EROS HOAGLAND/REDUX/EYEVINE

Military-service members can suffer brain injury and memory loss when exposed to explosions in enclosed spaces, even if they do not sustain overt physical injury.

NEUROSCIENCE

Memory-enhancement trials move into humans

Research suggests that electrodes could compensate for damaged tissue.

BY SARA REARDON

A strategy designed to improve memory by delivering brain stimulation through implanted electrodes is undergoing trials in humans. The US military, which is funding the research, hopes that the approach might help many of the thousands of soldiers who have developed deficits to their long-term memory as a result of head trauma. At the Society for Neuroscience meeting in Chicago, Illinois, on 17–21 October, two teams funded by the Defense Advanced Research Projects Agency presented evidence that such implanted devices can improve a person's ability to retain memories.

By mimicking the electrical patterns that create and store memories, the researchers found that gaps caused by brain injury can be bridged. The findings raise hopes that a 'neuroprosthetic' that automatically enhances flagging memory could aid not only brain-injured soldiers, but also people who have had strokes — or even those who have lost some power of recall through normal ageing.

Because of the risks associated with surgically placing devices in the brain, both groups are studying people with epilepsy who already have implanted electrodes. The researchers can use these electrodes both to record brain activity and to stimulate specific groups of neurons. Although the ultimate goal is to treat traumatic brain injury, these people might benefit as well, says biological engineer Theodore Berger at the University of Southern California (USC) in Los Angeles. That is because repeated seizures can destroy the brain tissue needed for long-term-memory formation.

Short-term memories are thought to be created when a part of the brain called the hippocampus aggregates sensory information, as well as the perception of space and time, and holds it readily accessible for a short while. Accessing the memory during that time will solidify it into a long-term memory. ▶

Key to this process is a signal that travels from one part of the hippocampus called CA3 to another, called CA1. Berger and his colleagues hypothesize that recreating that signal might restore the ability to solidify memories in people with damage to the hippocampus.

In one of the studies presented at the Chicago meeting, researchers asked 12 people with epilepsy to look at pictures and then recall up to 90 seconds later which ones they had seen. While the participants did this, the researchers recorded the firing patterns in both CA3 and CA1.

They then developed an algorithm that could use the activity of the CA1 cells to predict the pattern that was coming from CA3. Compared with the actual patterns, their predictions were accurate about 80% of the time.

By using this algorithm, the researchers should be able to stimulate the CA1 cells with a pattern that mimics an appropriate CA3 signal even if a person's CA3 cells are damaged, Berger says. In previous studies on monkeys trained to do the picture-recall task, receiving a juice reward when correct, his group has shown that stimulating CA1 with an appropriate pattern significantly improved the animals' performance (R. E. Hampson *et al.* *J. Neural Eng.* **10,** 066013; 2013).

USC biomedical engineer Dong Song, a member of the team, says that the group has tried the stimulation on a woman with epilepsy, but that it is too early to know whether it has improved her memory. He says that the researchers plan to apply it to more people in the coming months. Eventually, a device might be developed that would detect when the hippocampus is not efficiently encoding short-term into long-term memory and provide stimulation to support the process.

It is amazing that the memory-formation code can be so accurately predicted, says neurobiologist Howard Eichenbaum at Boston University in Massachusetts. But he cautions that mimicking it could be difficult if the CA1 cells are so badly damaged that they will not respond properly to stimulation. And he adds that because the hippocampus is so complex and receives inputs from many connections in the brain, stimulating it with the CA3 signal alone may not be enough.

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Thomas McHugh, a neuroscientist at the RIKEN Brain Science Institute in Tokyo, says that he has been following the team's work for years and has been consistently surprised at how well the approach has worked in animal models. "The data is convincing, but I'm still at a loss for understanding," he says. Many parts of the brain are organized in obvious ways: in the motor cortex, for example, stimulating a particular spot causes motion in a specific part of the body. But there is no such obvious organization in the hippocampus, so it is unclear why stimulating certain locations leads to predictable results.

A team at the University of Pennsylvania (Penn) in Philadelphia is taking a different approach to enhancing memory that requires an even less detailed understanding of how the process works.

The team exploits the fact that people's memory skills fluctuate over time depending on variables such as how much caffeine they have consumed or whether they are under stress. The team has found, again by working with people with epilepsy, that stimulating a region called the medial temporal lobe, which houses the hippocampus, improves memory that is functioning poorly. But when memory is functioning well, stimulation impedes it.

In a study that they presented at the Chicago meeting, Penn neuroscientist Daniel Rizzuto and his colleagues recorded brain activity in 28 people as they recalled a list of words. Using these patterns, the researchers developed an algorithm that predicted with high accuracy whether a person would remember a given word. By stimulating the brain only when a person read words that were likely to be forgotten, the researchers could boost performance by up to 140%.

Penn psychologist Michael Kahana says that the team has recorded from the brains of about 80 people in total and is seeking regulatory approval to use a more precise electrode array.

Although it would be useful from a basic-science viewpoint to discover why stimulation works so well, McHugh says, it may be worth developing therapies based on it even if it is not fully understood — as long as it can be proved to be safe and effective. ■

SPACE

Historic Rosetta mission to end with crash into comet

There were other options, but super close-up shots on descent will provide science bonanza.

BY ELIZABETH GIBNEY

A year since a probe called Philae made history by touching down on a comet, the team that pulled off the feat is plotting a different kind of landing. Next September, the European Space Agency will crash Philae's mothership Rosetta into the icy dust ball, but as gently as possible.

The dramatic act will bring the mission to an abrupt end — and give Rosetta's wealth of sensors and instruments their closest view of the comet yet. "The crash landing gives us the best scientific end-of-mission that we can hope for," says Rosetta project scientist Matt Taylor.

The collision will be emotional for the scientists, some of whom have worked on the mission since its inception in 1993. "There will be a lot of tears," says Taylor.

Launched in 2004, the Rosetta orbiter caught up with the comet 67P/Churyumov-Gerasimenko ten years later as the rock was travelling from deep in space towards the Sun — and dropped Philae onto the surface a few months later, on 12 November. Scientists have not heard from Philae since July, and don't know if they will do so again, but Rosetta's operations to survey the comet from orbit are in full swing. However, the orbiter can't keep up this work indefinitely. Funding for the mission runs out in September 2016 — and by that time 67P/Churyumov-Gerasimenko will be well on its way back out into deep space, where the solar-powered orbiter will receive too little sunlight to function.

Discussions about what to do with Rosetta when that happens have continued for more than a year. Rosetta flight director Andrea Accomazzo says that, ideally, Rosetta would hibernate while the comet remains in deep space, then be resurrected when 67P again approaches the Sun in 4 or 5 years' time. But the cold of deep space would probably damage the craft, Accomazzo says; others fear that fuel and other resources would run out. Moreover,