Cognition and Neurological Disorders

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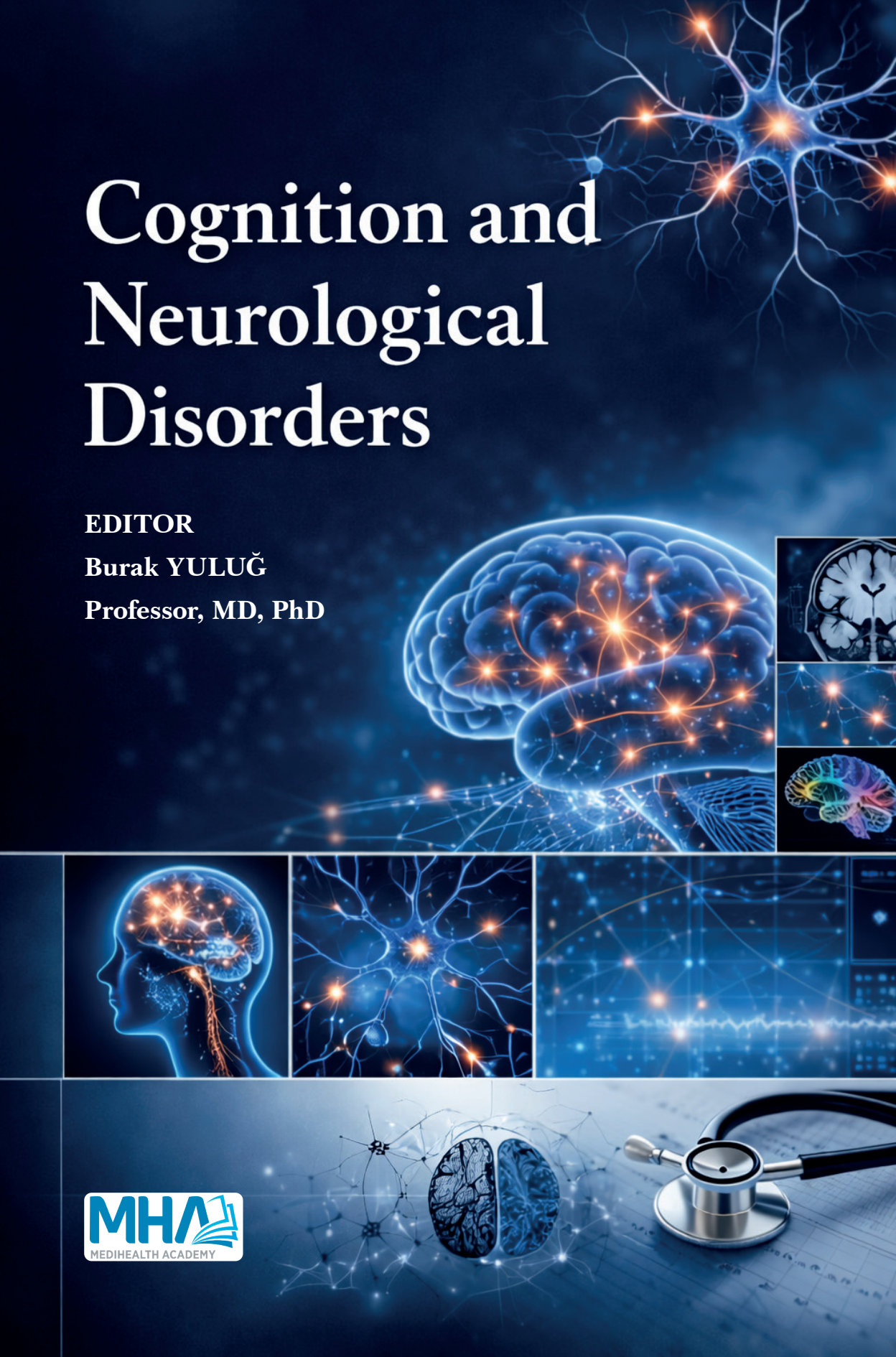

MHA
MEDIHEALTH ACADEMY

Contents

Chapter 7

Dementia Syndromes

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ABSTRACT

Dementia is a group of diseases characterized by decline in cognitive functions and functional impairment. Although Alzheimer's disease (AD) remains the most common subtype worldwide, other important forms such as dementia with Lewy bodies, frontotemporal dementia, and vascular dementia also contribute significantly to the global disease burden. The pathophysiology of dementia varies according to etiology and involves complex neurodegenerative, vascular, and protein aggregation mechanisms. Accurate diagnosis requires a comprehensive and multidisciplinary approach that includes a detailed clinical history, cognitive assessment using validated instruments such as the Mini-Mental State Examination, laboratory evaluation to exclude reversible causes, and neuroimaging to identify structural or vascular abnormalities. Advances in cerebrospinal fluid biomarkers and functional imaging techniques have improved diagnostic accuracy; however, their routine clinical application remains limited. Current treatment strategies are primarily symptomatic and aim to preserve cognitive and behavioral function. Pharmacological therapies focus on neurotransmitter modulation, particularly through acetylcholinesterase inhibitors and N-methyl-D-aspartate receptor antagonists such as memantine. Given the projected increase in dementia prevalence associated with global population aging, early recognition, structured diagnostic evaluation, and individualized management strategies remain essential components of care.

ALZHEIMER'S DISEASE (AD)

AD, the most common cause of dementia, is characterized by cognitive, functional, and behavioral impairment that typically begins with recent memory loss.[1] Pathological findings in the brain tissue of patients with AD are senile plaques and neurofibrillary tangles (NFTs).

