Psychopharmacology in Autism
FYI, It’s not likely the autism you’re treating.

Growing problem?
› Audience members with personal experience with autism or suspicion of it?
› My family.

Core symptoms v co-morbidity
› Social impairment
› Language impairment
› Obsessive interests and Repetitive behaviors
  • Any mixture of these can mimic symptoms of other disorders like ADHD, OCD, other disruptive behavior disorders.

Social impairment, low awareness, indifference can appear to be inattention.
Obsessive interests and repetitive behaviors can seem very like the obsessive and compulsive symptoms of OCD.
Confrontation of inflexibility or change in routine can bring on a lot of distress and look like the anxiety we see in other d/o’s but is it?

Case #1
› Jake is a 10 y/o boy with fairly longstanding and well established ASD diagnosis. Social interactions consistent with this but he is generally bright, happy, friendly, engaging (on his terms and topics of his interest). But he cannot sit still or focus on any one thing for as long as a minute it seems. In my office he opens and closes, locks and unlocks doors, turns white noise machine and computer monitors on and off dozens of times in the 20 to 30 minute appt.

› Responses to medications targeting attention, anxiety, obsessiveness and repetitive behaviors are much less predictable.

› Unfortunately, even though there are recognized differences in response there isn’t great evidence guiding us to Autism specific treatments for these symptoms.
Case #1 cont.

- Obsessions include elevators, garage doors, copy machines (will mimic the sound of the one at school almost endlessly). Can occupy himself sometimes for hours watching You Tube of these things over and over.

- He lives with his grandparents who are his guardians (parents incapable) and who are amazingly patient and tolerant with him and clearly care for him and in many ways enjoy him. At home his behavior is tolerated with mostly good humor to annoyance.

- In areas of interest he has an amazing memory and endless curiosity but at school they cannot get him to focus and settle long enough to accomplish much traditional learning at all.

- After several failed or poorly tolerated medication trials he had Genesight testing which was discouraging for benefit from stimulants or alpha adrenergics. Atomoxetine metabolized normally.

- Trials have included Adderall, guanfacine, aripiprazole, risperidone, atomoxetine and now Metadate (ongoing). Actually has tolerated most things but no appreciable response to anything.

- It can be normal even for children without autism to have scattered developmental abilities.

- It can make establishing expectations and judging impairment incredibly difficult.

- A child with autism (or really any developmental disability) and normal to even extraordinary abilities in certain areas (e.g. memory) too often has expectations set too high so deficit or disability is seen relative to an unrealistic developmental age/level when an appropriate assessment of this would suggest a milder or even no delay.

- Gastrointestinal d/o, sensory integration dysfunction, seizures, lowered IQ and learning disabilities, Fragile X and numerous other genetic differences, some vitamin deficiencies, sleep disorders, to name a few of the medical diagnoses.

- ADHD, Anxiety, OCD, Tourette, Depression, Gender dysphoria, Bipolar d/o and/or Disruptive Mood Dysregulation disorder(?).
Commonly co-morbid medication targets.

- ADHD, anxiety disorders, depression.
- Agitation, anger, mood lability, aggression. This warrants extended discussion so will take this last.

Strength of recommendation classes.

- Class I: Recommended
- Class Ila: Recommended in most cases
  - IIB: Recommended in some cases
- Class III: Not recommended

Strength of Evidence Categories

- Category A: Meta analyses of randomized controlled trials or multiple well done clinical trials.
- Category B: Meta analyses with conflicting conclusions, randomized controlled trials with small numbers.
- Category C: Expert opinion, consensus, case reports or case series.

Caveat: Many medications have been studied and marketed for conditions based almost as much on finding a niche/competitive foothold as they have for overall potential benefit (example SSRI’s).

Anxiety and Depression

Fluoxetine: For OCD ages 7 and older, major depression ages 8 and older.
  - Strength of recommendation class IIB
  - Strength of evidence category B
  - (Available in tablets, capsules and liquid)

Sertraline: OCD ages 6 and up
  - Strength of recommendation class IIB
  - Strength of evidence category B
  - (tab and liquid)

Citalopram: All uses off label for children

Escitalopram: Major dep. d/o 12 and older
  - Strength of recommendation class IIB
  - Strength of evidence category B

Venlafaxine: All pediatric uses off label

Desvenlafaxine: All pediatric uses off label

Duloxetine: Generalized anxiety d/o age 7 and above
  - Strength of recommendation class IIA
  - Strength of evidence category B

Bupropion: All pediatric uses off label
Medications cont.

