Psychotropic Medications Series Part 2:

Antipsychotics & Anxiolytics

Terry Broda, RN(EC), BScN, NP-PHC, CDDN
Elizabeth Kacew, RN(EC), MScN, NP-PHC

September 22, 2014

Antipsychotics & Anxiolytics

"Between 70% and 85% of persons with intellectual disabilities referred for **psychiatric** assessment are found to have one or more **untreated, undertreated, or undiagnosed** co-occurring **non-neuropsychiatric medical problems** influencing mental health and behaviour (Ryan and Sunada, 1997; Sundheim et al 1998). **Many** of these **conditions** can **produce delirium and/or psychosis** (Ryan et al 1998)."

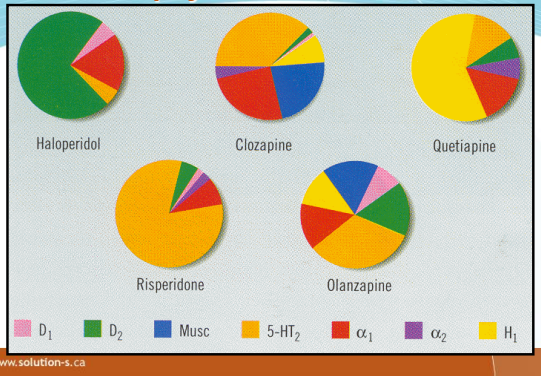
Antipsychotics & Anxiolytics

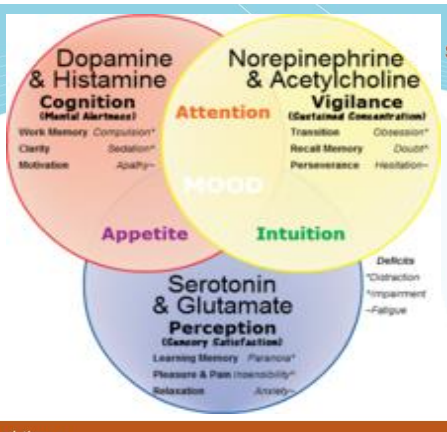
- **Observation** of the **nonverbal communications** of persons with intellectual disabilities can **offer clues** to **psychotic symptoms**:
  - such as **hallucinations, delusions, and paranoia**
- **Diagnostic** hypothesis is only considered **valid** if the **resulting treatment produces improved quality of life** and **function** and
- **provides relief of physical and/or emotional pain**.

Antipsychotics & Anxiolytics

- Non verbal indicators:
  - Covering eyes or ears
  - Fighting or shadow boxing with unseen
  - Staring into balk space/nodding, hearing conversation not heard by others
  - Unusual wrapping of objects in ears
  - Unprovoked glares of anger at strangers/or familiar faces
  - Exaggerated inspection of food/beverage items

Binding Affinities of Antipsychotics





Antipsychotics & Anxiolytics

Name	Primary Function	Notes
Acetylcholine	Muscle control, memory formation, sensory response	Imbalances can cause twitching or paralysis
Dopamine	Reward pathway, cognition, voluntary response	Imbalances cause Parkinsonian symptoms
Serotonin	Intestinal movement control, mood regulation, appetite, sleep, muscle control	Most antidepressants mimic effect of serotonin
Norepeinephrine	Fight or flight response, (increased HR, BG, O2 to brain)	
GABA	Inhibits CNS	Mediates muscle tone

Antipsychotics & Anxiolytics

COMMON SIDE EFFECTS:

- Dry mouth, blurred vision, flushing and constipation
- Drowsiness (sedation)
- Weight gain notably, clozapine and olanzapine.
- Movement disorders which include:
  - **Parkinsonism** - tremor and muscle stiffness
  - **Akathisia** - restlessness of the legs
  - **Dystonia** - abnormal movements of the face and body
  - **Tardive dyskinesia** (TD) - rhythmical, involuntary movements, such as lip-smacking and tongue-rotating movements

Antipsychotics & Anxiolytics

COMMON SIDE EFFECTS (part 2)

- Orthostatic Hypotension
- Prolongation of QTc interval (dizziness, fainting, palpitations, N & V)
- Galactorrhea / increased prolactin
- Sexual dysfunction
- Sun hypersensitivity

