Antipsychotics for Primary Care

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Disclosures

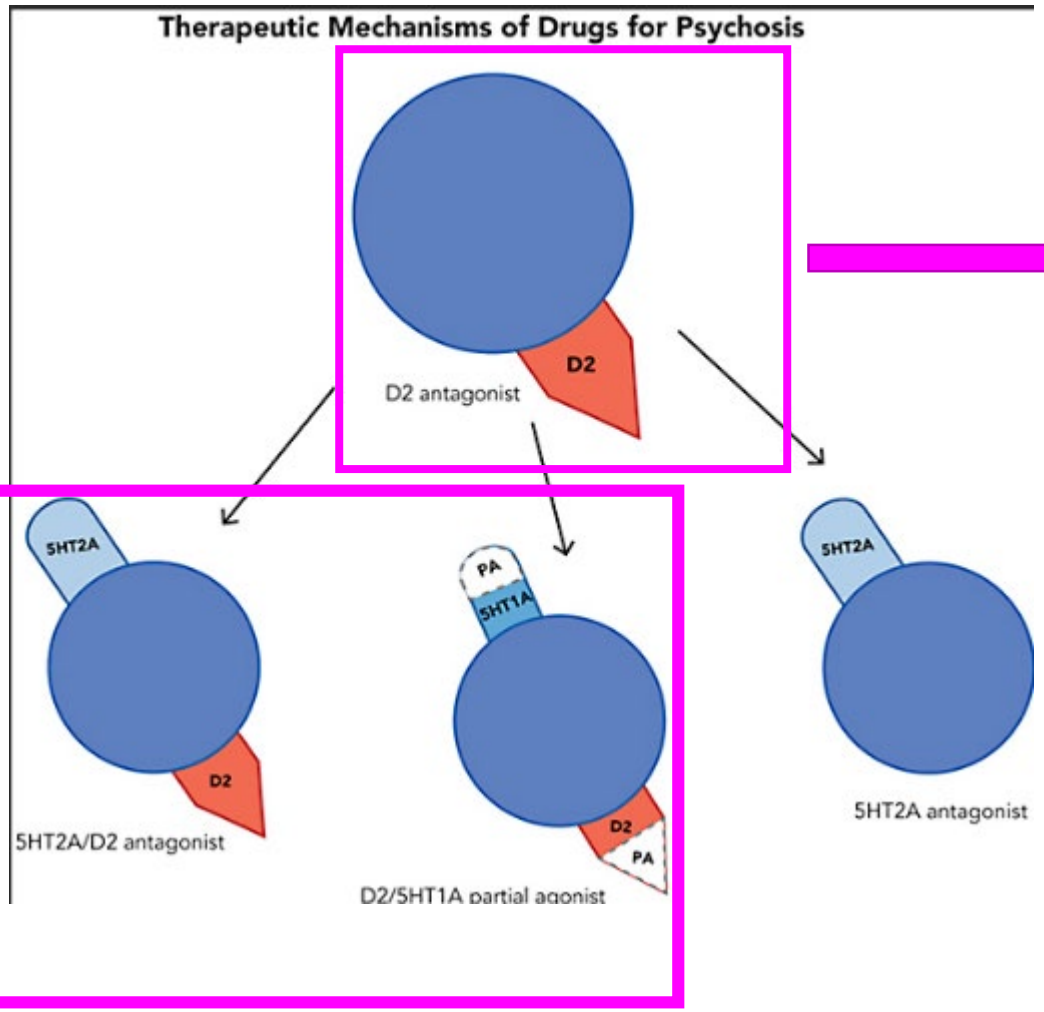
I have no relevant financial disclosures

Objectives

- State the basic mechanism of action of antipsychotic medications
- Review the indications and use of antipsychotic medications
- Describe major side effects of antipsychotic medications, how to monitor for these side effects, and how to treat these side effects

