Clinical assessment

Clinical changes in the early stages of Alzheimer’s disease (AD)

This content is intended for health care professionals only for educational and informational purposes and does not substitute for sound medical judgement or clinical decision making in the context of medical treatment

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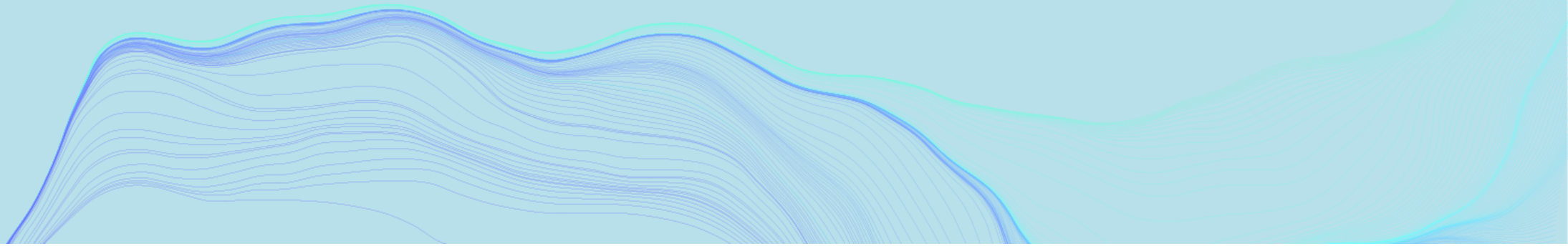
PIPN-M3142

Slide outline

Learning Zone

Understanding the domains of cognition



Domains of cognition

Cognition is not a unitary construct; it consists of different domains

Episodic memory
Recollection of past events and personal experiences[1,2]

Visuospatial functions
Concerned with the integration of space and visual form[3]

Executive functions
Thinking skills that assist with reasoning, planning, problem solving, and managing one's life[3]

Language
Verbal expression, language interpretation, and communication[1]

Attention
The capacity to focus and sustain concentration[1]

Attention
Monitor and process data in the surrounding environment to plan a motor action, e.g., imitate a hand gesture[5]

1. Harvey PD. Dialogues Clin Neurosci 2019;21:227–237; 2. Zilli EA, Hasselmo ME. Hippocampus 2008;18:193–209; 3. Mitchell, Meghan B., and Alireza Atri, 'Dementia Screening and Mental Status Examination in Clinical Practice', in Bradford Dickerson, and Alireza Atri (eds), Dementia: Comprehensive Principles and Practices (New York, 2014; online edn, Oxford Academic, 1 Nov. 2014); 4. Blair C. Curr Dir Psychol Sci 2016;25:3–7; 5.Ward M, et al. Dement Neuropsychol 2015;9:71–75

Clinical presentation by cognitive domain in AD

Episodic memory

- Forgetting recent personal and family events[1]
- Losing items around the home[1]
- Forgetting recent conversations[1]

Visuospatial functions

- Impaired perception of objects and faces[2]
- Inability to find the way in familiar surroundings[2]

Executive functions

- Struggle to follow a series of steps[1]
- Impaired judgment and problem-solving skills
- Repetitive questions[1]

Attention

- Impaired concentration[1]
- Losing track of thoughts[1]

Language

- Difficulty finding words[2]
- Struggling to follow a conversation[2]

Praxis

- Inability to perform a movement with a body part[3]
- Inability to imitate hand gestures[3]

In AD dementia, language and memory problems are closely related and overlap. In the early stages, impairments in semantic memory can occur e.g., naming and object recognition. Repetition and articulation remain relatively intact[4]

AD, Alzheimer's disease

1. Kipps CM, Hodges JR. J Neurol Neurosurg Psychiatry 2005;76(Suppl. 1):i22–i30; 2. Alzheimer's Society. The dementia guide. Available from: https://www.alzheimers.org.uk/sites/default/files/2020-03/the_dementia_guide_872.pdf (Accessed June 2023); 3. Ward M, et al. Dement Neuropsychol 2015;9:71–75; 4. Szatloczki G, et al. Front Aging Neurosci 2015;7:195;

Learning Zone

Definitions of Dementia and mild cognitive impairment (MCI)

Dementia

Dementia is defined by two key features:

1. **Cognitive impairment:** insidious, significant, progressive impairment across more than one cognitive domain[1]
2. **Functional impairment:** cognitive impairment (and/or concurrent neuropsychiatric symptoms [NPS]) has a clear impact on daily life activities, including social and occupational. The individual is no longer fully independent and requires assistance with activities of daily living[1,2]

