

Bioassay of Antidepressant Activity



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Depression

- A major depressive episode is associated with:
 1. a very **low mood**, which pervades **all aspects of life**
 2. an **inability to experience pleasure** in activities that were formerly enjoyed.

Depression

- Depressed people may be preoccupied with **THOUGHTS** and **FEELINGS** of:
 1. worthlessness
 2. guilt
 3. regret
 4. helplessness ★
 5. Hopelessness
 6. self-hatred

General Considerations

- According to the **monoamine hypothesis** of depression compounds exert **antidepressant activity** because they are capable of enhancing central
 1. noradrenergic and/or
 2. serotonergic functions.

Antidepressant

- A drug used to prevent or treat clinical depression.

Tests for antidepressant activity

- are based on the mechanism of action.

Classes of antidepressants

1. selective serotonin reuptake inhibitors (SSRIs)
2. serotonin–norepinephrine reuptake inhibitors (SNRIs)
3. tricyclic antidepressants (TCAs)
4. monoamine oxidase inhibitors (MAOIs)

Antidepressant bioassay methods

1. **Apomorphine-induced Hypothermia in Mice**
2. **5-Hydroxytryptophan Potentiation in Mice**

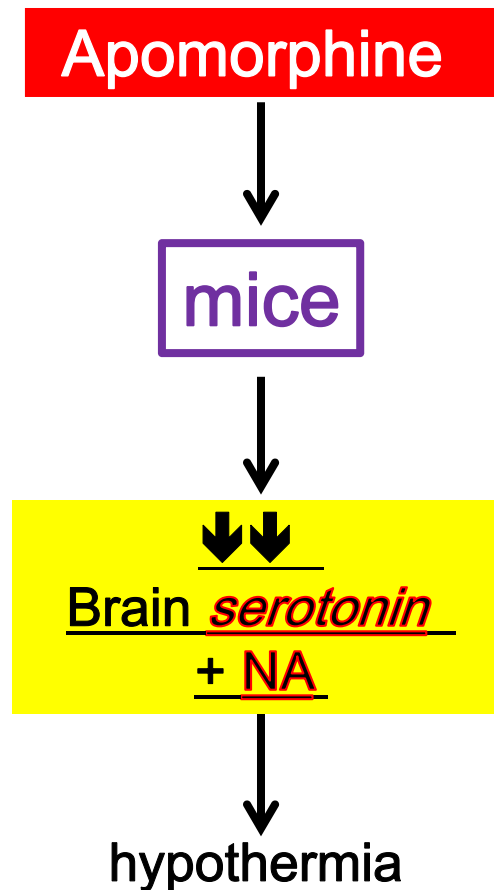
Depression evaluation

Forced Swim Test (to evaluate depression)

