



Treatment of psychosis

What do we mean by
“psychotic” or “psychosis”?

- Disorder of thought, e.g., delusion, ideas of reference
- Disorder of perception, e.g., auditory hallucinations
- Disorder of behavior, e.g., disorganized behavior

Examples of conditions that can cause psychosis

- schizophrenia/schizophreniform/brief psychotic disorder
- schizoaffective disorder
- mood disorders
- street drugs
- dementia
- delirium
- stroke
- brain tumors and other neurological disorders
- Nickelback's "Greatest Hits"


"I am not sick, I don't need help!"
Research on poor insight and how we can help improve adherence to treatments.

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The “dopamine hypothesis” of psychosis

- Psychosis is caused by “dysregulation” of dopamine (too much or too little dopamine activity in parts of the brain)

Psychosis can consist of both positive and negative symptoms

Positive (too <u>much</u> dopamine in mesolimbic part of brain)	Negative (too <u>little</u> dopamine in mesocortical part of brain)
delusions hallucinations disorganized speech disorganized behavior agitation	apathy anhedonia cognitive blunting emotional withdrawal

Four areas where dopamine activity appear important in psychosis

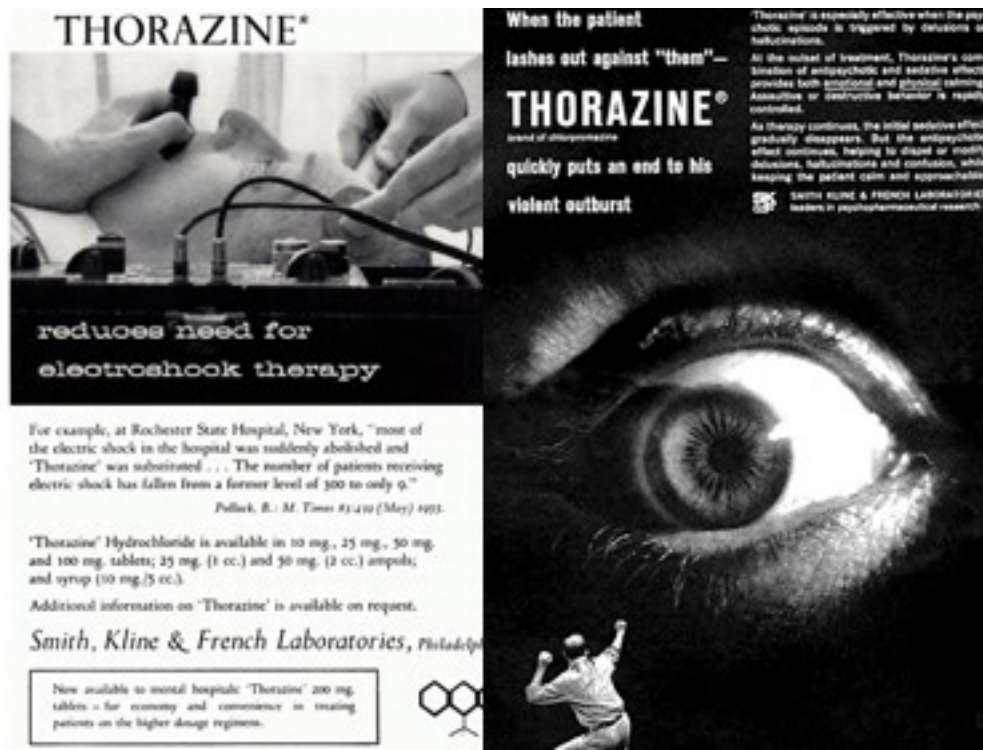
Tract (“area”)	Dopamine activity
Mesolimbic	Excess causes positive symptoms
Mesocortical	Deficit causes negative symptoms
Nigrostriatal	Deficit can cause movement disorders
Tubero-infundibular	Deficit can cause galactorrhea, amenorrhea

Antipsychotic medications (AKA “neuroleptics”)

