

# Memory & Learning

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Role of learning in behavior / personality development (behaviorism) → see p. Psyl >>

## DEFINITIONS AND PHYSIOLOGY

Characteristic of animals and particularly of humans is *ability to alter behavior on basis of experience*;

**Learning** is acquisition of information that makes this possible (i.e. process of acquiring new memories).

**Memory** is recording, retention and retrieval of that information.

On the basis of how information is stored and recalled:

1. Declarative memory
2. Reflexive memory

### 1. DECLARATIVE (S. EXPLICIT, RECOGNITION) memory: ≈ everyday sense of memory

a) memory for events (**episodic memory**)

b) memory for words, rules, language, etc (**semantic memory**).

- *depends* on conscious reflection for its acquisition and recall – relies on cognitive processes (evaluation, comparison, inference).
- often established in **SINGLE trial or experience** and can be expressed in *verbal declarative statements* (pvz. “vakar mačiau geltoną kanarėlę”).
- *damaged by amnesia!*

### 2. REFLEXIVE (S. IMPLICIT, NONDECLARATIVE, PROCEDURAL) memory

- *automatic (reflexive) quality* – formation / readout is *not dependent on awareness, consciousness, or cognitive processes* (such as comparison, evaluation), i.e. information is retrieved reflexively or incidentally.
- ACCUMULATES SLOWLY through **REPETITION over many trials**.
- paprastas kartojimas (jei pakartojama pakankamai daug kartų) įgauna reflexive learning pobūdį - **declarative** memory can be **transformed** into **reflexive** type by *constant repetition* (e.g. car drive learning first involves conscious cognitive process, but eventually driving becomes automatic and nonconscious).
- *not damaged by amnesia!*

REFLEXIVE memory forms:

A. **NONASSOCIATIVE LEARNING** (primitive form of learning - observed in animals at all levels of phylogenetic scale) - organism learns about properties of *single* stimulus (e.g. whether it is noxious or rewarding):

1. **HABITUATION** - *neutral (non-noxious) stimulus* is repeated many times: first time it is applied, it is novel and evokes reaction (orienting reflex or "what is it?" response); however, it evokes *less and less response* as it is repeated - eventually, subject becomes habituated to stimulus and ignores it.
2. **SENSITIZATION** (opposite to habituation) - repeated stimulus produces *greater response* if it is coupled (one or more times) with *unpleasant / pleasant stimulus* (e.g. *intensification of arousal value of stimuli* - mother who sleeps through many kinds of noise but wakes promptly when her baby cries).
  - sensitizing stimulus may override effects of habituation (e.g. after person is habituated to repetitive noise, strong pinch can restore response to noise).

Learning forms in animals:

**IMPRINTING** - *occurs primarily in birds*, and only during short period after hatching - birds learn to follow first large, moving object that they see (normally, birds are imprinted to follow their mothers, although they can also be imprinted to follow almost any animal, human, or object).

**EXPLORATION** - large *changes in environment* cause *fear*, whereas small changes lead to curiosity and *exploration*; if large changes do not produce overly threatening or painful stimuli, animal becomes habituated to fear and begins to explore; exploration does not satiate (as do eating, drinking, and sexual behavior) - every time change occurs in environment, exploration takes place.

B. **ASSOCIATIVE LEARNING** - organism learns about relation of *one stimulus to another (conditioned reflexes)*, i.e. organism incorporates meaningful information about its environment into its behavioral repertoire.

*CONDITIONED REFLEX* - reflex response to *stimulus that previously elicited little / no response*, acquired by repeatedly pairing stimulus with another *stimulus that normally does produce response*.

1. **CLASSIC CONDITIONING** involves relations between environmental events and responses (inherent reflexive) that they cause.

**Pavlov's classic experiment** - salivation induced by bell ring before placing meat in dog's mouth;

meat - **unconditioned stimulus (US)**; i.e. stimulus that elicits response without conditioning

bell-ringing - **conditioned stimulus (CS)**; i.e. initially neutral stimulus.

N.B. CS has to precede US!

