Psychotropic Update 2014

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Let’s start at the very beginning. . .

- Client’s story
- Diagnoses
- Baseline behaviors
- Functionality/ADLs
- Likes & Dislikes
- Medications
- Socialization

Effects of Medications

- Medications affect the production, flow, elimination, actions, and interactions of chemicals in the brain
  - In doing so, they influence (excite or inhibit) electrical flow in nervous system
  - They are neither sinister or magical
- Effective medication use may maintain or restore proper electrical and behavioral balance
- Effect depends on:
  - **Aggregate of influences on the brain**

Medications Commonly Causing Agitation/Behavior Disorders

- ↗ Anticholinergics
- ↗ Baclofen
- ↗ Cimetidine
- ↗ Corticosteroids
- ↗ Digoxin
- ↗ Amantadine
- ↗ Histamine$_2$-receptor antagonists

Delirium: Definition and Key Features

- A syndrome of acute brain failure
- Synonyms: “acute confusional state,” “encephalopathy”
- Typically multi-factorial
  - Results from
    interaction between
    vulnerable patient
    (usually with several
    predisposing factors) and
    one or more illnesses or conditions

Antidepressants +

Anafranil (tricyclic)	clomipramine	Marplan (MAOI)	isocarboxazid
Asendin	amoxapine	Nardil (MAOI)	phenelzine
Aventyl (tricyclic)	nortriptyline	Norpramin (tricyclic)	desipramine
Celexa (SSRI)	citalopram	Pamelor (tricyclic)	nortriptyline
Cymbalta (SNRI)	duloxetine	Parnate (MAOI)	tranylcypromine
Desyrel	trazodone	Paxil (SSRI)	paroxetine
Effexor (SNRI)	venlafaxine	Pexeva (SSRI)	paroxetine-mesylate
Elavil (tricyclic)	amitriptyline	Pristiq	desvenlafaxine (SNRI)
Emsam	selegiline	Prozac (SSRI)	fluoxetine
Lexapro (SSRI)	escitalopram	Remeron	mirtazapine
Ludiomil (tricyclic)	maprotiline	Sarafem (SSRI)	fluoxetine
Luvox (SSRI)	fluvoxamine	Sinequan (tricyclic)	doxepin
		Surmontil (tricyclic)	trimipramine
		Tofranil (tricyclic)	imipramine
		Tofranil-PM (tricyclic)	imipramine pamoate
		Vivactil (tricyclic)	protriptyline
		Wellbutrin	bupropion
		Zoloft (SSRI)	sertraline

Antidepressant Side Effects

Side Effects mainly seen in the 1st and 2nd weeks of treatment

- CNS – headache, restlessness
- CV – bradycardia. ^BP w/SSNRI's
- GI – nausea, diarrhea
- Labs – hyponatremia
- DERM – skin reactions

MAOI's (Parnate, Nardil), Tricyclics (Amitriptyline, etc), Tetracyclic (Remeron)

Anxiolytics

Anti-anxiety Medications (All of these anti-anxiety medications are benzodiazepines, except BuSpar)	
Ativan	lorazepam
BuSpar	buspirone
Klonopin	clonazepam
Librium	chlordiazepoxide
oxazepam (generic only)	oxazepam
Tranxene	clorazepate
Valium	diazepam
Xanax	alprazolam

Anxiolytics – Ativan to Xanax

- **Common Reactions**:
  fatigue, drowsiness, ataxia
- **Infrequent Reactions**:
  constipation, incontinence, urinary retention,
  dysarthria, blurred vision, diplopia, hypotension, nausea, dry mouth,
  skin rash, tremor
- **Paradoxical Effects**: confusion, depression, headache,
  libido changes, vertigo, memory disturbances, insomnia,
  hallucinations, anxiety, excited states
- **Interactions**:
  increased sedation with other psychotropics
  enhanced anticholinergic effects with antidepressants
  extension of half-life with antidepressants
  lowered clearance with combining with Cimetidine

ANTIPSYCHOTICS

Abilify	aripiprazole
Clozaril	clozapine
Fanapt	iloperidone
fluphenazine (generic only)	fluphenazine
Geodon	ziprasidone
Haldol	haloperidol
Invega	paliperidone
Latuda	lurasidone
Loxitane	loxapine
Moban	molindone
Navane	thiothixene
Orap (for Tourette's syndrome)	pimozide
perphenazine (generic only)	perphenazine
Risperdal	risperidone
Seroquel	quetiapine
Stelazine	trifluoperazine
thioridazine (generic only)	thioridazine
Thorazine	chlorpromazine
Zyprexia	olanzapine

