

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 'Central Neurotransmission' is overlaid in yellow on the mushroom's cap.

Central Neurotransmission

A red mushroom with white spots is the central focus of the image, resting on a bed of dry, brown grass. The mushroom's cap is bright red with irregular white patches, and its stem is a pale, almost white color. The background is a dense field of dry grass, creating a textured, natural setting. The overall lighting is somewhat dim, giving the scene a slightly somber or mysterious atmosphere.

**by the end of this lecture you
should be able to**

- **predict the consequences of giving drugs which interact with CNS neurotransmission**

8yr old farm Collie

- dosed with pour-on ivermectin 2 d ago
- ataxia
- blind
- tremors
- hypersalivation (may have vomited)
- generally depressed

definitions

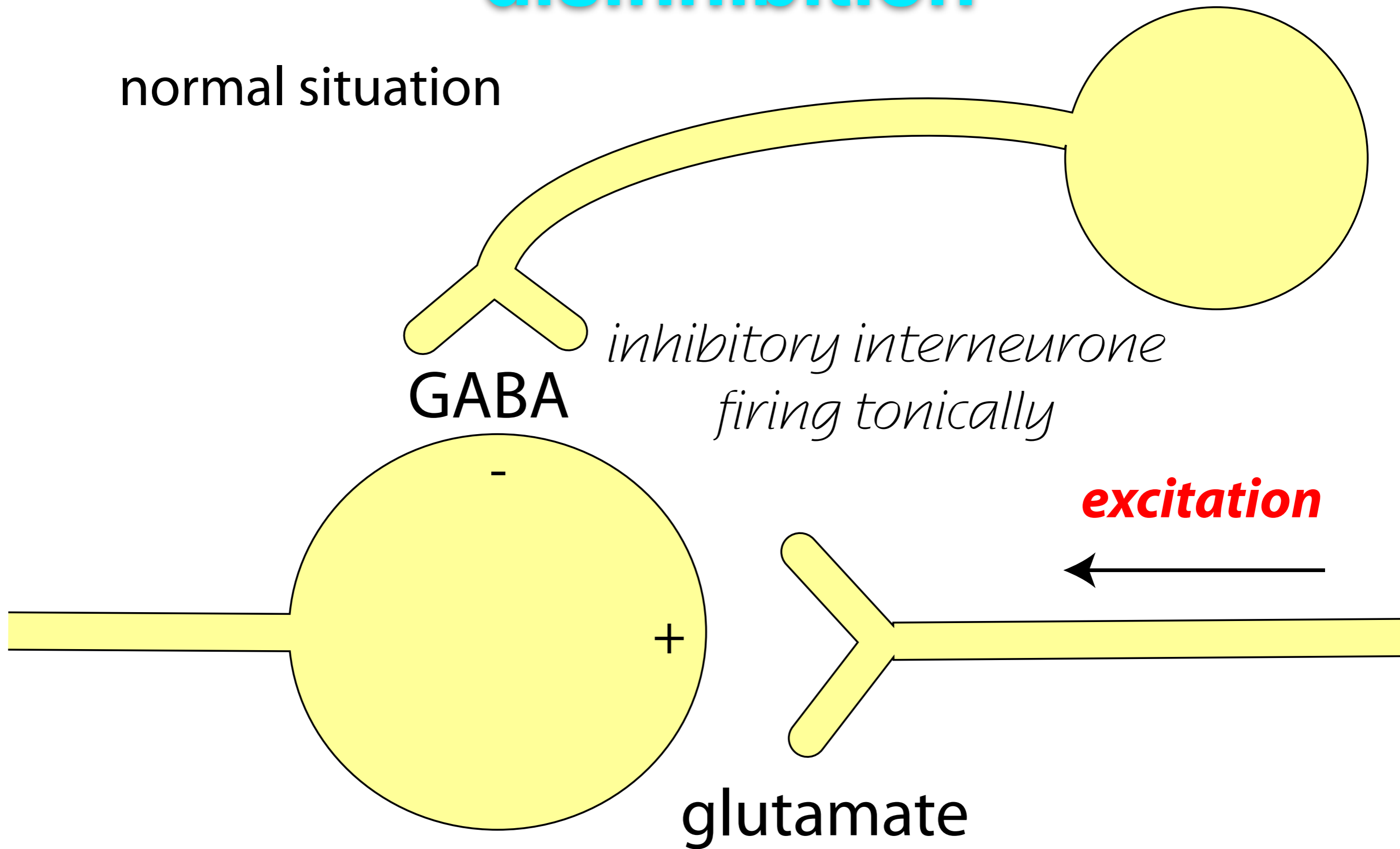
- **neurotransmitter**
 - acts rapidly, briefly & at short range
- **neuromodulator**
 - act more slowly and further away
 - responsible for most synaptic plasticity
 - not always from neurones

