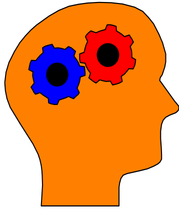
PSYCHOPHARMACOLOGY: "HEAD MEDS"



Rex S. Lott, Pharm.D., BCPP

Psychiatric Clinical Pharmacist
Boise VAMC

Professor
College of Pharmacy
Idaho State University
Clinical Associate Professor
University of Washington

PSYCHOPHARMACOLOGY: "Universal Truths"

- There are more drugs than there are truly different drugs
- Psychiatric medications treat symptoms not diagnoses
- Psychiatric medications rarely "cure" anything; they treat
- Therapeutic effects may be subtle; Side effects are often obvious
- "**Tincture of Time**"
  - Slow onset of therapeutic effects
  - Rapid appearance of side effects
- "Guidelines" and "Correct Procedures" do NOT always ensure good treatment.
- Typical psychiatric patients are not typical; most patients are unique; some are even more different than that;----------------

and then they change

PSYCHOPHARMACOLOGY: Common Side Effects:

Major Contributors to Non-Compliance & Treatment Failure

- **ANTICHOLINERGIC:**

Dry Mouth	Constipation
Blurred Near Vision	Urinary Hesitancy/Retention
Increased Heart Rate	Impaired Short-Term Memory

- **SEDATION:** Usually due to antihistamine effects
  - Not pleasant; Not alcohol-like
- **HYPOTENSION** = Low Blood Pressure
  - "Postural" = "Orthostatic": Blood pressure falls when standing.
- **WEIGHT GAIN; INCREASED CHOLESTEROL; DIABETES**
- **SEXUAL DYSFUNCTION**

PSYCHOPHARMACOLOGY: Terminology/Relationships

See accompanying handout diagram.

PSYCHOPHARMACOLOGY: Neurotransmitters in the "SOUP"

DOPAMINE: psychosis, pleasure/reward, appetite, Parkinson's Disease

ACETYLCHOLINE: side effects, memory, Alzheimer's Disease, GI function, "Housekeeping"

NOREPINEPHRINE: mood, excitement (fight/flight), appetite

SEROTONIN: mood, psychosis, appetite, aggression, sleep/wakefulness. Nausea, GI Side Effects

GABA (gamma amino butyric acid): anxiety, seizure control; sleep

HISTAMINE: side effects (sedation, weight gain)

PSYCHOPHARMACOLOGY

Schizophrenia, Psychosis & Antipsychotic Drugs

PSYCHOPHARMACOLOGY
Antipsychotic Medications

See accompanying diagram and table for antipsychotic medications.

PSYCHOPHARMACOLOGY: Clozapine

- Uniquely effective for "refractory" schizophrenia
- Effective for "negative" symptoms of schizophrenia
- Few EPS & NO Tardive Dyskinesia
- Common side effects:
  - Hypotension
  - Tachycardia
  - Excessive salivation
  - Sedation
  - **Weight Gain**
  - Constipation
- Serious (uncommon) side effects
  - Seizures
  - Agranulocytosis (Severe decrease in white blood cells with fulminant infection.

PSYCHOPHARMACOLOGY: Atypical Antipsychotics

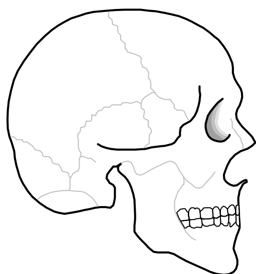
- Risperidone (Risperdal), Quetiapine (Seroquel), Ziprasidone (Geodon), Aripiprazole (Abilify), Paliperidone (Invega), Iloperidone (Fanapt), Asenapine (Saphris), Lurasidone (Latuda).
- **Possibly** more effective for "negative" symptoms of schizophrenia than first generation agents.
- Clearly fewer movement disorders / Tardive Dyskinesia
- Common side effects (variability between drugs):
  - **Weight Gain, diabetes, elevated cholesterol & triglycerides – significant with many**
  - Akathisia (Risperdal, Abilify, Geodon, Latuda)
  - Mild Sedation (varies – see table)