The number of affected individuals is predicted to increase significantly by 2050 due to the aging of the population.[2] Extracellular plaques consist of Aβ, while intracellular neurofibrillary tangles consist of p-tau. These neuropathological changes typically occur in the basal nucleus and then spread to other cortical and limbic regions.

AD is the most common type of dementia. Age is an important risk factor and increases after age 65.[3] Many prevalence studies show that AD is more common in women.[4] Although there are epidemiological studies showing that there is no relationship between education level and AD, low education level is now considered a potential risk factor.[5]

The most frequently studied occupational agents as risk factors for AD are organic solvents, pesticides, aluminum, and lead.[6] There are studies showing that the risk of AD is significantly increased in individuals who smoke two or more packs of cigarettes per day during midlife.[7] Heavy alcohol use in middle age has been reported to triple the risk of AD, especially in those carrying the ApoE-ε4 allele.[8]

There are studies indicating that a history of depression requiring treatment within the previous ten years increases the risk of AD.[9] Limited social relationships have been identified as an independent risk factor in major community-based cross-sectional and longitudinal observational studies conducted in Sweden and the United States.[10]

Results from epidemiological, neuroimaging and neuropathological studies have shown that vascular dementia, as well as vascular risk factors and vascular morbidity, are risk factors for Alzheimer's disease.[11]

Diagnostic Approach

A systematic and multidisciplinary approach is recommended for the evaluation of cognitive impairment:

- Comprehensive history focusing on the cognitive complaint, symptom onset and progression, functional status, and safety considerations.
- Thorough physical and neurological examination.
- Cognitive assessment using validated instruments such as the Mini-Mental State Examination (MMSE), Mini-Cog, and National Adult Reading Test.
- Laboratory investigations to exclude reversible causes, including complete blood count, metabolic panels, vitamin B12 and folate levels, and, when clinically indicated, infectious and autoimmune markers.
- Neuroimaging using magnetic resonance imaging (MRI) to identify structural, vascular, or inflammatory etiologies.
- Specialty consultations when required, including dementia specialists, neuropsychologists, social workers, or geriatric psychiatrists.

The MMSE remains widely used in clinical practice, with scores below 24 suggesting possible dementia; however, notable limitations exist in detecting subtle cognitive deficits, particularly those involving frontal lobe dysfunction, and in individuals with higher educational attainment.[12,13,14] The Mini-Cog provides an alternative brief screening tool with comparable sensitivity and specificity.[15]

Advanced diagnostic modalities such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT) may improve diagnostic accuracy in complex or atypical cases. Cerebrospinal fluid biomarker analysis for tau and amyloid-β also offers predictive value, although its routine clinical use remains limited.[16,17,18]

Lewy Body Dementia

Dementia with Lewy bodies (DLB) is the second most common cause of dementia.[19] DLB is more common in men. The clinical picture of DLB is part of a spectrum that includes dementia and parkinsonism. Prominent clinical features include impaired concentration, decreased verbal fluency, visual-spatial dysfunction, and psychomotor slowing. Patients with DLB are sensitive to neuroleptic drugs. Fluctuating levels of alertness, recurrent visual hallucinations, and the presence of parkinsonism are considered the key features required for a possible diagnosis of DLB.[19]

Frontotemporal Dementia Syndromes

Frontotemporal dementia (FTD) is a type of dementia that specifically affects the frontal and temporal lobes.[20] The underlying pathophysiology of FTD is that cholinergic function is preserved and is mostly associated with serotonergic deficiencies.[21]

Patients with FTD are typically younger than those with AD, often presenting before the age of 65, and the disease may progress more rapidly. Personality changes and socially inappropriate behavior are prominent early features. Patients frequently demonstrate early loss of insight, emotional blunting, and behavioral disinhibition.[22,23]

Vascular Dementia

Vascular dementia is the second most common type of dementia after AD. Patients often have vascular risk factors. Although many clinicians continue to rely on DSM-IV diagnostic criteria, various diagnostic criteria have been proposed.[24,25]

A causal relationship between dementia and cerebrovascular disease must be demonstrated. Decline in cognitive functions occurs after a recent stroke. Vascular dementia may occur with a sudden deterioration in cognitive functions.[24,25]

Table 1. Comparative clinical, pathological, and imaging features of major dementia subtypes[19-25]

Feature	AD	DLB	FTD	VaD
Core pathology	β-amyloid plaques + tau	α-synuclein (cortical Lewy bodies)	Tau / TDP-43 pathology	Cerebrovascular disease
Typical onset	Insidious, progressive	Fluctuating cognition	Early onset (<65 years)	Acute or stepwise
Early feature	Episodic memory loss	Hallucinations + fluctuations	Behavioral/ personality changes	Executive dysfunction
Memory	Early prominent	Mild early	Relatively preserved early	Variable
Attention	Preserved early	Fluctuating	Mild impairment	Impaired
Hallucinations	Late	Early prominent	Rare	Rare
Parkinsonism	Late	Early	Uncommon	Sometimes
REM sleep disorder	Rare	Common	Rare	Rare
Executive dysfunction	Late	Early	Early prominent	Early prominent
Progression	Gradual	Moderate	Rapid	Stepwise
Neuroimaging	Hippocampal atrophy	Relatively preserved	Frontal/temporal atrophy	Infarcts, white matter lesions
AChEI response	Good	Very good	Limited	Limited
Antipsychotic sensitivity	Normal	Severe	Variable	Variable