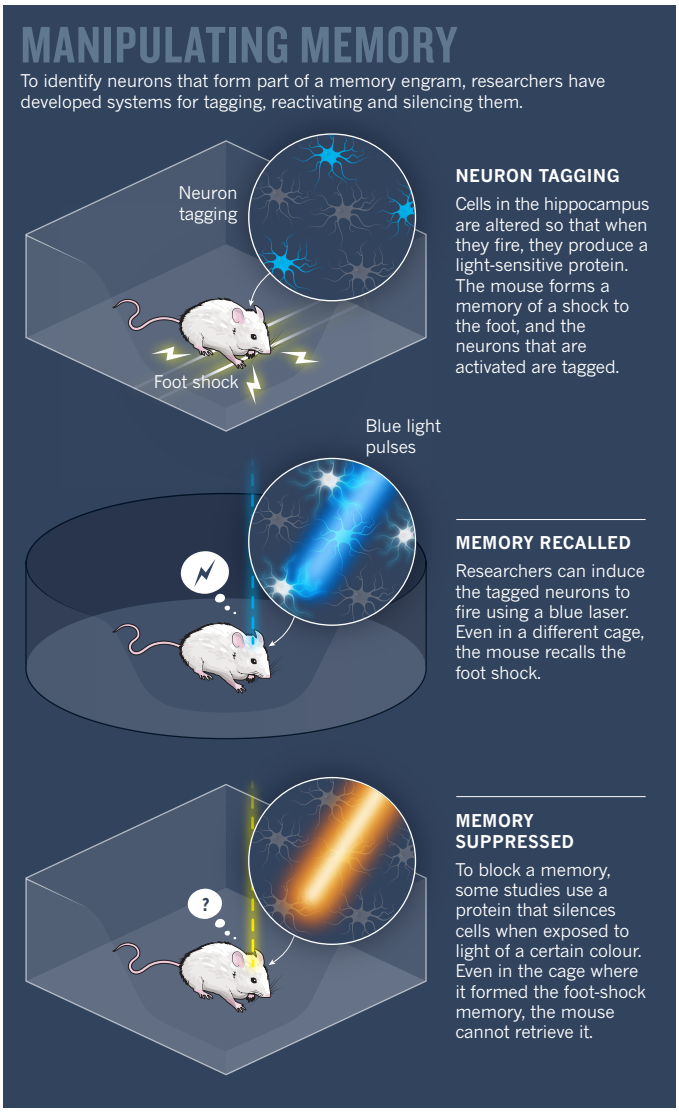

Chen. The results suggest that brains — even in higher-order regions that process memory, concepts and complex cognition — may be organized more similarly across people than expected.

MELDING MEMORIES

As new techniques provide a glimpse of the engram, researchers can begin studying not only how individual memories form, but how memories interact with each other and change over time.

At New York University, neuroscientist Lila Davachi is using MVPA to study how the brain sorts memories that share overlapping content. In a 2017 study with Alexa Tompary, then a graduate student in her lab, Davachi showed volunteers pictures of 128 objects, each paired with one of four scenes — a beach scene appeared with a mug, for example, and then a keyboard; a cityscape was paired with an umbrella, and so on. Each object appeared with only one scene, but many different objects appeared with the same scene[11]. At first, when the volunteers matched the objects to their corresponding scenes, each object elicited a different brain-activation pattern. But one week later, neural patterns during this recall task had become more similar for objects paired with the same scene. The brain had reorganized memories according to their shared scene information. "That clustering could represent the beginnings of learning the 'gist' of information," says Davachi.

Clustering related memories could also help people use prior knowledge to learn new things, according to research by neuroscientist Alison Preston at the University of Texas at Austin. In a 2012 study, Preston's group found that when some people view one pair of images (such as a basketball and a horse), and later see another pair (such as a horse and a lake) that shares a common item, their brains reactivate the pattern associated with the first pair[12]. This reactivation appears to bind together those related image pairs; people that showed this effect during learning were better at recognizing a connection later — implied, but never seen — between the two pictures that did not appear together (in this case, the basketball and the lake). "The brain is making connections, representing information and knowledge that is beyond our direct observation," explains Preston. This process could help with a number of everyday activities, such as navigating an unfamiliar environment by inferring spatial relationships between a few known landmarks. Being able to connect related bits of information to form new ideas could also be important for creativity, or imagining future scenarios.

In a follow-up study, Preston has started to probe the mechanism behind memory linking, and has found that related memories can merge into a single representation, especially if the memories are acquired in close succession[13]. In a remarkable convergence, Silva's work has also found that mice tend to link two memories formed closely in time. In 2016, his group observed that when mice learnt to fear foot shocks in one cage, they also began expressing fear towards a harmless cage they had visited a few hours earlier[14]. The researchers showed that neurons encoding one memory remained more excitable for at least five hours after learning, creating a window in which a partially overlapping engram might form. Indeed, when they labelled active neurons, Silva's team found that many cells participated in both cage memories.

These findings suggest some of the neurobiological mechanisms that link individual memories into more general ideas about the world. "Our memory is not just pockets and islands of information," says Josselyn. "We actually build concepts, and we link things together that have common threads between them." The cost of this flexibility, however, could be the formation of false or faulty memories: Silva's mice became scared of a harmless cage because their memory of it was formed so close in time to a fearful memory of a different cage. Extrapolating single experiences into abstract concepts and new ideas risks losing some detail of the individual memories. And as people retrieve individual memories, these might become linked or muddled. "Memory is not a stable phenomenon," says Preston.

Researchers now want to explore how specific recollections evolve with time, and how they might be remodelled, distorted or even recreated when they are retrieved. And with the ability to identify and manipulate individual engram neurons in animals, scientists hope to bolster their theories about how cells store and serve up information — theories that have been difficult to test. "These theories are old and really intuitive, but we really didn't know the mechanisms behind them," says Preston. In particular, by pinpointing individual neurons that are essential for given memories, scientists can study in greater detail the cellular processes by which key neurons acquire, retrieve and lose information. "We're sort of in a golden age right now," says Josselyn. "We have all this technology to ask some very old questions."■

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