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New Frontier: Head Transplants --- A Chinese surgeon has fused hundreds of mouse heads and bodies; next in his laboratory, monkeys

By Shirley S. Wang

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HARBIN, China -- Xiaoping Ren stood up after 10 hours hunched over an operating table and looked proudly at his patient, a small black mouse with a new brown head.

When he took a ventilator off the tiny creature's throat, the head began breathing spontaneously with its new body. An hour later, the body twitched, and, a few hours after that, the mouse opened its eyes, Dr. Ren recalls.

Since the July 2013 operation, he and his team at Harbin Medical University have done operations on nearly 1,000 more mice, testing various ways to help them survive longer than their record so far of one day after the surgery. A peer-reviewed international journal, *CNS Neuroscience & Therapeutics*, published the team's work in December.

Head transplants, at the extreme frontier of medicine, are inching toward reality. Dr. Ren plans to turn his surgical skills to monkeys this summer, hoping to create the first head-transplanted primate that can live and breathe on its own, at least for a little while.

If a breakthrough in this futuristic work comes, China might be where it happens. Since the mid-1990s, the Chinese government has been pouring money into scientific research, especially projects that are potentially high-impact or groundbreaking. China's investment in science and technology rose to 18% of the world's total research-and-development spending last year, from 10% in 2009, according to the Battelle Memorial Institute.

"China right now, they want to go to the top," said Dr. Ren. "If you think there's a really great benefit in research, China can put resources to support you."

One of China's ultimate goals, observers of its efforts say, is to be accepted as a scientific powerhouse. "The political leaders want to see the Chinese winning the Nobel Prize," said Cong Cao, a professor of contemporary Chinese studies at the University of Nottingham in the U.K.

Addressing science leaders last year, Chinese President Xi Jinping urged them to strive for breakthroughs as one of the keys to China's future. "Innovate, innovate, innovate," he said.

Some Chinese research has aroused controversy. A group from Guangdong province sparked a global outcry in April when it reported using a gene-editing tool on human embryos, work that could alter human patients' DNA in ways inheritable by their offspring. Some ethicists and scientists in Western countries called for a moratorium on such work. An international conference to discuss the implications of gene-editing technologies is now planned for this fall.

Controversy could surround Dr. Ren's research, too, as it becomes better known. Harbin-born, Dr. Ren studied and worked in the U.S. for more than 15 years before giving up a faculty position at the University of Cincinnati College of Medicine and returning to his hometown in northeast China three years ago. His wife and two daughters remain in the U.S., where he visits them several times a year.

In Harbin, he spends most of his waking hours on his research. He completed the laborious 2013 mouse operation in the early morning hours of a Saturday.

One reason Dr. Ren returned was to take advantage of the Chinese government's robust support for medical research. Another was that he doubted he could do the work he aspired to in the U.S.

A proposal for head-transplant experiments would face daunting obstacles in the U.S., both in terms of funding and ethical concerns, other researchers agree. But at Harbin Medical University, where Dr. Ren is director of the hand and microsurgical center, his work not only has won the approval of an ethics board but has received government and university grants totaling roughly 10 million yuan, or about \$1.6 million.

Head-transplant research isn't frivolous, Dr. Ren said. If such transplants could be perfected, he said, they might one day be able to help human patients who have intact brains but broken bodies, such as people with spinal-cord injuries, cancer and muscle-wasting diseases.

He doesn't want to oversell his team's progress. Dr. Ren wouldn't predict when he might try a human transplant.

"We want to do this clinically, but we have to make an animal model with long-term survival" first, said the researcher, an energetic and fast-talking 53-year-old. "Currently, I am not confident to say I can do a human transplant."

The prospect of head transplants in humans would raise unprecedented philosophical and ethical issues.

What would it mean for a person's identity to have a new body? And even if a human head transplant were possible, would it be right for one person to get a donor body that contained enough healthy organs to help several other people?

There is also the question of where donor bodies would come from. China, like many other countries, has a shortage of organ donors. Dr. Ren says donors could be found, such as accident victims.

