Neurodegenerative Diseases

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Disclosures/Conflicts of Interest

Dr. Aase has no conflicts of interest or disclosures to report.

Learning Objectives

1. Provide an overview of different types of dementia and their prevalence

2. Understand neurocognitive sequelae and their impact on patient functioning

3. Discuss common clinical issues related neurodegenerative diseases

Neurodegenerative Diseases

Today, the focus is on **dementia**, which is an umbrella term for a variety of neurodegenerative diseases (but not all of them).

Dementia per ICD-10

- *Dementia (F00-F03) is a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language, and judgement. Consciousness is not clouded. The impairments of cognitive function are commonly accompanied, and occasionally preceded, by deterioration in emotional control, social behaviour, or motivation. This syndrome occurs in Alzheimer disease, in cerebrovascular disease, and in other conditions primarily or secondarily affecting the brain.*

ICD-10 (2019)

Neurodegenerative Diseases: Risk Factors

Risk factors for dementia

- Increasing age
- Cardiovascular diseases (heart disease, hypertension, hyperlipidemia, DM, A-Fib, heart failure) and high BMI
- Inflammation
- Lower education levels/cognitive reserve
- OSA
- CVA
- Moderate to severe TBI

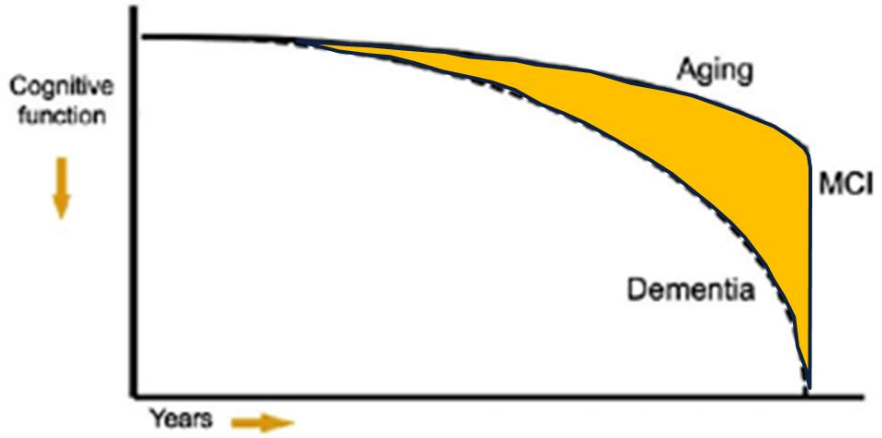
Hugo & Ganguli (2014); Stucky et al. (2014)

Neurodegenerative Diseases: MCI

Mild Cognitive Impairment (MCI)

- MCI is an intermediate stage between the expected decline of normal aging and the more pronounced decline of dementia.

- A critical factor that distinguishes MCI from dementia is the absence of functional impairment.



Slide adapted from Dr. Cady Block

Neurodegenerative Diseases: NCD

Minor	Major
Evidence of modest cognitive decline from a previous level of performance in one or more cognitive domains based on: 1) Concern of the individual, a knowledgeable informant, or the clinician that there has been a mild decline in cognitive function. 2) A modest impairment in cognitive performance, documented w/ neuropsych testing or another qualified clinical assessment.	Evidence of significant cognitive decline from a previous level of performance in 1 or more cognitive domains based on: 1) Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function. 2) Substantial impairment in cognitive performance, documented w/ neuropsych testing or another qualified clinical assessment.
These cognitive deficits do not interfere with the capacity for independence in everyday activities (e.g., complex iADLs such as paying bills or managing medications are preserved, but with greater effort, compensatory strategies, or accommodation)	These cognitive deficits interfere w/ independence in everyday activities (at minimum, requiring assistance with complex iADLs).
Deficits do not occur exclusively in the context of delirium & cannot be better explained by another mental disorder (e.g., major depressive disorder)	Deficits do not occur exclusively in the context of delirium & cannot be better explained by another mental disorder (e.g., major depressive disorder)
Cannot code behavioral disturbance (should be indicated in report, if relevant, but no code for this)	Can code behavioral disturbance & severity of functional impairment (if accompanied by psychotic symptoms, mood disturbance, agitation, or apathy; mild, mod, severe)
DSM-5 Code: 331.83 (G31.84) and should specify in writing possible/probably etiology	DSM-5 Code: Depends on probably or possible etiology (see p. 603-604 of DSM for diagnostic codes)

