Objectives
- Assessment and Diagnosis
- Treatment Options
  - Pharmacological
    - What are implications for or against pharmacological treatment?
  - Nonpharmacological
    - What nonpharmacological treatment options/management are there
    - How are patient/families referred for these

Cognitive Continuum

Normal

Mild Cognitive Impairment (MCI)

NCD-Dementia

NEUROCOGNITIVE DISORDER (NCD)

DSM 5

Major Neurocognitive Disorder (NCD)-dementia
  Alzheimer’s NCD

Dementia-DSM 5

There is evidence of substantial cognitive decline from a previous level of performance in one or more of the domains

The cognitive deficits are sufficient to interfere with independence
Benefits of having AD

- You never have to watch ‘reruns’ on TV
- You are always meeting ‘new’ people
- You don’t have to ‘remember’ whines of your spouse
- You can ‘hide’ your own Easter eggs

MILD COGNITIVE IMPAIRMENT (MCI)

- There is evidence of modest cognitive decline from a previous level of performance in one or more of the domains
- The cognitive deficits are insufficient to interfere with independence

MCI may increase your risk of later progressing to dementia 12% per year.
• 15 to 40% of patients with MCI can revert to normal cognitive state with lifestyle modification—Brain Wellness Program.

SAVE YOUR BRAIN:
- Eat a low fat diet
- Exercise
- Challenge your brain
- Reduce stress
- Socialize


• Cognitive training
• Blood pressure management for people with hypertension
• Increased physical activity

NORMAL COGNITIVE DECLINE
Normal Aging | Dementia
---|---
Not being able to remember details of a conversation or event that took place a year ago | Not being able to recall details of recent events or conversations
Not being able to remember the name of an acquaintance | Not recognizing or knowing the names of family members
Forgetting things and events occasionally | Forgetting things or events more frequently
Occasionally have difficulty finding words | Frequent pauses and substitutions when finding words
You are worried about your memory but your relatives are not | Your relatives are worried about your memory, but you are not aware of any problems
Making a bad decision once in a while | Poor judgment and decision-making
Missing a monthly payment | Inability to manage a budget
Forgetting which day it is and remembering it later | Losing track of the date or the season
Sometimes forgetting which word to use | Difficulty having a conversation

**ASSESSMENT AND DIAGNOSIS**

Alzheimer's Begins Years Before Symptoms Emerge

ASSESSMENT: HISTORY

Ask both the patient and a reliable informant about the patient’s:
- Date of onset of current condition, chronology and nature of symptoms
- Medical history
- Current medications & medication history
- Patterns of substance use or abuse
- Living arrangements

ASSESSMENT: PHYSICAL

Examine:
- Neurologic status
- Mental status
- Functional status (direct observation or informant report)

Include:
- Quantified screens of cognitive function
  - For example, Folstein’s MMSE, Mini-Cog, SLUMS, MoCA
- Neuropsychologic testing when presentation is atypical or if results are confounded by a high level of education or subtle changes
**ASSESSMENT: LABORATORY**

Routine

- CBC
- Na+, Ca++
- BUN/Cr
- Fasting glucose
- RPR
- TSH
- Vitamin B₁₂ level

Optional (based on clinical exam and suspicion)

- Liver function
- Folic acid
- Homocysteine/methylmalonic acid
- Urinalysis / Toxicology
- CSF analysis
- HIV testing

**ASSESSMENT: BRAIN IMAGING**

Consider imaging when:

- Onset occurs at age < 65 years
- Symptoms begin suddenly or progress rapidly
- There is evidence of asymmetric or focal neurologic deficits
- Clinical picture suggests normal-pressure hydrocephalus
- Patient has had recent fall or other head trauma

Consider:

- Noncontrast CT head scan
- MRI
- Positron emission tomography (PET) when diagnosis remains uncertain

**Magnetic Resonance Imaging (MRI)**

- Detects regional (medial temporal lobe) atrophy in AD
  - Entorhinal cortex, hippocampus, amygdala, and parahippocampus
- Even mildly affected individuals have:
  - 20-30% loss in entorhinal cortex volume
  - 15-25% loss in hippocampal volume
  - Ventricular enlargement

**18F-2-Fluoro-2-Deoxy-D-Glucose Positron Emission Tomography (FDG-PET)**

- Indirect measure of synaptic activity (glucose metabolism)
  - FDG-PET in AD may reflect:
    - Mitochondrial dysfunction
    - Oxidative stress
    - Abnormal synaptic plasticity
    - Excitotoxicity
    - Glial activation and inflammation
    - Reduced cerebral blood flow
    - Synapse loss and cell death

Amyloid Imaging

- In vivo surrogate for Aβ pathology
- Utilizes PET imaging of tracers that bind to Aβ
  - Pittsburgh Compound B (PiB)
- Amyloid binding is seen in 20-40% of cognitively normal elderly; indicative of impending AD?

Herrmann N et al. Drugs 2011;71(15):2031-65; Honig LS. Arch Neurol 2012; Epub

Assessment

2nd Visit (30-45mins) Discuss:
- Findings from the 1st visit
- Any other Neuroimaging- Amyloid PET scan ($3,000)
- Life Style modification and cognitive function
- Role of Medications/OTC
- Role of genetic testing- ApoE and others
- Professional/social concerns/documentation
- MCI research studies –MAYO CLINIC or U of Iowa
  - EARLY (Prevention AD Study)
  - ADNI-3 (Longitudinal Study for everyone - those will memory concerns and those with normal cognition)
  - NIC (Mild Cognitive Impairment)

Neurotransmitters

- ↓ Acetylcholine (Ach)
- ↓ Serotonin (5 HT)
- ↑ Glutamate

Risk Factors - Established

- Family history
- Down’s Syndrome
- APOE-E4 (whites)
- A. fibrillation

NEUROCHEMISTRY

RISK FACTORS FOR AD
CASES OF DEMENTIA COULD BE PREVENTED BY ADDRESSING THESE LIFESTYLE FACTORS

1 IN 3

DEMENTIA RISK REDUCTION

20% of dementia risk factors are potentially modifiable.

