BETTER OUTCOMES. TOGETHER.

KINARK

CHILDREN AND YOUTH

Antipsychotic Medications

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- What is psychosis?
- Why is treating psychosis important?
- How does someone become psychotic?
- How do antipsychotic medications work?
- What are the medications and how are they different?
- For what side effects do we need to monitor?
- Aside from psychosis, how else do we use antipsychotic medications?

What is psychosis?

"Psycho" – generally experienced in a pejorative or insulting manner

- Can be experienced as blocking a person's right to be heard, believed, listened to
- Comes with tremendous stigma

In simplest terms:

"impairment in a person's ability to distinguish what is real from what is not, often with impairment in the organization of thoughts"

What is psychosis?

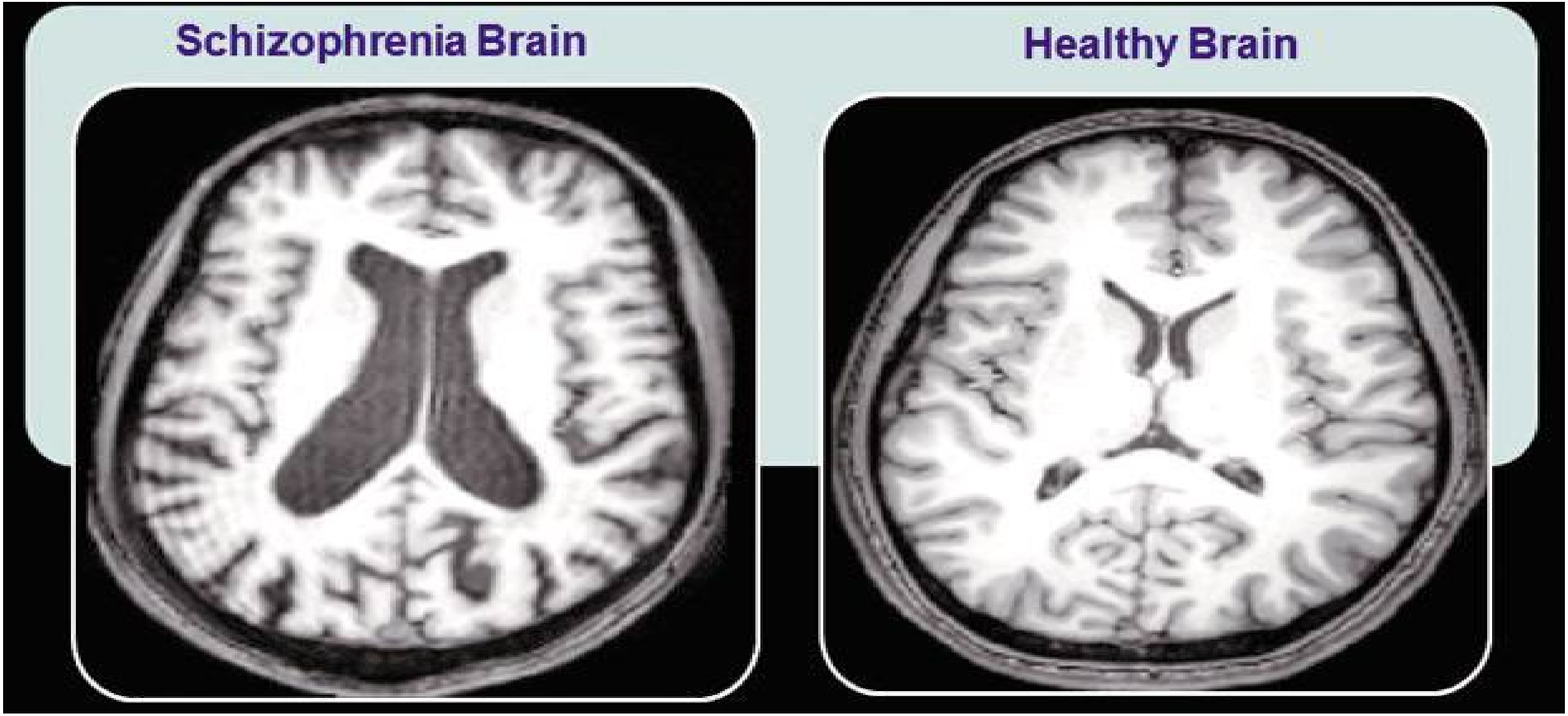
- Children are fluid in their understanding of reality (not psychosis) and are prone to hallucinations when medically ill (delirium, also not psychosis)

- Schizophrenia has age of onset around 19, but can present younger, highly atypical to present before puberty

- Psychosis can emerge from…
  - manic state in Bipolar Disorder (grandiose, religious themes)
  - depressed states (more common in post-partum, geriatric populations)
  - substance-induced states (methamphetamine, cocaine, cannabinoids)
  - other conditions (personality disorders, seizure disorders, intellectual disabilities, brain injuries) usually transiently

Why treat psychosis?

