Child and Adolescent Psychopharmacology

The Art, Science and Ethical Considerations

Stephen Luippold, PMHCNS-BC

2015

References


References


Psychiatric Disorders in Children and Adolescents

• 10-15% of children in USA are affected by significant psychiatric illness, 21% in those 9-17 years of age

• Only 20% of those affected receive treatment in a given year and 14.2% of youth reported psychotropic medication use

• The majority if youth prescribed medications had mental disorder with severe consequences, functional impairment, suicidality or associated behavioral or emotional difficulties

Child & Adolescent Psychopharmacology

• National Center for Health Statistics reports that 7.5% of U.S. children between ages 6 and 17 were taking medication for “emotional or behavioral difficulties” in 2011-2012

• The CDC reports a five-fold increase in the number of children under 18 on psychostimulants from 1988-1994 to 2007–2010

• The same report estimates that 1.3 percent of children are on antidepressants

• The rate of antipsychotic prescriptions for children has increased six-fold over this same period


Child & Adolescent Psychopharmacology

- Most Rx’s for stimulants and antidepressants are not from psychiatrist or psychiatric ARPN’s
- Majority of parents resist medications for their child
- Drug companies have reduced marketing budgets in the US
- Absence in biomarkers or lab tests for psychiatric diagnosis may lead to over or under-diagnosis
- Increased need and not over-treatment

FDA Approved Psychotropic Medications for Children and Adolescents

- **Stimulants:**
  - Methylphenidate — ADHD ≥ 6 years
  - Dexamphetamine — ADHD ≥ 6 years
  - Amphetamines — ADHD ≥ 3 years
  - Lisdexamfetamine — ADHD ≥ 6 years

- **SNRI and alpha-2-agonist**
  - Atomoxetine — ADHD ≥ 6 years
  - Clonidine — ADHD ≥ 6 years
  - Guanfacine — ADHD ≥ 6 years

- **Antidepressants**
  - Sertraline — OCD ≥ 6 years
  - Escitalopram — MDD ≥ 12 years
  - Fluvoxamine — OCD ≥ 7 years
  - Clomipramine — OCD ≥ 10 years
  - Fluoxetine — MDD ≥ 8 years and OCD ≥ 7 years

- **Antiepileptic Drugs**
  - Carbamazepine — Epilepsy From Infancy
  - Oxcarbazepine — Epilepsy ≥ 4 years
  - Lamotrigine — Epilepsy ≥ 2 years
  - Valproate — Epilepsy From Infancy
  - Topiramate — Epilepsy ≥ 2 years
  - Lithium — Bipolar Disorder ≥ 12 years

- **Antipsychotic Medications**
  - Risperidone — Schizophrenia ≥ 13 years
  - Bipolar Disorder ≥ 10 years
  - Irritability in Autism 5-16 years
  - Quetiapine — Schizophrenia ≥ 13 years
  - Bipolar Disorder ≥ 10 years
  - Aripiprazole — Schizophrenia ≥ 13 years
  - Bipolar Disorder ≥ 10 years
  - Irritability in Autism 5-16 years
  - Olanzapine — Schizophrenia ≥ 13 years
  - Bipolar Disorder ≥ 10 years

Pharmacokinetics in Children

- How the drug is absorbed, how it’s transformed in the liver, how it’s distributed in the body, how it’s excreted by the kidneys. Determines blood level of drug and used to determine dosage
- Kids are not “little adults” and relative mass of liver and kidney tissue is greater than in adults when adjusted for body weight
- Children have greater drug extraction during 1st pass through liver, lower bioavailability, faster metabolism and elimination
Pharmacokinetics
- Due to faster elimination, drug plasma half-life can be shorter in children and steady-state may be reached sooner
- More frequent dosing may be needed to maintain consistent therapeutic levels
- Drug distribution usually reaches adult levels by middle or last adolescence

Pharmacokinetics in Children
- Most important CYP 450 enzymes in pediatric psychopharmacology are CYP3A4 and CYP2D6 which are involved in the metabolism of most psychotropics used in this population
- CYP3A4, CYP2D6 reaches adult activity levels by 2 weeks of life
- Genetic polymorphism has been identified for multiple CYP genes including CYP3A4 and CYP2D6