- Mid-life hearing loss - 9%
- Failing to complete secondary education - 35%
- Smoking - 5%
- Physical inactivity - 3%
- Failing to seek early treatment for depression - 4%
- Type 2 Diabetes - 1%
- Obesity - 1%
- High blood pressure - 2%
- Social isolation - 2%
- Physiological Inactivity - 3%

Risk Factors Possible

- Low education attainment
- Physical inactivity
- Lack of social interaction
- High stress levels
- Previous head trauma

Risk Factors Possible (con.)

- Smoking
- Alcohol
- Health conditions

Risk Factors –Health conditions

- Stroke
- Midlife Hypertension
- Diabetes
- Midlife Obesity
- Depression
- Obstructive Sleep Apnea (OSA)
- Post Operative Cognitive Decline (POCD)

NON REVERSIBLE DEMENTIAS
Non reversible causes

Alzheimer’s (AD)
Vascular (VaD)
Frontotemporal (FTD)
Mixed (AD and VaD)
Lewy Body (DLB)

Dementia: Stages of Decline

- Early/mild: forgetfulness; short-term memory loss; misplaces items; trouble with complicated tasks; searches for words
- Middle/moderate: increased language problem; forgets major events; may need help dressing, cooking; may have a decrease in personal hygiene
- Late/severe: verbal communication dwindles; needs help eating, bathing; significant long-term memory loss; decline in motor abilities; does not recognize family members

Reversible (risk factors) causes of Dementia

DREVERSIBLE DEMENTIAS

- Drugs
- Emotional illness-depression
- Metabolic/endocrine disorders
- Eye/ear/environment
- Nutritional/neurologic
- Tumors/trauma
- Infection
- Alcoholism/anemia/atherosclerosis

ACETYL CHOLINE (ACH) IS REQUIRED FOR MEMORY
ANTICHOLINERGIC MEDICATIONS ARE BAD NEWS FOR MEMORY

APPROXIMATELY 50% OF THE OLDER POPULATION TAKES AT LEAST ONE ANTICHOLINERGIC DRUG.

KEEP CALM AND CARRY ON DEPRESCRIBING

The most common anticholinergic classes
• Tricyclic antidepressants
• First-generation antihistamines
• Bladder antimuscarinics
• Comprised >90% of all anticholinergic exposure.

REMOVE OFFENDING ANTICHOLINERGIC AGENTS

The most common drugs
Doxepin
chlorpheniramine
oxybutynin

http://www.pharmacytimes.com/contributor/timothy-o-shea/2015/02/frequently-prescribed-medications-linked-to-increased-dementia-risk
Popular OTC -anticholinergic

- Advil PM (pain and sleep)
- Benadryl (for allergies)
- Dramamine (for motion sickness)
- Excedrin PM (for pain and insomnia)
- Pepcid AC (acid reflux)
- Sominex (for insomnia)
- Tagamet (acid reflux)
- Tylenol PM (for pain and insomnia)

Drugs That May Cause Memory Loss

Antianxiety drugs
Narcotic painkillers
Sleeping aids
Incontinence drugs -Anticholinergics
Antihistamines
Cholesterol drugs
Antidepressant drugs
TCA

Drugs

- Regularly review medications and supplements
- Manage medications that could affect cognition
- Do frequent medication reconciliation

ANTSOLINERGIC DRUG BURDEN INDEX (DBI)

http://www.anticholinergicscales.es/calculate

ANTSOLINERGIC SIDE EFFECTS
Anticholinergic side effects

- Confusion
- Hallucinations
- Delirium
- Dry mouth
- Pupil dilatation/blurred vision
- Urinary retention
- Constipation
- Tachycardia

In addition, hypotension related to intensive treatment of hypertension and hypoglycemia related to intensive treatment of diabetes may also contribute to cognitive decline.

Primary goal of treatment

To enhance quality of life and maximize functional performance by improving or stabilizing cognition, mood, and behavior.
CHOLINESTERASE INHIBITORS (CHEI)

Medications

- Cholinesterase Inhibitors
  - Cognex
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Reminyl)

- Glutamate Receptors
  - Memantine (Namenda)

MEMANTINE

- Neuroprotective effect is to reduce glutamate-mediated excitotoxicity
- Modest benefit on cognition, ADLs, and behavior in AD
- Limited effect on cognition and no evidence to support widespread use in vascular dementia
- FDA-approved for moderate to severe AD
- Common adverse events: constipation, dizziness, headache

BRIAN WELLNESS – FOR US

NEUROPLASTICITY
INCREASE COGNITIVE RESERVE

NONPHARMACOLOGIC MANAGEMENT (1 of 2)
- Cognitive rehabilitation
- Supportive individual and group therapy
- Physical and mental activity
- Regular appointments every 3–6 months
- Family and caregiver education and support
- Attention to safety
  - Need for supervision, wandering, driving etc.

NONPHARMACOLOGIC MANAGEMENT (2 of 2)
- Environmental modification
  - Supportive strategies such as clocks, calendars, to-do list, visual clues, simple and compassionate communication style
  - Structure activities to match patient abilities

SUMMARY (1 of 2)
- Dementia is common in older adults but is not an inherent part of aging
- AD is the most common type of dementia, followed by vascular dementia and dementia with Lewy bodies
- Evaluation includes history with informant, physical & functional assessment, focused labs, & possibly brain imaging

SUMMARY (2 of 2)
- Primary treatment goals: enhance quality of life and maximize function by improving cognition, mood, behavior
- Treatment may involve both medications and nonpharmacologic interventions
- Community resources should be used to support patient, family, caregivers
4 PILLARS

- The Right Diet
- Physical Activity
- Brain Engagement
- Social Interaction (meaningful)

NUTRITION-FOOD FOR THOUGHT

SMART FOODS

- Blueberries
- Salmon
- Broccoli
- Spinach
- Red Wine/grape juice
- Dark chocolate/hot coco

MEDITERRANEAN DIET

EXERCISE- MOVING MORE

- Better blood flow and oxygenation
- BDNF
  - More neurogenesis - more brain cells
  - More synaptogenesis - more connection
- Less stress hormones
BRAIN POWER: Use it or lose it

Neurobics
It is NOT about getting the right answer,
It is the search that’s beneficial.

