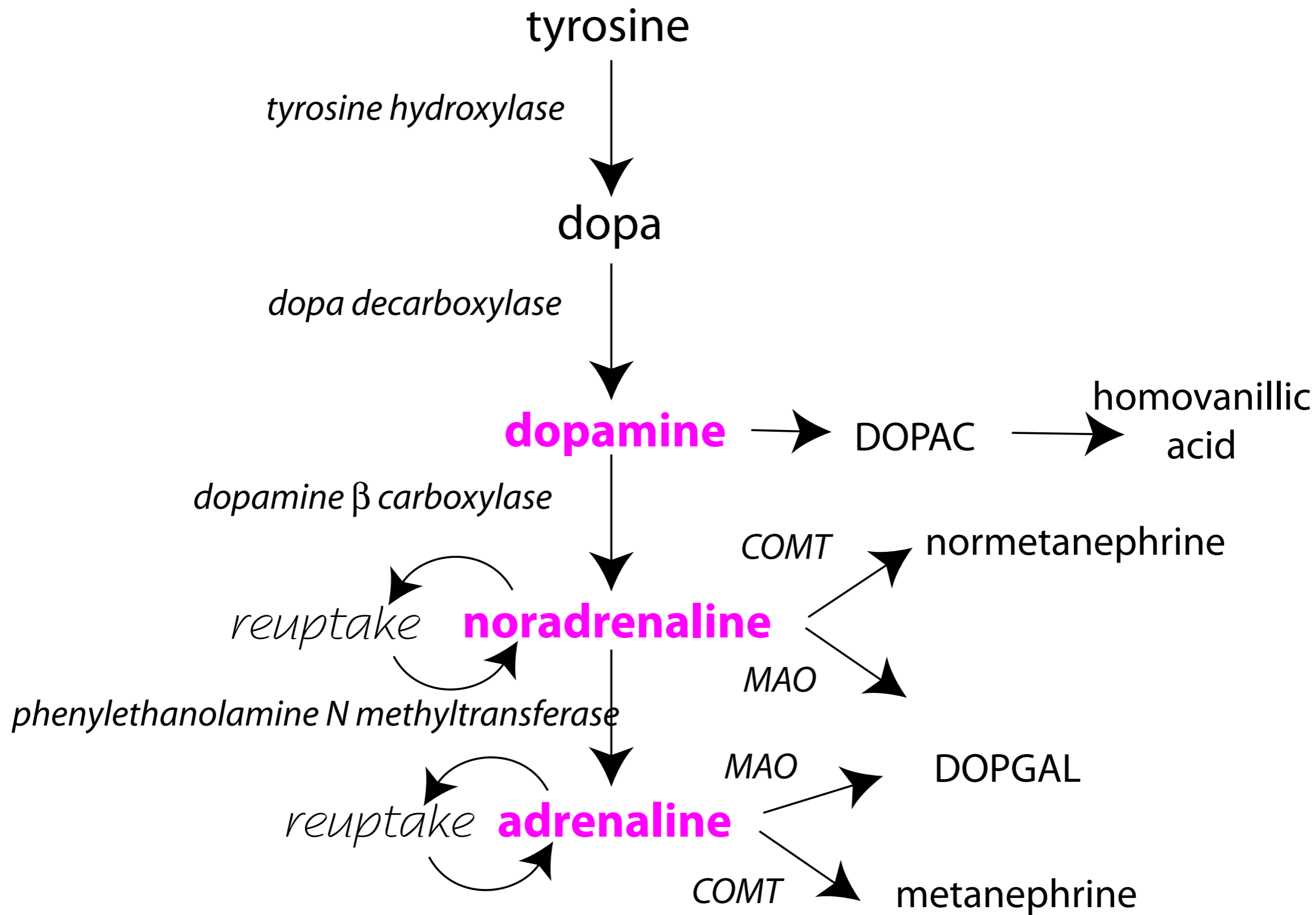


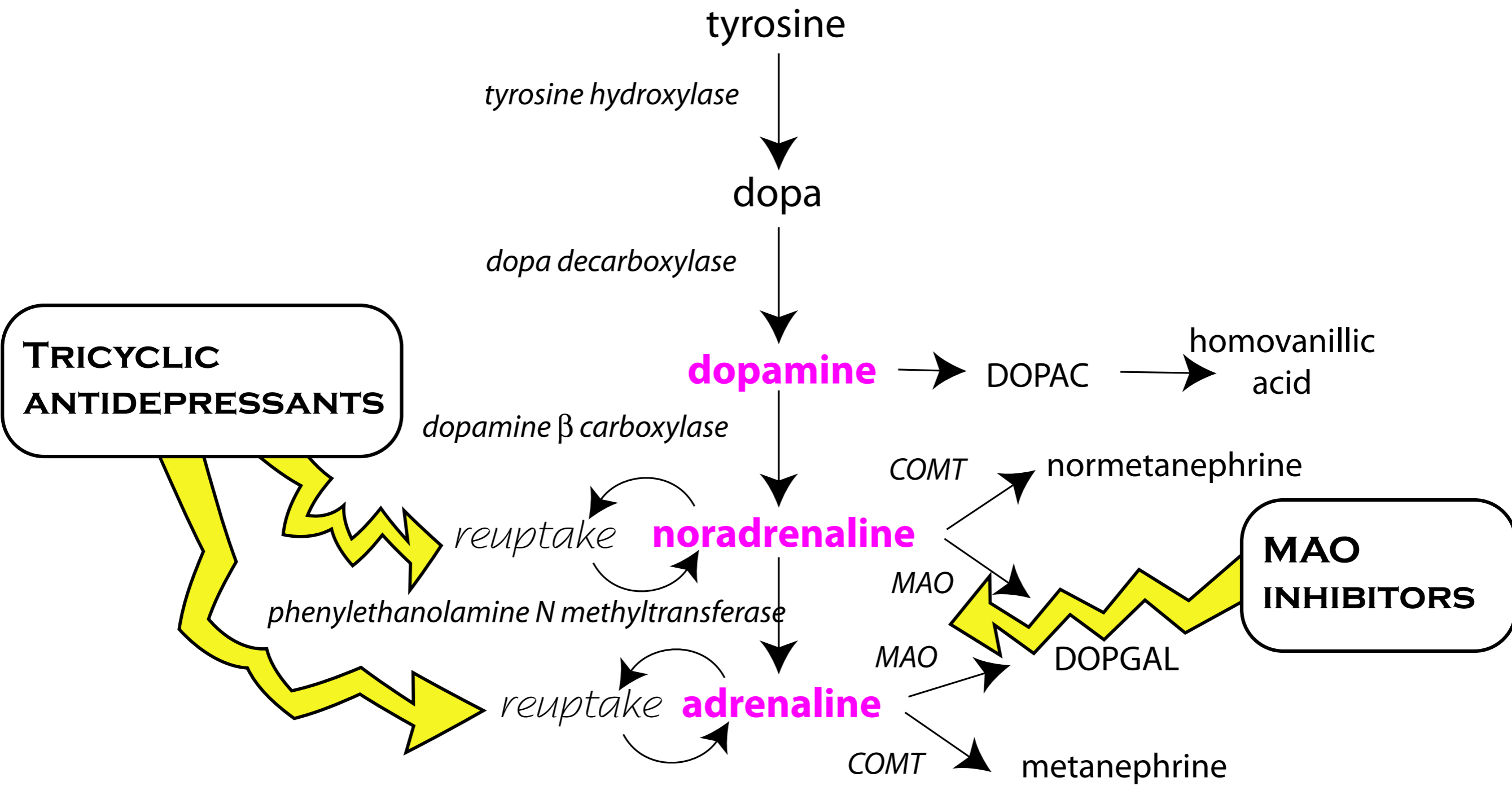
# sites of drug action



- **synthesis**
  - **false transmitters**
    - **methyl dopa**
    - **6 hydroxydopamine**
- **storage**
- **release**
- **receptor binding**
- **uptake**







# sites of drug action



- **synthesis**
- **storage**
  - **reserpine**
    - **blocks uptake into vesicles**
    - **causes NA depletion**
- **release**
- **receptor binding**
- **uptake**