Pharmacodynamics
- The biochemical and physiological effects of drugs on the body
- Developmental stage influences the response to a number of psychotropics
- Receptor density tends to peak in preschool years and gradually declines toward adult levels in adolescence
- Developmental psychopharmacology remains a research area of high ethical urgency

Meeting with the Child and their Parents
- Time should be spent alone with parent(s) and then with the child or adolescent
- A parent may not wish to discuss family/self history with the child present
- An adolescent may not discuss high risk behaviors in front of their parent

Evaluation Process
- Younger children have less differentiate emotions and limited experience with feelings/emotions
- A young chronically depressed or anxious child may view this as their normal state of being
- The younger the child the less accurate his or her time estimate
- Use concrete markers such as holidays or birthdays or other significant events

Cognitive and Psychological Considerations
- “Will this change who I am, make me a zombie, is it punishment?”
- Adolescent’s reaction to the “sick” role
- Adherence to treatment (across age span)
- Control issues (across the age span)
- Explaining medication to children in terms that they can understand
- Working with young, inexperienced parents who may have a psychiatric
Talking with the Child About Medications

• Communicating with children about medication is challenged by:
  Developmental shifts and their capacity to understand the information
  Their ability to use rationale judgment
  Presence of impaired cognitive functioning and judgment directly related to the psychiatric disorder

Talking with School-Aged Children about Psychiatric Medications

• School-aged (7-11) Piaget's concrete operations
• Children may describe medication effects as:
  “when I'm angry it helps me calm-down....It helps me pay attention....I don't worry too much....It slows my thinking down....It helps me not to cry so much....” or, as “sleepy....tired... more bored.... madder....”

Talking with Adolescents About Medications

• They may worry that their mind will be “controlled”
• Stigma or worried that they'll be labeled by family, friends or school
• They may externalize their problems and resist the notion that they may need a medication
• They may stop medications in order to drink or use recreational drugs

Talking with Parents about Psychiatric Medications

• Acknowledge that parents are experts on their child
• schools or agencies cannot force a parent to medicate their child
• Treat them as partners
• Provide up to date information
• Be up front with pros & cons, risks/benefits
• Medication is just part of the treatment plan

Talking with Parents

• “It' just a phase.”
• Discuss potentially serious risks of untreated mental illness in children & adolescents including: suicidal behavior, poor self-esteem, accidents, poor peer relationships, delayed attainment of developmental milestones and higher risk for substance abuse
• Reassurance of non-addictive nature of most medications should be emphasized

Ethical Considerations

Assent: The agreement obtained from those who are unable to enter a legal contract

– Conversation with a minor that conveys respect for their developing autonomy
– Provides an opportunity to educate the child about their illness and treatment
– May strengthen the therapeutic alliance
– Provides opportunities for them to ask questions
Assent and Consent

- The right of assent to or dissent from treatment belongs to the individual child or adolescent of minor age.
- The practitioner shall, whenever possible, obtain the assent of the minor and must obtain the consent of the legal guardian.
- Assent from the child is recommended by the American Academy of Pediatrics.

Ethics and Developmental Issues

- Most agree that preschoolers cannot give assent due to their egocentric, pre-logical, and magical thinking.
- School children (7-12) may be more likely to engage in treatment and report effects of medication if they are engaged in the process of informed assent.
- Children 12 years or older possess reasoning abilities and abstract thinking similar to adults.

Assent and Dissent

- When a child dissents but the guardian consents to treatment, it may be medically necessary to treat the individual minor without his or her assent.
- Consider the health needs of the child and the psychological ramifications of treating that child against his or her wishes.

Ethical Considerations

- **Beneficence**: A genuine concern for the health, well-being, and happiness of your patients.
  - The obligation to seek out and do good for patients.

Beneficence

- Our primary concerns are the welfare, functioning, and optimal development of children, these apply to individual children as well as to children as a group within society.
- Our judgments and actions should reflect these concerns, prioritizing them over familial or societal pressures.

Nonmaleficence

The obligation not to inflict harm and to avoid all actions that may have a detrimental effect on the child’s optimum development.