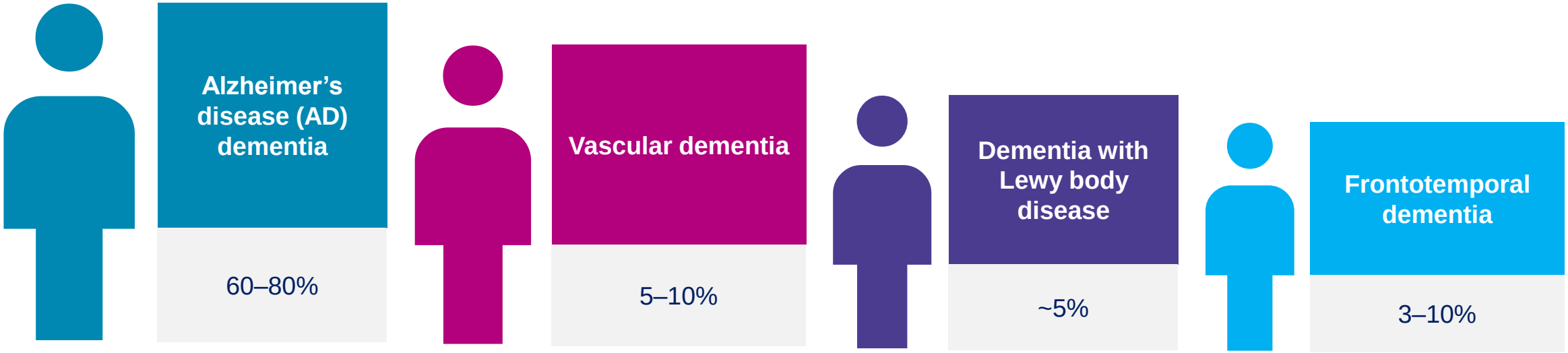
- Functional dependence is the primary feature differentiating dementia from MCI[3]
  - Current DSM-5 nomenclature refers to dementia as major neurocognitive disorder[3]

- ✓ Dementia is a clinical manifestation of an underlying neurodegenerative disease (or reversible condition impacting cognition)[4,5]
- ✓ AD is the most common neurodegenerative disease that eventually leads to dementia[3,4]

AD, Alzheimer's disease; DSM, Diagnostic and Statistical Manual of Mental Disorders; MCI, mild cognitive impairment; NPS, neuropsychiatric symptoms

1. Jack CR Jr, et al. Alzheimers Dement 2018;14:535–562; 2. McKhann GM, et al. Alzheimers Dement 2011;7:263–269; 3. Hugo J, Ganguli M. Clin Geriatr Med 2014;30:421–442; 4. University of California San Francisco. Available from: https://memory.ucsf.edu/dementia-overview (Accessed July 2023); 5. Chari D, et al. J Geriatr Mental Heath 2015;2:30–37

Types of dementia



Other causes of dementia: Mixed pathologies, hippocampus sclerosis, Parkinson's disease (similarities with LBD), chronic traumatic encephalopathy, progressive supranuclear palsy, corticobasal degeneration, Huntington's disease[1,2]

Percentages indicate the proportion of individuals with dementia
AD, Alzheimer's disease
1. Alzheimer's Association. 2023 Alzheimer's disease facts and figures. Alzheimers Dement 2023;19(4):1598-1695; 2. University of California San Francisco. Available from: https://memory.ucsf.edu/dementia-overview (Accessed July 2023)

Underlying etiologies of dementia

Dementia is a clinical syndrome that has multiple etiologies, including reversible conditions and progressive, neurodegenerative diseases[1,2]*

Neurodegenerative causes of dementia:

- **Alzheimer's disease[1]**
  - Clinical syndrome: Alzheimer's disease dementia
  - The most common cause of dementia

- **Cerebrovascular disease[3]**
  - Clinical syndrome: vascular dementia (VaD) / vascular cognitive impairment (VCI)
  - VaD/VCI and AD often co-occur, resulting in Mixed dementia[2]

- **Lewy body disease[4]**
  - Clinical syndrome: dementia with Lewy bodies (DLB)

- **Frontotemporal lobar degeneration[5]**
  - Clinical syndrome: frontotemporal dementia

Potential reversible causes of dementia[2]

- ✓ Idiopathic depression
- ✓ Vitamin B12 and/or folate deficiency
- ✓ Medications
- ✓ Hypothyroidism / hyperthyroidism
- ✓ Normal pressure hydrocephalus

*The following are examples of additional neurodegenerative causes of dementia: Parkinson's disease (similarities with LBD), chronic traumatic encephalopathy, progressive supranuclear palsy, corticobasal degeneration, Huntington's disease[1]

AD, Alzheimer's disease; DLB, dementia with Lewy bodies; LBD, Lewy body dementia; VaD, vascular dementia; VCI, vascular cognitive impairment

1. University of California San Francisco. Available from: https://memory.ucsf.edu/dementia-overview (Accessed July 2023); 2. Chari D, et al. J Geriatr Mental Heath 2015;2:30–37; 3. Smith EE. Clin Sci (Lond) 2017;131:1059–1068; 4. McKeith IG, et al. Neurology 2017;89:88–100; 5. Young JJ, et al. Ther Adv Psychopharmacol 2018;8:33–48