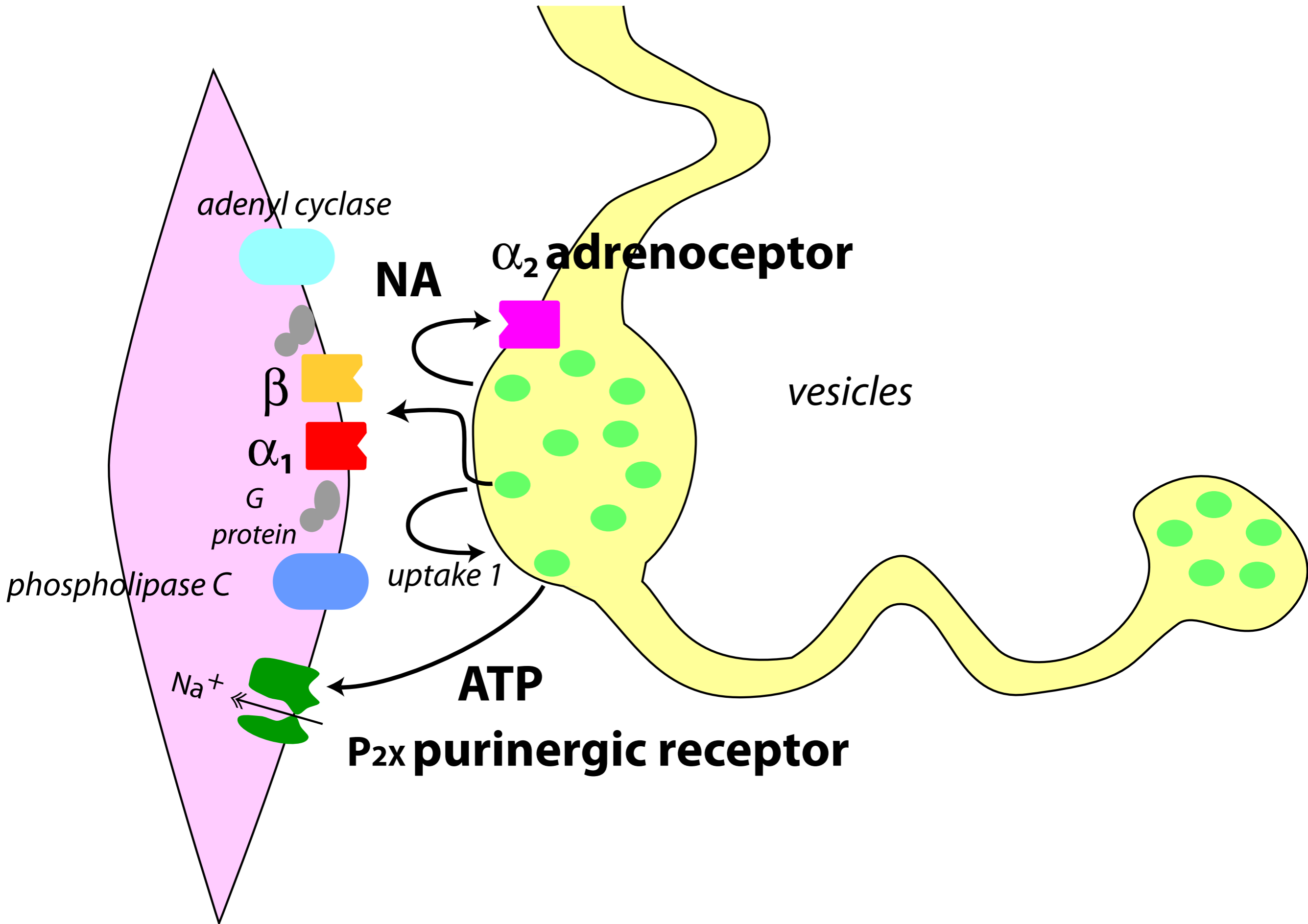
# sites of drug action

- **synthesis**
- **storage**
- **release**
  - **guanethidine**
  - **bretylum**
  - **Ca blockers**
- **receptor binding**
- **uptake**

# sites of drug action

A large, red, spotted mushroom with a white stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots. The stem is thick and white. The background is a dense field of dry, brown grass.

