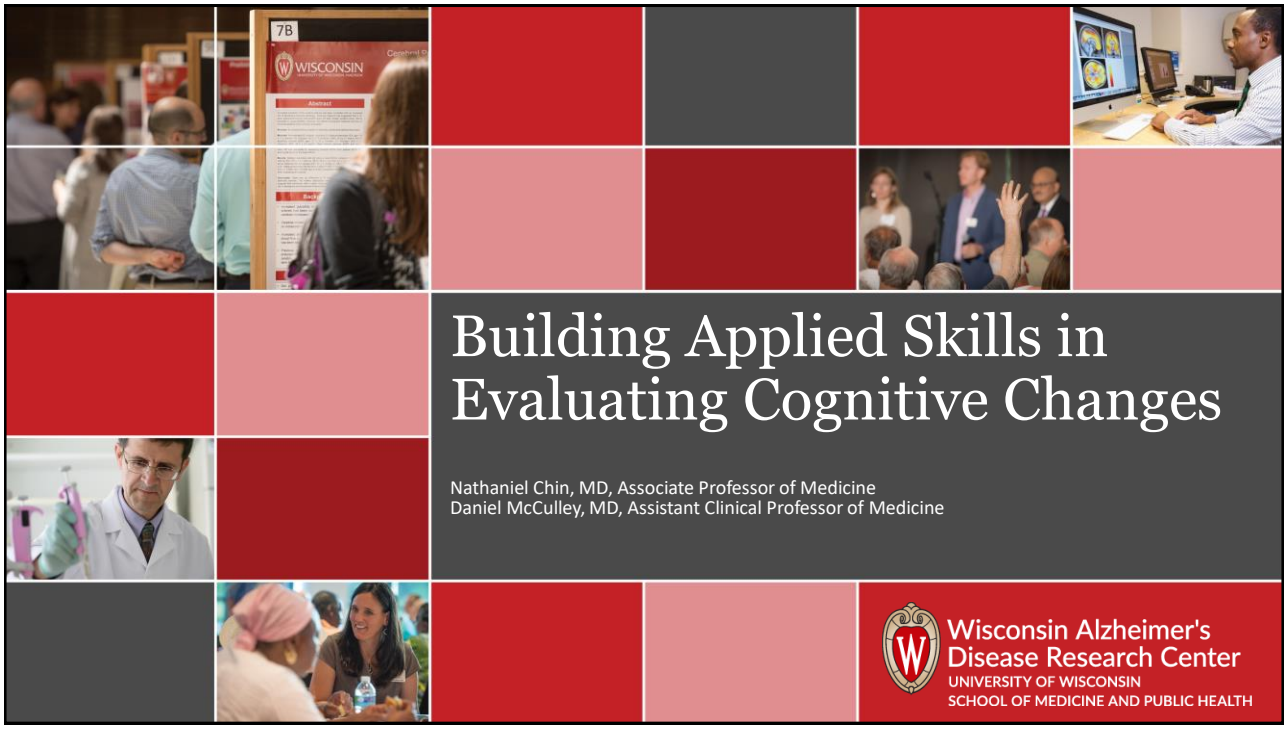

1

Disclosures

Nate Chin

- I have done consulting work for SVB Securities and NewAmsterdam
- My outside activities do not impact my presentation today.

Dan McCulley

- None

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2

Objectives

- Understand the importance of the early diagnosis of cognitive impairment
- Know the diagnostic criteria for MCI and Dementia
- Be able to name tools to use in the initial evaluation of cognitive changes
- Describe labs, imaging, and referrals that are commonly needed in the evaluation of cognitive changes
- Understand when to refer to a specialist
- Name resources to share with patients and their support team

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3

Sessions

- Session 1: The importance of early identification and diagnosis
- Session 2: The initial evaluation of cognitive concerns
- Session 3: What comes next?

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The importance of early identification and diagnosis

Nathaniel Chin, MD, Associate Professor of Medicine
Division of Geriatrics, UW School of Medicine and Public Health
Medical Director & Clinical Core Co-Leader, Wisconsin Alzheimer's Disease Research Center
Medical Director, Wisconsin Registry for Alzheimer's Prevention (WRAP) Study
Associate Director, Geriatric Memory Program, UW Health

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Session 1: The importance of early identification and diagnosis

https://www.mcmasteroptimalaging.org/age-well/health-care-and-health-service-delivery/early-disease-detection-%28non-cancer%29

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Let's start with terminology

- Mild cognitive impairment
- Dementia
- Alzheimer's disease
- Amyloid & tau
- Cognitive impairment
- Functional impairment
- Cognitive screening vs cognitive testing

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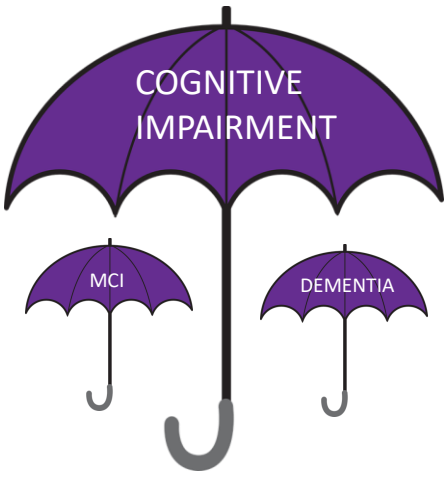
Cognitive impairment

- Subjective memory or thinking complaint
- Objective testing shows "low score"

- 2 types
  - Mild cognitive impairment (MCI)
  - Dementia

- Research only…for now
  - Subjective cognitive decline (SCD)



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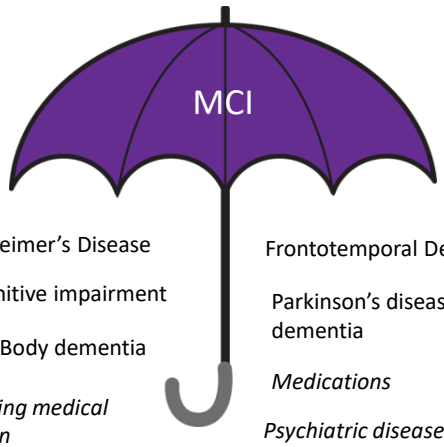
Mild cognitive impairment

- Memory/thinking complaint
- Decline from baseline ability
- Impairment on testing
- **No day to day functional impairment**



Alzheimer's Disease

Vascular cognitive impairment

Lewy Body dementia

Underlying medical condition

Frontotemporal Dementia

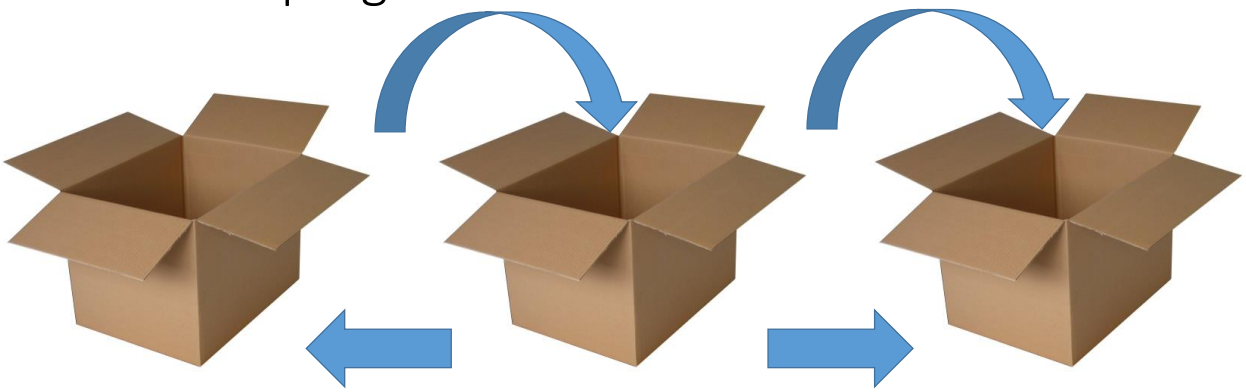
Parkinson's disease dementia

Medications

Psychiatric disease

9

MCI is a prognostic conundrum



Unimpaired **MCI** **Dementia**

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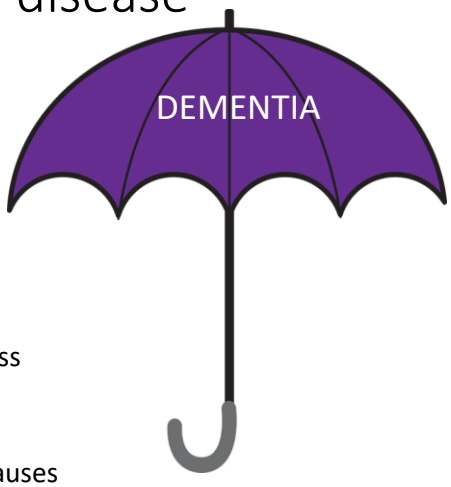
Dementia is a syndrome, not a disease

- NIA-AA Diagnostic Criteria 2011
- Cognitive symptoms that:
  - Represent a decline from previous level
  - Affect at least 2 thinking abilities on cognitive testing
  - Impairment in usual functional abilities
  - Chronic and persistent changes
  - Caused by a brain disease or injury
  - Are not explained by other medical or psychiatric illness
- Dementia due to AD
  - Memory is the primary complaint & ruled out other causes
  - Gradually progressive and with a documented decline



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Dementia vs Major Neurocognitive Disorder

- NIA-AA dementia criteria
  - Developed primarily by neurologists
  - More closely linked to pathology, biomarkers, and research definitions
  - Requires impairments in 2 or more cognitive domains
- DSM-V major neurocognitive disorder criteria
  - Developed by psychiatrists
  - Strongly linked to coding for various diagnoses
  - Requires impairments in 1 or more cognitive domains

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The difference between MCI and dementia is function

Mild Cognitive Impairment	Dementia
Concern regarding change in cognition (mild)	Cognitive loss (mild to severe)
Impairment in 1+ cognitive domains (usually memory)	Impairment in 2+ cognitive domains (usually includes memory)
Preservation of functional independence	*Functionally impaired*
Do not meet criteria for dementia	*Meet criteria for dementia*

Albert MS et al. *Alzheimer's & Dementia* 2011;7:270-279.

