

## Definitions

**Psychosis:** problems in thought, personality, behavior, bizarre irrational thinking

- Mental state involving detachment from the reality
- Madness; supernatural power
- Diagnosis by exclusion

### 2 main symptoms characterizing psychosis

- Delusion: Describes false bizarre fixed beliefs
- Hallucination: Sensory dysfunction
- Illusions? Misperception of stimulus

## Causes

■ Genetic? 1%

■ Normal?

■ Environmental (Stress)

■ Medical conditions:

1-Drugs (dopa like)

2-rapid withdrawal of opioid

3-brain tumour

4-Alzheimer and parkinson could manifest psychotic illnesses later

5-Electrolytes imbalance

6-Fetal infections

■ Drugs:

-Alcohol; Cannabis

-Cocaine; Amphetamine; MDMA

-K-opioid receptor agonists

-NMDA Antagonists: Amphetamine » increase release of dopamine in the brain

# Antipsychotic Drugs

=Neuroleptics, Major tranquilizers

## Signs and symptoms

### -Positive

- Hallucination & delusions
- Thought disorders
- Abnormal behaviors

### -Negative

- Social contacts: They withdraw from social contact
- Emotional responses: Depressed most of the time, loss of pleasure
- Decrease attention and memory
- Anxiety and depression -> Suicide

## Pathophysiology: Dopamine Hypothesis

### Pros:

■ D<sub>2</sub> agonists and dopamine releasers produce psychotic-like effects.

-Amphetamine, bromocriptine

■ Drugs block D<sub>2</sub> receptors produce psychotic-like effect.

-Ketamine, Phencyclidine

■ Antipsychotics are dopamine (D<sub>2</sub>) antagonists.

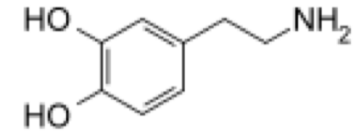
-Clozapine, Olanzapine

### Cons:

■ Antipsychotics are not always effective

■ Therapeutic effect is generally delayed

■ Newer antipsychotics have 5-HT antagonism (Pimavanserin)



## Dopamine

■ A catecholamine neurotransmitter

■ Projections:

-Substantia Nigra: Basal Ganglia -> Movement

-Ventral tegmental area: Mesolimbic pathway: Reward and cognition

-Arcuate nucleus: Pituitary gland: Inhibit prolactin secretion

■ Receptors:

-D<sub>1,5</sub> (Excitatory; Metabotropic; GPCR (Gs))

-D<sub>2,3,4</sub> (Inhibitory; Metabotropic; GPCR (Gi))

# Antipsychotic Drugs

## Principles

- The exact Pathophysiology is not well understood.
- Many people do not respond fully to medications or respond partially
- Therapeutic effect may be delayed several weeks
- Significant side effects → Main reason for non-compliance
- More effective against positive-symptoms → Negative symptoms are only treated by psychological therapy
- Use the minimum effective dose.

## Major S/E

- Hyperprolactinemia.
- Galactorrhoea
- Gynecomastia
- Sexual dysfunction: loss of libido.
- Neuroleptic malignant syndrome: Life threatening condition characterised by circulatory shock, high fever, seizures
- Tardive dyskinesia : Abnormal repetitive movements of facial muscles → irreversible effects
- Sedation??
- Hyperglycemia and diabetes.
- Weight gain??

## Clinical notes

- Most are effective against positive symptoms.
- Smoking increase metabolism of Clozapine
- Change the medication
- Injectable forms:
- Non-Compliance of the patient
- Acute psychotic agitation or mania
- Safe during pregnancy

Lees adverse effects

	Typical (First Generation)	Atypical (Second Generation)
Discovery	Older	Newer
Effectiveness	Partially	Better?
MOA	D2: Antagonist	D2: antagonist 5-HT: antagonist (5-HT3c)
Extrapyramidal S/E	+++++++	++

### Chlorpromazine

- The first neuroleptic (1952)
- Associated with sedation

### Haloperidol

- Antiemetic with cancer chemotherapy
- Amphetamine and LSD overdose

### Clozapine

- Decrease risk of suicide
- Has major side effects

### Aripiprazole

- Partial agonist at D<sub>2</sub>
- Olanzapine
- Risperidone
- Ziprasidone
- Amisulpride

## Other Antipsychotics

### Pimavanserin

- Approved in 2016.
- No dopamine action.
- 5-HT inverse agonist (i. e. antagonist)
- \$\$\$\$ - Very expensive
- Parkinson's disease psychosis.

## Antipsychotics: Other uses

- Anxiety Disorders: OCD
- Huntington Disease
- Autism
- Antiemetic

• **Antipsychotics can produce all of the following except:**

- A. Hyperglycemia
- B. sedation
- C. Weight loss
- D. Sexual dysfunction
- E. It can produce all of the above

• **Examples of typical antipsychotics:**

- A. Olanzapine
- B. Haloperidol
- C. Clozapine
- D. Ziprazidone
- E. All of the above

• **Dopamine (D1) receptors are:**

- A. Ionotropic excitatory
- B. Metabotropic excitatory
- C. Ionotropic Inhibitory
- D. Metabotropic inhibitory
- E. Voltage-gated receptors

• **A patient look at a tea cup, and he claims it is a bomb. This is an example of:**

- A. Dillusion
- B. Illusion
- C. Hallucination
- D. Schizophrenia
- E. Sounds like normal to me!