- Psychosis is neurotoxic – being psychotic kills brain cells!
- Treating early with antipsychotic medication is neuroprotective (keeps cells alive!)
- After multiple episodes of psychosis, individuals have less brain matter and don't return to their previous baseline functionality
- Compliance with medication is very important
- Challenging because youth typically aren't familiar with being sick, taking medication let alone the insight challenges of the illness itself


Schizophrenia Brain
Healthy Brain

Before Antipsychotics (Pre-1950s)

- Treatment for severe mental illness (often schizophrenia or psychosis) relied on **sedatives**, restraints, or institutional care
- Substances like **chloral hydrate**, **bromides**, and **barbiturates** were used primarily to *calm*, not treat symptoms

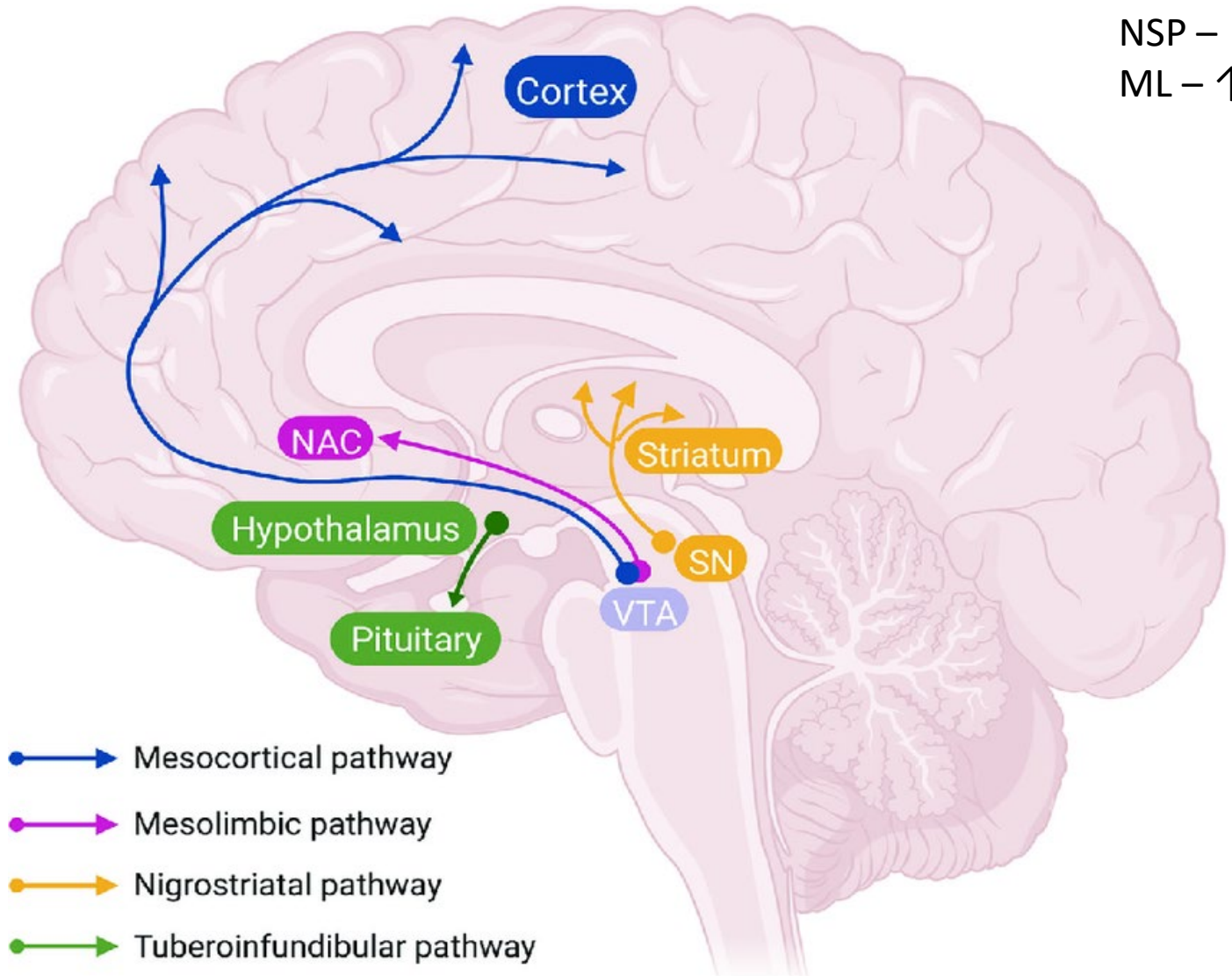
First Generation (Typical) Antipsychotics