Mechanism of Action

D2 Receptor Antagonism

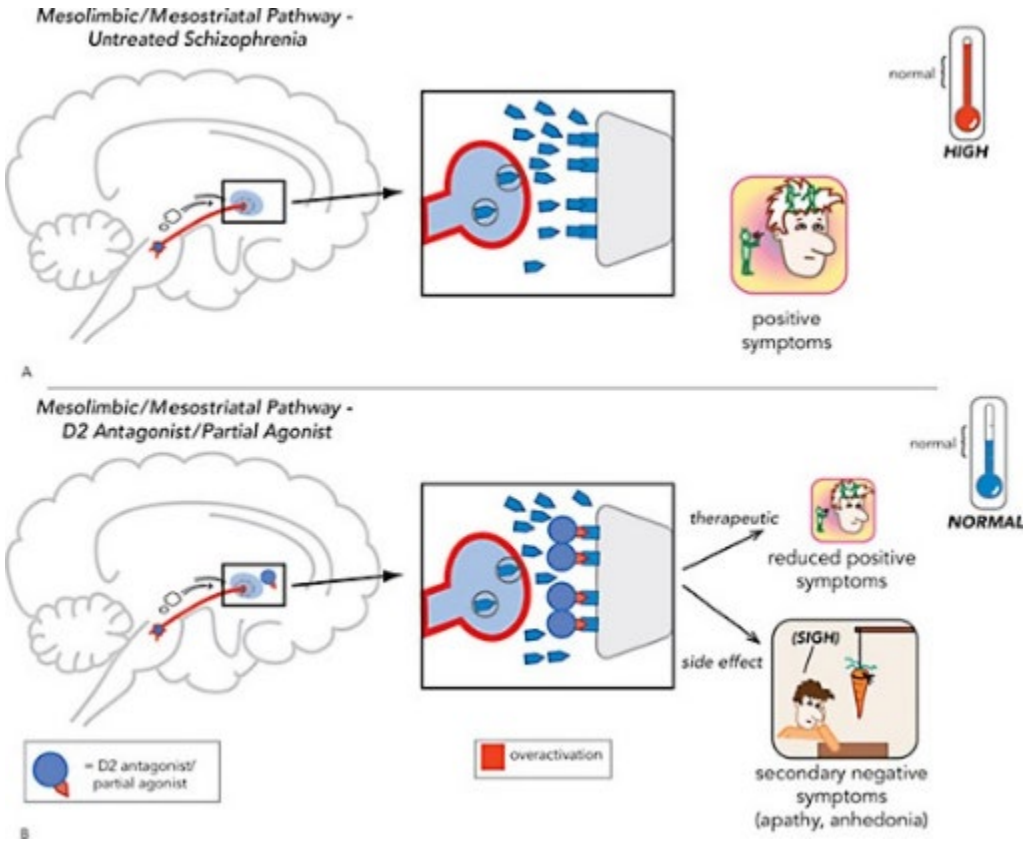


1st Generation or typical antipsychotics

2nd Generation or Atypical Antipsychotics

Stahl, S. (2021).

Mesolimbic/Mesostriatial Pathway



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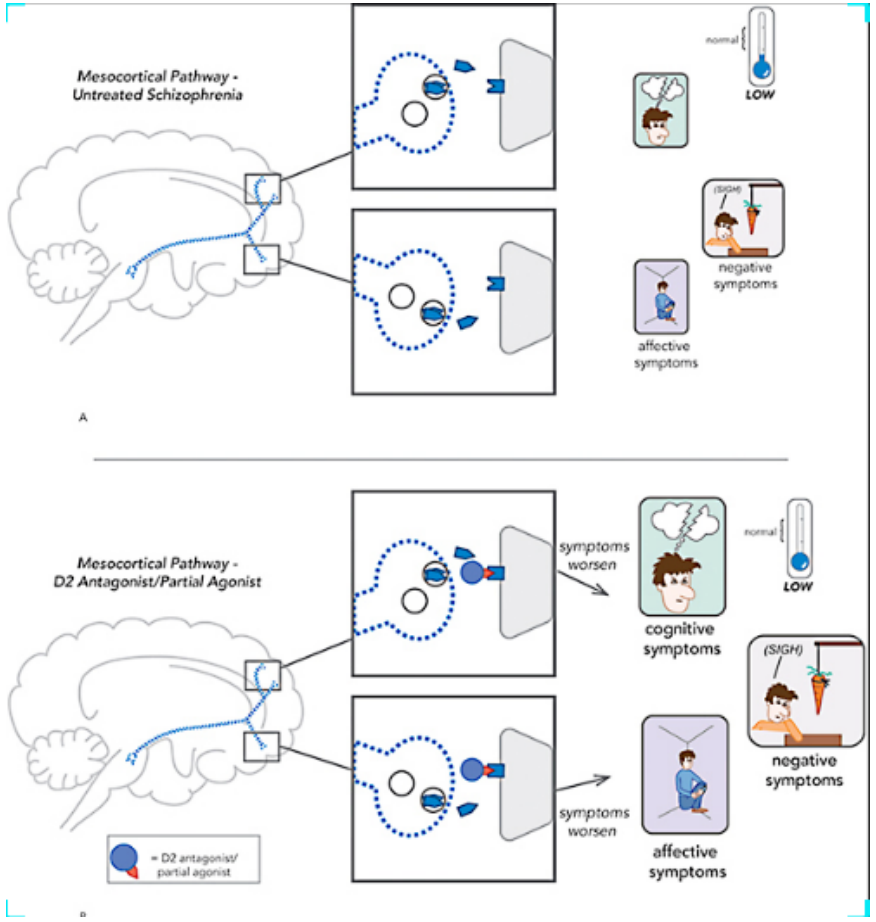
Mesocortical Pathway



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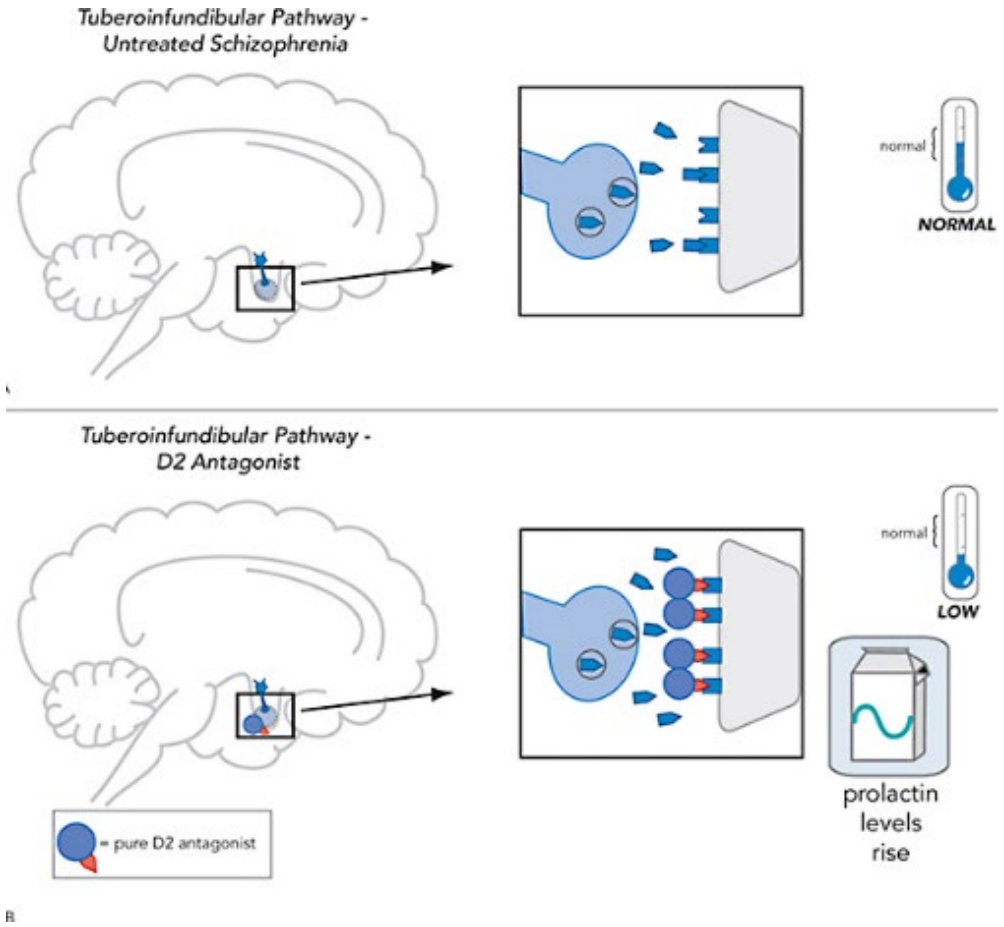
Tuberoinfundibular Pathway