Clinical characteristics of other neurodegenerative causes of dementia

VaD[1]	DLB[2]	FTLD[3,4]			LATE[5]
		bvFTD	**svPPA**	**nfvPPA**	
• **Variable cognitive profile:** domains affected depend on size and location of vascular lesion(s) • **Variable onset and time course** • **Variable non-cognitive features:** focal motor, sensory, and visual deficits	• **Dementia characterized by:** greater deficits in attention, visuospatial, and executive domains than in typical AD • **Prominent fluctuations** in cognition and alertness • **Visual hallucinations** • **REM sleep behavior disorder** • **Spontaneous motor features of Parkinsonism:** bradykinesia, rest tremor, rigidity	• Early impairment in social conduct • Prominent executive dysfunction	• Fluent output with progressive loss of meaning of words • Episodic memory often preserved	• Decline in verbal expression, dysfluent speech, grammatical changes • Memory and visuospatial function relatively preserved	• **Similar characteristics to what is observed in AD** (ie amnestic syndrome with **prominent episodic impairment**), but with more gradual decline over time • May have preserved verbal fluency, despite **profound deficiency in word list delayed recall** • Distinguished from FTLD with TDP-43 by epidemiology (generally affects older people) and anatomic distribution of proteinopathy

AD, Alzheimer's disease; bvFTD, behavioral frontotemporal dementia; DLB, dementia with Lewy bodies; FTD, frontotemporal dementia; FTLD, Frontotemporal lobar degeneration;
LATE, Limbic-predominant age-related TDP-43 encephalopathy; nfvPPA, non-fluent variant primary progressive aphasia; REM, rapid eye movement;
svPPA, semantic variant primary progressive aphasia; TDP-43, TAR DNA-binding protein 43; VaD, vascular dementia

1. Smith EE. Clin Sci (Lond) 2017;131:1059–1068; 2. McKeith IG, et al. Neurology 2017;89:88–100; 3. Bott NT, et al. Neurodegener Dis Manag 2014;4:439–454; 4. Young JJ, et al. Ther Adv Psychopharmacol 2018;8:33–48; 6. Nelson P, et al. Brain 2019:142;1503–1527

Clinical characteristics of AD with mixed pathologies

AD with vascular pathology

- Impairments of executive function and attention are likely to be an early symptom[1,2]
- Gait impairment more likely to be present[2]
- Particularly common amongst the elderly[2]

AD with DLB pathology

- Individuals may exhibit more severe NPS, such as delusions, hallucinations, and motor disturbances[3]
- Ages of dementia onset and death are younger than “pure” AD[3]

AD with other pathologies or comorbidities

LATE[4]

- Individuals tend to be of older age have faster decline and more severe cognitive impairment
- May exhibit more prominent neuropsychiatric disturbances

Obstructive sleep apnea[5,6]

- Sleep fragmentation and intermittent hypoxia may influence the cognitive profile of AD

Traumatic brain injury[7,8]

- Impairments in attention, episodic memory, and executive function are often affected

Depression and anxiety[9]

- Attention, psychomotor processing speed, executive function, and episodic memory are commonly affected

AD, Alzheimer’s disease; DLB, dementia with Lewy bodies; LATE, Limbic-predominant age-related TDP-43 encephalopathy; NPS, neuropsychiatric symptoms; TDP-43, TAR DNA-binding protein 43; VaD, vascular dementia

1. Karantzoulis S, Galvin JE. Expert Rev Neurother 2011;11:1579–1591; 2. Alzheimer’s Association. Alzheimers Dement 2023;19(4):1598-1695; 3. Chung EJ, et al. JAMA Neurol 2015;72:789–796; 4. Nelson P, et al. Brain 2019:142;1503–1527; 5. Andrade A, et al. J Alzheimers Dis 2019;64(Suppl. 1):S255–S270; 6. Kuo CY, et al. Front Aging Neurosci 2021;12:591737; 7. Wortzel HS, Arciniegas DB. Curr Treat Options Neurol 2012;14:493–508; 8. Model System Knowledge Translation Center. TBI factsheet. Available from: https://msktc.org/tbi/factsheets/Understanding-TBI/Brain-Injury-Impact-On-Individuals-Functioning#fsmenu8 (Accessed July 2023); 9. McAllister-Williams RH, et al. J Affect Disord 2017;207:346–352

Clinical characteristics of atypical presentations of AD

Atypical presentations of AD most often include syndromes in which the episodic memory impairment appears later in the disease course and non-amnestic focal cortical syndromes appear early[1]

Posterior cortical atrophy

- Associated with a variety of underlying pathologies, but AD is the most common underlying cause of PCA[2]
- Progressive decline in visuospatial, visuoperceptual, literacy, and praxic skills[2]
- Pathology affects parietal, occipital, and occipito-temporal cortex[2]
- Age of clinical onset is typically 50 to 65 years[2]

