Use of Antipsychotics & Anticonvulsants in IDDs

Joseph L. Calles, Jr., MD
joseph.calles@med.wmich.edu

Objective:

Identify and prevent the potential adverse interactions between antipsychotics and anticonvulsants used in the treatment of individuals with IDDs.

Notes:
The Use of Antipsychotics & Anticonvulsants in IDDs
33nd Annual DD Conference- April 18, 2017

Joseph L. Calles, Jr., M.D.
Department of Psychiatry
WMU Homer Stryker M.D. School of Medicine

Professional Information
- Associate Professor of Psychiatry, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI
- Consultant, Great Lakes Center for Autism Treatment and Research, Portage, MI
- Board Certified in General and Child & Adolescent Psychiatry
- Member, American Academy of Child & Adolescent Psychiatry (AACAP)
- Member, National Association for the Dually Diagnosed (NADD)

Disclosure
- There are no financial affiliations or compensations related to the content of this presentation.
Medications Discussed

**Antipsychotics:**
- aripiprazole (Abilify®, Aristada®)
- asenapine (Saphris®)
- brexpiprazole (Rexulti®)
- cariprazine (Vraylar®)
- clozapine (Clozaril®, FazaClo®, Venasect®)
- iloperidone (Fanapt®)
- lurasidone (Latuda®)
- olanzapine (Zyprexa®)
- paliperidone (Invega®)
- quetiapine (Seroquel®)
- risperidone (Risperdal®)
- ziprasidone (Geodon®)

**Anticonvulsants:**
- acetazolamide (Diamox®)
- brivaracetam (Briviact®)
- carbamazepine (Tegretol®, Carbatrol®, Equetro®)
- clobazam (Onfi®)
- divalproex sodium (Depakote®)
- eslicarbazine (Aptiom®)
- ethosuximide (Zarontin®)
- ezogabine (Potiga®)
- fosphenytoin (Cerebyx®)
- felbamate (Felbatol®)
- gabapentin (Neurontin®)
- lacosamide (Vimpat®)

**Anticonvulsants (cont.):**
- lamotrigine (Lamictal®)
- levetiracetam (Keppra®)
- methsuximide (Celontin®)
- oxcarbazepine (Trileptal®)
- perampanel (Fycompa®)
- pregabalin (Lyrica®)
- phenytoin (Dilantin®, Phenytek®)
- rufinamide (Banzel®)
- topiramate (Gabitril®)
- topiramate (Toppene®, Qudexy XR®, Trokendi XR®)
- vigabatrin (Sabril®)
- zonisamide (Zonegran®)
Presentation Overview

1. Epidemiology of psychopathology in IDDs
2. Epidemiology of epilepsy in IDDs
3. Epidemiology of psychopathology in epilepsy
4. The intersection of IDDs, MI and epilepsy
5. Pharmacotherapy of psychopathology in IDDs
6. Pharmacotherapy of epilepsy in IDDs
7. Pharmacotherapy of psychopathology in epilepsy

Presentation Overview

8. Pharmacotherapy of combined IDD, MI and epilepsy
9. Potential adverse events, drug-drug interactions, and proconvulsant effects in the treatment of comorbid disorders

Epidemiology of Psychopathology in IDDs
Epidemiology of Psychopathology: General

One study examined rates of behavior problems and psychopathology among children with DDs compared to both chronologic age (CA) and mental age (MA) matched comparison groups.

Significant group differences were found for ADHD, most notably the inattentive subtype, which was over three times as prevalent in the DD group. In the MA-match analyses, the DD group demonstrated significantly higher rates of the hyperactive subtype.

The prevalence of Social Phobia was significantly higher in the DD than the typical development sample for the MA-match analyses.