- Beneficence and Nonmaleficence requires the clinician to weigh the potential risks (side effects, cost, social stigma, inconvenience, family disapproval) against the benefits.
- You must consider the child’s developmental stage, medical history, family history, and previous response to medications.
Autonomy
• Children are not considered autonomous individuals in regard to health care and cannot give informed consent. Guardians are responsible for the health and welfare of their children.
• The practitioner must assist the patient and guardian in understanding and consenting to treatment.

Consent
• Topics for discussion includes:
  – Available scientific knowledge about the medication
  – FDA indication for use in children or the lack of alternative treatment options
  – Side effects
  – Potential adverse outcomes of non-treatment

Costea et al. 2008

Informed Consent
– Assessment of the patient's understanding of the information that you provided
– Assessment of the capacity of the patient or guardian to make the necessary decision
– Assurance that the patient has the freedom to choose among the medical alternatives without coercion or manipulation

Confidentiality
• The child & adolescent's right to privacy of communication is essential to your practice
• Certainty that what they say is confidential allows the child to reveal their feelings with the assurance that their discussions will not be shared without their consent
• At the outset, children and adolescents should be informed about their confidentiality rights and the limits on

Ethical Considerations
Special Populations
• Children who are developmentally disabled:
  – Requires careful risk/benefit assessment
  – Caregivers may have ulterior motives and want a child medicated for their own convenience
  – Pharmacotherapy may seem “easier” than therapy
  – The more vulnerable the child, the greater importance of a careful risk/benefit assessment

Justice
Distributive justice: fair distribution of health care services as guided by norms, policies or procedures agreed to by society
• Prescription practices are influenced by which medications in which drug classes are reimbursable or available in hospital or third-party payer formularies
• Rate of prescriptions may increase when there’s limited access to effective nonpharmacological treatment
Ethical Considerations
Off-label Prescribing
• Limited data regarding pediatric psychopharmacology
• Risk/benefit assessment may be more complex
• Caregivers must be educated about the rationale and potential risks/benefits of off-label use

Ethical Considerations
Special Populations
• Children in foster care or state ward
  - May have multiple caregivers involved including case workers, group home staff, attorneys, foster parents
  - Parents often lose ability to consent
  - The child’s best interest should guide treatment decisions
  - Do not overlook the child’s involvement and assent

Antipsychotic Drugs in Kids
• For youth 6-18 years-old, use of psychotropic medications was 3 x higher among youth in foster care than your in Medicaid overall
• Use of antipsychotics was 4 x higher among youth in foster care
• > one-half of youth in Medicaid who used antipsychotics had a dx of ADHD and no other dx
• Use of polypharmacy was 4 x higher among youth in foster care
• Rates of use of psychotropic drugs are

Polypharmacy in Children
• Kreider et al. 2014 cross sectional design used national Medicaid data to examine frequency of concurrent second-generation antipsychotics (SGAs) use with other classes of drugs
• Highest users of concurrent SGA were those in foster care and disability Medicaid programs
• Concurrent SGA use with other psychotropic classes increased over time,

General Goals of Psychopharmacology
• Diminish various pathological symptoms
• Augment the response to other therapeutic interventions
• Enhance social and academic functioning
• Enhance maturation and development
• Break cycle of failures, social & academic
• Change maladaptive behavioral patterns including aggressive behaviors

Baseline Assessment
• Physical Examination: height, weight, vital signs, general appearance. Begins upon introduction
• Developmental, medical, and family history
• Collateral information
• Tests may include CBC, liver/kidney, chemistry, hcg, lipids, prolactin, tox screen, EKG, EEG, imaging
• Psychometric tools: Achenbach’s, CBCL
Monitoring and Assessing Response

- Recheck patient after 1-2 weeks of starting treatment and be available for parents questions or concerns
- Monitor for side effects (observations, patient and parent interview, vital signs, height, weight, abdominal girth, and periodic lab tests)
- Re-administer psychometric tools
- Address issues that may contribute to nonadherence to treatment or manipulation of medication administration such as days or times given

Assessing Side Effects

- Important to discuss both physical and behavioral side effects to medications
- Physical: drowsiness, GI side effects, changes in appetite, headache, dizziness, vital signs, movement disorder (AIMS)
- Behavioral: agitation, nervousness, restlessness, insomnia, disinhibition, grandiosity, irritability