- **synthesis**
- **storage**
- **release**
- **receptor binding**
- **uptake**



receptor	transmitter	useful effects	agonist	antagonist
$\alpha 1$	adrenaline noradrenaline	vasoconstriction mydriasis	phenylephrine	prazosin
$\alpha 2$	adrenaline noradrenaline	(vasodilatation) sedation & analgesia	xylazine detomidine	yohimbine atipamezole
$\beta 1$	adrenaline (noradrenaline)	+ve inotropy tachycardia	dobutamine dopamine	atenolol metoprolol
$\beta 2$	adrenaline	bronchodilatation vasodilatation (muscle) uterine relaxation	salbutamol clenbuterol	propranolol (nonselective)
( $\beta 3$	adrenaline	lipolysis	SR58611A	SR59230A)

# $\alpha 2$ adrenoceptors

- presynaptic in periphery
- postsynaptic in CNS
- always inhibit the neurone they are on



# clinical use of agonists

- heart failure
  - adrenaline &  $\beta$ 1 agonists
- anaphylactic reactions
  - adrenaline
- delay parturition
  - clenbuterol
- sedation and analgesia
  - xylazine and  $\alpha$ 2 agonists

# clinical use of antagonists

- **slow heart**
  - **$\beta$ 1 blockers**
- **(vasodilatation)**
  - **$\alpha$ 1 blockers**
- **reversal of  $\alpha$ 2 sedation**
  - **$\alpha$ 2 blockers**

# sympathomimetics

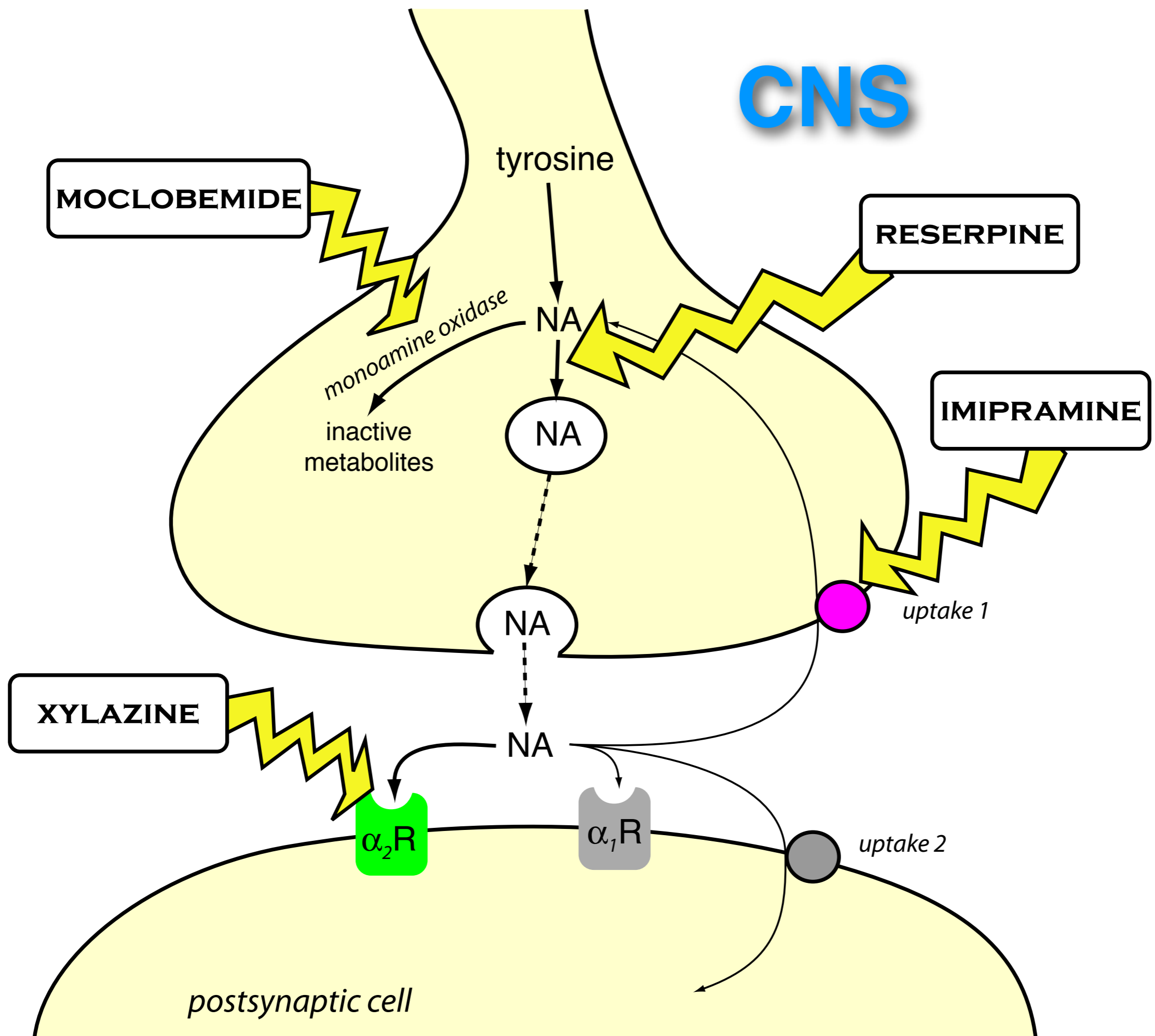
- **directly acting**
  - **at receptors**
- **indirectly acting**
  - **alter NA release / uptake**
  - **usually have some direct effect as well**
- **mixed**