effects

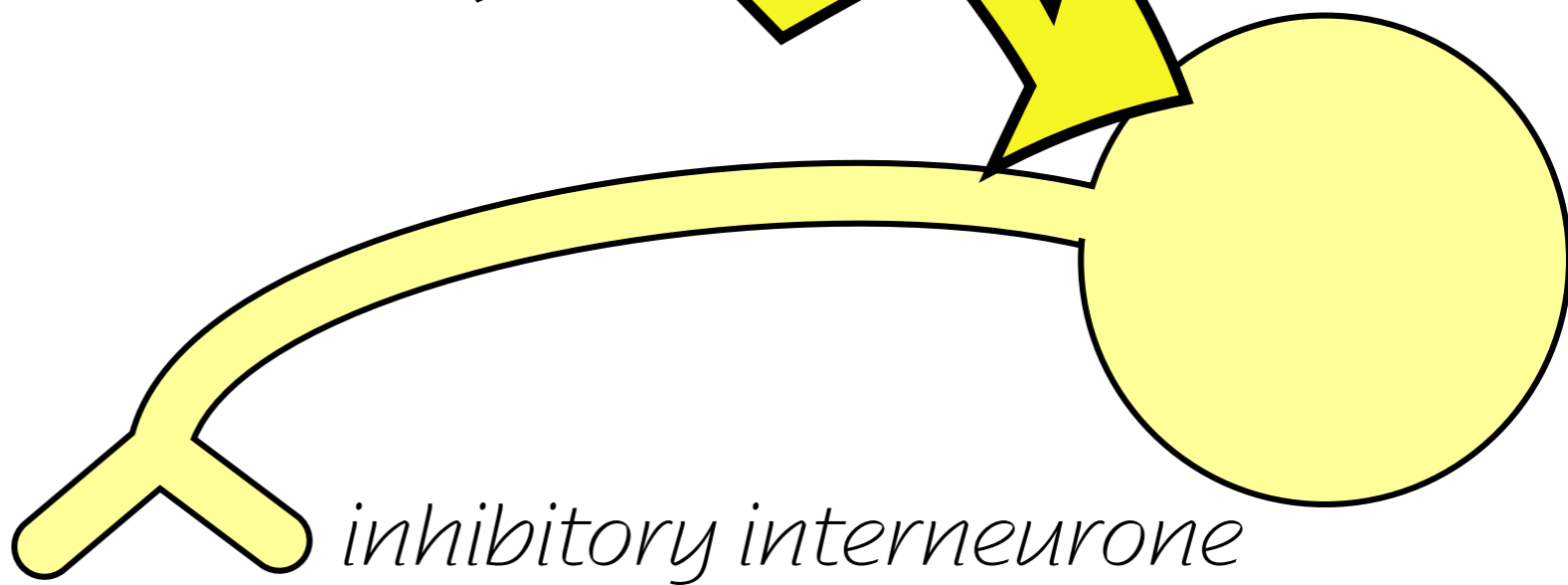
- behavioural - ? - cellular
- depend on
 - wiring (NGF etc)
 - receptor subtypes , distribution & numbers
 - transduction mechanisms
 - neuromodulators
 - their transduction mechanisms
 - all these can change!