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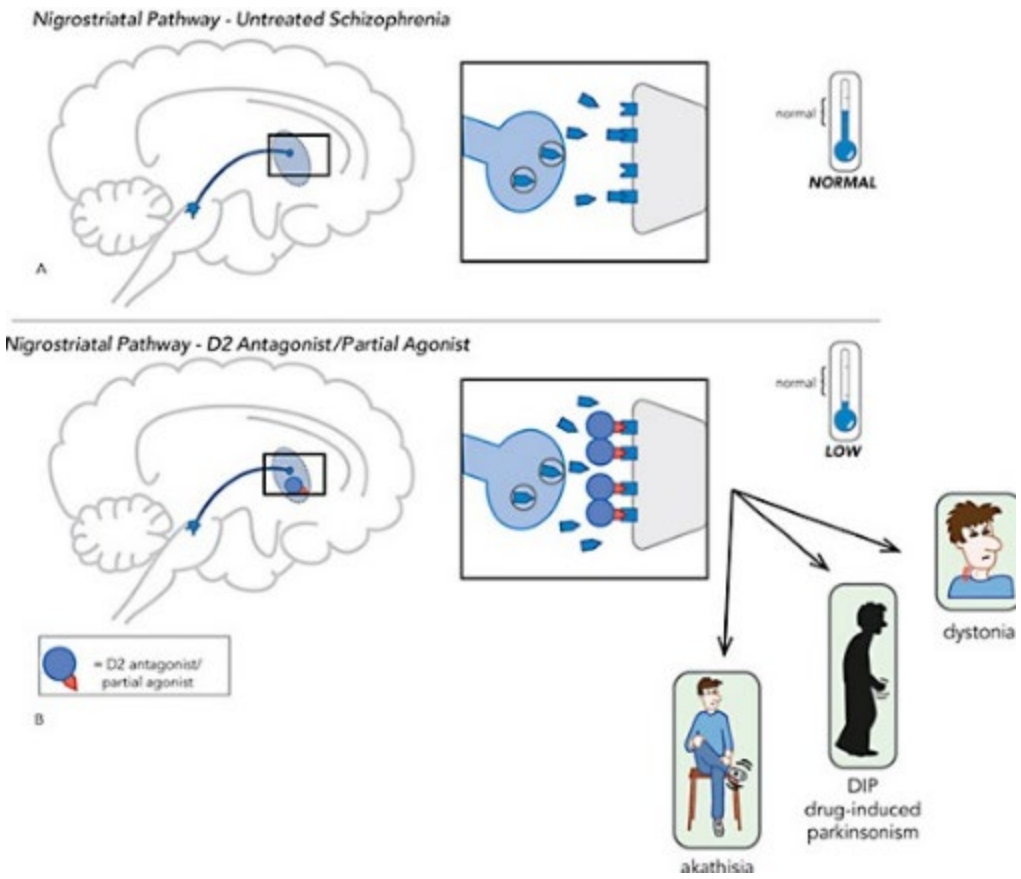
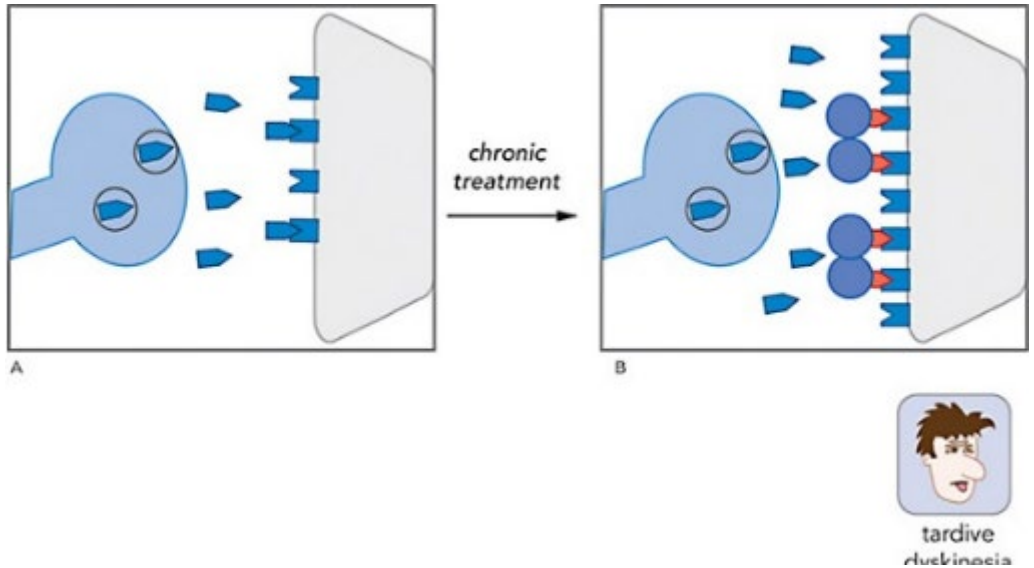
Nigrostriatal Pathway





