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EXPLORING THE BRAIN

Lecture 10

MEMORY

by

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GRESHAM LECTURE 10: Memory
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The first problem with studying memory is to be sure what it really means. In English at least, this single word can serve as an umbrella term for a diverse range of processes that may well be quite distinct. But there are many distinct types of brain process that fall under the general term 'memory'. The most basic and familiar distinction is between 'short-term' and 'long-term' memory. Short-term memory operates, for example, when we try and remember a series of numbers. Everything is fine so long as no one comes into the room, and indeed that there are no other distractions, because the strategy is usually to repeat the sequence in our minds over and over again. This process is highly vulnerable to interruptions: however even in the most ideal and silent of scenarios, it is surprisingly modest. The number of digits we can remember by simple repetition is on average a rather puny 7.

One of the most obvious questions to ask about short-term memory is how it relates to our more 'usual' memory. This less contrived type of memory process is 'long-term' and will occur without any need for repetition or rehearsal. So, do short- and long-term memory operate in parallel, in a completely independent way? It is well known that patients who remember nothing about what has happened to them beyond the immediate present, and who thereby exhibit an almost global 'amnesia', nonetheless have a short-term memory ability indistinguishable from non-amnesiacs. Clearly then the two processes can be separated, but does it work the other way? Could someone have a normal long-term memory even when the short-term memory ability was destroyed?

Impairments in short term memory are slippery to study. Long-term memory is not a single, one-step process but can be divided up into many different aspects. For each of these different aspects there appears to be a respective form of short-term memory. For example, young children who have a poor short-term memory for nonsense words particularly, also have, specifically, a poor long term memory for unfamiliar names of toys. Short term and long term memory appear to work not independently in parallel, but in series. First, short-term memory comes into operation: it is a transient, highly unstable and vulnerable process where attention and rehearsal are needed in order to lead into the more permanent and dormant long-term memory. Successful rehearsal in short-term memory will eventually lead to that special phone number being somehow retained in one's minds without constant attention to it.

Short-term memory operates to serve long term memory. But what do we mean by 'long term memory'? It turns out that, once more, this other basic category for the umbrella idea of 'memory', can itself be further broken down into two distinct phenomena. There is much that we learn and remember as we go through life: how to drive a car, the French for 'thank you' and what we did when Auntie Flo last came to visit. All these are examples of different types of memory at work. However, the odd one out in this list of three examples would be 'how to drive a car'. The memory for a fact, such as the French for 'thank you', or an event, such as the recent visit of Auntie Flo, requires that we should be making an explicit conscious effort. In contrast, driving a car, like many skills and habits, is almost performed on automatic pilot. This type of memory for skills such as driving is therefore referred to as 'implicit', because we do not need to actively and consciously remember how to do something: we just get in a car and drive. One sees a red light and the foot is 'automatically' on the brake. Not surprisingly, in contrast to this process, memory for events and facts can therefore be regarded as 'explicit' memory.

One of the most famous and intensively investigated case of complete loss of explicit memory is that of an individual 'HM'. H.M. had severe epilepsy, the condition where the patient at certain, unpredictable times will go be stricken with a seizure, massive convulsions of the body accompanied by loss of consciousness. In H.M.'s case, these epileptic seizures became so frequent that it was impossible for him to live a normal life.

And so in 1953, at the age of twenty seven, HM had part of his brain removed, to control the epileptic seizures. This operation was a great success. But it has never been performed since, because of the terrible consequence. Although the surgery cured the epilepsy, the net result of the operation was, for H.M., arguably far more crippling. What happened was that he could remember the events before his operation, that is to say up to about two years beforehand. But after that, and ever since the operation, he has remained constantly trapped in the present.

As a result of this condition H.M. has been unable to carry out any work that is any more than a simple act in the here and now. He has been given therefore rather monotonous jobs such as mounting cigarette lighters on cardboard displays. But even so he could not give a description of the place in which he worked, the nature of his job, nor the route along which he was driven every day.

