The Atlantic
SCIENCE

Scientists Partly Restore Activity in Dead-Pig Brains

Now what?

ED YONG
1:00 PM ET

FER GREGORY / SHUTTERSTOCK

The brain, supposedly, cannot long survive without blood. Within seconds, oxygen supplies deplete, electrical activity fades, and unconsciousness sets in. If blood flow is not restored, within minutes, neurons start to die in a rapid, irreversible, and ultimately fatal wave.

But maybe not? According to a team of scientists led by Nenad Sestan at Yale School of Medicine, this process might play out over a much longer time frame, and perhaps isn't as inevitable or irreparable as commonly believed. Sestan and his colleagues showed

this in dramatic fashion—by preserving and restoring signs of activity in the isolated brains of pigs that had been decapitated four hours earlier.

The team sourced 32 pig brains from a slaughterhouse, placed them in spherical chambers, and infused them with nutrients and protective chemicals, using pumps that mimicked the beats of a heart. This system, dubbed BrainEx, preserved the overall architecture of the brains, preventing them from degrading. It restored flow in their blood vessels, which once again became sensitive to dilating drugs. It stopped many neurons and other cells from dying, and reinstated their ability to consume sugar and oxygen. Some of these rescued neurons even started to fire. "Everything was surprising," says Zvonimir Vrselja, who performed most of the experiments along with Stefano Daniele.

There have long been signs that oxygen deprivation doesn't necessarily kill neurons as quickly as is often assumed. Still, Jimo Borjigin from the University of Michigan says that when she started studying brain activity in dying rats, "my colleagues told me that as soon as oxygen isn't there, every cell dies within minutes." Sestan's team "showed that cells are still intact not just a few minutes later, but a few hours later. This kind of study is long overdue."

Disembodied brains in jars are a familiar and disquieting science-fiction staple, but in those stories, the brains are alive, conscious, and self-aware. Those in Sestan's experiments were zero for three. Though individual neurons could fire, there were no signs of the coordinated, brain-wide, electrical activity that indicates perception, sentience, consciousness, or even life. The team had anesthetics on stand-by in case any such flickers materialized—and none did. "The pigs were brain-dead when their brains came in the door and by the end of the experiment, they were still brain-dead," says Stephen Latham, a Yale University ethicist who advised the team.

For that reason, "I don't see anything in this report that should undermine confidence in brain death as a criterion of death," says Winston Chiong, a neurologist at the University of California, San Francisco. The matter of when to declare someone dead has become more controversial since doctors started relying more heavily on neurological signs, starting around 1968 when the criteria for "brain death" were defined. But that diagnosis typically hinges on the loss of brain-wide activity—a line that, at least for now, is still final and irreversible. After *MIT Technology Review* broke the news of Sestan's work a year ago, he started receiving emails from people asking if he could restore brain function to their loved ones. He very much cannot. BrainEx isn't a resurrection chamber.

"It's not going to result in human brain transplants," adds Karen Rommelfanger, who directs Emory University's Neuroethics program. "And I don't think this means that the singularity is coming, or that radical life extension is more possible than before."

So why do the study? "There's potential for using this method to develop innovative treatments for patients with strokes or other types of brain injuries, and there's a real need for those kinds of treatments," says L. Syd M Johnson, a neuroethicist at Michigan

Technological University. The BrainEx method might not be able to fully revive hours-dead brains, but Yama Akbari, a critical care neurologist at the University of California, Irvine, wonders if it would be more successful if applied within minutes after death. Alternatively, it could help to keep oxygen-starved brains alive and intact while patients wait to be treated. “It’s an important landmark study,” Akbari says.

Such applications are a long way off, and even if they never materialize, “this is already an extraordinary breakthrough,” says Nita Farahany, a bioethicist at Duke University. Although neuroscientists can study lab-grown neurons, or peer at thin slices of brain tissue, these capture nothing of the three-dimensional intricacy that makes the brain the brain. By restoring some activity to postmortem pig brains, Sestan’s team has created a much better proxy for the real thing. The irony, of course, is that “the better the proxy, the sharper the ethical dilemmas,” says Farahany.