Exercise-cognitive
- Take classes
- Read regularly and keep a journal
- Stay up-to-date on technology

Activities associated with high cognitive function in older adults

Intellectually Engaging Activities
- Puzzles, discussion groups, reading, using the computer, playing bridge, playing board games, playing musical instruments, 27,31-33
- Careers that involve high complexity, 34-38
- High educational attainment, 39,42

Physical Activities
- Exercise, especially that which improves cardiovascular health, 40
- Gardening, 41
- Dance, 42

Social Engagement
- Travel, cultural events, 43
- Socializing with friends and family, 44

4 PILLARS
- The Right Diet
- Physical Activity
- Brain Engagement
- Social Interaction (meaningful)
Cognitive Impairment: Impact of Medications and Transitions

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CLINICAL ASSOCIATE PROFESSOR
UNIVERSITY OF IOWA COLLEGE OF PHARMACY

Objectives
- Evaluate a patient’s medication regimen for medications which have an anticholinergic effect and recommend alternative therapy.
- Discuss the use of antipsychotics in the treatment of neuropsychiatric symptoms associated with dementia.
- Appropriately monitor and attempt discontinuation of antipsychotics when used for the treatment of neuropsychiatric symptoms associated with dementia.
- Identify transitions of care issues involving medications and cognitively impaired patients.

Anticholinergic Burden

Why Are Anticholinergic Medications Used in Older Adults?
- Allergies
- Behavioral problems
- Depression
- Parkinson’s Disease
- Psychotic symptoms
- Urinary incontinence
- Treatment of side effects of other medications

Adverse Effects of Anticholinergics

<table>
<thead>
<tr>
<th>PERIPHERAL</th>
<th>CENTRAL NERVOUS SYSTEM</th>
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<tbody>
<tr>
<td>Blurred vision</td>
<td>Agitation</td>
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<tr>
<td>Constipation</td>
<td>Confusion</td>
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<tr>
<td>Dry mouth</td>
<td>Delirium</td>
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<tr>
<td>Impaired sweating</td>
<td>Hallucinations</td>
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<tr>
<td>Nausea</td>
<td>Memory impairment</td>
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<tr>
<td>Tachycardia</td>
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<tr>
<td>Urinary retention</td>
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</tr>
</tbody>
</table>

Anticholinergics and Dementia
- Dementia damage to cholinergic neuronal system
- Anticholinergic medications lead to further decline
- Block cholinergic response
- Patients with dementia are more susceptible to anticholinergic CNS adverse effects than general population
### Medications with Anticholinergic Properties

- Many lists and scales have been developed
- Increasing the number of medications with anticholinergic properties in a patient’s regimen will increase the risk of anticholinergic side effects

### Anticholinergic Risk Scale (ARS)

- Developed by Rudolph et al.
- Validated to estimate the extent to which a patient’s anticholinergic burden may lead to cognitive dysfunction and delirium
- Ranking of medications on a 3 point scale (1 low risk; 3 high risk)
- The ARS score is the sum of points for all medications on the patient’s regimen

#### ARS: Three Point Medications

- Amitriptyline
- Atropine
- Benztropine
- Carisoprodol
- Chlorpheniramine
- Chlorpromazine
- Cyproheptadine
- Dicyclomine
- Diphenhydramine
- Fluphenazine
- Hydroxyzine
- Imipramine
- Medclizine
- Oxybutynin

#### ARS: Two Point Medications

- Amantadine
- Baclofen
- Cetirizine
- Cimetidine
- Clozapine
- Cyclobenzaprine
- Desipramine
- Loperamide
- Loratadine
- Nortriptyline
- Olanzapine
- Prochlorperazine
- Pseudoephedrine/Triprolidine
- Tolterodine

#### ARS: One Point Medications

- Carbidopa/levodopa
- Entacapone
- Haloperidol
- Methocarbamol
- Metoclopramide
- Mirtazapine
- Paroxetine
- Pramipexole
- Quetiapine
- Ranitidine
- Risperidone
- Selegiline
- Trazodone
- Ziprasidone

### Anticholinergic Drug Scale (ADS)

- Includes all of the medications on the ARS plus many medications not normally thought of as anticholinergic
- Levels 1, 2 and 3 (3 most anticholinergic)
- Notable additions include (all level 2)
  - Disopyramide
  - Cabazapine
  - Oxcarbazepine

**CARNAHAN ET A. J Clin Pharmacol 2008;46:ADDENDUM**
Beers Criteria List of Anticholinergics

<table>
<thead>
<tr>
<th>Antihistamines</th>
<th>Antimuscarinics</th>
<th>Antiparkinsonian agents</th>
<th>Skeletal muscle relaxants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brompheniramine</td>
<td>Dantrolene</td>
<td>Atenolol (excludes atenolol)</td>
<td>Oxycodone</td>
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<tr>
<td>Gatainoramine</td>
<td>Flunarizine</td>
<td>Betaxolol</td>
<td>Orphenadrine</td>
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<td>Chlorpheniramine</td>
<td>Fluvastatin</td>
<td>Itopride</td>
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<td>Clemizoline</td>
<td>Fosfomycin</td>
<td>Trihexyphenidyl</td>
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<td>Cyproheptadine</td>
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<td>Dextropropoxyphene</td>
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<td>Hydralazine</td>
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<td>Hydroxyzine</td>
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<td>Methazolamide</td>
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<td>Oxyphenbutazone</td>
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<tr>
<td>Dizpropanol</td>
<td>Tridione</td>
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<tr>
<td>Dizpropanol</td>
<td>Triprolidine</td>
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</tbody>
</table>

Strategies to Minimize Risk

- Avoid use of medications with highest anticholinergic effect
- Those in level three
- Minimize use of medications in level two
- Minimize dose if use is necessary
- Seek alternative medications and non-pharmacological treatment
- Look at the entire medication list and eliminate unnecessary medications which anticholinergic properties to cut down on total anticholinergic burden