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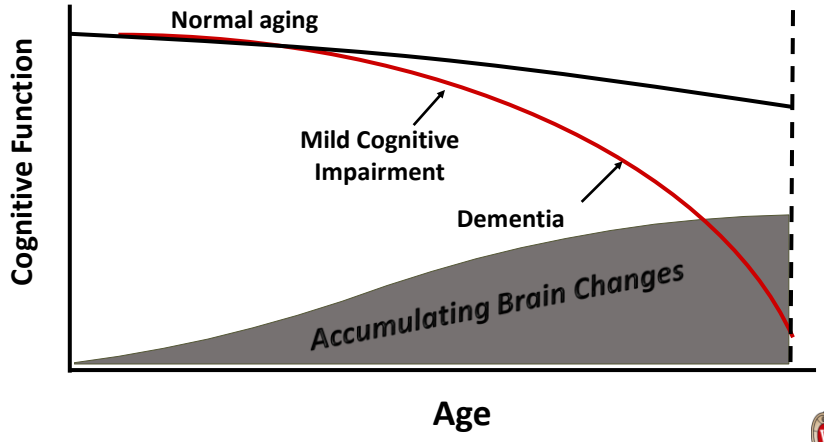
Neurodegenerative disease course



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Alzheimer's disease is many things to many people

- Two abnormal proteins called amyloid-β and tau
- One cause of progressing cognitive impairment
- Has a prolonged presymptomatic stage ~10-30 years
- Can be identified with PET and CSF biomarkers
- Other diseases may masquerade or co-occur with AD symptom expression
- Cerebrovascular disease commonly co-occurs with AD
  we tease them apart (imperfectly) with MRI and PET

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Brain changes in Alzheimer's Disease

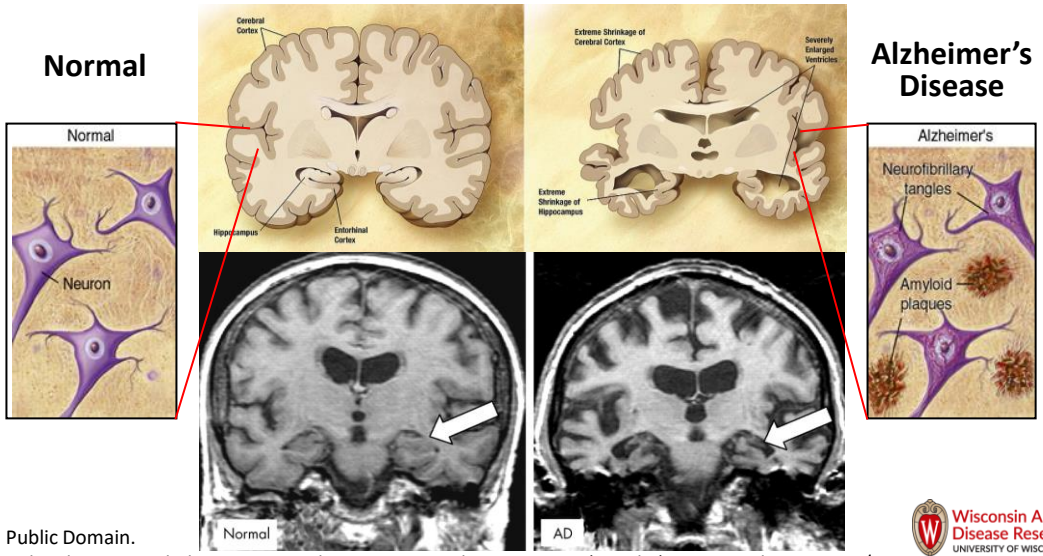

Figure: Public Domain.
MRI: van der Flier WM, Scheltens P. J Neurol Neurosurg Psychiatry 2005;76(Suppl V):v45–v52. doi: 10.1136/jnnp.2005.082149

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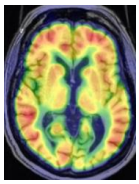
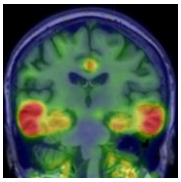
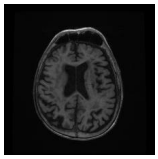
Alzheimer's disease has a sequence of events



Amyloid

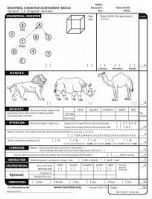


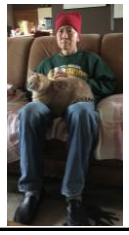
Tangles



Brain cell death

Mild cognitive impairment





Dementia

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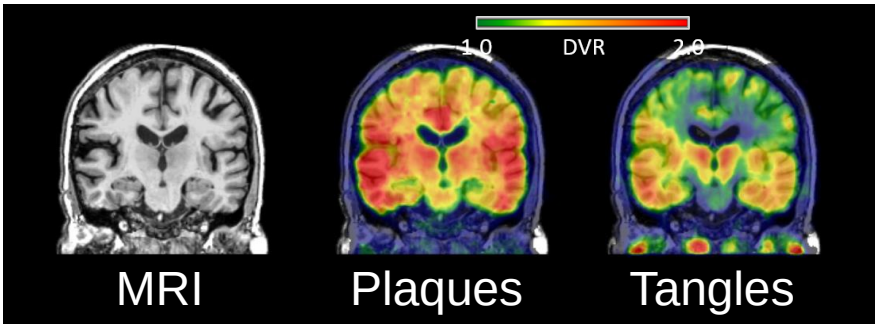
We can detect pathology without an autopsy

70-year-old person without memory symptoms



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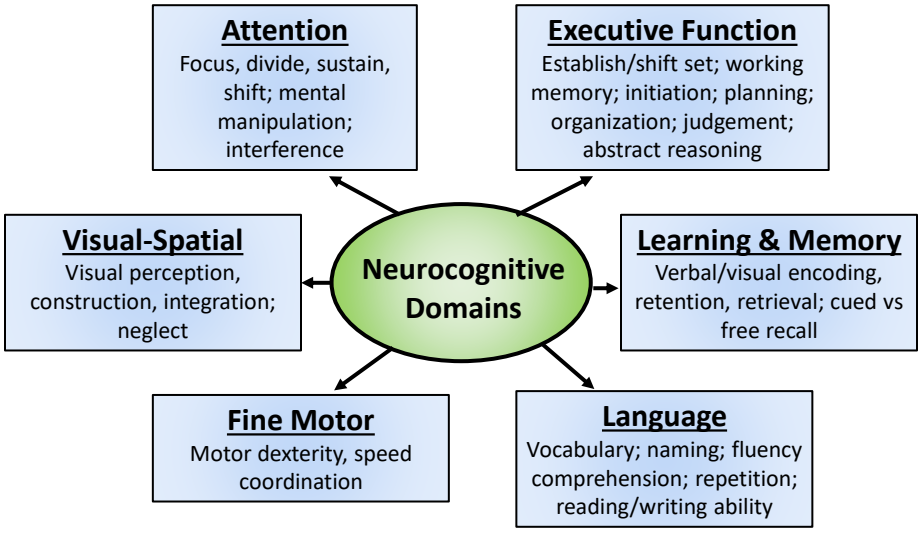

Premorbid Functioning: crystalized knowledge, word reading, vocabulary
Intelligence: Verbal & nonverbal IQ

