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Memories are made of this?

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When we think about memory, we tend to assume that ours is not particularly good (if it were, it would not have been that difficult to study for that last exam!). But the fact is that we all have a great memory, and that we use it all the time, to the point that we become unaware of it. Cristian Bodo explains.

When you find your way home after school without even having to think about it, when you recognise other members of your family and when you consider if it is best to stay at home doing homework or to go out with your friends, you are always using bits of information stored somewhere inside your brain that guide your actions and help you make decisions.

Can you imagine what it would be like if they were not there? This is precisely what happened to a man called Henry Molaison who, after a particularly difficult surgical operation in his brain, lost the ability to create new memories (Box 1). Henry would find himself lost all the time, because he could no longer remember how he had arrived at a particular place or recognise where it was. After being introduced to someone, he would start a lively conversation with his new acquaintance, but if the person left the room for a few minutes and then returned, Henry would start to introduce himself all over again. He could not work any more, because he did not remember how to get to his office.

Henry Molaison, whose damaged brain gave scientists insights into how memories are stored.

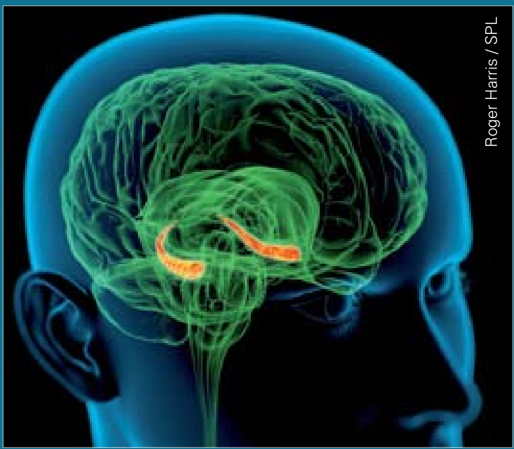
Searching for memories in the brain

Henry's story became famous among scientists who were trying to figure out how memory works. They all agreed that *something* had to change inside our brain every time that we commit something to memory, even when we do it unconsciously. This 'memory trace' has to remain there so that we can retrieve that particular piece of information when we need it. This can happen after just a few hours or after years, or even decades. However, what is it that changes exactly, and where in our brain are these memory traces stored?

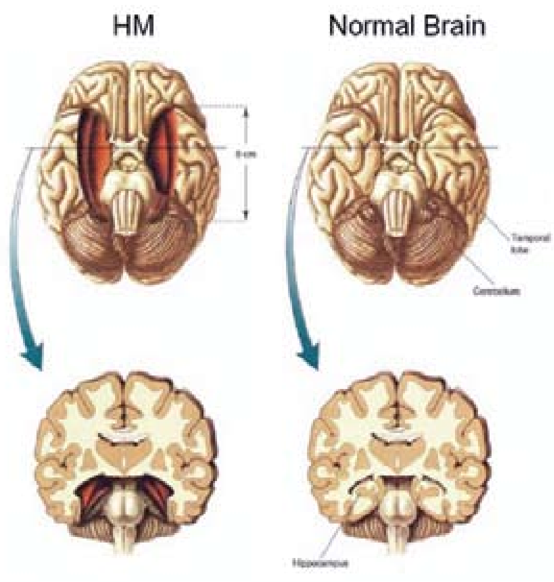
Although brain scientists have been working on this for a long time, we still don't have definite answers to these questions. We think that the **hippocampus** (Greek for seahorse, because its discoverer thought that it looked like one of those

Box 1 The hippocampus

The hippocampus is a brain structure belonging to the limbic system, present in humans and other mammals. It is a 'paired' structure, meaning that it is composed of two mirror-image halves in the left and right sides of the brain. Scientists have found that it works as a memory recorder, allowing us to store memory traces of what we see, hear, taste or feel, that we can later use to remember our past experiences. But no one knows for sure yet what these memory traces look like, or where in the brain they are being stored.



creatures) (Box 1) is essential for storing new memories. In fact, the hippocampus was precisely the part of the brain that got damaged the most during Henry's brain surgery, and so he provided an important clue to the people that were trying to understand memory. He had little problem remembering things that he had committed to memory before the operation, so it looked as if the hippocampus was essential to store new memory traces, but it was not the place of storage itself.



Henry Molaison's brain (on the left), showing the damage he suffered as a result of an operation, compared with a normal brain.