Alternatives to Antihistamines

- Antihistamines for allergies
  - Avoid first generation such as diphenhydramine and chlorpheniramine
  - Use second generation such as cetirizine or loratadine
  - Use intranasal normal saline rinses
  - Use intranasal steroids
- Antihistamines for sleep
  - Avoid use in older adults, risk greater than benefit
  - Use sleep hygiene and melatonin for sleep induction
  - Use trazodone 25-50 mg
  - Use mirtazapine 7.5 mg to no more than 15 mg HS for sleep

Alternatives to Antidepressants

- For depression
  - Avoid tricyclics and paroxetine
  - Use SSRIs (other than paroxetine), SNRIs and bupropion
- For neuropathic pain
  - Use SNRI, topical capsaicin, gabapentin, pregabalin or lidocaine patch
Alternatives to Antipsychotics

- For behavioral symptoms of dementia
- Avoid in the older adult if at all possible (more later on this)
- Use non-pharmacologic strategies
- If needed for behaviors use less anticholinergic atypical antipsychotics
  - Haloperidol, aripiprazole
- Look for and treat untreated conditions
- Pain
- Depression

Alternatives for Urinary Incontinence

- Antimuscarinics
- Use extended release formulations
- Less anticholinergic side effects
- Especially avoid ditropan immediate release
- Use non-pharmacological strategies
- Medications are not that effective for many types of incontinence
- Toileting schedule
- Pads

Case: JB

- JB is an 82 year-old male with BPH, HTN, Type 2 DM and neuropathy
- Medications
  - Tamsulosin 0.4 mg daily
  - Lisinopril 10 mg daily
  - Metformin 1000 mg twice a day
  - Amitriptyline 50 mg at bedtime started 2 weeks ago for neuropathic pain symptoms
- He returns to clinic today with increasing urinary symptoms of urinary hesitancy and retention
- What do you think is going on?
- What might we recommend for JB?

Antipsychotics In Dementia Care

- Very few drugs help for problem behaviors or psychosis in dementia
- Antipsychotics are the main drug treatment
- ~72% of LTCF residents get antipsychotics
- Varies by state and facility (~16.3-29.1%)
- Effectiveness is modest
- Serious side effects, including death
- Non-drug methods are preferred
- Caregivers may be poorly trained to use non-drug behavior management techniques

What does the behavior tell you?

- Wandering → Boredom
- Calling out → Loneliness
- Grabbing → Fear of pain
- Pushing → Desire for privacy
- Agitated → Over-stimulation
- Withdrawn → Under-stimulation
- Intrusiveness → Hunger, thirst
Assess the Person & Situation
- Identify, assess, treat, eliminate triggers to problem behaviors
- Unmet physical needs
- Unmet psychological needs
- Environmental causes
- Psychiatric causes

Monitor Outcomes & Adjust as Needed
- Track behavior problems
- Assure adequate "dose" (intensity, duration, frequency) of interventions
- Adapt/add interventions as needed to get the best possible outcomes
- Make sure all people working with the person understand and cooperate with the treatment plan and are trained as needed

Options for Pharmacologic Intervention
- Pain medications
- Antidepressants
- Sedative/Hypnotics
- Cognitive enhancers
- Antipsychotics

Pain Medications
- Empiric pain management protocol in nursing home residents with agitation
  - 8 week cluster RCT vs. usual care, n=352
  - Step 1: acetaminophen (68%)
  - Step 2: oral morphine (2%)
  - Step 3: buprenorphine patch (23%)
  - Step 4: pregabalin (7%)
- Agitated symptoms improved at 8 weeks with treatment vs. usual care, and worsened in 4 week washout

Antidepressants: The CitAD Trial
- Evaluate citalopram for efficacy for agitation in patients with Alzheimer’s disease
- RCT double blind placebo trial
- N= 186 followed for 9 weeks
- All received psychosocial intervention
- Citalopram 30 mg (n=94) Vs Placebo (n=92) [before dosing limitations]

Cit-AD Outcome Measures
- Primary Outcomes
  - Neurobehavioral Rating Scale agitation subscale (NBRS-A)
  - Alzheimer’s Disease Cooperative Study-Clinical Global Impression of Change (mADCS-CGIC)
- Other outcomes monitored
  - Cognition, ADRs (QT prolongation), ADLs caregiver stress
Cit-AD Results

- Citalopram group showed significant improvement in
  - NBRS-A and mADCS-CGIC scores
  - Caregiver stress scores
- Citalopram group had increase in ADRs
  - Worsening of cognition
  - QT Prolongation

Cit-AD Conclusions

- Addition of citalopram reduced agitation and caregiver stress
- However... cognitive decline and QT prolongation may limit use
- Need to study other SSRIs which are not as likely to result in QT prolongation

Benzodiazepines (BZD) and Other Sedatives/Anxiolytics

- Numerous studies demonstrate an association between BZD use and cognitive impairment
- Limited evidence of effectiveness for behavioral symptoms associated with dementia
- Not recommended for scheduled use due to adverse effects and likelihood of worsening cognition

Cognitive Impairment With Benzodiazepines (BZD)

- Billioti de Gage et al
  - Case control study of 1796 controls with a first diagnosis of dementia between 2000-2009
  - Exposure to BZD ascertained in a time window ranging form 5-10 years before index date
  - Use of BZD at any time significantly associated with increased risk of dementia
    - OR 1.51 95% CI (1.09-1.28)
    - Association stronger for long-acting compared with short acting BDZs

Cognitive Enhancers

- Cholinesterase Inhibitors and memantine
  - Small benefits seen in studies for cognition
  - Minimal to no benefit when studied for behavioral symptoms
  - Some evidence of efficacy in Lewy Body Dementia

Nuedexta® for Behaviors

- Dextromethorphan and Quinidine
- Off-label use for agitation in AD studied by Cummings et al
  - RCT with N=220
  - Primary outcome change in agitation using the NPI scale
    - 30% change considered significant
  - Treatment group improvement of 50.7%
  - Placebo group improvement of 26.4%
Nuedexta® Safety Concerns
- ADRs
  - Falls, diarrhea, UTIs, dizziness
  - Possible serotonin syndrome
- Drug interaction concerns
  - CYP2D6 inhibition by quinidine
    - Increases dextromethorphan concentration
    - Will interact with other CYP2D6 substrates
    - Also, concerns for other CYP2D6 inhibitors
      - Fluoxetine, paroxetine

Case: LM
- LM is an 85 year-old male with dementia (MoCA=14) recently admitted to our LTC dementia unit.
- He has been increasingly disruptive behavior with cares
- Current diagnoses
  - Alzheimer’s Dementia
  - Osteoarthritis
  - Depression

Case: LM
- Current medications
  - Donepezil 10 mg HS
  - Sertraline 50 mg daily
  - Acetaminophen 1000 mg 6 hr. prn pain
- Is LM a candidate for antipsychotic therapy for his behavioral symptoms?
- What do we recommend for LM?