Logopenic progressive aphasia

- Recognized as an atypical focal language variant of AD[3]
- Characterized as a primary phonological loop deficit leading to:[3]
  - Impaired sentence repetition and comprehension with slow spontaneous speech
  - Long, frequent word-finding pauses

Frontal variant

- Presents with disproportionate executive dysfunction and behavioral changes relevant to memory deficits[4]
- Often difficult to distinguish clinically from those with behavioral variant frontotemporal dementia[4]

AD, Alzheimer's disease; PCA, posterior cortical atrophy

1. Dickerson B, et al. CNS Spectr 2017;22:439–449; 2. Schott JM, Crutch SJ. Continuum (Minneap Minn) 2019;25:52–75; 3. Beber BS, et al. Dement Neuropsychol 2014;8:302–307; 4. Wong S, et al. Neurocase 2019;25:48–58

Mild cognitive impairment (MCI)

MCI defines the state between normal aging and dementia and is defined **by three key features**:[1]

1. Cognitive complaint, decline, or impairment: reported by the patient, a care partner, or clinician[1]
2. Objective evidence of impairment in ≥1 of the following domains: attention, executive function, visuospatial function, and episodic memory[1]
3. No dementia: performs ADLs independently. However, cognitive difficulty may have a mild but detectable impact on more complex activities, either self-reported or corroborated by a care partner[1,2]

- ✓ MCI can be caused by multiple underlying neurodegenerative pathologies[3]
- ✓ Current DSM-5 nomenclature refers to MCI as mild neurocognitive disorder[4]

Some individuals with MCI remain stable for many years and may even revert to normal cognition. Other individuals progress to dementia; indeed, there is significant heterogeneity in the MCI population[5,6]

AD, Alzheimer's disease; ADL, activities of daily living; DSM, Diagnostic and Statistical Manual of Mental Disorders; MCI, mild cognitive impairment

1. Alberts MS, et al. Alzheimers Dement 2011;7:270–279; 2. Mlinac ME, Feng MC. Arch Clin Neuropsychol 2016;31:506–516;
3. Dugger BN, et al. BMC Neurol 2015;15:146; 4. Hugo J et al. Clin Geriatr Med 2014;30:421–442; 5. Sugarman MA, et al. J Alzheimers Dis 2018;62:1841–1855;
6. Ganguli M, et al. J Am Geriatr Soc 2019;67:232–238

MCI subtypes

Individuals with MCI can be diagnosed as amnestic or non-amnestic, and as single or multiple domain

Amnestic MCI (aMCI)

- **Single domain:** impairment **only of episodic memory**, eg difficulty learning and recalling new information
- **Multiple domain**: impairment of episodic memory **and** in one or more additional domains:
  - ✓ Language
  - ✓ Attention
  - ✓ Visuospatial functions
  - ✓ Executive functions

Non-amnestic MCI (naMCI)

- **Single domain:** impairment in **only one non-memory** domain:
  - ✓ Language
  - ✓ Attention
  - ✓ Visuospatial functions
  - ✓ Executive functions
- **Multiple domain:** impairments in **more than one non-memory domain**

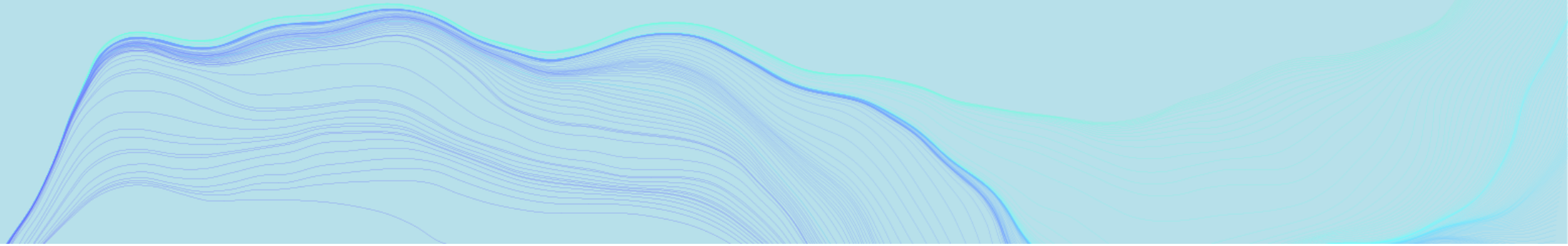
Individuals with aMCI are thought to have a higher risk of progressing to AD dementia; whereas, individuals with naMCI are thought to have a higher risk of conversion to non-AD dementia

AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment; MCI, mild cognitive impairment; naMCI, non-amnestic mild cognitive impairment

Csukly G, et al. Front Aging Neurosci 2016;8:52

Learning Zone

Understanding the functional and behavioral impairments in early stages of Alzheimer’s disease



