Psychopharmacology and Cognitive Disabilities

Handouts
Psychopharmacology and Cognitive Impairment

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<table>
<thead>
<tr>
<th>Disorder</th>
<th>Prevalence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depression</td>
<td>17%</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>5%</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>25%</td>
</tr>
<tr>
<td>Attention Deficit Disorder</td>
<td>7%</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>1%</td>
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</tbody>
</table>
Same prevalence rates seen across all levels of cognitive functioning

Those with intellectual disabilities: often disenfranchised
Drug Treatments: One Option
Require Medical Treatment

• Psychotic episodes
• Bipolar disorder
Much better Outcomes

• ADHD
• Severe depression
Being a skeptical consumer of research
Medical Approaches to treating Psychiatric Disorders
Early Approaches to Psychiatric Treatment:
A focus on Behavioral Control
Appropriate Drug Treatment

• Reducing suffering
• Improving quality of life
• Prevent brain damage
Pharmacokinetics

Liver Metabolism
Blood Levels

• Significant individual differences
• Hard to initially predict doses
Long-term Tolerability

... 

Quality of Life
ONSET of ACTIONS: PSYCHOTROPIC MEDICATIONS

• **FAST ACTING:** (30-45 minutes)
  > Benzodiazepines
  > Tranquilizers: (e.g. Xanax)
  > Stimulants (e.g. Ritalin)

• **SLOWER ONSET OF ACTION:** (weeks)
  > Antidepressants
  > Mood Stabilizers
  > Antipsychotics
Drug Dependency

• Addiction vs. Dependency
• Potentially Habit Forming:
  > Stimulants; Benzodiazepines
• No Evidence of Addiction Potential:
  > Antidepressants, Mood Stabilizers, Antipsychotics
Sequential Trials and Polypharmacy

- Having a clear strategy
- Tolerability issues
- Mono-therapy vs. combination treatments
The Role of the Family

• Supporting medication treatment; address fears
• Help with taking medications
• Family involvement: reducing relapses
• “Early warning signs”
Early Warning Signs List

• Physical Symptoms
• Change in daily activities
• Activity levels
• Sleep patterns
• Work, school, and social activities
• Sexual behavior
• Eating
• Substance use
Newer Antidepressants

trazodone
nefarazodone
fluoxetine
bupropion-X.L.
sertraline
paroxetine
venlafaxine-X.R.
desvenlafaxine
fluvoxamine
mirtazapine
citalopram
escitalopram
duloxetine
atomoxetine
Desyrel
Generic Only
Prozac\(^4\), Sarafem
Wellbutrin-X.L.\(^4\)
Zoloft
Paxil
Effexor-X.R.\(^4\)
Pristiq
Luvox
Remeron
Celexa
Lexapro
Cymbalta
Strattera
Antidepressants: Indications

• Major depression
• Dysthymia: chronic, mild depression
• Pre-menstrual dysphoria:
  (except Wellbutrin)
• Anxiety disorders (except Wellbutrin)
• Chronic pain (some)
Depression: Highlighting some Major Symptoms

• Mood changes:
  > sadness, depressed mood
  > irritability
  > anhedonia...disengagement
Depression: Highlighting some Major Symptoms

• **Physical Symptoms:**
  > sleep disturbances
  > appetite changes
  > fatigue...lethargy
  > decreased sex drive
  > headaches
State of the Art
Treatmen tOutcomes

• Depression * first drug: 30%
  second drug: 55%
  combinations: 65%

• Anxiety: 40-90%

* STAR-D: NIMH
Antidepressants: addiction potential: None
Treatment specifics

• Starting dose
  > start low...increase if tolerated
  > increase dose by 4-6 weeks if tolerated
Most Common Reasons for Lack of Effectiveness

• Inadequate dose
• Stopping treatments too early
Treatment specifics

• “Activation” an acute onset side effect
  > within hours after first dose
  > anxiety and insomnia
  > solution: treat for 4 weeks with tranquilizers (e.g. Ativan)
Treatment specifics

• Treating depression. Onset of actions
  > Depression 2-6 weeks
  > Pre-menstrual Dysphoria: within hours
Treatment specifics

• Onset of actions:
  > **Anxiety:** 2-3 weeks
  > **OCD: Obsessive-compulsive disorder:** slow, progressive improvement: one-12 months
  > **PTSD: Post traumatic stress disorder:** 35% response by 8 weeks; 58% by 9 months
Treatment specifics

• **Chronic Pain**: a few days...few weeks

• **Antidepressants that treat pain**:
  > amitriptyline: Elavil
  > nortriptoline: Pamelor
  > Effexor
  > Cymbalta
Treatment specifics: Depression

