Central Neurotransmission

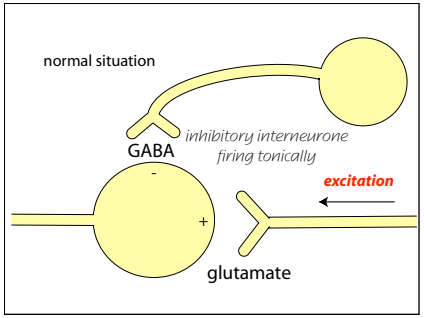
definitions

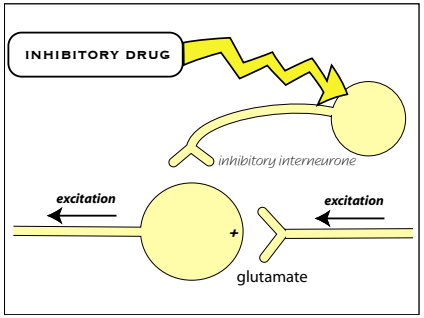
- neurotransmitter
  - acts rapidly, briefly & at short range
- neuromodulator
  - act more slowly and further away
  - responsible for most synaptic plasticity
  - not always from neurones

effects

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

disinhibition





time course

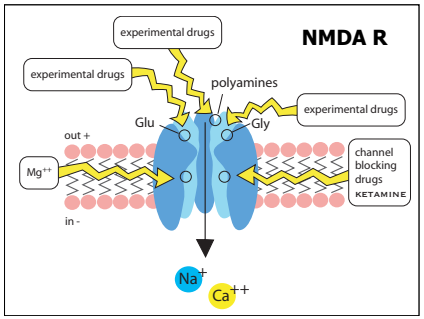
- **milliseconds**
  - **fast transmitters**
- **tens of ms**
  - **NMDA receptors**
- **seconds – minutes**
  - **neuromodulators**
- **minutes – days**
  - **receptor up / down regulation**
- **days – weeks (-never)**
  - **neurone reconnections**

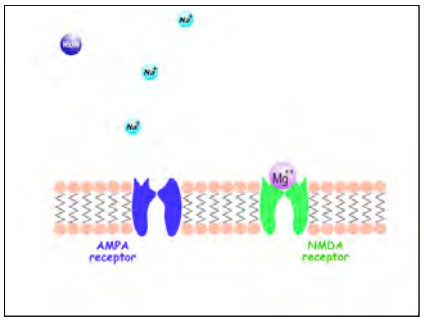
neurotransmitters

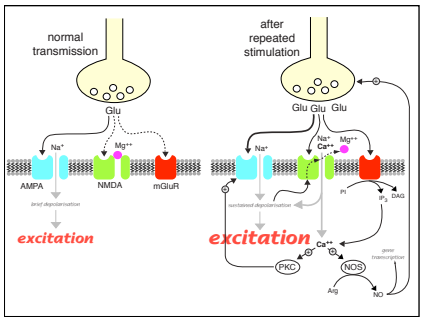
- **excitatory**
  - **glutamate**
- **inhibitory**
  - **GABA**
  - **glycine**
  - **catecholamines**
- **both / either**
  - **5HT**
  - **adenosine / ATP**

glutamate receptors

- **AMPA fast**
  - **normal transmission**
- **NMDA medium**
  - **wind up**
  - **pain**
  - **memory**
- **metabotropic slow (9 subtypes)**
  - **modulation?**
- **kainate fast**
  - **?**







glutamate

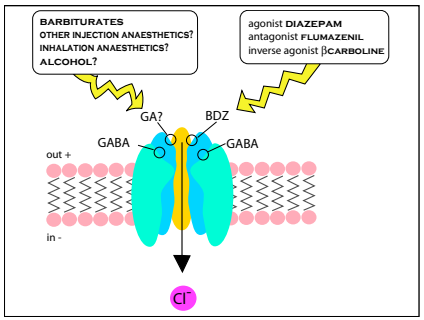
- energy metabolism
- excitotoxicity

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)

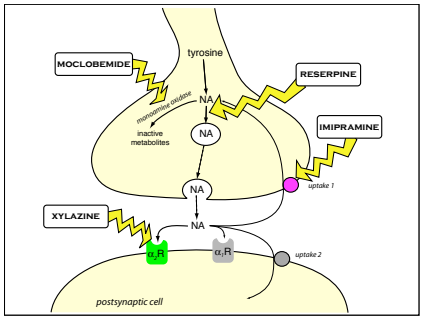


GABA / glycine receptors

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

monoamine receptors

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



noradrenaline

- **mostly postsynaptic α2**
- **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

- 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
  - encephalins, morphine – μ, δ R
  - some dynorphins – κ R
  - cannabinoids – CB1, CB2 R
  - magnesium?
  - zinc??

adaptive processes

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

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 a α_2 receptors, causes CNS depression**