Antipsychotic Update:
Considering Adverse Effects,
Monitoring Parameters, Drug
Interactions, Newer Medications,
& Newer Formulations to Better Manage
Unmet Clinical Needs

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October 11, 2019
Sarah E. Grady has nothing to disclose.
Objectives

- Demonstrate knowledge of mechanisms of action of second generation antipsychotics (SGAs) in order to accurately predict potential adverse effects of individual agents
- Develop a monitoring system to evaluate the tolerance of pharmacotherapy options for treatment
- Recognize the advantages and disadvantages of the newer partial dopamine agonists
- Compare and contrast the newer long-acting injections
- Discuss promising compounds being studied for management of negative symptoms
Demonstrate knowledge of mechanisms of action of second generation antipsychotics (SGAs) in order to accurately predict potential adverse effects of individual agents
Dopamine Tracts

- Nigrostriatal
  - Function: Movement
- Mesolimbic
  - Function: Arousal, memory, stimulus processing
- Mesocortical
  - Function: Cognition, communication, social function
- Tubero-infundibular
  - Function: Regulates prolactin release

First Generation Antipsychotics (FGA) Receptor Binding Profile - $K_I$ Values

<table>
<thead>
<tr>
<th></th>
<th>$D_2$</th>
<th>$5HT_{2A}$</th>
<th>$Alpha_1$</th>
<th>$H_1$</th>
<th>$M_1$</th>
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</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>3.6</td>
<td>3.6</td>
<td>0.3</td>
<td>3.1</td>
<td>32</td>
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<tr>
<td>Loxapine</td>
<td>11</td>
<td>4.4</td>
<td>42</td>
<td>4.9</td>
<td>120</td>
</tr>
<tr>
<td>Perphenazine</td>
<td>0.8</td>
<td>5.6</td>
<td>10</td>
<td>8.0</td>
<td>1500</td>
</tr>
<tr>
<td>Thiothixene</td>
<td>0.7</td>
<td>50</td>
<td>12</td>
<td>8</td>
<td>&gt;10,000</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>0.8</td>
<td>3.2</td>
<td>6.5</td>
<td>14</td>
<td>1100</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>1.2</td>
<td>57</td>
<td>12</td>
<td>1700</td>
<td>&gt;10,000</td>
</tr>
</tbody>
</table>
Potential Advantage of the SGAs over FGAs

- Lower risk of tremor, stiffness, restlessness, & dyskinesia
  - Rates vary widely amongst the individual SGAs
Pharmacologic Properties of SGAs: the “pines” - $K_I$ Values

<table>
<thead>
<tr>
<th></th>
<th>$D_2$</th>
<th>$5HT_{2A}$</th>
<th>$\text{Alpha}_1$</th>
<th>$H_1$</th>
<th>$M_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>160</td>
<td>5.4</td>
<td>1.6</td>
<td>1.1</td>
<td>6.2</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>31</td>
<td>3.7</td>
<td>110</td>
<td>2.2</td>
<td>2.5</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>380</td>
<td>640</td>
<td>22</td>
<td>6.9</td>
<td>37</td>
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<tr>
<td>Asenapine</td>
<td>1.4</td>
<td>0.1</td>
<td>1.2</td>
<td>1.0</td>
<td>&gt;10,000</td>
</tr>
</tbody>
</table>
Potential “Pine” Adverse Effects Predicated on Receptor Binding Profile

- Orthostatic hypotension
- Sedation
- Weight gain
- Anticholinergic (not Asenapine)
- Low risk - EPS

Pharmacologic Properties of SGAs: the “dones” - $K_I$ Values

<table>
<thead>
<tr>
<th></th>
<th>$D_2$</th>
<th>$5HT_{2A}$</th>
<th>$\text{Alpha}_1$</th>
<th>$H_1$</th>
<th>$M_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>3.2</td>
<td>0.2</td>
<td>5.0</td>
<td>20</td>
<td>$&gt;10,000$</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>4.2</td>
<td>0.7</td>
<td>2.5</td>
<td>19</td>
<td>$&gt;10,000$</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>6.8</td>
<td>0.6</td>
<td>18</td>
<td>63</td>
<td>$&gt;10,000$</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>1.0</td>
<td>0.5</td>
<td>48</td>
<td>$&gt;1,000$</td>
<td>$&gt;1,000$</td>
</tr>
<tr>
<td>Iloperidone</td>
<td>6.3</td>
<td>5.6</td>
<td>0.3</td>
<td>12</td>
<td>4900</td>
</tr>
</tbody>
</table>
Potential “Done” Adverse Effects Predicated on Receptor Binding Profile