HM can still remember strings of up to seven digits, thus demonstrating that short-term memory is indeed a separate process from the subsequent stage of long-term memory. Moreover, although HM appears to have lost his ability to remember in the long term, his brain has retained a different type of memory and that other type of long-term memory is just fine. H.M. can actually perform quite well at certain motor skills like tracing a star. However this task is not necessarily as easy as it sounds since the outline has to be traced while looking in a mirror: it is a demanding exercise in sensory motor co-ordination that improves with practice, like driving or riding a bicycle. Every day H.M. did indeed improve, showing that this other type of memory, implicit memory, was not processed in the same part of the brain as memories for events. Interestingly enough, HM was not conscious of remembering the *event* of learning to draw the star (an example of explicit memory), although his brain was quite happily getting better at doing so: implicit memory.

What is particularly relevant to our present discussion is that although HM cannot remember events occurring after his accident, past memories from long ago are still intact, trapped in the brain like a fly in amber. So these memories are obviously not dependent on the area that has been removed. It must be the case then, that no one brain region can be assuming the entire responsibility for the whole memory process of facts and events. Rather, memories must be somehow processed through one region, but consolidated elsewhere. In HM's case the damage must have intervened at the stage where a new memory is first processed. Hence all the memories that had already been consolidated, were safe; it is just that the memory for any new event or fact, was impossible.

The area that H.M. had had removed was the middle part of his 'temporal lobe', which lies on either side of the brain, as its name suggests, by the temples, just above the ears. This area also includes a region underneath the cortex called the 'hippocampus'. A considerable amount of clinical and experimental evidence has shown, subsequent to the case of H.M., that damage to this brain region results in an impairment in the laying down of memories.

However, even for this more specific aspect of memory, its initial consolidation, there is in addition another area that appears to be important: this is the area at the core of the brain named after the Greek for 'room' which is vital for the relaying of incoming sensory information on to the cortex. Just as the processing of hearing and vision each rely on a different part of the thalamus, so there is a specific area of the thalamus contributing to memory, the middle 'medial' region. We know that the medial thalamus contributes to memory because of one or two unfortunate and bizarre accidents, where people have ended up with either fencing foils or snooker cues up one nostril, thereby destroying the structure in the trajectory of the foil or cue, the medial thalamus. In such cases, the victims of these accidents have displayed amnesia for events. But unlike the examples of amnesia we have looked at so far, the problem has often only been temporary: memory has appeared to recover. Despite the fact that the amnesia can be temporary however, there is a permanent inability for memory of events that occurred while the amnesia lasted, presumably whilst the medial thalamus was malfunctioning. Hence, as for the hippocampus, the medial thalamus can also be viewed as important in the laying down, the consolidation, of memories.

Yet a further brain region seems to play a critical role because when it is damaged another, very specific type of memory impairment is seen: 'source amnesia'. Source amnesia is a specific loss of memory for when and where an event occurred. If there is thus no space or time reference, an event can no longer be differentiated from another, and there is no personal involvement of the individual with what has happened. Because events are unique and personal, whereas facts are generic and free of time and space frames of reference, it follows that source amnesia will primarily affect memory for events rather than for facts. So, whereas memory for both facts and events appear to rely on the integrity of the hippocampus and the medial temporal lobe, only memory for events seems affected by damage to this third area, the prefrontal cortex.

Interestingly enough, damage to the medial thalamus, which has connections with the prefrontal cortex, can also result in special type of errors of its own in the time-space allocation of memories. The problem for these particular patients is that memories can come forward inappropriately, out of context, when they are irrelevant to the speech and ideas of the present moment. The prefrontal cortex then is presumably having some influence not just in the way events are remembered as occurring at a certain time and place, but also in how they are associated with related events at presumably a similar time or place.

So far then, we have seen that for explicit memory of both events and facts, that clinical cases such as HM suggest that the hippocampus and medial thalamus play a role in laying down memories for some two years: these long-term memories are somehow 'stored' in the temporal lobe. Meanwhile the prefrontal cortex, with which the hippocampus and medial thalamus both have connections, co-ordinates facts with an appropriate time and space context to ensure that an event is remembered as a unique happening.