Mood Stabilizers

Depakote	divalproex sodium (valproic acid)
Eskalith	lithium carbonate
Lamictal	lamotrigine
lithium citrate (generic only)	lithium citrate
Lithobid	lithium carbonate
Neurontin	gabapentin
Tegretol	carbamazepine
Topamax	topiramate
Trileptal	oxcarbazepine

Lithium

Pluses

- Effective and noted at lower levels - 0.4-0.6 meq/L

Minuses

- Effects on thyroid
- Renally eliminated
  - Clcr 10-50 mL/minute: 50% to 75% of normal dose
  - Clcr<10 mL/minute: 25% to 50% of normal dose
  - Dialyzable (50% to 100%)
- Multiple Drug Interactions

Divalproex/Valproate/Valproic acid

Pluses

- Effective in treating acute symptoms of mania, depression and mixed.
- Often used in combination with antipsychotics better efficacy in reduction of mania and psychosis
- Better DOWN profile

Minuses

- Side effects noted esp more in elderly-> tremors, GI. Also issues with liver and blood dyscrasias.
- Drug drug Interactions
- Typical starting dose doe older individuals with bipolar disorder 250mg tid and titrate slowly to serum concentration of 50-125ug/ml. (ER has about 15% lower bioavailability than IR)

Lamotrigine

Pluses

- Well studied in individuals with mania and/or hypomania helped to prolong time to a depressive episode.

Minuses

- Life threatening rash especially with VPA, quick dose titration.
- Tolerability: GI, CNS

Carbamazepine

Pluses

- Effective in treatment of acute bipolar mania yet with some comparative trials may not have been as effective as VPA.

Minuses

- Tolerability: up to 50% of pts experience side effects especially neurological. Less likely are skin rashes, blood dyscrasias and liver impairment.
- Drug Interactions!

ADD/ADHD Medications

ADHD Medications (All of these ADHD medications are stimulants, except Intuniv and Straterra.)	
Adderall	amphetamine
Adderall XR	amphetamine (extended release)
Concerta	methylphenidate (long acting)
Daytrana	methylphenidate patch
Desoxyn	methamphetamine
Dexedrine	dextroamphetamine
Dextrostat	dextroamphetamine
Focalin	dexmethylphenidate
Focalin XR	dexmethylphenidate (extended release)
Intuniv	guanfacine
Metadate ER	methylphenidate (extended release)
Metadate CD	methylphenidate (extended release)
Methylin	methylphenidate (oral solution and chewable tablets)
Ritalin	methylphenidate
Ritalin SR	methylphenidate (extended release)
Ritalin LA	methylphenidate (long-acting)
Strattera	atomoxetine
Vyvanse	lisdexamfetamine dimesylate

Antipsychotic Medications Are Dangerous?

They have risks

- Both minor and more substantial
- Are they more significant than other medications?

Is primary problem the medications or is it improper use by those who don't understand what they are doing?

- Wrong medications
- Inappropriate use without adequate understanding
- Excessive dose
- Problematic combinations
- Not addressing other factors affecting brain function / dysfunction