---

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>DD Sample</th>
<th>MA Match Sample</th>
<th>CA Match Sample</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD inattentive</td>
<td>32.1</td>
<td>26.1</td>
<td>26.1</td>
<td>2.03</td>
<td>0.005</td>
</tr>
<tr>
<td>ADHD hyperactive</td>
<td>42.6</td>
<td>26.1</td>
<td>26.0</td>
<td>3.08</td>
<td>0.000</td>
</tr>
<tr>
<td>Social Phobia</td>
<td>21.0</td>
<td>11.4</td>
<td>11.4</td>
<td>2.03</td>
<td>0.040</td>
</tr>
</tbody>
</table>

* 
* p < .05

---

A UK study found that more than a third - 40.9% (clinical diagnoses) or 35.2% (DC–LD diagnoses) - of an adult, ID cohort had mental ill-health.

Those point prevalence rates were higher than those observed in the UK general population.

---

Caplan, et al., 2015

Cooper, et al., 2007c
Epidemiology of Psychopathology: Self-injurious Behavior

- A UK study found the point prevalence of self-injurious behavior (SIB) to be 4.9%, the 2-year incidence 0.6%, and the 2-year remission rate 38.2%.
- At any point in time, the point prevalence of SIB was accounted for by both new onset, and by enduring SIB, with enduring SIB predominating.

Epidemiology of Psychopathology: Aggressive Behavior

- The same UK group found the point prevalence of aggressive behavior was 9.8%, 2-year incidence was 1.8%, and, for the adults who had aggressive behavior, the 2-year remission rate was 27.7%.
- Prevalence was accounted for by both new onset aggressive behavior and enduring aggressive behaviors.
Epidemiology of Psychopathology: Psychosis

Cooper’s group found the point prevalence of psychosis to be 2.6%-4.4% depending upon the diagnostic criteria used; 2-year incidence of psychotic episode was 1.4%, 2-year incidence of first episode of psychosis was 0.5%, and, of people in episode at entry, the remission rate in the 2-year period was low, at 14.3%.

Cooper, et al., 2007a

Epidemiology of Psychopathology: Mood Disorders

Cooper’s group also found that the point prevalence of affective (mood) disorders was higher in the ID population (than that reported previously for the general population): 3.8% for depression and 0.6% for mania.

In addition, 1.0% had bipolar disorder, currently in remission, and 0.1% first episode of mania, currently in remission.

Cooper, et al., 2007b

Epidemiology of Epilepsy in IDDs
Epidemiology of Epilepsy in IDDs

- A review article reported that in general samples of people with IDs, the pooled estimate (from 38 studies) of epilepsy prevalence was 22.2%.
- For samples of people with Down syndrome, excluding two studies focusing on older people, the prevalence rate was lower, with the pooled estimate (from 11 studies) being 10.3%.

Robertson, et al., 2015

Epidemiology of Epilepsy in IDDs

- A systematic review of outcomes in ASDs found that the overall percentage of participants with epilepsy at follow-up ranged between 1.8% in those under 12 years of age (the majority of whom did not have an ID) and 23.7% of those over 12 years of age, of whom the majority did have an ID.
- These are significantly greater percentages than those reported in the literature for the general population, but are similar to those found for IDs.

Woolfenden, et al., 2012

Epidemiology of Epilepsy in IDDs

- The causes of IDDs and epilepsy are increasingly recognized to be genetic, based on: chromosomal microarray analysis to identify copy number variants; gene panels; and, whole-exome sequencing.
- A specific genetic diagnosis may guide care by pointing to comorbid disorders and best therapy.

Devinsky, et al., 2015
Examples of recurrent copy number variants associated with ID, epilepsy, and other neurodevelopmental phenotypes

<table>
<thead>
<tr>
<th>Copy number variant</th>
<th>Deletion or duplication</th>
<th>Associated phenotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1p21.3</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>1q21.1</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>2q31.3</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>6q27</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>9p29</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>16p11.2.2 (5q13.32q21.32)</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>15q14.3-q15.2</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>15q13.3</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
<tr>
<td>15q24.1</td>
<td>Deletion</td>
<td>ID, CHARGE, Epilepsy,</td>
</tr>
</tbody>
</table>

Epidemiology of Epilepsy in IDDs

The prevalence of epilepsy increases with the severity of the IDD. Among 692 patients with childhood-onset epilepsy followed for 20-30 years, 147 (21%) had IDD with epilepsy. Of those 147 cases, 53% had severe/profound IDD compared to 24% with moderate IDD and 24% with mild IDD.