disinhibition

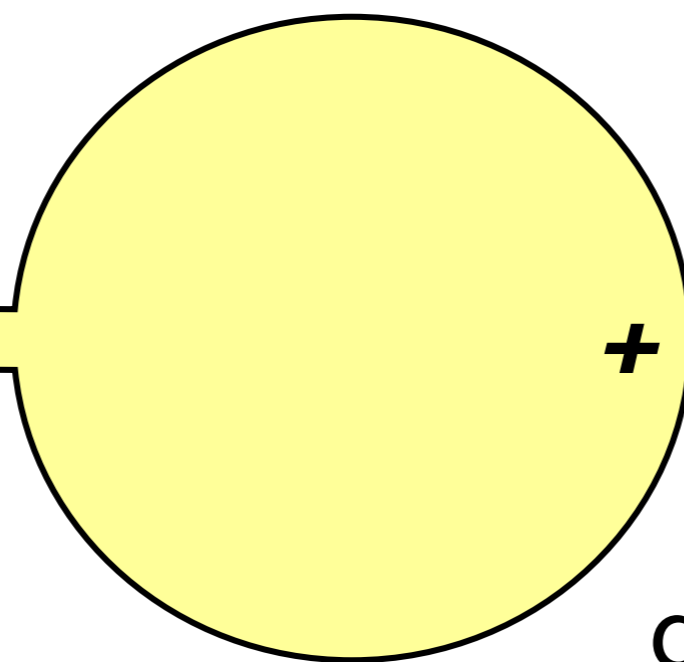
normal situation



INHIBITORY DRUG

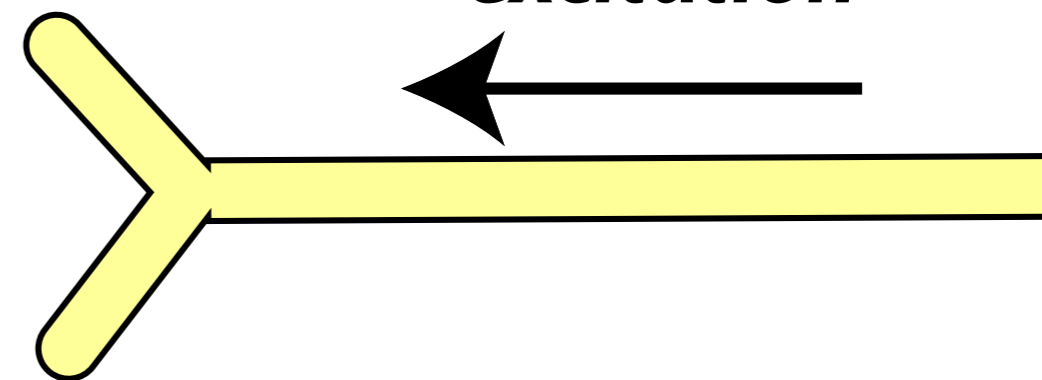


excitation



glutamate

excitation



time course

- **milliseconds**
 - fast transmitters
- **tens of ms**
 - NMDA receptors
- **seconds - minutes**
 - neuromodulators
- **minutes - days**
 - receptor up / down regulation
- **days - weeks (-never)**
 - neurone reconnections

neurotransmitters

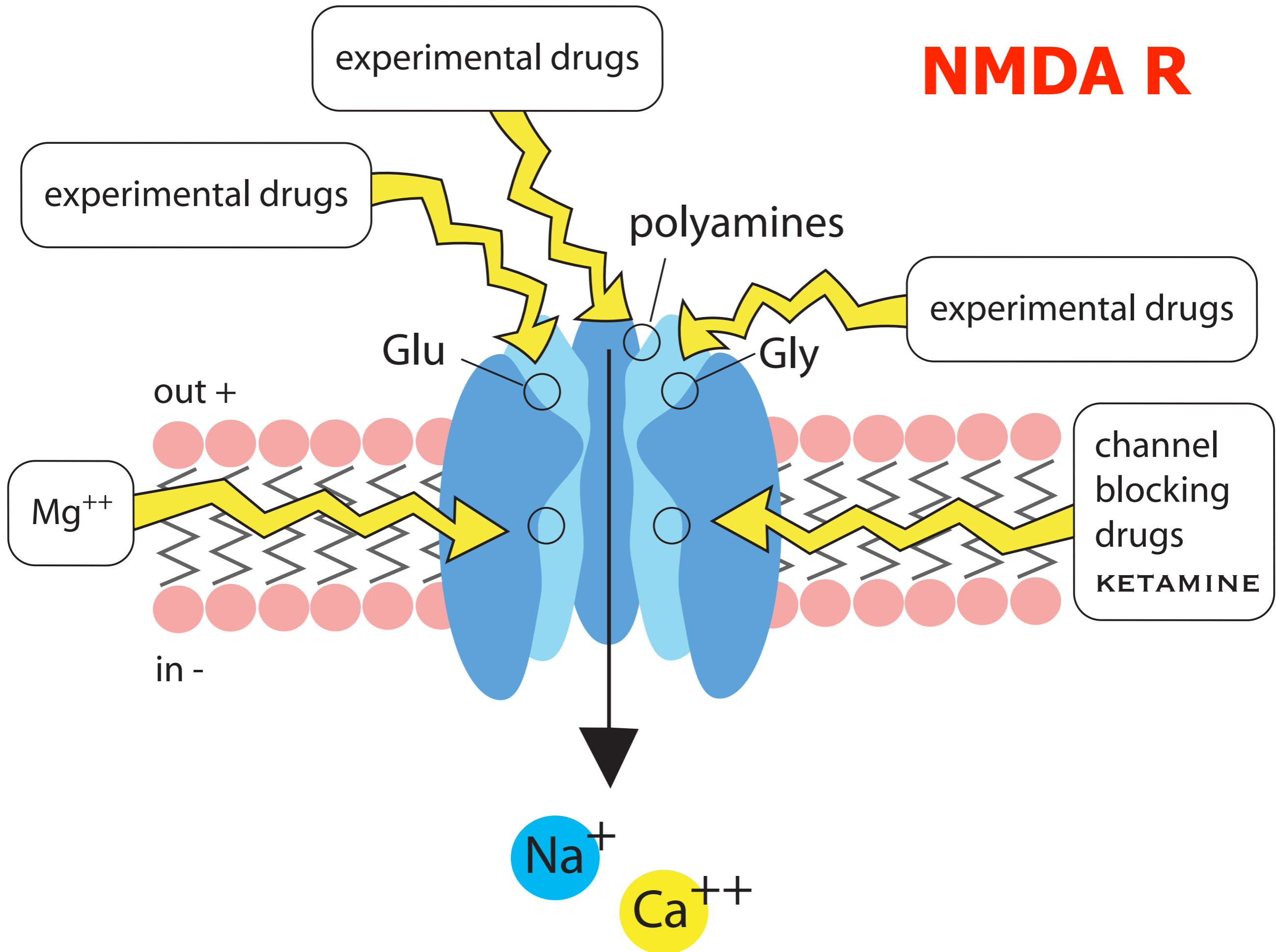
A large, red, gilled mushroom with white spots on its cap, growing on a bed of dry pine needles. The mushroom is the central focus of the image, with its cap showing a gradient from red to orange and yellow. The background is a dense layer of dry, brown pine needles.

