

Antipsychotic Medications

used to treat psychoses;
aka "neuroleptics", "major tranquilizers", or "anti-schizophrenics"

Schizophrenia Symptoms

- Hallucinations
- Delusions
- Disorganized speech
- Disorganized behavior
- These are called "positive (+) symptoms"
- (abnormalities that have been "added" to the person's behavior and mental processes)
- Normal emotion lost
- Decreased motivation; apathy
- Decreased social interaction
- Decreased speech
- These are called "negative (-) symptoms" – normal behaviors that have decreased

Phenothiazines: First Generation Antipsychotics

- 1950's - *chlorpromazine (*Thorazine) became the first and prototypic antipsychotic
- chemically complex – blocks or decreases the action of DA, NE, ACh and histamine
- Others: Mellaril (thioridazine), Stelazine (trifluoperazine), Prolixin (fluphenazine) & ~6 others (all the generics end in "azine")
- Differ in potency & degree of side effects
- Inexpensive and long-acting; injectable forms are available

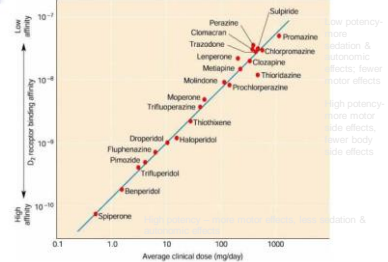
Dopamine Hypothesis

- Schizophrenia is associated with excessive response to DA in limbic & cortical regions

Support for the DA Hypothesis

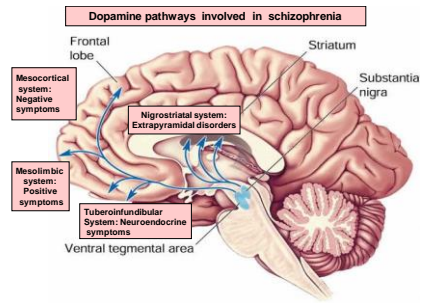
- effectiveness of typical antipsychotics almost perfectly correlated with DA blockade
- drugs which ONLY block DA are highly effective: *butyrophenone *Haldol (haloperidol)
- drugs which *increase* DA can cause paranoid schizophrenic states (e.g. amphetamine psychosis)
- brains of schizophrenics do show some abnormalities in DA activity
- BUT: not the only neurotransmitter affected- growing evidence that serotonin & glutamate also involved
- Blockade of DA receptors by typical antipsychotics primarily decreases "positive" symptoms.

Effectiveness of neuroleptics is highly correlated with binding affinity to DA receptors



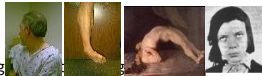
Main Side Effects

- *Extrapyramidal Motor Disorders
 - Dry mouth, blurred vision, constipation
 - Sedation, decreased response to stimuli
 - Postural hypotension
 - Disturbed hypothalamic functions; skin photosensitivity
- As with mood stabilizers, side effects can lead to significant noncompliance.



Extrapyramidal Motor Effects

- Parkinson's-like decreased movement (ε over 30%)
 - involuntary movements of face & limbs (dyskinesia) in 20%
 - compulsive restlessness (akathisia) in 20% (2) & internal, emotional sense of agitation
 - sometimes strong involuntary muscle spasms (dystonias) (2%)
- often must take drug motor side-effects



Tardive Dyskinesia (TD)



- Neurological symptom that may appear after months of use. More common the longer the use, the higher the dose or the older the patient.
- Involuntary movements of lips, tongue, jaw, face, eyelids &, less often, the body
- Unlike other extrapyramidal symptoms, TD may increase if drug is discontinued (may be long-lasting or permanent in some)

http://www.youtube.com/watch?v=BRbRctqj_k

Second Generation (SGA) or "Atypical" Antipsychotics

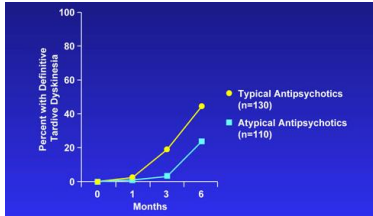
- Prototype: Clozaril (clozapine) (1989)
- **Block selected D2 & 5HT2 receptors**
- Fewer extrapyramidal side effects
- Helped 30-33% previously unresponsive patients
- Improved "negative" symptoms and disorganization; largest decrease in suicides
- Side effect: wt. gain, constipation, sedation
- BUT can cause deadly agranulocytosis in 1-2% so requires blood monitoring

More Atypical Antipsychotics

- risperidone (Risperdal) But may cause wt. gain, high blood sugar, & diabetes
 - olanzapine (Zyprexa)
 - quetiapine (Seroquel)
 - ziprasidone (Geodon)
 - lurasidone (Latuda)
- Warning: increased risk of death when used for dementia-related psychosis in elderly
- aripiprazole (Abilify) may be "new generation" – not a DA blocker

Must weigh side effects/risks against cost

Some will still have EPS



Neuroleptic Malignant Syndrome

- Medical emergency - possibly life-threatening event in 1-2%; may not be recognized
- severe rigidity, may not be able to swallow or speak or move eyes
- catatonia, confusion, agitation, or coma possible
- autonomic effects, high fever; unstable vitals
- Antipsychotics must be stopped; need to be in ICU to control vitals
- <http://www.youtube.com/watch?v=7ldQtYmggDQ>

Other Uses for Antipsychotics

- Other psychotic conditions
- Bipolar disorder; add-on for depression, anxiety
- Borderline personality disorder
- As an add-on for treatment of major depression & some anxiety disorders (OCD, PTSD)
- Some developmental disorders like autism
- Symptoms of Huntington's Disease & Tourette syndrome
- Treat aggression, agitation, delusions of dementia
- anti-nausea, anti-itching (e.g. Compazine)
 - <http://www.radiolab.org/blog/radiolab-blog/2011/aug/09/damn-it-basal-ganglia/>
- treat intractable hiccups; slow premature ejaculation
- preanesthetic calming