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 ($LD_{50}$ 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 Serotoninergic)**
  - 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)

• Extrapyramidal 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)

• 1st 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)

• 2nd 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)

- 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\textsuperscript{nd} 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)
- Lamotrigine (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?