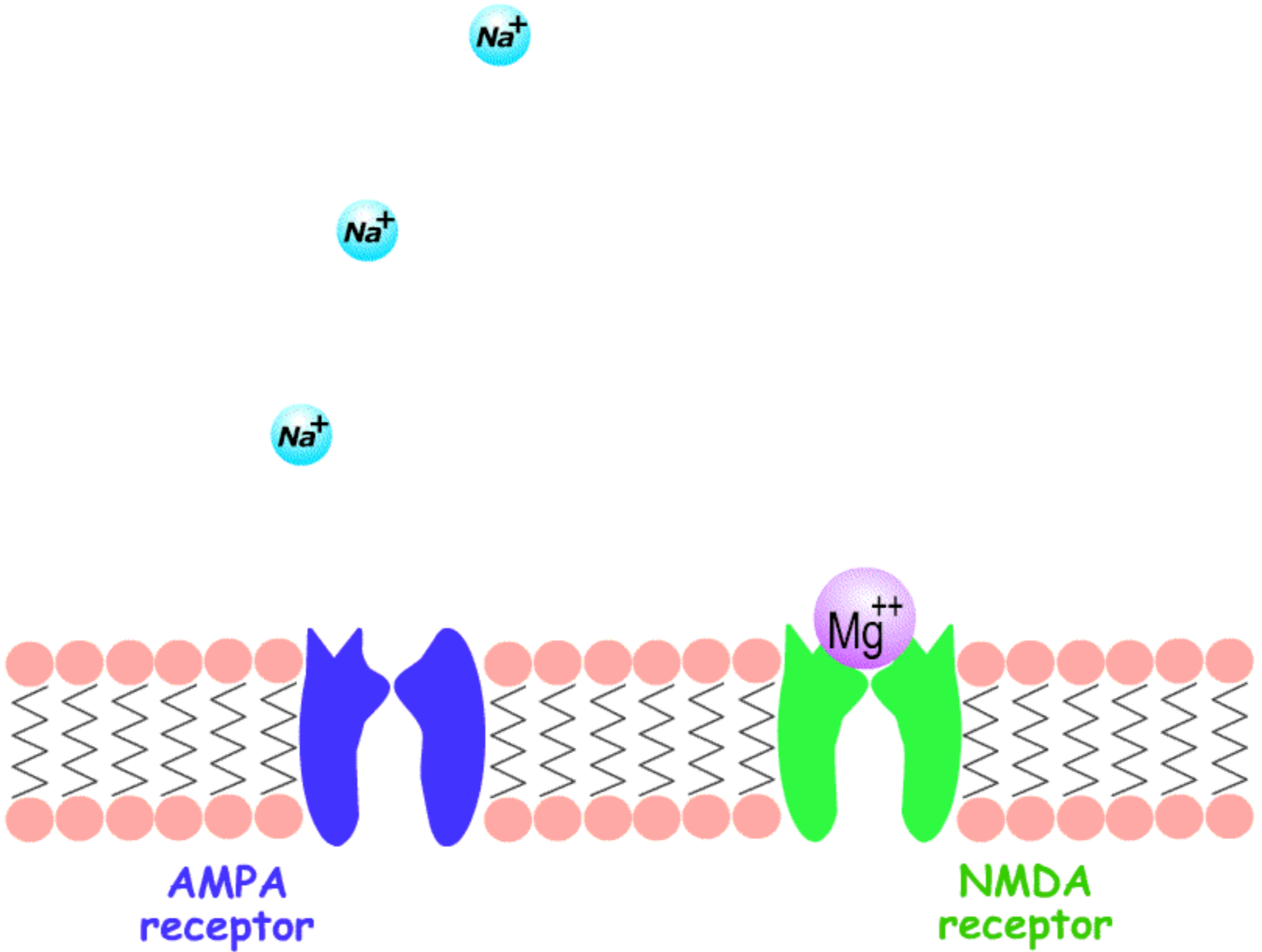
- **excitatory**
 - glutamate
- **inhibitory**
 - GABA
 - glycine
 - catecholamines
- **both / either**
 - 5HT
 - adenosine / ATP