Atypical Antipsychotics

Risperidone (Risperdal (M-tab) + Consta)
Clozapine (Clozaril)
Olanzapine (Zyprexa (Zydis))
Quetiapine (Seroquel)
Ziprasidone (Zeldox /Geodon)
Paliperidone (Invega + Sustenna)
Asenapine (Saphris –>S/L)
*Aripiprazole (Abilify)

Legend
( ) Fast dissolving
+ IM Long-acting
* 3rd generation

www.solution-s.ca

Atypical Antipsychotics

Indications in Individuals with Developmental Disabilities

- Schizophrenia and related psychotic disorders
- Adjunctive mood stabilizers in Bipolar Disorder
- Adjunctive treatment in Obsessive-Compulsive Disorder
- Tic Suppression in Tourette's Syndrome
- Symptomatic treatment in Pervasive Developmental Disorders
- Conversion strategy to reduce risk of Tardive Dyskinesia

www.solution-s.ca

Atypical Antipsychotics

Unique Properties

- Potent dopamine (D_2) and Serotonin (5-HT_2) antagonism
- Less occurrence of extrapyramidal adverse effects
- Decreased theoretical risk of Tardive Dyskinesia
- Greater impact on negative symptoms of schizophrenia

www.solution-s.ca

Side Effects of Atypical Antipsychotics

"I must be losing weight! I can see the tips of my toes."

Weight Gain by Individual Atypical Antipsychotic Drug

	Weight gain(kg/month)
Olanzapine*	2,3
Quetiapine	1,8
Clozapine*	1,7
Risperidone	1,0
Ziprasidone	0,8

*Risk of dyslipidemia & diabetes also elevated, 2004

Atypical Antipsychotics

SE CLOZARIL

- Agranulocytosis…FATAL!
- Regular bloodwork:
  - CBC & different weekly X 26 weeks
  - Every 2 weeks thereafter
  - If stable after one year, every 4 weeks
- Important to check if person has a fever (symptom of infection)

Atypical Antipsychotics

SOLUTION-S

CONSIDERATIONS:

- Ziprasidone WITH food
- Asenapine WITHOUT food, under the tongue & DO NOT SWALLOW!
- Avoid grapefruit juice
- Zydis -> aspartame

Typical Antipsychotics

SOLUTION-S

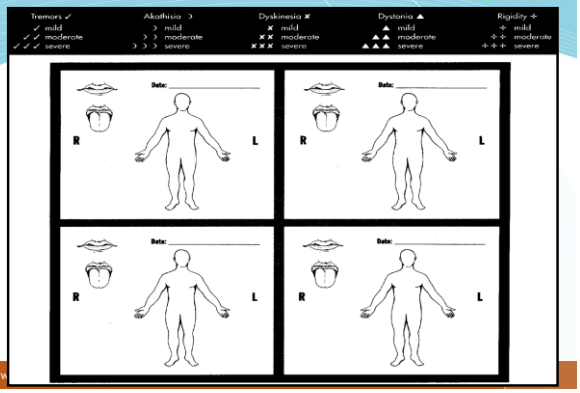
- Haldol (haloperidol)
- Loxapac (loxapine)
- Largactil (chlorpromazine)
- Nozinan (methotrimeprazine)
- Clopixol (zuclopenthixol)

Videos

SOLUTION-S

- http://www.youtube.com/watch?v=_dnK578aZdo
- http://www.youtube.com/watch?v=W_3bbpFjI68
- http://www.youtube.com/watch?v=FUr8ltXh1Pc

EPS Assessment



Examination & Checklist for EPS

Monitored on a regular basis means every person receiving drug therapy must be assessed at least once:

1. Every 3 to 6 months
2. After the initiation of a new psychotropic medication or a dose increase

Acute Dystonia

Clinical Signs/Symptoms

Motor Symptoms	Psychological Symptoms	Differential Diagnosis	Risk
Briefly sustained or fixed abnormal movement e.g., torticollis (30%) tongue (25%) trismus (14.6%) oculogyric crisis (6%) laryngospasm	• fear • anxiety	• malingering • seizure • catatonia	• high potency first-generation antipsychotics (FGAP) • young males • first exposure to FGAP

Treatments

- Lorazepam S/L
- Benztropine IM
- Diphenhydramine IM
- Rx antiparkinsonian as prophylaxis
- Decrease the dose
- Change Rx