Courtesy of Dr. Tori Williams

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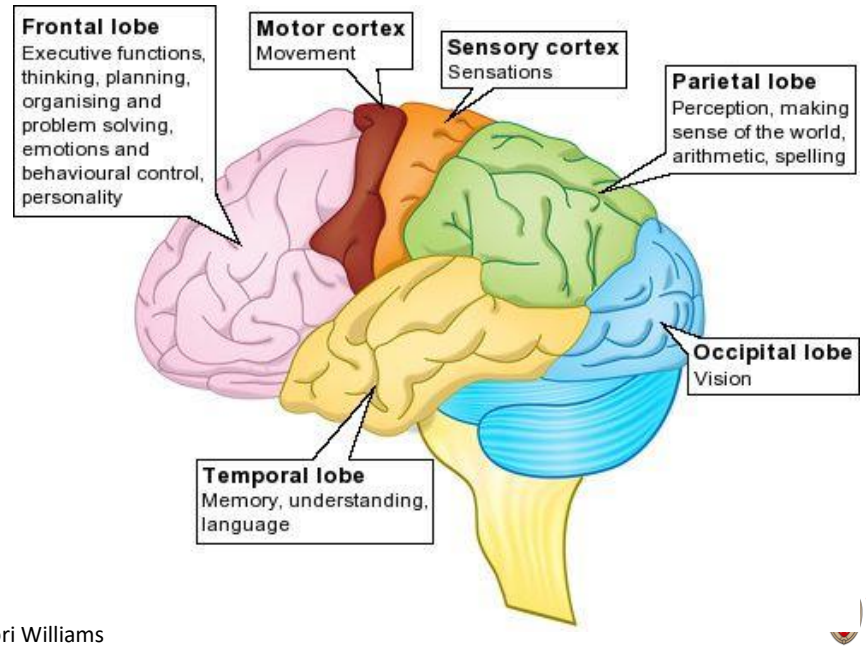

Courtesy of Dr. Tori Williams

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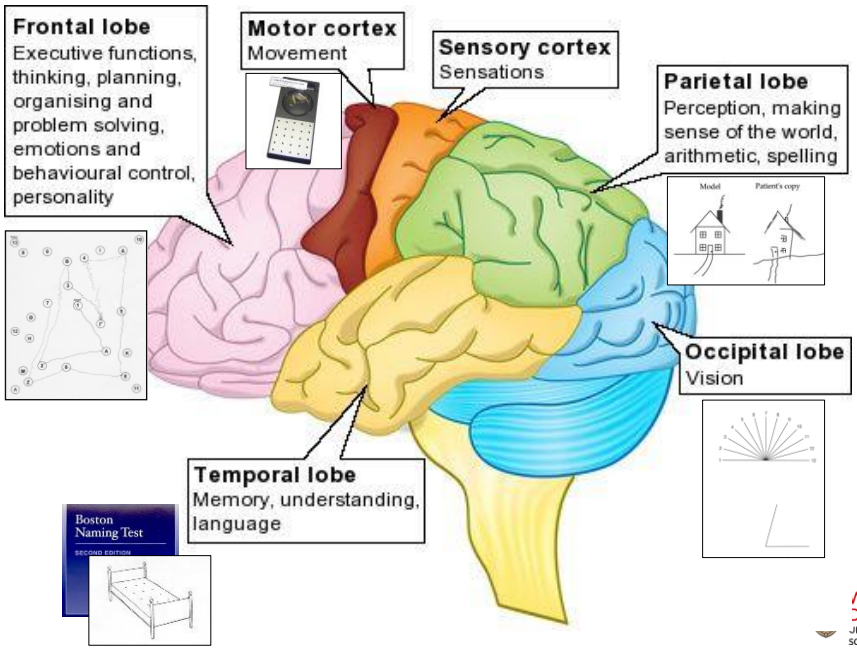

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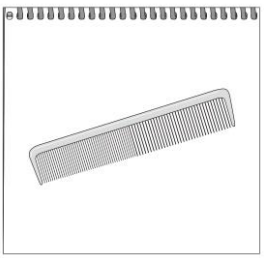
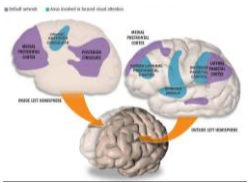
"What is this called?"

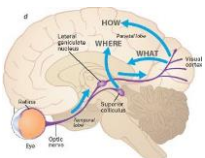


Not so simple….

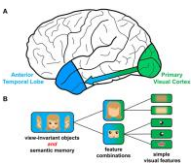
- No one test measures a single cognitive domain.
- Evaluating profile of observed performance across tests is critical.
  - Some tests have built-in comparison conditions (i.e., Stroop)



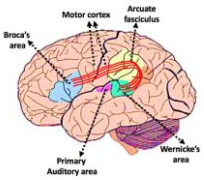
Attention Network



Visual Perception



Semantic Access



Language Output

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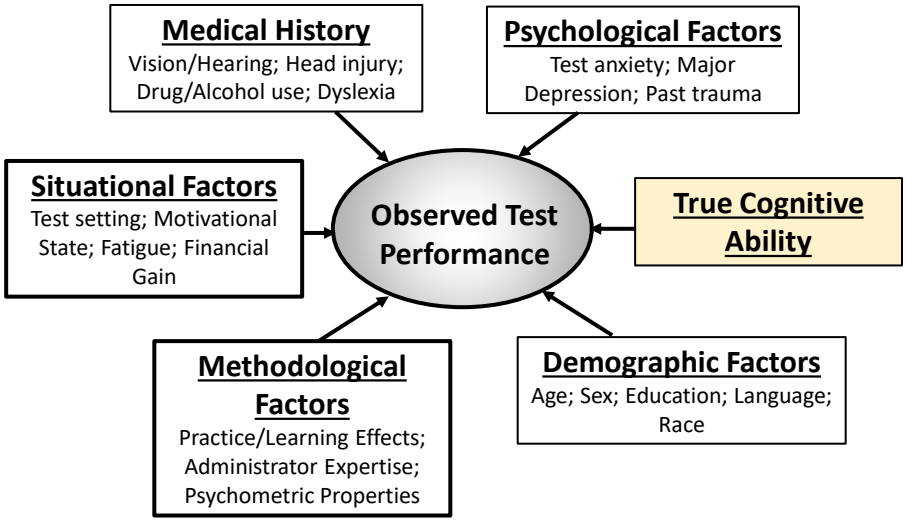
Factors Affecting Test Performance



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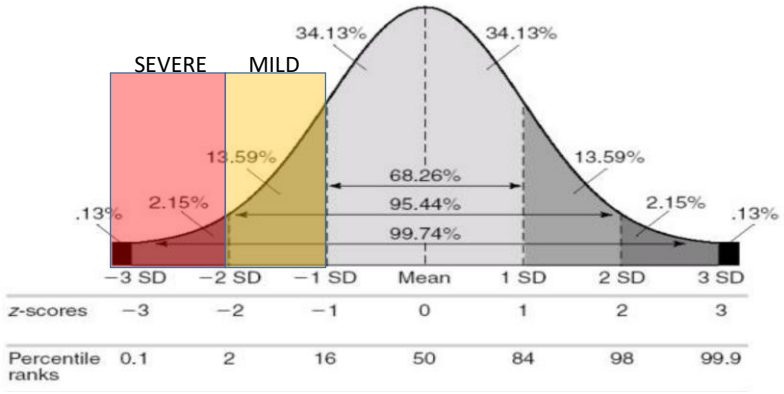
Establishing Cognitive Impairment

How do we define impairment in cognitive performance?



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Neuropsychological Profile Analysis

Alzheimer's Disease

	Raw Score	Standard	Percentile	Description
GENERAL COGNITION				
[illegible]	[illegible]			Normal
MoCA	21 /30	-1.19	12	Low Average
[illegible]	[illegible]			
ATTENTION / PROCESSING SPEED				
Trailmaking Part A (0 errors' 24/24 CL)	45 sec	-0.47	31	Average
Number Span Forward - Total	6 /14	-0.78	21	Low Average
Number Span Forward - Span Length	6 /9	-0.38	35	Average
Number Span Backwards - Total	5 /14	-0.62	26	Average
Number Span Backwards - Span Length	5 /8	0.31	62	Average
WAIS-R Digit Symbol	24	8	25	Average
LANGUAGE				
MINT	14 /32	-7.52	1	Impaired
Animal Fluency	9	-1.84	3	Borderline
Vegetable Fluency	6	-1.68	4	Borderline
F+L Words	28	0.53	69	Average
F+L+C Words	39	11.00	63	Average
F Words	15	0.59	72	Average
L Words	13	0.34	63	Average
VISUOSPATIAL				
Benson Figure Copy	17 /16	1.21	88	High Average
MEMORY				
Benson Delay (11% retained; Recog = Y)	2 /16	-3.07	1	Impaired
Craft Immediate - Verbatim	7 /44	-1.72	4	Borderline
Craft Immediate - Paraphrase	9 /25	-1.07	14	Low Average
Craft Delay - Verbatim (0% retained)	0 /44	-2.47	1	Impaired
Craft Delay - Paraphrase (0% retained)	0 /25	-3.09	1	Impaired
RAVLT Total Learning (2, 3, 3, 4, 5)	17 /75	-2.68	1	Impaired
RAVLT Distractor List	2 /15	-1.19	12	Low Average
RAVLT Short Delay	4 /15	-1.37	8	Borderline
RAVLT Long Delay (0% retained)	0 /15	-2.92	1	Impaired
RAVLT Recognition (TP=2; TN=2)	13 %	2	1	Impaired
EXECUTIVE FUNCTIONING				
Trailmaking Part B (5 errors; 24/24 CL)	144 sec	-0.72	23	Low Average
Clock Drawing Test	1 /3	---	---	Impaired
MOOD				
GDS-15 (Depression Symptoms)	3 /15	---	---	Minimal