# sites of drug action

A large, red, spotted mushroom with a white stem, growing in a field of dry grass. The mushroom has a bright red cap with numerous white spots. The stem is thick and white. The background is a dense field of dry, brown grass.

- **synthesis**
- **storage**
- **release**
- **receptor binding**
- **uptake**

# CNS



MOCLOBEMIDE

RESERPINE

IMIPRAMINE

XYLAZINE

tyrosine

NA

NA

NA

NA

$\alpha_2R$

$\alpha_1R$

uptake 2

uptake 1

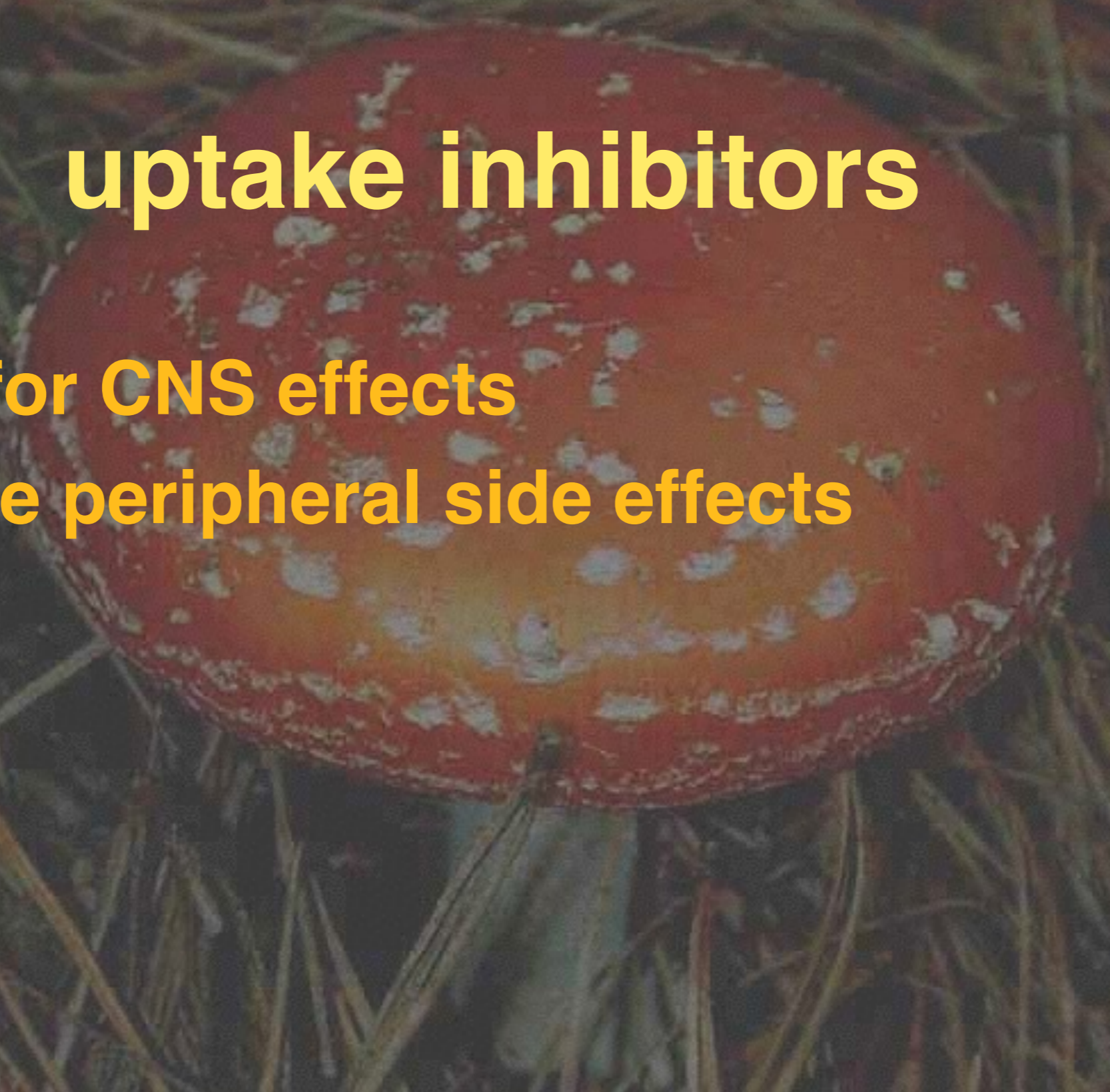
monoamine oxidase

inactive metabolites

postsynaptic cell

# uptake inhibitors

- **used for CNS effects**
- **beware peripheral side effects**



# uptake inhibitors

- **tricyclic antidepressants**
- **“selective” serotonin uptake inhibitors (SSRIs)**
- **monoamine oxidase inhibitors**
- **(cocaine)**
- **(amphetamine)**

# co-transmission

- vesicle released at synapse
- mixture of transmitters in vesicle
  - noradrenaline
  - ATP
  - neuropeptide Y (& in separate vesicles)
  - others???
- mixture may not always be the same



# co-transmission

- **ATP**
  - P2x purinoceptors responsible for fast transmission
    - > 7 subtypes
    - CNS as well as smooth muscle & peripheral nerves
  - P2y purinoceptors ??
  - potentiates effects of noradrenaline
- **peptides**
  - neuropeptide Y
  - chromogranin??