Slide courtesy of Dr. Cady Block

Diagnosing MCI vs. Dementia

DSM-5

Neurocognitive Disorders (NCD)

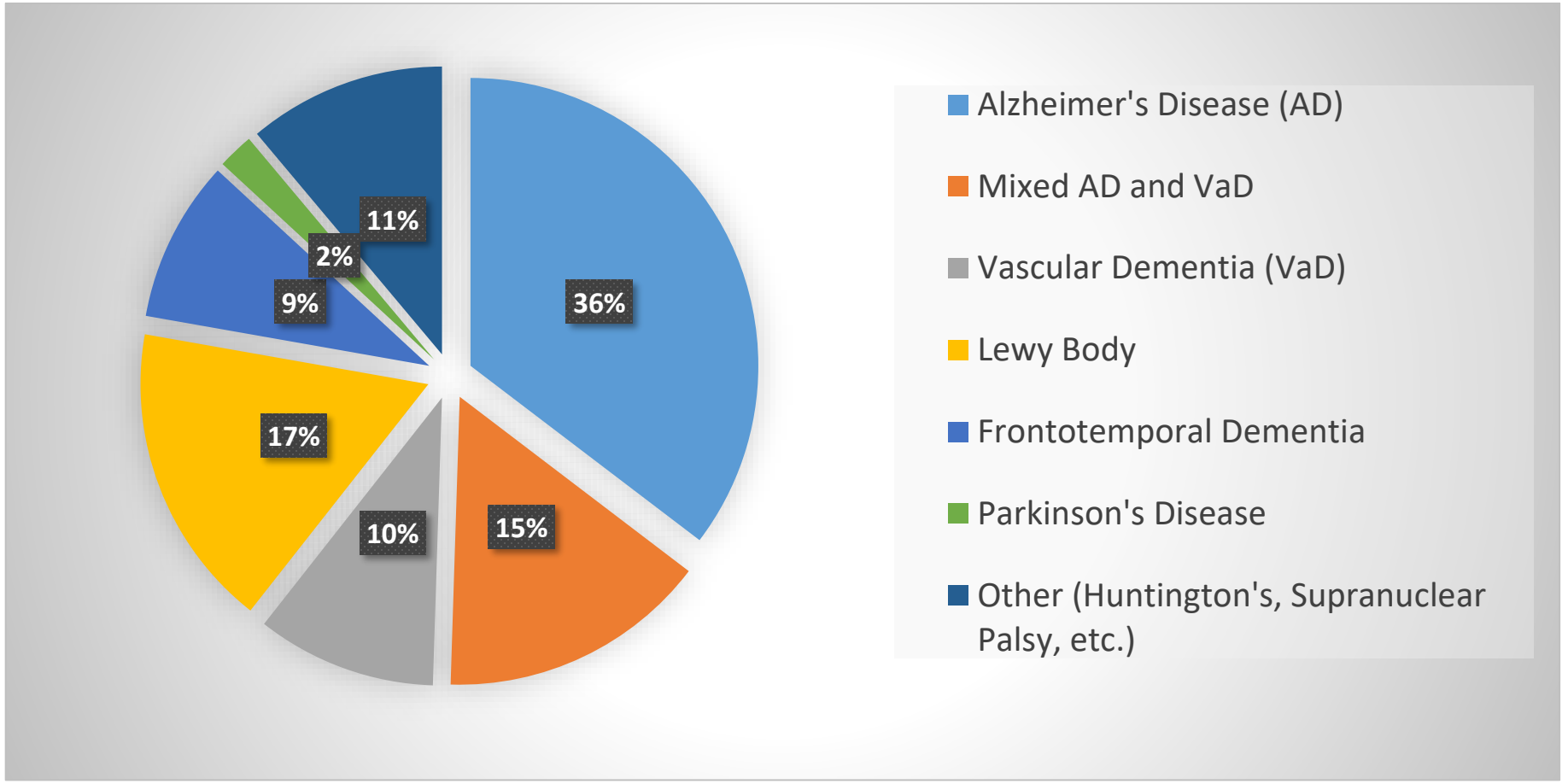
- Note: These are not solely due to neurodegenerative processes.
- “MCI” is typically used to reference prodromal or subtle decline due to presumed neurodegenerative condition.
- ~10% conversion to dementia per year

DSM-5 NCD Options

NCD due to Alzheimer’s Disease
Frontotemporal NCD
NCD with Lewy Bodies
Vascular NCD
NCD due to HIV Infection
NCD due to TBI
Substance/Medication Induced NCD
NCD due to Prion Disease
NCD due to Parkinson’s Disease
NCD due to Huntington’s Disease
NCD due to Another Medical Conditions (e.g., metabolic condition, immune disorder, structural lesions, neurological conditions)
NCD due to Multiple Etiologies
Unspecified NCD