Akathisia

Clinical Signs/Symptoms

Motor Symptoms	Psychological Symptoms	Differential Diagnosis	Risk
• Foot shifting • Pacing • Rocking	• Agitation • Restlessness • Decreased concentration	• Psychotic exacerbation	• High potency first-generation antipsychotics (FGAP) • Elderly • Female • Anemia • SSRIs

Treatments

- Antiparkinsonians NOT EFFECTIVE
- Diazepam, clonazepam, lorazepam
- ß-blocker
- Decrease the dose
- Change Rx

Parkinsonism

Clinical Signs/Symptoms

Motor Symptoms	Psychological Symptoms	Differential Diagnosis	Risk
• Tremor • Bradykinesia • Rigidity • Akinesia (masked facies, decreased arm swing) • Pill rolling movements	• Poor concentration attention • Bradyphrenia	• Depression • Negative symptoms of psychosis	• High potency first-generation antipsychotics (FGAP) • Elderly • Female • Neurological disorders

www.solution-s.ca

Treatments

- Decrease the dose
- Change Rx
- Antiparkinsonian
  - Caution side effects: anticholinergic symptoms, exacerbation of psychosis, decrease cognition, unmask / ↑ TD
  - Less use of anticholinergic medication w/ Olanzapine, Seroquel

www.solution-s.ca

Classification of Movement Disorders

Type	Characteristics
Classical Tardive Dyskinesia	Lip smacking and pursing Tongue side to side movement (bon-bon) Tongue protrusion (Fly-catcher) Chewing movements Respiratory Dyskinesia Pelvic thrusting Choreoathetoid limb movements Tapping, side to side foot movements Marching in place
Tardive Dystonia	Similar to Idiopathic Torsion Dystonia Generalized or Focal/Segmental
Tardive Tic	Motor and Vocal Tics
Tardive Akathisia	Subjective restlessness or need to move
Withdrawal Emergent Syndrome	Transient, 6-12 weeks duration Begins immediately following abrupt discontinuation of neuroleptics Children > Adults Generalized Chorea

www.solution-s.ca

Tardive Dyskinesia (TD)

Diagnostic Criteria:

- History of three months total cumulative neuroleptic use
- Dyskinesia of lingual-facial-buccal muscle (most common), upper face, limb, trunk
- Movements which are repetitive, stereotyped in appearance and distribution
- Most common is choreoathetoid movements (classical TD)
- Motor impersistance is NOT a feature
- Gait is usually not affected

Tardive Dyskinesia Risk Factors

Variable	Factor	Determinant of Increased Risk
Patient Characteristics	• Age • Gender • Diagnosis • Previous EPS • Diabetes Mellitus (NIDDM)	• Increased risk with age (>55 years) • Female (slightly higher) • Affective disorder • Risk 2 to 3 times higher • Risk 50-100% higher
Drug Characteristics	• Type of neuroleptic • Dose/Duration • Continuous vs. intermittent	• Typical neuroleptics have similar liability • Positive correlation with total drug exposure • Higher with intermittent treatment

Tardive Dystonia

Clinical Signs/Symptoms		Risks
Motor • **Sustained muscle contractions** • **Blepharospasm** • **Sustained jaw opening (83%)** • **Torticollis (50-65%)** • **Arm hyperextension (42%)** • **Back arching/flexion/leaning (35%)** • **Hand flexion/grasp-like**	**Psychological** • **Distress** • **Mobility dysfunction** • **Embarrassment**	• **Abnormal birth** • **Abnormal development** • **Neurological disorders** • **Mental retardation** • **Male, younger age** • **Earlier onset**

NMS : F-E-V-E-R

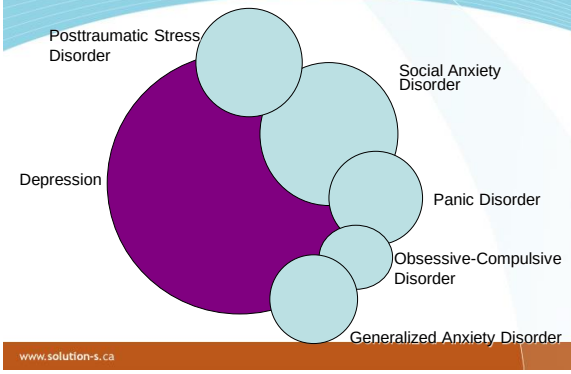
(d/t blockage of dopamine receptors)

