# NEWS IN FOCUS





SCOTT OLSON/GETTY IMAGES

**The pigs whose brains were used in the study had been killed at a slaughterhouse for meat.**

NEUROSCIENCE

# Pig brains kept alive for hours outside body

*A system that revives pig brains after death raises a slew of ethical and legal questions.*

**BY SARA REARDON**

In a challenge to the idea that brain death is final, researchers have revived the disembodied brains of pigs four hours after the animals were slaughtered. Although the experiments stopped short of restoring consciousness, they raise questions about the ethics of the approach — and, more fundamentally, about the nature of death itself. The current legal and medical definitions of death guide protocols for resuscitating people and for transplanting organs.

Details of the research appear in a paper[1] published on 17 April in *Nature*. Scientists at Yale University in New Haven, Connecticut, hooked the organs up to a system that pumped in a blood substitute. The technique restored some crucial functions, such as the ability of cells to make energy and remove waste, and helped to maintain the brains' internal structures.

"For most of human history, death was very simple," says Christof Koch, president and chief scientist of the Allen Institute for Brain Science in Seattle, Washington. "Now, we have to question what is irreversible."

In most countries, a person is considered to be legally dead when brain activity ceases or when the heart and lungs stop working. ▶

The brain requires an immense amount of blood, oxygen and energy, and going even a few minutes without these vital support systems is thought to cause irreparable damage.

Since the early twentieth century, scientists have conducted experiments that keep animals' brains alive from the moment the heart stops, by cooling the brains and pumping in blood or a substitute. But how well the organs functioned afterwards is unclear[2]. Other studies have shown that cells taken from brains long after death can perform normal activities, such as making proteins[3]. This made Yale neuroscientist Nenad Sestan wonder: could a whole brain be revived hours after death?

Sestan decided to find out — using severed heads from 32 pigs that had been killed for meat at a slaughterhouse near his lab. His team removed each brain from its skull before fitting the organ with a catheter. Four hours after death, the scientists began to pump a preservative solution into the brain's veins and arteries.

The system, which the team calls Brain*Ex*, mimics blood flow by delivering nutrients and oxygen to brain cells. The preservative solution also contained chemicals that stop neurons from firing, to protect them from damage and to prevent electrical brain activity from restarting. Despite this, the scientists monitored the brains' activity throughout the experiment and were prepared to administer anaesthetics if they saw any signs that the organs might be regaining consciousness.

The researchers tested how well the brains fared during a six-hour period. They found that neurons and other brain cells had restarted normal metabolic functions, and that the brains' immune systems seemed to be working. The structures of individual cells and sections of the brain were preserved — whereas cells in control brains that did not receive the preservative solution collapsed. And when scientists applied electricity to tissue samples from the treated brains, they found that individual neurons could still carry a signal.

But the researchers never saw coordinated electrical patterns across the entire brain that would indicate sophisticated activity. They say that restarting such function might require an electrical shock, or preserving the brain in solution for an extended period to allow cells to recover from any damage they sustained while deprived of oxygen.

Sestan, who has used the system to keep pig brains alive for up to 36 hours, has no immediate plans to try to restore electrical brain activity. His goal is to find out how long his team can sustain an isolated brain's metabolic and physiological functions.

***"We just flew a few hundred metres, but can we really fly?"***

"It is conceivable we are just preventing the inevitable, and the brain won't be able to recover," Sestan says. "We just flew a few hundred metres, but can we really fly?" Brain*Ex* is far from ready for use in people, he adds, not least because it is difficult to use without separating the brain from the skull.

Still, the development of technology with the potential to support sentient, disembodied organs has broad ethical implications for animals and people. "There isn't really an oversight mechanism in place for worrying about the possible ethical consequences of creating consciousness in something that isn't a living animal," says Stephen Latham, a bioethicist at Yale who worked with Sestan's team. He says that doing so might be justifiable in some cases — for instance, if it enabled scientists to test drugs for degenerative brain diseases on the organs, rather than on people.

The latest study also raises questions about whether brain damage and death are permanent. Lance Becker, an emergency-medicine specialist at the Feinstein Institute for Medical Research in Manhasset, New York, says that many physicians assume that even minutes without oxygen can cause fatal harm. But the pig experiments suggest that the brain might stay viable for much longer than previously thought, even without outside support. "We may have vastly underestimated the ability of the brain to recover," Becker says.

That could have consequences for organ donation. In parts of Europe, emergency responders who cannot revive a person sometimes preserve organs for transplantation by pumping oxygenated blood through the body — but not the brain. If technology such as Brain*Ex* becomes widely available, the ability to extend the window for resuscitation could shrink the pool of eligible organ donors, says Stuart Youngner, a bioethicist at Case Western Reserve University in Cleveland, Ohio. "There's a potential conflict here between the interests of potential donors — who might not even be donors — and people who are waiting for organs," he says.

In the meantime, scientists and governments are left to navigate quandaries related to the possibility of creating a conscious brain without a body. "This really is a no-man's land," says Koch. "The law will probably have to evolve to keep up." He wants a broader ethical discussion to take place before anyone tries to induce awareness in an isolated brain. "It is a big, big step," Koch says. "And once we do it, it's impossible to reverse it." ■ SEE COMMENT, P.299 & P.302

1. Vrselja, Z. *et al. Nature* **568**, 336–343 (2019).
2. White, R. J., Albin, M. S. & Verdura, J. *Science* **141**, 1060–1061 (1963).
3. Verwer, R. W. *et al. FASEB J.* **16**, 54–60 (2002).

ASTROPHYSICS

# Black hole imaged for first time

*Picture created by Event Horizon Telescope is one of the strongest confirmations yet of Einstein's general relativity.*

**BY DAVIDE CASTELVECCHI**

Astronomers have finally glimpsed the blackness of a black hole. Using a global network of radio telescopes, they have for the first time produced a picture of an event horizon — a black hole's perilous edge — against a backdrop of swirling light.

"We have seen the gates of hell at the end of space and time," said astrophysicist Heino Falcke of Radboud University in Nijmegen, the Netherlands, at a press conference in Brussels on 10 April.

The picture, created by the Event Horizon Telescope (EHT) collaboration, made the front pages of newspapers around the world. Scientists hailed it as a historic achievement — and one of the strongest confirmations yet of Albert Einstein's general theory of relativity.

The image of a glowing, ring-like structure shows that a supermassive black hole 6.5 billion times the mass of the Sun lies at the centre of the galaxy M87, around 16 megaparsecs (55 million light years) away. The 'shadow' at its centre contains the event horizon, a spherical surface that represents a point of no return.

The results, comparable to recognizing a doughnut on the Moon's surface, were unveiled by the EHT in seven press conferences on four continents. The findings were published in *The Astrophysical Journal Letters*[1–6].

"When I was a student, I never dreamt that anything like this would be possible," says astrophysicist Roger Blandford at Stanford University in California. "It is yet another confirmation of general relativity as the correct theory of strong gravity."

Event horizons are the defining feature of black holes. To a nearby observer, they should