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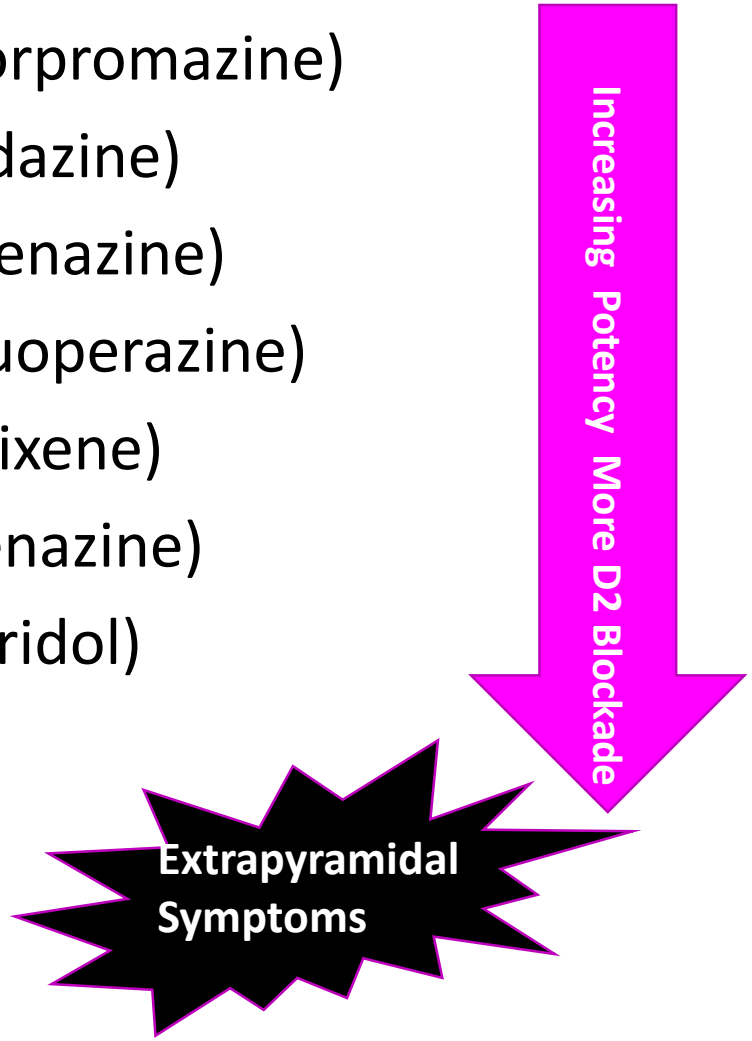
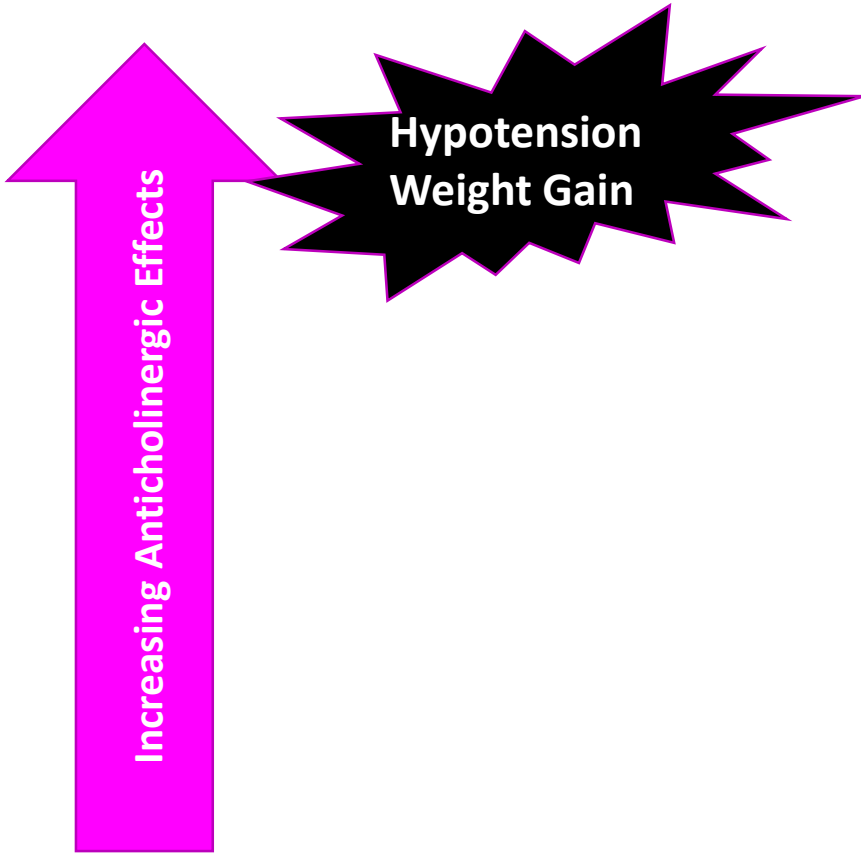
First Generation Antipsychotics

- Thorazine (chlorpromazine)
- Mellaril (thioridazine)
- Trilafon (perphenazine)
- Stealzine (thifluoperazine)
- Navane (thiothixene)
- Prolixin (fluphenazine)
- Haldol (Haloperidol)