- powerful US must be associated with pleasant or unpleasant affect:
  - a) stimulation of *brain reward system (positive reinforcement)*;
  - b) stimulation of *brain avoidance system* or painful shock to skin (**negative reinforcement**).
- **UNCONDITIONED REFLEX** - elicited by US directly, without conditioning;
- **CONDITIONED REFLEX** - caused by CS alone, without US.
- if CS is presented *repeatedly without US*, conditioned reflex eventually dies out (*extinction* or *internal inhibition*).
- if animal is disturbed by *external stimulus immediately after CS*, conditioned response may not occur (*external inhibition*).
- if conditioned reflex is *reinforced from time to time* by again pairing CS and US, conditioned reflex *persists indefinitely*.
- somatic, visceral, and other neural changes can be made to occur as conditioned reflex responses;

conditioning of *visceral* responses is called **BIOFEEDBACK** (e.g. volitional changing of heart rate, BP; changes are too small to apply in clinical practice).

- if two different stimuli (CS and very similar stimulus) are so nearly identical that they cannot be distinguished, conditioned animal becomes upset, whines, fails to cooperate, and tries to escape - Pavlov called these symptoms **EXPERIMENTAL NEUROSIS**; if connections between frontal lobes and rest of brain are cut, animals still fail to discriminate but their failure does not upset them; **prefrontal lobotomy** (cuts connections between frontal lobes and deeper brain portions) were at one time used in humans to *relieve tensions* caused by delusions, compulsions, phobias, intractable pain (delusions and other symptoms are still there, but they no longer bother patient).

**2. OPERANT (INSTRUMENTAL) CONDITIONING** - animal is taught to perform task ("operate on environment" – not reflexive action [as in classic conditioning]) in order to obtain reward / avoid punishment; it is **trial-and-error learning** - behaviors that are rewarded will increase, and behaviors that are punished will decrease.

**conditioned avoidance reflexes** - permit animal to avoid unpleasant event (e.g. animal is taught that by pressing bar it can prevent electric shock to feet – it is called **negative reinforcement** of behavior).

**food aversion conditioning** - animal exposed to taste of food develops strong aversion to food if tasting is coupled with injection of drug that produces nausea or illness.

- response is very strong - can sometimes be learned with CS-US **single pairing**, even if CS and US are separated by hour or more ← survival value (avoiding poisons) - brain is genetically "programmed" to food aversion responses!

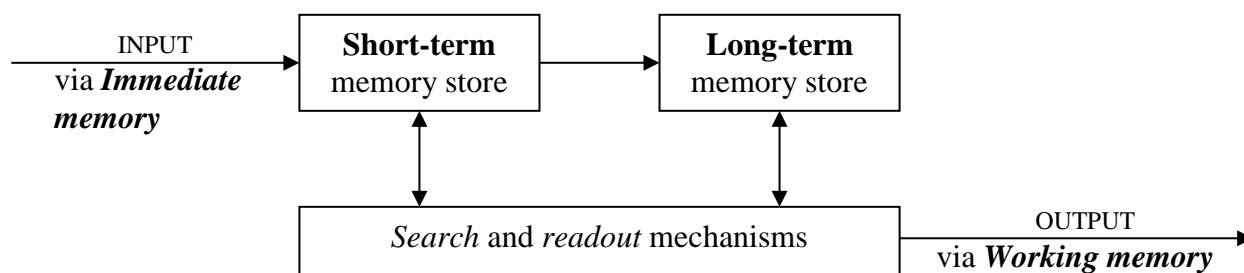
if child's *temper tantrum* (stimulus) is followed by parental attention or gratification (response), this behavior is rewarding to child and therefore reinforces behavior. Ignoring tantrum or isolating child briefly is change in response that removes reinforcement and extinguishes behavior.

**C. HABITS, SKILLS (S. PROCEDURAL MEMORY)** - improved performance on certain tasks (pvz. gramatikos taisyklių taikymas praktikoje).

**D. PRIMING (S. REPETITION PRIMING)** - facilitation of word / object recognition by prior exposure to it (e.g. improved word recall when presented with first few letters of it).

## NEURAL BASIS OF MEMORY

### MEMORY STAGES



**SHORT-TERM memory** (lasts seconds to hours) – processing (encoding) in **parahippocampal gyrus** and **hippocampus** lays down long-term changes in synaptic strength (becomes long-term memory).