- “Conventional” (AKA “first generation” or “typical”) antipsychotics (old school)
- “Atypical” (“second generation”) antipsychotics (newer)

Some of the “conventional” antipsychotics

- chlorpromazine (Thorazine)
- fluphenazine (Prolixin)
- **haloperidol (Haldol) - currently widely used**



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When the patient lashes out against “them”—

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brand of chlorpromazine

quickly puts an end to his violent outburst

reduces need for electroshock therapy

For example, at Rochester State Hospital, New York, “most of the electric shock in the hospital was suddenly abolished and ‘Thorazine’ was substituted . . . The number of patients receiving electric shock has fallen from a former level of 300 to only 9.”

Pollack, B.: *N. Y. Times* 83:410 (May) 1973.

“Thorazine” Hydrochloride is available in 10 mg., 25 mg., 50 mg. and 100 mg. tablets; 25 mg. (1 cc.) and 50 mg. (2 cc.) ampuls; and syrup (10 mg./5 cc.).

Additional information on “Thorazine” is available on request.

Smith, Kline & French Laboratories, Philadelphia

Now available to mental hospitals: “Thorazine” 200 mg. tablets — for economy and convenience in treating patients on the higher dosage regimen.

Thorazine® is especially effective when the psychotic episode is triggered by delusions or hallucinations.

At the outset of treatment, Thorazine’s combination of antipsychotic and sedative effects provides both emotional and physical calming. Agitative or destructive behavior is rapidly controlled.

As therapy continues, the initial sedative effect gradually disappears. But the antipsychotic effect remains, helping to disperse or modify delusions, hallucinations and confusion, while keeping the patient calm and approachable.

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Tyrant in the house?



"Thorazine" can control the agitated, belligerent attitude and help the patient to live a composed and useful life.

When "Thorazine" is administered to the agitated adult there is a marked decrease in the toxic-making influence of tension, irritability, abnormality, excessive talking and "hyper-vigilance" - pacing or restlessness.


On "Thorazine" therapy, the patient often finds more regular eating and sleeping habits and regains in his personal hygiene. As the patient becomes more reliable and cooperative, he is able to live a composed and useful life.

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for prompt control of
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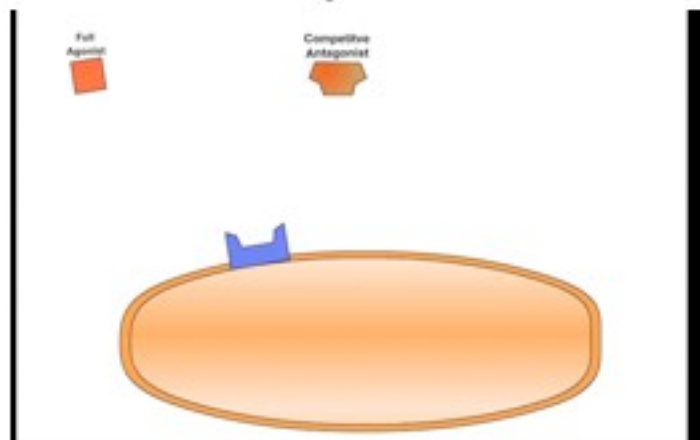
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In the over 1,000,000 children in whom "Thorazine" has been used, poisoning or agranulocytosis has never been reported.

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*U.S. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

“Conventional” or “typical” antipsychotics are dopamine antagonists



Effects of the “typical” antipsychotics

Tract	Dopamine activity	Effect of dopamine block
Mesolimbic	Excess causes positive symptoms	Relieves positive symptoms
Mesocortical	Deficit causes negative symptoms	Worsens negative symptoms
Nigrostriatal	Deficit can cause movement disorders	Can cause movement disorders
Tubero-infundibular	Deficit can cause prolactinemia	Can cause prolactinemia

Movement disorders are some of the most troubling side effects of antipsychotic medications

- EPS - extrapyramidal symptoms
- TD - tardive dyskinesia
- NMS - neuroleptic malignant syndrome