- **F**ever: hyperthermia & diaphoresis
- **E**ncephalopathy: abrupt onset confusion, stupor
- **V**ital sign instability: BP unstable, tachycardia
- **E**nzyme elevation: CPK (creatinine phosphokinase, hepatic enzymes)
- **R**igidity: "lead pipe" rigidity (generalized)

Withdrawal Symptoms

- N & V, diaphoresis, myalgia, insomnia, anxiety, confusion (rebound cholinergic effects) (within days after D/C)
- Psychosis (2-3 weeks after D/C)
- Dyskinesia (2-4 weeks after D/C)
- Dystonia, parkinsonism, akathesia (within days after D/C)

Spectrum of Depression and Anxiety Disorders



ANXIOLYTICS (*benzodiazepines)

Valium*	➢ Diazepam
Ativan*	➢ Lorazepam
Rivotril*	➢ Clonazepam
Serax*	➢ Oxazepam
Xanax*	➢ Alprazolam
Lectopam*	➢ Bromazepam
Dalmane*	➢ Flurazepam
Restoril*	➢ Temazepam
Librium*	➢ Chlordiazepoxide
Buspar	➢ *Buspirone*

Indications for use of benzodiazepines

Clear Indications	Probable Indications	Possible Indications
• Panic • Generalized anxiety • Social Phobia • Mania/agitated schizophrenia	• Coping difficulties with anxiety • Acute insomnia related to stress • Sleep-wake cycle disturbance	• Akathisia • Tourette Syndrome • Severe agitation (emergency/ crisis)

Use of Benzodiazepines

- Useful but NOT recommended as first-line
- For short periods (less than 4 months)
- Side effect profile
  - Sedation
  - Reduced coordination
  - Impaired cognition
- Risk of dependency/tolerance
- Withdrawal symptoms/rebound anxiety

****(decrease gradually: 10 - 25% every 1- 4 weeks.)**

Benzodiazepines

Class	Medication
1. Long half-life (>13hrs) & high potency	Clonazepam (Rivotril) Clobazam (Frisium) (*AED)
2. Long half-life (>13hrs) & low potency	**Chlordiazepoxide (Librium) **Diazepam (Valium) **Flurazepam (Dalmane) Nitrazepam (Mogadon) ***(**active metabolites)***
3. Short half-life (<13hrs) & high potency	Lorazepam (Ativan) Alprazolam (Xanax)
4. Short half-life (<13hrs) & low potency	Oxazepam (Serax) Temazepam (Restoril)

Benzodiazepines

Persons w/ IDD are at an increased risk of exhibiting behavioral side effects, possibly due to :

- Decreased tolerance threshold to frustration
- More stressful living environments (group homes lacking privacy, with rigid structure, & limited trained staff) in combination with their own limited social skills & coping strategies
- **These side effects can appear from the 2nd to the 7th day or up to 55 days after starting/increasing the Rx (average = 23 days)

Buspirone

Indications

- **Anxiolytic**
- **Anti-aggressive properties**
- **Anti-depressant and anti-obsessional properties**
- **No anticonvulsant properties**

Dosage

- Begin 5 mg bid – tid
- Max. 45-60 mg/day
- Takes effect in 2-4 weeks
- *NOT effective as a PRN

Pharmacology

- 5HT1A partial agonist

Adverse Effects

- Little sedation
- Headaches, dizziness, GI upset
- No tolerance to date
- May precipitate hypomania in the elderly

Interactions

- Increased neuroleptic serum levels (+ risk EPS)
- Increased benzodiazepine levels
- Case reports of Serotonin syndrome with SSRIs & trazodone

SOLUTION·S
29-2450 Lancaster
Ottawa, Ontario K1B 5N3
T 613 249-8593
F 613 249-0198
info@solution-s.ca
www.solution-s.ca

SOLUTION·S

Surprising Drug Interactions

SOLUTION·S

Grapefruit & Grapefruit Juice

- Fresh or frozen, it can increase or less frequently, decrease the effects of certain drugs by interfering with their metabolism & elimination, **resulting in serious adverse reactions.**
- As little as 250 ml (1 cup) can cause significant increased blood levels of certain drugs.
- **These effects can last up to 3 days or longer!**