Clinical features of behavior and functional ability

Behavior and functional ability are also important clinical features in AD[1–3]

Functional ability

Ability to perform basic and complex activities[3]

Basic activities of daily living related to self-maintenance[4,5]

- Bathing
- Dressing
- Grooming
- Mouth care
- Toileting
- Transferring from bed to chair
- Walking
- Climbing stairs
- Eating

Complex activities related to independent living[4,6]

- Managing finances
- Driving / using public transport
- Shopping
- Cooking
- Managing medications
- Housework

Behavior

Social behavior and psychological status[1,2]

Neuropsychiatric symptoms include[7,8]:

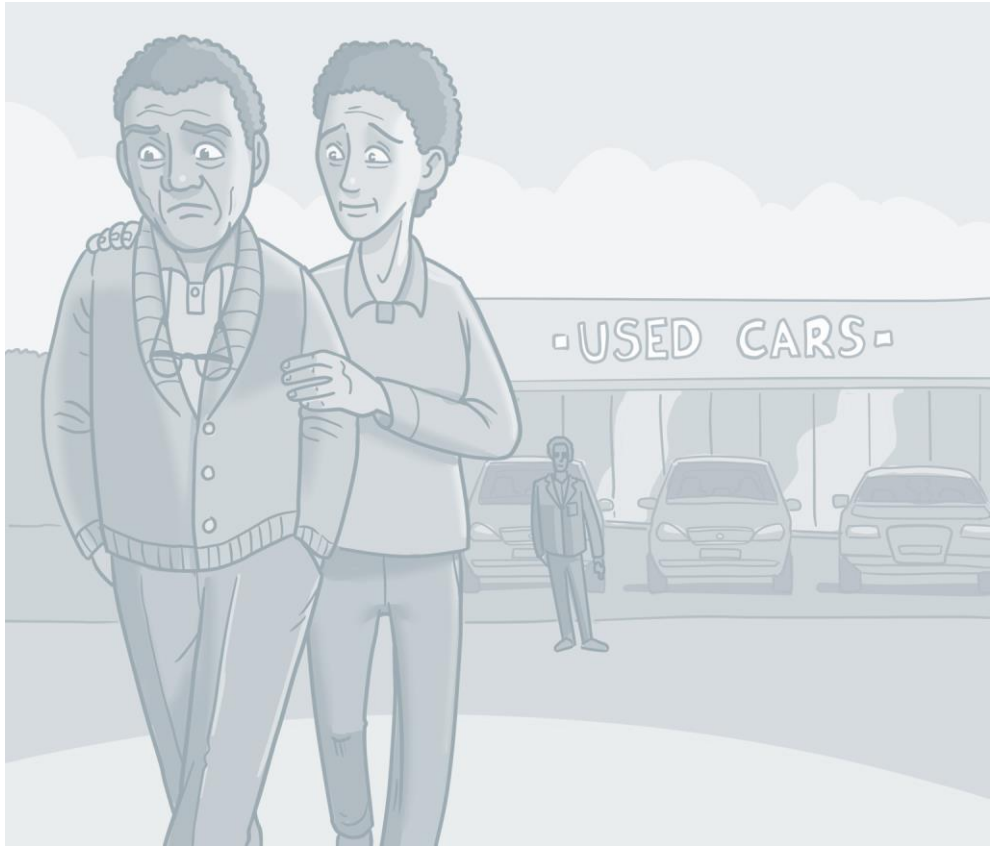
- Depression
- Anxiety
- Irritability
- Apathy
- Disinhibition
- Agitation
- Aggression
- Psychosis
- Hallucinations
- Sleep disturbances

1. Fernández M, et al. BMC Neurol 2010;10:87; 2. Sachdev PS, et al. Nat Rev Neurol 2014;10:634–642; 3. Jutten RJ, et al. Alzheimers Dement (Amst) 2017;8:26–35; 4. Mlinac ME, Feng MC. Arch Clin Neuropsychol 2016;31:506–516; 5. Jekel K, et al. Alzheimers Res Ther 2015;7:17; 6. Book S, et al. BMC Psychiatry 2018;18:308; 7. Lanctôt KL, et al. Alzheimers Dement (N Y) 2017;3:440–449; 8. Eikelboom WS, et al. Neurology 2021;97:e1276–e1287

Impairments in functional ability

- The ability to perform BADLs and IADLs is dependent on cognitive, motor, and perceptual abilities[1]
- **BADLs** are strongly correlated with motor functioning and coordination, remaining preserved until later stages of disease[2]
- **IADLs** require greater cognitive organization and can be impaired during early stages of cognitive decline[1]
- Past aMCI and naMCI criteria state that individuals should experience no "substantial interference with work, usual social activities, or other activities of daily living"[3,4]
- Since these criteria were initially proposed, research studies have shown that individuals with both aMCI and naMCI commonly experience mild deficits in IADLs[3,5,6]