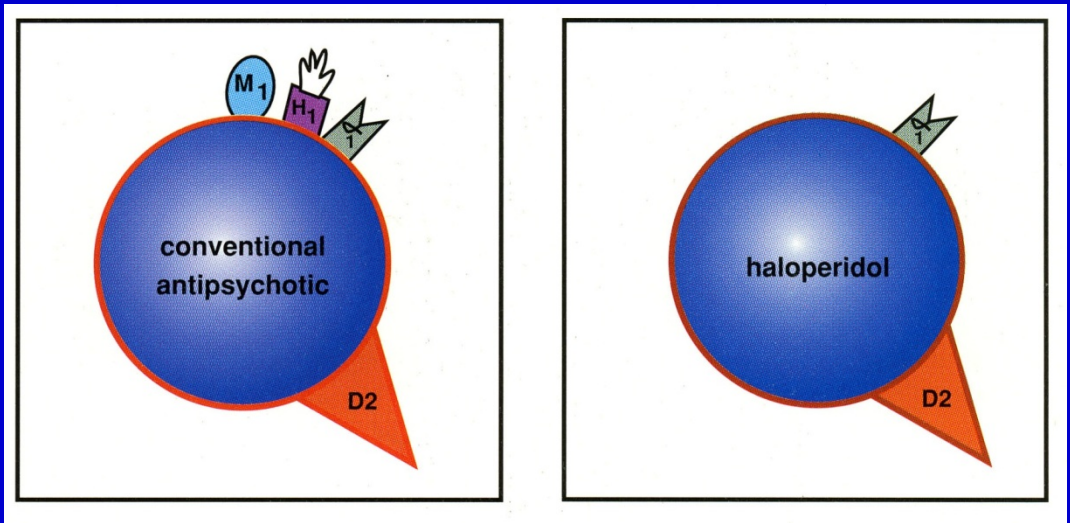
Antipsychotics

- Often used
- Reduction in non-psychotic symptoms
  - Excitement
  - Hostility
  - Restlessness
  - Tension
  - Agitation
  - Anxiety
  - Aggression
  - Uncooperativenesss
  - Irritability
- Occasional worsening of behavior
- No therapeutic effect
  - Wandering
  - Apathy
  - Withdrawal
  - Hypersexuality
  - Symptoms of executive dysfunction

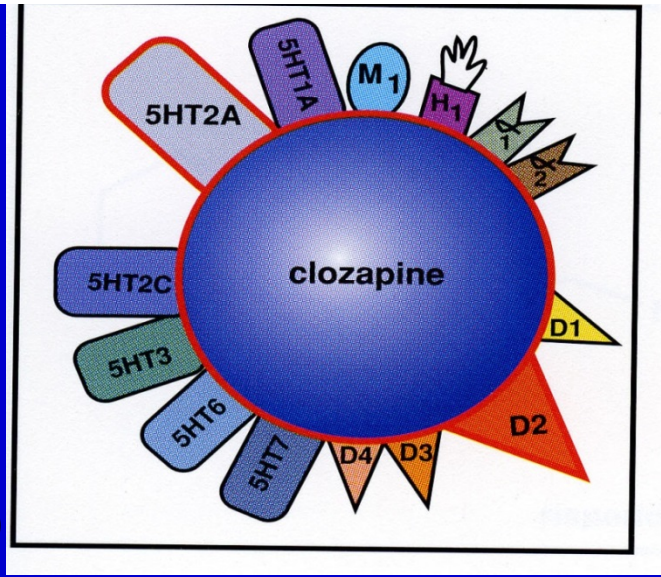
Tariot, 1996

Example of Second Generation Antipsychotics: Clozapine

- First Generation "Typical" Antipsychotics



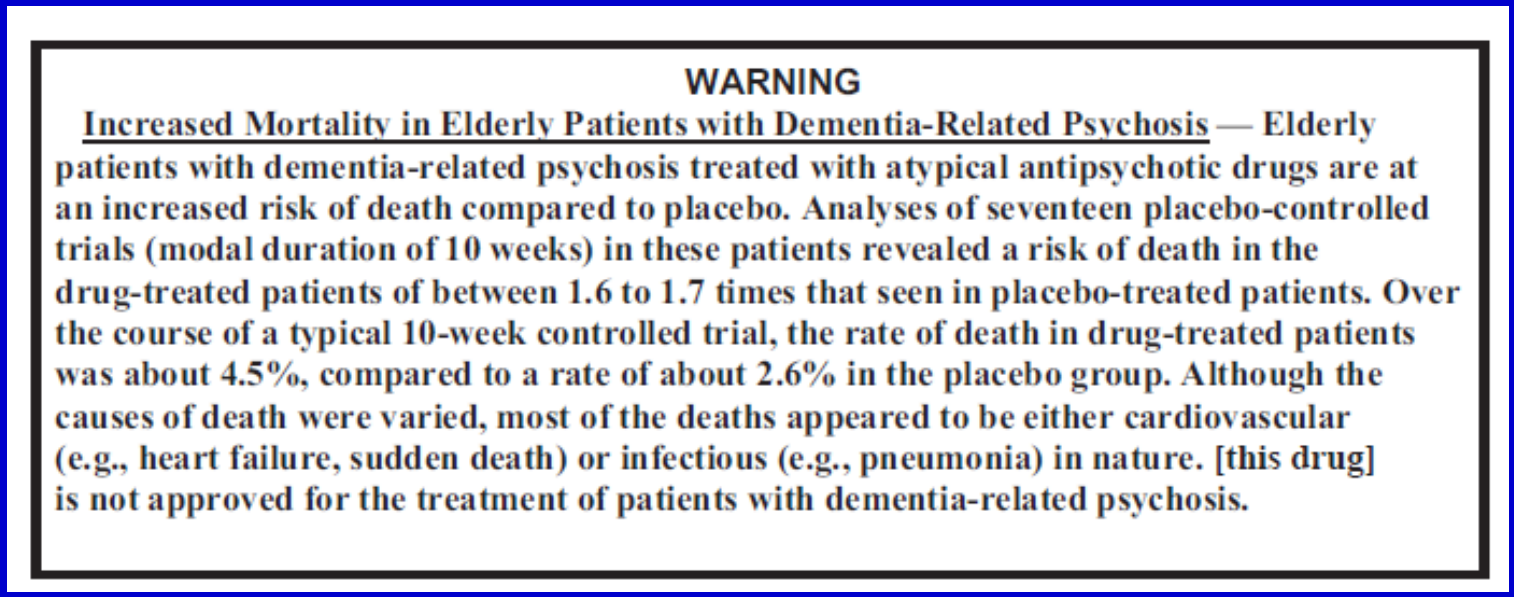
- Second Generation "Atypical" Antipsychotics



