Diagnosis and Treatment of Dementia
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Outline
- When is screening happening?
  - Clinic screening tools
  - Memory Clinic Diagnostics
  - Expected progression
  - Pharmacologic Therapies
  - Non-pharmacologic Therapies

When are clinicians screening?
- Annual Wellness Visit (required)
- Health report
- Patient reports problems (sens 45-55%, spec 75-85%)
- Family reports problems (sens ~95%, spec ~85%)
- Clinician suspicion
- All patients >80 (NIA, USPSTF)

Normal aging
- “Occasional” and “Temporary” memory lapses
- Decline with normal aging:
  - Processing speed
  - Rapid novel problem solving
  - Delayed recall
- Stable:
  - Vocabulary
  - Fund of information

Cognitive ability changes
- “Crystallized ability” stays the same
  - Information/skills gained from experience
- “Fluid intelligence” declines
  - Flexible reasoning and novel problem-solving
  - Decreased learning efficiency (takes longer/repetition)
  - “Tip-of-the-tongue” phenomenon (word-finding)
- Slowed reactions (both mental and physical)

Someday, I aspire to disclosures...
A few off-label drug uses, marked by:

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Dementia Types:
- Alzheimer's disease ~55% of all dementia
- Vascular dementia ~10-15% of all dementia
- Lewy body dementia ~20% of all dementia
- Frontotemporal Dementia
- Parkinson's disease
- Parkinson's plus syndromes
- Normal Pressure hydrocephalus
- Traumatic Brain injury
- Cerebral Amyloid Angiopathy
- Rarer: HIV, Toxin-induced (Alcohol, Wilson's, etc), CJD, CADASIL, Corticobasilar, Huntington's, PTLD, autoimmune

Before Memory Clinic
- Some sort of screening test
- More story:
  - Slope of decline
  - Meds to stop
  - Comorbidities to address
- Neuro Exam
- Tests:
  - TSH, B vitamins, Vit D, CMP, CBC
  - Head Imaging

MiniCog
- 3-word recall
- Clock Draw Test
  - Score: 1 pt/word, 1 pt clock numbers, 1 pt clock hands
  - <3 = dementia
  - Sensitivity/Specificity ~75-85%
  - PPV 0.34, NPV 0.98
  - Highly validated
  - No education/language bias (studied!)
  - 3-5 minutes

MMSE
- Score: >24 = normal, add 1 point if ≤12 years education
- Proprietary ($1-5/test)
  - Oldest (1975), most studied
  - Sensitivity ~70%, Specificity ~85-89%
  - PPV ~0.6, NPV ~0.9
  - Takes ~10 min

SLUMS
- Score: >25 or 27 = normal, >20 or 21 = MCI
- Free!
- Takes ~10 min
- Sensitivity/Specificity ~90
- Less well-studied
  - Mostly at VA

MoCA
- Score: >26 = normal, 18-25 = MCI, add 1 pt for ≤12 yrs education
- Better screen for MCI
  - MMSE sens 71%, MoCA sens 83%
  - Sensitivity ~95%, Specificity ~90%
  - Moving towards being proprietary
  - More executive function: more types of dementia
  - Takes ~15 min
  - More versions: many languages, visually impaired, low education
  - Requires more training (has a user manual)
What are we testing?

Areas of cognition:
- Immediate memory
- Delayed memory
- Attention
- Visuospatial/construction
- Language
- Executive function

Memory Clinic?

- Scoring well, but a clear clinical problem
- Atypical symptoms (not "just Alzheimer's")
- Complicated comorbidities
- Patient/family disagrees

WAI Memory Clinics

A comprehensive, team approach to dementia diagnosis, treatment, and support for the patient and caregiver.

- Supports the PCP
- Empowers the patient and caregiver
- Reduces crisis visits
- Decreases caregiver burnout

Inter-Professional Model

Inter-professional Practice
- Integrate skill sets
- Share knowledge
- Organize planning

Medical Evaluation
- Battery of key cognitive domains

Differential diagnostic algorithm
- Analysis of hx, burden, ADLs, etc.