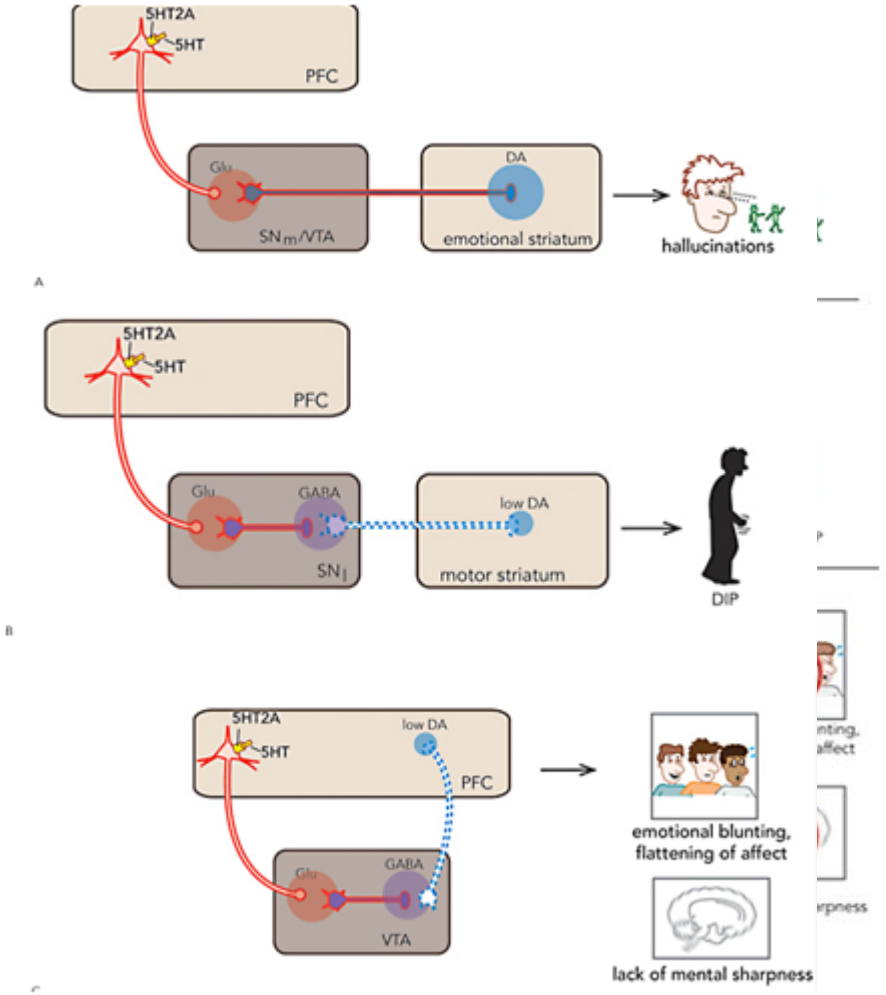
Haloperidol and Fluphenazine

- Most commonly used Typical or 1st generation antipsychotics in treating schizophrenia
- Highly potent, more risk for Extrapyramidal side effects
- Both come in long acting formulations.
- Haldol comes in a short acting formulation to treat acute agitation

Second Generation Antipsychotics

- Abilify (aripiprazole)
- Latuda (lurasidone)
- Geodon (ziprasidone)
- Saphris (asenapine)
- Fanapt (Illoperidone)
- Invega (paliperidone)
- Risperdal (risperidone)
- Seroquel (quetiapine)
- Clozaril (clozapine)
- Zyprexa (Olanazpine)

Increasing metabolic side effects



Stahl, S. (2021).

General Guidelines for Prescribing

- APA Recommends individuals with Schizophrenia be treated with antipsychotic medication
- Typically Start with a second generation or Atypical Antipsychotic due to side effect burden
- After failure of 2 antipsychotics can try adding Clozapine

Pearls

Aripiprazole (ABILIFY)

- D2/5HT2C Partial Agonist→ Low side effect profile
- Higher incidence of Akathisia
- Reduces Hyperprolactinemia
- FDA Indications: Schizophrenia, Bipolar DO (Maintenance), Depression (adjunctive treatment) Autism Related Irritability
- Long Acting Injectable Forms
  - Abilify Maintena
  - Abilify Aristada and Initio

Stahl, S. (2021).

Lurasidone (LATUDA)

- FDA Indications: Schizophrenia, Bipolar Depression
- Must take with at least 500 calories of food

Ziprasidone (GEODON)

- FDA Indications: Schizophrenia, Manic or Mixed Episodes of Bipolar and Bipolar Maintenance, Acute Agitation
- Must take with at least 500 Calories
- Also available in a short acting injection for acute agitation

Asenapine (SAPHRIS)

- FDA Indications: Schizophrenia, Mixed or Manic Episodes of Bipolar (with or without psychosis)
- Sublingual formulation, must remind patients to not eat or drink for at least 10 minutes offer

Iloperidone (FANAPT)

- FDA Indications: Schizophrenia
- Titrate slowly to prevent othrostatis

Paliperidone (INVEGA)

- FDA Indications: Schizophrenia
- Prone to Hyperprolactinemia
- Active Metabolite of Risperidone
- Available in 3 forms of Long Acting Injections
  - Invega Sustenna: given every 4 weeks
  - Invega Triniza: given every 3 months
  - Halfyeara: Given every 6 months

Risperidone (RISPERDAL)

- FDA Indications: Schizophrenia
- Available in sublingual forms
- Hyperprolactinemia
- Doses higher than 6 mg/day associated with higher risk of EPS
- Available in 2 forms of Long Acting Injections
  - Risperdal Consta given every 2 weeks, must stay refrigerated
  - Persisaris given every 4 weeks, must stay refrigerated, is given SQ

Quetiapine (SEROQUEL)

- FDA Indications: Schizophrenia, Bipolar, Depression (adjunctive tx)
- Comes in IR and XR Formulations
- IR can be abused
- Least likely to cause EPS
- Titrate slowly can cause orthostatis

Clozapine (CLOZARIL)

- FDA Indications: Treatment Resistant Psychosis
- Must register with Clozapine REMS to prescribe, requires frequent blood monitoring
  - First 6 months: Weekly
  - Second 6 months: Every other week
  - After 12 months: Monthly
- Shown to reduce violence and suicide in individuals with schizophrenia

Olanzapine (ZYPREXA)

- FDA Indications: Schizophrenia and Bipolar
- Comes in Short Acting Injection for acute agitation, note this cannot be combined with IM Ativan
- Long Acting Injection—Replrev is not prescribed due to monitoring requirements
- Also comes in sublingual formulations