- EPS
- Prolactin elevation
- Orthostatic hypotension
- Sedation
- Weight gain
EPS Trends Among SGAs

Risperidone, Paliperidone

Olanzapine, Asenapine, Ziprasidone, Iloperidone, Aripiprazole

Quetiapine, Clozapine
Anticholinergic Trends Among SGAs

- Clozapine
- Olanzapine, Quetiapine
- Risperidone, Paliperidone, Ziprasidone, Iloperidone, Asenapine, Aripiprazole
Orthostasis Trends Among SGAs

- Iloperidone, Clozapine, Quetiapine, Risperidone
- Paliperidone
- Olanzapine, Asenapine, Ziprasidone, Aripiprazole
Sedation Trends Among SGAs

- Clozapine, Quetiapine
- Olanzapine, Asenapine
- Risperidone, Paliperidone, Ziprasidone, Iloperidone, Aripiprazole
Develop a monitoring system to evaluate the tolerance of pharmacotherapy options for treatment
Metabolic Complications

- Proposed weight gain mechanisms
  - Serotonin 2C receptor antagonism
  - Histamine receptor antagonism
  - Peripheral variables unrelated to appetite

- Proposed hyperglycemia mechanisms
  - Muscarinic cholinergic subtype 3 receptor antagonism

- Proposed hyperlipidemia mechanisms
  - Unknown

- It is possible for an individual to have hyperglycemia, hyperlipidemia, or both independent of weight gain

Potential Metabolic Complications

- Clozapine, Olanzapine (high risk)
- Risperidone, Paliperidone, Quetiapine (medium risk)
- Ziprasidone, Aripiprazole (low risk)
### ADA/APA Guidelines for Metabolic Monitoring of Antipsychotics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
<th>Quarterly</th>
<th>Every year</th>
<th>Every 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical History</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Fasting Glucose of A1c</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Fasting Lipids</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Treatment of Metabolic Complications

- Switch to agent associated with a low risk of weight gain, hyperglycemia, & hyperlipidemia if possible
- If not possible, implement nonpharmacologic strategies
- Many medications studied for antipsychotic-induced weight gain
- Metformin or other antidiabetic agents can be initiated for hyperglycemia
- Statins can be prescribed for hyperlipidemia
Pharmacologic Interventions Studied for AP-related Metabolic Changes

- Amantadine
- Aripiprazole
- Atomoxetine
- D-fenfluramine
- Dextroamphetamine
- Famotidine
- Fluoxetine
- Intranasal insulin
- Metformin
- Metformin with sibutramine
- Modafinil
- Nizatidine
- Orlistat
- Phenylpropanolamine
- Reboxetine
- Rimonabant
- Rosiglitazone
- Sibutramine
- Telmisartan
- Topiramate
- Zonisamide

Pharmacologic Interventions for AP-related Adverse Effects in Schizophrenia: Weight Outcomes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mean difference in weight (kg)</th>
<th>95% CI</th>
<th>RCTs</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>3.17</td>
<td>1.90 - 4.44</td>
<td>10</td>
<td>711</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>2.13</td>
<td>1.39 - 2.87</td>
<td>3</td>
<td>260</td>
</tr>
<tr>
<td>Topiramate</td>
<td>5.20</td>
<td>0.84 - 9.55</td>
<td>2</td>
<td>120</td>
</tr>
<tr>
<td>Reboxetine</td>
<td>1.90</td>
<td>0.72 - 1.90</td>
<td>2</td>
<td>79</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>2.86</td>
<td>1.01 - 4.72</td>
<td>3</td>
<td>66</td>
</tr>
</tbody>
</table>
Hyperprolactinemia

- Risperidone, Paliperidone, FGAs (high risk)
- Partial dopamine agonists (negligible risk)
APA Monitoring Guidelines for Hyperprolactinemia

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen for symptoms of hyperprolactinemia</td>
<td>Screen for symptoms of hyperprolactinemia at each visit &amp; then annually</td>
</tr>
<tr>
<td>Women - menstruation</td>
<td></td>
</tr>
<tr>
<td>Men - ejaculatory &amp; erectile function</td>
<td></td>
</tr>
<tr>
<td>Both genders - galactorrhea, libido</td>
<td></td>
</tr>
<tr>
<td>Prolactin level if clinically indicated</td>
<td></td>
</tr>
</tbody>
</table>
Treatment of Hyperprolactinemia