Impact-Patient Care
- Quality diagnostic process
- Optimization of patient, family, population outcomes

Impact-Clinicians
- Earlier diagnosis
- Improved coordination of care
- Improved management of co-morbidities
- Improved connection of families to resources
- Improved support to PCP

Memory Clinic Team

- Geriatric Family Specialist:
  - Caregiver informant collection
  - Functional screens
  - Family burden
  - Ongoing patient and caregiver support and resources

- Neuropsychology:
  - Administer/analyze cognitive evaluations
  - i.e. Cognistat/ RBANS
  - Offer cognitive therapies recommendations

- Physician:
  - Specialized dementia training
  - Comprehensive assessment
  - Lab review
  - Medical exam
  - Polypharmacy

Team:
- Provides recommendations and management plan back to PCP

Comprehensive History

- Symptoms at onset
- Time course and pattern of cognitive decline
- Past and present function at higher level tasks
- Safety concerns
- Other associated symptoms
- Depression, tremor, frequent falls, visual hallucinations, stroke and/or transient ischemic attack symptoms, ataxia, urinary incontinence, agitation, personality changes, etc...
Past Medical/Surgical History
- Vascular risk factors/history of vascular disease
- Coronary artery bypass surgery
- Other major central nervous system (CNS) event (e.g., TBI with LoC)
- Hearing and/or vision loss
- Obstructive sleep apnea
- Alcohol or other substance abuse
- Depression, anxiety, posttraumatic stress disorder, or other psychiatric illness
- Other neurologic disease (Parkinson’s, ALS, seizure)
- History of malignancy or with or without prior treatment with chemotherapy

Pertinent History
- All medications and supplements
- Correlation of dose change/initiation with cognitive symptoms
- Family, friends, and other social support
- Use of community resources
- Educational and Work history
- Military history (including exposure to combat or blast injuries)
- Hobbies and other daily activities
- Family history of vascular, neurologic or psychiatric disorders

Physical Exam
- General appearance & Mental status
- behavior, attitude, mood, affect, insight, judgment, thought content, thought process, speech, language
- Cranial nerves
- Motor function and integration
- strength, tone, cogwheeling
- Sensory function
- Coordination
- Deep tendon reflexes
- Gait & balance

Differential Diagnosis
- Depression/anxiety
- Substance abuse
- Encephalitis: infectious or ischemic
- Sleep apnea/hypopnea

Imaging
- CT head: rule out vascular disease, tumor
- MRI: Lacunar infarcts, CAA, infection/inflammation, paraneoplastic tumors
- PET-CT glucose: Alzheimer’s vs FTD

Image copied from: Cleveland Clinic (my.clevelandclinic.org)
Imaging

- Amyloid PET scans
  - Approved for equivocal cases
- Tau PET scans
  - Still in research

10-year-old woman with cognitive decline (pre-MCI)

Diagnostic Testing: Lumbar Puncture

- CSF Aβ-42 (Aβ-42:40 ratio), T-tau, P-tau Thr181 & Thr231
  - All 3 abnormal = valid for early prodromal AD
  - All 3 normal = rules out AD
  - Combine with imaging to ↑ accuracy in indeterminate cases

CSF Biomarkers

- One type of amyloid, two types of tau

CSF Biomarkers

- CSF tau levels
- CSF amyloid levels

Summary

- Comprehensive Interprofessional Evaluation
- Extensive history from multiple sources
- Comprehensive neurocognitive testing
- Increasing use of advanced imaging and biomarkers

Treatment

- Progression
- Pharmacologic
- Non-pharmacologic
- BPSD addressed elsewhere

Alzheimer’s Progression

- FAST stages
- Behavioral Changes
**FAST Stages:**

1. Normal adult
2. Normal adult with mild memory changes (normal older adult)
3. MCI
4. Mild dementia
5. Moderate dementia
6. Moderately-severe dementia
   - Difficulties with ADLs, continence
7. Severe dementia
   - Complete motor loss, speech loss, hospice eligible at stage 7b

**Behavior: Early Changes**

- ↓ tolerance for chaos
- ↑ rigidity, possessiveness, self-focus
- ↓ sense of boundaries
- Social graces maintained
- Stressful for families (different person with strangers)
- Routines increasingly important

**Mid changes:**

- ↓ conversational retention (1/4 words lost)
- ↑ repetition, perseveration
- ↑ anxiety
- ↑ confabulation (“filling in the gaps”)
- Circadian changes/sun-downing
- No reasoning with them
- Gait becomes small/shuffling
- ↓ fine motor skills

