PRECLINICAL SCREENING OF ANXIOLYTICS

CONTENTS

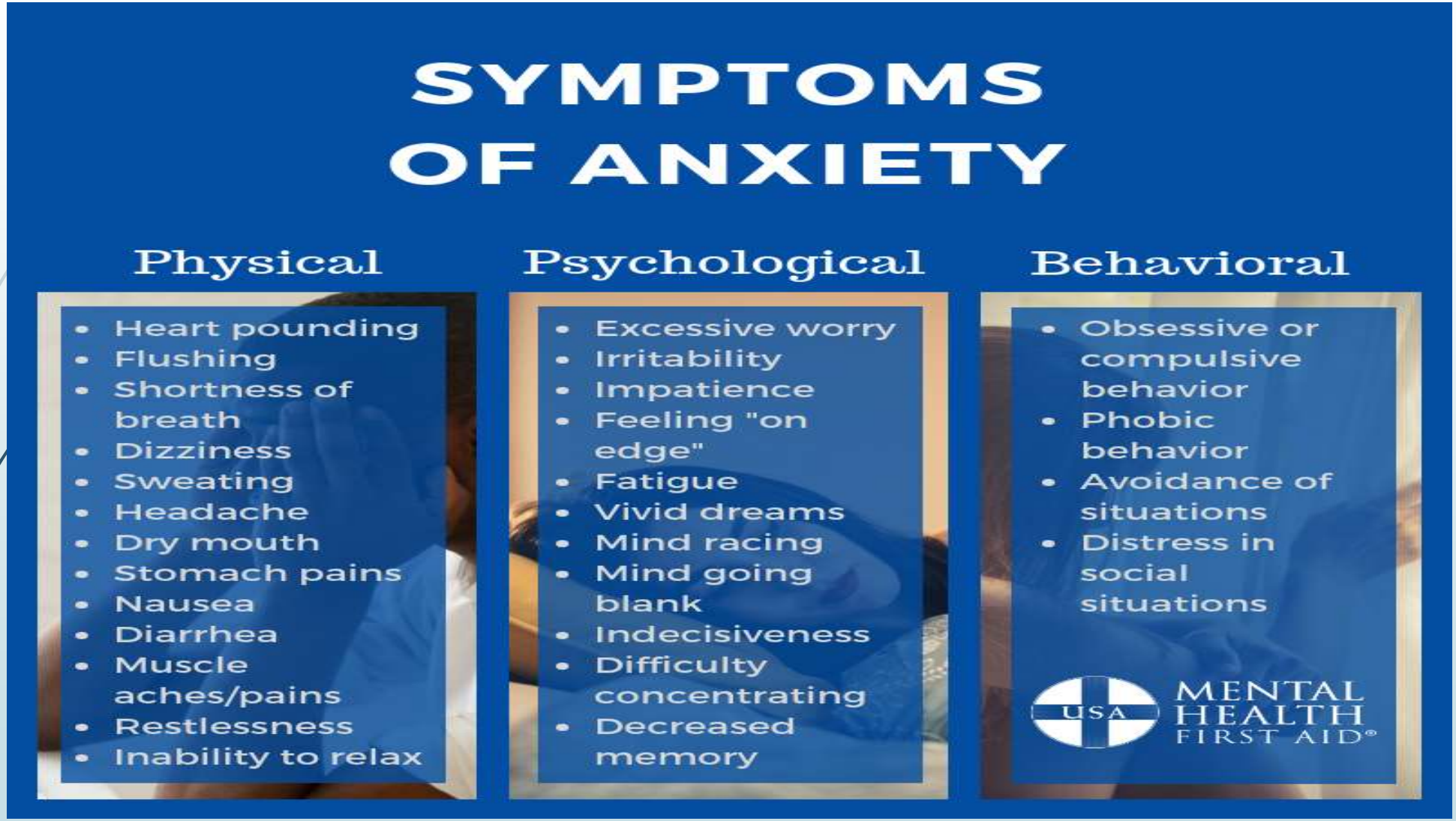
- Introduction
- Symptoms of anxiety
- Types of anxiety
- Anti-anxiety drugs
- Preclinical evaluation of anxiolytics
- In-vivo methods

INTRODUCTION

- Anxiolytic or anti-anxiety are those drugs which are used to reduce the symptoms of anxiety and treat the anxiety disorder.

ANXIETY

- A feeling of worry or fear, especially about the future is known as anxiety.
- It is an emotional state, unpleasant in nature associated with uneasiness, discomfort and concern or fear about some defined or undefined future threat.


