Major Neuro cogntive Disorder

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Cognition & Cognitive disorders

- Cognition includes memory, language, orientation, judgment, conducting interpersonal relationships, performing actions (praxis), and problem solving.

- Cognitive disorders reflect disruption in one or more of these domains and are frequently complicated by behavioral symptoms

DEFINITION

- Dementia, referred to as major neurocognitive disorder in the DSM-5, is marked by severe impairment in memory, judgment, orientation, and cognition.
- Dementia refers to a disease process marked by progressive cognitive impairment in clear consciousness.

- Dementia does not refer to low intellectual functioning because these are developmental and static conditions, and the cognitive deficits in dementia represent a decline from a previous level of functioning.

- Dementia involves multiple cognitive domains and cognitive deficits cause significant impairment in social and occupational functioning.

- There are four types of dementias based on etiology:
  - Alzheimer's disease
  - dementia of Lewy bodies
  - vascular dementia
  - frontotemporal dementia

- The critical clinical points of dementia are the identification of the syndrome and the clinical workup of its cause.

- The disorder can be progressive or static

- permanent or reversible

- An underlying cause is always assumed, although, in rare cases, it is impossible to determine a specific cause.

- The potential reversibility of dementia is related to the underlying pathological condition and to the availability and application of effective treatment.

- Approximately 15 percent of people with dementia have reversible illnesses if treatment is initiated before irreversible damage takes place.

EPIDEMIOLOGY

- With the aging population, the prevalence of dementia is rising.
- The prevalence of moderate to severe dementia in different population groups is:

  - 5 % in the general population> 65 y/o
  - 20 to 40 % in the general population> 85 y/o
  - 15 to 20 % in outpatient general medical practices

- the most common type of dementia: Alzheimer's disease 50 to 60 %

- The second most common type of dementia: vascular dementia: related to cerebrovascular diseases: 15 to 30 % of all dementia cases

- Vascular dementia is most common in persons between the ages of 60 and 70 and is more common in men than in women.

- coexisting vascular dementia and dementia of the Alzheimer's type: 10 to 15 %

- Other common causes of dementia: each representing 1 to 5 % of all cases:
  - head trauma
  - alcohol-related dementias
  - movement disorder-related dementias: Huntington's disease and Parkinson's disease

ETIOLOGY

- The most common causes of dementia in individuals older than 65 years of age are:
- (1) Alzheimer’s disease
- (2) vascular dementia
- (3) mixed vascular and Alzheimer’s dementia

- Other illnesses that account for approximately 10 %:
- Lewy body dementia
- Pick’s disease = frontotemporal dementias
- normal-pressure hydrocephalus (NPH)
- alcoholic dementia
- infectious dementia, such as HIV or syphilis
- Parkinson’s disease

- Many types of dementias evaluated in clinical settings can be attributable to reversible causes, such as:

- metabolic abnormalities (e.g., hypothyroidism)
- nutritional deficiencies (e.g., vitamin B12 or folate deficiencies)
- dementia syndrome caused by depression

Possible Etiologies of Dementia

Degenerative dementias
- Alzheimer's disease
- Frontotemporal dementias (e.g., Pick's disease)
- Parkinson's disease
- Lewy body dementia
- Idiopathic cerebral ferrocalcinosis (Fahr's disease)
- Progressive supranuclear palsy

Miscellaneous
- Huntington's disease
- Wilson's disease
- Metachromatic leukodystrophy
- Neuroacanthocytosis

Psychiatric
- Pseudodementia of depression
- Cognitive decline in late-life schizophrenia

Physiologic
- Normal-pressure hydrocephalus

Metabolic
- Vitamin deficiencies (e.g., vitamin B_{12}, folate)
- Endocrinopathies (e.g., hypothyroidism)
- Chronic metabolic disturbances (e.g., uremia)

Tumor
- Primary or metastatic (e.g., meningioma or metastatic breast or lung cancer)