Stucky et al. (2014); Slide adapted from Dr. Cady Block

Dementia Prevalence by cause



- Global prevalence rates for dementia (1980-2009) in individuals over age 60 found a rate of 5-7%
- Age-specific prevalence ranges from 0.1% at ages 60-64 to 8.6% at age 95.
- Prevalence rates double ever 4-5 years

Hugo & Ganguli (2014); Schoenberg & Scott, 2011; Stucky et al. (2014); Slide adapted from Dr. Cady Block

Neuropsychological Evaluation for NDs

Gathering information through a variety of methods:

- Medical Records Review
- Clinical Interview
- Collateral Interview
- Neuropsychological Testing

Overall goal to assist with differential diagnosis and treatment planning.

Can assist in identifying areas of clinical importance for the patient and family members to consider and address.

Neuropsychological Evaluation for NDs

Any given evaluation is a “snapshot” in time to determine the severity of a patient’s symptoms in the context of their overall clinical presentation.

We must consider important rule-outs for a patient’s self-reported symptoms, such as:

- Normal aging
- Psychiatric disturbance (e.g., Major Depression)
- Delirium
- Neurodevelopmental disorders
- “Modifiable” factors (e.g., situational stressors, reversible medical problems, substance use)

Neuropsychological Evaluation for NDs

Estimating "premorbid" or baseline functioning is critical

- Use of overlearned tasks (verbal) and demographic factors

Differential diagnosis by examining performance patterns and considering base rates.

- Different neurodegenerative diseases have different neurocognitive patterns commonly observed.
- Progression patterns also can vary, and mixed presentations/comorbidities interact frequently.
- Neuropsychological performance patterns are often correlated with neuroimaging.

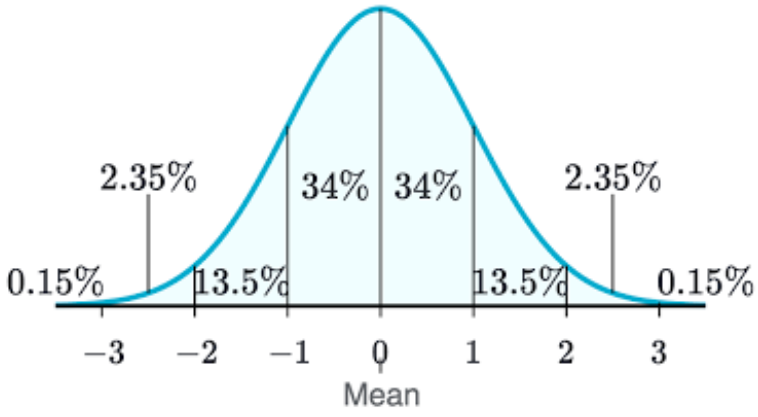
Performance on measures of neuropsychological functioning can also be predictive of outcomes.

- For example, performance on measures of verbal memory and semantic processing can be predictive of whether there is progression from MCI to Alzheimer's disease

Belleville et al. (2017); Pantel et al. (2004)

Neuropsychological Evaluation for NDs

- Neuropsychological testing data are typically interpreted in the context of performance relative to an appropriate normative sample.
- In optimal circumstances, demographic factors are taken into account when interpreting norms.
- Patterns based on cognitive domains are critical for understanding a patient's level of cognitive functioning.
- Some cognitive domains have "downstream" effects (e.g., attention/processing speed).



Neuropsychological Evaluation for NDs

- Neuropsychologists assess for particular domains in almost all dementia evaluations.
- Specialty measures can be utilized depending on the case factors and referral questions.
- **Example:** *Prospective Memory* deficits are common in NDs and have been associated with daily functioning (external validity).