Devinsky, et al., 2015
Epidemiology of Epilepsy in IDDs

- Seizure type is also influenced by the severity of the IDD. Focal epilepsies predominate in those with mild IDD (69%; 17% with symptomatic generalized epilepsy), similar to those with normal intelligence, while symptomatic generalized epilepsies predominate in those with severe IDD (67%; 29% with focal epilepsy).
- Seizure type is related to rates of remission, with some types being more treatment-resistant.

Devinsky, et al., 2015

---

Epidemiology of Psychopathology in Epilepsy
Epidemiology of Psychopathology in Epilepsy

In the task force report from the International League Against Epilepsy (ILAE), the authors note that epidemiological studies in a number of different countries, and over a long period of time, have yielded reasonably consistent results with regard to the rates of psychiatric disorder in children with epilepsy, which have ranged from around 35% to 50%.

Sillanpää, et al., 2016

Epidemiology of Psychopathology in Epilepsy

ADHD is under-diagnosed and under-treated in children with epilepsy. Approximately 30% of children with epilepsy have ADHD. There is a broad differential diagnosis for the causes of ADHD symptoms in children with epilepsy, including the epilepsy itself and some antiepileptic drugs.

Besag, et al., 2016b

Epidemiology of Psychopathology in Epilepsy

Anxiety and depression are common in children and adolescents with epilepsy, affecting one-quarter to one-third of patients. Multiple epilepsy-related, psychological and genetic-familial factors have been implicated in causing anxiety and depression in patients with epilepsy.

Dunn, et al., 2016
Epidemiology of Psychopathology in Epilepsy

- The overall research evidence suggests that schizophrenia-like psychosis is believed to be 6 to 12 times more likely to occur in people with epilepsy than in the general population.

Mendez, et al., 1993

The Intersection of IDDs, MI, and Epilepsy

- The previously cited ILAE task force report also noted that the prevalence of psychiatric disorder in children with complicated epilepsy, usually implying accompanying intellectual disability, is much higher, well over 50%.

Silvennoinen, et al., 2016
In another study, investigators looked at: (a) associations between epilepsy (or epilepsy-related factors) and neuropsychiatric comorbidities in patients with ID and (b) between ID and neuropsychiatric comorbidities in patients with epilepsy.

van Ool, et al., 2016

There was an indication that having epilepsy was significantly related to higher rates of negative mood symptoms in adults and elderly with ID, including depressive symptoms, negative mood, and mood swings. Having epilepsy was, however, not associated with emotional disturbances. Most studies also did not demonstrate a significant association between the presence of epilepsy and behavioral problems.

van Ool, et al., 2016

Generally, the results indicated that more severe epilepsies (including generalized seizures), greater seizure severity, higher seizure frequency, and higher number of seizure types, were risk factors for behavioral problems and psychiatric disorders.

van Ool, et al., 2016
The Intersection of IDDs, MI, and Epilepsy

- Having ID was related to higher rates of ASD, postictal psychosis, and both psychotic and nonpsychotic disorders.
- The degree of the ID seemed relevant with respect to behavioral problems, a more severe ID being significantly associated with more behavioral problems in adults with epilepsy.

van Dal, et al., 2016

Summary of findings on neuropsychiatric outcomes in patients with ID and epilepsy

<table>
<thead>
<tr>
<th>Factors contributing to the genesis and persistence of psychiatric disorders in patients with IDDs and epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
</tr>
<tr>
<td>ASD</td>
</tr>
<tr>
<td>ADHD</td>
</tr>
<tr>
<td>ID</td>
</tr>
<tr>
<td>ID</td>
</tr>
<tr>
<td>ID</td>
</tr>
</tbody>
</table>

van Dal, et al., 2015
Pharmacotherapy of Psychopathology in IDDs

Pharmacotherapy of SIB

In the UK, an expert panel's (all 258 consultant members on the mailing list of the Royal College of Psychiatrists' Learning Disability Faculty) first choices of medications for SIB were:

