

# Psychopharmacology

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# Fundamentals of Pharmacology

- Significant overlap in symptoms/disease states treated within a given class
  - Antidepressants treating anxiety
  - Antipsychotics treating mania
- Significant development in receptor specificity
- Exact reason many medications work is unclear

# Fundamentals (cont)

- Off-label prescribing
  - Potential risk of unexpected side-effects
- Significant placebo response
- Minimal placebo-active drug difference
  - Less prominent with antipsychotics
- Frequent cytochrome P-450 and protein binding interactions

# Antidepressants

- Commonly prescribed across all disciplines of medicine
- Initially came to the market in the 1950's (TCA's and MAOI's)
- Black box warning for increased risk of suicidal ideation in children/adolescents
- Multiple uses:
  - Depression, anxiety, sleep, chronic pain, migraine prophylaxis, enuresis

# Antidepressants

- Monoamine Oxidase Inhibitors (MAOI)
  - Originally developed to treat tuberculosis
  - Inhibits the enzyme that degrades monoamines (dopamine, norepinephrine, epinephrine, serotonin)
  - Tyramine reaction = (potentiates release of NEpi → pressor effect → malignant hypertension); avoid foods with elevated levels of tyramine
  - Drug-drug interactions (to avoid serotonin syndrome and malignant hypertension)
  - Newest is Emsam (selegiline) patch, others are phenelzine (Nardil) and tranylcypromine (Parnate)
  - Less commonly used given the restrictions

# Antidepressants

- Tricyclic Antidepressants (TCA)
  - Originally developed as anesthetics
  - Inhibits the reuptake of norepinephrine, serotonin, dopamine in a non-selective manner
  - The original “gold standard”
  - Complicated side-effects due to muscarinic and histaminic blockade
  - Therapeutic window assessed via plasma levels
  - EKG changes (increased QTc, QRS intervals)
  - Lethal in overdose (LD<sub>50</sub> is 2000-3000mg)

# Antidepressants

- Tricyclic Antidepressants (cont)
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor)
  - Imipramine (Tofranil)
  - Desipramine (Norpramin)
  - Doxepin (Sinequan)
  - Amoxepine (Ascendin)

# Antidepressants

- Selective Serotonin Reuptake Inhibitors (SSRI)
  - Generally first line treatment due to favorable side-effect profiles
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil, Pexeva)
  - Sertraline (Zoloft)
  - Fluvoxamine (Luvox)
  - Citalopram (Celexa), Escitalopram (Lexapro)



# Antidepressants

- SNRI's
  - Venlafaxine (Effexor XR)
  - Duloxetine (Cymbalta)
- NDRI's
  - Bupropion (Wellbutrin)
- NaSSA (Noradrenergic/Specific Serotonergic)
  - Mirtazapine (Remeron)
- SARI (Serotonin-2 Antagonists/Reuptake Inh.)
  - Nefazodone (Serzone)
    - Not as commonly prescribed due to concerns of hepatotoxicity
  - Trazodone (Deseryl)
    - Generally used as a hypnotic
    - 1/10,000 risk of priapism

# Antipsychotics

- “Neuroleptics” “Major Tranquilizers”
- Class of medications helped to “de-institutionalize” patients from state hospital systems
- Generally used to treat psychotic disorders, severe depression, severe anxiety (rare)
- Cause of significant side-effects in a vulnerable population

# Antipsychotics (cont)

- Extrapiramidal side-effects
  - Due to dopamine-acetylcholine imbalance
  - Parkinsonism
  - Dystonia
  - Akathisia
  - Tardive dyskinesia
- Neuroleptic Malignant Syndrome
- Metabolic Syndrome (Syndrome X)
  - Dyslipidemia, increased abdominal fat, insulin resistance, hypertension
- Black box warning for risk of cerebrovascular adverse events in elderly with dementia; increased mortality in elderly with dementia

# Antipsychotics (cont)

- 1<sup>st</sup> Generation (“Typicals”)
  - Potency (based on ability to produce EPS)
    - Low-potency
      - Chlorpromazine (Thorazine)
      - Thioridazine (Mellaril), Mesoridazine (Serentil)
    - Mid-potency
      - Perphenazine (Trilafon)
      - Thiotixine (Navane)
      - Trifluoperazine (Stelazine)
    - High-potency
      - Haloperidol (Haldol)
      - Trifluoperazine (Prolixin)

# Antipsychotics (cont)

- 2<sup>nd</sup> Generation (“Atypicals”)
  - Significant for their decreased tendency to cause EPS
  - Probably more effective for treating the negative symptoms of schizophrenia
  - Cost is an issue (to individuals & systems)
  - Clozapine (Clozaril)
    - Frequent WBC monitoring (agranulocytosis)
    - Prominent side-effect burden

# Antipsychotics (cont)

- 2<sup>nd</sup> Generation (cont)
  - Risperidone (Risperdal)
    - Available as elixir, depot injectable “Risperdal Consta” and dissolving tablet “M-Tab”
  - Paliperidone (Invega)
    - Metabolite of risperidone
  - Olanzapine (Zyprexa)
    - Available as dissolving tablet “Zyprexa Zydis”
  - Quetiapine (Seroquel)
    - Least potent of all 2<sup>nd</sup> generation antipsychotics
  - Ziprasidone (Geodon)
  - Aripiprazole (Abilify)

# Mood Stabilizers

- Most are also anticonvulsants
- Used to treat mania, depression, anxiety, agitation/aggression
- Lithium (Eskalith, Lithobid)
- Carbamazepine (Tegretol)
- Oxcarbazepine (Trileptal)
- Divalproex (Depakote)
- Lamotragine (Lamictal)

# Anxiolytics

- Anxiety is a common co-morbid symptom with many psychiatric diagnoses
- Generally short-term treatment until underlying psychiatric illness better treated
- Risk of abuse/dependence
- Antidepressants and antipsychotics (rarely) used long-term



# Anxiolytics

- Benzodiazepines
  - Anxiety, catatonia, hypnotic, alcohol withdrawal
  - Quick onset of action
  - Intoxication and withdrawal reactions similar to alcohol
  - Lorazepam (Ativan), diazepam (Valium), alprazolam (Xanax), clonazepam (Klonopin), midazolam (Versed)

# Anxiolytics (cont)

- Buspirone (Buspar)
  - Generalized Anxiety Disorder is the only indication

Questions?