Common Neuropsychological Domains
Attention
Processing Speed
Language
Visuospatial/Constructional
Memory
Executive Functioning
Sensorimotor
Functional and Psychiatric

Hering et al. (2018)

Neuropsychological Evaluation & COVID-19

Important to consider the context of COVID-19

Alterations in practice are occurring and may persist over time

- Risk/benefit analysis due to health vulnerability
- Consideration of delaying evaluation
- Modifications to the evaluation process to mitigate risk
  - Tele-Neuropsychology (direct to patient home)
  - In-clinic hybrid models (virtual testing from another room)
  - Mitigated in-person evaluations (with PPE and physical precautions)
  - Creative combinations of the above
- Because testing is only one component of the evaluation process, creativity can help to address referral questions and minimize risk

Bilder et al. (in press)

Sequelae of Types of Dementia

Alzheimer's Disease

- Most patients diagnosed during their 70s
- Higher prevalence among ethnic minorities
- Familial variant can be earlier onset (ages 40-60) with more rapid decline

Clinical/cognitive presentation

- 5-15 years in duration
- Insidious deficits in memory acquisition and storage
- Later, amnesia, aphasia, visuospatial deficits, executive dysfunction, and apathy
- Progressive decline in functioning
- Anosognosia (lack of insight into deficits later in the disease)

Lezak et al. (2012); Stucky et al. (2014)

Assessment of Memory

Memory is best understood in stages

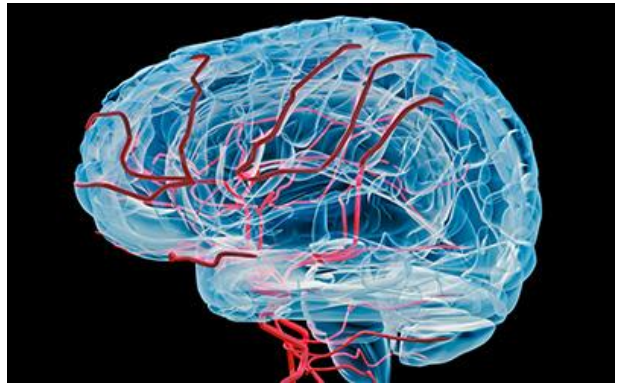
- *Acquisition (or encoding) where information is learned*
  - Assessed in clinic with repeated trials of stimuli
- *Storage/Consolidation*
  - Transfer of transient memory to a state of greater permanence
- *Retrieval (via free recall or recognition)*
  - How much of the information can the patient spontaneously retrieve after varying amounts of time?
  - Sometimes after being presented with distractor stimuli to detect interference
  - Recognition paradigms are easier – they provide cues/reminders
- **Key distinction** – in AD, impaired recognition (or rapid forgetting) often distinguishes it from subcortical dementia presentations where recognition is typically spared.

Note – screening measures do not assess all of these things!

Sequelae of Types of Dementia

Vascular Dementia

- Attributable to ischemic and/or hemorrhagic events that create cognitive and functional deficits
- Heterogeneous in presentation based on the pathology/location
- Can present independently or combined with other dementias
- 2.4% prevalence rate in adults over 70 (likely an underestimate)



Clinical/cognitive presentation

- No uniform pattern given the heterogeneous presentation
- Common areas are attention, processing speed, executive function, deficits in free recall (due to fronto-striatal deficits)
- Increased depression symptoms

Lezak et al. (2012); Stucky et al. (2014)

Sequelae of Types of Dementia

Lewy Body Dementia

- ~20% of all dementias
- Characterized by parkinsonism and cognitive decline
- Shares clinical features with Parkinson's disease and AD
- Onset average in late 50s; average 7 years survival time

Clinical/cognitive presentation

- Onset of motor and cognitive symptoms within 1 year of each other
- Fluctuating cognition with variable attention/alertness
- Visuoperceptual deficits, deficits in free recall, verbal and executive decline
- Key clinical features include visual hallucinations, neuroleptic sensitivity, and sometimes the presence of REM behavioral disorder

Lezak et al. (2012); Stucky et al. (2014)

Sequelae of Types of Dementia

Frontotemporal Dementia

- A group of neurodegenerative disorders sharing overlapping pathologies and clinical features. Varying prevalence estimates (9-20% of dementias).
- Median survival rates range from 3 to 8 years
- Typically earlier onset – ages 40-65, average 54 years. Later onset is rare.

Clinical/cognitive presentation – 3 variants

- *Behavioral variant* – insidious onset beginning with behavioral changes (and a lack of insight).
- Executive/Memory deficits followed by global impairment.
- Most common of the variants

Lezak et al. (2012); Stucky et al. (2014)

Sequelae of Types of Dementia

Clinical/cognitive presentation – 3 variants of FTD

- *Language variant* or *Primary Progressive Aphasia* – 3 distinct subtypes with language deterioration and relatively preserved other cognitive functions until later in the disease.
  - *Progressive nonfluent aphasia* – Impaired comprehension of sentences, agrammatism in language production, apraxia of speech (effortful and halting)
  - *Semantic dementia* – Impaired confrontation naming, impaired comprehension of words, spared speech production
  - *Logopenic* – Impaired single-word retrieval, impaired repetition