Antidepressant bioassay methods

1. Apomorphine-induced Hypothermia in Mice

Principle



Antidepressant bioassay methods

1. Apomorphine-induced Hypothermia in Mice

Principle

antidepressants

mice

↑↑
Brain serotonin

+ NA

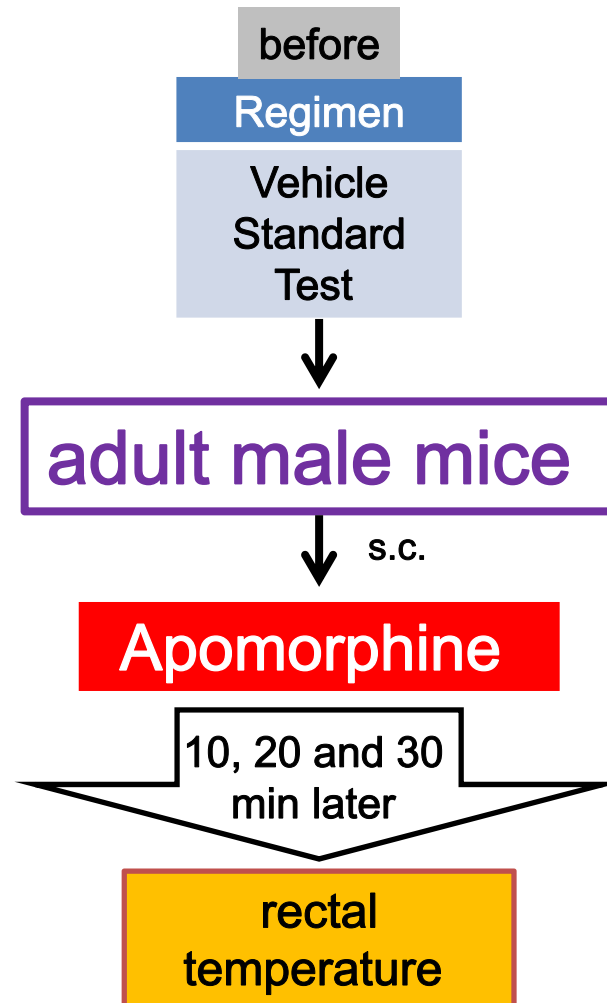
prevent

Apomorphine-induced hypothermia

Antidepressant bioassay methods

1. Apomorphine-induced Hypothermia in Mice

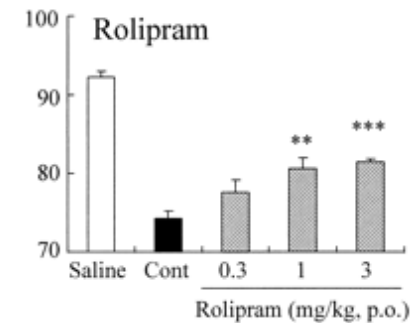
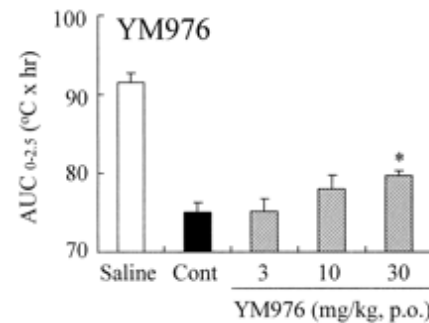
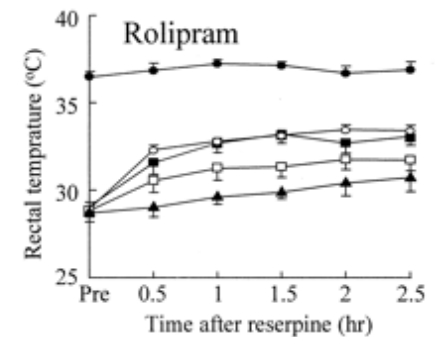
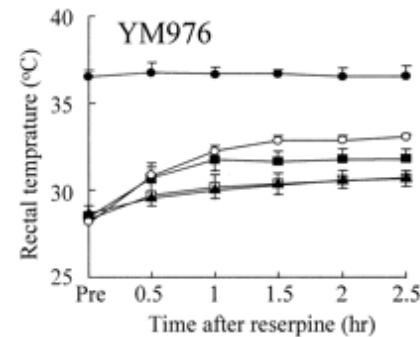
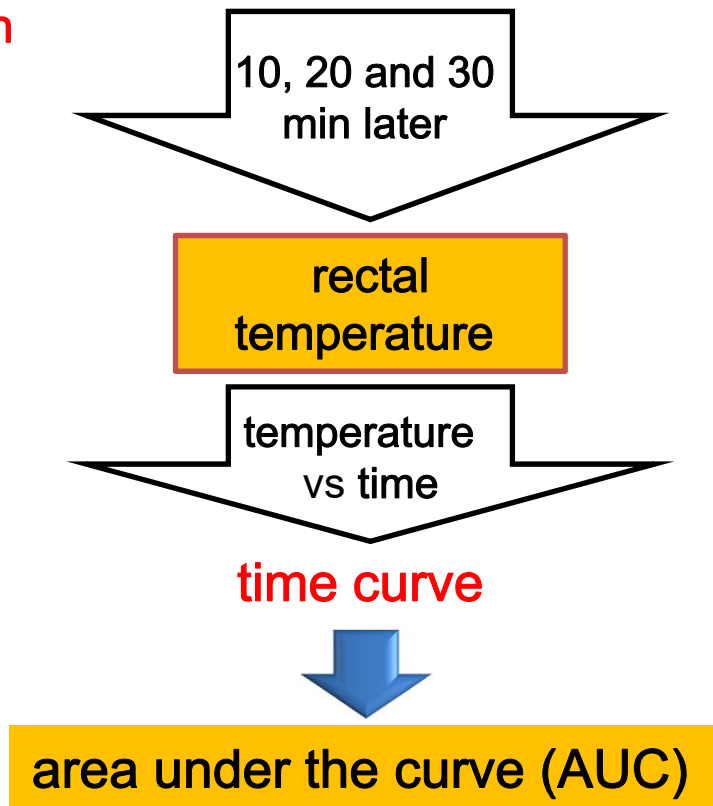
Procedure



