#### **DUKE DEMENTIA FAMILY SUPPORT PROGRAM**

#### **Caregiver Connections** An Educational Webinar Series With The Experts

#### The presentation will begin shortly. Thank you for your patience!

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# Medications & Dementia

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# Disclosures

• No disclosures



# Outline

- Background
- Symptomatic Treatments:
  - Memory & Thinking
  - Depression & Anxiety
  - Behaviors
  - Sleep
- Disease-Modifying Medications:
  - Anti-amyloid antibodies



# What do we mean by mild cognitive impairment (MCI) and dementia?

#### Normal Cognition



- I notice subtle changes in my memory and thinking
- Cognitive assessment is normal.
- These changes <u>do not</u> interfere with my day to day activities.

#### Mild Cognitive Impairment (MCI)

- There are changes in my memory and thinking that I and others notice.
- These changes are picked up on cognitive assessments.
- These changes <u>do not</u> interfere with my day to day activities.
- These changes aren't caused by another medical or psychiatric problem.

#### **Dementia**

- There are changes in my memory and thinking that
   I and others notice.
- These changes are picked up on cognitive assessments.
- I <u>need extra help with day</u> to day activities.
- These changes aren't caused by another medical or psychiatric problem.

# MCI and dementia are "umbrella" terms

- MCI and dementia are syndromes or "umbrella" terms which describe a group of symptoms that occur together.
- They describe cognitive symptoms and their impact on function.
- They don't tell us what's going on in the brain that is causing the symptoms.
- There are different diseases that can cause MCI and dementia.



# What diseases cause MCI/dementia?

#### **Alzheimer's Disease**

- Accounts for 60-80% of dementia
- Progressive cognitive decline typically beginning with short-term memory



#### Vascular Cognitive Impairment

- Often co-occurs with AD
- Dementia primarily caused by cerebrovascular disease or impaired cerebral blood flow

#### Lewy Body Disease

- Accounts for 30% of dementia
- Progressive cognitive decline with cognitive fluctuations, visual hallucinations, REM sleep behavior disorder, and Parkinsonisms

#### $\alpha$ Synuclein



80% Have AD Neuropathology

### **Frontotemporal Disease**

- Typically presents in 50s
- Accounts for ~10% of dementia in ≤65 years
- Includes behavioral variant and nonfluent and semantic primary progressive aphasia.



And Others

# **Types of Treatment**

### Symptomatic Treatments

- Address symptoms of disease, but do not affect the disease process or address underlying issue that caused the disease
- Medications are available for cognitive, mood, and behavioral symptoms

### Disease-Modifying Treatments

- Addresses the underlying problem causing the disease, which slows down or preventing disease progression
- Anti-amyloid antibodies for Alzheimer's Disease

# **Cognitive Symptoms**

### Cholinesterase Inhibitors

- Increase acetylcholine in the brain.
- Includes:
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Razadyne)

### NMDA-Receptor Antagonists

- Decreases excessive glutamate signaling in the brain.
- Includes:
  - Memantine (Namenda)

### Cholinesterase Inhibitors



- Rivastigmine (Exelon)
- Galantamine (Razadyne)

- Increase acetylcholine in the brain.
- Appear to work similarly well across stages.
- Benefits are generally modest.
- May work better in Dementia with Lewy Bodies.
- No evidence of benefit in frontotemporal dementia.

### Cholinesterase Inhibitors



- (Aricept)
- Rivastigmine (Exelon)
- Galantamine (Razadyne)

### Side Effects

- Upset stomach, nausea, diarrhea, and decreased appetite occur in 20-30% of people.
- Insomnia, vivid dreams, and other sleep problems These side effects may be more common with donepezil.
- Less commonly, can slow the heart rate and cause muscle cramps.
- Cholinesterase inhibitors are generally safe.

### NMDA-Receptor Blocker



- Memantine (Namenda)

- Decreases excessive glutamate signaling in the brain.
- Helps improve memory and thinking and function.
- Benefits are generally modest at best and may be greater in more advanced disease.
- Limited evidence of benefit in Lewy Body disease.
- Not recommended in frontotemporal dementia.

### NMDA-Receptor Blocker



- Memantine (Namenda)

### Side Effects

- Generally, well tolerated. Most common side effect is dizziness.
- Can rarely increase confusion and hallucinations.

# Affective (Mood) Symptoms



- Depression
- Anxiety
- Apathy

- Mood changes are common in cognitive impairment
- Sometimes mood symptoms can occur before cognitive changes
- The evidence that common antidepressants help depression in AD is mixed.
- Cholinesterase inhibitors and memantine can sometimes help with affective symptoms.

