COMMENTARY

Anatomy and neurophysiology of memory

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Abstract

Memory is the glue that binds our mental life. Memory can be ultra short memory, short term memory and long term memory. A given neural system participates in several forms of memory. Working memory is regarded as the "mental workspace." Recent experiments show that memory processing during sleep serves an adaptive function. Best studied mechanisms underlying neural plasticity are long term potentiation and long term plasticity. Hippocampal formation (HF) and linked regions of medial temporal lobe in interaction with parts of the prefrontal cortex plays a critical role in the encoding of episodic memory. Interaction between the amygdala and the HF is important for emotional memories especially those with a fearful and aversive character. Acetylcholine is the neurotransmitter associated with declarative memory. Neuroimaging has confirmed the importance of basal ganglia and cerebellum for procedural memory. A reduction of activation to a primed stimulus is consistently found either in modality specific regions or in cortical regions like lateral semantic region for semantic priming. Conditioning, both classical and Pavlovian, has been considered as type of implicit memory. Dorsolateral prefrontal cortex is important for item storage during work. Tests of thought depend on simultaneous storage and manipulation of information that are considered executive in nature. An episodic buffer is thought to play a role in the interface between working and episodic memory.

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Memory is defined as the ability to store, retain and retrieve information. Memory is not a unitary function but consists of several forms that can be dissociated neutrally. Memory is the glue that binds our mental life. Memory is a special case of the general biological phenomenon of neural plasticity. Plasticity of nerve cells and synapses is the basis of memory.

According to duration of retaining of information, memory can be ultra short memory (lasts minutes to second and known as echoic or sensory memory), short term memory (briefly held by a process of rehearsal and capacity limitation) and long term memory (can last lifespan of person, no capacity limitation and due to changes in neuronal structure and connectivity and rehearsal). Memory may be declarative memory about facts and events and nondeclarative memory consisting of skills and habits (striatum and cerebellum), priming (neocortex), simple classical conditioning (amygdala) and nonassociative learning.

Semantic memory is memory of facts or information that is independent of episodic memory. It is stored in neocortex and can be retrieved without the engagement of medial temporal lobe (MTL) structures. Procedural memory is gradual acquisition of sensorimotor or cognitive skills through repeated exposure. Priming is facilitation of response to an item if it was previously encountered. Déjà vu is intense feeling of familiarity without recall. Variety of learning systems may mediate performance. A given neural system participates in several forms of memory e.g. hippocampal formation (HF) is critical for episodic memory and is also thought to play a role in learning.

Working memory is a specific form of short term memory that is necessary for task at hand but not present in the environment. It is regarded as the "mental workspace" and critical for information manipulation and goal directed adaptive behaviour.

Sleep and memory

Freud noted that dreams can reveal fragments of recent experiences in the form of day residues. Recent experiments show that memory processing during sleep serves an adaptive function. Sleep after initial learning facilitates the memory function. Sleep related facilitation can be seen for different types of memory. Memory is specifically aided during periods of deep sleep especially in non rapid eye movement (NREM) stage 3 and 4 sleep (slow wave sleep). In animals the phenomenon of hippocampal replay in which activity patterns are expressed during the day are later observed during sleep. Declarative memories acquired during waking can be processed during sleep that can influence the likelihood of subsequent memory retrieval when awake.

Facilitation of declarative memory is typically manifest as a reduction in the amount of forgetting that occurs not as an improvement in memory.

Anatomy

Left MTL is concerned with memory for spoken and written text. Damage leads to impaired memory for spoken and written text. Left cerebral hemisphere is concerned with memory associated with words. Damage leads to difficulty in remembering verbal material such as word lists and stories. Right MTL is concerned with spatial analysis. Damage leads to impaired learning of spatial arrays whether layouts are examined by vision or touch. Right cerebral hemisphere is concerned with verbal memory encoded without verbal labels. Damage leads to impaired memory for faces, spatial layouts and other nonverbal material.

Cellular and molecular mechanisms of memory

Most impressive examples are of neural plasticity. Plasticity is the ability of the neurons in the nervous system for enduring changes triggered by external events. Best studied mechanisms underlying neural plasticity are long term potentiation (LTP) and long term plasticity (LTD).

Neural plasticity may be short term and long term. Short term plasticity lasts seconds to minutes, depends on specific synaptic events and increases neurotransmitter release. Long term plasticity lasts for longer duration. It depends on new protein synthesis, physical growth of nerve processes and increase in the number of synaptic processes.

Long term potentiation

Stimulating presynaptic fibres in hippocampus with brief pulse of high frequency impulses leads to an increase in responsiveness of the postsynaptic cells to low frequency stimulation. It can last for weeks. Initiation depends on multiple second messenger mechanisms. It is maintained by changes in gene transcription factors and changed patterns of protein synthesis and phosphorylation. The two types are early LTP and late LTP.

Long term plasticity

It is the process that is triggered when presynaptic stimulation is lower causing less calcium influx through N-methyl-d-aspartate (NMDA) receptors and the preferred activation of calcineurin, a protein phosphatase. LTP and LTD together combine to modulate synaptic strength. The active field of neural network modeling has shown that in principle changes in synaptic efficacy by LTP and LTD can produce efficient mechanisms to encode, store and retrieve information. This proposal of modeling of neural network was first made by neurophysiologist Dr Donald Hebb.[1]

Declarative or episodic memory

Neural systems

HF and linked regions of MTL in interaction with parts of the prefrontal cortex plays a critical role in the encoding of episodic memory. Interaction of HF with amygdala is important for emotional memories. HF consists of hippocampus proper, the entorhinal cortex and the adjacent peripheral and parahippocampal cortices which interact with entorhinal cortex and in turn receive projection from all other neocortical areas with parietal, dorsal, occipital and prefrontal regions primarily projecting to parahippocampal gyrus and temporal cortex to perirhinal cortex. In this way HF is bidirectionally connected to the rest of the brain. Neural imaging studies have shown that activation of HF is observed during successful encoding and retrieval of episodic information.