- *Motor variant* – 3 distinct subtypes with progressive deterioration of motor functions, concurrent with other cognitive and psychological symptoms
  - *Progressive supranuclear palsy* – Impaired downward gaze, bradykinesia, executive dysfunction
  - *Corticobasal degeneration* – Asymmetric limb apraxia, alien limb syndrome, visuosptail dysfunction, executive dysfunction
  - *FTD with upper motor neuron disease* – impaired memory and executive functions, speech deficits, disinhibition and personality changes, numerous motor symptoms

Lezak et al. (2012); Stucky et al. (2014)

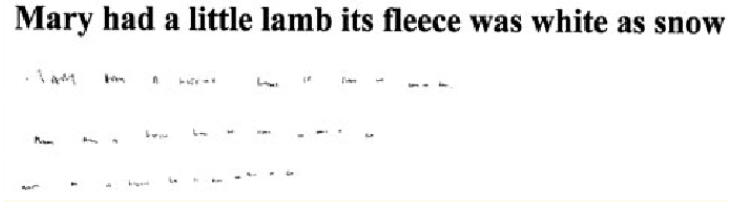
Sequelae of Types of Dementia

Parkinson's Disease (PD)

- Movement disorder due to dysfunction of frontal-subcortical network
  - Resting tremor, rigidity, postural instability, bradykinesia, other features
- Second most common ND overall
- 20-30% of people with PD develop dementia, usually if over 70

Clinical/cognitive presentation

- Cognitive problems more likely in non-tremor subtypes
- Motor symptoms and processing speed have downstream effects.
- Dysarthria, hypophonia, micrographia, impaired initial learning, reduced mental flexibility
- Higher incidence of depression and anxiety



Lezak et al. (2012); Stucky et al. (2014)

Sequelae of Types of Dementia

Huntington's Disease

- Terminal autosomal dominant movement disorder
- 1/10,000-1/20,000 prevalence
- Disease duration 17-20 years
- Onset typically ages 30-50

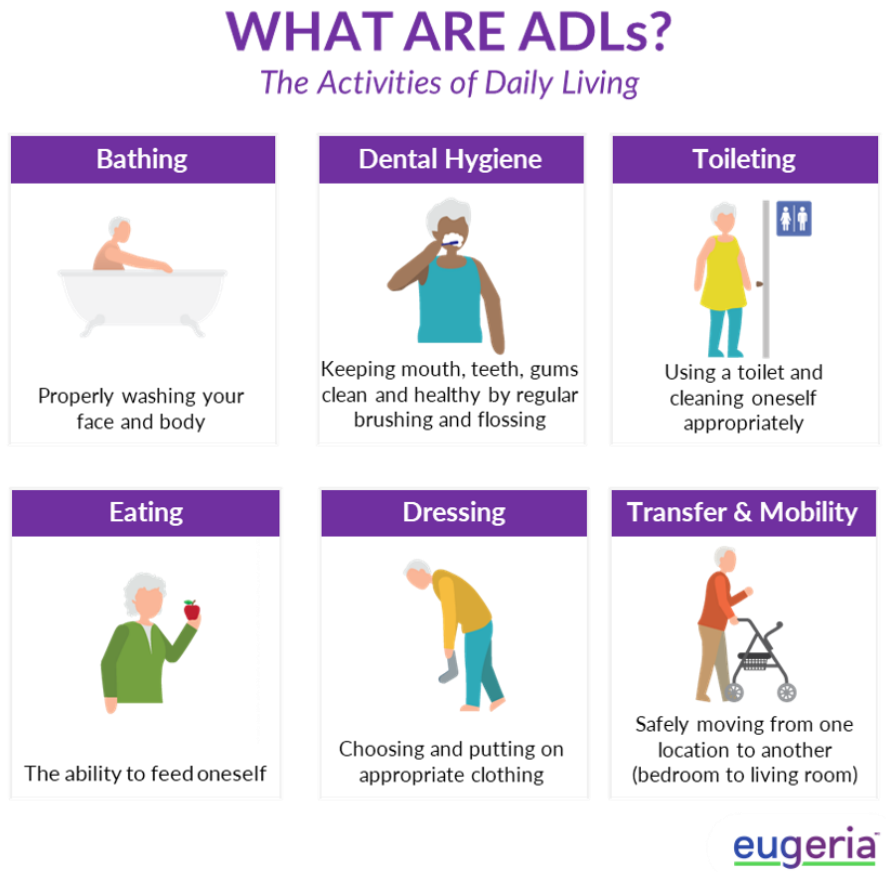
Clinical/cognitive presentation

- Chorea (involuntary dance-like movements)
- Eventual problems with dysarthria and dysphagia
- Impaired attention, processing speed, visuospatial, learning, executive functions
- Psychiatric problems and a high rate of suicide completion (7.3%)

Lezak et al. (2012); Stucky et al. (2014)

Common Clinical Issues

Assessment of functional status includes consideration of iADLs/ADLs.