**WORKING memory** (very short-term memory) located in **prefrontal cortex**:

- a) keeps initial information input (**IMMEDIATE memory**)
- b) keeps information available, while individual plans action based on it (pvz. pasižiūrime į užrašų knygutę telefono numerį ir tada šį numerį renkame); nukreipus individo dėmesį, working memory turinys dingsta – i.e. information is held in working memory only as long as it is useful for solving problem at hand.

**LONG-TERM memory** (stores memories in **neocortex** for years and sometimes for life).

- long-term memory is organized by **meaning (semantics)** rather than by **perceptual characteristics** of experience (e.g. people remember content of sentence far better than specific order of words or font in which sentence was seen; people remember set of related words (e.g. fruits) better than set of unrelated words).
- two types of long-term memory are distinguished:
  - 1) **RECENT memory** (secondary memory) - new learning; **primarily damaged by amnesia!**
  - 2) **REMOTE memory** (tertiary memory) - retrieval of old established information.
- **short-term memory is very vulnerable** - subject to disruption by **trauma** and various **drugs**, whereas **long-term memory traces are remarkably resistant to disruption**.
- **TRAUMATIC AMNESIA:**
  - dysfunction of **short-term memory** (RETROGRADE & ANTEGRADE AMNESIA) – **recently acquired memories are readily disrupted!**
  - disrupted **search-readout mechanisms** – po kurio laiko *atmintis peritrauminiams įvykiams atsistato* (vadinasi, informacija buvo sėkmingai užkoduota ir išlaikyta in short-term memory store!).
- **memory is always undergoing continual change with time** – bėgant laikui **short-term memory** konvertuojama į **long-term memory** (relatively stable; tačiau bėgant laikui, be jokių traumų, there is gradual loss of stored information or diminished capacity to retrieve it).

Goetz: “Textbook of Clinical Neurology”:

- anatomiškai tokio dalyko kaip **SHORT-TERM memory** nėra; short-term memory dažniausiai vadinama:
  - a) **long-term memory dalis**, kai atgaminame informaciją praslinkus sekundėms ÷ minutėms nuo įvykio;
  - b) **attention**

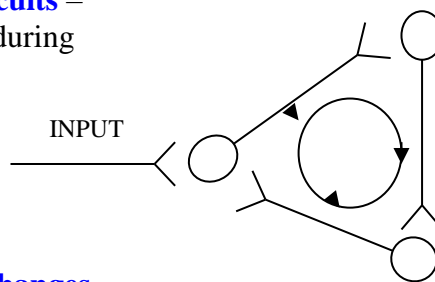
N.B. individual who cannot repeat back even single digit or word is having **deficit in attention** not **deficit in any sort of memory!**
- teiginys “**information must go through SHORT-TERM memory in order to reach LONG-TERM memory**” yra:
  - a) *teisingas*, jeigu **SHORT-TERM memory** laikysime **ATTENTION sinonimu** (people do not remember that which they do not notice!)
  - b) *neteisingas*, jeigu **SHORT-TERM memory** laikysime **IMMEDIATE memory sinonimu** – mat informacija patenka *lygiagrečiai* (ne nuosekliai!) į **IMMEDIATE memory** ir į **LONG-TERM memory**; in long-term memory iš karto prasideda informacijos praradimo procesas (todėl ir atrodo, kad egzistuoja efektyvesnė “short-term memory”).

## MEMORY MECHANISMS

### 1. **Very brief memory:**

- a) for visual events (ICONIC MEMORY)  $\approx$  250 msec. trukmės - due to brief **retinal afterimages** – **photochemical process** in sensory receptor (retina).
- b) for auditory events (ECHOIC MEMORY)  $\approx$  1-2 sek. trukmės.

2. **Short-term memory** – **reverberatory circuits** – *dynamic process* (does not involve any enduring physical changes in neurons):



3. **Long-term memory** is related to **plastic changes**.

