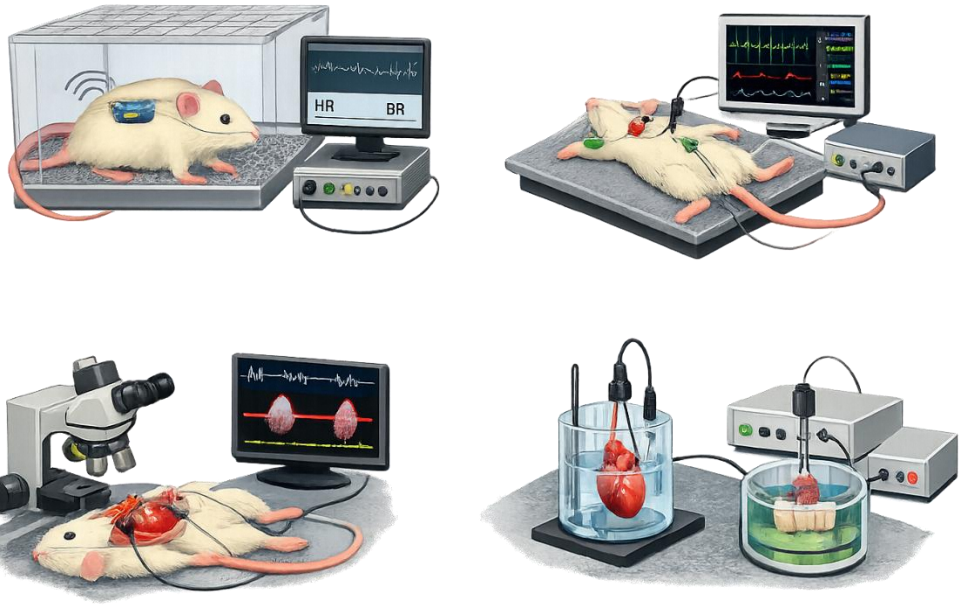
Preclinical Screening Models for ANS Activity

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What is the Autonomic Nervous System (ANS)?

- The Autonomic Nervous System (ANS) is the part of the nervous system that controls involuntary functions in the body.
- **These include:**
  - Heart rate
  - Blood pressure
  - Breathing
  - Digestion
  - Pupil size
  - Sweating
  - Urine output
- The ANS is divided into two major branches:
  - **Sympathetic Nervous System (SNS):**
    - "Fight or flight" responses (increases heart rate, opens airways, etc.)
  - **Parasympathetic Nervous System (PNS):**
    - "Rest and digest" functions (slows heart rate, stimulates digestion, etc.)
- Drugs acting on the ANS are used for many medical conditions, such as hypertension, asthma, heart problems, digestive issues, and more.

Why is screening needed?

- Before using any new drug that acts on the ANS, it must be tested in animal models to determine:
    - **What part of the ANS it affects**
    - **How strong its action is**
    - **Whether it has side effects on vital organs**

General Screening Approaches for ANS Drugs



A. In Vivo Models (Whole Animals)

- These models involve giving the drug to live animals **(usually rats, mice, cats, dogs)** and **observing changes in:**
    - Heart rate (tachycardia or bradycardia)
    - Blood pressure (hypertension or hypotension)
    - Pupil size (mydriasis or miosis)
    - Intestinal movement (increased or decreased)
    - Urine output or salivation
- **Common procedures:**
    - Blood pressure and heart rate are measured using cannulated animals connected to pressure transducers.
    - Pupil size is observed in animals after drug administration.
    - Gastrointestinal motility is tested by giving charcoal meal and measuring how far it moves through the intestine.

B. Isolated Organ Preparations (Ex Vivo Models)

- **These models use isolated organs such as:**
    - Ileum (intestine) – for parasympathetic activity
    - Vas deferens – for sympathetic activity
    - Trachea – for bronchodilation/constriction
    - Heart (Langendorff preparation) – for cardiac effect
- **Additional points:**
    - The organs are placed in an organ bath, supplied with oxygenated fluid, and connected to a recording system.

- Drugs are added to see how the tissue contracts or relaxes.
- Helps to determine the receptor type involved (e.g., alpha, beta, muscarinic, nicotinic).

C. Use of Antagonists for Confirmation

➢ To confirm whether the drug acts on the sympathetic or parasympathetic system, blocking agents are used:

- **Atropine –** blocks parasympathetic (muscarinic) receptors
- **Propranolol –** blocks sympathetic beta receptors
- **Phentolamine –** blocks alpha receptors
- If the effect of the test drug is stopped by one of these blockers, it suggests what type of receptor it acts on.

Screening Models for Sympathomimetics

What are sympathomimetics?

- Sympathomimetic drugs are drugs that stimulate the sympathetic nervous system.
- They mimic the action of adrenaline (epinephrine) and noradrenaline (norepinephrine).
- They act on adrenergic receptors, which are of **two main types:**
  - Alpha receptors **(α1, α2)**
  - Beta receptors **(β1, β2, β3)**
- **Different sympathomimetic drugs** may act on one or more of these **receptors to produce effects such as:**
  - Increased heart rate and blood pressure
  - Bronchodilation (airway opening)
  - Pupil dilation
  - Decreased digestion
  - Increased blood glucose

Why is screening important?

- **To check:**
  - Which adrenergic receptors are involved
  - Potency and duration of action
  - Specific effects (e.g., heart vs lungs)
  - Side effects like excessive stimulation

Common screening models:

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