Medications to avoid w/ GRAPEFRUIT

- *Amiodarone p.o. (Cordarone)
- Aripiprazole (Abilify)
- Atorvastatin (Lipitor)
- Buspirone (Buspar)
- Carbamazepine(Tegretol)
- Clomopramine (Anafranil)
- Dextromethorphane (DM)
- *Diazepam p.o. (Valium)
- *Erythromycin p.o.
- Estrogens
- Fluvoxamine (Luvox)
- Fluoxetine (Prozac)
- Itraconazole (Sporanox)
- Lovastatin (Mevacor)
- Methadone
- *Methylprednisolone p.o.
- *Midazolam p.o. (Versed)
- Montelukast (Singulair)
- Nifedipine (Adalat)
- Pimozide (Orap)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)
- Sertraline (Zoloft)
- Sildenafil (Viagra)
- *Simvastatin p.o. (Zocor)
- Tamoxifen
- Trazodone (Desyrel)
- Ziprasidone (Zeldox)

***if given IV, no interaction noted**

Effects of Tobacco on Rx

SOLUTION-S

- Increased metabolism of fluvoxamine by 25% (via CYP182)
- Increased clearance of cyclic anti-depressant (induction via CYP182)
- Decreased plasma levels of chlorpromazine, haloperidol, fluphenazine, thiothixene, clozapine & olanzapine by 20-100% (induction)
- Increased clearance of diazepam & chlordiazepoxide (induction)

Effects of Caffeine on Psychotropics (coffee, tea, cola)

SOLUTION-S

With SSRIs:

- Increased jitteriness & insomnia
- Increased caffeine levels with fluvoxamine, half-life increased from 5hrs to 31hrs !

With antipsychotics:

- Increased akathisia & agitation
- Increased levels of clozapine (competition for metabolism via CYP1A2)

Effects of Caffeine on Psychotropics (coffee, tea, cola)

With drugs that treat EPS:

- May offset benefits of Rx by increasing tremor & akathisia

With anxiolytics & sedatives:

- May counteract sedation & increase insomnia

With lithium:

- Increased renal excretion of lithium resulting in decreased plasma levels
- May increase lithium tremor

Medical Hazards of Obesity

- **Hypertension**
- **Blood Lipid abnormalities**
- **Coronary Heart Disease**
- **Diabetes Mellitus**
- **Gallbladder Disease**
- **Respiratory Disease**
- **Cancer**
- **Gout**
- **Arthritis**
- **(Low Self Esteem)**
- **(Birth Defects)**

Abnormal Involuntary Movement Scale (AIMS)

Patient identification: _____ Date: _____

Rated by:

- Either before or after completing the examination, observe the patient unobtrusively at rest (*e.g.*, in waiting room).
- The chair to be used in this examination should be hard and firm, without arms.
- After observing the patient, he/she may be rated on a scale of 0 (none), 1 (minimal), 2 (mild), 3 (moderate), and 4 (severe), according to the severity of symptoms.
- Ask the patient whether there is anything in his/her mouth (*i.e.*, gum, candy, *etc.*) and, if there is, to remove it.
- Ask patient about the current condition of his/her teeth. Ask if he/she wears dentures, and if teeth or dentures bother the patient now.
- Ask patient whether he/she notices any movement in mouth, face, hands or feet. If yes, ask to describe and to what extent they currently bother patient or interfere with his/her activities.

0 1 2 3 4	Have patient sit in chair with hands on knees, legs slightly apart, and feet flat on floor. (Look at entire body for movements while in this position)
0 1 2 3 4	Ask patient to sit with hands hanging unsupported. If male, between legs; if female and wearing a dress, hanging over knees. (Observe hands and other body areas)
0 1 2 3 4	Ask patient to open mouth. Do this twice. (Observe tongue at rest within mouth)
0 1 2 3 4	Ask the patient to protrude tongue. Repeat. (Observe abnormalities of tongue movement)
0 1 2 3 4	Ask the patient to tap thumb, with each finger, as rapidly as possible for 10-15 seconds; separately with right hand, then with left hand. (Observe facial and leg movements)
0 1 2 3 4	Flex and extend patient's left and right arms. (One at a time)
0 1 2 3 4	Ask patient to stand up. (Observe in profile; observe all body areas again, hips included)
0 1 2 3 4	Ask patient to extend both arms outstretched in front with palms down. (Observe trunk, legs and mouth)*
0 1 2 3 4	Have patient walk a few paces, turn and walk back to chair. Repeat. (Observe hands and gait)*

*Activated movements