ABSTRACT:
Memory disturbances have been the clinically fascinating as well as challenging situation for physicians. This review discusses the types of memory and the clinical situations and causes of memory impairment. The symptom analysis of memory disturbance through history and clinical examination of lobar functions is an imperative tool to classify the clinical syndrome, diagnose its cause and treat it accordingly. Finally, a brief description of amnestic syndromes emphasises why every emergency clinician should also be well versed with memory functions as it is not something which is only done by neurologists or involves elaborate neuropsychological batteries.

INTRODUCTION:
Memory in health and disease has been the focus of medical studies worldwide. Memory is the recording, retention, and retrieval of knowledge. It accounts for all knowledge gained from experience--facts that are known, events that are remembered, and skills that are gained and applied. Scientific measurement of memory began in the late 1800s with Ebbinghaus’ monograph and turned the study of memory away from philosophers and toward experimentalists. Studies of dementia, brain atrophy and memory decline, and trauma in relation to amnesia were conducted by several neurological luminaries including Samuel Wilks, Jean Esquirol, and Alois Alzheimer. Linkage of memory with emotional elements was presented by James Papez, whose anatomical studies form much of the basis of modern knowledge of memory circuitry. Well over a hundred years ago Ribot proposed that memory is encoded by changes in connections between the brain’s ‘nervous elements’ and becomes stabilized (resistant to disruption) during the first several minutes following its acquisition.

TYPES OF MEMORY:
- **Working memory**: a multi component psychological system that mediates the temporary processing and storage of internal representations that guide and control action. Information is held in working memory only as long as it is useful for solving a problem at hand.
- **Declarative Memory**: the everyday sense of memory and is responsible for the learning and remembrance of new events, facts, and materials.
  - **Episodic memory**: recent and remote: remembrance of personal experiences that took place at a particular place and time.
  - **Semantic memory**: recent and remote: knowledge of generic information, such as the meaning of a word.
- **Non declarative/Implicit Memory**: retrieved reflexively or incidentally. Remembering how to swim or ride a bicycle belong in this category. Implicit forms of memory include perceptual, motor, and cognitive skill learning (sometimes referred to as procedural memory).

Consolidation is the process of sorting and storing information. Initial packaging is done in the primary and secondary association cortices. Then they are transferred to a master computer in the hippocampus which sorts and organizes the data. The hippocampus then transfers the consolidated data to the cortex. Ultimately the hippocampal cortex is free to receive more information.

NORMAL MEMORY PATHWAY- ANATOMY AND PHYSIOLOGY:
In 1937, the neuroanatomist Papez published a study describing an anatomical circuit that involved a number of central nervous
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system nuclei and pathways that are important in aspects of memory and emotion. The concept of a circuit is particularly important in dealing with memory, since lesions anywhere along the pathway may interrupt memory function, although the coloration of the deficit may be particularly influenced by the specific nuclei or path that is damaged (figure 1).

The two prominent cortical areas are the cingulate cortex and the hippocampus of the temporal lobe. Diffuse cortical impulses travel into the hippocampus, traverse the midline fornix pathway to the mammillary bodies of the hypothalamus, and continue to the anterior and dorsal thalamus. From these regions, information projects to the midline cingulate cortex, which finally projects diffusely to cortical regions.

Model for working memory:

Alan Baddeley and Graham Hitch proposed a Model of Working Memory in 1974, in an attempt to describe a more accurate model of short-term memory (figure 2). Baddeley & Hitch proposed their tripartite working memory model as an alternative to the short-term store in Atkinson & Shiffrin’s ‘multi-store’ memory model.

Anatomy of declarative memory:

Long-term memories are thought to be stored in the neocortex, the neocortical location reflecting the content of the memory. Thus, knowledge about the visual appearance of a tool may be stored separately, perhaps near the visual neocortex. The hippocampal complex has reciprocal connections with higher-order association cortices, and it is hypothesized that the hippocampal complex somehow binds or relates multiple features about an event or fact across physically disparate neocortical regions. Over time, the features somehow become consolidated and no longer require the hippocampal complex for binding. Diencephalic regions linked to declarative memory include the dorsomedial and anterior nuclei of the thalamus, the mammillary bodies, the mammillothalamic fiber tract connecting the medial hippocampal complex to the anterior thalamic nuclei, and the ventroamygadalofugal fiber tract connecting the amygdala to the dorsomedial nuclei.