### Memory traces are localized in different places throughout CNS

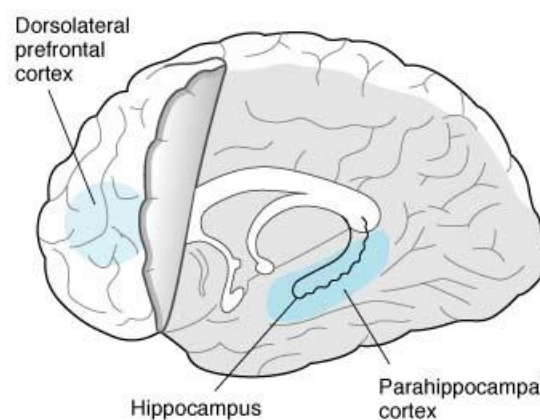
- Pavlovas galvojo, kad learning is limited to **neocortex**.
- although cortical lesions can seriously disrupt learning, animals can *RELEARN* certain tasks even they are **completely decorticated!**
- kai kuriuos paprastus sąlyginius refleksus galima išmokyti dalyvaujant **tik nugaros smegenims!** (jas chirurgiškai izoliavus nuo brain).
- **ALL REGIONS OF NERVOUS SYSTEM** appear to contain neurons with properties needed for memory storage – *even after extensive lesions, some traces of memory can remain* (brain has *capacity to reconstruct* a good reproduction from memory leftovers).

### REFLEXIVE and DECLARATIVE memories involve different neuronal circuits:

#### DECLARATIVE MEMORY

- encoding involves:

1. **WORKING MEMORY** in **frontal lobes**: *central executive* (in prefrontal cortex) → "rehearsal systems" (*verbal system* for retaining verbal memories, and parallel *visuospatial system* for retaining visual & spatial aspects).  
↓
2. Processing in **parahippocampal gyrus** and **hippocampus** to convert to **SHORT-TERM MEMORY**;



Lesions of these structures (e.g. Alzheimer's disease) → **widespread (domain-independent)** declarative memory deficits:

- 1) striking defects in **SHORT-TERM MEMORY** - cannot form new long-term memories.
- 2) intact **WORKING MEMORY** – patients perform adequately as long as they concentrate on what they are doing; however, if they are distracted for even very short period, all memory of what they were doing and proposed to do is lost.
- 3) intact **REMOTE MEMORY** (retain old pre-lesion memories).
- 4) **REFLEXIVE MEMORY** processes are intact - capable of new learning.
  - **bilateral** damage → **global** amnesia;
  - **unilateral** left- or right-sided lesions → **material-specific** memory dysfunctions (verbal or nonverbal, respectively).

**Diencephalon (mamillary bodies)** – connections:

- a) → fornix → hippocampus.



b) → mamillothalamic tract → thalamus → prefrontal cortex → basal forebrain (**nucleus basalis of Meynert**)\* → diffuse cholinergic projection to **all neocortex**, amygdala\*\*, hippocampus.

\*severe loss in Alzheimer's disease (+ atrophy of parahippocampal gyrus & hippocampus) and in Parkinson's dementia.

\*\***amygdala** (closely associated with hippocampus) - not critical for declarative memory; amygdala plays role in emotional modulation of memories - encodes **emotional memories** (amygdaloid lesions make animals less fearful – role in fear conditioning); many memories have emotional component or "color" (i.e. memories can be pleasant or unpleasant).

in humans, events associated with strong emotions are remembered better than events without emotional charge; in patients with *bilateral lesions of amygdala*, this difference is absent.

**PAPEZ CIRCUIT** (p. A138 (4) >>) participates in memory-emotions correlation.

3. **LONG-TERM MEMORIES** - visual, olfactory, auditory, etc - are located in **cortical regions** concerned with these functions.

- once long-term memories have been established, they no longer require hippocampal complex (long-term memories are resistant to retrograde amnesia).
- long-term memories can be **recalled by large number of different associations** (e.g. memory of vivid scene can be evoked not only by similar scene but also by sound or smell associated with scene and by words such as "scene," "vivid," and "view").
- **damage to neocortical region** results in **domain-specific memory deficits** - both loss of previously acquired memory (stored in that area) and inability to acquire new memories (to be stored in that area); e.g. patients with left temporal lesions lose specific knowledge about names of animals, tools, or people.
- **cholinergic system** is critical for **long-term** declarative memories (vs. **catecholamines** - important role in **working memory**).