PSYCHOPHARMACOLOGY: Acute EPS vs. Tardive Dyskinesia

	ACUTE EPS	TARDIVE DYSKINESIA
ONSET	**Early:** Days to Months	**Late:** Years
DOSE RELATED	Clearly	Possibly
REVERSIBLE	**YES**	Approx. 30 - 40 %
SYMPTOMS	Varied; Usually **lack of movement**	**Movement**: Repetitive, Stereotyped

PSYCHOPHARMACOLOGY:

Depression



PSYCHOPHARMACOLOGY: "Antidepressants"

INDICATIONS

- Affective Disorders
  - Depression (Unipolar & Bipolar
  - Seasonal Affective Disorder
- Anxiety Disorders
  - Generalized Anxiety Disorder
  - Panic Disorder (TCA's, SSRI's, MAOI's)
  - Obsessive-Compulsive Disorder (SSRI's & Anafranil)
  - Post-Traumatic Stress Disorder (SSRIs)
- Enuresis (TCA's)
- ADHD (TCA's -- ??SSRI's?? -- Bupropion)
- Chronic Pain Syndromes (TCA's, Venlafaxine, Duloxetine)

PSYCHOPHARMACOLOGY:
Antidepressants

See Accompanying tables.

PSYCHOPHARMACOLOGY:
Antidepressants

Choice of Antidepressant

- Diagnosis
- Past response history -- patient or close relative
- Side Effect Profile
  - SSRI/SNRI **>** Tricyclics **<>** MAOI's
  - Bupropion vs anxiety
- Co-Morbidity (e.g., pain syndromes)
- Ease of prescribing & administration
- Cost
  - Pharmaceutical Industry -- indigent medication programs
  - Long-term, Big Picture vs Short-term, Small Picture

PSYCHOPHARMACOLOGY:
Antidepressants

Patient/Client Education

- Antidepressants DO:
  - **"Correct"/ "Normalize"** Abnormal Brain Function
  - **Return** person to "normal" (baseline) mood
  - **Allow** person to experience emotions/moods normally
- Antidepressants DON'T:
  - Cause euphoria
  - "Make" people happy
- Antidepressants are NOT:
  - "Stimulants" or "Uppers" (BUT may precipitate mania)
  - "Addicting" (BUT may cause withdrawal discomfort when stopped abruptly)

PSYCHOPHARMACOLOGY: Antidepressants

Duration of Therapy

Prevent Relapse Vs Prevent Recurrent Episodes

- **First or isolated episode**:
  - Continue treatment 6 - 12 months after remission of symptoms
  - Full therapeutic doses
  - GOAL: Maintain therapeutic response and prevent relapse of current episode
- **3 or more episodes of Major Depressive Illness:**
  - Indefinite duration (prophylaxis) – Prevention of recurrence of new episodes
  - FULL therapeutic doses
  - Possibly life-long treatment

PSYCHOPHARMACOLOGY: Antidepressants

Antidepressants in the Elderly

- Pseudodementia
- **Dosing**: In general, conservative.
  - "Start low", "Go slow", ---- BUT GO SOMEWHERE
- Adverse Side Effects -- especially with Tricyclics:
  - Hypotension (falls)
  - Sedation
  - CNS Anticholinergic Effects (delirium)
  - Peripheral Anticholinergic Effects (constipation, etc.)