Anatomy of Nondeclarative Memory

Nondeclarative memory reflects adaptive plasticity within neural systems that occurs in the course of the support by those systems of particular forms of behavior. Thus, motor-skill learning has been linked to pyramidal, extrapyramidal, and cerebellar motor systems. Specific basal ganglia and cerebellar areas appear to support the working memory capacity of particular frontal regions.

The specific roles of different neurotransmitters in memory are just beginning to be appreciated. The cholinergic system appears to be critical for the acquisition of long-term declarative memories. Cholinergic function decreases somewhat with age and greatly in patients with Alzheimer’s disease, and these changes may contribute importantly to corresponding reductions in declarative memory ability. The catecholamines appear to have an important role in working memory. Dopaminergic function is decreased in patients with Parkinson’s disease, who have reduced working memory capacity. There is some evidence that dopamine agonists can improve working memory capacity in patients with Parkinson’s disease and in healthy subjects.

SYMPTOM ANALYSIS OF MEMORY DISTURBANCES:

Any damage to a neocortical region results in both the loss of previously acquired memory, or knowledge, stored in that area and an inability to acquire new memories involving that kind of knowledge. For example, patients with left temporal lesions lose specific knowledge about the names of animals, tools, or people, depending on the location of the lesion. Thus, neocortical damage is thought to result in domain-specific memory deficits in which the loss of old memories and the inability to gain new memories reflect the kind of knowledge represented in that neocortical region.

In contrast, damage to medial temporal lobe, diencephalic, and basal forebrain regions yield widespread, or domain-independent, declarative memory deficits. Global amnesia can arise from damage to any one of these regions, even if the other regions remain intact.

Immediate memory stores appear to be located in posterior neocortical regions, the location reflecting the modality (auditory or visual) and material (verbal or nonverbal) of the briefly retained information. For immediate auditory memory, left and right temporal-parietal cortices, respectively, mediate auditory verbal and nonverbal material. For immediate visual memory, left and right occipitoparietal cortices, respectively, mediate immediate verbal and nonverbal material. Thus, a reduced ability to immediately recall aurally presented digit strings occurs in patients with left temporal-parietal lesions.

Working memory processes that support selective aspects of declarative memory have been linked to the dorsolateral frontal
cortex and to basal ganglia and cerebellar areas that are directly or indirectly linked to the dorsolateral frontal cortex. The prevailing view is that there are discrete dorsolateral frontal areas that direct the rehearsal of the immediate memory stores. Thus, keeping a spatial location in mind may involve a right-frontal area that directs the maintenance of that information in a right parietal area, whereas keeping a word in mind may involve a left-frontal area that directs the maintenance of that information in a left temporal or parietal area. Specific basal ganglia and cerebellar areas appear to support the working memory capacity of particular frontal regions.

<table>
<thead>
<tr>
<th>Table 1: Clinico-anatomical correlates of memory disorder</th>
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<td><strong>Anatomic Site of Damage</strong></td>
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<td>Frontal lobe</td>
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<td>Basal forebrain</td>
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<td>Ventromedial cortex</td>
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<td>Hippocampus and parahippocampal cortex</td>
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<td>Fornix</td>
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<td>Mammillary bodies</td>
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<td>Dorsal and medial dorsal nucleus thalamus</td>
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<td>Anterior thalamus</td>
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<td>Lateral temporal cortex</td>
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<td>Parietal lobe</td>
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<th>Table 2: Causes of memory disturbances</th>
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<td><strong>Etiological categories</strong></td>
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<tr>
<td>Structural developmental disorders</td>
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<td>Hereditary and degenerative disorders</td>
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<td>Acquired metabolic causes</td>
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<td>Toxicity and deficiency</td>
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<td>Infectious disorders</td>
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<td>Neurovascular disorders</td>
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<td>Neurological disorders</td>
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<td>Demyelinating disorders</td>
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<td>Trauma</td>
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<td>Sleep disorders</td>
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<td>Iatrogenic</td>
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**TYPES OF MEMORY DISTURBANCES AND CAUSES:**

Any disease affecting the structures critical for regulating memory storage can cause the amnestic syndrome. Etiologies for medial temporal lobe damage include surgical resection, herpes encephalitis, paraneoplastic encephalitis, posterior cerebral artery distribution ischemia, anoxia, and seizures. The mediodorsal thalamic nucleus and adjacent regions may be injured by infarction, tumors, and penetrating injuries.

