AUTONOMIC NERVOUS SYSTEM 3 of 5

ADRENERGIC ANTAGONISTS

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OUTLINE

- Action of receptor stimulation
- Which drugs
- α_1 and α_2 receptors
- Non selective α blockers
- Selective α blockers
- Classification of β blockers
- Uses of β blockers
- Adverse effects β blockers

PHYSIOLOGICAL ACTION OF RECEPTOR STIMULATION

- α_1 receptors

Mydriasis

Vasoconstriction (peripheral)

Uterine contraction

Sweating

Ejaculation

Bladder sphincter contraction

Intestinal relaxation

- β receptors

Increased automaticity	β_1
Increased contractility	β_1
Vasodilatation (muscles)	β_2
Bronchial, uterine, intestinal relaxation	β_2
Hypokalaemia, hepatic glycogenolysis	β_2
Detrusor relaxation	β_2

WHICH DRUGS

α antagonists

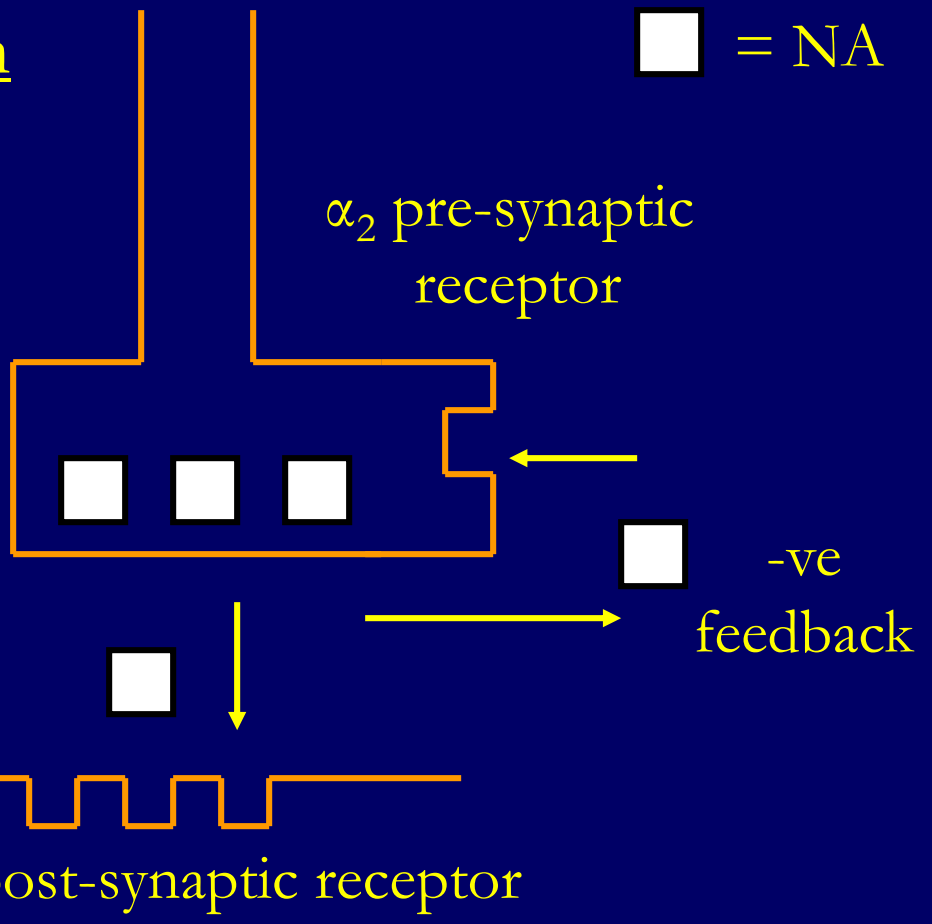
- Phentolamine
- Phenoxybenzamine
- PRAZOSIN
- Doxazosin
- Labetalol

β antagonists

- PROPRANOLOL
- Sotalol
- Timolol
- ATENOLOL
- Metoprolol
- Pindalol
- Labetalol

α-RECEPTOR ACTIVITY

Diagrammatic representation of a synapse



NA activates α_1 and α_2 receptors

NON-SELECTIVE α ANTAGONISTS (1/3)

- Phentolamine

Reversible competitive antagonist

Administered i.v. ⟶ brief effect

Uses: adrenal hypertensive crises

- phaeochromocytoma
- MAOI-sympathomimetic interaction

NON-SELECTIVE α ANTAGONISTS (2/3)

- Phenoxybenzamine

Powerful non selective, irreversible binding

Effects last 2 days

Better treatment for phaeochromocytoma hypertensive crisis

Administered orally or i.v.

NON-SELECTIVE α ANTAGONISTS (3/3)

- Adverse effects of combined block:

  Reflex tachycardia & postural hypotension

Standing activates baroreceptors and releases NA ⟶ no vasoconstriction (α_1), no negative feedback (α_2) ⟶ unopposed β action: tachycardia and vasodilatation

SELECTIVE α_1 ANTAGONISTS

- Prazosin, Doxazosin

α_2 negative feedback not blocked ⟶

less reflex tachycardia and postural hypotension

- Useful anti-hypertensive agents
- Theoretically in peripheral vascular disease
- Increases urine flow rates in benign prostatic hypertropy

β RECEPTOR ANTAGONISTS CLASSIFICATION (1/3)

- Pharmacodynamic classification

Pure antagonists:

- Non selective β blockers e.g. sotalol, timolol, PROPRANOLOL
- Selective β_1 blockers e.g. ATENOLOL, metoprolol

β RECEPTOR ANTAGONISTS CLASSIFICATION (2/3)

- Partial antagonists i.e. have some agonist activity too – 'intrinsic sympathomimetic activity' (ISA)

e.g. pindolol (non selective), acebutalol (selective) and labetolol (non selective α and β blockade as well as ISA)

β RECEPTOR ANTAGONISTS CLASSIFICATION (3/3)

- Pharmacokinetic classification

Lipid soluble: propranolol, metoprolol, labetalol, timolol

Extensive first pass metabolism, widely distributed (large V_D), crosses blood-brain barrier

β RECEPTOR ANTAGONISTS CLASSIFICATION (3/3)

Water soluble: atenolol, sotalol

Excreted unchanged by kidneys ($T_{1/2}$ increased in renal failure)

Less widely distributed (less CNS adverse effects)

β RECEPTOR ANTAGONISTS USES

CVS

- Angina
- Hypertension
- Dysrhythmias
- MI
- Portal hypertension

Eye

- Glaucoma

Endocrine

- Hyperthyroidism
- Phaeochromocytoma

CNS

- Anxiety
- Migraine prophylaxis
- Essential tremor
- Alcohol and opiod withdrawal

β RECEPTOR ANTAGONISTS ADVERSE EFFECTS

- Bronchospasm
- Cardiac failure
- Heart block
- Hypotension
- Reduced peripheral circulation
- Hypoglycaemia

N.B. practolol

First β1 selective agent (1970)

Extensively tested

After 4 years: oculo-muco-cutaneous syndrome (fibrosis)

Withdrawn

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