Atypical Antipsychotics: **FDA's Boxed Warning**

FDA requires that drug manufacturers include a boxed warning (black-box warning) on the product's labeling to warn prescribers and consumers of these risks

- Physicians are not prohibited from prescribing a drug in the presence of the condition(s) specified in the boxed warning.
- In April 2005, FDA required manufacturers of these drugs to include a boxed warning regarding the increased risk of mortality in elderly patients with dementia



WARNING

Increased Mortality in Elderly Patients with Dementia-Related Psychosis — Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. [this drug] is not approved for the treatment of patients with dementia-related psychosis.

Properties of Atypical Antipsychotics

Atypical Antipsychotic	EPS	PROL	TD	ACH	SZ	OH	LFTs	SED	WT GAIN	NMS	AGRAN	TX REFR	Lipid	DM	QTc
ARIPiprazole (Abilify®)	No	No	Uncommon	Very low	Low	Low	Low	Low	Very low	Yes	?	Maybe	Very low	Very low	Low
Asenapine (Saphris®)	Yes	No	Uncommon	Very low	Low	Low / moderate	Low	Moderate	Low	Yes	?	No	Very low	Very low	Low
CloZAPine (Clozaril®)	No	No	Uncommon	High	DD	High	Low	High	High	Yes	Yes	Yes	High	High	Low
Iloperidone (Fanapt™)	No	No	Uncommon	Very low	Low	Low / moderate	Low	Low	Low / moderate	Yes	?	No	Very low	Very low	Moderate
Lurasidone (Latuda®)	Yes	Yes	Uncommon	Very low	Low	Low	Low	Moderate	Very low	Yes	?	No	Very low	Very low	Low
OLANZapine ZyPREXA®	Yes	Yes	Uncommon	Moderate	Low	Low / moderate	Low / moderate	Moderate	High	Yes	Yes	Maybe	High	High	Low
Paliperidone (Invega™)	Yes	Yes	Uncommon	Very low	Low	Moderate	Low	Low	Low	Yes	?	Maybe	Low	Low	Low
QUEtiapine (SEROquel®)	No	No	Uncommon	Moderate	Low	Moderate	Low / moderate	Moderate	Moderate	Yes	Yes	Maybe	Moderate	Low / moderate	Moderate
RisperiDONE (RisperDAL®)	Yes	Yes	Uncommon	Very low	Low	Moderate	Low	Low	Low / moderate	Yes	Yes	Maybe	Low	Low / moderate	Low
Ziprasidone (Geodon®)	Yes	Yes	Uncommon	Very low	Low	Low	Low	Low	Very low	Yes	Yes	Maybe	Very low	Very low	Moderate

DR EPS = dose related extrapyramidal symptoms; **PROL** = prolactin elevation (may cause amenorrhea, galactorrhea, gynecomastia, impotence); **TD** = tardive dyskinesia; **ACH** = anticholinergic side effects (dry mouth, blurred vision, constipation, urinary hesitancy); **SZ** = seizures; **OH** = orthostatic hypotension (blood pressure drops upon standing); **LFTs** = increased liver function test results; **SED** = sedation; **WT GAIN** = weight gain; **NMS** = neuroleptic malignant syndrome; **AGRAN** = agranulocytosis (without white blood cells to fight infection); **TX REFR** = efficacy in treatment refractory schizophrenia; **Lipid** = lipid abnormalities; cholesterol and/or triglyceride elevations; **DM** = diabetes (based on case reports);

Side Effects for Atypical Antipsychotics

All of the atypical antipsychotics cause side effects. The chart below shows the side effects for adults taking an atypical antipsychotic for an off-label condition compared with those taking placebo. There are fewer studies of off-label use for some of the atypicals, especially quetiapine (Seroquel®) and ziprasidone (Geodon®). Because most off-label studies lasted less than 6 months, there is limited evidence about longer term side effects.