- Antipsychotics - 49.1%
- Antidepressants - 25.9%
- Anti-anxiety drugs - 11.1%

Unwin & Deb, 2008

Pharmacotherapy of SIB

The expert panel's first choices of atypical antipsychotics for SIB were:

- Risperidone - 74.1%
- Olanzapine - 12.0%
- Quetiapine - 0.9%

Unwin & Deb, 2008
Pharmacotherapy of SIB

- The expert panel’s first choices of *antidepressants* for SIB were:
  - Citalopram - 32.4%
  - Fluoxetine - 22.2%
  - Sertraline - 11.1%
  - Escitalopram - 9.3%

Unwin & Deb, 2008

Pharmacotherapy of Aggression

- In the UK, an expert panel’s (all 258 consultant members on the mailing list of the Royal College of Psychiatrists’ Learning Disability Faculty) first choices of medications for *aggression* were:
  - Antipsychotics - 80.6%
  - Anti-anxiety drugs - 12.0%
  - Antidepressants - 6.5%

Unwin & Deb, 2008

Pharmacotherapy of Aggression

- The expert panel’s first choices of *atypical antipsychotics* for aggression were:
  - Risperidone - 76.7%
  - Olanzapine - 13.0%
  - Quetiapine - 1.9%

Unwin & Deb, 2008
Pharmacotherapy of Aggression

- The expert panel's first choices of antidepressants for aggression were:
  - Citalopram - 35.2%
  - Fluoxetine - 19.4%
  - Sertraline - 13.0%
  - Escitalopram - 10.2%

Unwin & Deb, 2008

Pharmacotherapy of Psychosis

- Any antipsychotic medication can be used to treat psychotic symptoms in individuals with IDDs, with the atypical agents being preferred over older agents.
- The choice of agent will be determined by the trade-off between efficacy and tolerance (side effect profile).

Pharmacotherapy of Mood Disorders

- The selective serotonin reuptake inhibitors (SSRIs) are the preferred medications for the treatment of depression in individuals with IDDs.
- The atypical antipsychotics are first line treatments for bipolar disorder/mania, unless there is comorbid epilepsy, in which case anticonvulsants with good mood stabilizing properties should be used first.
Pharmacotherapy of Epilepsy in IDDs

Therapy to control seizures should be individualized, with drug selection based on seizure types, epilepsy syndrome, concomitant medications, and comorbid disorders.

There are limited comparative antiepileptic drug data in the IDD with epilepsy population.

Devereux, et al., 2015
Pharmacotherapy of Epilepsy in IDs

- A Cochrane Review on pharmacological interventions for epilepsy in people with IDs determined that, in general, AEDs that are proven to be effective in the general epilepsy population are also effective for refractory epilepsy in people with ID.
- It was not possible for the authors to comment on the relative efficacy of medications, making clinical decisions difficult.

Jackson, et al., 2015

Pharmacotherapy of Epilepsy in IDs

- The treatment of refractory epilepsy does seem to differ if IDs are present.
- A Canadian study found that patients with ID were currently taking, and had been previously exposed to, a greater number of different AEDs. Patients with ID were also more likely to be taking at least one older AED and were more commonly treated with benzodiazepines.

Fridhandler, et al., 2012

Pharmacotherapy of Epilepsy in IDs

- A more recent study assessed the efficacy of newer AEDs in individuals with Angelman syndrome (AS) (~80-90% with AS have epilepsy).
- Newer AEDs, such as levetiracetam, lamotrigine, and clobazam, and, to a lesser extent, topiramate, appeared to be as effective- if not more so- as valproic acid and clonazepam, while offering more favorable side effect profiles.

Shaaya, et al., 2016
Pharmacotherapy of Epilepsy in IDs

- Another genetic syndrome with high prevalence of epilepsy (up to 90%) is tuberous sclerosis complex (TSC).
- A Dutch study of children with TSC and epilepsy found that vigabatrin was used by 94% of children, and was the first treatment in 48%.
- Vigabatrin was more effective than other AEDs (including VPA) when prescribed as first treatment.