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**Table 1:** Clinico-anatomical correlates of memory disorder

**Table 2:** Causes of memory disturbances

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whereas damage to the fornix may occur with tumors, trauma, infarcts, and surgery (e.g., removal of a colloid cyst or bilateral fornix transection in patients with temporal lobe epilepsy). The basal forebrain (e.g., septal nuclei) may be damaged by ruptured anterior communicating artery aneurysms. The memory defects in Alzheimer’s disease are likely related to pathology in multiple areas, including the entorhinal cortex, parieto-occipital regions, and the frontal lobes; these patients are much more impaired by their memory problems because of associated cognitive deficits, such as impaired strategy and planning. Unilateral amnestic stroke may involve the territories of the posterior cerebral, anterior choroidal, or thalamic penetrating arteries. In 85% of patients with unilateral stroke-associated amnesia, the left hemisphere is affected; left amygdalohippocampal or diencephalic dysfunction may result in a particular vulnerability to global amnesia. Other aetiologies associated with memory disturbances occurring chronically are listed in Table 2.

### Cortical versus Subcortical dementia

The distinction between cortical and subcortical dementia is not absolute because most of these diseases are not limited to either cortical or subcortical regions, and therefore many patients exhibit elements of both kinds of dementia. There are declarative memory deficits (e.g., recall and recognition) seen in persons with Alzheimer’s disease or amnesia. Impairments in speed of mental processing, working memory, reasoning, and strategic memory (e.g., recall) are evident in nondemented patients with striatal diseases, including patients with early Parkinson’s disease. Parkinson’s or Huntington’s disease often have deficits in procedural forms of memory, motoric and nonmotoric, that remain intact in patients with Alzheimer’s disease and amnesia. Table 3 shows the differences between cortical and subcortical dementia.

### WHAT IS “MILD COGNITIVE IMPAIRMENT”? 

MCI refers to subtle cognitive impairment, especially in elderly persons, that is readily recognized by the patient and companions but does not qualify, in degree, as actual dementia. MCI becomes clinically relevant when cognitive impairment impacts on quality of life, such as making poor financial decisions or disrupting personal interactions. The same type of neuropsychiatric symptoms not uncommonly seen with dementia can be part of MCI. Screening tests for such deficit, even when the Mini-Mental State Examination score is normal, are becoming increasingly pertinent. For example, a recently introduced Memory Impairment Screen is reported to be a reliable alternative test for the detection of early dementia. Short-term follow-up studies showed that on average 10 to 15% of the subjects with MCI progress to dementia each year. A majority of subjects with MCI do not progress to dementia at the long term. Age strongly influences the dementia risk. MCI often represents the predementia stage of a neurodegenerative disorder in elderly subjects but rarely in younger subjects. Studies on progression of MCI to dementia have classified patients into cognitive complaints, aging-associated cognitive decline (AACD), mild functional impairment, amnestic and non amnestic MCI.

### TRANSIENT AMNESTIC SYNDROMES

Amnesia refers to a relatively circumscribed deficit in declarative memory that cannot be accounted for by impairments in attention, language, motivation, reasoning, or other nonmnemonic abilities. It is defined by a behavioral syndrome and not by etiology or lesion location. The amnesia is described as global if it extends to both verbal and nonverbal information.