Common Clinical Issues

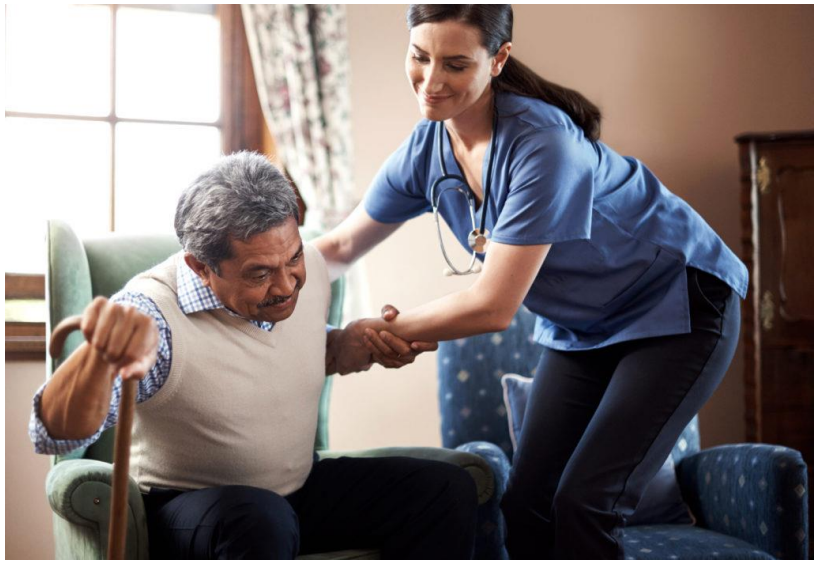
A number of clinical questions require case-by-case consideration when working with neurodegenerative disorders.

Level of supervision

- Depending on the "snapshot" of the patient's current cognitive and functional status, varying recommendations for level of supervision may be appropriate.

Functional needs

- Some patients may be able to manage iADLs/ADLs while others may require some level of assistance. Functional deficits will vary based on the type of neurodegenerative clinical presentation that is seen (e.g., apathy vs. cognitive deterioration).



Common Clinical Issues

Rehabilitation considerations

- Some patients may benefit from specific therapies, environment management, and compensatory memory strategies.

Driving

- Driving is a significant issue for consideration. Neuropsychological test results combined with clinical and collateral information can inform recommendations. Often, a behind-the-wheel driving assessment is a reasonable recommendation.

Employment

- Individuals still working need consideration of their capacity to continue to do so, if workplace accommodations or assistance may be appropriate, and if transitioning to retirement or long-term-disability may be appropriate options.

Common Clinical Issues

Capacity

- An important component of neuropsychological evaluations is an assessment of a patient's capacity to make medical and financial decisions. If a neurodegenerative disorder prognosis suggests certain decline, we often encourage patients to consider advance directives and other late-life issues along with trusted family.

Need for mental health intervention/support

- Neurodegenerative disease presentations involve varying degrees of insight that can impact adjustment to a diagnosis. Some involve specific and challenging neuropsychiatric symptoms. The impact on family members can be an enormous challenge. We routinely recommend mental health interventions when appropriate, and also link patients and caregivers to resources for peer support.

Common Clinical Issues

Risk factor modification

- We frequently recommend lifestyle interventions and appropriate referrals for sleep, medically-approved exercise, nutrition, fall-precautions, reducing social isolation, etc.

Addressing comorbidities

- Referrals are frequently made for comorbid health considerations that can interfere with treatment and also contribute to cognitive sequelae (e.g., noncompliant or untreated OSA).

Follow-up evaluations

- Sometimes, re-evaluation is indicated to track disease progression and update recommendations, and/or to assess response to interventions.

Summary

Today's goals were to:

1. Provide an overview of different types of dementia and their prevalence
2. Understand neurocognitive sequelae and their impact on patient functioning
3. Discuss common clinical issues related neurodegenerative diseases

Questions?

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