Overwater, et al., 2015

Pharmacotherapy of Psychopathology in Epilepsy

- A previously cited article noted that about 70% of children with ADHD and epilepsy will benefit from standard treatment, such as methylphenidate.
- To date, there appears to be no firm evidence that the usual treatments for ADHD are likely to exacerbate seizures.

Besag, et al., 2016b
Pharmacotherapy of Psychopathology in Epilepsy

- Although studies of treatments for depression and anxiety, in populations with epilepsy, are limited, another article cited previously commented that SSRIs and cognitive behavioral therapy (CBT) are currently accepted treatments.
- The SSRIs and the SNRIs do not reduce seizure threshold, and may even lessen the chance of seizures.

Duan, et al., 2016

Pharmacotherapy of Psychopathology in Epilepsy

- The AED pregabalin has been recommended as a first-choice treatment for generalized anxiety disorder in adults with epilepsy, but no data exists for treatment of children with anxiety and epilepsy.

Mula, 2016

Pharmacotherapy of Psychopathology in Epilepsy

- If psychosis is not drug-induced and requires antipsychotic treatment, it should not normally be withheld on the basis of possible seizure exacerbation (see the last section of this presentation).
- For postictal psychosis, the antipsychotic treatment can be withdrawn slowly when the psychotic features have resolved, but further antipsychotic treatment might be required if there are future episodes.

Besag, et al., 2016a
Pharmacotherapy of Psychopathology in Epilepsy

- Psychosis in association with the prescription of some antiepileptic drugs can also occur in children and adolescents.
- If the psychosis is drug-induced, a review of the antiepileptic medication is indicated. (see the last section of this presentation).

Besag, et al., 2016a

Pharmacotherapy of Combined IDD, MI and Epilepsy

There are no studies that specifically address the treatment of individuals with this clinical triad.

Some experts have made recommendations for AED selections in those with IDDs and epilepsy.

Given that several AEDs are also used to treat psychiatric disorders, suggested AEDs can be considered as first or second choices to treat epilepsy and some comorbid psychiatric disorders in individuals with IDDs:

Shanker, et al., 2015
Making a treatment choice: initial treatment

The use of AEDs is better-suited to treat bipolar disorder, less so for some anxiety and depressive disorders, and not for psychotic disorders (unless they derive from the epilepsy itself).

Other classes of psychotropic medications can be used in individuals with the clinical triad, but must be used cautiously to avoid drug-drug interactions and other adverse effects.
Potential Adverse Events, Drug-Drug Interactions, and Proconvulsant Effects in the Treatment of Comorbid Disorders

Adverse Events
- The previously cited ILAE task force reported on adverse cognitive and behavioral effects of AEDs in children.
- They distinguished the older AEDs from the newer, and newest, AEDs.
- A striking finding was the lack of information on children.

Adenkorng, et al., 2016

- The authors surmised that there may be negative cognitive effects with phenobarbital, phenytoin, topiramate and zonisamide.
- Adverse behavioral effects were associated with phenobarbital, valproate, gabapentin, topiramate, levetiracetam and zonisamide.

Adenkorng, et al., 2016
Adverse Events

- With regard to cognitive effects, valproate, carbamazepine (CBZ), gabapentin and oxcarbazepine appear to be neutral.
- CBZ appears to be neutral with regard to behavioral effects.
- Positive cognitive effects have been reported with lamotrigine (LTG) and levetiracetam.
- Positive behavioral effects have been reported with LTG.

Aldenkamp, et al., 2016

Adverse Events

- Although the data on adolescents with psychosis is somewhat limited, there seems every reason to recommend starting at low doses and escalating the dose slowly when AEDs that have a documented association with psychosis, such as vigabatrin and topiramate, are being prescribed.