Extrapyramidal symptoms (EPS) are usually short-term (not permanent) movement disorders

- akathisia - “restlessness”
- rigidity
- tremor
- acute dystonias (like intense “muscle cramps”)

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Acute dystonia



Tardive dyskinesia (TD)

- Involuntary movement disorder of tongue, mouth, fingers: chewing, lip-smacking, blinking, grimacing
- Risk of TD increases with exposure to neuroleptic medication - ~3-5% / year for typical antipsychotics
- All antipsychotics, whether typical or atypical (except clozapine) carry risk
- Screen using Abnormal Involuntary Movement Scale (AIMS)



Neuroleptic malignant syndrome (NMS)

- Rare, but can be fatal
- Symptoms: muscle rigidity, fever, confusion
- Have abnormal lab values
- Treatment: stop antipsychotics, needs hospitalization

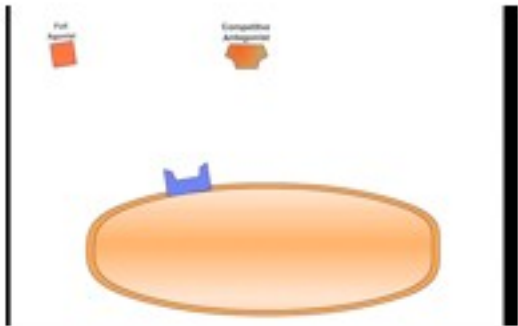
The “atypicals” (second generation antipsychotics)

- clozapine (Clozaril)
- risperidone (Risperdal)
- olanzapine (Zyprexa)
- quetiapine (Seroquel)
- ziprasidone (Geodon)
- aripiprazole (Abilify)

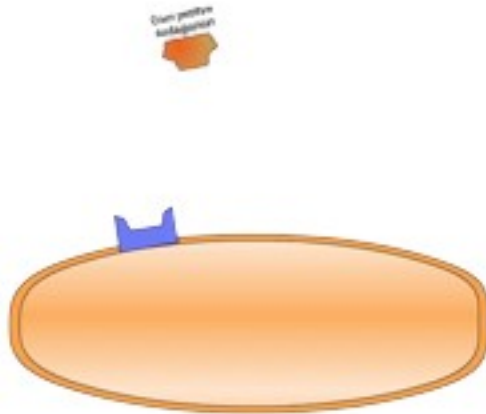
How do “atypical” antipsychotics work?

- They are dopamine antagonists just like the “typicals”.
- BUT “atypicals” may “dissociate” or drop off the dopamine receptor faster than do “typical” antipsychotics.

“Typical” antipsychotics are dopamine antagonists that persistently bind to dopamine receptors



This “quick release” of “atypical” antipsychotics appears to decrease side effects like movement disorders



How do “atypical” antipsychotics work?

- They are dopamine antagonists just like the “typicals”.
- BUT “atypicals” may “dissociate” or drop off the dopamine receptor faster than do “typical” antipsychotics.
- AND they are also serotonin (2A) antagonists - this causes dopamine release in certain areas of the brain.

	TYPICALS		ATYPICALS	
Tract	Effect on dopamine	Overall effect	Effect on dopamine	Overall effect
Mesolimbic	↓	Relieves positive symptoms	↓ from dopamine block	Improves positive symptoms
Mesocortical	↓	Worsens negative symptoms	↑ from serotonin 2A block	Improves negative symptoms
Nigrostriatal	↓	Can cause movement disorder	↑ from serotonin 2A block	Lessens risk of movement disorder
Tubero-infundibular	↓	Can cause prolactinemia	↑ from serotonin 2A block	Lessens risk of prolactinemia

Side effects of atypicals

- Sedation
- Weight gain: can lead to diabetes and metabolic syndrome, elevated lipid levels
- Low blood pressure
- Reduced risk of EPS, TD, NMS, but risk still present

Monitoring patients on atypical antipsychotics

All need regular:

- weight, waist measurement
- blood pressure checks
- fasting glucose and lipid level checks
- AIMS testing