Johnson adds that no animals died for the sake of the study: The team sourced brains from pigs that had been killed for food. “Thousands of sentient animals have been killed in studies searching for neuroprotective treatments that have not borne fruit,” she says. “Meanwhile, millions of animals are killed for food every year, and that’s a potentially rich source of experimental brains that would involve no additional harm.”

The study still needs to be replicated by other independent teams. And before anyone takes the technique further, or even contemplates the possibility of human trials, there are several ethical issues to consider. For example, is the team *really* sure that the part-revived brains have no consciousness? Latham, the Yale ethicist, feels confident. Even people under anesthesia show signs of coordinated, brain-wide electrical activity, he says, so the absence of such signals strongly suggests that “we don’t even have the possibility of consciousness showing up.”

But consciousness is still hard to define, much less measure. And no one has ever had to measure it in a brain that lacks a body. How would you assess awareness, pain, or suffering “in a brain that has restored circulation and neural function, but that’s disconnected from external sensation?” asks Steven Hyman, a neuroscientist at the Broad Institute of Harvard and MIT. “This is a very hard scientific problem and policy issue.” As Johnson says, “I think it’s very unlikely that consciousness or sentience could be restored in a several-hours-dead brain but I’m also pretty sure that if it was, we wouldn’t know that it was.”

It’s also unclear *why* the pig brains never regained coordinated activity. Is it because the team waited for four hours? Is it because they only treated the brains for six hours? Was it something about the way the pigs were killed? Or is it because they added chemicals that dampen neural activity to the fluid that they pumped through the brains? (They did this because excessive firing helps to kill neurons in oxygen-starved brains.) And if that’s the case, could isolated brains gain consciousness if the blockers were removed?

Possibly, and that would certainly blur the line between living and dead. But that experiment is emphatically not on the cards. The team’s next and only step is to try

BrainEx for longer periods of time. If that leads to signs of coordinated activity, "we'd have to close down the research for a while," Latham says, "because there's no institutional body for us to consult. We'd need to create one." Current regulations on animal research exclude individuals that were either raised for food, or that have died. There's nothing that covers the grey area posed by an isolated brain with signs of cellular activity and may or may not be conscious.

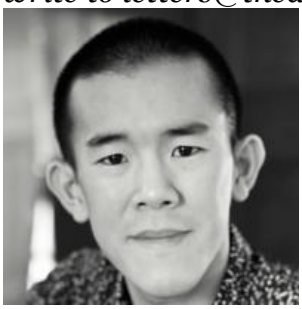
This illustrates a problem that I wrote about last year: Advancements in neuroscience—from preserving postmortem tissue to growing blobs of brain tissue in a dish—are outpacing the ethical frameworks that help us think about such research. Sestan's team "recognized that they were up against a blurred line, and did everything they could to seek guidance—more than many researchers would have," Farahany says. "But the truth is that there wasn't guidance."

In a commentary that accompanies the new study, she and others suggest several immediate guidelines. Don't remove the neural activity blockers until we know what they do. Don't do similar studies without anesthetics. Prioritize research into ways of detecting neural signals that might indicate sentience or consciousness. Be transparent. With those principles in place, an organization like the National Institutes of Health or the National Academies of Sciences, Engineering, and Medicine should convene groups of scientists and citizens to discuss the ethical boundaries of this research and draw up clear guidelines.

"First we have to figure out how to do this work ethically in animals," Farahany says. If one eventually could revive a dead brain to the point of consciousness, "what comes with that and what doesn't? Are memories intact? Are self-identities intact? How would we answer those questions if you can't ask an animal?"

And what might change if researchers move from isolated brains to brains that are still inside the skulls of their owners? Or to human trials? Could that increase the already big shortage of transplantable organs, if the point at which medical interventions are futile becomes blurry? These are all questions for the distant future, but it's worth having answers before the future becomes the present.

We want to hear what you think about this article. Submit a letter to the editor or write to letters@theatlantic.com.



ED YONG is a staff writer at *The Atlantic*, where he covers science.