Psychotic Disorders in Childhood

Epidemiology

Psychotic symptom prevalence: 17% among children age 9-12 and 7.5% among adolescents age 13-18
Childhood Schizophrenia: Same DSM-V criteria same as for adults but harder to diagnose
Age of onset prior to age 12 or puberty is very rare, less than 1 case per 10,000 population
Rate of new cases significantly increases during late adolescents with prevalence of 1%
Insidious onset; Gender ratio across

Childhood-Onset Schizophrenia

Etiology

No definite single etiology of schizophrenia identified and may be multifactorial
1st degree relatives of children with schizophrenia have higher prevalence rate of schizophrenia
Possible link to CNS infections early in life
Neuroimaging: Childhood-onset schizophrenia show cortical gray matter and cortical volume loss at 1% to 3% per year during first 5 years
Environmental: prenatal stress, increased cortisol levels, underdeveloped hypothalamus

Differential Diagnosis

- PTSD or Acute Stress Disorder, Bipolar Disorder, ADHD, ASD
- Stress and anxiety are most common cause of hallucinations in preschool children. Typically will endorse auditory or visual hallucinations without negative symptoms
- Cultural context is important when assessing symptom

HPI

- Assess course of behavioral changes, academic and social decline, isolative behaviors, diminished self-care, development of odd beliefs or suspicions, loss of interest in activities.
- Parents may have observed child talking self, coming to parents room more frequently at night
- Increased levels of inattention or disruptive behavior
- Hallucinations vs. Imaginary friend, ask “do you want these to go away?”
Antipsychotic Use in Children

- Children have a greater density of D1-D2 receptors which suggest a greater sensitivity to the beneficial and adverse effects of antipsychotics
- Start low: 50% of adult starting dose
- Evidence supports the early recognition and treatment of psychotic symptoms in childhood to avert progression to more severe forms of psychotic illnesses
- Decision to treat is influenced by degree of symptoms, global functioning and family history

Neuroprotection and Neurogenesis

- Schizophrenia, bipolar disorder and recurrent major depression demonstrate atrophic brain changes
- 2nd gen antipsychotics are known to have neuroprotective properties, promotion of new nerve cell development
- Neuroprotection should be considered in the risk/benefit analysis when considering pharmacotherapy

Atypical Antipsychotic Medications FDA Approved for Children/Adolescents

- Olanzapine (Zyprexa) Schizophrenia for ages 13 and older, Acute/mixed mania for ages 13 and older
- Risperidone (Risperdal) Schizophrenia for ages 13 and older, acute/mixed mania ages 10 and older, autism related irritability for ages 5-16
- Quetiapine (Seroquel) Schizophrenia 10-17, acute mania ages 10-17,
- Aripiprazole (Abilify) Schizophrenia for ages 13 and older, acute/mixed mania ages 10 and older, Autism related

Atypical Antipsychotics

- Clozapine: (Clozaril) No FDA approval for use in children
- Ziprasidone (Geodon) No FDA approval for use in children
- Lurasidone (Latuda) No FDA approval for use in children
- Iloperidone (Fanapt) No FDA approval for use in children

Atypical Antipsychotics Mechanism of Action

- May have faster rate of dissociation from D2 receptors
- Higher affinity for serotonin receptors, specifically the 5-HT2A family
- The simultaneous blocking of D2 and S2 receptors is thought to account for the increased efficacy in improving negative symptoms of schizophrenia
- Consequently, these drugs have a lower incidence of EPS compared to 1st gen antipsychotics

Atypical Antipsychotic Drugs and Side Effect

- Drowsiness, dizziness
- GI: dry mouth, constipation
- CV: hypotension, tachycardia
- Hyperglycemia, Weight-gain, Metabolic Syndrome
- Hyperprolactinemia
- QTc prolongation
- NMS
- EPS
Acute Dystonic Reaction: Muscular hypertonicity and tonic contractions neck, mouth, tongue, eyes
- Max risk hours to 5 days of starting therapy or dose increases
- Untreated may last from few minutes to hours
- Painful and frightening
- Benadryl 25-50mg PO or IM, Cogentin 1-2mg

Parkinsonism: Tremor, cogwheel rigidity, drooling
- Max risk 5 to 30 days after starting therapy
- Responds to benztropine (Cogentin) 1-2mg PO bid