- Switch antipsychotic to agent associated with low risk
  - Olanzapine
  - Quetiapine
  - Aripiprazole
- Augment with aripiprazole
- Dopamine agonists
  - Not generally recommended


**APA Monitoring Guidelines for Drug-Induced Movement Disorders**

<table>
<thead>
<tr>
<th></th>
<th>EPS</th>
<th>Assess for rigidity, tremor, &amp; akathisia</th>
<th>Q2w during acute phase of treatment &amp; at each visit during maintenance phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tardive dyskinesia</td>
<td></td>
<td>AIMS</td>
<td>Assess every 6 months with FGAs &amp; every 12 months with SGAs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>If patient is at increased risk, complete every 3 to 6 months</td>
</tr>
</tbody>
</table>
Dystonia

- Risk factors
  - Young male patients, high potency FGAs

- Treatment
  - Benztropine 1-2 mg IM
  - Diphenhydramine 25-50 mg IM

Akathisia

- Usually takes days to weeks to appear
- May occur with many antipsychotics

**Treatment:**
- Propranolol 30-120 mg/day
- Benzodiazepines - lorazepam 1-2 mg/day, clonazepam 0.5-1 mg/day
- Anticholinergics - benztropine 1.5-8 mg/day
- Mirtazapine 15 mg/day
- Amantadine 100 mg/day
- Cyproheptadine 8-16 mg/day

Pseudoparkinsonism

- Usually occurs 1-2 weeks after initiation of therapy
- Risk factors: female, age > 40, high potency FGAs
- Treatment:
  - Benztropine 1-2 mg bid
  - Trihexyphenidyl 1-3 mg tid
  - Diphenhydramine 25-50 mg bid

Tardive Dyskinesia

- Prevention is key!
  - Use antipsychotics for appropriate purposes
  - Use the lowest effective dose
  - Use anticholinergics only when indicated & for shortest amount of time

- Treatment
  - Discontinue offending antipsychotic if possible
  - Switch to second generation antipsychotic (SGA) if taking FGA
  - FDA approved for TD: Valbenazine
  - FDA approved for TD: Deutetrabenazine
  - American Academy of Neurology Updated Recommendations:
    - Deutetrabenazine & Valbenazine - level A
    - Clonazepam & Ginkgo biloba - level B
    - Amantadine & tetrabenazine - level C


# Vesicular Monoamine Transporter 2 (VMAT-2) Inhibitors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tetrabenazine (Xenazine®)</th>
<th>Deutetrabenazine (Austedo®)</th>
<th>Valbenazine (Ingrezza®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pivotal trials leading to FDA approval</td>
<td>Not applicable</td>
<td>ARM - TD, AIM - TD</td>
<td>KINECT 2, KINECT 3</td>
</tr>
<tr>
<td>Half-life (hr) of active metabolites</td>
<td>5 - 7</td>
<td>9 - 10</td>
<td>15 - 22</td>
</tr>
<tr>
<td>Special considerations for administration</td>
<td>None</td>
<td>Take with food</td>
<td>None</td>
</tr>
<tr>
<td>Initial dose (mg/day)</td>
<td>12.5</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Titration (mg/week)</td>
<td>12.5</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>Usual dose range (mg/day)</td>
<td>50 - 100 divided in 3 doses a day Recommended maximum: 200</td>
<td>24-48 divided in 2 doses a day</td>
<td>40 - 80 as 1 dose a day</td>
</tr>
</tbody>
</table>
Vesicular Monoamine Transporter 2 (VMAT-2) Inhibitors

- Adverse effects
  - Somnolence
  - Insomnia
  - Depression
  - Suicidality
  - Neuroleptic malignant syndrome
  - Akathisia
  - Parkinsonism
  - Dysphagia
  - QTc prolongation
  - Hypotension
  - Hyperprolactinemia

- Cost

Recognize the advantages and disadvantages of the newer partial dopamine agonists
Pharmacologic Properties of SGAs: Partial Agonists - $K_I$ Values

<table>
<thead>
<tr>
<th></th>
<th>$D_2$</th>
<th>$5HT_{2A}$</th>
<th>Alpha$_1$</th>
<th>H$_1$</th>
<th>M$_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>1.6</td>
<td>8.7</td>
<td>26</td>
<td>28</td>
<td>6800</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>0.4</td>
<td>0.5</td>
<td>19</td>
<td></td>
<td>&gt;1,000</td>
</tr>
<tr>
<td>Cariprazine</td>
<td>0.6</td>
<td>19</td>
<td>130</td>
<td>23</td>
<td>&gt;1,000</td>
</tr>
</tbody>
</table>
Potential Partial Dopamine Agonists
Adverse Effects Predicated on
Receptor Binding Profile