Antipsychotics: Typical and Atypical
- Evidence supports modest symptom improvements with:
  - Haloperidol (Haldol®)
  - Olanzapine (Zyprexa®)
  - Risperidone (Risperdal®)
  - Aripiprazole (Abilify®)
  - Quetiapine (Seroquel®)
  - Less supportive evidence
- Research does not support use of other antipsychotics in dementia

AHRQ Summary of Efficacy: Atypical Antipsychotics

<table>
<thead>
<tr>
<th></th>
<th>Aripiprazole</th>
<th>Olanzapine</th>
<th>Quetiapine</th>
<th>Risperidone</th>
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<tbody>
<tr>
<td>Dementia</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Dementia Overall</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Dementia Psychosis</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Dementia Agitation</td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
</tbody>
</table>

Legend:
++ = Moderate or high evidence of efficacy
+ = Low or very low evidence of efficacy
+/- = Mixed results

Evidence for the Use of Antipsychotics for Behavioral Disturbances
- CATIE-AD
  - Time to discontinuation was primary outcome
  - Olanzapine, Quetiapine, Risperidone no better than placebo
  - Time to discontinuation due to lack of efficacy favored Olanzapine and Risperidone
  - Time to discontinuation due to adverse effects favored placebo

Antipsychotics and Mortality in Dementia

- Black Box Warning issued in 2004
- Elderly with dementia-related psychosis treated with these drugs at increased risk for death compared to placebo
- Consistent across all antipsychotics
- Accumulating evidence suggests conventional antipsychotics have a higher risk
  - Relative risk = 1.6-1.7
  - Absolute risk = 3.5% vs. 2.3% with placebo
- Number Needed to Harm (NNH) = 83
- Number Needed to Treat (NNT) = 5-14

More Evidence of Harm

- Increased risk of acute kidney injury in adults >65 receiving atypical antipsychotics
  - Not part of Black Box Warning
  - Population based cohort study RR 1.73 (95% CI 1.55-1.92)
- All-cause mortality
  - RR 2.39 (2.28-2.50)
  - NNH = 27

Use of Antipsychotics for Behavioral Problems in Dementia

- May be used after other approaches fail
- FDA status
  - Antipsychotics are not indicated for the treatment of dementia-related psychosis
- Should discuss the risk of increased mortality with patients and families

Important Areas to Discuss When Considering Antipsychotics

- Information gathering
  - What are the overall patient goals and what are the specific goals of treatment
  - Good time to share prognosis and correct unrealistic assumptions
  - Why do they think the patient is having these behaviors?
- Share the facts
  - What has been tried
  - The goals for treatment
  - Offer all alternative treatments
  - Risks of treatments

Use of Antipsychotics for Behavioral Problems in Dementia

- Clearly document treatment targets before starting drug therapy
  - Frequency
  - Severity
  - Time of day
  - Environmental or other triggers
- Use quantitative and qualitative descriptions
  - Be specific (biting rather than agitation)
- Continue to document during use

Potentially Appropriate Antipsychotic Treatment Targets

- Hallucinations
- Delusions (note: memory problems are often mistaken for delusions, e.g. thinks people are stealing lost items)
- Aggressive behavior (especially physical)
Appropriate Antipsychotic Treatment Targets
- If the symptom (hallucination, delusion or aggressive behavior) presents a danger to the patient or others
- Or causes the patient to experience
  - Inconsolable or persistent distress
  - Significant decline in function
  - Substantial difficulty receiving needed care

Dementia Type-Specific Issues
- Frontotemporal Dementia
  - Some efficacy with trazodone and SSRIs
- Parkinson’s Disease / Lewy Body Dementia
  - Tolerate antipsychotics poorly
  - Reduce anti-Parkinson med doses for psychosis
- Pimavanserin (Nuplazid®) NEW for Parkinson's Disease psychosis

Pimavanserin (Nuplazid®)
- New antipsychotic with no effect on dopaminergic receptors
- Less likely to cause exacerbation of Parkinson's symptoms
- Indicated only for psychosis associated with Parkinson’s Disease
- Adverse effects
  - Peripheral edema
  - Cognitive impairment
  - Nausea
  - Constipation
- Has the same antipsychotic Black Box Warning regarding mortality

Monitoring Antipsychotic Use
- Start with a time limited trial
- Monitor for effectiveness
- Specific target behaviors
- Monitor for adverse effects

Antipsychotic Adverse Effects
- Sedation
- Postural hypotension
- Falls
- Extrapyramidal
- Parkinsonism
- Cerebrovascular
- Mortality
- Urolithiasis and cardiac
- Metabolic side effects (weight gain, etc.)
Managing Adverse Effects

- Options
- Dose Reduction
- Change Drug
- Discontinue the Medication

Case: TS

- TS was started on haloperidol for severe neuropsychiatric behaviors including throwing a chair at his roommate, biting caregivers repeatedly and hitting residents in the hallway
- Since initiation of haloperidol 0.5 mg BID, his behaviors have subsided however he has developed a tremor and unstable gait
- What should we do?