• Treat until asymptomatic
• Continue for 6 months:
  • Gradual discontinuation
• Long-term treatment
Risks

• Can aggravate bipolar disorder
• Lowers seizure threshold
• Paxil: can cause cognitive impairment
• Impact on suicidality
Impact on Prescribing

CDC: Lubell, et al. 2007

• 1950-1990: suicides increased 300%  (ages: 10-24)
• 1988: newer drugs on the market
• 1990-2003: suicides ↓ 29%  (ages: 10-24)
• 30-40% decrease in prescriptions for antidepressants for kids and teens
• 2003-2004: teenage suicides increased by 18%
Who is at Risk?

- Unsuspected or undiagnosed bipolar disorder
- Suicide and depression: in general always need to exercise caution
Antipsychotic Medications
Atypical Antipsychotics

- SEROQUEL
- RISPERDAL
- ZYPREXA
- GEODON
- ABILIFY
- INVEGA
- FANAPT
- SAPHRIS
Antipsychotics: Indications

• Schizophrenia
• Drug induced psychosis
• Bipolar mania
• Bipolar depression: Seroquel
Antipsychotics: Indications

• Psychotic symptoms: neurological diseases
  (e.g. Alzheimer’s disease)

• Aggression
State of the Art
Treatment Outcomes
(medication treatment only)

• Texas Medication Algorithm Project
• CATIE: Clinical Antipsychotic Trials of Intervention Effectiveness
Antipsychotics
Addiction potential: None
Treatment specifics

• Acute agitation: psychosis or mania: antipsychotics may be combined with tranquilizers
• Reduces agitation within hours
Treatment specifics

• Psychotic symptoms: onset of actions: several to many weeks
• Onset of action with mania: 10 days+
• Aggression: days to weeks
Atypical Antipsychotics: Metabolic Side Effects

- Weight gain
- Increased Cholesterol and triglycerides
- Hyperglycemia
- Type II Diabetes
Metabolic Side Effects

- **Most common:**
  > Zyprexa; Clozaril; Symbyax

- **Moderate:**
  > Seroquel, Risperdal, Invega

- **Least Likely:**
  > Abilify, Geodon
Metabolic Side Effects

- Requires periodic monitoring

  - blood glucose
  - cholesterol
  - triglycerides
  - weight and body mass index
Bipolar Disorder
Bipolar I

Three Treatment Targets
Medications for Bipolar Disorder

• Lithium
• Certain Anticonvulsants:
  > Depakote
  > Tegretol
  > Equatro
  > Trileptal
  > Lamictal
• Antipsychotics
State of the Art
Treatment Outcomes

• Using best practice guidelines
  STEP-BD: NIMH

• 58% achieved recovery

• 2 year follow-up: 48% relapsed
Realistic Medical Prophylaxis

• In adults: if treated early and if medication compliant:
  30% true cessation of episodes

• Realistic Good Outcome:
  > 75% reduction in episode frequencies
  > Reduce severity and hospitalizations
But...

More than half are chronically non-compliant
Lithium and Anticonvulsant Mood Stabilizers:

Addiction potential: None
Treatment Specifics: Three Phases

• Emergency treatment
• Stabilize the current mood episode
• On-going treatment: preventing recurrences
Lithium

• Significant lab monitoring...before and during treatment
• Very toxic in overdose
• Good results in bipolar disorder
• Marked reduction in suicides (7-fold reduction)
Anti-convulsants

• Depakote
• Tegretol
• Equetro
• Trileptal
• Lamictal (not for mania; treats bipolar depression)
Side Effects Common to Most Anticonvulsant Anti-Manic Drugs

- Nausea
- Lethargy/Sedation
- Tremor
- Weight Gain
- Rash
Risks

• More potentially dangerous side effects
• Birth defects
• Lithium: highly toxic
• Very high rates of non-compliance
Stevens-Johnson Syndrome
Risks

• Significant side effects

• Poor compliance:
  long-term tolerability

• Poor outcomes:
  > Episodes increasingly severe
    and harder to treat
  > High rates of suicide: 20%
Tranquilizers

Benzodiazepines
### Tranquilizers: for Anxiety

<table>
<thead>
<tr>
<th>Diazepam</th>
<th>Valium</th>
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<tbody>
<tr>
<td>Chlordiazepoxide</td>
<td>Librium</td>
</tr>
<tr>
<td>Prazepam</td>
<td>Centrax</td>
</tr>
<tr>
<td>Clorazepate</td>
<td>Tranxene</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Klonopin</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Ativan</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Xanax, XR</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>Serax</td>
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### Tranquilizers: for Insomnia

