Memory systems

Les systèmes mnésiques

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Abstract – Two recent findings are summarized here that bear on the organization of memory and brain systems. First, the capacity for simple recognition of familiarity (a form of declarative memory) depends on the hippocampal region in both humans and nonhuman primates. Second, probabilistic classification learning (a form of nondeclarative memory akin to habit learning) depends on the caudate nucleus and putamen. These findings are related to the classification of long-term memory and current understanding of the participating brain systems. (© Académie des sciences / Elsevier, Paris.)

amnesia / declarative memory / nondeclarative memory / hippocampus / basal ganglia

1. Introduction

As the papers in this symposium illustrate, the problem of memory can be usefully investigated at many levels of analysis: from questions about synaptic change to questions about human cognition. Between these poles are many important matters about what memory is, what brain systems are involved, and what jobs they do. This article addresses two issues concerning the organization of memory and brain systems.

The first issue concerns the medial temporal lobe memory system, where damage causes an amnesic syndrome, a condition that historically has been one of the richest sources of information about the nature of memory. The second issue concerns the fact that the role of the medial temporal lobe in memory is narrower than once thought. It is needed for just one kind of memory. The major distinction is between the capacity for conscious memory for facts and events (declarative memory), which depends on the medial temporal lobe system, and a collection of nonconscious, nondeclarative memory abilities, which depend on other brain systems. In the case of nondeclarative memory, performance changes as the result of experience, and in this sense deserves the term memory, but the change in performance occurs without requiring any conscious memory content or even the experience that memory is being used.

2. The amnesic syndrome and its animal model

In human amnesia, memory is impaired against a background of normal intellectual function. The hallmark of the deficit is profound forgetfulness. Material that is presented for study can be perceived and comprehended, and it can be held in short-term memory. Thus, even severely amnesic patients can appear normal at first meeting. They can carry on an intelligent conversation, and they can hold small amounts of material in mind, such as a telephone number, so long as they are permitted to rehearse it. Amnesic patients also have intact access to their remote past. The difficulty comes when they attempt to recollect material that was presented a few minutes before. They cannot form and maintain new long-term memories. It has been known for decades that this memory deficit is associated with bilateral lesions of the medial temporal lobe or midline diencephalon [1, 2]. Detailed neurohistological examination of a few other patients has revealed the importance of the hippocampal formation, which lies within the medial temporal lobe [3, 4]. An animal model of human amnesia was established in the monkey in the early 1980s [5, 6]. Systematic and cumulative work over the next 10 years, using the animal model, succeeded in identifying the system of structures in the medial temporal lobe essential for declarative memory [7, 8]. This system includes the hippocampal region (i.e., the hippocampus proper, the dentate

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gyrus, the subicular complex), the entorhinal cortex, and the adjacent perirhinal and parahippocampal cortices.

3. Recognition memory and the hippocampal region

One fundamental memory ability is the capacity to recognize what is familiar, as opposed to what is novel. Tests of recognition memory have figured prominently in work with the animal model of human amnesia. Recognition memory can be tested in both humans and monkeys, sometimes with identical tests, and it has proven to have a similar neural substrate. The visual paired-comparison test is a simple test of familiarity that depends on the spontaneous tendency of humans and nonhuman animals to seek novelty [9]. In the test, two identical pictures are presented side by side for visual inspection for a period of a few seconds.

Then, either immediately or after a delay of minutes or even hours, two pictures are again presented. One of the pictures is the same picture that was presented just before, and the other picture is a new one. The subject (human or monkey) is allowed to view the two pictures for 5 s, while eye movements are recorded. The finding in normal subjects is that they spend about twice as much time looking at the new picture compared to the old picture.

When the test pictures are presented immediately after the sample pictures, amnesic patients and monkeys with bilateral lesions of the hippocampal region behave similarly. The patients and the monkeys look at the old picture as long as normal subjects, consistent with the fact that medial temporal lobe damage spares short-term memory. However, when a delay is introduced between the sample pictures and the test pictures, neither the patients nor the operated monkeys discriminate between the novel and familiar pictures [10, 11]. These findings demonstrate the importance for memory of the hippocampal region itself, and the ease with which its contribution can be demonstrated when an appropriate test is used. There has been a suggestion that recognition memory can escape impairment in those patients with lesions limited to the hippocampal region [12]. However in other studies, amnesic patients, including those who at autopsy proved to have damage limited to the hippocampal formation or even the CA1 field of the hippocampus, also demonstrated unmistakable impairment on several tests of recognition memory [13].