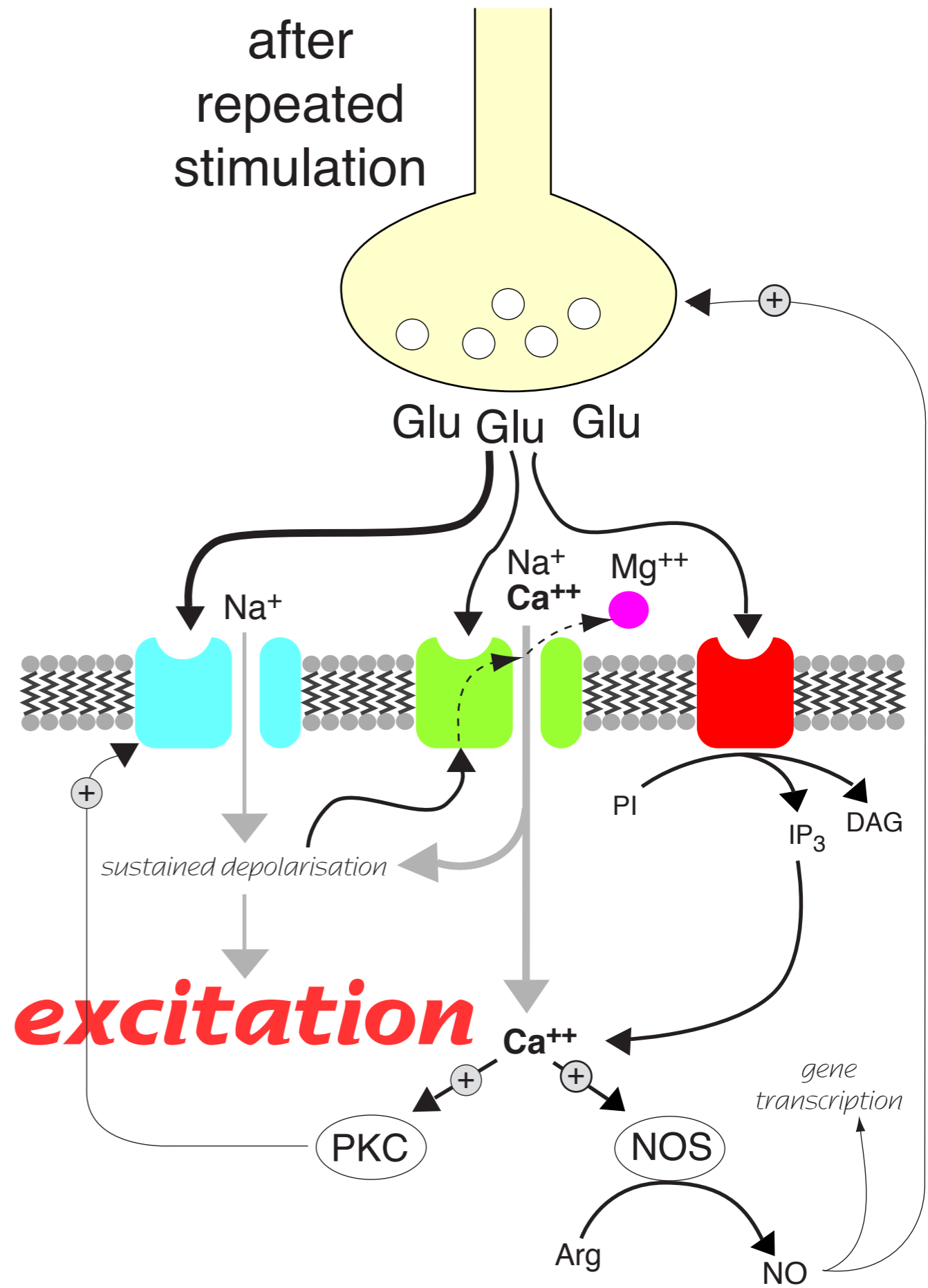
