

## **Practical Psychopharmacology of Autism Spectrum Disorders**

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## Off-Label Use Of Medication

In this presentation, all discussion of use of medication refers to “**off-label**” use other than risperidone and aripiprazole for irritability in children and adolescents with autistic disorder

## Evaluation

- Diagnosis
- Physical Examination
- Neuropsychological Testing
- Genetic Testing
- Electroencephalogram (EEG) and/or Brain Imaging (CAT scan or MRI scan)

## Treatment Options

- Behavior therapy
- Speech and Language therapy
- Occupational therapy
- Physical therapy
- Social skills therapy
- Special educational services (academic vs. life skills track)
- Treatment of comorbid medical problems, including seizures
- Vocational training
- Pharmacotherapy

## Target Symptoms for Medication

- Motor hyperactivity and inattention
- Interfering ritualistic behavior
- Aggression, self-injury, severe tantrums
- Mood disturbances: depression, bipolar
- Anxiety
- Others: sleep disturbances, pica, inappropriate sexual behavior

## **Motor Hyperactivity and Inattention**

- Psychostimulants: methylphenidate, dextroamphetamine
- Alpha-2 agonists: guanfacine, clonidine, Intuniv
- Non-stimulants: atomoxetine, bupropion, tricyclic antidepressants

## **Psychostimulants**

- Work quickly
- Side effects: reduced appetite, insomnia, tics
- May cause behavioral worsening
- May need to be given multiple times per day
- Need new prescription each month

## **Alpha-2 Agonists**

- Need to monitor blood pressure and heart rate
- Can be sedating
- Generally don't make symptoms worse
- 2/3 need to be given 2-3 times per day
- Intuniv now FDA-approved for ADHD in children

## **Non-Stimulants**

- Atomoxetine: effective in ADHD; preliminary studies in developmental disabilities. May take longer to work than stimulants. Generally won't make tics worse. May help with comorbid mood and/or anxiety.

## **Non-Stimulants (Cont'd)**

- Bupropion: has been shown to be effective for ADHD. Not well-studied in developmental disabilities. Can lower the seizure threshold and should NOT be given to a patient with a history of seizures or active seizure disorder. Can make tics worse.

## **Non-Stimulants (Cont'd)**

- Tricyclic antidepressants: not well-studied in developmental disabilities. Associated with side effects including: dry mouth, blurry vision, constipation. Can lower the seizure threshold. Can affect cardiac rhythm.

## **Ritualistic Behavior**

- Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Fluoxetine
  - Fluvoxamine
  - Sertraline
  - Paroxetine
  - Citalopram
  - Escitalopram

## **SSRIs**

- Data indicate SSRIs may be more effective in post-pubertal vs. pre-pubertal individuals with developmental disabilities
- Side effects: insomnia, sedation, stomach upset, sexual dysfunction, weight gain
- Can generally be given once a day
- Concern about increasing suicidal thinking/behavior

## **Aggression Severe Tantrums/Self-Injury**

- Typical antipsychotics
- Atypical antipsychotics
- Mood stabilizers
- Alpha-2 agonists
- Naltrexone

## **Aggression (Cont'd)**

- Typical Antipsychotics
  - Haloperidol
  - Thioridazine
  - Chlorpromazine
- Side effects: acute extrapyramidal symptoms (EPS), tardive dyskinesia (TD), sedation, weight gain, drooling



## **Aggression (Cont'd)**

- Atypical Antipsychotics
  - Clozapine
  - Risperidone
  - Olanzapine
  - Quetiapine
  - Ziprasidone
  - Aripiprazole
  - Paliperidone

## **Clozapine**

- Common side effects include weight gain, sedation, drooling
- Can lower the seizure threshold
- Agranulocytosis and need for careful blood monitoring

## **Risperidone**

- Well-studied in autism (FDA approval) and mental retardation associated with behavioral dyscontrol
- Common side effects: weight gain, sedation (transient), drooling, elevated prolactin