Side Effects of Antipsychotic Medications

Research and analysis

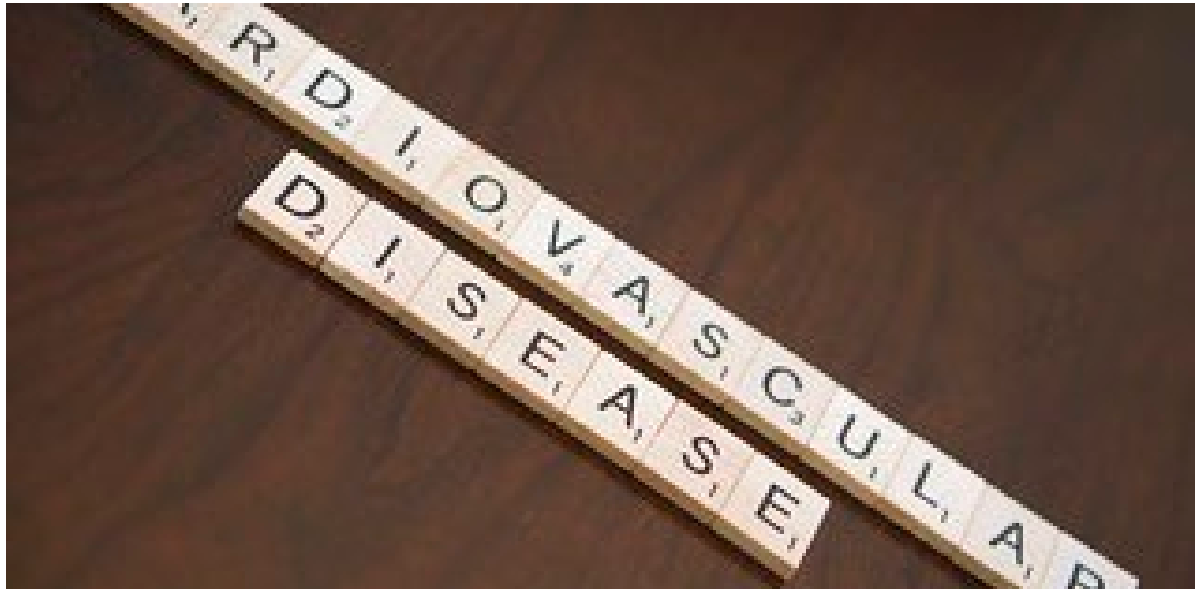
Severe mental illness (SMI) and physical health inequalities: briefing

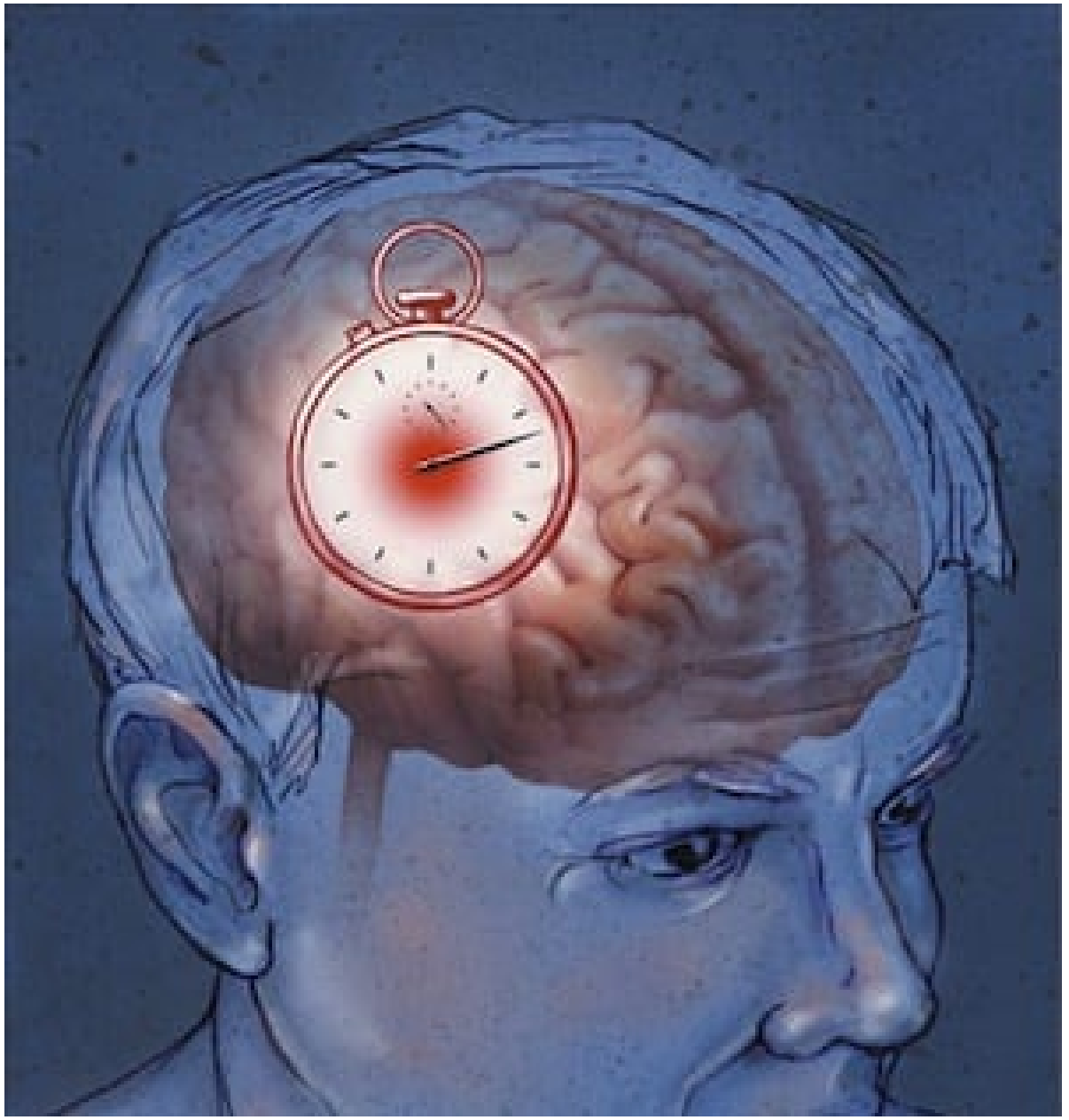
Glucose, cholesterol and blood pressure in type II diabetes: A longitudinal observational study comparing patients with and without severe mental illness