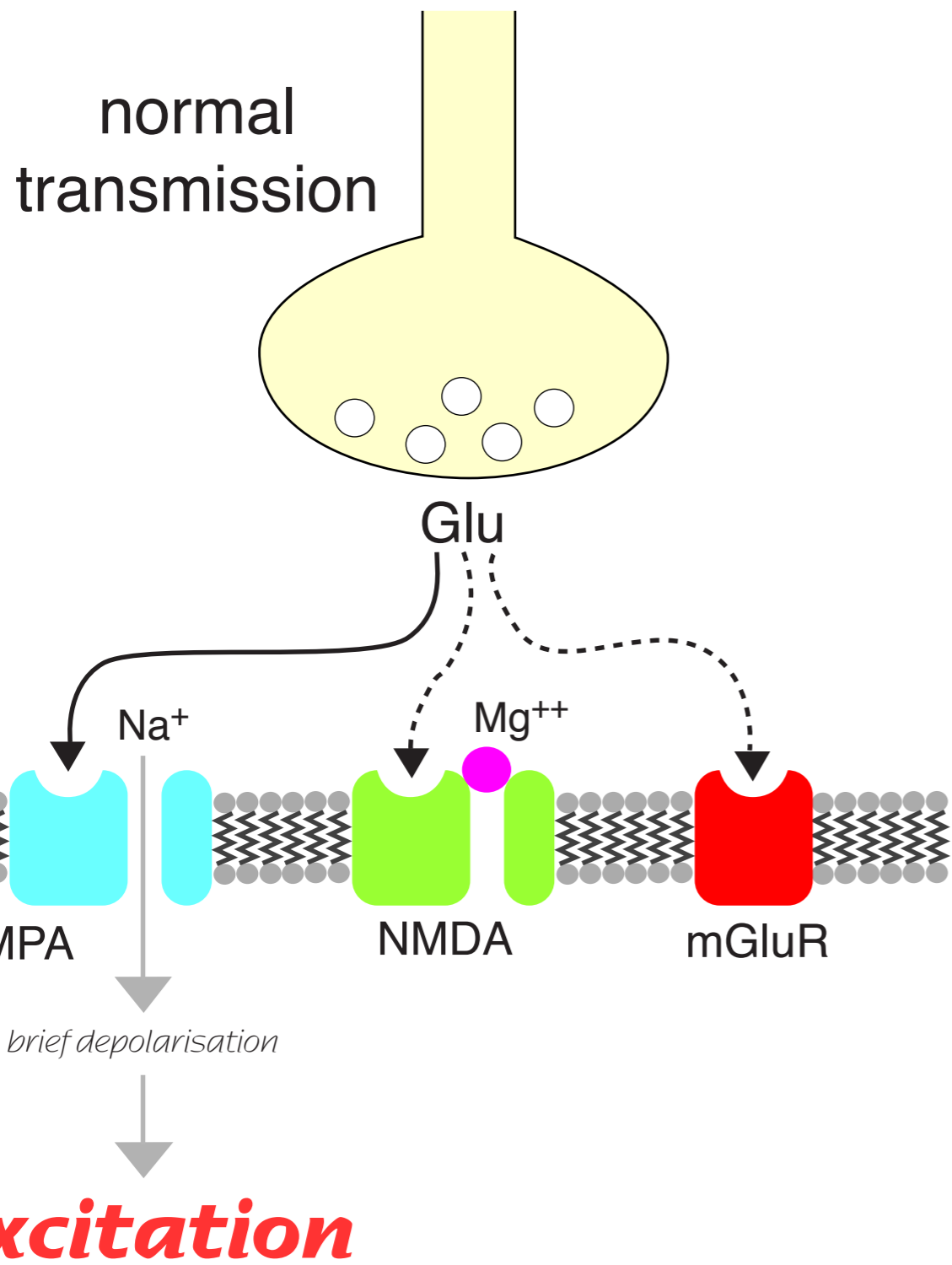
glutamate receptors

