



a form of declarative memory. Other forms include the conscious recall of episodes from personal experience (i.e., episodic memory), and factual knowledge (i.e., semantic memory) that can be consciously recalled and stated (i.e., declared). Declarative memory involves consciously *knowing that* Patients with amnesia resulting from lesions of the medial temporal lobes or midline diencephalic structures have deficits of declarative memory.

Nondeclarative memory encompasses several distinct and neuroanatomically less clearly localized functions related to the performance of specific learned motor, cognitive, or perceptual tasks. Nondeclarative (procedural) memories involve unconsciously *knowing how* Deficits in nondeclarative memory may involve various areas of association neocortex, depending on the nature of the task (e.g., parietal-temporal-occipital junction cortex for visual perceptual tasks, frontal association cortex for motor tasks). Patients with amnesia resulting from lesions of the medial temporal lobes tend to perform normally on tests of nondeclarative memory.

Anterograde amnesia is the inability to learn new information. It commonly occurs after brain injury or in association with dementia. The inability to recollect prior information is retrograde amnesia. Both types of amnesia usually occur together in brain injury syndromes, although the extent of one type or the other may vary. The degree of anterograde amnesia after head injury correlates with the severity of the injury.

Isolated Disorders of Memory Function

Memory can be impaired in relative isolation as a consequence of head injury, thiamine deficiency (i.e., Korsakoff's syndrome), benign forgetfulness of aging, transient global amnesia, or psychogenic disease.

Head injury typically results in retrograde amnesia in excess of anterograde amnesia, with both forms stretching out over time from the discrete event. As time passes, these disrupted memories gradually return, although rarely to the point at which the events immediately surrounding the trauma are recalled.

Korsakoff's syndrome is characterized by the near-total inability to establish new memory. Patients often confabulate responses when they are asked to convey the details of their current circumstance or to relay the content of a recently presented story. Deficiency of thiamine and other nutritional deficiencies in the context of chronic alcoholism are the most common underlying causes. Thiamine is a necessary cofactor in the metabolism of glucose, and thiamine must be replenished at the same time glucose is administered whenever a comatose patient is seen in the emergency department.


Aging is associated with mild loss of memory, exhibited by difficulty in recalling names and by forgetfulness for dates. Population-based assessments of neuropsychological function have demonstrated that poor performance on delayed-recall tasks is the most sensitive indicator of cognitive change with

advancing age. Verbal fluency, in contrast, remains intact with advancing age, and vocabulary may increase with time, even into old age.

Transient global amnesia is a dramatic memory disturbance that affects older patients (>50 years). Patients usually have only one episode; occasionally, episodes recur over the course of several years. Patients have complete temporal and spatial disorientation; orientation for person is preserved. Near-total retrograde and anterograde amnesia persists for various periods, typically 6 to 12 hours. Patients are often anxious and may repeat the same question over and over again. Transient global amnesia may be confused with psychogenic amnesia, fugue state, or partial complex status epilepticus. Transient global amnesia is thought to reflect underlying vascular insufficiency to the hippocampus or midline thalamic projections.

Unlike patients with organic memory disturbances, patients with psychogenic amnesia typically have inconsistent loss of recent and remote memory, relatively more loss of emotionally charged memory (rather than relatively less loss of such memory in organic disease), and an apparent indifference to their own plight; they ask few questions. Most characteristically, patients with psychogenic amnesia tend to express disorientation to person (asking, *Who am I?*), a phenomenon seldom seen in organic memory disturbance.

Patients with severe depression may exhibit pseudodementia. Vegetative signs, including changes in appetite, weight, and sleep pattern, are common, whereas signs of cortical impairment, such as aphasia, agnosia, and apraxia, are rare. Memory and bradyphrenia improve with antidepressant therapy. Depression often coexists with other causes of dementia, such as AD, Parkinson's disease, and vascular dementia.

 For a deeper discussion on this topic, please see Chapter 402, "Alzheimer's Disease and Other Dementias," in Goldman-Cecil Medicine, 25th Edition.

SUGGESTED READINGS

- Bateman RJ, Xiong C, Benzinger TLS, et al: Clinical and biomarker changes in dominantly inherited Alzheimer's disease, *N Engl J Med* 367:795–804, 2012.
- Carrillo MC, Brashear HR, Logovinsky V, et al: Can we prevent Alzheimer's disease? Secondary "prevention" trials in Alzheimer's disease, *Alzheimers Dement* 9:123–131, 2013.
- Castellani RJ, Perry G: Pathogenesis and disease-modifying therapy in Alzheimer's disease: the flat line of progress, *Arch Med Res* 43:694–698, 2012.
- Iqbal K, Flory M, Soininen H: Clinical symptoms and symptom signatures of Alzheimer's disease subgroups, *J Alzheimers Dis* 37:475–481, 2013.
- Ling SC, Polymenidou M, Cleveland DW: Converging mechanisms in ALS and FTD: disrupted RNA and protein homeostasis, *Neuron* 79:416–438, 2013.
- McKhann GM, Knopman DS, Chertkow H, et al: The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging and the Alzheimer's Association workgroup, *Alzheimers Dement* 7:263–269, 2011.
- Perry DC, Miller BL: Frontotemporal dementia, *Semin Neurol* 33:336–341, 2013.