Neurocognitive model: role of MTL in episodic memory

MTL binds memories and their instance specific context and then stores their code for later retrieval. Bulk of hippocampal cortical input is segregated over two pathways – one which conveys spatial information while the other conveys information regarding items and objects. Hippocampus proper ensures the memory retrieval will be unambiguous. Representational overlap in the entorhinal cortex combined with the pattern separation system in the hippocampus proper enormously increases the storage capacity of the memory store and allows accurate recall of episodic memories. Recent work has shown that recollection is predominantly mediated by hippocampus proper while familiarity has been linked to perirhinal cortex. Interaction between the amygdala and the HF is important for emotional memories especially those with a fearful and aversive character. Neuroimaging has shown that encoding and retrieval is associated with the activation of lateral prefrontal region with HF that is supported by anatomical tracts such as uncinate fasciculus. Current evidence, though not clear, suggests that the neocortex is the ultimate store of memories and that engrams are stored in a distributed pattern of synaptic connection over a large group of neurons.

On a molecular level, glutaminergic neurotransmission is crucial to support LTP mechanisms that support the neural plasticity essential for memory formation. Acetylcholine is the neurotransmitter associated with declarative memory. Muscarinic receptor blockade impairs episodic memory and degeneration of cholinergic neurons in the basal nucleus

of Meynert is a prominent finding in Alzheimer's disease.

Assessment and neuropsychology

Numerous tests of episodic memory can be used for clinical purposes. Well known batteries include Wechsler memory scale III which involves verbal memory stores, verbal paired associates, visual memory for scenes, faces etc. Immediate and delayed recall of these tests is assessed. There are many standardised verbal list learning tests that involve differing degrees of semantic relatedness among words and minor differences in administration. These include California verbal learning test, Hopkin's verbal learning test and selective reminding test. They are alternate but equivalent forms that reduce practice effects when administered repeatedly. A comprehensive test of memory should include multiple trials of a word list to assess learning rate or slope, measures of immediate and delayed memory, recognition test in which the subject must decide whether an item has been studied or not, tests of visual and verbal memory that preferentially engage the right or left MTL system that are thought to be material specific to the same degree.

Implicit memory

Neural systems

Procedural memory: Neuroimaging has confirmed the importance of basal ganglia and cerebellum for procedural memory. It has demonstrated the time variant activation of primary and secondary motor cortex during skill learning. Learning of repetitive sequences in the so called "open loop" tasks in which visual feedback is delayed depends on the integrity of the dorsal striatum and its interaction with cortex. This extends to skills that are not motor such as prediction of probabilistic sequence and planning of complex tasks. Importance of cerebellum is in "closed loop" tasks that require continuous visuomotor feedback as well as error control. The cerebellum has been proposed to play a role in creating new stimulus response mapping.

Priming

Neuroimaging suggests that neural substrate of priming lies in the neocortex. A reduction of activation to a primed stimulus is consistently found either in modality specific regions or in cortical regions like lateral semantic region for semantic priming. It represents neural assemblies that are optimised by the pruning of unnecessary connections. As a result, there is earlier activation and facilitated response to a primed stimulus.

Fear conditioning and extinction

Amygdala has a key role to play in fear conditioning. Different subnuclei of this complicated structure are implicated in establishing and storing fear conditioning memory traces. Extinction depends on the interaction of amygdala and the cingulate gyrus.

Assessment and neurophysiology

There is no commercially available test for implicit memory, procedural memory or habit formation. Various motor skills can be learnt incrementally such as motor pursuit or mirror tracing. Probabilistic learning can occur when there is acquisition of information or representation that reflects underlying structural irregularities in the input. This can occur in tasks as seemingly disparate tasks such as weather prediction tasks and artificial grammar. Implicit memory can occur even when system of recollection is dysfunctional. Priming is memory without awareness reflected on improvements in accuracy or reaction time during testing which is demonstrated in a variety of tasks like word stem completion or the so called repetition priming. Conditioning, both classical and Pavlovian, has been considered as type of implicit memory.

Working memory

Neural systems

Dorsolateral prefrontal cortex (DLPFC) is considered important for working memory whose functioning is required for both simple maintenance of information over a delay and manipulation of that information. DLFPC activation is observed in conjunction with activity of post cortical areas that receive input from a variety of specialised sensory cortices chiefly inferior parietal lobule which is connected strongly and bidirectionally with DLPFC. DLPFC is important for item storage during work.

Assessment and neuropsychology

Classical test of simple working memory is digit span test which involves repetition of short sequence of digits. Tests of thought depend on simultaneous storage and manipulation of information that are considered executive in nature e.g. letter-number span is a highly correlated test with a nonverbal formally dissimilar problem solving tasks like the Wisconsin card sort. The card sort calls upon abilities such as abstraction, set shifting and response to examiner feedback. Computerised validated battery of frontal lobe tests known as "cantab" which is based on comparative and pharmacologic challenge literature as well as human lesion studies. Widely commercially available test of cognitive control is called "stroop."

Working memory is thought to be a limited capacity system that holds information on line when the stimulus is no longer present. That the working memory is a capacity limited system comes from the extensive work done in this field by Muller.[2,3] An episodic buffer is thought to play a role in the interface between working and episodic memory. A central execution is involved in allocation of cognitive resources during the dual tasks and in the manipulation of the information.

Further Readings

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