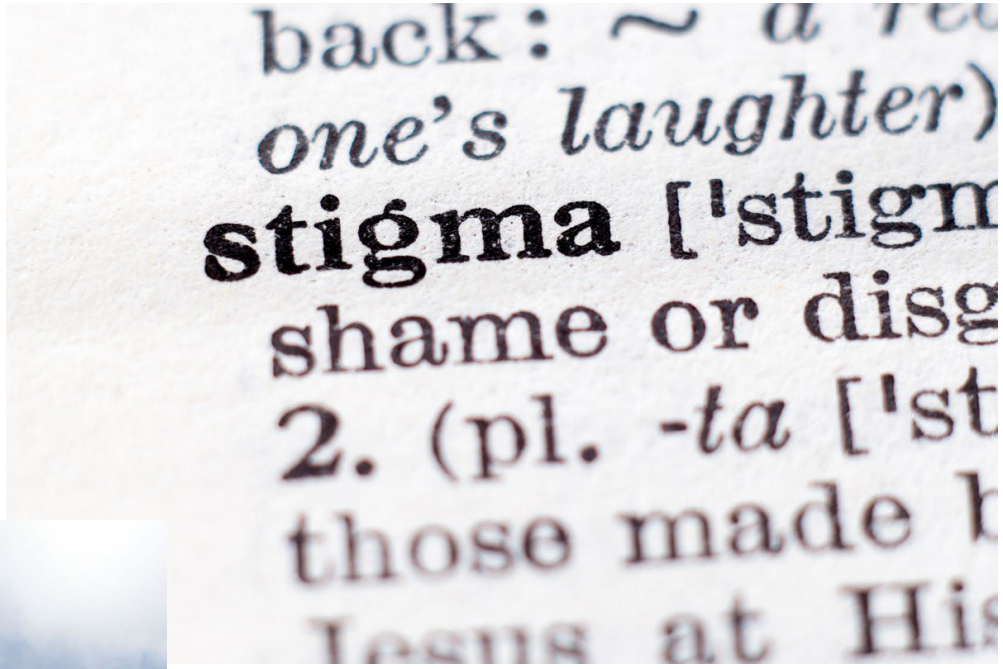
Robert Smith[1,2] | Lu Han[1] | Shehzad Ali[1,3] | Stephanie L. Prady[1] | Joanne Taylor[1] | Tom Hughes[4] | Ramzi A. Ajjan[5] | Najma Siddiqi[1] | Tim Doran[1]

- People with severe mental illness (SMI) have a life expectancy of 15–20 years less than the general population, partly due to increased risk of physical disease, including type II diabetes (T2DM) and cardiovascular disease.

DIABETES


CARDIOVASCULAR
DISEASE





Sedentary Lifestyle

Metabolic Syndrome

**3 of 5 of these are required

Insulin Resistance (indicated by the following):

- Type 2 diabetes
- Impaired Fasting Glucose
- Impaired Glucose tolerance

Elevated BP: BP >/= 140/90 and/or on antihypertensive medications

Plasma TG >/= 150 mg/dL

HDL Cholesterol

- Men: <35
- Women <39

Obesity (BMI > 30 kg/m2, waist to hip ratio (> 0.9 inches in men and > 0.85 inches in women)

Renal Function/Kidney Disease Urinary albumin excretion rate >/= 20 ug/min or albumin:creatine ratio >/= 30 mg/g

https://www.heart.org/en/health-topics/metabolic-syndrome/about-metabolic-syndrome, Goldberg (2019)

Treatment

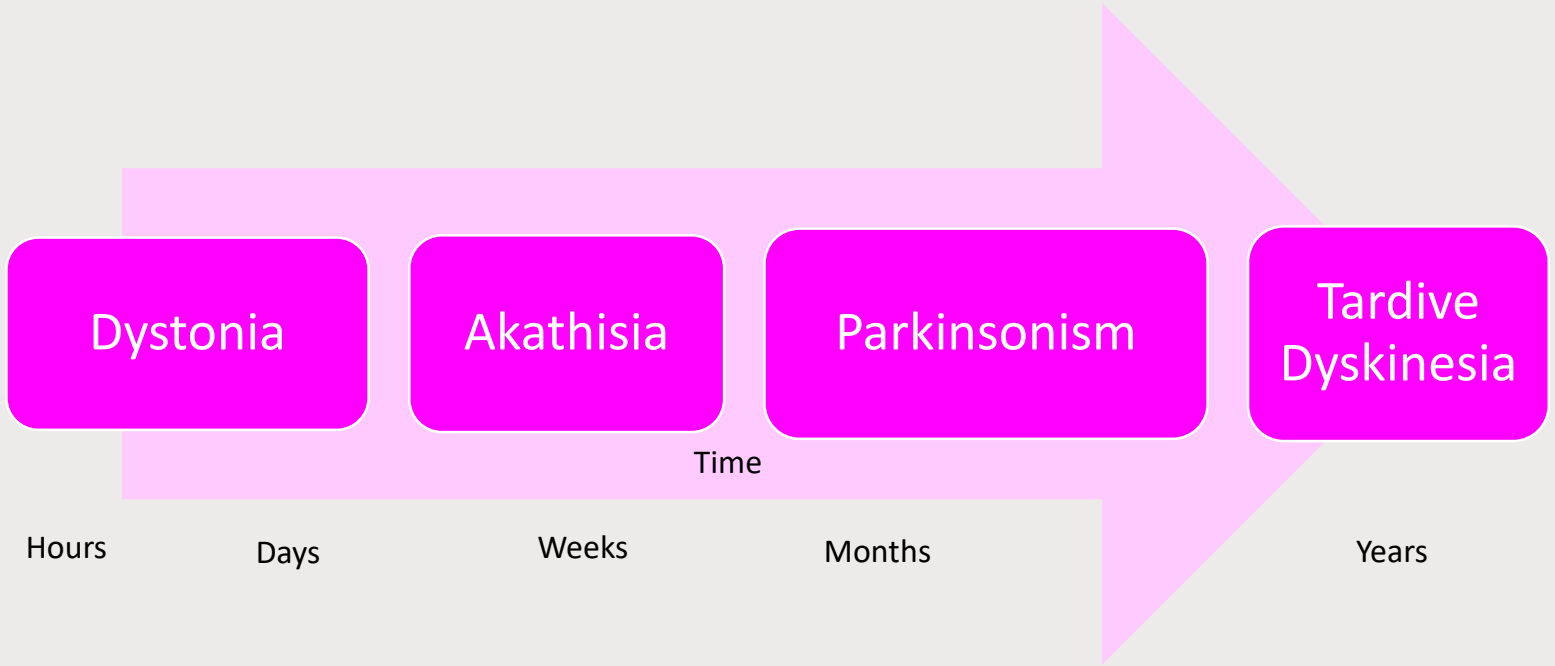
- Consider treatment with an antipsychotic that has a lower propensity for weight gain (if able)
  - Aripiprazole, Ziprasidone, perphenazine, lurasidone
- Multi-layered approach
  - Medication
  - Life-style Modification with diet and exercise.