Non-human animal models in memory research

One problem with studying how memories are created in humans is that we have limited access to our own brain: the procedures that are required to obtain tissue samples are likely to cause permanent damage to our brain structures. That is why lab animals have proved to be so useful in memory research. Non-human animals use their memory for their survival in the wild: they need to remember how to get to their lairs, where to find food, what is good to eat and what is poisonous, who are their relatives or members of their group and what their predators look like.

This natural ability to remember things that are important to them can be used by scientists in the lab. If an animal is offered a reward such as a piece of candy each time it performs a task, it will quickly memorise how to complete the task. By comparing the brains of rodents (rats and mice) before and after they have learned a particular task, the scientists have looked at differences in structure, in the pattern of connection between neurons and in electrical activity.

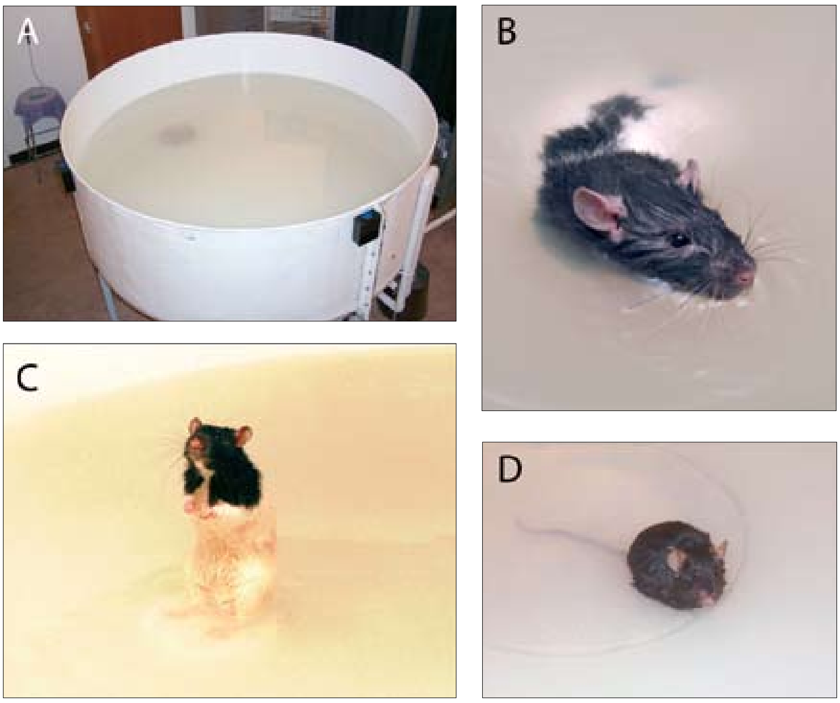
One common task that lab animals will perform is the 'water maze'. This consists of a big circular pool, filled with cloudy water and with a small platform hidden somewhere under the surface. Rodents don't like to swim, and so they want to find the platform to stand on when you put them in the pool. Since they cannot see it, at first they search at random, but they gradually learn how to locate it using cues in the environment.

This test is useful to measure 'spatial memory', the kind that helps you to find your bearings on a familiar environment. After some time the animal is put back in the tank without the platform but it will look for it where it originally was. Animals with experimentally impaired memory simply search at random, having no memory of the earlier training.

Using this method it was discovered that a substance called glutamate, produced by neurons, is essential for creating new memories. When glutamate was blocked in the brains of experimental animals, they became incapable of

A water maze; the mouse learns to swim to the platform using the surrounding objects to orient itself; the overhead camera records its route.

storing simple memories and learning new tasks, while those in the control group had no problem doing this. Furthermore, by looking closely at the brain circuits in the two groups, scientists discovered that glutamate helped to store new memories by strengthening the connections between the neurons. This in turn suggested to them that the strength of the connections between individual neurons may be a good indicator of how vivid a memory is, or how hard it is to lose it.