Vascular Dementia

	Raw Score	Standard	Percentile	Description
GENERAL COGNITION				
[illegible]	[illegible]			Normal
MoCA	21 /30	-1.19	12	Low Average
[illegible]	[illegible]			
ATTENTION / PROCESSING SPEED				
Trailmaking Part A (0 errors' 24/24 CL)	66 sec	-1.64	5	Borderline
Number Span Forward - Total	4 /14	-1.65	5	Borderline
Number Span Forward - Span Length	4 /9	-1.92	3	Borderline
Number Span Backwards - Total	2 /14	-2.05	2	Impaired
Number Span Backwards - Span Length	2 /8	-2.00	2	Impaired
WAIS-R Digit Symbol	16	6	9	Borderline
LANGUAGE				
MINT	30 /32	0.10	53	Average
Animal Fluency	16	-0.47	31	Average
Vegetable Fluency	13	0.38	64	Average
F+L Words	20	-0.41	33	Average
F+L+C Words	36	10.00	50	Average
F Words	11	-0.28	38	Average
L Words	9	-0.51	30	Average
VISUOSPATIAL				
Benson Figure Copy	17 /16	1.21	88	High Average
MEMORY				
Benson Delay (70% retained; Recog = Y)	12 /16	0.38	64	Average
Craft Immediate - Verbatim	16 /44	-0.42	33	Average
Craft Immediate - Paraphrase	17 /25	0.67	75	Average
Craft Delay - Verbatim (75% retained)	12 /44	-0.71	24	Low Average
Craft Delay - Paraphrase (82% retained)	14 /25	0.16	56	Average
RAVLT Total Learning (4, 5, 6, 7, 8)	30 /75	-0.95	17	Low Average
RAVLT Distractor List	4 /15	0.06	52	Average
RAVLT Short Delay	4 /15	-1.37	8	Borderline
RAVLT Long Delay (0% retained)	0 /15	-2.92	1	Impaired
RAVLT Recognition (TP=12; TN=15)	90 %	11	63	Average
EXECUTIVE FUNCTIONING				
Trailmaking Part B (5 errors; 24/24 CL)	205 sec	-1.84	3	Borderline
Clock Drawing Test	1 /3	---	---	Impaired
MOOD				
GDS-15 (Depression Symptoms)	3 /15	---	---	Minimal

- Measures of global cognition (MMSE, MoCA, SLUMS, etc) are useful in identifying risk for dementia and/or monitoring progression over time.
- Dementia must be caused by a brain disease….

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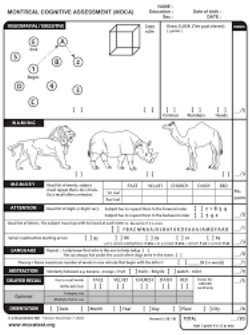
Cognitive screening

- Mini-Mental State Examination (MMSE)
- Saint Louis University Mental Status Exam (SLUMS)
- Montreal Cognitive Assessment (MoCA)
- Mini-cog
- Memory Impairment Screen (MIS)
- Brief Alzheimer's Screening Test (BAS)
- General Practitioner assessment of Cognition (GPCOG)
- AD8 Informant Interview (not a test)



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Cognitive screening & testing

- Well-trained staff should administer test
- Stick to the guidelines of the instrument
- Results should be discussed with patient/family

- Performance testing is an objective measurement to potentially identify cognitive changes beyond normal aging
- May not reflect what a person feels or others witness
- Artificial process (quiet, isolated room, specific tasks)

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What are *the* functional abilities?

Instrumental Activities of Daily Living

- Making and keeping appointments
- Managing medications
- Managing finances
- Driving
- Meal preparation and cooking
- Household chores
- Use of technology
- Maintaining hobbies

Basic Activities of Daily Living

- Dressing
- Bathing
- Toileting
- Transferring
- Walking
- Eating

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Functional impairment

- Compare current abilities to baseline
- Start with IADLs
  - Most complex are: managing finances, medications, appointments
- Collateral historian is key
  - Ideally someone who lives with the patient (spouse, child)
  - Patient endorsement is more confirmation than identification
- Compensatory strategies are okay and expected in MCI
- Rare, infrequent mistakes may not be impairments
  - Objective impairments are easier to identify- missed payments, ER visits due to medication non-adherence
- Impairments must be due to cognition, not due to mood or physical limitations

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Establishing Functional Impairment

Challenges:

- Cognitive versus physical/sensory deficits
  - Higher incidence of comorbidities in community-based samples
  - Residing in assisted care facilities
- Lack of insight due to cognitive impairment
  - Informant report is preferred
  - Frequency of contact with participant
- Limited familiarity/knowledge in distinguishing dementia from typical aging
  - "They are doing better than I am!"

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How to diagnose cognitive impairment?

- **Cognitive and functional history**
  - Cognitive symptoms
  - Functional changes, if any
- **Cognitive testing**
  - Cognitive screening instrument
- Evaluate for reversible causes, specifically delirium & mental health
  - History
  - Labs
  - Brain imaging
- Physical exam
- Labs and head imaging

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Cognitive history

- Symptom identified
  - Patient, family, provider, routine screening
- Patient and collateral historian
- Cognition
  - Onset, course
  - Specific symptoms and stories
  - Medical changes during this time
    - Including head injuries, acute illnesses, surgeries
- Mood, personality, behavior
- Sleep, hearing
- Review medical history, medications, family history, substance history

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Early symptoms

- Symptoms depend on the part of the brain affected
  - **MEMORY**: forgetting recent events or conversations, repeating stories and questions, misplacing items
  - **LANGUAGE**: word finding, problems understanding words, problems reading or writing
  - **VISUO-SPATIAL**: problems getting lost, difficulty recognizing people, difficulty understanding spatial relationships
  - **EXECUTIVE FUNCTION**: problems with reasoning, organizing, multi-tasking, problem solving
  - **ATTENTION**: Problems with focus, difficulty following a conversation
- Earliest symptoms are thinking ability and not daily function

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Functional history

- Collateral historian is key
- Patient perspective important
- Inquire about specific safety concerns or events/issues noticed by family
- Check list approach reviewing IADLs and then BADLs

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Look for reversible causes

- Medication reconciliation
- Mood assessment
- Evaluate alcohol intake or other substances
- Evaluation sleep and rule out sleep apnea
- Kidney, liver, or thyroid issues
- Hearing or vision issues
- Chronic infections
  - Syphilis, Lyme disease, HIV, Covid19
- Acute infections
  - UTI, cellulitis, pneumonia, viral colds
- Brain imaging for subdural hematoma or NPH

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Cognitive screening

- Not the same as cognitive testing or neuropsychological testing
- Not diagnostic testing
  - Some exceptions
- Explain the test and purpose of testing before administering

- MMSE
  - Well-studied, quick, costs $
- SLUMS
  - Similar to MMSE, less evidence than MMSE, free
- MoCA
  - Better for MCI, well-studied, many languages, cost $, more training

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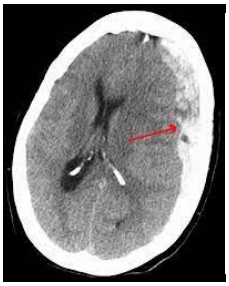
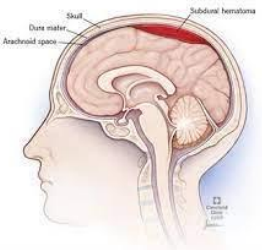
Blood work & head imaging

- Labs
  - Kidney function, electrolytes
  - Liver function
  - Thyroid function
  - Anemia
  - Vitamin deficiencies





- Brain imaging
  - Rule out brain mass, subdural hematoma
  - Evaluate for: atrophy, chronic small vessel disease

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Diagnose the syndrome first

- Evaluate for cognitive impairment
  - Is this normal aging or something more?
  - Could this be reversible?
- Evaluate for functional impairment due to cognitive disability
  - Is there functional decline? Is there functional impairment?
  - If so, is it due to the thinking changes or something else?
- From here, you'll have a sense of normal vs MCI vs dementia
- Cognitive screening can help support your suspicion…or not

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Etiologies are harder to determine

- Ruling out the most common neurodegenerative conditions
  - LBD and PD = history, physical exam
  - Cerebrovascular disease = comorbid conditions, brain scan
  - Frontotemporal disease = history
- Ruling in Alzheimer's disease
  - History
  - Cognitive testing profile (memory predominant)
  - Amyloid biomarkers
  - Not APOE
- Family history of Alzheimer's disease means less than you think

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Use the evaluation to talk about brain health