Traumatic
- Dementia pugilistica, posttraumatic dementia
- Subdural hematoma

Infection
- Prion diseases (e.g., Creutzfeldt-Jakob disease, bovine spongiform encephalitis, Gerstmann-Sträussler syndrome)
- Acquired immune deficiency syndrome (AIDS)
- Syphilis

Cardiac, vascular, and anoxia
- Infarction (single or multiple or strategic lacunar)
- Binswanger's disease (subcortical arteriosclerotic encephalopathy)
- Hemodynamic insufficiency (e.g., hypoperfusion or hypoxia)

Demyelinating diseases
- Multiple sclerosis

Drugs and toxins
- Alcohol
- Heavy metals
- Irradiation
- Pseudodementia due to medications (e.g., anticholinergics)
- Carbon monoxide

Neuropathology

- The neurotransmitters that are most often implicated in the pathophysiological condition of Alzheimer's disease: acetylcholine and norepinephrine, both of which are hypothesized to be hypoactive in Alzheimer's disease.

- The primary cause of vascular dementia: multiple areas of cerebral vascular disease, resulting in a symptom pattern of dementia.

- Vascular dementia most commonly in men, with preexisting hypertension or other cardiovascular risk factors.

- parietal-temporal distribution of pathological findings in Alzheimer's disease

- Pick's disease is characterized by a preponderance of atrophy in the frontotemporal regions.

- Lewy body disease is a dementia clinically similar to Alzheimer's disease and often characterized by hallucinations, parkinsonian features, and extrapyramidal signs.

Clinical Criteria for Dementia with Lewy Bodies (DLB)

The patient must have sufficient cognitive decline to interfere with social or occupational functioning. Of note early in the illness, memory symptoms may not be as prominent as attention, frontosubcortical skills, and visuospatial ability. Probable DLB requires two or more core symptoms, whereas possible DLB only requires one core symptom.

Core features

- Fluctuating levels of attention and alertness
- Recurrent visual hallucinations
- Parkinsonian features (cogwheeling, bradykinesia, and resting tremor)

Supporting features

- Repeated falls
- Syncope
- Sensitivity to neuroleptics
- Systematized delusions
- Hallucinations in other modalities (e.g. auditory, tactile)

DSM-5 Diagnostic Criteria for Major Neurocognitive Disorder (Dementia)

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on:
   1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and
   2. A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

B. The cognitive deficits interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).

C. The cognitive deficits do not occur exclusively in the context of a delirium.

D. The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).

Specify whether due to:

Alzheimer's disease
Frontotemporal lobar degeneration
Lewy body disease
Vascular disease
Traumatic brain injury
Substance/medication use
HIV infection
Prion disease
Parkinson's disease
Huntington's disease
Another medical condition
Multiple etiologies
Unspecified

Coding note: Code based on medical or substance etiology. In some cases, there is a need for an additional code for the etiological medical condition, which must immediately precede the diagnostic code for major neurocognitive disorder.

Specify:

Without behavioral disturbance: If the cognitive disturbance is not accompanied by any clinically significant behavioral disturbance.

With behavioral disturbance (*specify* disturbance): If the cognitive disturbance is accompanied by a clinically significant behavioral disturbance (e.g., psychotic symptoms, mood disturbance, agitation, apathy, or other behavioral symptoms).

Specify current severity:

Mild: Difficulties with instrumental activities of daily living (e.g., housework, managing money).
Moderate: Difficulties with basic activities of daily living (e.g., feeding, dressing).
Severe: Fully dependent.

DIAGNOSIS AND CLINICAL FEATURES

- The diagnosis of dementia is based on the clinical examination, including a mental status examination, and on information from the patient's family, friends, and employers.

- Memory impairment is typically an early and prominent feature in dementia, especially in dementias involving the cortex, such as dementia of the Alzheimer's type.