1952: Chlorpromazine

- Discovered accidentally when a surgical anesthetic (chlorpromazine) was found to reduce agitation and delusions.
- First drug to *specifically reduce psychotic symptoms*, creating the modern era of psychiatric pharmacology.
- **Other major FGAs**
  - **Haloperidol** (1958)
  - **Fluphenazine**
  - **Perphenazine**
  - **Loxapine**
- **Impact**
  - Dramatically reduced institutionalization and allowed more people to return to community living.
  - But caused significant **extrapyramidal symptoms (EPS)**: tremors, rigidity, akathisia, dystonia, and risk of **tardive dyskinesia**.

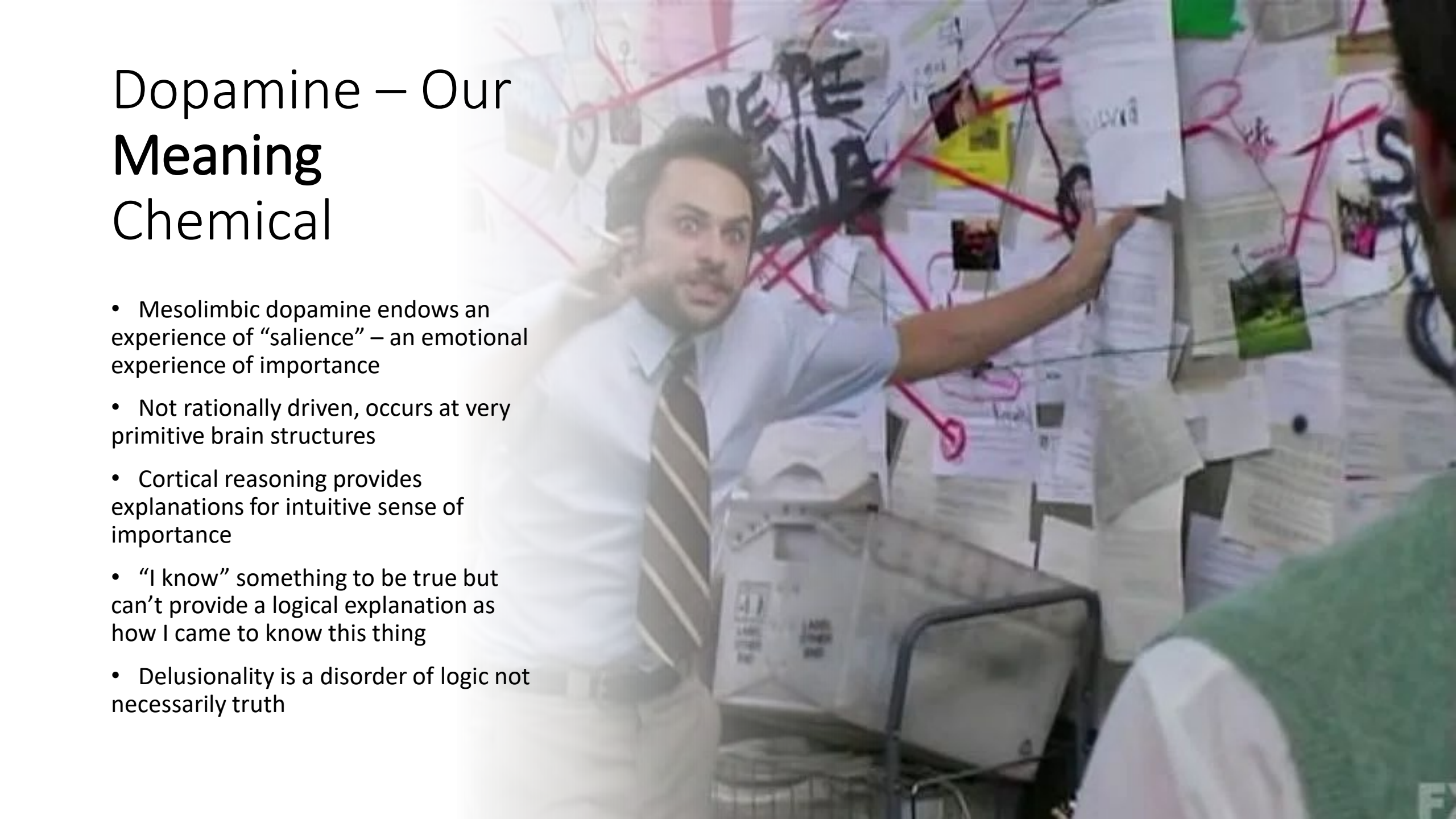
DOPAMINE PATHWAYS

TIP – Prolactin↓
NSP – ↓dopamine=↓movement
ML – ↑dopamine = ↑psychosis



Dopamine – Our **Meaning** Chemical

- Mesolimbic dopamine endows an experience of “salience” – an emotional experience of importance
- Not rationally driven, occurs at very primitive brain structures
- Cortical reasoning provides explanations for intuitive sense of importance
- “I know” something to be true but can’t provide a logical explanation as how I came to know this thing
- Delusionality is a disorder of logic not necessarily truth



Second Generation (Atypical) Antipsychotics

- **Clozapine (1971)**
  - First atypical antipsychotic
  - In addition to blocking the dopamine receptor, also blocks the 5-HT2 receptors (serotonin)
  - Effective for **treatment-resistant schizophrenia**
  - Lower EPS rates but risk of **agranulocytosis** → required monitoring
- **Other SGAs (blocking dopamine and serotonin receptors)**
  - **Risperidone** (Risperdal)
  - **Olanzapine** (Zyprexa)
  - **Quetiapine** (Seroquel)
  - **Ziprasidone** (Zeldox)
  - **Paliperidone** (Invega)
  - **Asenapine** (Saphris)
  - **Lurasidone** (Latuda)
- **Impact**
  - Tended to have fewer movement side effects
  - But introduced new issues: **weight gain**, **metabolic syndrome**, **diabetes risk**

Third Generation Antipsychotics – Dopamine Modulators

- **Dopamine partial agonists**:
  - Aripiprazole (Abilify)
  - Brexpiprazole (Rexulti)
  - Cariprazine (Vraylar)

Features

- More “stabilizing” effect on dopamine, not full blockade