Akathisia: Motor restlessness and intense need for movement
- Beta-blocker such as propranolol or benzodiazepines
- Consider lowering dose of antipsychotic

Tardive Dyskinesia: Late onset movement disorder associated with dopamine blocking agent
- Remove offending agent
- Conduct AIMS every 3 months and document

Metabolic Syndrome
- Weight gain, dyslipidemia, insulin resistance, hyperglycemia
- Weight gain typically occurs within first 4-12 weeks
- H1 and 5HT2C blocking effects of antipsychotic may interfere with leptin-mediated appetite suppression
- SGA-induced Type 2 Diabetes likely multifactorial
- Lipid abnormalities are largely r/t weight gain

Risperidone (Risperdal)
- Schizophrenia age 13> start 0.5mg daily with increases of 0.5mg-1.0mg in intervals no less than 24 hours as tolerated to recommended dose of 3mg/day
- Autism ages 5-16 start 0.25mg/day for patients <20kg and 0.5mg/day for >20kg with minimum 4 days before dose increase, with max dose 2.5mg
- Bipolar >9 years age 0.5mg daily with increases 0.5 to 1mg occurring no less 24

Olanzapine (Zyprexa)
- Schizophrenia: age 13-17 start 2.5-5mg/day with dose increments 2.5-5mg over several days and target dose of 10mg/day
- Acute or mixed mania ages 13-17 start 2.5-5mg day with dose range 2.5-20mg/day
- Tablets 2.5, 5, 7.5, 10, 15, and 20mg
- Zydis 5, 10, 15 and 20mg tabs
- IM 10mg vial

Quetiapine (Seroquel)
- Schizophrenia adolescents age 13-17 dosing schedule:
  - Day 1: 25mg twice daily
  - Day 2: twice daily dosing totaling 100mg
  - Day 3: twice daily dosing totaling 200mg
  - Day 4: twice daily dosing totaling 300mg
  - Day 5: twice daily dosing totaling 400mg
- Flexible dose range 400 to 800mg daily
- Acute Mania 10-17 years: as above with flexible dose range 400-600mg a day
### Aripiprazole (Abilify)
- **Schizophrenia** ages 13-17:
  - Initial dose of 2mg daily then titrate to 5mg after at least two days and then to target dose of 10mg daily after two additional days
- **Autism** ages 6-17:
  - 2mg/day with increase to 5mg/day, with subsequent increases to 10 or 15mg/day.
  - Dose adjustments at intervals no less than one week
- **Acute Mania** 10-17 years
  - Initial dose of 2mg daily then titrate to 5mg after at least two days and then to target dose of 10mg daily after two additional days
Tablets: 2, 5, 10, 15, 20 and 30mg
Oral solution: 1mg/ml and Injection 7.5mg/ml for IM

### Asenapine (Saphris)
- **Manic or mixed episodes** associated with bipolar I disorder: ages 10–17 years.
- FDA’s approval was based on the results of a 3-week study involving 403 pediatric patients, including 302 who received Asenapine twice a day in 2.5-mg, 5-mg, or 10-mg doses

### Risperidone & Aripiprazole
- Risperidone has been the most thoroughly studied antipsychotic for treating severe irritability associated with ASD
- Two large RPC studies lead to FDA approval in 2006 for treating severe irritability associated with ASD
- 2009 aripiprazole became the second agent approved by the FDA for managing irritability in children 6-17 years-old with autism

### Case Examples
- **Jacob**: 19-year-old with autistic spectrum disorder and comorbid bipolar disorder
- **Nathaniel**: 12-year-old autistic spectrum disorder and comorbid psychosis
- **James**: 17-year-old ASD and schizophrenia
- **Jose**: 5-year-old with global developmental delay and hyperactivity

Review of literature regarding Autistic Spectrum Disorder (ASD) and comorbid psychiatric illnesses
Ethical considerations: Vulnerable population

### Autistic Spectrum Disorder (ASD)
- Autistic spectrum disorder (ASD) occurs in all racial, ethnic, and socioeconomic groups
- Five times more common among boys than among girls
- CDC estimates that about 1 in 68 children has been identified ASD
- Broader definition of ASD and better efforts in diagnosis
- A true increase in the number of people with an ASD cannot be ruled out.