- Reversible causes = empowering your patient
- Brain health = optimizing brain abilities
- Lifestyle interventions = maintaining brain abilities and delayed decline
- Regardless of the person's cause for cognitive impairment, brain health is the foundation of care

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Talk to the patient about syndrome and then etiology

- Initial evaluation is about understanding symptoms and impact
- No diagnosis is needed immediately
  - Concern for memory impairment, concern for memory loss
- But don't hesitate to tell someone "concern for MCI"
- Explaining the difference between normal aging, MCI, dementia is valuable
  - You are functionally intact, so you do not have dementia at this time
- Then talk about "brain diseases" as possible causes, AND, reversible causes that will be evaluated

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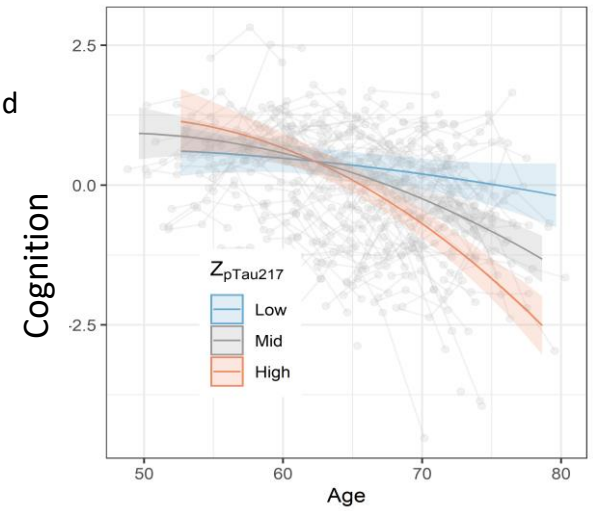
Advanced testing

- Not needed to diagnose the syndrome and start care
- PET scans
  - FDG-PET
  - Amyloid & Tau
- DAT scan
- Lumbar puncture - CSF
  - Amyloid and Tau
  - Inflammatory processes
  - Multiple sclerosis
- Blood based biomarkers
  - Amyloid and Tau
  - Inflammation, neurodegeneration
  - Predictive power



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Barriers to the evaluation

- No reported complaint
- No time or follow up
- No collateral historian
- Not screening or getting bad screening
- Relying on screening too much
- Absence of systems to help evaluate cognition and function

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Tips of the clinician

- Don't feel pressured to diagnose and don't promise a diagnosis
- Utilize a team, when possible
- Utilize multiple visits
- Talk about brain health while doing the evaluation

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Tools to help with the process

- Standard process for evaluation
  - History → Reversible conditions → Cognitive screening
  - Physical exam → Lab work → Brain imaging
  - Potential referrals: sleep clinic, counseling, pharmacy
- Utilize questionnaires (validated is better but homegrown is good)
  - AD8, Short IQCode, ECog-12
  - GDS, PHQ9
  - GAD7, GAS
  - FAQ, Lawton IADL
  - STOP-BANG, Insomnia Severity Index
  - Neuropsychiatric Inventory (NPI)

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AIMS Public Health

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Research article

The physician's Alzheimer's disease management guide: Early detection and diagnosis of cognitive impairment, Alzheimer's disease and related dementia

Allison B. Reiss[1], Donna de Levante Raphael[2], Nathaniel A. Chin[3] and Vivek Sinha[4,*]

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Benefits of an early diagnosis

- Can help explain symptoms, personality changes, behavioral changes
  - Provides an answer to patient and family suspicions/concerns
- Earlier interventions
  - Access to right services and support
  - Medications
- Maintain a good quality of life
- Patients can participate in their care and discuss future care options
- Patients can participate in their own legal and financial decisions
- Helps patients and family prepare for future functional change and potential safety issues
  - Allows family members and friends to develop new roles of support
- Gives time for families and care partners to become more educated

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Benefits of an early diagnosis

- Address brain health and mental health
- Address chronic diseases with a new lens
- Make earlier referrals
- Monitor for functional changes (ie driving) and safety issues
- Connect patient/family to community organizations
- Address advanced directives and future care planning
- Refer to clinical research

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Memory clinic process

- Detailed 1-hr interview with patient and family
  - Cognitive, functional, behavioral/psychiatric history
- Cognitive testing
  - RBANS, Cognistat = 1 hour
- Physical exam
  - Full neurological exam
- Lab testing
  - CMP, CBC, TSH, B12
  - HIV, RPR, Vitamin levels
- Brain scans
  - MRI or CT
- Advanced studies
  - FDG-PET
  - Lumbar puncture
- Education and feedback
- Referral to appropriate resources, including research
- Advanced care planning

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Session 2: The Initial Evaluation of Cognitive Concerns

Dan McCulley, MD

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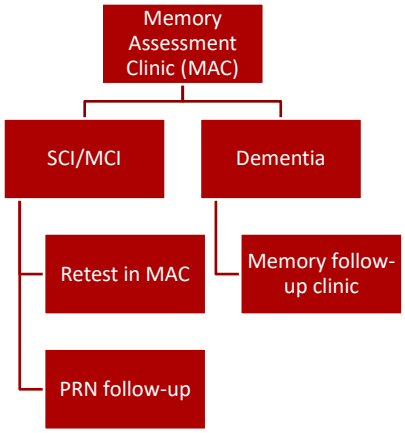
UW Memory Clinic

- Old Model:
  - 1 hour of neuropsychological testing
  - SW interviews informant
  - MD discussed diagnosis and recommendations



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Issues with Old Process

- Labs and imaging often not done before the visit
- Some patients had unrecognized/undertreated OSA, depression, anxiety, polypharmacy, etc which complicated the diagnosis
- 1 hour of testing is stressful and may not needed for some patients who clearly have dementia

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MTC Clinic

- SW calls an informant before visit
  - Cognitive history
  - IADLs/ADLs
  - Safety
  - POA documents
  - Recommends resources
- MA calls patient before visit
  - Memory ROS
  - Geriatric ROS
  - GDS for Depression
  - STOP-Bang for OSA risk

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MTC Clinic

- MD/NP visit
  - Review SW and MA history
  - Review chart and medications
  - Cognitive history from patient
  - Cognitive testing, informant questionaries
  - Physical exam
  - Provide preliminary diagnosis if able
  - Order needed labs and imaging
  - Order needed referrals
  - Discuss healthy brain habits

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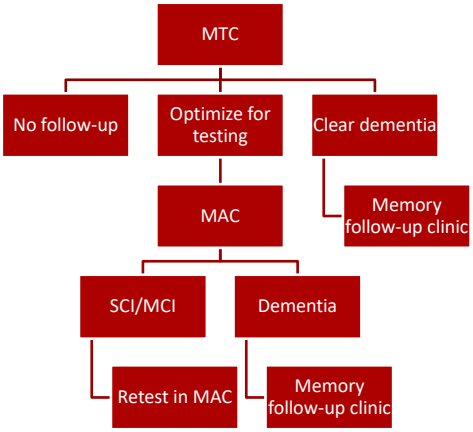
MTC Clinic

- New model



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Simplified Criteria for Diagnosis

Mild Cognitive Impairment (~ Mild Neurocognitive Disorder)

- Memory or other thinking changes that are worse than expected for aging

Dementia (~ Major Neurocognitive Disorder)

- Memory or thinking changes that are starting to interfere with day to day activities
- Driving, doing finances, managing medications, and arranging/keeping appointments are often the earliest changes

	Change from Baseline	Impairment on testing	Functional changes
MCI	+	+	-
Dementia	+	+	+

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What is needed for a diagnosis?

	Change from Baseline	Impairment on testing	Functional changes
MCI	+	+	-
Dementia	+	+	+

- DSM-5 criteria
  - Impairments not due to delirium or a mental health disorder
  - Need to have an impairment in at least 1 cognitive domain
    - Attention
    - Executive function
    - Learning and memory
    - Language
    - Perceptual - motor
    - Social cognition

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Ideal Initial Evaluation

- History from patient
- History from informant
- Cognitive testing
- Evaluate function
- Look for reversible causes
  - Depression and anxiety
  - Medications, substances
  - OSA
- Order labs and imaging
- Refer as needed

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Cognitive History

- Patient
  - Timeframe
  - Symptoms
  - Initiating event
  - Family history
- Informant
  - Timeframe
  - Symptoms
  - Function
  - Safety concerns

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Tools

- Patient
  - Cognition
    - **MoCA**
    - SLUMS
    - Mini-Cog
  - Mental Health
    - **GDS**
    - PHQ-9
    - GAD-7
  - Sleep Apnea
    - **STOP-BANG**
    - Berlin
- Informant
  - Changes
    - **Short IQCODE**
    - AD8
  - Function
    - **IADLs/ADLs**
    - FAQ
  - Staging
    - **QDRS**
    - DSRS
    - FAST