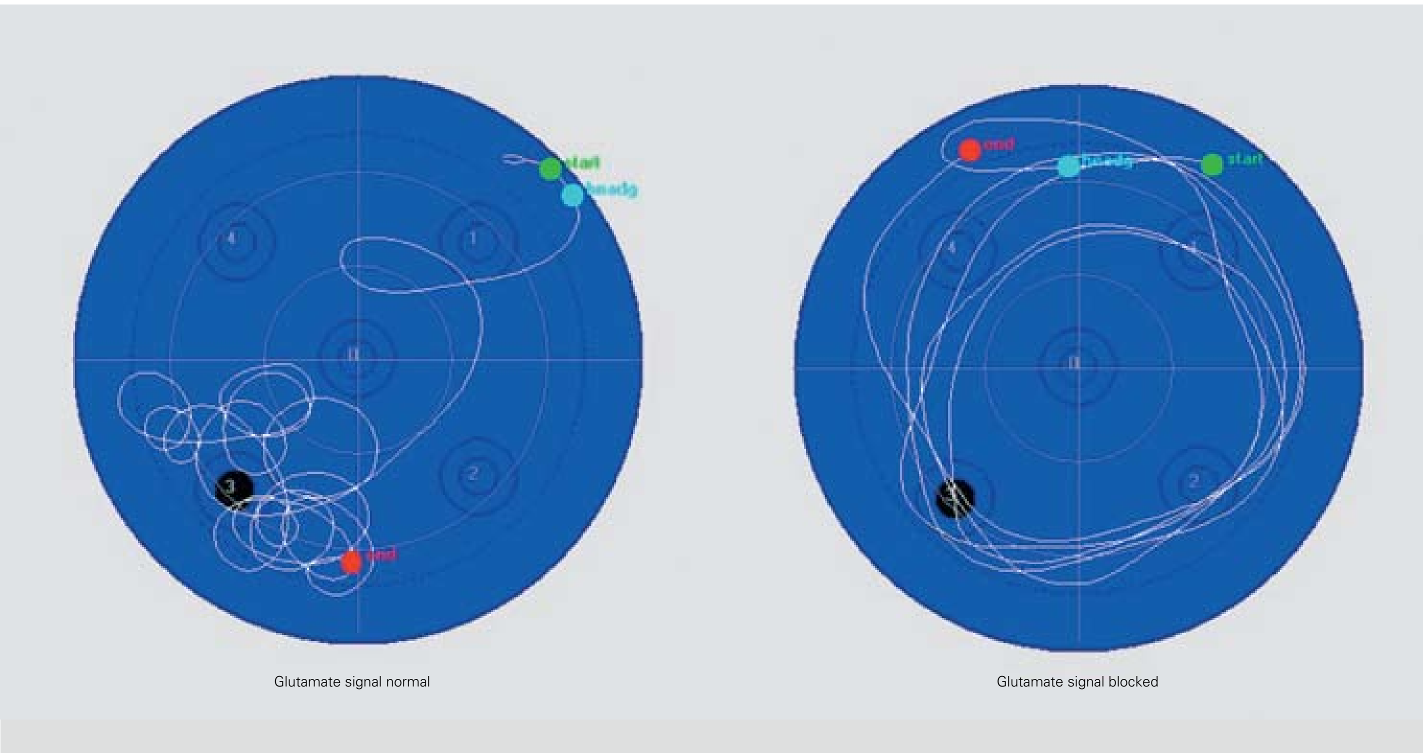
A *A typical water maze, 2 m diameter. The 'hidden' platform is visible from this angle but cannot be seen from water level.* ***B*** *A rat swimming in the pool.* ***C*** *A rat that has reached the platform and is looking around at external cues.* ***D*** *A mouse on the platform. The hidden platform is usually made bigger for mice so that they can find it more easily. The key point about the water maze is that the animals have to use 'spatial memory' to find the hidden platform.*

Why do we study memory?

The ability of the brain to create new memories based on our sensory perceptions is essential to live our lives and to function in a society. Imagine how terrifying it would be to suddenly find yourself in a place that you don't recognise, surrounded by complete strangers, without a clear idea of who you are, why you are there and what you are supposed to do next. And yet, this bleak scenario often becomes a reality for millions of people all over the world.

Our memory system is regularly targeted by several neurodegenerative (nerve destroying) diseases. Alzheimer's disease is the most famous and widespread of them. They leave patients in a state of great vulnerability as they progress. Since this disease becomes more common in old age, and people tend to live longer nowadays, the number of individuals affected is expected to increase in the future. That is why it is so important to find answers to our questions about memory. Therefore, not only is it interesting in itself, because it can potentially teach us something fundamental about how we function and who we are, but it can also help us to develop more effective therapies to fight these diseases.

Cristian Bodo works for the scientific journal Nature Reviews Neuroscience



Results of an experiment in which normal mice and those with the glutamate signal blocked were put in a water maze. The mice had already been trained to find the platform earlier but the glutamate blocked ones just forgot and swam around in circles!