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Memory consolidation involves time-limited participation of MTL

The theory of memory consolidation in humans proposes that the medial temporal lobe (MTL) plays a key role in memory retrieval, and that its involvement in the process of consolidation takes place over a period of time. The MTL is a system of brain structures which includes the hippocampal formation, entorhinal cortex, perirhinal cortex, parahippocampal cortex and the amygdala. This time-determined process begins at the molecular and cellular level of the hippocampus, and it may take only minutes to hours to complete the first phase of consolidation. According to theory, these newly acquired memories are subsequently anchored in the hippocampal formation in the course of time. Such reminiscences may remain in the hippocampus for several years – as in episodic memory – before the entorhinal cortex assumes the process of consolidation, a process which can allow it to participate in recall over decades. Thus the primary function of the MTL is to guide the development of memory consolidation to produce stable mnemonic representations in the neocortex. As a result, the MTL eventually becomes irrelevant in recall of remote memories of the past.

This time-limited theory of memory consolidation is based on a wealth of data originating from studies in patients with circumscribed lesions of the MTL, as well from experimental studies in animals. It has often been reported in humans that lesions to the MTL produce retrograde amnesia in which recently acquired memories are lost, whereas recollection of memories from the remote past remain intact. Evidence of this kind has been used to support the assumption that there is a fundamental difference in the process consolidating the memory of events occurring far in the past from those which recently took place.

Nevertheless, despite these convincing aspects, the classical concept of memory consolidation was challenged in 1997 by the multiple memory trace theory, an alternative theory based on the assumption that synaptic connections between MTL and neocortex increase when an event is frequently recalled. Although both theories recognise the crucial role of MTL in supplying neocortex with memory data, the process by which this transfer takes place is described as being completely different. According to the multiple memory trace theory, older memories accumulate large numbers of connections, whereas as recent ones command only relatively few links between the two brain systems. Lesions to the MTL reek greater havoc to the more recently established synaptic connections of recent memory simply because older reminiscences possess a larger set of interactions.

In order to determine which of these theories accurately explains brain memory processing, it is necessary to determine whether MTL functions according to a time-limited dynamic process, as in consolidation theory, or to the time-invariant static procedure predicted by the theory of multiple memory trace. Haist et al. [1], using functional magnetic resonance imaging (fMRI) in connection with remote memory assessment in humans, have brought forth evidence suggesting that memory consolidation takes place in the MTL according to a dynamic time-dependent process, and is not the result of an increase in synaptic links due to repeated memory retrieval. The authors also provide evidence indicating that the entorhinal cortex may be able to support memory consolidation up to 20 years after the learning event.

Methods

Haist et al. selected 8 healthy older adults of 60–70 years of age who described themselves as avid consumers of popular media and news reports. They were required to perform the famous face test in which they recalled and recognised the names of well-known people – entertainers, artists, athletes – in twenty-eight photographs from six decades of the 20th century, i. e. from the 1940s to the 1990s. This classical neuropychological test was used in examining the memories of older subjects because it allows a retrospective study which extends over the many years required to observe the entire consolidation process. During the recognition of faces from a particular decade, whole brain activity was measured using a gradient-recalled single-shot echoplanar imaging method sensitive to the blood oxygen level-dependent (BOLD) signal change. The participants were tested in eight separate runs using a recall memory test versus no-task resting control format. Six runs tested the recollection of famous faces from a specific decade, whereas photographs of non-famous individuals (recent and remote) were tested separately in two runs.

Results

The results of the Haist et al. study showed that participants' famous face recognition scores (87.6 ± 2.1 %) were higher than the recall scores (47.7 ± 4.1 %) for all of the six decade test conditions. The performance of test subjects was identical to that of control subjects of a previously conducted famous face test of amnesiac individuals suffering temporally graded memory loss. The authors note that the high level of recognition indicates that the study participants were substantially familiar with the faces from each decade.

The anterior hippocampus and amygdala of the right hemisphere were significantly activated, as determined by fMRI, in the recollection of famous faces in the 1990s test condition, while activation of the amygdala was also seen in the 1960s condition. Haist et al. point out that a temporal gradient was observed in the right hemisphere MTL since the percent signal change for the 1990s condition exceeded the mean percent signal change of the other decade conditions in 7 of the 8 study participants. Activation of the hippocampal formation by decades other than the 1990s did not exceed the statistical threshold. The posterior parahippocampal cortex of the right hemisphere was also activated, but it was not temporally graded. The authors note their results agree with other neuroimaging studies showing a bias for right hemisphere MTL activation in face processing studies.