Antidepressant bioassay methods

1. Apomorphine-induced Hypothermia in Mice

Evaluation



Antidepressant bioassay methods

1. Apomorphine-induced Hypothermia in Mice

Evaluation

Antidepressant

```
graph TD; A[Antidepressant] --> B[↑ Brain 5HT+NE content]; B --> C[↑ rectal temperature  
↑ area under the curve (AUC)];
```

↑ Brain 5HT+NE content

↑ rectal temperature
↑ area under the curve (AUC)

Antidepressant bioassay methods

2. 5-Hydroxytryptophan Potentiation in Mice

Principle

5-Hydroxytryptophan

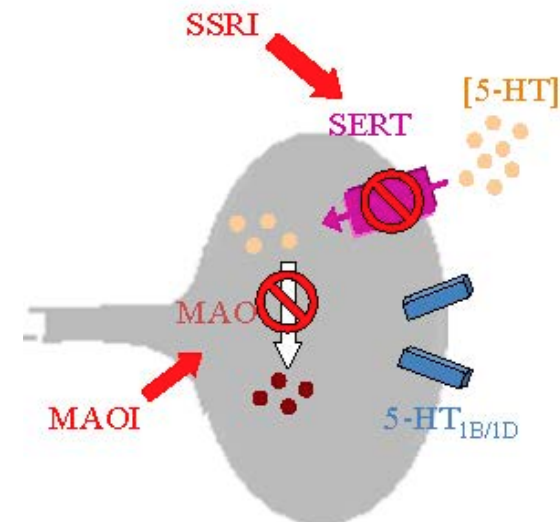
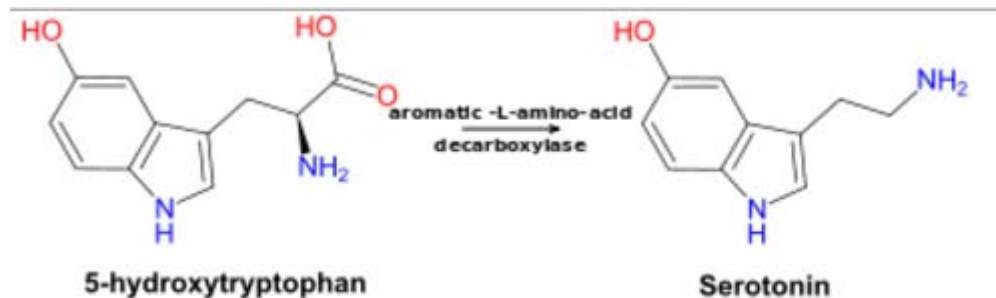