SYMPTOMS OF ANXIETY
Physical
Heart pounding
Flushing
Shortness of breath
Dizziness
Sweating
Headache
Dry mouth
Stomach pains
Nausea
Diarrhea
Muscle aches/pains
Restlessness
Inability to relax
Psychological
Excessive worry
Irritability
Impatience
Feeling "on edge"
Fatigue
Vivid dreams
Mind racing
Mind going blank
Indecisiveness
Difficulty concentrating
Decreased memory
Behavioral
Obsessive or compulsive behavior
Phobic behavior
Avoidance of situations
Distress in social situations
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TYPES OF ANXIETY

- Social anxiety
- Obssessive Compulsive disorder
- Phobia
- Post-traumatic anxiety

ANTI-ANXIETY DRUGS

BENZODIAZAPENE	AZAPIRONES	SEDATIVE-ANTIHISTAMINIC	BETA BLOCKERS
Diazepam	Buspirone	Promethazine	Atenolol
Alprazolam	Ipsapirone	Hydroxyzine	Propanolol
Lorazepam	Gepirone	Chlorphenamine	Bisoprolol
Delorazepam		Clemastine	

PRECLINICAL EVALUATION OF ANXIOLYTICS

- In-vitro Methods
- In-vivo methods

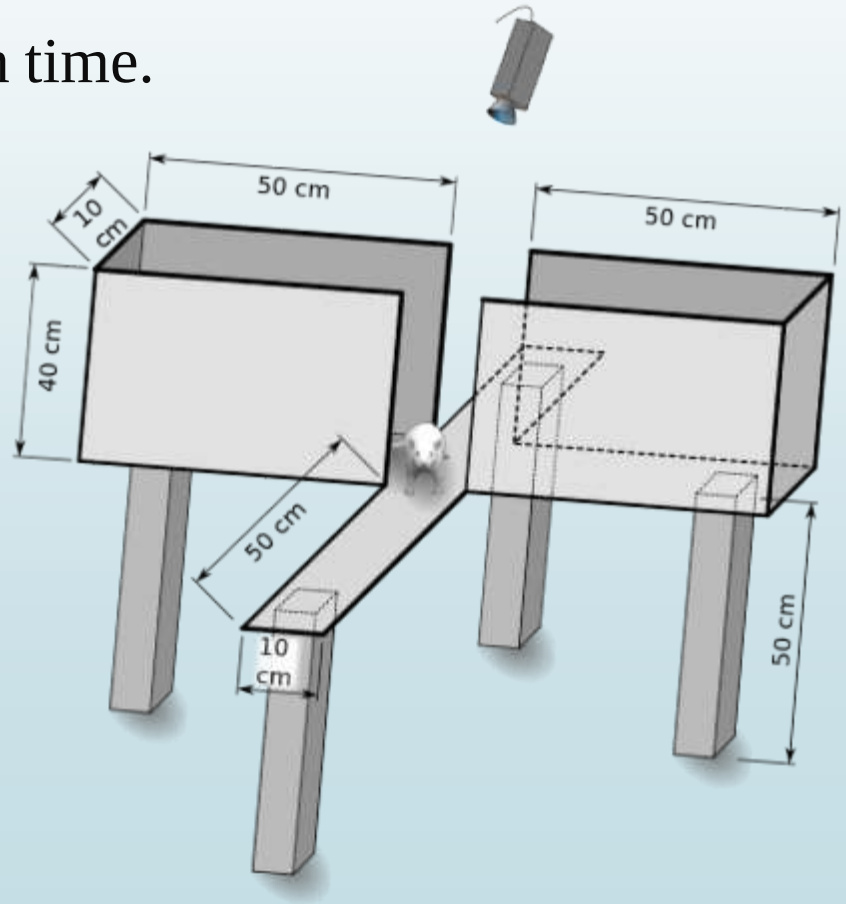
- Our main focus here would be In-vivo.

IN VIVO METHODS

- Elevated plus-maze test
- Light-dark model
- Vogel lick conflict test
- Social interaction

Elevated Plus Maze Test

- Most widely used method; **male mice** used.
- For selective identification of anxiolytics and anxiogenic drugs.
- **Anxiolytics-** decrease anxiety, increase open arm exploration time.
- **Anxiogenics-** decrease open arm exploration time.
- 2 open arms and 2 closed arms of 50×10×40 cm dimensions.
- Open roof arrangement.
- Two open arm are opposite to each other.
- Maze elevated at 50cm height.



EXPERIMENTAL DESIGN

- **GROUP 1-** Control
- **GROUP 2-** Standard
- **GROUP 3-** Test treated with dose **X**
- **GROUP 4-** Test treated with dose **2X**

METHODOLOGY

Mice weighing around 200gm housed in pairs for10 days prior to testing; 6 animals selected for each group.

Test drug administered 30 min prior to experimentation by I.P. route.

The mice is then placed in the centre of the maze facing one of the enclosed arms.