- **AMPA fast**
 - normal transmission
- **NMDA medium**
 - wind up
 - pain
 - memory
- **metabotropic slow (15 subtypes)**
 - modulation?
- **kainate fast**
 - ?

NMDA R







glutamate

A photograph of a mushroom with a bright red cap and white spots, growing on a bed of dry pine needles. The mushroom is the central focus of the image.

- energy metabolism
- excitotoxicity

neurotransmitters



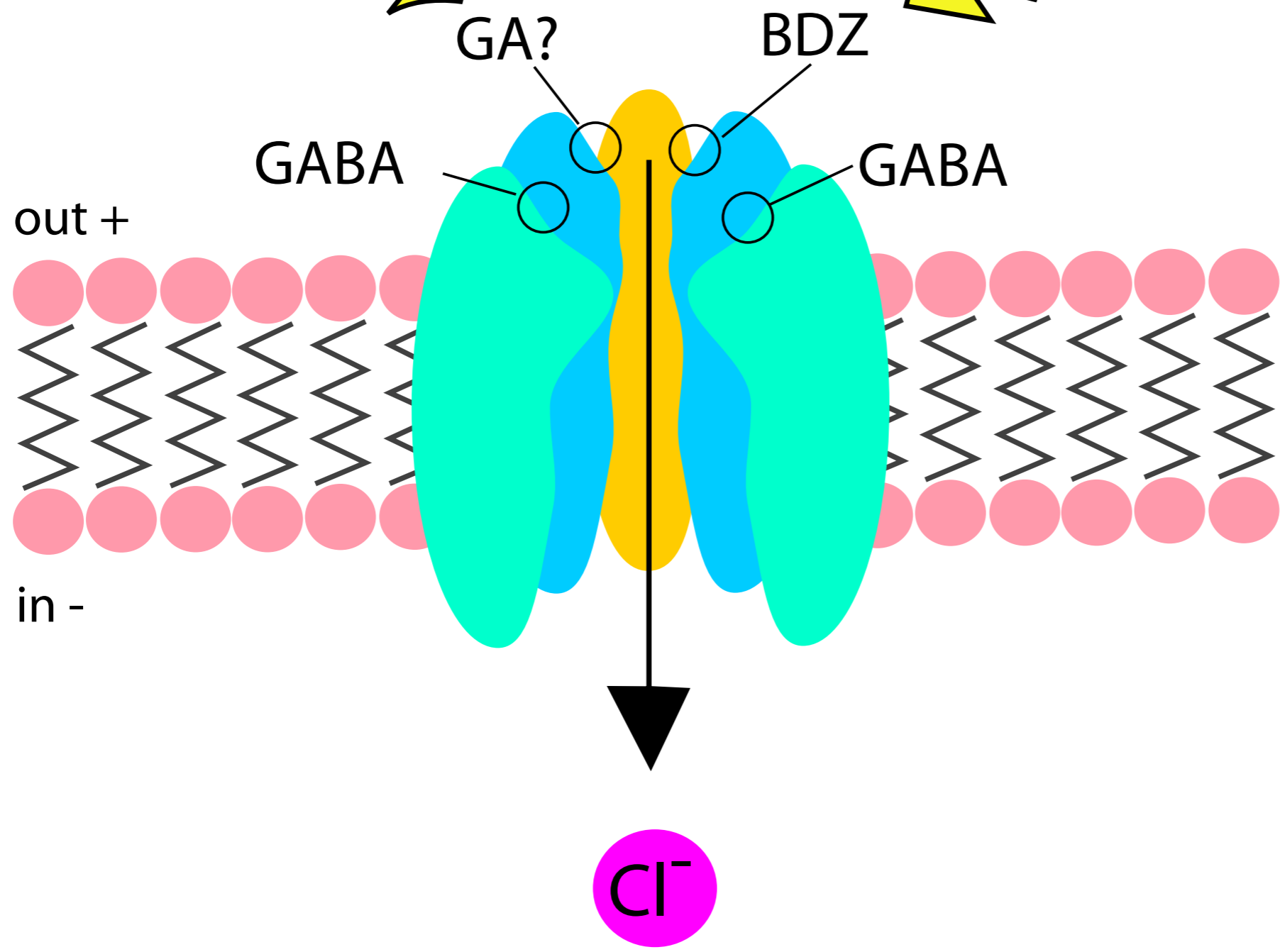
- **excitatory**
 - **glutamate**
- **inhibitory**
 - **GABA**
 - **glycine**
 - **catecholamines**
- **both / either**
 - **5HT**
 - **adenosine / ATP**

GABA / glycine receptors

- **GABA_A**
- **glycine**
 - postsynaptic chloride channels
- **GABA_B**
 - presynaptic, G protein coupled
- **glycine / NMDA**
 - on NMDA receptor
- **glutamate (nematodes)**

BARBITURATES
OTHER INJECTION ANAESTHETICS?
INHALATION ANAESTHETICS?
ALCOHOL?