PSYCHOPHARMACOLOGY: Antidepressants

Adverse Side Effects

- **Activation, Insomnia, Sleep Disturbance, Mania risk in bipolar disorder**
- **Sedation** -- most prominent with TCA's
  - » Mirtazepine (Remeron®) & Paroxetine (Paxil®)
- **Anticholinergic** -- prominent with TCA's
- **Cardiovascular Effects** -- most prominent with TCA's
- **Weight gain** -- Less with SSRI's & Wellbutrin
- **Sexual Dysfunction** -- prominent with SSRI's
  - Less likely with Bupropion, Vilazodone & Mirtazapine
- **Gastrointestinal Distress** -- prominent with SSRI's
- **Tremor** -- most prominent with TCA's

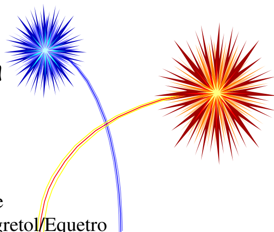
PSYCHOPHARMACOLOGY: Antidepressants

"SEROTONIN SYNDROME"

- **Agitation & Mental Status Changes (Confusion)**
- **Fever, Shivering, Sweating**
- **Muscle twitching & Tremor**
- **Hyperreflexia, Incoordination**
- **Diarrhea**
- **Risk Factors:**
  - ⇒Combined MAOI & SSRI Therapy
  - ⇒SSRI's use alone (less common)
  - ⇒Hours after addition of SSRI therapy
  - ⇒Serotonin-Active Antidepressants **+** St. John's Wort (??)

PSYCHOPHARMACOLOGY: Mood Stabilizers

Calming the Storm & Keeping it Calm



Lithium
Valproate = Depakote
Carbamazepine = Tegretol/Equetro
Lamotrigine = Lamictal
Atypical Antipsychotics

PSYCHOPHARMACOLOGY Mood Stabilizing ("Anti-Manic") Medications

See Accompanying Table

PSYCHOPHARMACOLOGY: Lithium & Mood Stabilizers

INDICATIONS

- Bipolar Disorder
- Atypical Affective Disorders & Dysthymia
- Schizo-Affective Disorder
- Major Depressive Disorder
- ↓ Risk of Suicide in bipolar disorder (LITHIUM ONLY)
- "Augmentation" of other psychoactive medications
- Intermittent Explosive Disorder
- Mood lability in Post-Traumatic Stress Disorder

PSYCHOPHARMACOLOGY: Lithium

Lithium Blood Levels

- 3 - 5 days to stabilize after any dose change
- Minimum (trough) blood levels - 12 hours after dose
- Blood levels are NOT therapeutic goals or patient outcomes
- Acute Treatment of Mania: 0.8 - 1.5 mEq/L
- Prophylaxis/Maintenance: 0.5 - 1.2 mEq/L

PSYCHOPHARMACOLOGY: Lithium

Lithium Adverse Side Effects

- Dose-Related
  - » Nausea, diarrhea (minimized by taking with food)
  - » Polyuria & Polydipsia
  - » Fine "action" tremor
- Drug-Related
  - » Weight gain
  - » Acne; Alopecia
  - » Hypothyroidism
  - » Changes in kidney function

PSYCHOPHARMACOLOGY: Lithium

Lithium Intoxication

- Usually with blood levels above 1.5 - 2.0 mEq/L
- Predisposed: Dehydration, poor intake, other drugs
- Symptoms:
  - Nausea, vomiting, diarrhea
  - Slurred speech; staggering gait
  - COARSE tremor
  - Lethargy ⇒ stupor ⇒ coma ⇒ seizures ⇒ death

PSYCHOPHARMACOLOGY: Valproate & Carbamazepine

- Antiepileptic Drugs -- happen to also treat mania
- Alternatives to or combinations with lithium
  - ~30% (+++?) don't respond adequately to lithium
  - Substantial number may respond to Carbamazepine or Valproate
- Carbamazepine & Valproate occasionally combined
- Carbamazepine + lithium ⇒ occasional neurologic side effects:
  - » Confusion, disorientation
  - Combination is used with some success

PSYCHOPHARMACOLOGY: Carbamazepine (Tegretol)