fast

ATP

noradrenaline

peptide co-transmitters

inflammatory mediators

slow

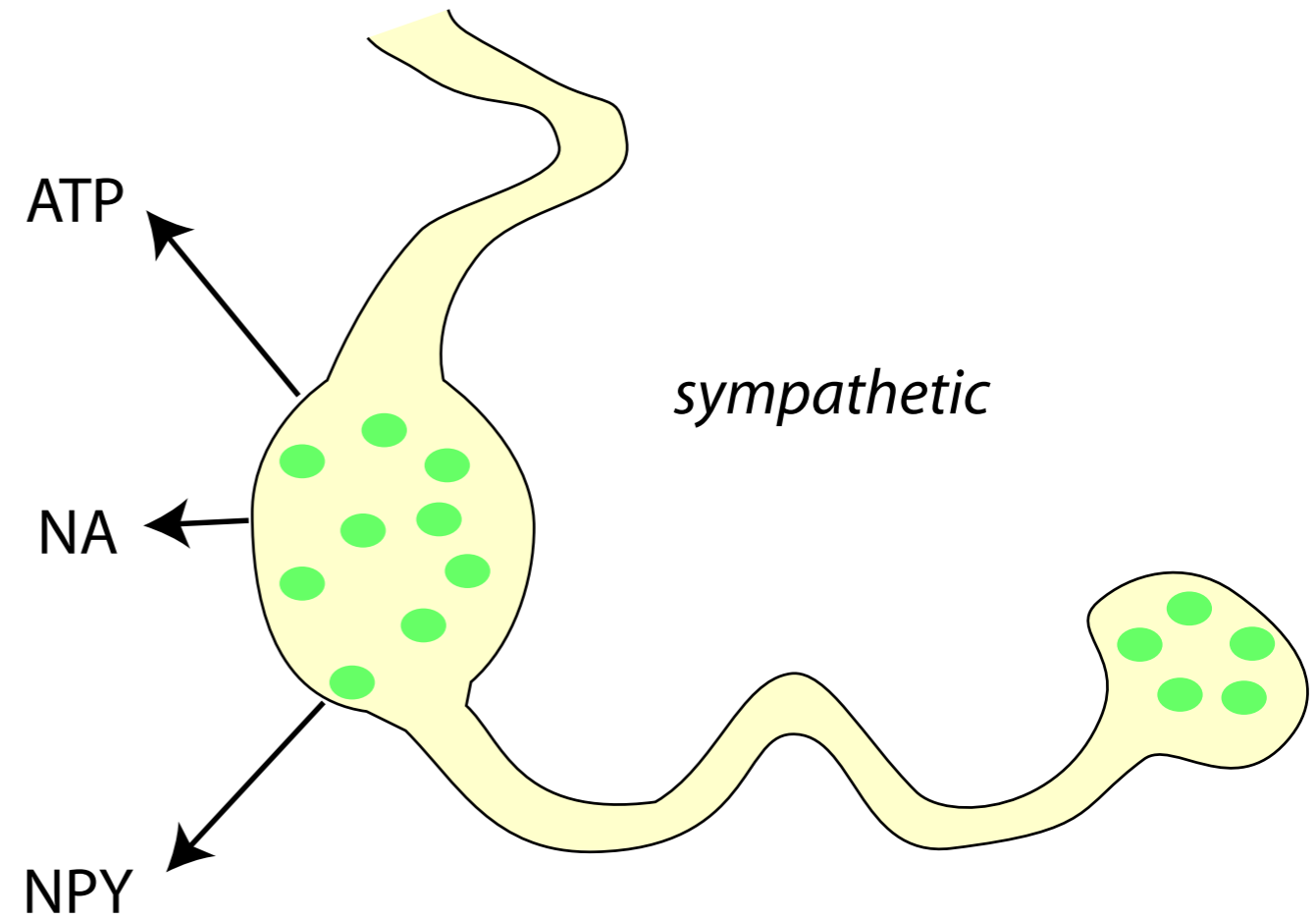
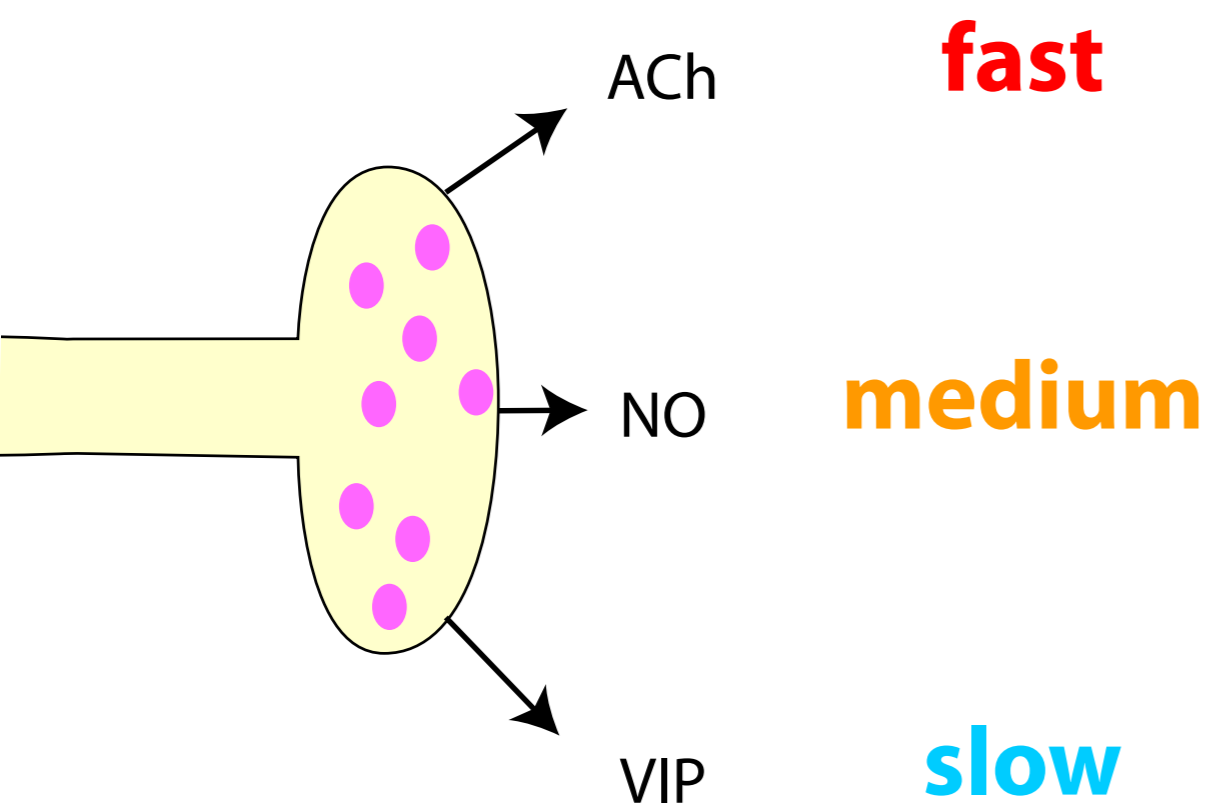