agonist **DIAZEPAM**
antagonist **FLUMAZENIL**
inverse agonist **βCARBOLINE**



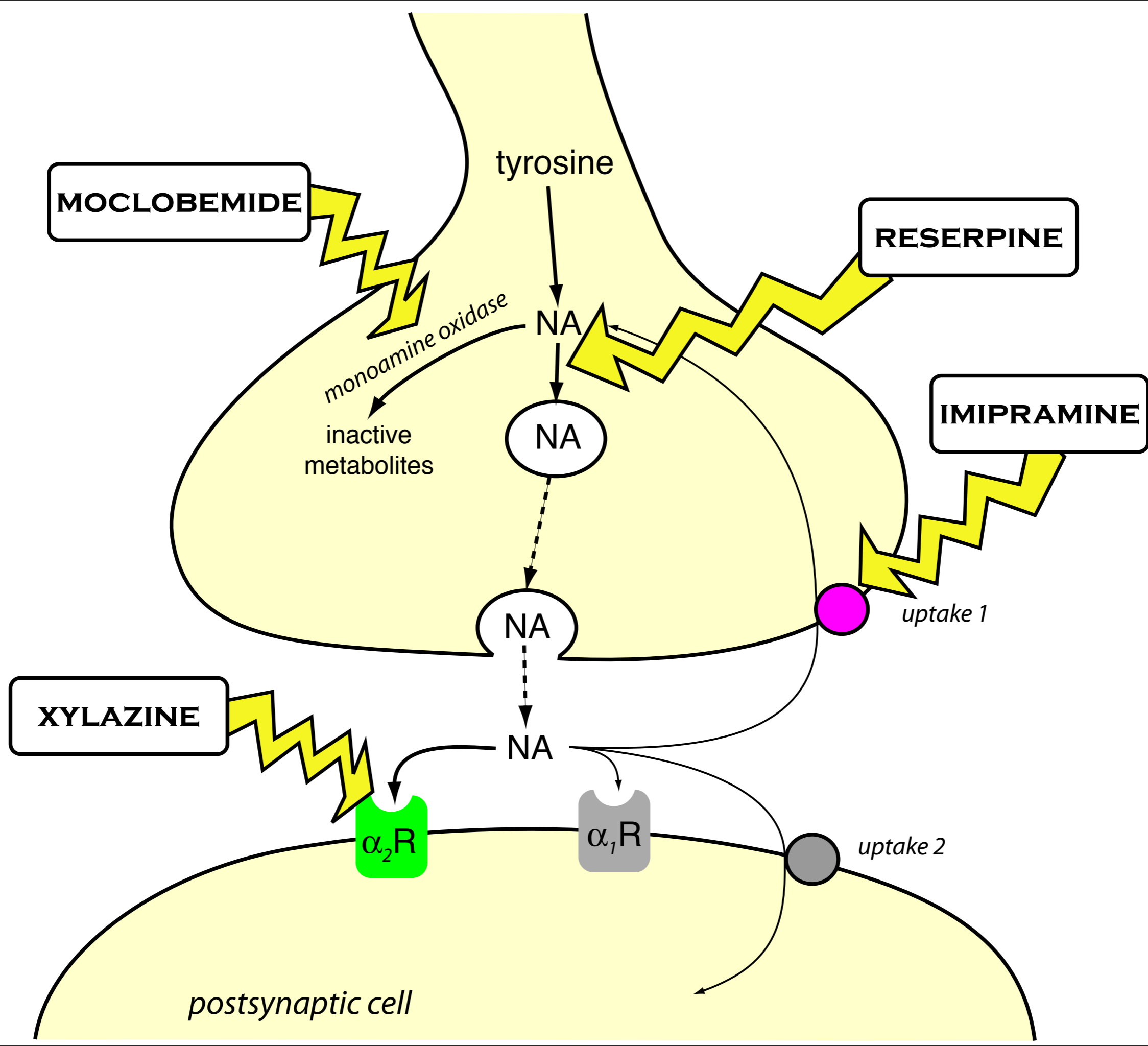
GABA / glycine receptors

- **GABA_A**
- **glycine**
 - postsynaptic chloride channels
- **GABA_B**
 - presynaptic, G protein coupled
- **glycine / NMDA**
 - on NMDA receptor
- **glutamate (nematodes)**

monoamine receptors

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.

- **noradrenaline**
- **dopamine**
- **5HT**
- **octopamine**



noradrenaline

- **mostly postsynaptic α_2**
- **mostly inhibitory**
- **alertness, pain, blood pressure**



imidazolines

- I1
 - blood pressure
- I2
 - depression?? MAO
- I3
 - insulin release

dopamine

- **currently 5 receptors**
- **D2**
 - **reward pathway**
 - **pituitary hormone release**
 - **nigrostriatal pathway**
 - **vomiting**

5HT receptors in brain

- $5HT_{1A}$ - mood / emotion, pain?
- $5HT_{1C}$ - CSF secretion, motor function
- $5HT_{1D}$ - motor function
- $5HT_2$ - stereotypy, mood / emotion, hallucinations
- $5HT_3$ - anxiety, emesis, pain?
- + 9 other subtypes!

reuptake inhibitors

A photograph of a red mushroom with white spots, likely a fly agaric, resting on a bed of dry pine needles. The mushroom is the central focus, with its vibrant red cap and white spots contrasting against the brown, needle-covered ground. The lighting is somewhat dim, giving the scene a natural, slightly somber feel.

- **human antidepressants**
- **used to alter animal behaviour**

other fast transmitters

- **acetylcholine**
 - nAChR, mAChR
- **histamine**
 - H1, H2, H3
- **adenosine, ATP, AMP**

purinergic receptors

- **adenosine**
 - A1 and A2 R - G protein coupled
 - presynaptic inhibition
- **ATP**
 - P2x (ionotropic) P2y (metabotropic)
 - co-transmission in periphery, nociception

neuromodulators

- **excitatory**
 - substance P
 - neurokinins A & B
 - cholecystokinin
 - nitric oxide, carbon monoxide
 - arachidonic acid / prostaglandins
 - etc, etc

neuromodulators

- **inhibitory**
 - enkephalins, morphine - μ , δ R
 - some dynorphins - κ R
 - cannabinoids - CB1, CB2 R
 - magnesium?
 - zinc??

adaptive processes

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- **cfos, cjun**
- **growth factors**

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central neurotransmitters

- glutamate is the main excitatory transmitter
- glutamate acts at AMPA (fast), NMDA (medium) and mGlu (slow)
- GABA is the main inhibitory transmitter, acting at GABA_A receptors
- neuromodulators act slowly to amplify or reduce transmission
- noradrenaline, acting at α_2 receptors, causes CNS depression