Side Effects & Toxicity

- **Common - nuisance - related to dose:**
  - Drowsiness
  - Dizziness, clumsiness, staggering
  - Diplopia (double vision)
  - Nausea, vomiting, heartburn
- **Uncommon - not clearly related to dose**
  - Rash
  - Liver damage (rare)
  - Bone marrow damage (very rare)
  - Low blood sodium
  - Low white blood cells
  - Teratogenic Risk

PSYCHOPHARMACOLOGY: Valproate (Valproic Acid/Divalproex)

Dosing & Interactions

- 750 - 4000 (+) mg/day
  - Guided by patient's response
  - Blood levels of possible significance
- May slow elimination of many other medications:
  - Antidepressants
  - Other Antiepileptic Medications
  - Carbamazepine
  - **Lamotrigine (Lamictal®)**

PSYCHOPHARMACOLOGY: Valproate (Valproic Acid/Depakote)

Side Effects & Toxicity

- **Common**
  - Nausea & Gastrointestinal Irritation (Depakote may be less problem)
  - Sedation (usually only early)
  - Weight Gain (common and often significant)
  - Tremor ("Action")
- **Uncommon/Rare**
  - Edema
  - Liver damage (young children)
    - Rare in adults
- **Significant Teratogenic Risk**

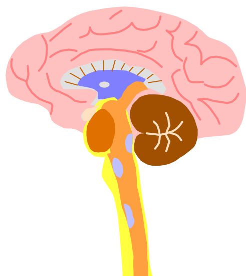
PSYCHOPHARMACOLOGY: Anti-Anxiety Agents & Hypnotics

Some "Mufflers"

A "Gyroscope"

&

"Perfect" Sleeping Pills!!



PSYCHOPHARMACOLOGY:
Benzodiazepines (Valium Family)

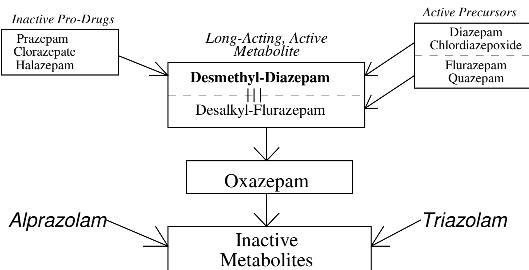
Medical / Therapeutic Use

- Improves functioning
- Controlled by MD
- Legal Use
- Stable doses

Abuse / Misuse

- Social / Recreational Use
- Impaired functioning
- Controlled by user
- Illegal use
- Large, unstable/escalating doses
- Poor / no symptom response
- No family monitoring / supervision
- Frequent (too) refills of Rx

PSYCHOPHARMACOLOGY:
Benzodiazepines (All really same drug)



PSYCHOPHARMACOLOGY:
Benzodiazepines

INDICATIONS

- Generalized Anxiety Disorders (NOT Preferred)
- Panic Disorder (Maintenance – NOT Useful "PRN")
- Insomnia & Other Sleep Disorders
- Treatment of Antipsychotic Side Effects
- Antidepressant augmentation / acceleration
- Non-Psychiatric Indications
  - Muscle Spasms
  - Seizures
  - Alcohol/Sedative Withdrawal
  - Anesthesia

PSYCHOPHARMACOLOGY: Benzodiazepines

Adverse Side Effects

- **"Mufflers"**
  - Drowsiness & Fatigue
  - Decreased cognitive/intellectual functioning
  - Shut out the world
- Dizziness, Ataxia, Weakness, Incoordination
- Anterograde Amnesia
  - Higher doses or high potency drugs
  - ANY benzodiazepine
- Paradoxical Rage / Disinhibition (uncommon, but….)
- Rebound Sleep Disturbance with Discontinuation