4. Nondeclarative memory: habit learning and the neostriatum

Despite their severe impairment on conventional memory tasks of recall and recognition, amnesic patients perform normally on many other tasks that assess, for example, the capacity for skill and habit learning, simple forms of conditioning, and the phenomenon of priming [14]. The implication is that the kinds of learning and memory that are intact in amnesia depend on different brain structures than the medial temporal lobe and diencephalic structures damaged in amnesia. As an illustration of the kind of memory ability that is intact in amnesia, consider a task of probablistic classification learning. This kind of learning is analogous to the habit learning tasks studied in experimental animals. Volunteer subjects attempt to learn a set of associations. The associations are not obvious, and their probablistic structure defeats the normal tendency to simply memorize what needs to be learned. What happens in this task is that participants decide on each trial which of two weather outcomes (rain or sunshine) will occur based on a set of one, two, or three cues (out of four possible cues) that appear on a computer screen [15]. Each cue is independently associated to a weather outcome with a fixed probability, and the two outcomes occur equally often. On each trial subjects respond by pressing a key to record their choice, and feedback is given immediately after each choice (correct or incorrect). Amnesic patients learned gradually to predict the correct weather outcome, and they learned across 50 trials at the same rate as normal subjects, improving from 50 % correct (chance performance) to about 65 % correct [15]. Despite the intact performance of the amnesic patients on the weather prediction task, they were markedly impaired at answering factual questions about the training episode that they had just completed. In contrast to amnesic patients, 20 patients with nondementing Parkinson's disease were impaired at learning this same probablistic learning task. After 50 training trials, the patients were not performing above chance levels [16]. Parkinson's disease is associated with prominent pathology in the caudate nucleus and the putamen. These findings support the idea that probablistic classification learning is akin to habit learning, which in rodents appears to depend on the integrity of the caudate-putamen [17]. Note that the learning deficit in patients with Parkinson's disease appeared on a task that had no essential motor component. Thus, the basal ganglia are important for some kinds of habit learning, even when motor skill learning is not required [18].

5. Multiple memory systems

An important lesson from recent work on memory, and from the findings summarized here, is that memory is not a single entity. *Figure 1* illustrates how long-term memory can be divided into several parallel memory systems. Declarative memory is the kind of memory impaired in amnesia. It refers to the capacity for conscious recollections about facts and events.

It is especially suited for one-trial learning, at forming and maintaining an association between two arbitrarily different pieces of material. Thus, it is good at associating

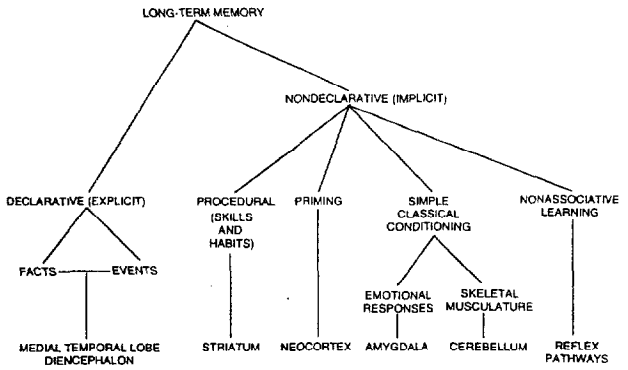

Figure 1. A taxonomy of long-term memory systems together with the brain structures critical for each system.

In addition to its importance in emotional learning, the amygdala also has a modulatory influence on the strength of other forms of memory.

the various aspects of a context that are present at a particular time and place, thereby creating a memory for an episode.

It is also well suited for connecting the pieces of information needed to acquire a new fact (e.g., Angel Falls are located in Venezuela). Declarative memory depends on the interaction between the medial temporal/diencephalic structures damaged in amnesia and widespread areas of neocortex where information is processed and ultimately stored in long-term memory.

Nondeclarative memory is not itself a brain-system construct. Rather, it is an umbrella term that encompasses several different kinds of nondeclarative memory. Nondeclarative forms of memory have in common the feature that memory is nonconscious. Memory is expressed through performance and does not require any reflection on the past or even the knowledge that memory is being influenced by past events. It is sometimes pointed out that declarative memory is knowledge about the external world, and it is either true or false; nondeclarative memory is about performance, and it is neither true nor false.

The principal forms of nondeclarative memory and their associated brain substrates, as currently understood, are as follows: 1) memory for skills and habits has an essential dependence on the neostriatum, which serves as a target of cortico-striatal pathways; 2) perceptual priming depends on changes within perceptual processing pathways of the neocortex [19, 20] other forms of priming (e.g., conceptual priming) have not been adequately studied with neuroimaging; 3) simple classical conditioning can be divided into the conditioning of skeletal musculature, which has an essential dependence on the cerebellum [21] and 4) emotional learning, for example fear conditioning, which has an essential dependence on the amygdala [22]. The amygdala is also a source of modulation for both declarative and nondeclarative memory [23]. Thus, the amygdala is probably responsible for the fact that emotionally arousing (declarative) memories are usually remembered better than neutral (declarative) memories; 5) nonassociative learning (habituation and sensitization) is a robust form of behavioral memory that is well-developed even in invertebrate animals who do not, so far as is known, have a capacity for declarative memory.

Habituation and sensitization occur as changes within the same reflex pathways that exhibit the altered behavior [24].

The idea that there are multiple forms of memory, each supported by a distinct brain system, has been central to recent work on memory. What has been learned about the identity of these memory systems, their operating characteristics, and their anatomical foundations sets the stage for some fundamental biological questions: 1) Where in each system do the synaptic changes occur that actually store the record of experience? 2) For each system, what are the molecular and cellular mechanisms underlying synaptic change? 3) Are these mechanisms common to all forms of memory, or are there differences in the mechanisms used by different memory systems? In the coming years, these questions can be expected to be at the forefront of work that investigates memory and neuronal plasticity at the level of cells and synapses.

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