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>flurazepam</td>
<td>Dalmane</td>
</tr>
<tr>
<td>temazepam</td>
<td>Restoril</td>
</tr>
<tr>
<td>triazolam</td>
<td>Halcion</td>
</tr>
<tr>
<td>estazolam</td>
<td>ProSom</td>
</tr>
<tr>
<td>quazepam</td>
<td>Doral</td>
</tr>
<tr>
<td>zolpidem</td>
<td>Ambien</td>
</tr>
<tr>
<td>zaleplon</td>
<td>Sonata</td>
</tr>
<tr>
<td>eszopiclone</td>
<td>Lunesta</td>
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Tranquilizers: Indications

• Severe situational stress
• Some forms of insomnia
• Anxiety Disorders
Tranquilizers: Indications

• Acute Mania
• Agitation
• Withdrawal from alcohol
State of the Art
Treatment Outcomes
(medication treatment only)

• No large scaled studies
Treatment Specifics

• Onset of actions
• Short-term versus Long-term use
• Dependency and abuse potential
Benzodiazepine use: HMO Setting  
(Samari, 2007)

- N: 2440
- Treated for 2 years with tranquilizers
- Percent of those requesting increased doses: 1.6 %
Treating Anxiety in Substance Abusing Clients

- Non-habit forming alternatives:
  - Hydroxyzine: Atarax; Vistaril
  - Clonidine (alpha-2 agonist)
  - Inderal (beta blocker)
  - Gabapentin: Neurontin
Treating Anxiety in Substance abusing clients

• Non-habit forming alternatives:
  > SSRIs
  > BuSpar (buspirone): generalized anxiety

• Onset of actions: 2-4 weeks
Camomile and GAD

- Significant reduction in anxiety vs. Placebo
- Dose: 200 mg. Per day
- Some required 600 mg per day
- Tea: 400-600 mg

(Amsterdam, J, 2009)
Nightmares

• **Minipress**: Prazosin (antihypertensive) (alpha-1 adrenergic antagonist)
• 8 week study. Ss: 40 veterans
• Average dose: 13 mg (start at 1 mg) vs. placebo
• Distressing dreams: 0.94 (effect size)
• Quality of sleep: 1.0
ADHD: Course of the Disorder

Childhood.........Adolescence.........Adulthood

Full Syndrome...
(100)

“H” drops out........

Remission Rate: 33%
(66)
“Inattentive Subtype”
ADD

• A different disorder...unlike ADHD
• No good medication treatment options
ADHD “like” behavior
Pharmacologic Treatments
STIMULANTS

Methylphenidate
(e.g. Ritalin)

Dextroamphetamine
(Dexedrine)

Amphetamine
(Adderall)
Results from MTA study: aggressive dosing
State of the Art
Treatment Outcomes
(medication treatment only)

• Individual medications, alone 72%
• Sequential trials: 92%
Stimulants
Addiction Potential

It depends...
RISKS

• Potentially habit forming in non-ADHD clients
• Safest drugs in Psychiatry
RISKS

• Problematic if incorrect diagnosis
Consequences of Mis-Diagnosis and Stimulant Treatment

- Pre-schizophrenic: psychosis
- Agitated Depression: ↑ agitation
- Situational Stress: ↑ anxiety

neglecting psychological issues
But... Failure To Treat

• Increased risk of Substance Abuse
RISKS

• Cardiac concerns
Pre-Treatment cardiac screening

If family history of heart disease or SIDS; Fetal drug exposure or:
dizziness, tachycardia, chest pain, or syncope:
Baseline EKG
Omega-3
Fatty Acids:
essential fatty acids
Omega-3 and Depression

- Fish oil: Much better bio-availability
- 1-2 grams a day (EPA + DHA)
- 6 published studies: major depression
  - all: add-on studies
  - all significant better than placebo
Cochrane Data Base: Systematic Studies

• Meta analysis: St. John’s Wort
• Dosing: 900-1800 mg per day
• St. John’s Wort; equal efficacy to prescription antidepressants
• Linde, et al. (2008)
ST. JOHN’S WORT TREATMENT

- Reasons for use
- 900-1800 mg per day
- Three, divided doses
- Onset of actions
- Cost: $1.00 per day
Risks: ST. JOHN’S WORT

- Benign side effects profile
- Watch for Drug-Drug Interactions!
- Can ignite mania in bipolar
Limitations of Psychiatric Medication Treatments