Discontinuing Antipsychotics

- Continue medication only if there is clear evidence of efficacy
- Many do not experience exacerbation of agitation when medication withdrawn

Discontinuing Antipsychotics

- Use periodic gradual dose reductions (GDR) to assess continued need yearly
- Probably much sooner on initial prescription, e.g. 3 months max, but monitor closely for relapse
- If used in delirium, DC or taper after resolution
- Consider 25% decrease every 4-6 weeks as a general GDR guideline

Relapse Risk After Discontinuation: ADAD Trial

- Patients with Alzheimer’s disease with psychosis or agitation/aggression
- Treated with risperidone for 16 weeks
- Responders then randomized to one of three regimens
  - Continued risperidone for 32 weeks
  - Continued risperidone for 16 weeks then 16 weeks of placebo
  - Continued use of placebo only for 32 weeks

ADAD: Results

- First 16 weeks
  - Relapse rate greater in placebo group than other two groups
    - Chi^2 42.16, P<0.001
    - OR 3.19 (1.71-5.97)
- Second 16 weeks
  - Relapse rate greater in the group that switched from risperidone to placebo
    - 48% vs. 35%, P=0.02
    - HR 4.88 (95% CI 1.08-21.98)
ADAD: Implications

- Increased relapse rate but not everyone relapsed
- Still can make a case for a trial reduction or discontinuation to evaluate for continued need
- Need good behavioral symptom documentation
- To evaluate effect of discontinuation
- If need to justify re-institution of medication

Back to TS

- Four months later, LM is maintained on antipsychotic therapy
- His behaviors are well controlled and his tremor has disappeared
- What should we do?

Transitions of Care

Complications at Transitions

- Increased use of health-care system
- Hospital readmission
- Medication misadventures
- Adverse events
- Interruption of therapy
- Polypharmacy
- Increased medication expense

Case: MB

- MB is an 82 year-old female who developed SOB and fever at LTC facility admitted to hospital with pneumonia
- Other pertinent diagnosis include
  - Hypertension
  - Atrial fibrillation
  - Type 2 Diabetes

Case: MB

- Admission complicated by an increase in cognitive impairment and several episodes of delirium which were treated with the hospital delirium treatment protocol
- It is hospital day four, her pneumonia has been treated and she is cleared for discharge despite continued confusion and a significant decline in cognitive function from baseline
## Discharge Medication Orders for MB

**PRE-HOSPITAL MEDICATIONS**
- Metformin 1000 mg twice a day
- Lisinopril 20 mg daily
- Omeprazole 20 mg daily
- Sertraline 50 mg daily
- Warfarin 5 mg daily
- Acetaminophen 1000 mg tid prn pain/temp

**DISCHARGE SUMMARY MEDICATIONS**
- Pantoprazole 40 mg daily
- Levofloxacin 500 mg x 5 days
- Lisinopril 20 mg daily
- Insulin sliding scale
- Sertraline 25 mg daily
- Warfarin 3 mg daily
- Trazodone 50 mg q 6 hr pm agitation/panic
- Acetaminophen 500 mg q 6 hr pm pain
- Haloperidol 0.5 mg tid pm agitation

## Medication Reconciliation

- Metformin not on discharge summary however insulin is
- Metformin held during hospital stay and replaced with insulin
- Not caught in discharge planning
- Warfarin dose differs
- Need to verify when next INR is due
- Drug interaction between warfarin and levofloxacin which likely resulted in lower dose of warfarin
- Dose will need to be adjusted when levofloxacin is finished

- Omeprazole
  - Pantoprazole is hospital formulary PPI and automatically substituted for omeprazole
- Sertraline dose was reduced
  - Something to do with delirium and meds ordered for that as inpatient??
- Addition of haloperidol and trazadone
  - Likely part of delirium treatment which should be discontinued!

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**Thank you!**

**WHAT QUESTIONS DO YOU HAVE?**
Supporting Families through Transitions of Care

Fewer than 50% of people with Alzheimer’s disease or their caregivers reported being told of their diagnosis.

Getting the Diagnosis
Emotions run High

- SHOCK & DENIAL - You will probably react to learning of the loss with numbed disbelief. ...
- PAIN & GUILT - ...

Getting the Diagnosis
Emotions run High

- ANGER & BARGAINING - ...
- "DEPRESSION", REFLECTION, LONELINESS -

Getting the Diagnosis
Emotions run High

- THE UPWARD TURN - ...
- RECONSTRUCTION & WORKING THROUGH - ...
- ACCEPTANCE & HOPE -

A recent study of caregivers’ experience with the diagnostic process reported that it took >2 years after the initial physician visit for some patients to receive a dementia diagnosis.
Caregiving Basics

Take Good Care of Yourself
- Find moments of joy
- Manage Stress
- Respite
- Coping with change

Understanding the Diagnosis

Why Early Dementia is Not Detected/ Disclosed

Presentation Issues
- Patients are often retired and life consists of over-learned routines and/or spouse intervenes to compensate for cognitive impairment
- Patients work hard to "cover" cognitive deficits

Clinical Constraints
- Perception that memory loss is normal aging
- Diagnostic uncertainty
- Fear of causing emotional distress
- Lack of disease-modifying treatment
- Lack of time or support

Support from Care Providers
- Partner with your doctor
- Care Provider Options

Conversations about Dementia
- Respect the person with the Diagnosis Right to Know
  - Do they want to talk about it
  - Learn more
    - Principles for a Dignified Diagnosis [www.alz.org](http://www.alz.org)
    - I Have Alzheimer’s Disease [www.alz.org](http://www.alz.org)
- Telling Family and Friends
  - Relationships may change
  - Educate them about what they can expect
Conversations about Dementia

Getting Help in the Workplace
- Disclosing the diagnosis to HR
  - For the caregiver that is still working
  - For the person with the diagnosis that is still working

Benefits of Timely Diagnosis

Patients/Caregivers
- Lessened anxieties about the unknown diagnosis.
- A better chance of benefiting from treatment for symptoms
- Alter care plans of comorbid conditions to reflect patients' cognitive impairment
- Plan for the future

HCPs
- Can better address:
  - Delirium during hospitalization and its adverse outcomes
  - Frequent hospitalizations due to diabetes and hypertension
  - Medication side effects and nonadherence
  - Treatable comorbidities

The Basics of Alzheimer’s Disease and other Dementia

Brain failure…it is an irreversible, progressive brain disease that slowly destroys memory and thinking skills.