Besag, et al., 2016a

<table>
<thead>
<tr>
<th>Older AEDs</th>
<th>Phenobarbital</th>
<th>Phenytoin</th>
<th>Valproate</th>
<th>Carbamazepine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuraxial</td>
<td>Tegretol</td>
<td>Lamictal</td>
<td>Tegretol</td>
<td>Lamictal</td>
</tr>
<tr>
<td>Other AEDs</td>
<td>Lamotrigine</td>
<td>Gabapentin</td>
<td>Valproate</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Neuraxial</td>
<td>Lamotrigine</td>
<td>Gabapentin</td>
<td>Valproate</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Other AEDs</td>
<td>Lamotrigine</td>
<td>Gabapentin</td>
<td>Valproate</td>
<td>Carbamazepine</td>
</tr>
</tbody>
</table>

Note: Lined-out drugs not available in the US
Aldenkamp, et al., 2016
Adverse Events

A study that evaluated the use of the newer AED perampanel in patients with ID and epilepsy found that behavioral adverse effects were present in 40.3%. Most common were aggression, agitated behavior, disruptive behavior, and mood symptoms.

Snoeijen-Schouwenaars, et al., 2017
### AED, antidepressant, and antipsychotic drug-drug interactions

<table>
<thead>
<tr>
<th>AED</th>
<th>TCA</th>
<th>Non-TCA</th>
<th>SNRI</th>
<th>MAOI</th>
<th>Antidepressants</th>
<th>Antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Sodium valproate</td>
<td>Lamotrigine</td>
<td>Topiramate</td>
<td>Oxcarbazepine</td>
<td>Carbamazepine, lamotrigine, oxcarbazepine, topiramate</td>
<td>Carbamazepine, lamotrigine, oxcarbazepine, topiramate</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Phenytin</td>
<td>Carbamazepine</td>
<td>Lamotrigine</td>
<td>Oxcarbazepine</td>
<td>Carbamazepine, lamotrigine, oxcarbazepine, topiramate</td>
<td>Carbamazepine, lamotrigine, oxcarbazepine, topiramate</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Phenytoin</td>
<td>Carbamazepine</td>
<td>Lamotrigine</td>
<td>Oxcarbazepine</td>
<td>Carbamazepine, lamotrigine, oxcarbazepine, topiramate</td>
<td>Carbamazepine, lamotrigine, oxcarbazepine, topiramate</td>
</tr>
</tbody>
</table>

(Mostly from Epocrates)

### AED, antidepressant, and antipsychotic drug-drug interactions

<table>
<thead>
<tr>
<th>AED</th>
<th>TCA</th>
<th>Non-TCA</th>
<th>SNRI</th>
<th>MAOI</th>
<th>Antidepressants</th>
<th>Antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tagamet</td>
<td>Tagamet</td>
<td>Tagamet</td>
<td>Tagamet</td>
<td>Tagamet</td>
<td>Tagamet</td>
<td>Tagamet</td>
</tr>
<tr>
<td>Zyban</td>
<td>Zyban</td>
<td>Zyban</td>
<td>Zyban</td>
<td>Zyban</td>
<td>Zyban</td>
<td>Zyban</td>
</tr>
<tr>
<td>Celexa</td>
<td>Celexa</td>
<td>Celexa</td>
<td>Celexa</td>
<td>Celexa</td>
<td>Celexa</td>
<td>Celexa</td>
</tr>
<tr>
<td>Serzone</td>
<td>Serzone</td>
<td>Serzone</td>
<td>Serzone</td>
<td>Serzone</td>
<td>Serzone</td>
<td>Serzone</td>
</tr>
<tr>
<td>Pristiq</td>
<td>Pristiq</td>
<td>Pristiq</td>
<td>Pristiq</td>
<td>Pristiq</td>
<td>Pristiq</td>
<td>Pristiq</td>
</tr>
<tr>
<td>Zyprexa</td>
<td>Zyprexa</td>
<td>Zyprexa</td>
<td>Zyprexa</td>
<td>Zyprexa</td>
<td>Zyprexa</td>
<td>Zyprexa</td>
</tr>
<tr>
<td>Prozac</td>
<td>Prozac</td>
<td>Prozac</td>
<td>Prozac</td>
<td>Prozac</td>
<td>Prozac</td>
<td>Prozac</td>
</tr>
</tbody>
</table>