### Autistic Spectrum Disorder and Comorbid Psychiatric Illnesses
- Recognition and treatment of psychiatric illness in those with developmental disability is often overlooked
- Psychiatric symptoms may be falsely attributed to the underlying developmental disorder and simply dismissed
- This may lead to incorrect choice of treatment or no treatment at all
- Symptoms of ASD and schizophrenia
Case Study
Jacob
- 19-year-old non-verbal male diagnosed with Autistic Spectrum Disorder (ASD)
- Removed from group home due to severe aggression and self-injurious behaviors
- Treated in the community by a psychiatric APRN
- Has care attendants through DMH
- Multiple past mediation trials and adverse effects

Case Study
Jacob
- Mother reports a marked change in behavior over past 3 months. Episodic behaviors...severe insomnia, severe aggression, self-injurious behavior, increase in self-stimulatory behaviors, increase "OCD" traits such as repeatedly spitting on mattress and rubbing it with his hands and taking his clothes on and off and other disruptive behaviors

Jacob
- Past Medication Trials:
  - Abilify caused nausea and vomiting
  - Risperidone constipation and nausea
  - Trazodone increased "OCD and pica"
  - SSRI's increased agitation and insomnia (activation)
  - Perphenazine (Trilafon) increased aggression & “OCD”
  - Clonidine increased aggression and “OCD”

Jacob
- Home medications:
  - Naltrexone 50mg daily
  - Clorazepate 3.75 q am, 7.5mg qhs
  - Claritin 10mg daily
  - Multivitamin

Hospital medications: Haldol 2mg IM every 4 hours PRN, Lorazepam 2mg every 6 hours PRN

Jacob in ED for 3 days
- Exam: restless, agitated jumping on & off stretcher. Throwing pillows & other objects. Loud guttural noises and engaging in self-stimulatory behaviors,
- No involuntary or purposeless movements, tics or tremors and no pain behavior
- Family History: Father with Asperger’s, Half-brother with autism, maternal uncle with schizophrenia, maternal aunt w bipolar

Jacob
- Admitted to a medical unit awaiting appropriate placement
- Began to taper lorazepam and continue clorazepate
- Added quetiapine 25mg twice daily
- Daily follow-up visits with Jacob and daily meetings with his mother
- Multiple security calls placed each day due to violent behavior
Jacob

**Day 5:** No change in aggression and Mother is reporting a significant “OCD” symptoms
Multiple calls made to security by staff
Still not sleeping
Continuing to slowly taper lorazepam
Increased quetiapine to 50mg bid

**Day 7:** Continued unprovoked aggression,
Course tremor bilateral upper extremities but no cogwheeling or rigidity noted on exam
Continue lorazepam taper and D/C the PRN haloperidol

**Day 8:** No longer having tremors
Increased quetiapine 50mg bid and 100mg at bedtime and 25mg bid PRN agitation

**Day 10:** Severe aggression continues. Grabbed and bit his mother, pacing in room and attempting to leave his room and taking his clothes off
Multiple calls to security last evening/night
Long discussion with Mother including another review of his medication history. Here, Mother discloses her history of bipolar disorder. ????
Run to office to review the literature

Literature on ASD and Comorbid Bipolar Disorder

- Biederman et al. 2013, looked at the comorbid occurrence of bipolar disorder and ASD
- Hypothesized that in youth with bipolar, the clinical correlates of bipolar disorder will be comparable irrespective of the comorbidity with ASD
- Results: 30% (47/155) of bipolar I probands met criteria for ASD
- Clinically significant minority of youth with

Literature

- Similar clinical features of mania was observed in youth with bipolar I disorder irrespective of the comorbidity with ASD.
- Mania was characterized by predominantly irritable mood, long duration and highly episodic course with mixed symptoms and severe impairment
- ASD youth with bipolar I experienced mania at an earlier age and more often with grandiosity

- Gotham et al. looked at data collected from 165 participants (n=109 with ASD; n=56 with non-spectrum developmental delay)
- Both anxiety and depressive symptoms were greater in ASD participant
- Findings supported previous claims that individuals with ASD are at particular risk for affective and anxiety-specific problems
Literature

- Howell et al. 2011 reported a growing body of evidence to suggest that a significant percentage of those with ASD have comorbid psychiatric disorders that may cause significant clinical impairment.
- Several studies suggest that ASD may share common vulnerability genes with bipolar disorder.
- Repeated studies show the possibility of increased sensitivity to medication adverse effects as well as decreased efficacy in those with ASD.