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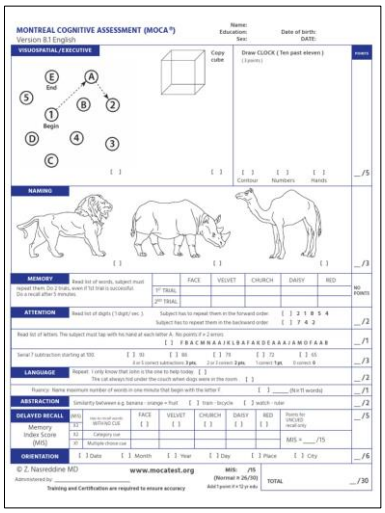
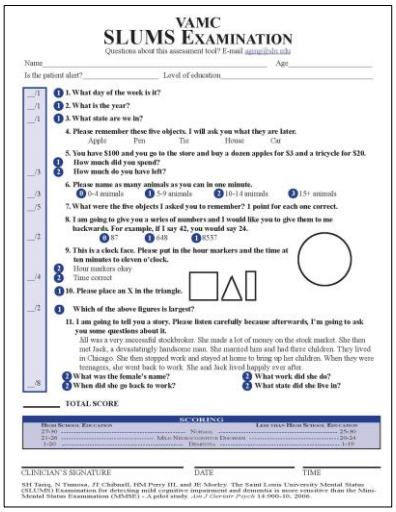
Cognition Tools

- MoCA
  - Good for diagnosing MCI or dementia
  - ~ Sn 0.9; Sp 0.8
  - Other versions available: 5-minute, blind/telephone, hearing impaired, low education
  - Should do online training to use



Cognition Tools

- SLUMS
  - Not as good as MoCA, especially for MCI



Case 1

- 68 year old man presents to memory clinic
- Seen by PCP 3 months prior
  - No complaints about memory from patient
  - SLUMS done and scored 18/30
  - Diagnosed with dementia and referred to our clinic
  - Told to "get affairs in order" and start planning to move to a nursing home within the next few years

SCORING		
High School Education		Less than High School Education
27-30----------	----------Normal----------	----------25-30
21-26----------	----------MNCD*----------	----------20-24
1-20----------	----------Dementia----------	----------1-19

*Mild Neurocognitive Disorder

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Case 1 Continued

- 68 year old man in memory clinic
  - Patient and family report no changes from baseline in memory or thinking
  - No changes in function
  - Testing showed mild deficits in learning and memory
  - Had significant learning disabilities in school
  - Dx: lifelong learning issues, not dementia or MCI

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Cognition Tools

- SLUMS scoring guide leads to errors
  - Need to look for a change from baseline to diagnose MCI (Mild Neurocognitive Disorder) and dementia
  - Need to look for functional changes to diagnose Dementia (Major Neurocognitive Disorder)

High School Education		Less than High School Education
27-30----------	----------al----------	----------25-30
21-26----------	----------Mi----------	----------20-24
1-20----------	----------Demen----------	----------1-19

*Mild Neurocognitive Disorder

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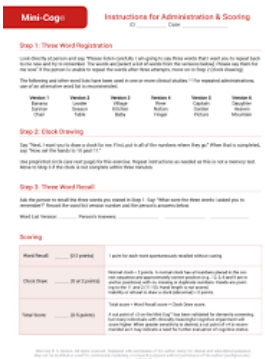
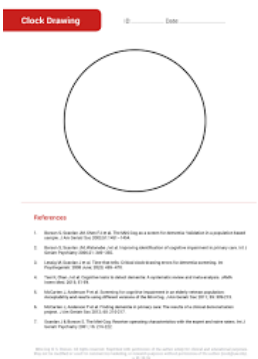
Patient Tools

- Mini-Cog
  - Not good for the diagnosis of MCI
  - Good Sn and Sp for dementia vs no dementia (~ 0.9, 0.85)





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Informant Tools

- Change from baseline
  - **Short IQCode**
  - AD8
- Function
  - **Lawton IADLs**
  - **Katz ADLs**
  - FAQ
- Staging
  - **QDRS**
  - DSRS
  - FAST

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Informant Tools

- Short IQCode
  - 16 questions
  - Average scores, for a total score of 1-5
  - Scores > 3.4 increase odds of cognitive impairment
  - Other cutoffs used in some studies (> 3.3, 3.38, 3.5)

Compared with 10 years ago how is this person at:

	1	2	3	4	5
1. Remembering things about family and friends e.g. occupations, birthdays, addresses	Much improved	A bit improved	Not much change	A bit worse	Much worse
2. Remembering things that have happened recently	Much improved	A bit improved	Not much change	A bit worse	Much worse

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Informant Tools

- AD8
  - 8 questions
  - 2 or more increases risk of cognitive impairment

Remember, "Yes, a change" indicates that there has been a change in the last several years caused by cognitive (thinking and memory) problems.	YES, A change	NO, No change	N/A, Don't know
1. Problems with judgment (e.g., problems making decisions, bad financial decisions, problems with thinking)			
2. Less interest in hobbies/activities			

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Informant Tools

- IADLs
  - Medications, finances, appointments, driving, meal prop/cooking, household chores, shopping, phone/technology usage
- ADLs
  - Bathing, dressing, toileting, transferring, continence, feeding
- Descriptors
  - Independent, has difficulty but does by self, requires assistance, dependent on others to do, never did at baseline

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Informant Tools

- Functional Activities Questionnaire (FAQ)
  - 10 areas
  - Score of 9 or more out of 30 increases risk of cognitive impairment

1.	Writing checks, paying bills, balancing checkbook
2.	Assembling tax records, business affairs, or papers
3.	Shopping alone for clothes, household necessities, or groceries
4.	Playing a game of skill, working on a hobby
5.	Heating water, making a cup of coffee, turning off stove after use
6.	Preparing a balanced meal
7.	Keeping track of current events
8.	Paying attention to, understanding, discussing TV, book, magazine
9.	Remembering appointments, family occasions, holidays, medications
10.	Traveling out of neighborhood, driving, arranging to take buses

- Dependent = 3
- Requires assistance = 2
- Has difficulty but does by self = 1
- Normal = 0
- Never did [the activity] but could do now = 0
- Never did and would have difficulty now = 1

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Informant Tools

- Quick Dementia Rating System (QDRS)
  - 10 areas, total score out of 30
  - 2 - 5.5 = consistent with MCI
  - 6 - 30 = consistent with dementia
    - Cutoffs for mild, moderate, and severe dementia

1. Memory and recall _____C

0 No obvious memory loss or inconsistent forgetfulness that does not interfere with function in everyday activities

0.5 Consistent mild forgetfulness or partial recollection of events that may interfere with performing everyday activities; repeats questions/statements, misplaces items, forgets appointments

1 Mild to moderate memory loss; more noticeable for recent events; interferes with performing everyday activities

2 Moderate to severe memory loss; only highly learned information remembered; new information rapidly forgotten

3 Severe memory loss, almost impossible to recall new information; long-term memory may be affected

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Other Staging Tools

- Dementia Severity Rating Scale (DSRS)
- Functional Assessment Staging Tool (FAST)
  - Used to qualify for hospice

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Look for Reversible Causes

- Mental health
  - GDS
  - PHQ-9
  - GAD-7
- Medications/substances
  - Alcohol
  - Benzos, TCAs, sleep meds, allergy meds, bladder meds
  - Cannabis
- Sleep apnea
  - STOP-BANG
  - Bicarb 28 or higher

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Labs and Imaging

- Labs:
  - CBC, CMP, B12, TSH
  - HIV and syphilis if at risk
  - In our clinic:
    - B1, B6, B9 (folate)
    - +/- vitamin D and homocysteine
  - In the right person:
    - PTH, lipid panel, A1c, …
  - UA not needed unless they have symptoms of a UTI
- Imaging
  - MRI w/o contrast preferred
  - CT head w/o contrast

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Case 2

- 70 y/o woman with 2 years of memory changes
- Seen by PCP 9 months prior
  - SLUMS score of 19/30
  - Labs including B12 and TSH WNL
  - MRI with age expected changes
  - Diagnosed with dementia likely due to Alzheimer's disease
  - Told to start Prevagen

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Case 2 Continued

- 70 y/o woman with 2 years of memory changes
- In our clinic:
  - Patient and family report no functional changes
  - Testing showed an impairment in memory
  - Diagnosed with MCI

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Case 2 Continued

- 70 y/o woman with 2 years of memory changes
- Work-up from our clinic:
  - B12 that PCP had ordered was “normal” but 230 (normal 220-900)
  - MMA and homocysteine confirmed she had a B12 deficiency
  - Sleep referral placed due to snoring and daytime fatigue, dx with moderate OSA
  - Dx: MCI due to B12 deficiency and OSA, not dementia due to Alzheimer’s disease

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Case 2 Continued

- Key Points:
  - Must evaluate function to diagnose dementia
  - Need to evaluate for reversible causes
  - "Normal B12" can still be a deficiency
    - Consider MMA and homocysteine if B12 < 300
  - Prevagen is expensive and has no biological plausibility for improving memory