- Early in the course of dementia, memory impairment is mild and usually most marked for recent events; people forget telephone numbers, conversations, and events of the day.

- As the course of dementia progresses, memory impairment becomes severe, and only the earliest learned information (e.g., a person's place of birth) is retained.

Psychiatric and Neurological Changes

- Personality
- Hallucinations and Delusions
- Mood
- Cognitive Change
- Catastrophic Reaction
- Sundowner Syndrome

Major Clinical Features Differentiating Pseudo dementia from Dementia

Pseudodementia	Dementia
Clinical Course and History	
Family always aware of dysfunction and its severity	Family often unaware of dysfunction and its severity
Onset can be dated with some precision	Onset can be dated only within broad limits
Symptoms of short duration before medical help is sought	Symptoms usually of long duration before medical help is sought
Rapid progression of symptoms after onset	Slow progression of symptoms throughout course
History of previous psychiatric dysfunction common	History of previous psychiatric dysfunction unusual
Complaints and Clinical Behavior	
Patients usually complain much of cognitive loss	Patients usually complain little of cognitive loss
Patients' complaints of cognitive dysfunction usually detailed	Patients' complaints of cognitive dysfunction usually vague
Patients emphasize disability	Patients conceal disability
Patients highlight failures	Patients delight in accomplishments, however trivial
Patients make little effort to perform even simple tasks	Patients struggle to perform tasks
	Patients rely on notes, calendars, and so on to keep up
Patients usually communicate strong sense of distress	Patients often appear unconcerned
Affective change often pervasive	Affect labile and shallow
Loss of social skills often early and prominent	Social skills often retained
Behavior often incongruent with severity of cognitive dysfunction	Behavior usually compatible with severity of cognitive dysfunction
Nocturnal accentuation of dysfunction uncommon	Nocturnal accentuation of dysfunction common
Clinical Features Related to Memory, Cognitive, and Intellectual Dysfunctions	
Attention and concentration often well preserved	Attention and concentration usually faulty
"Don't know" answers typical	Near-miss answers frequent
On tests of orientation, patients often give "don't know" answers	On tests of orientation, patients often mistake unusual for usual
Memory loss for recent and remote events usually severe	Memory loss for recent events usually more severe than for remote events
Memory gaps for specific periods or events common	Memory gaps for specific periods unusual[a]
Marked variability in performance on tasks of similar difficulty	Consistently poor performance on tasks of similar difficulty

Normal Aging

- Aging is not necessarily associated with any significant cognitive decline, but minor memory problems can occur as a normal part of aging.

- They are distinguished from dementia by their minor severity and because they do not interfere significantly with a person's social or occupational behavior.

COURSE AND PROGNOSIS

- The classic course of dementia is an onset in the patient's 50s or 60s, with gradual deterioration over 5 to 10 years, leading eventually to death.

- The age of onset and the rapidity of deterioration vary among different types of dementia and within individual diagnostic categories.

- The average survival expectation for patients with dementia of the Alzheimer's type is approximately 8 years, with a range of 1 to 20 years.

- After dementia is diagnosed, patients must have a complete medical and neurological workup because 10 to 15 percent of all patients with dementia have a potentially reversible condition if treatment is initiated before permanent brain damage occurs.

- The course of the dementia varies:
  - steady progression: Alzheimer's type
  - worsening dementia: vascular dementia
  - a stable dementia: in dementia related to head trauma

TREATMENT

- The first step in the treatment of dementia is verification of the diagnosis.

- Preventive measures are important, particularly in vascular dementia. Such measures might include:
- changes in diet, exercise
- control of diabetes and hypertension
- Pharmacological agents: antihypertensive, anticoagulant, antiplatelet agents

Psychosocial Therapies

- Recent memory is lost before remote memory in most cases of dementia, and many patients are highly distressed by clearly recalling how they used to function while observing their obvious deterioration.

- Emotional reactions ranging from depression to severe anxiety to catastrophic terror can stem from the realization that the sense of self is disappearing.

