Taste Learning and Memory in Aging

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Declarative memory includes semantic, episodic, and spatial memory, and in humans involves conscious recall.[1] Visual recognition memory is a type of episodic memory, while taste recognition memory leading to taste acceptance or aversion is conventionally classified as a type of nondeclarative memory not requiring conscious effort to recall (Fig 1). Dissociations between declarative and nondeclarative memory in rodents are based on the effects of aging and adult brain damage.

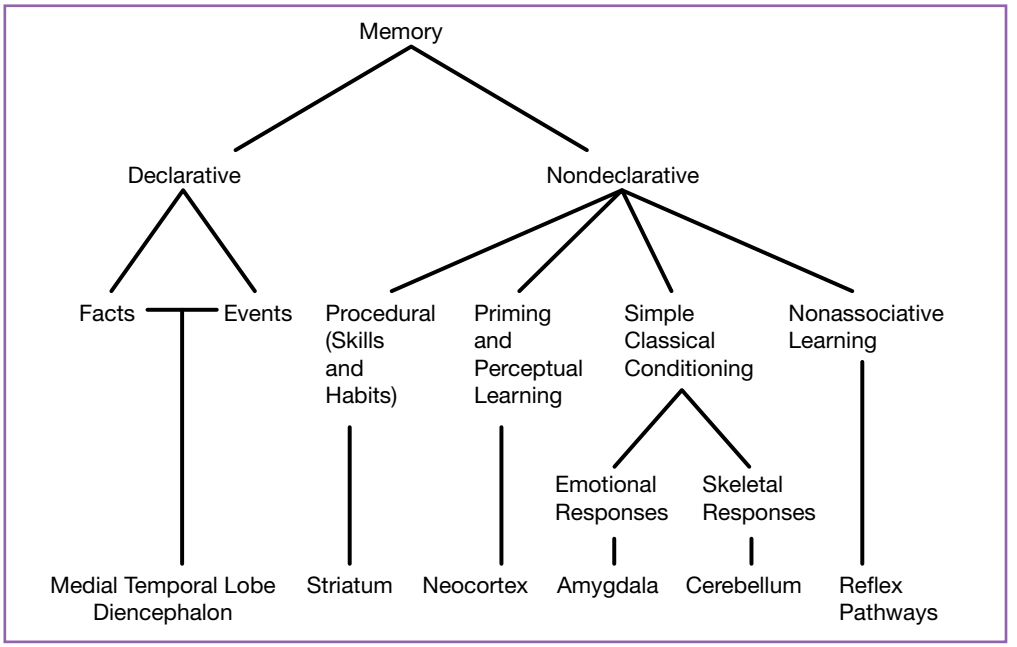

Fig 1. Declarative and nondeclarative memory systems.[1]

Source: Squire LR. Memory systems of the brain: a brief history and current perspective. *Neurobiol Learn Mem.* 2004;82(3):171-177. Reprinted by permission of Elsevier.

Performance in declarative memory tasks typically is impaired by aging and lesions of the hippocampal system, including the hippocampus and related cortical areas. In accordance with a nondeclarative memory classification of aversive taste recognition memory, previous animal studies have shown that taste aversion learning does not require the hippocampal integrity and is not impaired, but even improved, at advanced ages.[2] Nevertheless, conditioned taste aversion exhibits

learning and memory phenomena, such as blocking[3,4] and context-dependency,[5,6] requiring an intact hippocampus in adults,[7-10] and decaying during aging.[11,12]

Research on safe taste recognition memory has pointed to the amygdala's role in the taste neophobic response and its habituation when the taste is recognized as familiar and safe. However, the results are controversial regarding the impact of aging in taste neophobia, indicating a critical role of previous aversive experiences.[13]

The Institute of Neurosciences, Center for Biomedical Research (CIBM), University of Granada, Spain, has used object recognition memory and habituation of taste neophobia tasks in order to compare the effect of aging and damage of the hippocampal system in visual and taste recognition memory, respectively. First, the spontaneous object recognition (SOR) memory task is based in the rodent's natural tendency to explore novel objects. It requires at least two sessions. The acquisition session in which the rat is allowed to explore two identical objects is followed after a variable interval by a similar retention session in which one of the objects is substituted by a novel one. The time that the rat spends exploring the novel vs the familiar object is used as an index of memory.

Second, taste neophobia is evidenced in decreased consumption of a novel taste solution compared to previous water intake during baseline and to later exposures as long as the taste becomes familiar. Habituation of taste neophobia refers to the increased intake of a familiar taste that was not followed by aversive consequences, thus showing safe taste recognition memory.

CIBM results in rats support a deleterious effect of aging, both in visual and taste recognition memory. Using a systematic approach with standard everyday objects to study the performance of aged rats in SOR memory tasks at various retention intervals, CIBM researchers identified age-related deficits at the 24-hour interval, but not at shorter intervals (10 seconds, 60 seconds, and 1 hour). A retention deficit in aged rats at the longer interval is consistent with most of the previous reports, but previous results were controversial regarding shorter intervals.