Munesue et al. 2008

- For most medications, limited data are available regarding efficacy in ASD populations.
- Currently only 2 medications—risperidone and aripiprazole—have U.S. FDA indication for use in autism.
- Metabolic side effects are common and pose a risk to overall health, generally limiting their use to those with the most severe symptoms.

Politte et al. 2014

Jacob

- **Day 11**: Added Depakote for mood-stabilization.
- Weight: 62 kg; 20mg/kg; 1200mg/daily.
- We started him on 1000mg/daily.
- Labs on admission including LFT’s, Chem, CBC with diff were all WNL.
- Getting serum levels will be tough.

Day 15: Now with less aggression but still having periods of agitation.
- Sleep remains poor.
- Quetiapine now at 50mg bid and 100mg qhs and 25mg bid PRN agitation.
- Day 16: Episodes of agitation but no aggression.
- Quetiapine 25mg helped with agitation.
- Slept 6 hours last night.

Day 20: Sleeping through the night with no aggression or agitation.
- Depakote now up to 1250mg daily with blood level of 75.
- Quetiapine 50mg bid 100mg qhs and 25mg bid PRN agitation or sleep.
- QTc 425.
- Appears to be tolerating his medication regimen well.

Day 31: Discharged to home with his mother.
- Discharge medications: Depakote 1250mg daily, Seroquel 50mg bid and 150mg qhs, clorazepate 3.75mg qd and 7.5mg qhs.

Jacob

- Day 11: Added Depakote for mood-stabilization.
- Weight: 62 kg; 20mg/kg; 1200mg/daily.
- We started him on 1000mg/daily.
- Labs on admission including LFT’s, Chem, CBC with diff were all WNL.
- Getting serum levels will be tough.

Day 15: Now with less aggression but still having periods of agitation.
- Sleep remains poor.
- Quetiapine now at 50mg bid and 100mg qhs and 25mg bid PRN agitation.
- Day 16: Episodes of agitation but no aggression.
- Quetiapine 25mg helped with agitation.
- Slept 6 hours last night.

Day 20: Sleeping through the night with no aggression or agitation.
- Depakote now up to 1250mg daily with blood level of 75.
- Quetiapine 50mg bid 100mg qhs and 25mg bid PRN agitation or sleep.
- QTc 425.
- Appears to be tolerating his medication regimen well.

Day 31: Discharged to home with his mother.
- Discharge medications: Depakote 1250mg daily, Seroquel 50mg bid and 150mg qhs, clorazepate 3.75mg qd and 7.5mg qhs.
Nathaniel

- 14-year-old male with autistic spectrum disorder (ASD), ADHD and developmental delay
- Home meds: Wellbutrin SR 100mg bid and clonidine 0.2mg qhs
- Brought to ED after he wrapped a belt around his neck and tied it to window for 20-30 minutes
- 3 weeks prior he overdosed on Benadryl and one month prior to that he wrapped cord around his neck

Nathaniel

- Reports hearing 2 different male voices
- Differentiates this from his own thoughts
- Voices are command and have been telling him to kill himself, other times state “don’t do it.”
- Fairly new onset of AH
- Call to his therapist who reports a recent (3+ months) fascination with zombies and mentioned wanting to die and come back as a zombie

Nathaniel

- No aggressive behavior toward others
- Behaviors are a clear change from baseline
- He shows an inability to distinguish fantasy from reality that is a clear change from baseline
- Parents could not identify any particular stressor or event leading to behaviors

Literature on ASD and Comorbid Psychotic Disorders

- Sullivan et al. 2013 looked at whether ASD and traits predict psychotic experiences (PE) in early adolescents
- Prospective cohort study n=5,359 analyzing data reported on those who had autistic traits, diagnosis of ASD and PE at age 12 years
- Results showed that a diagnosis of ASD increased the odds of of psychotic experiences almost 3-fold