SIDE EFFECTS	OLANZAPINE (Zyprexa®)	RISPERIDONE (Risperdal®)	ARIPIPRAZOLE (Abilify®)	QUETIAPINE (Seroquel®)	ZIPRASIDONE (Geodon®)
Weight gain	▬▬▬	INSF	INSF	INSF	INSF
Cardiovascular problems	▬	▬	▬▬▬	INSF	INSF
Stroke	▪	▪	INSF	INSF	INSF
Extrapyramidal symptoms (uncontrollable movements)	▬	▬	▬	INSF	▬
Agitation	INSF	INSF	▬	INSF	INSF
Gait disturbance	▬	▬	INSF	INSF	INSF
Fatigue	▬	▬	▬	INSF	INSF
Sleepiness	▬	▬	▬	▬▬▬	▬
Headache	□	INSF	INSF	INSF	INSF
Cognitive problems	▪	INSF	INSF	INSF	INSF
Pain	INSF	INSF	▬▬▬	INSF	INSF
Gastrointestinal symptoms	INSF	□	▬	▬	INSF
Urinary symptoms	▬	▪	▬▬▬	INSF	INSF
Skin problems	INSF	INSF	▬	INSF	INSF
Dry mouth	▬	INSF	INSF	▬▬▬	INSF

The length of the bar indicates how many people typically experience the side effect.

▬▬▬ 21–50% ▬ 11–20% ▬ 5–10% ▪ Less than 5% □ The harmful side effect occurred more often in people taking placebo (inactive substance) than in people taking the drug.

INSF = Insufficient evidence.

Common Problems with Antipsychotics

- Parkinsonism
  - Bradykinesia
  - Rigidity
  - Tremor
  - Gait
  - Decreased postural reflexes
  - Masked faces
  - Drooling
- Sedation
- Acute dystonic reaction
- Akathisia
- Tardive dyskinesia
- Neuroleptic malignant syndrome
- Falls/fractures

Clinical Presentation of EPS: Akathisia

Motor symptoms	Pacing, rocking, shifting foot to foot
Mental symptoms	Restlessness, inability to relax, poor concentration, irritability
Differential diagnosis	Psychotic agitation
	Idiopathic syndrome, such as restless-legs syndrome

Casey DE. *Int Clin Psychopharmacol* 1997;12(suppl 1):19–27.

Clinical Presentation of EPS: Dystonia

Motor symptoms	Briefly sustained or fixed abnormal postures of the eyes, tongue, face, neck, limbs, trunk
Mental symptoms	Fear, anxiety
Differential diagnosis	Manipulation, hysteria, seizures, catatonia
	Idiopathic syndrome, such as focal or segmental dystonia

Casey DE. *Int Clin Psychopharmacol* 1997;12(suppl 1):19–27.

Clinical Presentation of EPS: Parkinsonism

Motor symptoms	Tremor, rigidity, bradykinesia (akinesia), mask face, decreased arm swing
Mental symptoms	Bradyphrenia, cognitive impairment
Differential diagnosis	Negative symptoms of psychosis, depression
	Idiopathic syndrome, such as Parkinson's syndrome

Casey DE. *Int Clin Psychopharmacol* 1997;12(suppl 1):19–27.

Pharmacotherapy Principles

- Choose medication based on prominent behavior feature
- Avoid interactions with other medications
- Initiate with lowest possible dose
- Titrate slowly to lowest effective dose
- Visible effects can take several weeks
- Reevaluate at regular intervals
- Be aware of Federal regulations

"The goal of treatment in residents with behavior disturbances is not to just make them quiet… it is to calm
without impairing function."

Alan Siegel, MD, Yale University

- Positive outcome for patient
- Less burden for the caregivers

Evaluation of Treatment Plan

- Target Symptoms are controlled
- Maximize functionality of patient
- Treatment compliance

QUESTIONS ?

or COMMENTS ?