Common Irreversible Causes of Dementia
- Alzheimer’s disease
- Multi-infarct or vascular dementia (Small strokes)
- Parkinson’s disease (sometimes)
- Lewy Body disease
- Fronto-lobe diseases (i.e. Pick’s)
- Creutzfeldt-Jakob disease
- Huntington’s disease
- Head trauma
- Alcoholism
10 Warning Signs

- Memory changes that disrupt daily life
- Challenges in planning and solving problems
- Difficulty completing familiar tasks
- Confusion with time or place
- Trouble understanding visual images and spatial relationships
- New problems with words in speaking or writing
- Misplacing things and losing the ability to retrace steps
- Decrease or poor judgment
- Withdrawal from work or social activities
- Changes in mood or personality

Common Reversible Dementia

- Infection (i.e. UTI)
- Medications
- Dehydration
- Malnutrition
- Vitamin deficiencies
- Depression

The Importance of Communication in Elder Care

- A social connection is critical for all people, even the elderly with dementia
- Choose interpersonal communication over “task” talk.
- Invite them to share their stories

Communication Barriers

- Lack of opportunities
- Ignoring Talk
- Task Talk
- Elderspeak

Elderspeak

- Baby talk
- Diminutives (terms of endearment)
- Incorrect pronoun use
- Speak loudly and slowly
- Shorten statements
- Overly caring or controlling

Managing Challenging Behaviors
Meaningful Interactions

- Approach from the front
- Approach slowly
- Offer hand, palm up
- Address them by name
- Introduce yourself
- Get to eye level

Challenging Behaviors.....

- May be a way to communicate
- Behavioral Symptoms-
  - Irritability, anxiety, or depression
  - Sleep changes
  - Physical or verbal outbursts
  - Emotional distress
  - Restlessness, wandering

Find Ways to Respond....

- Are needs being met?
  - Don’t forget dignity
  - Create great life experiences
  - Adapt or change surroundings
  - Did my reaction make it worse?
  - “Tell me about that…”

Emotional Memory

- Emotional memory is NOT lost
- While a person with dementia will lose cognitive memory, they will not lose how you make them feel.
- Create moments of joy

Emotional Memory

“I’ve learned that people will forget what you said, people will forget what you did, but people will never forget how you made them feel.”

Maya Angelou

Legal and Financial Planning for the Future
As Baby Boomers Age
Incidence and Costs Will Rise

In 2017, Alzheimer’s and other dementias will cost the nation $259 billion. By 2050, these costs could rise as high as $1.1 trillion.

Legal Planning

• Make plans for health care and long-term care
• Seek the Advice of the professionals
• Elder Law Attorney
• Iowa Legal Aide
• Financial planning
• IPOST
• Powers of Attorney

Who is Eligible?

• All Medicare beneficiaries who are cognitively impaired are eligible to receive the services under the new code.
  - Persons diagnosed with Alzheimer’s, other dementias, or mild cognitive impairment.
  - Persons without a clinical diagnosis who, in the judgment of the clinician, are cognitively impaired.

Required Service Elements

- Cognition-focused evaluation, including a pertinent history and examination of the patient
- Medical decision making of moderate or high complexity (defined by the E/M guidelines)
- Functional assessment (for example, ADLs and IADLs), including decision-making capacity
- Use of standardized instruments to stage dementia
- Medication reconciliation and review for high-risk medications, if applicable
- Evaluation for neuropsychiatric and behavioral symptoms, including depression and including use of standardized instruments
- Evaluation of safety (for example, home safety), including motor vehicle operation, if applicable
- Identification of caregiver(s), caregiver needs, social supports and the willingness of caregiver to take on caregiving tasks
- Advance care planning and addressing palliative care needs, if applicable and consistent with beneficiary preference
- Creation of a care plan, including initial plans to address any neuropsychiatric symptoms and referral to community resources as needed (for example, adult day programs and support groups); the care plan must be shared with the patient and/or caregiver along at the time of initial education and support.
When, Where and By Whom?

Who Can Bill?
- Physicians, nurse practitioners, and physician assistants, clinical nurse specialists and certified nurse midwives

How Often?
- No limit on number of times code can be billed.

Where?
- Services have to be provided face-to-face

Reimbursement

- Medicare reimbursement rates can vary slightly based on the setting in which the service is provided and geographic location.
- Estimated $238 reimbursement rate for G0505 billed by a physician in a non-facility setting

Alzheimer’s Association Cognitive Impairment Care Planning Toolkit

G0505

Effective January 1, 2017
- Two distinct activities –
  1) assessment of the patient
  2) establishment of a care plan
- Both are shared with the patient and caregiver, along with education.

Note: Currently a Medicare Benefit

- Will become a CPT code in 2018.
- CMS will cover G codes, whereas private insurers typically wait until a CPT code is available.

Toolkit Development

- Expert Workgroup convened
- CMS defined the “what”; the toolkit helps answer the “how”
- Available at www.alz.org/careplanning
Toolkit

Service Elements of Planning Care for Dementia

- Use of medications/aide in care
- Use of the Functional Abilities Questionnaire
- Use of the Alzheimer’s Disease Assessment Scale (ADAS-Cog)
- Use of the Mini-Mental State Examination (MMSE)
- Use of the Nursing Home Assessment of Dual Special Needs (NHANES)

Additional Resources

- Support Groups
- Education
- Social Engagement
  - Melodies Choir
  - Memory Cafe
- Annual Conference
- Trial Match
- Volunteer Opportunities

Additional Resources from the Alzheimer’s Association

- Alz.org
- 800.272.3900
- Aging Resources
- Lifelong Links

Local Resources

- Alz.org
- 800.272.3900
- Aging Resources
- Lifelong Links

Voices of Alzheimer's Nothing About Us without us

Alzheimer's Story, Balboa Park, 1-23-17 HD.mp4
An Interdisciplinary Approach to Falls Prevention (Medical to Therapy)

Dr. David Demarest, PhD
Gail McGaughy, MS, PT, CBS
Sue Sandahl, MA, OTR/L, CBS
Tammy Miller, COTA/L, BS, CBS, CCM

Objectives

- Identify the scope of the problem as it relates to impact of falls
- Identify the components of our rehab program that works in conjunction with a medical provider with the same overall focus of fall prevention
- Address fall prevention and intervention programming

A Little About Us…

- On With Life was the dream of eight Des Moines area families who came together to support each other and help build a post-acute (our inpatient) program for their loved ones and others with brain injury
- From this we have continued to grow to include multiple branches of our program:
  - Post Acute Inpatient
  - Long Term Care for Youth and Younger Adults
  - Supported Community Living
  - Neuropsychology Services
  - Outpatient Neuro Rehabilitation
- Working with individuals with neurologic deficits and diseases as well as those with brain injuries from accidents, strokes, etc.