(Mostly from Epocrates)

### AED and antipsychotic drug-drug interactions

<table>
<thead>
<tr>
<th>AED</th>
<th>TCA</th>
<th>Non-TCA</th>
<th>SNRI</th>
<th>MAOI</th>
<th>Antidepressants</th>
<th>Antipsychotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>AED</td>
<td>AED</td>
<td>AED</td>
<td>AED</td>
<td>AED</td>
<td>AED</td>
<td>AED</td>
</tr>
</tbody>
</table>

(Derived from Epocrates)
AED and antipsychotic drug-drug interactions

**Abnormalities for antipsychotics (every 10 mg):**
AED= antiepileptic
ASD= aripiprazole
BDZ= benzodiazepine
CAR= cariprazine
CLZ= clozapine
DLX= divalproex
LBR= lurasidone
OXR= olanzapine
POX= paliperidone
QU= quetiapine
RS= risperidone
ZIP= ziprasidone

**Abnormalities for anticonvulsants (left column):**
AED= antiepileptic
BDZ= benzodiazepine
CLZ= clozapine
LBR= lurasidone
OXR= olanzapine
POX= paliperidone
RS= risperidone
ZIP= ziprasidone

**Proconvulsant Effects: Antipsychotics**

<table>
<thead>
<tr>
<th>Incidence Rate of Failure by Antipsychotic Drug</th>
<th>No. of Patients</th>
<th>Incidence of Abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>No. of Patients</td>
<td>Incident Rate (%)</td>
</tr>
<tr>
<td>ECT</td>
<td>1,000</td>
<td>10.0</td>
</tr>
<tr>
<td>Lithium</td>
<td>1,000</td>
<td>10.0</td>
</tr>
<tr>
<td>Proconvulsant</td>
<td>1,000</td>
<td>10.0</td>
</tr>
</tbody>
</table>

(Wu, et al., 2016)

**Proconvulsant Effects: Antipsychotics**

(Wu, et al., 2016)
Proconvulsant Effects: Antidepressants

| Antidepressant drug classes | Drug names | Side effects in patients with IDD
|-----------------------------|------------|-----------------------------|
| Serotonin reuptake inhibitors (SSRIs) | Fluoxetine, paroxetine, sertraline | Cerebellar ataxia, anxiety, serotonin, neuropsychiatric 
| Select serotonin reuptake inhibitors (SNRIs) | Venlafaxine, duloxetine, desvenlafaxine | Agitation, suicidal thoughts, nausea, orthostatic hypotension, sweating, gastrointestinal disturbances, fatigue, somnolence, nausea 
| selective norepinephrine reuptake inhibitors (SNRIs) | Bupropion | Agitation, suicidal thoughts, nausea, orthostatic hypotension, sweating, gastrointestinal disturbances, fatigue, somnolence, nausea 
| Tricyclic antidepressants | Imipramine, amitriptyline, clomipramine | Agitation, suicidal thoughts, nausea, orthostatic hypotension, sweating, gastrointestinal disturbances, fatigue, somnolence, nausea

Johannessen-Landmark, et al., 2016

Conclusions

- Individuals with combined IDDs, epilepsy and psychiatric disorders are complex and difficult to treat.
- AEDs can have adverse cognitive and behavioral effects.
- Some psychotropic medications can increase the risk of seizure activity.

Conclusions

- There are no medications that treat the underlying, core features of IDDs, so the focus of treatment is controlling seizure activity and reducing psychiatric symptoms.
- Initial treatment should target the most distressing and/or impairing symptoms.
- Use of medications should follow the “start low, go slow” approach.
Conclusions

- Try to use the least number of medications, choosing agents that can serve more than one function, e.g., AEDs that are also good mood stabilizers.
- It is a safe assumption that any clinical deterioration in patients on medications could be from the medications themselves, including side effects (e.g., constipation or urinary retention).

Questions?

References


## References


References