Functional impairment in individuals with MCI due to AD or mild to moderate AD dementia is also linked to changes in brain pathology, including hippocampal atrophy[7]



AD, Alzheimer's disease; aMCI, amnestic mild cognitive impairment; IADL, instrumental activities of daily living; MCI, mild cognitive impairment; naMCI, non-amnestic mild cognitive impairment

1. Mlinac ME, Feng MC. Arch Clin Neuropsychol 2016;31:506–516; 2. Book S, et al. BMC Psychiatry 2018;18:308; 3. Brown PJ, et al. Arch Gen Psychiatry 2011;68:617–626; 4. Albert MS, et al. Alzheimers Dement 2011;7:270–279; 5. Teng E, et al. Dement Geriatr Cogn Disord 2010;30:189–197; 6. Jekel K, et al. Alzheimers Res Ther 2015;7:17; 7. Sabbagh M, et al. J Alzheimers Dis Rep 2021;5:207–211

The link between impairments in function and cognition

Functional changes in individuals with AD, such as impact on BADL and IADL, correlate with cognitive decline[1,2]

- **Executive functions** have been shown to correlate with functional performance in both BADL and IADL[1]
- **Processing speed** and **attention** have been shown to correlate with IADL but not BADL[3]
- **Visuospatial skills** have been demonstrated correlations with IADL and BADL[4]

AD, Alzheimer's disease; BADL, basic activities of daily living; IADL, instrumental activities of daily living

1. Mlinac ME, Feng MC. Arch Clin Neuropsy 2016;31:506–516; 2. Liu-Seifert H, et al. J Alzheimers Dis 2015;47:205–214; 3. Clemmensen FK, et al. BMS Geriatr 2020;20:513; 4. Fukui T, Lee E. Am J Alzheimers Dis Other Demen 2009;24:313–321

Neuropsychiatric symptoms (NPS)

Neuropsychiatric symptoms (NPS) are the behavioral and psychiatric symptoms of dementia associated with neurodegenerative disease[1,2]

NPS are common in mild cognitive impairment (MCI) and dementia and include disturbances in mood, perception, and behavior; they are often referred to as behavioral and psychological symptoms of dementia (BPSD)

Mild behavioral impairment (MBI) is another term used to describe the very early NPS evidenced prior to cognitive decline[1,3]

- **NPS in MCI and dementia have been found associated with the following**:
  - Poorer outcomes[1]
  - Greater caregiver burden[1]
  - Greater functional impairment[5]
  - Higher rates of institutionalization[1]
  - Poorer QOL[1]
  - Accelerated progression to severe dementia or death[6]

Definition of MBI

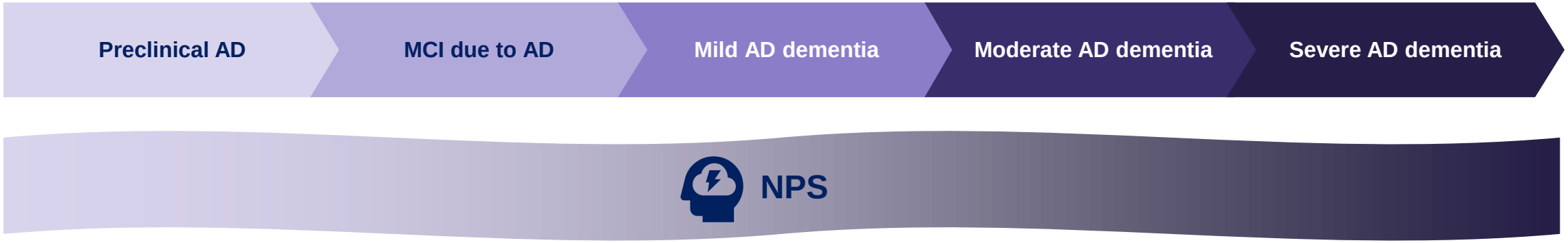
- MBI describes the emergence at ≥50 years of age of sustained and impactful NPS, as a precursor to cognitive decline and dementia[3]
- MBI describes NPS, which are not captured by conventional psychiatric nosology, that persist for at least 6 months, and occur in advance of or combined with MCI[1]

AD, Alzheimer's disease; BPSD, behavioral and psychological symptoms of dementia; ISTAART, Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment; MBI, mild behavioral impairment; MCI, mild cognitive impairment; NPS, neuropsychiatric symptoms; QOL, quality of life

1. Ismail Z, et al. Alzheimers Dement 2016;12:195–202; 2. Burhanullah MH, et al. Am J Geriatr Psychiatry 2020;28:64–71; 3. Ismail Z, et al. J Alzheimer Dis 2017;56:929–938; 4. Yang AN, et al. J Nutr Health Aging 2020;24:237–241; 5. Ginsberg TB, et al. J Am Osteopath Assoc 2019;119:96–101; 6. Peters ME, et al. Am J Psychiatry 2015;172:460–465