The Facts

- 1 in every 3 older adults (65+) fall every year.
  - Less then half tell their doctor
  - Falling once doubles your chances of falling again
- 1 in every 5 falls causes serious injury (broken bones or a head injury)
- Every year, 2.5 million older adults are seen in ER’s for injuries from falls
- Over 700,000 older adults are hospitalized from fall injury every year
  - 250,000 of these being hip fractures
  - Medical costs are $34 Billion every year
- Falls are the most common cause of head injuries

What Happens After…..

- Not all falls cause injury – but they do instill fear
  - Limbs everyday and social activities
  - Increased weakness from decreased activity
  - Depression and anxiety
- Injuries can happen
  - Limited mobility
  - Limited independence
  - Broken bones (most common are wrist, arm, ankle, hip)
  - Head injuries (particularly when using blood thinners)

Leading Causes of Brain Injury
• Gait and cognition are interrelated in older adults - declines in attention, psychomotor processing, problem-solving, and spatial awareness can have significant impact on fall probability

• Gauchard et al. (2006): persons with cognitive deficits mildly beyond normal aging were twice as likely to have fallen in the past and showed twice as many falls

• Depression correlates with the incidence of falls (Debaere et al., 2010), and severity of depression correlates with greater incidence rates (Jørgensen et al., 2012)

• Depression is related to a higher chance of recurrent falls - 3.3 to 2.2 times more likely (Stekelenburg et al., 2002)
Mild Cognitive Impairment (MCI)

- 3% of the population has Mild Cognitive Impairment (MCI), a precursor between normal aging and Alzheimer’s Disease.
- Structural differences are seen in persons with MCI - decreased white matter integrity in posterior areas of brain and gray matter reductions in the temporal lobe and other areas.
- MCI is associated with greater cognitive dysfunction and these brain changes and with an increased risk of falls. Mechanisms not well understood, however.

Back to Normal Aging

- Even in healthy adults, there is significant loss in gray and white matter, especially in the frontal and next, in the parietal lobe.
- What does the parietal lobe do? Visual-spatial/visual-perceptual skills are primary, navigation/pathfinding, spatial sense/spatial awareness.

What’s psychological and what’s biological...

- Loss of white matter over time - associated with reduced mental processing speed and working memory. White matter hypointensity on scanning predicted falls over the following 12 months (Ren et al., 2013).
- As we age, what has been automatic needs to become more under conscious control - have to pay attention more, in driving, in walking, in problem-solving (though “overlearned” skills are still in play). “Motor automaticity” is reduced - it’s why older persons start looking at their feet more.
- BUT - guess what we use to attend in a more focused fashion? The frontal lobe! (You’re screwed if you do; you’re screwed if you don’t)

More regarding depression

- In depressed patients, gray and white matter integrity is reduced in the frontal areas.
- White matter pathology is observed in the prefrontal region in depressed patients.
Our Program

- Our comprehensive program looks to:
  - To decrease risk of injury
  - Improve independence
  - Increase quality of life

- Utilizes a medical and therapy component

Treatment Course

- Medical Evaluation
  - From this, if appropriate you are referred for additional assessment by PT/OT

- Physical and Occupational Therapy Assessment
  - Strength, Vision, Balance, Coordination, Cognition
  - Home modification recommendations
  - Home exercise program

The Medical Perspective

Detailed Medical History
  - Acute, chronic, aging

Medications
  - Side effects, dosages

Falls Checklist/Questionnaire
  - Identify their frequency of falls, concerns, issues

Medical (continued)

Recommendations for continued care (as appropriate):
  - Metabolic/Bloodwork
  - Cardiac:
    - EKG, Echo, Holter Monitor
    - Neurologic:
    - EEG
  - Other:
    - Podiatry Consult
    - Formal Vision Evaluation
    - PT/OTEval and treatment
    - Primary Care Physician Follow Up

Physical and Occupational Therapy Evaluation, Treatment, Recommendations

- Evaluation
  - Falls History
    - How often? Reasons? Injuries?
  - Home Environment
    - Layout? Steps? Flooring? Lighting?
  - Family/Caregiver Supports
    - Education
  - Pain
    - Where? Frequency?
  - Personal Goals
    - What’s important to them?

Physical Therapy

- Strength
- Range of Motion
- Coordination
- Sensation
- Vestibular Function/Dizziness,
- Balance
- Gait/Walking
**Occupational Therapy**

- Activities of Daily Living
  - Bathing, Dressing, Grooming
- Instrumental Activities of Daily Living
  - Homemaking Skills: Cooking, Cleaning, Laundry
  - Home Maintenance: Yardwork, Fix-it Projects
- Driving
- Strength
- Range of Motion
- Coordination
- Vision/Visual Perception
- Cognition
- Reaction Time

**Physical and Occupational Therapy**

**Evaluation, Treatment, Recommendations**

- Physical Therapy
  - Exercise
  - Stretching
  - Balance Training
  - Gait Training
  - Vestibular Training
  - Proprioceptive Training

- OT Treatment
  - Safety Training
  - Adaptive Equipment Training
  - Organization and Planning
    - Planner/Calendar
  - Exercise
    - Home program
  - Reaction Time Training
  - Vision Training

**Insurance**

- Medical Evaluation
  - Billed through the medical provider as a regular appointment
- Therapy Assessment
  - PT/OT benefits through insurance plan

**To Get Started....**

- Medical Evaluation Scheduled
- Physical Therapy Evaluation
- Occupational Evaluations
- Specialist Referrals
- Contact with PCP
Questions?