- Lower risk of weight gain and sedation (varies)
- Less EPS compared to FGAs, and fewer metabolic effects compared to many SGAs

Uses and Worries – Typical antipsychotics

- Haloperidol and loxapine, still used in treatment of acute agitation (intramuscularly, orally)
- High risk of movement disorders (Parkinsonism, Akathisia, Dystonia, Dyskinesia)
- High risk of prolactin elevation (breast development, galactorrhea)

MOVEMENT RATINGS: Rate highest severity observed. Rate movements that occur upon activation one less than those observed spontaneously. Circle movement as well as code number that applies.		RATER Date
Facial and Oral Movements	**1. Muscles of Facial Expression** e.g. movements of forehead, eyebrows periorbital area, cheeks, including frowning blinking, smiling, grimacing	0 1 2 3 4
	2. Lips and Perioral Area e.g., puckering, pouting, smacking	0 1 2 3 4
	3. Jaw e.g. biting, clenching, chewing, mouth opening, lateral movement	0 1 2 3 4
	4. Tongue Rate only increases in movement both in and out of mouth. NOT inability to sustain movement. Darting in and out of mouth.	0 1 2 3 4
Extremity Movements	**5. Upper (arms, wrists,, hands, fingers)** Include choreic movements (i.e., rapid, objectively purposeless, irregular, spontaneous) athetoid movements (i.e., slow, irregular, complex, serpentine). DO NOT INCLUDE TREMOR (i.e., repetitive, regular, rhythmic)	0 1 2 3 4
	6. Lower (legs, knees, ankles, toes) e.g., lateral knee movement, foot tapping, heel dropping, foot squirming, inversion and eversion of foot.	0 1 2 3 4
Trunk Movements	**7. Neck, shoulders, hips** e.g., rocking, twisting, squirming, pelvic gyrations	0 1 2 3 4
Global Judgments	**8. Severity of abnormal movements overall**	0 1 2 3 4
	9. Incapacitation due to abnormal movements	0 1 2 3 4
	10. Patient's awareness of abnormal movements. Rate only patient's report No awareness 0 Aware, no distress 1 Aware, mild distress 2 Aware, moderate distress 3 Aware, severe distress 4	0 1 2 3 4
Dental Status	**11. Current problems with teeth and/or dentures**	No Yes
	12. Are dentures usually worn?	No Yes
	13. Edentia?	No Yes
	14. Do movements disappear in sleep?	No Yes

