Drug Receptor Interactions

1

agonist

- A drug which interacts with a specific receptor to produce a response
  - ie, it has efficacy

2

efficacy

- The ability to produce a response after binding

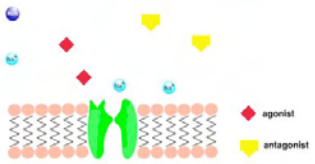
3

antagonist

- A drug which occupies a receptor stopping an agonist getting in
- it produces no effect on its own
  - ie, it has no efficacy

4

competitive antagonist



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inverse agonist

- A drug which occupies a receptor to produce the opposite effect to an agonist
  - ie, it has negative efficacy
- it is also blocked by an antagonist
- constitutive activation required

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partial agonist

- a drug which occupies a receptor and produces a resonse which is smaller than that of a full agonist
  - ie it has low efficacy

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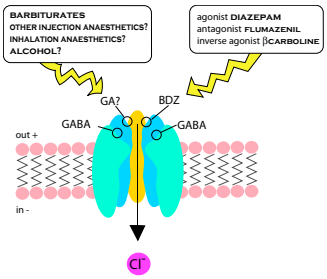

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affinity

- The tendency of a drug to bind to receptors

$$K_A = \frac{1}{K_D}$$

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affinity

- high affinity drug
  - high occupancy at low concentration
- low affinity drug
  - high occupancy at high concentration

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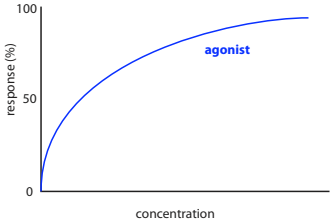
concentration response curves



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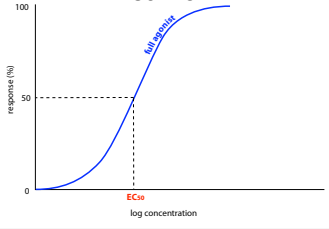
log concentration response curve



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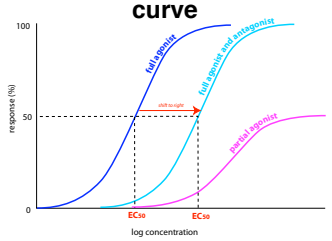
log concentration response curve



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antagonism

- competitive
  - reversible
  - irreversible
- non-competitive
  - usually channel blockers
- physiological
- chemical
- pharmacokinetic

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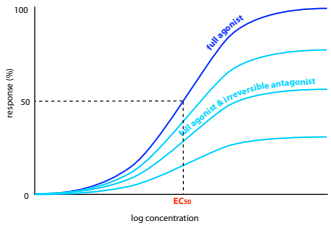
irreversible antagonist



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binding assays

- tissues homogenised
- cell membranes collected
- incubated with radioligand
- recovered by filtration & washed
- radioactivity measured
- K_D and B_{max} calculated

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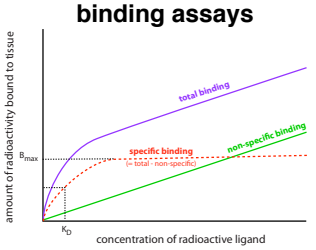
binding assays



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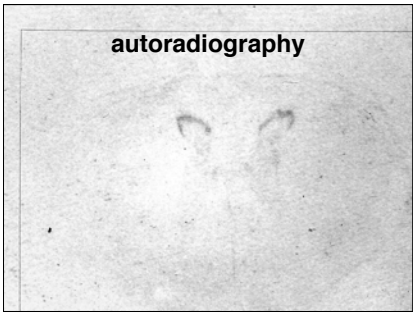
autoradiography



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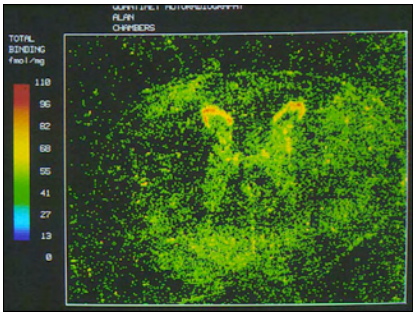

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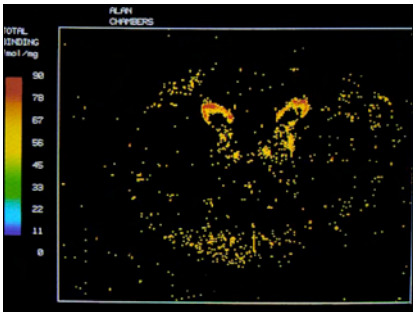

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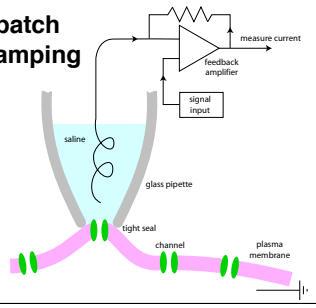
patch clamping



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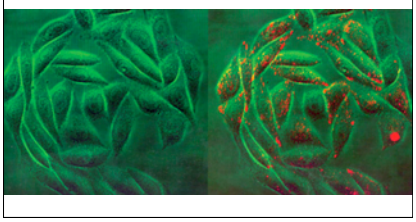
receptor activation assays



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receptor numbers

- change with use
- up and down regulation

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receptor reserve

- = spare receptors
- more receptors in tissue than required for full response
- partial agonists may produce a full response in a tissue with many spare receptors
- common in smooth muscle

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desensitisation / tachyphylaxis (receptors)

- receptor down regulation
- conformation changes
- transducer changes
- mediator depletion

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tolerance (animals)

- increased metabolism
- adaptation
  - progession of disease
- drugs pumped out

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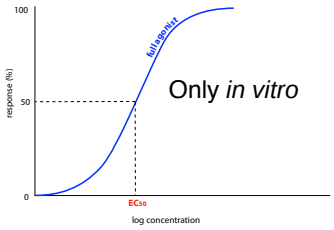
EC_{50}



Only *in vitro*

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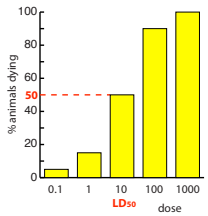
ED_{50}



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therapeutic ratio

- an index of a drug's safety

$$= \frac{LD_{50}}{ED_{50}}$$

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therapeutic ratio

- difference between effective dose and dose which produces side effects is clinically important
- LD_{50} ethically unacceptable

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What would you do?

- thoracotomy
- premed: buprenorphine (partial agonist)
- intra-op: fentanyl (full agonist)
- recovery: naloxone (antagonist)
- post op analgesia?

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drug receptor interactions

- agonists produce an effect
- competitive antagonists block the effect but the blockade can be overcome by increasing the agonist concentration
- drugs can be compared using EC_{50} values in vitro and ED_{50} values in vivo
- therapeutic index is a measure of how safe a drug is

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