# Affective (Mood) Symptoms



- Escitalopram (Lexapro)
- Citalopram (Celexa)
- Sertraline (Zoloft)
- Talk Therapy

- Mood changes are common in cognitive impairment
- Sometimes mood symptoms can occur before cognitive changes
- The evidence that common antidepressants help depression in AD is mixed.
- Low dose stimulants like Ritalin are sometimes used for apathy.
- Cholinesterase inhibitors and memantine can sometimes help with affective symptoms.

# Behavioral Symptoms



- Agitation
- Delusions
- Hallucinations
- Paranoia
- Wandering
- Disinhibition

- Behavioral symptoms can occur in 60-90% of people living with dementia.
- Symptoms often peak in the late afternoon or evening (sundowning).
- Behavioral symptoms are more common in more advanced stages of disease.
- Behavioral symptoms worsen memory and thinking and reduce day to day function.

# Behavioral Symptoms



 Non-Drug Strategies

- The initial approach to behavioral symptoms should focus on identifying and addressing potential triggers:
  - Medication side effects
  - Untreated pain
  - Delirium
  - Sleep problems
  - Vision & hearing problems
  - Boredom
  - Depression and anxiety
  - Communication

# Behavioral Symptoms



- Trazodone
- Antipsychotics
- Pimavanserin (Nuplazid)
- Nuedexta
- Brexpiprazole (Rexulti)

- Medications are sometimes required to manage behavioral symptoms.
- Cholinesterase inhibitors, memantine, and antidepressants should be started before trying other medications.
- Low-dose trazodone at night can sometimes help, especially in people with trouble sleeping.
- Antipsychotics are used as a last resort as they can have serious side effects.
- Newer medications like Pimavanserin, Nuedexta, and Brexpiprazole may help, but they are expensive and its unclear if they are more effective.



- Pimavanserin (Nuplazid)
- Brexpiprazole (Rexulti)

### Antipsychotic Side Effects

- Can cause sedation, increase the risk of falls, and some have anticholinergic side effects that can worsen memory and thinking.
- Sometimes these medications can cause abnormal movements, Parkinsons like symptoms, and tardive dyskinesia.
- People with Lewy Body disease can have severe side effects with these medications.
- There is a small, 1-2%, increased risk of death in people with dementia who take these medications.



- 25-35% of people with Alzheimer's disease will have sleep disturbances.
- REM sleep behavior disorder (acting out dreams) is also common in Lewy Body disease.
- Evaluation should focus on addressing factors contributing to poor sleep and optimizing sleep hygiene.
- Z-drugs (Ambien) and anti-histamines like Tylenol PM or Benadryl should be avoided.
- Melatonin, low dose trazodone or newer sleep medications like Suvorexant (Belsomra) or daridorexant (Quviviq) are preferred.

# Alzheimer's Disease

The most common cause of dementia



# Anti-Amyloid Therapy

#### **Before Treatment**

**After Treatment** 





Does getting rid of amyloid help memory and thinking?

### Lecanemab (Leqembi)

#### **Amyloid PET Scan**

**Before Treatment** 



1.Dyck, C. H. van et al. Lecanemab in Early Alzheimer's Disease. New Engl J Med (2022) doi:10.1056/nejmoa2212948.

# Anti-Amyloid Side Effects

- Most concerning side effect of anti-amyloid antibodies is *Amyloid Related Imaging Abnormality* (ARIA).
- Anti-amyloid antibodies can cause brain swelling (edema) or small areas of bleeding (hemorrhage).
- Most cases of ARIA are asymptomatic. Common ARIA-related symptoms can include dizziness, headache, confusion, fatigue.
- There have been some deaths related to ARIA.



<u>ARIA-E</u>

Edema or Swelling

ARIA-H Hemorrhage or Bleeding

## Pros & Cons of Anti-Amyloid Antibodies

#### **Potential Benefits**

- More time in the milder stages of the disease with more independence and better day to day function. More time spent living at home.
- For people with MCI due to Alzheimer's disease, this might mean delaying progression to dementia by 3 years.

#### Potential Downsides

- Spending hours every other week at an infusion center.
- Some people may have significant out of pocket costs.
- Side effects can include brain swelling, bleeding, and death.

# Medications in Dementia

#### **Behavioral Medications**

#### Talk Therapy or SSRIs

#### Cholinesterase Inhibitor or Memantine

#### **Anti-Amyloid Antibodies**

#### Physical Activity, Lifestyle, & Sleep

For behavioral symptoms that do not respond to
other treatments and non-drug strategies, we use more potent medications at low doses.

For depression and anxiety, talk therapy and/or an antidepressant can help. SSRIs may also help with behavioral symptoms and memory/thinking.

Cholinesterase inhibitors and memantine can help with affective and behavioral symptoms in addition to helping memory and thinking.

Anti-amyloid antibodies may be appropriate for people with early Alzheimer's disease.

Managing symptoms in dementia should begin by addressing physical activity, lifestyle, and sleep as these can worsen cognition and contribute to behaviors.

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