FTD: Pharmacological Management Strategies

Brice McConnell, MD, PhD
Assistant Professor of Neurology
University of Colorado Denver
Department of Neurology, Behavioral Neurology Section

Disclosures: None

FTD: Pharmacological Management Strategies

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Example</th>
<th>Effect</th>
<th>Proposed Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-depressants</td>
<td>Citalopram, paroxetine, sertraline, venlafaxine</td>
<td>300 mg qam (bid) or (qhs)</td>
<td>20 mg to 200 mg/day</td>
</tr>
<tr>
<td>Anti-epileptics</td>
<td>Oxycontin, aprindine, memantine, clonazepam</td>
<td>300 mg qam (bid) or (qhs)</td>
<td>5 mg to 40 mg/day</td>
</tr>
<tr>
<td>Anti-agitation</td>
<td>Clozapine, haloperidol, quetiapine</td>
<td>300 mg qam (bid) or (qhs)</td>
<td>50 mg to 600 mg/day</td>
</tr>
</tbody>
</table>

Approved from Tsai R, Boxer A. (Neurochem 2016)
## Cholinesterase Inhibitors

### Galantamine
- Randomized, placebo-controlled study of 36 patients (bv-FTD and PPA), eight weeks of treatment.
- Not associated with improvements in behavior (possible trend for efficacy for aphasia).  
  [Kemper A et al. Dement Geriatr Cogn Disord 2008]

### Donepezil
- Open-label study, 12 patients with FTD received donepezil and 12 did not, six months of treatment.
- No significant difference in behavior between the groups.
- Four patients on donepezil had worsened disinhibition and compulsive behaviors (improved with discontinuation of the medication).  
  [Medeiros MF et al. J Neuropsychiatry 2007]

### Rivastigmine
- Open-label study, 20 patients with probable FTD received rivastigmine, 20 patients did not, 12 months of treatment.
- Rivastigmine group had improved mood, behavioral symptoms, and reduced caregiver stress.
- Cognitive measures were not changed.  
  [Moretti R et al. Drugs Aging 2004]

---

### Bottom Line: Cholinesterase inhibitors are not recommended (may worsen behavioral problems)

## Serotonergic Medications

### Fluoxetine
- Open-label study, 5 patients with FTD received drug, 3 months of treatment.
- Data suggestive of improvements in behavior.  

### Sertraline
- Open-label study, 5 patients with FTD received drug, 3 months of treatment.
- Data suggestive of improvements in behavior.  

- Open-label study, 16 patients with FTD received drug, 6 months of treatment.
- Improved behavior (stereotypies) with medication.  
  [Mendez M et al. Movement Disorders 2005]

- Open-label study, 4 patients with sv-FTD received drug, 2-4 weeks of treatment.
- Improved behavior (decreased NPI-Q) with medication.  
  [Proctor O et al. J Neuropsychiatry 2009]
## Serotonergic Medications

### Paroxetine
- Double-blind randomized cross-over, 10 patients with FTD, 6 weeks of treatment
  - No improvements in behavior or executive function measures
  - De Deu J et al. J Neuropsychiatry 2004
- Open label, randomized, controlled, 8 patients with FTD received paroxetine compared to 8 with FTD receiving placebo, 14 months of treatment
  - Improvements in behavior, and caregiver stress with paroxetine

### Citalopram
- Open label, 15 patients with FTD, 6 weeks of treatment
  - Improvements in behavior (NPI) and frontal behavioral index

### Trazodone
- Double-blind, placebo-controlled crossover, 26 patients with FTD, 12 weeks of treatment
  - Improvements in behavior (NPI), MMSE unchanged
  - Lebert F et al. Dement Geriatr Cogn Disord 2004

---

**Bottom Line:** Serotonergic medications seem to be helpful, but data is limited

---

## Antipsychotics

### Olanzapine
- Open label, 17 patients with FTD, 24 months of treatment
  - Improvements in behavior and caregiver stress (some concerns for somnolence)

### Quetiapine
- Case report, 3 patients with FTD
  - Improvements in behavior (reduced agitation)
  - Chow T, Mendez M. Am J Alzheimers Dis Other Demen 2002
- Double-blind crossover, 8 patients with FTD crossed to quetiapine and dextroamphetamine, 4 weeks of treatment
  - No improvements in behavior (NPI) with quetiapine