Take Home Points: Metabolic Syndrome

	Initially	3 mo	6 mo	Annually
Blood Pressure	X	X	X	X
Weight	X	X	X	X
Lipids	X	X		X
A1C	X	X		X

- Screen regularly for metabolic Syndrome
- Complete metabolic labs at least annually
- Treat or refer to treatment to prevent metabolic syndrome
- Encourage life-style modifications

Extrapyramidal Symptoms Spectrum



https://www.ncbi.nlm.nih.gov/books/NBK534115/ https://psychiatryonline.org/doi/10.1176/appi.books.9781615371624.as49

Dystonia

- Typically occurs **acutely** over hours to days after starting an antipsychotic medication
- Can include: Torticollis, trismus, tongue protrusion, pharyngeal constriction, laryngospasm, blepharospams, oculogyric crisis
- Treatment: administration of **Antimuscrinic agent** (benztropine, trihexyphenidyl) or **Antihistamine** (diphenhydramine) these agents can reverse things rather quickly
- https://youtu.be/Rio44_GC0cs

https://www.ncbi.nlm.nih.gov/books/NBK534115/ https://psychiatryonline.org/doi/10.1176/appi.books.9781615371624.as49

Akathisia

- Often described as **an inner restlessness**, evidenced by pacing, foot taping, difficulty sitting still
- Akathisia Risks
  - Insomnia
  - Violence
  - Self-Harm
  - Suicide Attempts
- Treatment:
  - Try lowering dose of offending agent
  - Beta Blockers, Anti-muscarinic agents, benzodiazepines

https://www.ncbi.nlm.nih.gov/books/NBK519543/#:~:text=to%20remain%20still.-,It%20is%20a%20neuropsychiatric%20syndrome%20that%20is%20associated%20with%20psychomotor,cases%20the%20movement%20is%20repetitive. https://www.ncbi.nlm.nih.gov/books/NBK534115/ https://psychiatryonline.org/doi/10.1176/appi.books.9781615371624.as49

Drug induced Parkinsonism

- Signs:
  - Tremor (resting)
  - Muscular rigidity
  - Slowing of movements- shuffling gait
  - Masked Facies
- Rabbit Syndrome: Another variant includes perioral and jaw tremor
- DIP Typically presents symmetrically while Parkinson presents asymmetrically

Tardive Dyskinesia

- Typically Late onset Months to Years after starting antipsychotic medication
- Hyperkinetic, irregular movements, non-rhythmic
- Risk Factors: Duration of exposure, advanced age, female sex, diagnosis of affective DO
- Sometimes irreversible
- Lower incidence associated with Clozapine, Quetiapine, and Olanzapine.
  - Note any exposure to 1st gen AP increases risk for developing TD
- Avoid Anticholinergic Meds→ can worsen TD
- VMAT-2 Inhibitors should be offered to all individuals with TD regardless of the severity (Delphi Panel 2020, APA Practice Guidelines for Schizophrenia 2020, AAN Guidelines 2013, 2018)

https://www.ncbi.nlm.nih.gov/books/NBK534115/ https://psychiatryonline.org/doi/10.1176/appi.books.9781615371624.as49 Goldberg (2019), https://doi.org/10.1176/appi.books.9780890424841 https://pubmed.ncbi.nlm.nih.gov/31995677/ https://pubmed.ncbi.nlm.nih.gov/29454493/

Take Home Points EPS

- Evaluate for EPS at every visit, note timing of symptoms compared to when medication was started
- Dystonia: Diphenhydramine, Benztropine, or trihexyphenidyl
- Akathisia: BB
- Parkinsonism: Benztropine, Amantadine, trihexyphenidyl
- Tardive Dyskinesia: 1st Line Tx for TD is VMAT-2 Inhibitors (should be offered regardless of severity)
- https://www.youtube.com/watch?v=ucrV4ljDKuE

https://www.ncbi.nlm.nih.gov/books/NBK534115/ https://psychiatryonline.org/doi/10.1176/appi.books.9781615371624.as49 Goldberg (2019), https://doi.org/10.1176/appi.books.9780890424841 https://pubmed.ncbi.nlm.nih.gov/31995677/ https://pubmed.ncbi.nlm.nih.gov/29454493/

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