is a serotonin precursor

Pargyline



is a MAO inhibitor
inhibits breakdown
of serotonin



Antidepressant bioassay methods

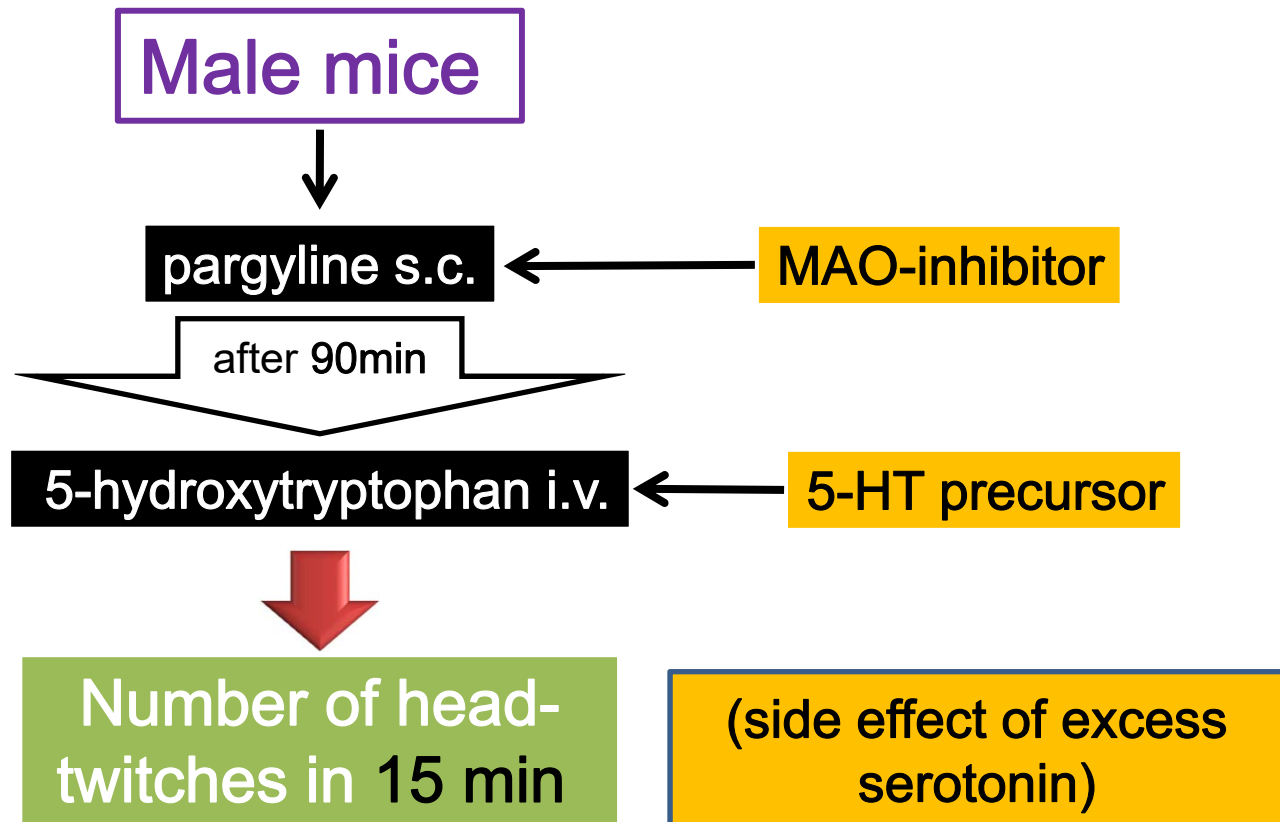
2. 5-Hydroxytryptophan Potentiation in Mice

- This test is specific for **antidepressants** that **block** the **re-uptake** of **serotonin**
- Therefore, in the presence of **5-hydroxytryptophan** (**serotonin precursor**) and **pargyline** (**MAO inhibitor**), **antidepressants potentiate serotonin effects**.
- This may lead to the appearance of **serotonin side effects**, such as **serotonin syndrome**.