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Case 3

- 75 y/o woman with 2 year of gradual memory decline presents to the memory clinic for a second opinion
- Seen by a community neurologist 6 months prior
  - IADLs/ADLs not documented
  - "Difficulty with serial 7s"
  - No labs or imaging done
  - Diagnosed with "early onset" Alzheimer's dementia and started on Donepezil
- Neurologist started memantine at a 3 months follow-up because patient had loose stools and stopped the donepezil

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Case 3 Continued

- 75 y/o woman with 2 year of gradual memory decline
- In our clinic:
  - MoCA was 21/30
  - No functional changes
  - Labs showed a B6 and B9 (folate) deficiency and low normal B12 (normal MMA)
  - MRI showed significant microvascular disease
  - Dx: Mild Neurocognitive Disorder (MCI) due to cerebrovascular disease and B6 and B9 deficiencies
  - Further labs showed a LDL of 190
  - Statin started and recommended controlling other vascular risk factors

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Case 3 Continued

- Key points:
  - Must evaluate function to diagnose dementia
  - Serial 7s alone is not sufficient to diagnose MCI or dementia
  - Head imaging should be done in almost all cases
  - Early onset Alzheimer's refers to an onset of Alzheimer's prior to age 65
  - Memantine has been shown to be effective for moderate or worse stage dementia due to Alzheimer's disease

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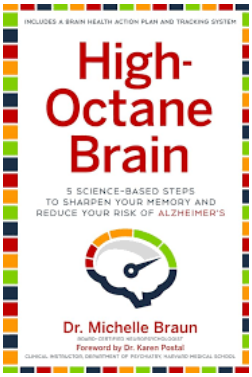
Brain Health

- Discuss evidence-based habits for brain health
- Without something concrete to do many patients will depend on supplements and unproven recommendations
- In our clinic we discuss:
  - Exercise
  - MIND/Mediterranean diet
  - Quality sleep
  - Stress reduction
  - Cognitive activity
  - Social activity
  - Avoiding risky substances
  - Treating hearing loss
  - …



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Dementia Prevention and Risk Reduction

The Lancet Commissions

Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission

Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

https://doi.org/10.1016/S0140-6736(20)30367-6

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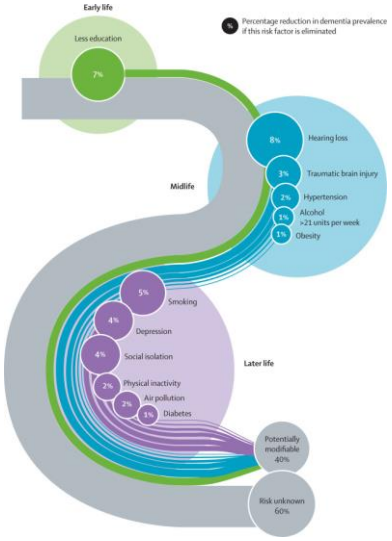
Dementia Prevention and Risk Reduction



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Case 4

- 70 y/o woman seen in consult for 2 years of progressive memory changes
- In clinic
  - Function on borderline of an impairment
  - MoCA 19/30
  - Labs normal
  - MRI normal
  - Dx: borderline of MCI and dementia

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Case 4 Continued

- 70 y/o woman seen in consult for 2 years of progressive memory changes
- Medications include amitriptyline and zolpidem
- Physically inactive
- Eats a significant amount of processed food
- Poor sleep hygiene

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Case 4 Continued

- 70 y/o woman seen in consult for 2 years of progressive memory changes
- Recommendations:
  - Switched amitriptyline to escitalopram
  - Stopped zolpidem, initially switched to low dose doxepin (3mg) for sleep maintenance insomnia which was eventually stopped
  - Discussed sleep hygiene
  - Discussed importance of physical activity and healthy diet

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Case 4 Continued

- 70 y/o woman seen in consult for 2 years of progressive memory changes
- 3 month follow-up- small subjective improvement in cognition
- 1 year follow-up: MoCA increased from 19 to 22, no subjective continued decline
- 2 year follow-up: MoCA stable at 21, no subjective continued decline

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Case 4 Continued

- Key Points:
  - Look at medications
  - Discuss healthy habits, especially exercise
  - Don't assume everyone has a neurodegenerative disorder and will continue to decline

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Key Points from Session 2

- MCI and dementia requires a decline from baseline
- Dementia requires a functional impairment
- Take advantage of tools
  - MoCA, Mini-Cog
    - SLUMS scoring table is incomplete
  - Use informant questionaries:
    - AD8 or short IQCODE
    - FAQ is good tool for function
- A vague diagnosis is better than an inaccurate specific diagnosis
- Evaluated for reversible causes
- Talk about habits for brain health

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Session 3: What comes next?

- Landscape of memory care is changing
- Biomarkers & MAB therapy have/will enter clinics
- The fundamentals of evaluation syndromes remain the foundation
  - First step and occurring before biomarkers
- Standard process for evaluating cognitive complaints can help organize the visit and improve effectiveness

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Benefits of an early diagnosis

- Can help explain symptoms, personality changes, behavioral changes
  - Provides an answer to patient and family suspicions/concerns
- Earlier interventions
  - Access to right services and support
  - Medications
- Maintain a good quality of life
- Patients can participate in their care and discuss future care options
- Patients can participate in their own legal and financial decisions
- Helps patients and family prepare for future functional change and potential safety issues
  - Allows family members and friends to develop new roles of support
- Gives time for families and care partners to become more educated

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Benefits of an early diagnosis

- Address brain health and mental health
- Address chronic diseases with a new lens
- Make earlier referrals
- Monitor for functional changes (ie driving) and safety issues
- Connect patient/family to community organizations
- Address advanced directives and future care planning
- **Initiate disease modifying therapy sooner**
- **Refer to clinical research**

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Advanced care planning

- Medical-legal preparation
  - HC-POA & Financial POA
  - Advanced directives & Living will
- Discussion of type of care to receive during disease
  - Surgery
  - Cancer screening
  - Management of chronic medical conditions
- Planning for future changes
  - Home health care, Adult activity centers
  - Living environment
  - Safety considerations

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Medications

- Cognitive enhancers
- Mental health
- Sleep medications
- Adjustment to medications used for other conditions

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Other medications

- Mental health
  - Medications for anxiety and depression
- Sleep medications
  - Discourage Benadryl, consider melatonin
  - Prescription sleep medications
- Supplements
  - No effective “brain supplement”
  - Vitamin deficiencies should be repleted
- Adjustment to medications used for other conditions

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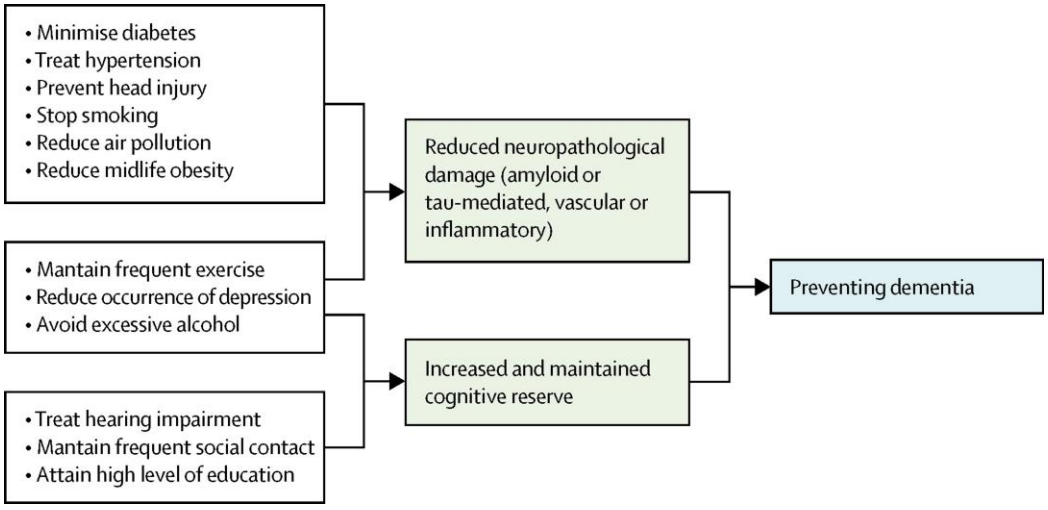
Modifiable risk factors of dementia



Livingston et. al 2020
The Lancet 2020 396413-446DOI: (10.1016/S0140-6736(20)30367-6)

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Addressing modifiable risk factors may impact disease course

- Sleep
- Physical activity
- Diet
- Cognitive activity
- Stress reduction
- Social activity
- Hearing/Vision
- Smoking cessation
- Oral hygiene

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How do we do it?