- Patients often benefit from a supportive and educational psychotherapy in which the nature and course of their illness are clearly explained.

- They may also benefit from assistance in grieving and accepting the extent of their disability and from attention to self-esteem issues.

- Any areas of intact functioning should be maximized by helping patients identify activities in which successful functioning is possible

- Clinicians can help patients find ways to deal with the defective ego functions:
  - keeping calendars for orientation problems
  - making schedules to help structure activities
  - taking notes for memory problems

- Psychodynamic interventions with family members of patients with dementia may be of great assistance.

- Those who take care of a patient, as they watch a family member gradually deteriorate struggle with feelings of:
  - guilt
  - grief
  - anger
  - exhaustion

- Clinicians must also be aware of the caregivers' tendencies to blame themselves or others for patients' illnesses and must appreciate the role that patients with dementia play in the lives of family members.

Pharmacotherapy

- benzodiazepines for insomnia and anxiety
- antidepressants for depression
- antipsychotic drugs for delusions and hallucinations
- but should be aware of possible idiosyncratic drug effects in older people (e.g., paradoxical excitement, confusion, and increased sedation)
- In general, drugs with high anticholinergic activity should be avoided.

- cholinesterase inhibitors used to treat mild to moderate cognitive impairment in Alzheimer’s disease:
  - Donepezil
  - rivastigmine
  - galantamine
  - tacrine

- Donepezil is well tolerated and widely used.
- Tacrine is rarely used because of its potential for hepatotoxicity.
- Memantine: NMDA antagonist: protects neurons from excessive amounts of glutamate, which may be neurotoxic. The drug is sometimes combined with donepezil.

Drug (Brand)	Formulation	Indications	Starting Dose	Titration	Dosage Range
Tacrine (Cognex)	10-, 20-, 30-, 40-mg capsules	Mild to moderate AD dementia	10 mg 4 times a day	Increase by 10 mg 4 times a day (40 mg total daily) every 4 weeks	40–160 mg daily with 4 times a day dosing
Donepezil (Aricept)	5-, 10-, 23-mg tablets 5-, 10-mg disintegrated tablets	Mild to moderate and severe AD dementia	5 mg daily	Increase to 10 mg after 4 weeks. Increase to 23 mg daily after 3 months	10–23 mg daily
Rivastigmine (Exelon, Exelon	1.5-, 3-, 4.5-, 6-mg oral solution	Mild to moderate AD dementia Major	4 mg twice a day 8 mg daily	By 1.5 mg twice a day every 4	3–6 mg daily for oral preparation.

Galantamine (Razadyne, Razadine ER)	4-, 8-, 12-mg tablets 8-, 16-, 24-mg extended-release capsules 4-mg/mL oral solution	Mild to moderate AD dementia	1.5 mg twice a day 4.6-mg transdermal patch	Increase by 4 mg twice a day every 4 weeks. Increase by 8 mg every 4 weeks for extended release	4–12 mg in divided doses for oral preparation. 8–24 mg daily for extended release
Memantine (Namenda, Namenda XR)	5-, 10-mg tablets 7-, 14-, 21-, 28-mg extended-release capsules 10-mg/5-mL oral solution	Moderate to severe AD dementia	5 mg daily 7-mg extended-release formula	By 5 mg daily in weekly intervals. Increase by 7 mg daily extended-release formula	10–20 mg daily in divided dose for oral preparation. 7–28 mg daily for extended release
Memantine XR and donepezil combination (Namzaric)	14-mg memantine ER/10-mg donepezil capsules	Moderate to severe Alzheimer disease when patient	14-mg memantine ER/10-mg donepezil daily		

Take Home Message…

- The most common form of dementia: Alzheimer’s disease
- Main NTs in Alzheimer’s disease: Ach & Nepi
- Pick disease: FTD : personality change
- DLB: EPS

Thanks

For your attention