PSYCHOPHARMACOLOGY: Buspirone

Psycho-Pharmaco-Gyroscopic

- Serotonin-Active -- Non-benzodiazepine
- Delayed onset
- Subtle effects -- overall stabilization
- Some possible mild antidepressant activity
- Minimal Side Effects -- nausea
- NOT sedating; NOT abusable
- NOT usually accepted by patients

PSYCHOPHARMACOLOGY: "Z" Drugs (Ambien, Sonata, Lunesta)

Psycho-Pharmaco-Perfection

- Close to "Ideal" Hypnotics -- "Pure" Benzodiazepine-like sedative -- **CLAIMS**
  - Rapid onset; short half-life
  - ?? Minimal rebound insomnia??
  - Low risk of anterograde amnesia (????? Sleep eating)
- Minimal effect on normal sleep architecture
- Probable low abuse potential; low risk of withdrawal symptoms (??????)

PSYCHOPHARMACOLOGY: "Z" Drugs

- Zolpidem (Ambien & Ambien CR)
- Zaleplon (Sonata)
- EsZopiclone (Lunesta) -- Butterfly wings

PSYCHOPHARMACOLOGY: Panic Disorders

- **Benzodiazepines (usually only temporarily used)**
  - Alprazolam (Xanax) -- 3 - 4 mg/day (Up to 12 mg)
  - Clonazepam (Klonopin) -- 1 - 3 mg/day (?or more?)
  - Larger doses often needed
- **Antidepressants (TCA's & SSRI's)**
  - **LOW** starting doses
- **MAOI's**

PSYCHOPHARMACOLOGY: **Obsessive-Compulsive Disorder**

- Drug therapy: some help
- CBT is primary treatment
- SSRI antidepressants (Prozac, etc) are the only effective form of drug therapy
  - Anafranil (clomipramine) TCA that is an SSRI
- High doses; delayed onset; prolonged therapy & then, not a dramatic response rate.

PSYCHOPHARMACOLOGY: Pharmacotherapy of ADHD

MYTHS

- Medication response confirms diagnosis
- Loss of response to stimulants at puberty
- ADHD is "outgrown
- ADHD doesn't occur in adults
- Sugar and food additives cause/worsen ADHD
- ADHD symptoms occur in all settings at all times

PSYCHOPHARMACOLOGY: Pharmacotherapy of ADHD

Medications for ADHD

- **Stimulants** -- methylphenidate, dextroamphetamine
- **Non-stimulant:** atomoxetine (Strattera)
- **Antidepressants** --
  - TCA's (norpramine, imipramine, nortriptyline) (NOT Recommended)
  - SSRI's & Venlafaxine
  - Bupropion
- **Central Antihypertensives:**
  - Clonidine (Catapres)
  - Guanfacine (Tenex)

PSYCHOPHARMACOLOGY: Pharmacotherapy of ADHD

Stimulant Effects in ADHD

- Not "paradoxical" sedation
  - **Stimulation** of Inhibitory Pathways?
  - Improved filtering of inputs?
- **Therapeutic Goal:** Symptomatic control sufficient for productive school/social participation
- 70% response to initial trial; alternative stimulants effective in additional 25%.

PSYCHOPHARMACOLOGY: Pharmacotherapy of ADHD

Stimulants - Adverse Side Effects

- Anorexia, Nausea, Vomiting
- Insomnia
- Growth Suppression (Temporary)
- Elevated blood pressure & cardiac rhythm changes
- Depression
- Psychosis & Mania (VERY unlikely)
- Dysphoria, Irritability, & Withdrawal
- Tics (**may** indicate Tourette's Syndrome)

PSYCHOPHARMACOLOGY: Pharmacotherapy of ADHD

ADHD in ADULTS

- Diagnostic Confusion
  - Sociopathy
  - Bipolar Disorder
  - Substance Abuse (self-medication)
- Treatment -- careful attention to dosage
  - Stimulants
  - Tricyclic Antidepressants
  - Clonidine
  - SSRI's
  - Bupropion