Parameters measured during next 5 minutes

- Time spent in the open arms.
- Entries into open arms.
- Time spent in closed arms.
- Entries in closed arms.
- Total arms entries.

Anxiolytic effect indicated by-

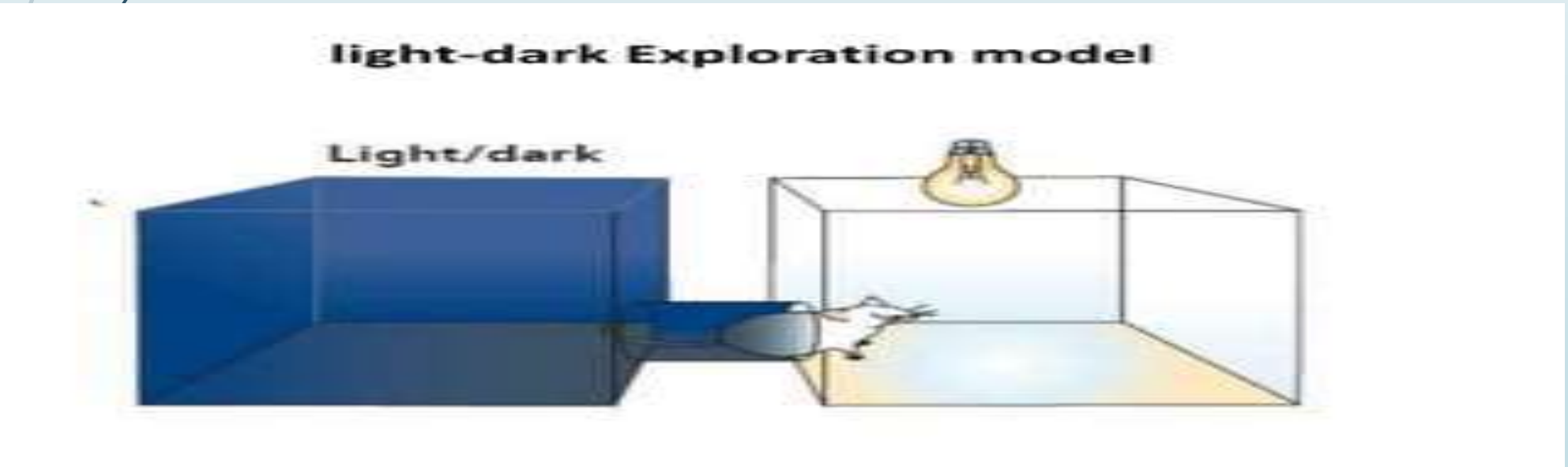
- Increase in the proportion of time spent in open arms.
- Increase in the proportion of entries into open arms.

EVALUATION OF RESULTS

- Motor activity and open arm exploratoy activity determined.
- Benzodiazepines and valproate increase motor activity and exploratory time.

LIGHT- DARK MODEL

- Rodents- have exploratory activity.
- Animals placed in a chambered system, where they can freely moves brightly-light open field and a dark corner.
- After treatment with anxiolytic- show more crossing between the two chambers and more locomotor activity.
- Number of crossing between the light and dark sites is recorded.



METHODOLOGY

- Apparatus- a dark and a light chamber divided by a photocell equipped zone.
- Polypropylene animal cage (44×21×21 cm) is darkened with black spray over 1/3rd of its surface.
- A partition containing 13cm(L) , 5cm (H) opening is used for separating the dark one- third if the cage.
- This activity rest on an activity monitor which counts total locomotor activity.
- An electronic system consisting of 4 sets of photocells across the partition.
- It automatically counts movements through the partition and record the time spent in the light and dark compartments.

- Animals- treated 30 min before the test with drugs or vehicle given i.p. placed in the cage and also observed for 10 min.
- Groups of 6-8 animals used for each dose.

- **EVALUATION:-**
- No. of crossings through the partition between the light and dark chambers compared with total activity counts during the 10 min.
- Locomotor activity also monitored.
- Anxiolytics like diazepam and meprobamate increase locomotor activity and no. of crossings.

VOGEL LICK CONFLICT TEST

- **Source of anxiety:**

  thirsty rats are administered shocks while licking water.

- **Animals used:**

  Sprague dawley rats

METHODOLOGY

A water bottle with metal drinking tube is fitted to the animal housing.

Electric circuit is connected between drinking tube and floor of cage.

Drugs given, after 30 minutes rats placed in cage and allowed to drink water and shock given after 20 licks.

After 3 minutes next shocks are given for every 12^{th} lick.

No. of shock delivered in 3 minutes noted for each animal, no. of shock received after treatment compared with control.

PARAMETERS MEASURED

- Number of accepted punishments (electric shock).

ANXIOLYTIC EFFECT

- Statistically significant increase in the number of accepted shocks.