COMMON:	BASELINE	MON	TUE	WED	THUR	FRI	SAT	SUN
Blurred Vision								
Constipation								
Dizziness								
Drooling								
Dry mouth								
Muscle Stiffness								
Nervousness								
Skin – Itchy								
Skin Rash								
Sleepiness/ Tiredness								
Tremors/ Slowed Movements								
Unable to Sit Still								
Urinating Trouble								
Weight Gain								
RARE BUT SERIOUS (NOTIFY MEDICAL):	BASELINE	MON	TUES	WED	THUR	FRI	SAT	SUN
Extreme stiffness or lack of movement, very high fever, mental confusion, irregular pulse rate, eye pain **(EMERGENCY RESPONSE)**								
Fever, sore throat, yellowing of eyes/skin, easy bruising								
Seizure								
Stiffness of Tongue								
Sustained involuntary muscle contraction								
Sudden stiffness and inability to breathe or swallow **(EMERGENCY RESPONSE)**								

Uses and Worries – Risperidone

- Available in dissolvable tablet (M-tab), liquid and long-acting injectable (Risperdal Consta, every 14 days)
- Can almost be considered a first-generation antipsychotic (higher risk of dystonia, EPS, hyperprolactinemia)
- Weight gain, metabolic side effects, sexual side effects common
- Difficulty with visual accommodation also common (notable when switching from long-distance to short-distance, change in lighting)

Uses and Worries – Paliperidone

- Active metabolite of Risperidone
- Available in long-acting injectable form
  - Invega Sustenna (every 28 days)
  - Invega Trinza (every 90 days)

Uses and Worries – Clozapine

- Most effective antipsychotic but due to monitoring and challenging side effects, reserved for treatment-resistant conditions
- Monitoring includes weekly blood draws to monitor white blood cell production
- Commonly causes drooling, weight gain, fatigue
- Can cause seizures, arrhythmias
- Has an anti-suicide property independent of pharmacological mechanism
- Sometimes used to treat movement disorders

Uses and Worries – Olanzapine

- Chemically related to clozapine
- Very good anti-manic agent, better mood stabilizer properties than Risperdal/typical antipsychotics
- Available in short-acting injectable form and orally dissolving tablet (Zydis)
- Very high risk of weight gain, fatigue
- Patients preferred experience of being on olanzapine in large studies despite side effects

Uses and Worries – Quetiapine

- Indicated for use in Bipolar Disorder to treat manic and depressed states
- Available in extended release oral formulation (Seroquel XR)
- Calming due to histamine-blocking properties (similar to Gravol/Benadryl)
- Orthostatic hypotension (dropping blood pressure upon standing) is common
- Often used off-label for anxiety, insomnia
- Low-affinity, dosing for schizophrenia usually upwards of 300-600 mg daily
- Weight gain very common and problematic in off-label uses

Uses and Worries – Lurasidone

- Must be taken with meals for absorption
- Akathisia and restlessness are very common
- Use was strongly promoted for treatment in Bipolar Disorder more commonly than psychotic disorders, primarily for mixed states
- Weight neutral, good metabolic profile

Uses and Worries – Aripiprazole

- At low doses (under 10 mg) used to treat depression as adjunct to traditional anti-depressant
- Works as mood-stabilizing agent/anti-psychotic in dosing greater than 15 mg daily
- Also available as long-acting injectable (Abilify Maintena, every 28 days)
- Often causes akathisia at lower doses
- “Shouldn’t” cause dyskinesia but not uncommon

Antipsychotic Use for Other Conditions

- Bipolar Disorder – most antipsychotics also used to treat different phases of Bipolar Disorder (treatment of mania, prevention of mania)
- Tic Disorder
- Obsessive-Compulsive Disorder
- Delirium
- Responsive Behaviours in Dementia
- Autism Spectrum Disorder
- Nausea, Cannabis Hyperemesis
- Eating Disorders

Thank You For Listening!