### Risperidone
- Case report in one patient with FTD, 16 months of treatment
  - Stabilization of cognitive decline
Antipsychotics

Apiprazole

- case report, 1 patient with FTD, 24 months of treatment
- improvements in behavior (sexually inappropriate vocalizations)

Bottom Line: Antipsychotics may be helpful, but a discussion is needed for increased mortality and possible extrapyramidal side effects

Seizure Medications

Topiramate

- case series, 3 patients with FTD, 6 weeks of treatment
- improvements in behavior (abnormal eating)

- case report, 1 patient with FTD, 6 months of treatment
- improvements in behavior (alcohol consumption, but not other behavioral issues)

Valproic Acid

- case series, 3 patients with FTD
- improvements in behavior (reduced agitation)
  Chow T, Mendez M. Am J Alzheimer’s Dis Other Dement 2002

Carbamazepine

- case report, 1 patient with FTD, 6 months of treatment
- improvements in behavior (sexually inappropriate behavior)
Seizure Medications

**Bottom Line:** Seizure medications may help, but little data is available

---

Other Medications

**Memantine**
- open label, 3 patients with FTD, 3 months of treatment
  - improvements in behavior (NPI)
  - Stenmark A et al. Alzheimer Dis Assoc Disord 2007

- open label, 21 patients with FTD, 13 patients with semantic dementia, 9 patients with nonfluent aphasia, 26 weeks of treatment
  - improvements in behavior (NPI) in FTD patients
  - Swanberg MM. Alzheimer Dis Assoc Disord 2007

- double-blinded, randomized, placebo-controlled study, 23 patients with bvFTD received memantine and 26 did not, 26 weeks of treatment
  - no significant difference in behavior or cognition between the groups

- double-blinded, randomized, placebo-controlled study, 39 patients with bvFTD or semantic dementia received memantine and 42 did not, 26 weeks of treatment
  - no significant difference in behavior or cognition between the groups (more patients in memantine group had worsening of cognition)

**Bottom Line:** Memantine is not recommended (may worsen cognition)
Other Medications

**Dextroamphetamine**
- double-blinded crossover, 8 patients with FTD crossed to quetiapine and dextroamphetamine, 4 weeks of treatment
- some improvements in behavior (NPI) with dextroamphetamine

**Selegiline**
- case series, 3 patients with FTD, 3 months of treatment
- improvements in behavior (NPI)

**Oxytocin**
- double-blinded, randomized, placebo-controlled crossover, 20 patients with FTD, 1 dose of treatment
  - improvement in behavior (NPI) in evening of dose

- double-blinded, randomized, placebo-controlled crossover, 23 patients with FTD, 1 week of treatment
  - tolerated and safe, possible trend toward improvements in behavior

**Bottom Line:** Limited data for stimulants, MAOIs, and oxytocin

Other Medications

**Non-Pharmacologic**

**The ABC Model**
(A) Antecedent → (B) Behavior → (C) Consequences
- Modifying the antecedent or consequences to improve safety and reduce impact on caregivers
- Successes that behaviors are a result of the disease process
- Successful strategies include avoiding triggers and modifying reactions to triggers that cannot be avoided
  - Merrilees J. Alzheimer Dis Assoc Disord 2007
  - Smith M, et al. Geriatr Mental Health Train Ser 2005

**The DICE Model**
(D) Describe → (I) Investigate → (C) Create → (E) Evaluate
- Similar to the ABC model, but the process is more delineated
- Provides a structure for clinician to work with caregiver on specific interventions
Summary: Symptom Management

- Non-pharmacological strategies are considered first-line treatment for behavioral issues
- Cholinesterase inhibitors are not recommended (may worsen behavioral problems)
- Memantine is not recommended (may worsen cognition)
- Serotonergic medications seem to be helpful, but data is limited
- Antipsychotics may be helpful, but must discuss increased mortality and possible extrapyramidal side effects
- Seizure medications may help, but little data is available
- Limited data for stimulants, oxytocin, MAOIs