Antidepressant bioassay methods

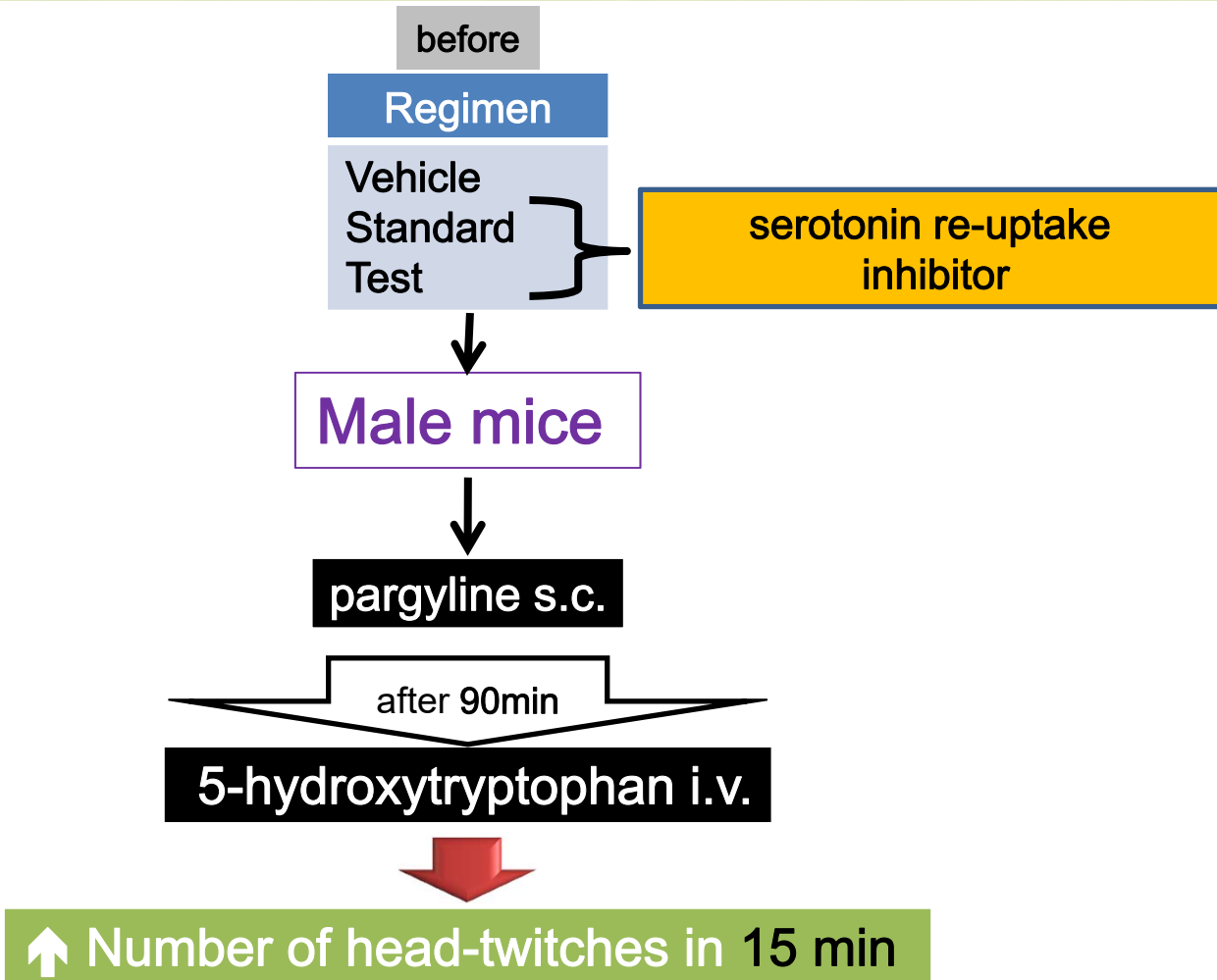
2. 5-Hydroxytryptophan Potentiation in Mice