**Mid-late changes:**

- Tunnel vision:
  - Cannot recognize time/space/whole object or person
- Lack of danger sense/insight
- Repetition is soothing
- Hypersensitivity of hands, mouth, genitals – agitation with care
- Focused on immediate needs: imposing, demanding
- Agitation with inability to describe needs

**Late changes:**

- Fine motor skills gone
- Picks up objects; cannot use them.
- Mimics body actions; cannot follow directions.
- Forgets familiar people/faces.
- Cannot initiate; difficulty task-switching.
- Reliant on emotional response for comfort, vocal tones.
- Memory of basic bodily functions ↓
- ↑ startle reflex
- ↑ bed sores, loss of ambulation, complete ADL dependence

**Agitation/Aggression in dementia**

- 20-40% of people with dementia
- 33% in SNFs are on anti-psychotics (GAO)
- 14% overall on anti-psychotics
- >50% are on for >1 year
Pharmacologic Therapies

- Acetylcholinesterase Inhibitors
  - Donepezil (Aricept)
  - Rivastigmine (Exelon – patch better)
  - Galantamine (Razadyne)
- Memantine
  - NMDA receptor antagonist
  - FDA approved for moderate to severe dementia
  - No evidence for use in mild dementia
  - Adjunct with acetylcholinesterase inhibitors?
    - No evidence of superiority
    - Theoretically more calming
    - No difference between XR and short acting
- Vitamin E
  - VA trial: double-blind RCT 613 patients 2007-2012
    - Vitamin E 2000 IU daily, Memantine 20 mg daily, placebo
    - Mild-moderate dementia, slower functional decline compared to other groups
    - Delay 19%, ~6 months compared to placebo
    - Decreased caregiver burden compared to other groups
    - Memantine and memantine + Vitamin E equivalent
    - Side effect: increased bleeding, ?CV events (miniscule)

Exercise!

- Physical inactivity RF for cognitive decline
- ↑ BDNF and IGFs pathways in brain
- ↑ Neurogenesis, especially in dentate gyrus, vasculature
- Can ↓ hippocampal loss in high-risk older people (APOE-4)

Exercise During Dementia

- Am J Geriatric Psychiatry 2007:
  - Metanalysis of trials
  - Exercise benefit >> memory meds
- Aging Res Rev 2016:
  - Exercise improved cognition (SMD: 0.42)
  - Aerobic better, high & low intensity both work
Treatment

- Supplements?
  - Many work great in mice!
  - Eg docosahexaenoic acid (DHA)
  - Prevogen?
    - No evidence it’s better than placebo

- Diet:
  - Mediterranean and “MIND” Diet
  - Data is on prevention, not treatment

Social Activity & Brain Games

- Cognitive stimulation for patient
- Some suggestion of improved mood, orientation, global functioning
- Decreases loneliness, improves outlook in early Alzheimer’s
- Respite for Caregiver
- Decreases depression and anxiety for both patients and caregivers
- Memory Cafes, Early Memory Loss Support Groups, Senior Centers

Music

- “Whole Brain Activity”
- Recognition of familiar tunes maintained across all stages of dementia
- Decreases anxiety, agitation
- Singing may increase recall of familiar people
- Effect can last hours to days after “treatment”

Caregiver Burden

- 60% report high stress levels
- Worse health: Spend 8% more per year on personal health care needs
- 18 billion hours unpaid care per year = $221 billion
- 70% have work-related difficulties because of caregiving
- Average lifetime income loss: ~250,000-300,000
- >$33 billion in lost revenue to economy
- Can’t enjoy their relationship with loved one

Caregiver support

- Resources and Education:
  - Websites
  - Local ADRC and/or dementia specialists
  - Respite
  - Adult Day Centers/Senior Centers
  - Automate as much as possible
  - Technology (GPS trackers, Alarmed pill boxes, etc)
  - Caregiver support groups
  - Exercise!

Now you know...

- Memory clinic for complex cases
- Interprofessional evaluation
- Medications are few, somewhat useful
- Non-pharmacologic treatments equally important
Thanks!!

Acknowledgments
Wisconsin Alzheimer’s Institute
http://www.wai.wisc.edu/
Wisconsin Registry for Alzheimer’s Prevention (WRAP)
Wisconsin Alzheimer’s Disease Research Center (ADRC)
http://www.adrc.wisc.edu

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