**Transient Global Amnesia (TGA)**

TGA—the term was coined by Fisher and Adams over 50 years ago—is characterised by an acute inability to retain new information (anterograde amnesia). The retrograde amnesia can extend as far back as weeks or months. Many patients with TGA repeatedly ask the same questions and seem to be confused and disoriented in time and place. However, loss of self-awareness and consciousness excludes typical TGA. The most widely used diagnostic criteria is by Caplan et al (Table 3). Causes include ischaemia, migraine, epileptic seizure, venous congestion, and psychological disturbances. DWI abnormalities in TGA have been published, most patients with TGA have small punctate DWI lesions in the lateral hippocampal formation. Patients with TGA and DWI abnormalities have a higher incidence of carotid atherosclerosis than those with normal DWI (Table 4).
discharges on EEG, concurrent onset of other seizure types, and a response to anticonvulsant therapy.\textsuperscript{35} These episodes tend to be more numerous than TGA, are relatively brief and characteristically occur on waking. A persistent impairment of retrograde memory is a common accompaniment of TGA. There is circumstantial evidence that this may be the result of disruption of memory consolidation, related to recurrent ictal activity in mesial temporal structures.

Korsakoff syndrome

It refers to a persistent state of mental dysfunction characterized by memory impairment associated with confabulation.\textsuperscript{36} Approximately 80\% of patients with acute Wernicke's encephalopathy develop Korsakoff syndrome. The classic clinical triad of Wernicke's encephalopathy consists of mental status changes, ophthalmoplegia, and gait ataxia. Pathologically, patients show capillary proliferation and petechiae; spongy degeneration of astrocytes with neuronal preservation occurs in midline structures of the brain, such as the medial thalamic nuclei, mammillary bodies, periaqueductal gray area of the mesencephalon, and pontine tegmentum. The lesions in the thalamus and mammillary bodies probably account for the confusion, memory loss, and confabulation. The pontine tegmental lesions may cause the oculomotor palsies, and the truncal ataxia may result from the midline cerebellar degeneration. Cellular injury in these regions may be due to the inhibition of ATP synthesis and the induction of abnormal carbohydrate metabolism.

Post-traumatic amnesia (PTA)

A coup contusion occurs at the site of impact in the absence of a fracture. A contrecoup contusion occurs in the brain diametrically opposite the point of impact. Acceleration/ deceleration forces may cause tearing of nerve fibers at the moment of impact, which is called shearing injury or diffuse axonal injury, especially in the temporal and inferior frontal regions. Measurement of the duration of post-traumatic amnesia (PTA) is common practice, serving as an important index of the severity of traumatic brain injury (TBI) and a predictor of functional outcome. In addition to attentional, orientation and memory impairments, prevalent manifestations found among confused patients after TBI included sleep–wake cycle disturbance, decreased daytime arousal, fluctuation in cognitive and behavioural symptom severity, motor agitation, affective lability, and perceptual and thought process abnormalities.\textsuperscript{37} As duration of PTA is influenced by injury severity, evaluating the severity of confusion at a set time after injury potentially reduces the confounding influence of evaluation results with those of duration of TBI recovery. The Delirium Rating Scale-Revised-98 (DelRS-R98), The Galveston orientation and amnesia test (GOAT) are certain scoring systems testing delusions,\textsuperscript{38} psychomotor behaviour, aspects of cognition (attention, language, visuospatial disturbance, short term memory and long-term memory), presence of a physical disorder accounting for symptoms, sleep–wake cycle disturbance, thought process abnormalities, lability of mood and fluctuation of symptoms. They have been shown to have a good correlation in predicting late outcome after TBI.

CONCLUSION

Memory disturbances can variously affect the Papez circuitry or the neocortical areas which have consolidated memory reserves. Various domains of memory disturbances point out to their respective localization and associated history and clinical features help in diagnosing the underlying etiology. Arrival at a possible diagnosis helps in definitive treatment, rehabilitation and prognostication of amnestic state.

Apprehension of dementia in elderly patients reporting memory decline should be objectively documented by screening and detailed cognitive batteries. Reassurance to patients with normal aging associated cognitive decline and even to those with MCI and low risk profile of progression goes a long way in improving associated psychological consequences. On the other hand early detection of dementia offers such patients early treatment and thus a potential to delay their progression to advanced dementia.

Acute and subacute amnestic syndromes are to be approached in a different way depending upon the underlying clinical syndrome. Timely detection and intervention can improve the further clinical course. These syndromes are usually misdiagnosed in an emergency clinical setting and thus the entities need to be known by physicians and emergency interns.

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