In addition, several regions of the brain outside the MTL – such as the right and left hemisphere fusiform gyrus and inferior occipital gyrus – were also significantly activated in all decade test conditions of the authors' study.

Haist et al. subsequently carried out a linear trend analysis of the changes in functional activity of several brain regions across all test decades. The results showed that the entorhinal cortex of the right hemisphere was associated with linear decrease in functional activity from recent to remote decades. The mean percent fMRI signal change of the entorhinal region of interest (ROI) in the right hemisphere for the 1990s and 1980s conditions exceeded the more remote decade conditions in 6 of the 8 participants. The authors point out that no other brain region showed similar effects, not the hippocampal formation or the fusiform cortex. In addition, Haist et al. were able to show that activity changes in the entorhinal cortex equalised to baseline levels in test conditions of the 1970s, 1960s and 1950s, but fell during the recall of famous faces of the 1940s. This means that recall of faces from the 1940s represents memories different from those formed as adults, i. e. represent the very remote memories of youth which are not consolidated by the MTL. The results of the entorhinal cortex activation were verified by employing a pair-wise comparison the fMRI activity data from the 1990s and 1980s conditions with the combined data from the 1970s, 1960s and 1950s. Haist et al. conclude that right the hemisphere entorhinal cortex is involved in memory consolidation for up to twenty years.

Discussion

The authors point out that the study of remote memory assessment in humans is complicated because of the difficulty in designing studies which can assess the consolidation of memory stretching back over several decades. The use of the famous face test, however, allows study participants to recognise photographs of people known to the public at a particular decade, going back to the remote past. Using this test procedure, while monitoring fMRI signals of whole brain activity, Haist et al. were able to demonstrate the extensive participation of the entorhinal cortex region of the MTL in remote memory functions. This finding agrees with volumetric measurements of the MTL in patients exhibiting severe retrograde amnesia, the extent of which showed a positive correlation with the size of lesions to the parahippocampal and entorhinal cortices. Lesions of the hippocampus, however, showed no such correlation. Nevertheless, lesions to the CA1 subfield of the hippocampus have been shown to produce retrograde amnesia restricted to a few years, whereas damage to the MTL resulted in longer retrograde amnesia. The authors conclude that these results agree with their fMRI findings.

The study by Haist et al. is the first one to produce evidence in normal humans indicating that the entorhinal cortrex could be involved in memory consolidation lasting up to decades. By contrast, this study shows that hippocampal function is limited to only a few years in the consolidation of memory required by the famous face test. Since certain areas of the neocortex are involved in the original processing of visual stimuli, it would appear that these regions could also be involved in memory consolidation, even if no evidence of a reverse linear trend of activity increasing across decades was observed. This means that MTL participates in acts of memory like a scaffold does in the construction of a building. Once sufficient memory consolidation is achieved, the neurobiological scaffold MTL is no longer needed to sustain long-term memory.

The authors emphasise that their study does not support the hypothesis which assumes MTL to be the locus of multiple memory traces supporting long-term memory retrieval. Their findings unambiguously provide evidence that hippocampal formation does not play a static role in remote memory function, as suggested by the multiple memory trace theory. Results of the Haist et al. study demonstrate participation of MTL in long-term declarative memory to be time-limited in healthy adults, however the entorhinal cortex may be involved in memory consolidation reaching back several decades.

In a News and Views section article in the November 2001 issue of Nature Neuroscience, Howard Eichenbaum [2] from the Laboratory of Cognitive Neurobiology of Boston University notes that while consolidation through various stages may be slow, it has the advantage of facilitating an update of memory data. This means that new memories can be interleaved with the pre-existing organisation of knowledge in the neocortex. In other words, the brain brings with it a neurobiological framework which allows new experiences to shape our view of the world. Eichenbaum contends that since humans are confronted with a large body of relevant knowledge, which is frequently supplemented by new information, the process of memory consolidation can go on for several decades. This again demonstrates that the brain functions according to a dynamic principle, which does not resemble the static operations of a digital computer.

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