- 6 Pillars of Brain Health
  - Physical Activity
  - Food
  - Sleep
  - Cognitive Activity
  - Social Activity
  - Stress Reducing Activity

Physical Activity: 150-300 minutes per week of aerobic activity

Food: MIND Diet or Mediterranean diet

Sleep: Restorative sleep, 7-9 hours each night

Cognitive Activity: Daily enjoyable *yet* challenging activity that requires focus and thinking

Social Activity: Enjoying time with other people

Stress Reducing Activity: Daily intentional activity to unwind and relax

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Research, support groups, county resources

- Clinical trials
  - Pharmaceutical and lifestyle studies
  - Biomarker studies
- Community organizations
  - Alzheimer's Association
  - Alzheimer's Foundation of America
  - AARP (Global Council on Brain Health)
- Aging and Disability Resource Centers (WI)
  - Dementia care specialists

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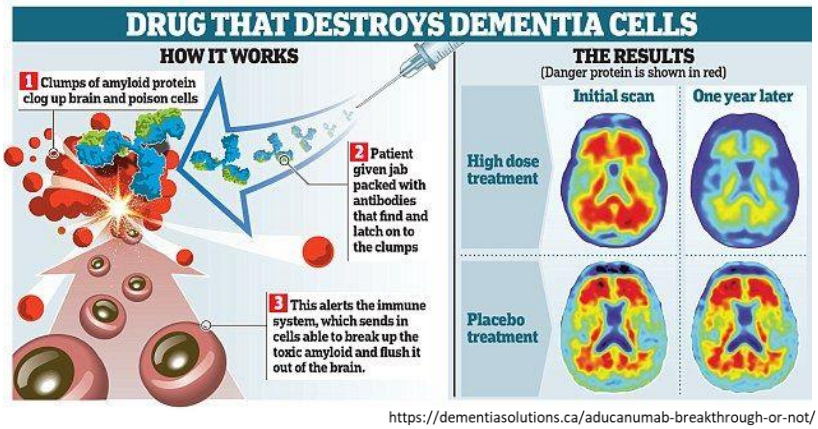
Treatments that Target Amyloid

- Aducanumab & Lecanemab
- Monoclonal antibody
- Infusion therapy removes aspects of amyloid-beta



https://dementiasolutions.ca/aducanumab-breakthrough-or-not/

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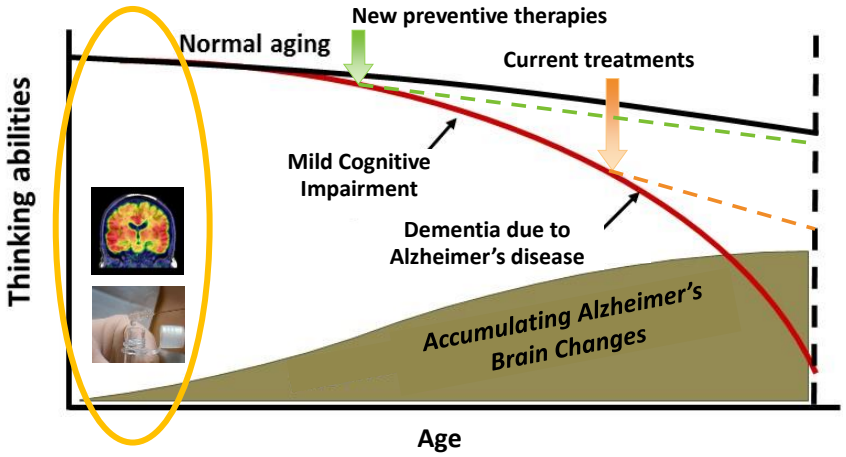
Developing New Therapies



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What is a biomarker?

- Objective measure collected from blood, other body fluids, or tissues that captures normal or abnormal biological processes and conditions

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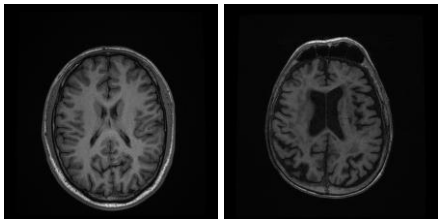
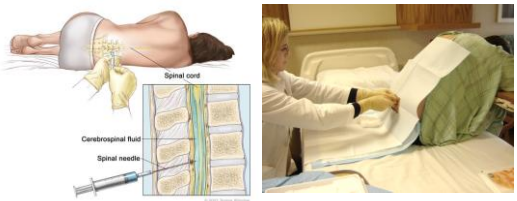
What are the current biomarkers in memory clinics?

MRI of brain, transverse section

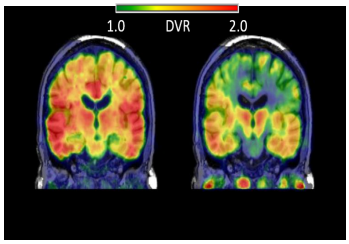


younger patient older patient



N Engl J Med 355;13 www.nejm.org September 28, 2006

PET Scans



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Why are blood-based biomarkers a good thing?

- Access
  - Better representation
- Less invasive and less risk
- Cost-effective & Time-effective
  - Scalable
- Like CSF, blood can be stored for future use

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What are the current blood-based biomarkers in AD research?

- Amyloid-beta (AB), ratio AB42/40, p-tau, NfL, t-tau, GFAP
  - P-tau seems to be the best
    - Elevated levels indicate amyloid PET positivity
    - Really elevated levels indicate tau PET positivity
    - *WRAP publication: Plasma pTau-217 in preclinical Alzheimer's disease*
    - *not just the type of p-tau, but the molecule and system used to measure
  - AB42/40 available in clinic
    - ~20% false positive rate
  - Neurofilament light (NfL): non-specific for neurodegeneration
  - Total tau (t-tau): non-specific for neuronal injury
  - Glial fibrillary acidic protein (GFAP): non-specific for brain inflammation

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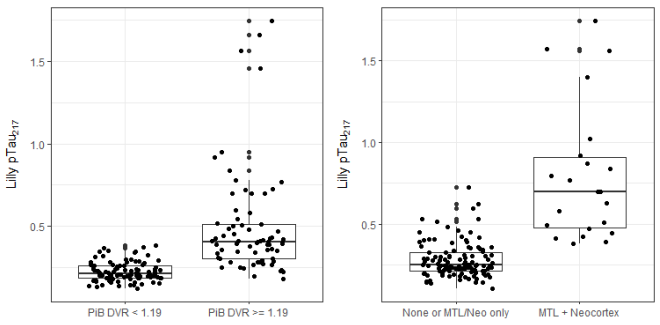
How valid are the blood-based biomarkers?

- Many studies show validity of AB ratio & p-tau
  - *Using PET as gold standard
  - Studied across the cognitive spectrum and age spectrum
  - *Most studied in well educated White individuals



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Can a blood-based biomarker diagnose MCI or dementia?

- **No**

- MCI and dementia are clinical diagnoses
  - Based on symptoms, cognitive testing, and clinical evaluation

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For those with MCI or dementia, can the blood-based biomarker diagnose AD?

- Depends
  - Clinical history and cognitive testing still matter
  - Type of biomarker matters
    - NfL, t-tau, GFAP = NO
  - Can support a diagnosis of AD
    - *Only tells us about AD, not the other causes
- AB42/40 = elevated amyloid, does not indicate tau
- Ptau217 = elevated amyloid, may indicate elevated tau

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Can blood-based biomarkers predict who will develop cognitive symptoms?

- Possibly…likely

- Similar to PET scans, there is a relationship
  - Some blood-based biomarkers show association with eventual cognitive decline
  - More work needed to validate

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Can blood-based biomarkers predict who will develop AD or MCI/dementia?

- Possibly

- Not everyone with amyloid develops tau
  - Some biomarkers may help differentiate this

- Not everyone with amyloid and tau develop MCI/dementia
  - People can have amyloid for 20-30 years without symptoms
  - Some biomarkers may help differentiate this

- Greater predictive power can occur as the accuracy of tests improve & the diversity of tests increases

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Where do biomarkers fit in a memory evaluation?

- ?
- To be determined

- Biomarkers have a role in diagnostics, prognostics, and understanding mechanisms

- People first. Understanding the experience and concerns of the patient/family is pivotal to care (including diagnosis). Diagnosing the syndrome is listening to people.

- Biomarkers are the tools used by clinicians after listening

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Starting with the syndrome

- Normal → SCD → MCI → Dementia
  - Ruling out conditions while evaluating for brain diseases
- History → Cognitive screening → Blood work & imaging → memory visit
- Structured interviews, validated questionnaires, cognitive tests
- Take advantage of tools
  - MoCA, Mini-Cog, SLUMS (remember the SLUMS scoring table is incomplete)
  - Use informant questionaries:
    - AD8 or short IQCODE for change from baseline
    - FAQ is a good tool for function
- Utilize a team and follow a process
  - Example: MTC has asynchronous SW help, MA support
- Refer to the memory clinic

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Referrals to the memory clinic

- Complex and atypical cases
- Possible MCI cases
  - Those needing thorough cognitive testing
  - Those with persistent symptoms despite normal scores on cognitive screening
  - Those with persistent symptoms after reversible causes have been corrected
- Dementia cases
  - Atypical presentations
  - Those with mild stage dementia who need further evaluation to see if they qualify for the new Alzheimer's medications

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What are the barriers for you?

- History collecting?
- Cognitive screening?
- Diagnosis?
- Care planning?
- Treatments?
- Communication?
- Clinic structure?
- Staffing?

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Comments and Questions

Thank you for listening!

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