Autistic Spectrum Disorder and Comorbid Psychiatric Illnesses

- Early small studies found an increase incidence of autism in childhood-onset schizophrenia (COS)
- An NIMH longitudinal study of COS confirmed these findings….25% of the 75 children diagnosed with COS had a lifetime diagnosis of ASD
- There is evidence of for neurodevelopmental connections between the spectra of ASD and psychotic illnesses

Literature on ASD and Comorbid Psychotic Disorders

- Wachtel & Shorter, 2013 concluded that there may be a “vulnerability punch” giving those with ASD at baseline with higher risk of comorbid psychiatric illness including psychosis
- Another review found “schizophrenic-type illness” in 10% of patients with ASD, leading to the proposal that ASD might be a “vulnerability factor” for the development of psychosis
Nathaniel
- Discussion with his outpatient psychiatrist
- Start aripiprazole (Abilify) 5mg daily
- Continued home medications
- Admitted to inpatient psychiatric hospital for further evaluation and treatment

James
- 17-year-old Haitian male diagnosed with “high functioning autism”
- Came to my office with his mother and older sister who voiced concern for a change in behavior including:
  - Withdrawing from family and friends
  - Loss of interest in activities & academic decline
  - Family reports that he is not interacting and sits in his room with shades drawn
  - “He’s not himself”

James
- James stood outside my office in a fixed position
- I eventually coaxed him to enter my office
- He was wearing a winter coat in May
- He sat facing a wall and was noticeably responding to internal stimuli
- His speech was sparse, perseverative
- Thought processing was blocked
- Denied SI or HI
- This was a marked change in baseline presentation

James
- Medical work-up and imaging was WNL
- Long discussion with family and James regarding diagnosis and treatment
- Family was very resistant to suggestions for inpatient psychiatric hospitalization
- Mother minimized James’ illness but agreed to treatment
- Started Risperidone 0.5mg twice daily and to return in one week

James
- Referred him for therapy with a colleague who speaks Haitian creole
- Over the course of weeks, Risperidone was titrated to 1mg bid
- James showed some improvement with diminished positive symptoms but continued to exhibit negative symptoms
- Risperidone was increased to 1.5mg twice daily
- James continued to show modest improvement but continued to experience a decline in his overall level of function

Jose
- 5-year-old male with global developmental delay who was diagnosed with autism while in Puerto Rico
- Born at 29 weeks weighing 2lbs
- Recent EEG, MRI normal
- No h/o seizures, no regression or loss of skills
- No expressive language
- Mother brought him into my office for evaluation and treatment of “hyperactivity” and self-injury with
<table>
<thead>
<tr>
<th>Jose Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Highly irritable, arching spine and screaming as his mother is holding him</td>
</tr>
<tr>
<td>• I asked that she let him stand at which point he ran head-first into a wall, turned around and ran head-first into the opposite wall</td>
</tr>
<tr>
<td>• He then threw himself onto the floor and was banging his head and screaming</td>
</tr>
<tr>
<td>• Mother appeared exhausted but deeply committed to caring for her child</td>
</tr>
<tr>
<td>• Started Risperidone Solution 0.25mg daily and return in 2 weeks, sooner PRN</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Jose’s Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Risperidone titrated to 0.25mg bid but not tolerated due to drooling</td>
</tr>
<tr>
<td>• Dose increased to 0.125mg in the am and 0.25mg in pm</td>
</tr>
<tr>
<td>• One-month later self-injury and irritability has clearly diminished</td>
</tr>
<tr>
<td>• “Hyperactivity” has decreased by “60%”</td>
</tr>
<tr>
<td>• Had initial experienced drooling when starting risperidone and that has ceased</td>
</tr>
<tr>
<td>• Conduct in school is much better and he is sleeping well</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I Did Mention Art</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Anna Freud pinpoints as a key ingredient of healing: empathy and compassion</td>
</tr>
<tr>
<td>• Maimonides proclaimed: “The physician should not treat the disease but the patient who is suffering from it.”</td>
</tr>
<tr>
<td>• Psychiatric nurses know that empathy is gained through an understanding of the individual you’re treating. An understanding, not just of their neurobiology, but of their culture, history, literature, “heroes,” music, creative influences and what moves them?</td>
</tr>
</tbody>
</table>