- EPS
- Orthostatic hypotension
- Sedation
- Weight gain

# Partial Dopamine Agonists

<table>
<thead>
<tr>
<th></th>
<th>Aripiprazole</th>
<th>Brexpiprazole</th>
<th>Cariprazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA Indications</td>
<td>Schizophrenia, Bipolar I Disorder, Major Depressive Disorder (adjunct), Autism, Tourette Syndrome</td>
<td>Schizophrenia, Major Depressive Disorder (adjunct)</td>
<td>Schizophrenia, Bipolar I Disorder</td>
</tr>
<tr>
<td>Half-life</td>
<td>75 hours</td>
<td>91 hours</td>
<td>Cariprazine: 2-4 days DCAR 1-2 days DDCAR 1-3 weeks</td>
</tr>
</tbody>
</table>

**Half-life** refers to the time it takes for the concentration of the drug in the body to decrease by half. For Aripiprazole, the half-life is 75 hours; for Brexpiprazole, it is 91 hours; and for Cariprazine, it is 2-4 days (DCAR) and 1-2 days (DDCAR) with a 1-3 weeks delay.
Iowa Medicaid Coverage of Partial Dopamine Agonists – October 1, 2019

- Aripiprazole tablets - Step 1
- Brexpiprazole (Rexulti) - Step 3
- Cariprazine (Vraylar) - Step 3
Drug Interactions
Patient Case

- 37 y/o male brought to BMC by group home staff with increased delusions and hallucinations. He was released from BMC about 3 weeks ago on the following medications:
  - Clozapine 400 mg HS
  - Depakote ER 1500 mg HS
  - Lisinopril 20 mg daily
  - Docusate 100 mg BID

Patient states that he has been taking his medications. Group home staff confirms this.
Potential Drug Interactions with Antipsychotics

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Major CYP450</th>
<th>Increase AP</th>
<th>Decrease AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine, Olanzapine, Asenapine, Loxapine, Thiothixene, Trifluoperazine</td>
<td>1A2</td>
<td>Fluvoxamine, ciprofloxacin, other 1A2 inhibitors</td>
<td>Cigarette smoking*, other 1A2 inducers</td>
</tr>
<tr>
<td>Risperidone, Iloperidone, Haloperidol, Chlorpromazine, Fluphenazine, Loxapine, Perphenazine, Brexpiprazole</td>
<td>2D6</td>
<td>Fluoxetine, paroxetine, other 2D6 inhibitors</td>
<td>2D6 inducers</td>
</tr>
<tr>
<td>Quetiapine, Aripiprazole, Lurasidone, Ziprasidone* (1/3), Cariprazine, Haloperidol, Iloperidone, Loxapine, Pimozide</td>
<td>3A4</td>
<td>Fluvoxamine, ketoconazole, other 3A4 inhibitors</td>
<td>Carbamazepine, rifampin, other 3A4 inducers</td>
</tr>
</tbody>
</table>
Compare and contrast the newer long-acting injections
"Done" Injections

<table>
<thead>
<tr>
<th></th>
<th>Risperidone Microspheres</th>
<th>Risperidone Extended Release</th>
<th>Paliperidone Palmitate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual dosage range (mg)</td>
<td>25 - 50</td>
<td>90 - 120</td>
<td>39 - 234</td>
</tr>
<tr>
<td>Usual dosage interval</td>
<td>Q 2 wk</td>
<td>Q 4 wk</td>
<td>Q 4 wk</td>
</tr>
<tr>
<td>Injection site</td>
<td>Deltoid or gluteal</td>
<td>Subcutaneous in the abdomen</td>
<td>Deltoid or gluteal</td>
</tr>
<tr>
<td>Half-life (days)</td>
<td>3 - 6</td>
<td>9 - 11</td>
<td>25 - 49</td>
</tr>
<tr>
<td>Storage</td>
<td>Refrigerator</td>
<td>Refrigerator</td>
<td>Room temperature</td>
</tr>
<tr>
<td>Oral Supplementation</td>
<td>3 wk</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
Risperidone Extended Release (Perseris™)

- FDA approved for Schizophrenia in adults
- Establish tolerability with oral risperidone
- May be initiated at 90 mg or 120 mg
- Supplementation with oral risperidone not recommended
- Giving more than 1 dose per month is not recommended
# Other SGA Injections