Procedure



Antidepressant bioassay methods

2. 5-Hydroxytryptophan Potentiation in Mice



Depression evaluation

Forced Swim Test

Principle

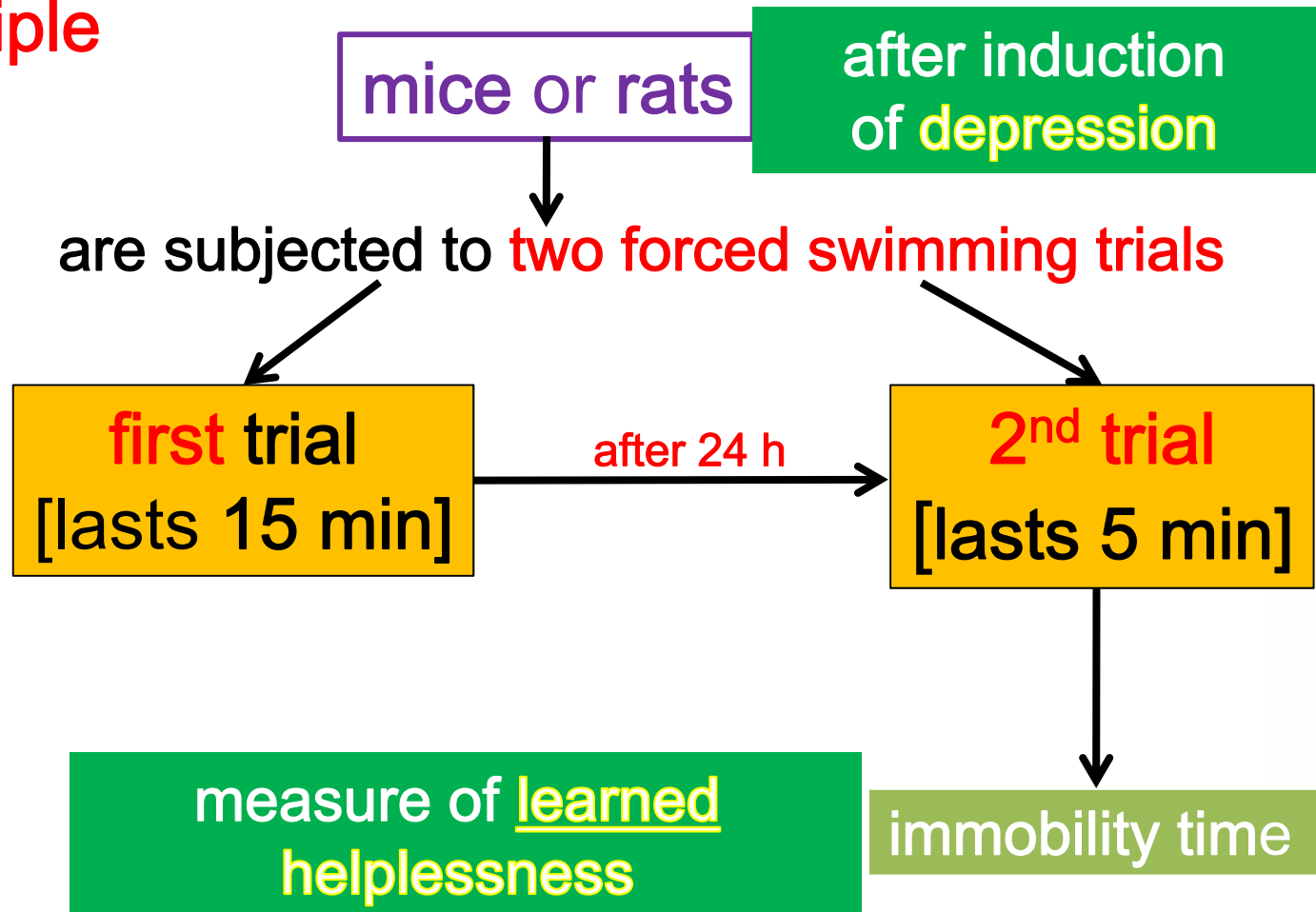
The test is most frequently used to examine the "learned helplessness" response common in animal models of depression.



Depression evaluation

Forced Swim Test

Principle



Depression evaluation

Forced Swim Test

Procedure

mice or rats

before

Regimen

Vehicle
Standard
Test

2nd trial

[lasts 5 min]

↓ immobility time



Before 2nd trial
antidepressants
administration