## **Olanzapine**

- Only small controlled studies in developmental disabilities
- Common side effects: weight gain (at times significant), has been associated with glucose and lipid dysregulation, sedation

## **Quetiapine**

- No controlled studies in developmental disabilities
- Common side effects: weight gain (may be less prominent than with clozapine and olanzapine), sedation, orthostatic hypotension if dose increased too quickly

## **Ziprasidone**

- No controlled studies in developmental disabilities
- Common side effects: sedation (transient), occasional insomnia or behavioral activation. Not associated with significant weight gain
- Should not be given to patients with cardiac problems
- Must be taken with food

## **Aripiprazole**

- FDA-approved for “irritability” in children and adolescents with autism.
- Common side effects: EPS and nausea/vomiting if given at too high a starting dose. Occasionally transient sedation or activation.
- Most weight-neutral other than ziprasidone
- No prolactin elevation

## **Paliperidone**

- Major active metabolite of risperidone
- Potentially fewer drug-drug interactions
- Once daily dosing
- Potentially less weight gain and prolactin elevation

## **Aggression (Cont'd)**

- Mood Stabilizers
  - Valproic acid
  - Lithium
  - Carbamazepine
  - Gabapentin
  - Topiramate
  - Lamotrigine

## **Valproic Acid**

- A controlled study in autism found no drug vs. placebo difference
- Common side effects: sedation, weight gain
- Need to monitor blood level for therapeutic range and to follow liver function tests
- May be useful in patients with seizures and aggression

## **Lithium**

- No controlled studies in developmental disabilities
- Common side effects: tremor, polydipsia, polyuria, weight gain
- Need to monitor blood for therapeutic range and to follow kidney and thyroid function

## **Carbamazepine**

- No controlled studies in developmental disabilities
- Common side effects: dizziness
- Need to monitor blood level for therapeutic range and to follow blood count and sodium level

## **Gabapentin**

- No controlled studies in developmental disabilities
- Common side effects: some sedation, some weight gain
- No need to monitor blood levels
- Not particularly effective on a clinical basis

## **Topiramate**

- No controlled studies in developmental disabilities
- Common side effects: sedation, cognitive dulling. Not associated with weight gain
- No need to monitor blood levels

## **Lamotrigine**

- Controlled study in autism found no drug vs. placebo difference
- Must increase the dose very slowly
- Steven's – Johnson rash

## **Aggression (Cont'd)**

- Alpha-2 Agonists
  - Guanfacine: not particularly effective for aggression
  - Clonidine: can be effective for aggression. Need to balance sedation vs. clinical benefit
- Need to monitor blood pressure and heart rate



## **Aggression (Cont'd)**

- Naltrexone
  - Not effective on a clinical basis
  - No significant side effects
  - Need to monitor liver function

## **Mood - Depression**

- SSRIs
- Bupropion
- Venlafaxine (elevated blood pressure)
- Mirtazapine (weight gain, sedation)
- Duloxetine
- Tricyclic antidepressants

## **Mood - Bipolar**

- Valproic acid
- Lithium
- Carbamazepine
- Gabapentin
- Topiramate
- Lamotrigine (Steven's Johnson Syndrome)

## **Anxiety**

- Mirtazapine (weight gain, sedation)
- Buspirone
- SSRIs (low dose)

## **Sleep Disturbance - Insomnia**

- Melatonin
- Clonidine
- Trazodone (priapism)
- Mirtazapine
- Tricyclic Antidepressant (Doxepine, Amitriptyline)
- Chloral Hydrate
- Benzodiazepines (Paradoxical rxt'm)
- Diphenhydramine (Paradoxical rxt'n)

## **Pica**

- SSRIs
- Behavioral strategies

## **Inappropriate Sexual Behavior**

- SSRIs
- Hormonal strategies
- Behavioral strategies

## **Lurie Center for Autism**

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<http://www.massgeneral.org/children/services/treatmentprograms>

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Questions?

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