**ADHD**
Methylphenidate: Ages 6 and up
Strength of recommendation class IIa
Strength of evidence category B
(multiple names, durations of action and delivery mechanisms)

**ADHD**
Adderall and similar (dextedrine, Vyvanse) Age 3+
for ADHD and Age 6+ for Narcolepsy
SOR IIb, SOE Cat. B
Atomoxetine (Strattera) 6+
SOR IIb, SOE Cat. B

Medications cont.

**ADHD**
Clonidine (Catapres, Kapvay) and guanfacine
(Tenex, Intuniv) Age 6+.
Both are SOR IIb and SOE Cat. B
Mood lability, agitation, Tourette, psychosis
Antipsychotics (risperidone 5+, aripiprazole 6+, quetiapine 10+, olanzapine 13+). Risperidone for ASD irritability SOR IIb, SOE Cat. A. All the rest IIb and Cat. B at best.

ADHD cont.

› I will not spend time on specific dosing recommendations beyond your questions.

› One major caveat is that in patients with developmental delays in general I would say that response is much less predictable and side effects seem more likely and many times more difficult to manage (e.g. appetite or sleep effects).

› For that reason it can make sense to start lower though ultimate doses maybe typical.

Anxiety disorders

› I am going to defy DSM-V and combine discussion of OCD with GAD and separate those from phobias, panic and PTSD.

› OCD and GAD can be very tricky to diagnose due to the symptom overlap between ASD and those. The rigidity and adherence to routine along with the perseveration, obsessive interests and repetitive behaviors could all potentially support ASD or OCD or GAD.
Anxiety cont.

- Panic and specific phobias maybe not much different than general population? Couldn’t find much data and my clinical experience equivocal.

- PTSD, also didn’t find a lot of data on the relative incidence of this but reduced reporting ability and some of social symptoms maybe increase potential for this being present but unrecognized?

Anxiety cont.

- SSRI’s, SNRI’s, potentially alpha adrenergics, low dose atypicals (likely more appropriate if other targets present, e.g. agitation/agression). PRN’s often problematic but maybe antihistamines, atypical (olanzapine, risperidone), cautious trial of benzo. For the latter couple suggest consultation.

- With SSRI and SNRI would follow the start low, go slow approach at almost any age.

Depression

- Thought to be more likely to present in somewhat higher functioning patients and in adolescence. Among the symptoms that can be harder to assess are the social withdrawal and anhedonia. This pattern of onset maybe due to growing self awareness of difference and difficulties with social interactions/relationships.

Agitation/aggression

- Taken in isolation this is a very non-specific symptom cluster. Many potential causes including the co-morbidities already covered. There are some ASD typical triggers or patterns though (e.g. disruption of routines or frustration of pursuit of fixations).

- Not necessarily exclusive to ASD among the developmental disability category either.

- If suspicion that one of the other co-morbidities may be underlying (including medical) target that first.

Agitation/aggression cont.

- Medications with specific designation/approval for this.
- Atypical antipsychotics risperidone and aripiprazole.
- Medical cannabis – Autistic Spectrum d/o is a certifying diagnosis for use this in Minnesota since July 18’.

Agitation/aggression

- Risperidone, most studied and with strongest recommendation, Aripiprazole also indicated but….

- Length of studies not great, dosing recommendations uncertain, side effects not benign (metabolic and weight changes, potential for EPSE e.g. dystonia, dyskinesia).

- Longer term clinical response vs. short term sedation. Risk of chasing a ghost?
Agitation/aggression cont.

- Not clearly indicated or recommended but sometimes tried
  - Mood stabilizers
  - Alpha adrenergics or stimulants without an ADHD diagnosis
  - Analgesics without a clear pain source
  - Beta blocker
  - Benzodiazepine with unclear anxiety diagnosis
  - Trazodone
  - Medical cannabis (ASD a qualifying diagnosis in Mn but testing data pretty limited)

Medical cannabis

- Qualifying Conditions:
  - Cancer associated with severe/chronic pain, nausea or severe vomiting, or cachexia or severe wasting
  - Glaucoma
  - HIV/AIDS
  - Tourette Syndrome
  - Amyotrophic Lateral Sclerosis (ALS)
  - Seizures, including those characteristic of Epilepsy
  - Severe and persistent muscle spasms, including those characteristic of Multiple Sclerosis.
  - Inflammatory bowel disease, including Crohn’s disease
  - Terminal illness, with a probable life expectancy of less than one year*
  - Intractable pain
  - Post-Traumatic Stress Disorder
  - Autism
  - Obstructive Sleep Apnea

Medical cannabis cont.