**Working memory** – PREFRONTAL CORTEX

**Short-term memory** – PARAHIPPOCAMPAL GYRUS, HIPPOCAMPUS

**Long-term memory** – various parts of ASSOCIATION NEOCORTEX

### Strangeness & Familiarity

- some **parts of TEMPORAL lobes** change interpretation of one's surroundings - helps individual adjust to environment (in strange surroundings, one is alert and on guard, whereas in familiar surroundings, vigilance is relaxed).
- dysfunction → **“déjà vu”, “jamais vu” phenomena**.  
“déjà vu” occurs from time to time in *normal* individuals, but it may be aura (immediately preceding seizure in *temporal lobe epilepsy*).

### Memory circuit of the brain

- major pathway for memory, including long-term storage and recognition memory:

**entorhinal cortex** → glutamatergic perforant pathway → **hippocampus**: **dentate gyrus** (granule cell layer) → mossy fibres → **CA3** → Schaffer collaterals → pyramidal neurons in **CA1** → **subiculum** → fimbria → precommissural **fornix** → septal nuclei, ventral striatum → **cingulate** → **entorhinal cortex**

**basal forebrain** (septal nuclei and NBM) → postcommissural **fornix**\* → anterior nuclei of the **thalamus**

**mammillary bodies** → mammillothalamic tract

\*some fibres from the fornix also pass through the anterior commissure to the contralateral hippocampus.

## REFLEXIVE MEMORY

(pvz. sąlyginiai refleksai) pažeidžiama suardžius šias struktūras:

- 1) **amygdala**
- 2) **nucl. dentatus, nucl. interpositus** (**cerebellum** in learning! e.g. well characterized participation in classic conditioning)

N.B. does not involve processing in hippocampus!

- some investigators argue that **striatum** is involved (learning of some habit tasks is disrupted by lesions of basal ganglia).
- reflexive memory is **more diffuse** in its neural representation.
- each specific form of reflexive memory is closely linked to specific brain structures:
  - IMMEDIATE memory** stores are located in **posterior neocortical regions** - location reflecting modality (auditory or visual) and material (verbal or nonverbal):
    - immediate auditory memory - temporal-parietal cortices (left for verbal, right for nonverbal material).
    - immediate visual memory - occipitoparietal cortices (left for verbal, right for nonverbal material).
- memory processes depend on same brain regions that mediate performance in any given domain (e.g. motor-skill learning has been linked to pyramidal, extrapyramidal, and cerebellar motor systems).

## INTERCORTICAL TRANSFER OF MEMORY

- if animal is conditioned to respond to visual stimulus with one eye covered and then tested with blindfold transferred to other eye, it performs conditioned response.
- this is true even if *optic chiasm* has been cut (visual input from each eye goes only to ipsilateral cortex).
- memory transfer occurs in **anterior portion of corpus callosum**; if it is cut, no memory transfer occurs.

## MOLECULAR BASIS OF MEMORY

Key to memory is **alteration in STRENGTH of selected SYNAPTIC CONNECTIONS!**

- this occurs during *change from short-term working memory to long-term memory*.
- alteration involves **gene activation & protein synthesis** → **long-term potentiation (LTP)** and **long-term depression (LTD)** smulkiau žr. SYNAPTIC PHYSIOLOGY
  - acquisition of long-term learned responses is **prevented** if, *within 5 minutes* after each training session, animals are anesthetized, given electroshock, subjected to hypothermia, or given drugs that block protein synthesis.
  - if these interventions are performed *4 hours after* training sessions, there is **no effect** on acquisition.
  - human counterpart of this phenomenon is **TRAUMATIC AMNESIA**.

**HABITUATION** is due to **Ca<sup>2+</sup>** decrease in sensory endings → transmitter release↓; **long-term habituation** is due to ↓number of presynaptic terminals.

**SENSITIZATION** is due to action potential prolongation in these endings with resultant increase in intracellular **Ca<sup>2+</sup>** (neurotransmitter release↑); **long-term sensitization** is due to ↑number of presynaptic terminals.

**CLASSIC CONDITIONING:** US acts presynaptically on neurons activated by CS - this leaves free  $\text{Ca}^{2+}$  in cell, leading to long-term change in **adenylyl cyclase** molecule; when this enzyme is activated by CS, more **cAMP** is produced → closes  $\text{K}^+$  channels → prolongs action potentials.

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**Viktor's Notes<sup>SM</sup> for the Neurosurgery Resident**

Please visit website at [www.NeurosurgeryResident.net](http://www.NeurosurgeryResident.net)