Neuropsychiatric symptoms: trajectory across the AD clinical continuum

- NPS are prevalent across the entire clinical AD spectrum[1]
- Unlike cognitive decline that progressively deteriorates with disease progression, the course of NPS follows a relatively stable pattern across all clinical AD stages[1]
- **Affective symptoms, such as anxiety and depression, remain stable throughout the cognitive spectrum[2]**



AD, Alzheimer's disease; MCI, mild cognitive impairment; NPS, neuropsychiatric symptoms

1. Eikelboom WS, et al. Neurology 2021;97:e1276–e1287; 2. Wiels WA, et al. Front Psychiatry 2021;12:707580.

Apathy as an early marker and risk factor for AD

Apathy is a common NPS in dementia and a risk factor for cognitive decline in MCI and mild AD dementia:[1,2]

- Apathy and anxiety are clinical manifestations of early stages of AD[2]
- Presence of **apathy can predict which individuals with amnestic MCI will progress to AD**[1]
  - The risk of progressing from amnestic MCI to AD was ~7-fold higher in individuals with apathy compared to those without apathy[1]

Apathy can be used to distinguish between AD and bvFTD:[3]

- Apathy has different profiles across the disease course of AD and bvFTD:
  - In early disease (<5 years post-onset), emotional apathy is greater in bvFTD than AD
  - In late disease (>5 years since onset), executive apathy was greater in AD than bvFTD

Measuring apathy:[4]

  - Neuropsychiatric Inventory apathy sub-scale (NPI-Q-apathy)
  - Apathy Evaluation Scale

AD, Alzheimer's disease; bvFTD, behavioral variant frontotemporal dementia; DAIR, Dementia Apathy Interview and Rating; DCA, diagnostic criteria of apathy; MCI, mild cognitive impairment; NPI-Q-apathy, Neuropsychiatric Inventory Questionnaire apathy; NPS, neuropsychiatric symptoms

1. Palmer K, et al. J Alzheimers Dis 2010;20:175–183; 2. Johansson M, et al. Neurobiol Aging 2020;85:74–82; 3. Wei G, et al. J Neurol 2020;267:1086–1096; 4. Lanctôt K, et al. Am J Geriatr Psychiatry 2021;29:81–89

Deciphering between a psychiatric disorder and early neurodegeneration

Psychiatric disorder

- Depression and other psychiatric conditions have been linked to problems with thinking, concentration, and memory[1]
- The domains of executive function, working memory, episodic memory, attention, and psychomotor processing speed are commonly affected in individuals with depression and other psychiatric conditions[1]

Neuropsychiatric symptoms (NPS)

- Individuals with higher levels of NPS are more likely to progress to AD and less likely to revert to normal cognition[2]
  - More severe mood and hyperactivity symptoms during assessments (i.e., NPI-Q) may increase the likelihood of progressing from MCI to AD dementia[2]
- Presence of NPS, especially depression, in patients with MCI, may cause a higher likelihood of cognitive deterioration, representing early neurodegeneration[3]

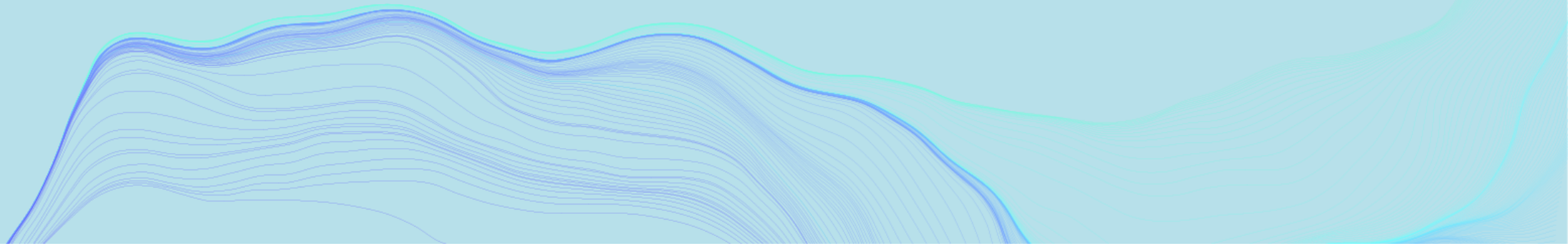
- **Deciphering between a psychiatric disorder and NPS can be complex[4]**
  - **When cognitive symptoms wax and wane in relation to mood symptoms, depression is most likely to be the root cause of cognitive decline[4]**

AD, Alzheimer's disease; MCI, mild cognitive impairment; NPI-Q, Neuropsychiatric Inventory Questionnaire; NPS, neuropsychiatric symptoms