# **non-adrenergic non- cholinergic transmission**

- **nitric oxide**
- **vasoactive intestinal peptide**
- **neuropeptide Y**
- **gonadotrophin releasing hormone**
- **5 hydroxytryptamine**
- **$\gamma$  aminobutyric acid**
- **dopamine**

# NANC transmission

*parasympathetic*



various stimuli



*nitric oxide synthase*

arginine + oxygen

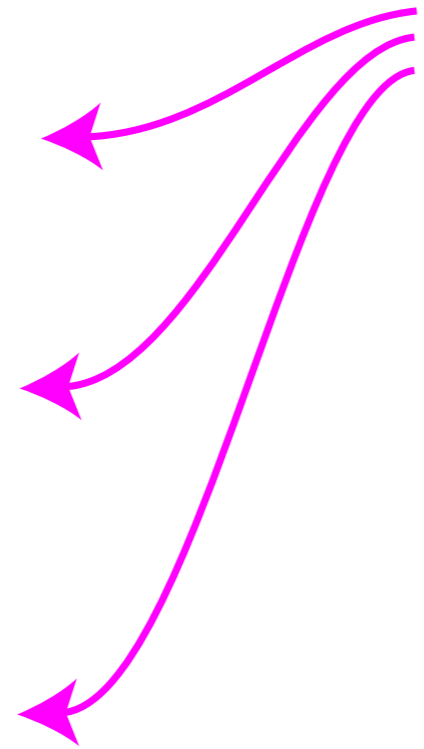


**NO** + citrulline

guanylate cyclase

other enzymes  
containing haem

peroxynitrite  
free radicals



O<sub>2</sub>

N<sub>2</sub>O<sub>4</sub>



H<sub>2</sub>O

NO<sub>3</sub><sup>-</sup> + NO<sub>2</sub><sup>-</sup> + H<sup>+</sup>

# NANC transmission

A photograph of a red mushroom with white spots, likely a Amanita muscaria, growing on a bed of pine needles. The mushroom is the central focus, with its bright red cap and white spots contrasting against the dry, brownish-green needles. The background is a dense layer of these needles, creating a textured, natural setting.

- **nitric oxide**
  - relaxes smooth muscle
  - neuronal excitation
  - excitotoxicity

# oxides of nitrogen

- nitric oxide - NO
  - vasodilator & neuromodulator
- nitrous oxide - N<sub>2</sub>O
  - anaesthetic gas
- nitrogen dioxide - NO<sub>2</sub>
  - environmental pollutant
- do not mix them up!!!

# NANC transmission

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- **nitric oxide**
  - **nitroergic neurones**
  - **2% of brain neurones**



**What would you do?**



# downer cow



- given dexamethasone 10 mins earlier to induce calving
- now gone down
- some swelling around perineum
- shaking / muscle twitching
- grunting respiration

# problems

- **histamine release**
  - **vasodilatation**
  - **increased vascular permeability**
  - **smooth muscle contraction**
  - **cardiac stimulation**
  - **increased abomasal secretions**

# treatment?

- **adrenaline**
  - route?
- **antihistamines?**



# **(nor)adrenergic transmission**

- **NA synthesised from tyrosine & stored in vesicles**
- **release requires calcium**
- **NA binds to a variety of adrenergic receptors throughout the body**
- **action terminated by reuptake**
- **all these processes can be affected by drugs**
- **ATP co-transmission important**