- Risks for use by children, adolescents, and young adults
  - Use of medical cannabis in children, adolescents, and young adults should be approached with special caution. There is evidence that recreational use of marijuana during the active period of brain development through young adulthood can lead to cognitive impairment. There is also an association between recreational use of marijuana in this population and onset of psychotic mental illness such as schizophrenia. Much remains unknown about who is at risk and whether these risks with recreational marijuana use apply to use of products with high levels of THC – to children, adolescents, and young adults with serious disease and incapacitation symptoms despite all conventional medical treatments.

Cannabis for ASD

Table 1: Count (%) of Active Patients by Condition* as of March 31, 2019

<table>
<thead>
<tr>
<th>Qualifying Condition</th>
<th>Patients Certified: N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaucoma</td>
<td>110 (1%)</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>92 (1%)</td>
</tr>
<tr>
<td>Tourette Syndrome</td>
<td>112 (1%)</td>
</tr>
<tr>
<td>ALS</td>
<td>37 (1%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>1,831 (12%)</td>
</tr>
<tr>
<td>Severe and Persistent Muscle Spasms</td>
<td>1,831 (12%)</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease, Including Crohn's Disease</td>
<td>474 (3%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1,139 (9%)</td>
</tr>
<tr>
<td>Terminal Illness</td>
<td>1,518 (11%)</td>
</tr>
<tr>
<td>Intractable Pain</td>
<td>9,974 (64%)</td>
</tr>
<tr>
<td>Pain: Traumatic Stress Disorder</td>
<td>2,624 (17%)</td>
</tr>
<tr>
<td>Autism Spectrum Disorder</td>
<td>481 (3%)</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>669 (5%)</td>
</tr>
<tr>
<td>Total</td>
<td>15,687</td>
</tr>
</tbody>
</table>

Medical cannabis for ASD

- Age (y) 0-4, 5-17, 18-24, 25-35, 36-49, 50-64, 65+
- Mean Age (53)

- Autism Spectrum Disorder -19(4%), 287(59%), 102(21%), 48(10%), 20(4%), 5(1%), 2(1%), 16.3 (10.1)

- How might it work?
  - Who can certify? MD/DO, PA, NP that sign up on State site [https://www.health.state.mn.us/people/cannabis/index.html].
  - What happens after? Can be some up front and yearly cost for patient. Connected with dispensary and they provide medical cannabis product. Typically CBD>>THC to start with. Feedback to certifying provider?
### Case #2
- 13 y/o male inpatient with a longstanding diagnosis of ASD with severe limitations in communication, admitted due to suspected GI pain and accompanying severe agitation and self injury (head banging and self hitting and biting to the point of injury). Psychiatry consulted and at the point of first visit he was in PICU and under Precedex (dexmedetomidine) sedation. Medical team completed their w/u and treatment, then proceeded with rapid sedation withdrawal and discharge home.

### Case #2 cont.
- In home environment his agitation recurred just as severely and resulted in re-hospitalization. Risperidone and analgesics provided some improvement but still clearly struggled with episodic agitation and SIB and was not returned to baseline mood or functioning.
- Based upon a seizure d/o diagnosis he was certified for a medical cannabis trial and seemed to have a fairly prompt and very positive response.

### Case #3
- 15 y/o with severe ASD (needing very substantial support). Lives with grandparents who struggle to manage his behavior and this struggle is increasing with time and changes in everyone’s ages and his size. Fixation on vacuums and after a period of relative extinction of this was inadvertently re-triggered and now grandparents have felt compelled to accommodate this in an attempt to avoid agitation and aggression. Treatment with several medications tried with some providing initial response which was not maintained.
- What to do?

### Take home messages
- Lack of effective treatments for core ASD symptoms.
- Core symptoms can be very hard to differentiate from those caused by other conditions.
- Treatment responses can be transient, elusive and lead to escalating treatments (dosages and numbers of medications).
- Environmental and behavioral treatments and supports are often critical.

### Take home cont.
- There are clearly roles for medication trials if symptom presence, severity and impairment are present (again largely if not fully targeting co-morbidities).
- Stay humble when predicting response. Go low and slow and be diligent for usual and unusual SE’s.
- Be diligent in eliminating medications without persisting benefit.
- While there is a lot not known about medical cannabis there are situations where certification and trial (with discussion of potential ill effects) is likely very appropriate. But try and be clear what you are treating and tracking response.

### Questions/further discussion