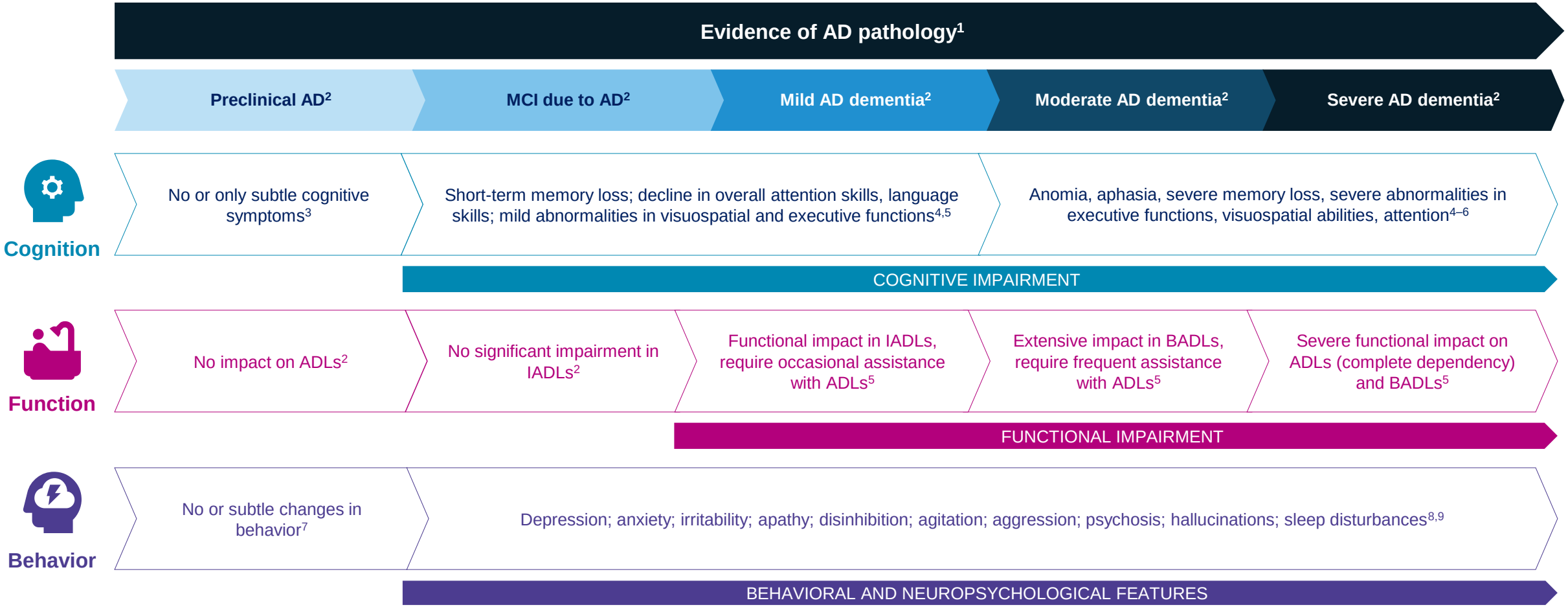
1. McAllister-Williams RH, et al. J Affect Disord 2017;207:346–352; 2. Sugarman MA, et al. J Alzheimers Dis 2018;62:1841–1855; 3. Yang AN, et al. J Nutr Health Aging 2020;24:237–241; 4. Galvin JE. Curr Geriatr Rep 2018;7:19–25

Learning Zone

Alzheimer’s disease: Clinical continuum



The AD clinical continuum and disease staging



AD, Alzheimer's disease; ADL, activities of daily living; BADL, basic activities of daily living; IADL, instrumental activities of daily living; MCI, mild cognitive impairment

1. Aisen PS, et al. Alzheimers Res Ther 2017;9:60; 2. Jack CR Jr, et al. Alzheimers Dement 2018;14:535–562; 3. Harada CN, et al. Clin Geriatr Med 2013;29:737–752; 4. Kazim SF, Iqbal K. Mol Neurodegener 2016;11:50
5. Mayo Clinic. Alzheimer's stages: How the disease progresses. https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/in-depth/alzheimers-stages/art-20048448 (Accessed April 2023); 6. Kipps CM, Hodges JR. J Neurol Neurosurg Psychiatry 2005;76(Suppl. 1):i22–i30;
7. Ismail Z, et al. Alzheimers Dement 2016;12:195–202; 8. Eikelboom WS, et al. Neurology 2021;97:e1276–e1287; 9. Lanctôt KL, et al. Alzheimers Dement (N Y) 2017;3:440–449.

Examples of important changes to patients in the early stages of the disease continuum

Forgetting a list of items

Forgetting names of people and common items

Misplacement of items

Forgetting dates or appointments

Loss of ability to follow instructions

Forgetting to take medications

Forgetting dates to pay bills on time

Confusion regarding date and time

Loss of independence

Change in mood

Hartry A, et al. Alzheimers Dement (Amst) 2018;10:498–508

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