After discarding other potential explanations, CIBM explored the role of the object used, applying a 1-hour retention interval. In two different experiments, CIBM researchers dissociated the effect of object complexity, often related with ambiguity, and perceptual similarity. Thus, the pairs of objects used were either complex (ie, formed by 30 Lego® bricks of different colors, but very different in shape or very similar pyramids differing only in the number of planes [pentagon versus hexagon-based pyramids]). Surprisingly, old rats did not exhibit difficulties in recognizing

simple geometric forms 1 hour after the acquisition, even if they were very similar, but evidenced recognition memory deficits using complex forms, even if they were very different.[14] This supports a selective age-related decay of memory processes involved in SOR memory.

Previous research on the effect of aging in safe taste recognition memory also yielded controversial results. CIBM researchers previously reported a reduced neophobic response and its habituation in old rats previously subjected to conditioned aversions to a different taste.[13] Later findings in naïve-aged rats indicated similar taste neophobia in old and younger adult rats. However, the habituation of taste neophobia is selectively impaired by aging. Thus, while younger adult rats recognize the taste as familiar and safe after one exposure, old rats require 4 exposure days. This indicates an age-related decay of taste recognition memory similar to that found in visual recognition memory.

Likewise, recognition memory seems to depend on temporal lobe areas, such as the perirhinal cortex (PRh), independently of the sensory modality. With respect to SOR memory, a growing number of studies point to the PRh as the critical brain area, although the hippocampus also is reported to have involvement. Consistently, laboratory results have shown that PRh neurotoxic lesions by N-methyl-D-aspartate (NMDA) interfere with object recognition memory, while dorsal hippocampal lesions selectively impair place-object recognition memory in adult rats. In fact, age-related deficits in SOR memory are attributed to decay of PRh function.

With respect to taste recognition memory, treatments that inhibit protein synthesis[15] or block cholinergic neurotransmission[16] in PRh interfere with the habituation of taste neophobia. CIBM also reported the first results indicating that a familiar taste solution induces increased c-Fos expression in the medial PRh,[17] thus supporting the involvement of the area in taste familiarity detection. Such an increase in PRh activity was abolished by amygdala lesions that impaired habituation of taste neophobia (Fig 2).[17] This suggests that the PRh might contribute to a widespread neural network involved in safe taste memory consolidation.

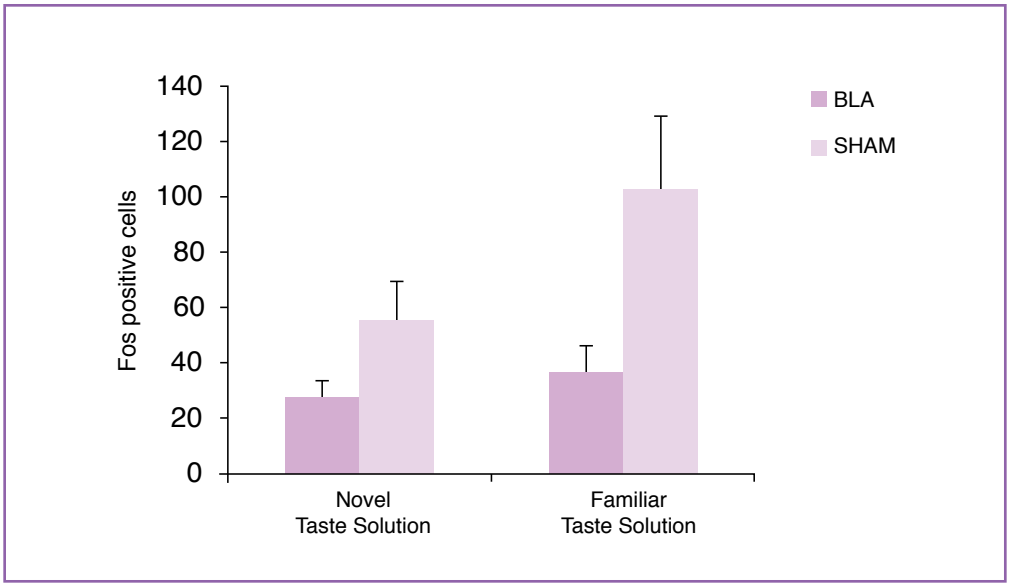

Fig 2. Increased number of Fos positive cells in the perirhinal cortex induced by a familiar taste solution.[17] Such increment was abolished by basolateral amygdala lesions.

BLA=basolateral amygdala (neurotoxic) lesion, SHAM=sham lesion

Source: Gómez-Chacón B et al. Basolateral amygdala lesions attenuate safe taste memory-related c-fos expression in the rat perirhinal cortex. *Behav Brain Res.* 2012;230(2):418-422. Reprinted by permission of Elsevier.

Although visual, but not taste recognition, memory in humans seems to rely on a conscious effort to recall and each memory modality depends on independent brain sensory systems, the results obtained in animal models point to shared brain processes that are similarly affected by age-related decay and that can result in functional improvement with choline dietary supplementation.[18,19] It is possible to propose the PRh as a shared component of the neural circuit required for taste and visual recognition memory, thus distinct mechanisms relying on PRh and the amygdala for safe taste memory and in PRh and the hippocampus for visual recognition memory are conceivable.

Therefore, functional and anatomical dissociation among shared and independent recognition memory processes involving the temporal lobe and related areas require further research. It is expected that bringing together memory tasks previously used in different and separate fields will prompt a new view to the concepts and classifications of memory.

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