<table>
<thead>
<tr>
<th></th>
<th>Olanzapine Pamoate</th>
<th>Aripiprazole Monohydrate</th>
<th>Aripiprazole Lauroxil</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual dosage (mg)</strong></td>
<td>150 - 600</td>
<td>400</td>
<td>441 - 1064</td>
</tr>
<tr>
<td><strong>Usual interval dosing</strong></td>
<td>Q 2-4 wk</td>
<td>Q4 wk</td>
<td>Q4-8 wk</td>
</tr>
<tr>
<td><strong>Injection Site</strong></td>
<td>Gluteal</td>
<td>Gluteal</td>
<td>Deltoid or Gluteal</td>
</tr>
<tr>
<td><strong>Half-life (days)</strong></td>
<td>25 - 49</td>
<td>30 - 47</td>
<td>54 - 57</td>
</tr>
<tr>
<td><strong>Storage</strong></td>
<td>Room temperature</td>
<td>Room temperature</td>
<td>Room temperature</td>
</tr>
<tr>
<td><strong>Oral Supplementation</strong></td>
<td>None</td>
<td>2 wk</td>
<td>None if Initio given</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 wk if Initio not given</td>
</tr>
</tbody>
</table>
Iowa Medicaid Coverage of LAIs - October 1, 2019

- Risperdal Consta - Step 2
- Perseris - Step 2
- Invega Sustenna - Step 2
- Invega Trinza - Step 2
- Zyprexa Relprevv - Step 2
- Abilify Maintena - Step 2
- Aristada - Step 2
Discuss promising compounds being studied for management of negative symptoms
Treating Unmet Needs of Patients with Persistent Negative Symptoms

- Negative symptoms contribute to
  - Reduced quality of life
  - Increased functional disability
  - Increased burden of illness
  - Poorer long-term outcomes
- Negative symptoms are prominent & persistent in ¼ of patients with schizophrenia
- Estimated to occur in ½ of outpatients at any given time

Chue P, Lalonde J. Addressing the unmet needs of patients with persistent negative symptoms of schizophrenia: emerging pharmacological treatment options. Neuropsychiatr Dis Treat. 2014; 10; 777-789.
Antidepressants

- One meta-analysis of 23 studies found overall efficacy for the treatment of negative symptoms
  - 8 showed positive results
  - 15 showed negative results
- A Cochrane systematic review demonstrated the same outcome as the aforementioned meta-analysis
  - Authors cautioned that only 5 of 139 studies met the required standards to evaluate the effect on potential confounding symptoms (depressive symptoms, for example)


Antipsychotics

- A few studies have been conducted comparing the effects of monotherapy with different antipsychotics, with no differences among agents reported.

- A trial of asenapine versus olanzapine found that neither drug differed significantly at 26 weeks.

- A systematic review of the efficacy of clozapine monotherapy identified 6 studies:
  - Findings favored clozapine.
  - Findings also confounded by difficulty interpreting results as the population was mostly treatment refractory.

NICE guideline on core interventions in the treatment & management of schizophrenia in adults 2010


Other Options That Have Been Studied

- Psychostimulants
- NSAIDs
- N-acetyl cysteine
- Minocycline
- 5HT-3 antagonists
- Lamotrigine
- Memantine

Chue P, Lalonde J. Addressing the unmet needs of patients with persistent negative symptoms of schizophrenia: emerging pharmacological treatment options. Neuropsychiatr Dis Treat. 2014; 10; 777-789.
Emerging Options

- NMDA receptor function enhancers
- Nicotine acetylcholine receptor agonists
NMDA Receptor Function Enhancers

- Studies have found preliminary evidence that increasing NMDA activation though glycine site agonists (D-serine) improves negative symptoms
- Sarcosine, a glycine reuptake inhibitor has been found to improve negative symptoms in studies


Nicotinic Acetylcholine Receptor Agonists

- Agents active at alpha-7 nicotinic receptors being developed
- It is thought that targeting cognitive symptoms with nicotinic receptor agonists may improve negative symptoms
- These agents have shown mixed results

EnVivo Pharmaceuticals, Inc. Study of EVP-6124 as an adjunctive pro-cognitive treatment in schizophrenia on chronic stable atypical antipsychotic therapy. 2014 http://clinicaltrials.gov
Summary

- “Pines” may be associated with more metabolic complications, while the “dones” may be associated with more EPS
- Metabolic monitoring is recommended
- Partial dopamine agonists differ slightly in indication, half-life, & binding to non dopamine receptors
- The new long-acting risperidone injection allows for a longer injection interval, but may have some dosing constraints
- Further research is needed for optimal management of negative symptoms of schizophrenia