But is there a particular brain region where a memory is finally laid down? This was the question that the psychologist Karl Lashley spent his life trying to answer some fifty years ago. Lashley trained rats on a memory task in mazes, and then removed different portions of cortex to see if he could identify where the memory 'engram' might be stored. To his surprise and consternation, removal of different parts of the cortex did not result in a precise matching between one specific area and the retention of a specific memory. Rather, the more amounts of cortex were removed, irrespective of specificity of region, the worse the rats became at the memory task. Perhaps not surprisingly then, the entire cortex plays an important role in the storage of memory.

In line with Lashley's evidence from rats, are the clinical cases reported by Penfield, a neurosurgeon who stimulated the brains of awake patients and found that in certain cases, the stimulation evoked 'memories'. If the same area was stimulated by Penfield on different occasions, then different memories were elicited: it would be like finding different videos at different times in the same attic storage cupboard. Conversely, the same memories could be generated from stimulating different areas: again, imagine how bizarre it would be to find the same video in different storage cupboards. No one has yet shown definitively how these phenomena can be explained, in terms of brain functioning. One possibility, however, is that each time Penfield stimulated, albeit at the same site, he was activating a different circuitry of neurons, where each particular circuit might participate in a particular memory. Similarly, when stimulating in another locus, Penfield may have sometimes been activating a circuit he had activated before, but simply from a different triggering point: once the same circuit was activated, from whatever triggering point, the 'memory' would be the same.

An interpretation of Penfield's findings then, is that memory is somehow associated with overlapping circuits of neurons. Any one neuron could be the member of all number of different circuits: it would be the specific combination in each case that distinguished one circuit from another. Each circuit would contribute to the phenomenon of a memory, so that no single brain cell or exclusively committed group of cells is wholly responsible: instead the memory would be 'distributed'.

But how do the memories actually become consolidated in the cortex in the first place? We have seen that all types of memory first enter the highly transient and dissociable phase of short-term memory: but short- term memory only lasts at most for half an hour. In contrast is the striking case of HM where, although he had perfect recall of all that had happened early in his life, could not remember anything from the period of *two years* preceding his operation. For the hippocampus and medial thalamus to consolidate memories then, it is not just a matter of a few minutes, but of a substantial period of time.

No one really knows yet exactly how the hippocampus and medial thalamus might be working over a period of years, in conjunction with the cortex, to lay down memories that will, eventually, no longer depend on the integrity of these subcortical structures. One attractive idea however draws on the idea of a memory being composed of otherwise arbitrary elements, brought together for the first time in the event or the fact to be remembered. The role of the hippocampus and medial thalamus would be to ensure that these disparate, previously unassociated elements, are now associated and thus somehow bound into a cohesive 'memory'. Some mechanism would therefore be needed to recruit these different and remote neuronal populations into a working network.

It is possible to imagine that, initially, the cohesiveness of the working cortical network that represents the 'memory', depends on an ongoing dialogue with the hippocampus and medial thalamus. However, as the network becomes established, seemingly over a period of several years, then gradually the subcortical structures become less important, such that eventually, as we saw with HM, an established memory can remain intact, freed up from, and entirely independent of, the hippocampus. One metaphor might be that of scaffolding: whilst a building is being established, the removal of the scaffolding would lead to the collapse of the edifice: however once the building is completed, the scaffolding is redundant.

If explicit memory for events and facts depends on an initial dialogue between the cortex and certain subcortical structures, perhaps this same arrangement could also apply to the laying down of skills and habits, implicit memory. Certain 'habits', such as remembering sequences or making a certain type of movement in an appropriate context without needing to think about it, can all be performed adequately in amnesiac patients with medial temporal lobe damage. However patients suffering from disorders of the basal ganglia such as Parkinson's disease and

Huntington's Chorea have seemingly no problem explicitly remembering facts and events. Instead, their problem is that they are no longer able to perform the 'habit' of an appropriate sequence of movement, or of recognising the next in a sequence of items that had been shown to them over and over again and which normally would have been 'implicitly' remembered.

We can see then that memory is multi-faceted and multi-stage. It is more than a mere 'function' of the brain, as it encapsulates individuals' inner resources for interpreting, in an exquisitely unique fashion, the world around them. It is a cornerstone of the mind.