Robert Truog, director of the Center for Bioethics at Harvard Medical School, said that though head-transplant work has "profound implications for personal identity," there is no reason it ethically shouldn't be done if it has been vetted by institutional review boards. "I imagine this is something we're going to see over the next however many years," he said, "and I imagine it will be done overseas."

Princeton University bioethicist Peter Singer, when the work was described to him, said he believes it is too speculative at this stage to be done in primates.

Another expert found the concept of head transplants appalling. "The whole idea is ridiculous," and not worth the effort or the sacrifice of animals, said Arthur Caplan, a bioethicist at New York University School of Medicine.

The idea, though, has a long history. As early as the start of the 20th century, American scientist C.C. Guthrie attempted to implant a second head on a dog's body. The head exhibited only basic reflexes. In the 1950s, first Russian and then Chinese scientists did similar grafts with a little more success, the second head reported able to do such things as drink.

Two decades later, Robert J. White, a professor at Case Western Reserve University in Ohio, did a head transplant in a rhesus monkey. The monkey looked around and tried to bite a researcher's hand but wasn't able to breathe on its own, according to media reports at the time.

For that experiment, the late Dr. White was dubbed "Dr. Frankenstein," a reputation he would play up over his career, especially around Halloween, according to George Stamatis, who directed public affairs at the medical school when Dr. White was a faculty member.

Most recently, an Italian neurosurgeon, Sergio Canavero, made the striking statement that he would attempt a human head transplant in two years' time and said he had identified a patient willing to provide the head. Dr. Ren said Dr. Canavero has asked him to collaborate on testing the procedure in animals, and he has agreed. Dr. Canavero declined to comment.

Dr. Ren began thinking about head transplants a decade ago. As a surgeon, he always dreamed of fixing the seemingly unfixable.

In 1996, he moved to the U.S. for five years of microsurgery training at the University of Louisville School of Medicine, joining a team that was a pioneer in hand transplants.

He moved on to a faculty position at the University of Cincinnati, where for a dozen years he studied one of the big challenges in organ transplants: preventing ischemia, or lack of oxygen, in donor organs.

Eventually, he recalled, he began thinking "What's the next frontier?" In his field, that would be a head transplant.

"In the U.S., people would be very shocked" at the notion, Dr. Ren said. He remembered a storm of criticism from ethicists that the University of Louisville team and others provoked with hand transplants in the late 1990s, and again with face transplants soon after.

Dr. Ren moved back to China in 2012, though he has continued to hold an adjunct position at Loyola University Chicago. Loyola officials said the university has nothing to do with his head-transplant work.

Not only would funding and approval for this work be easier to get in China, but so would laboratory animals. Dr. Ren believes he will be able to obtain monkeys called long-tailed macaques, which are small and friendly animals, from colonies in Suzhou in the south of China. They will need time to adjust to the cold in Harbin, where the high averages six degrees Fahrenheit in January. He anticipates he can just call the local airport after they arrive and have them shipped to the university.

At Harbin, Dr. Ren has established a large, gleaming laboratory and assembled a team that includes a neurosurgeon, a cardiovascular expert, a spinal-cord regeneration specialist and an immunologist. A common remark from his colleagues is that they at first thought his research was a crazy idea, but they slowly got on board with the collaboration. "It's a huge challenge, but it's exciting," one said.

Outside the lab, Dr. Ren likes to kid around with his students, who say he sometimes gives them fatherly encouragement about their studies and has a beer with them.

In their mouse experiments, Dr. Ren and his team are testing the idea that although the spinal cord and brain contain an enormous number of nerves, only a small fraction need to regenerate for the head-transplanted animal to be able to breathe and perform basic reflexes.

Perhaps the two biggest hurdles are preventing immune rejection and keeping the brain healthy while it is disconnected, he said. Even five minutes without oxygen could leave permanent brain damage.

The first step of the operation is to make what is known as a "clean trauma," a sharp cut using a diamond-bladed knife to separate the head that will receive a new body. As for the body that will be donated, its head is also separated, but at midbrain. That leaves this body's heart able to beat.

Because a brain needs continuous oxygen, one of Dr. Ren's first steps is to temporarily attach blood vessels from the donor body, whose heart is still pumping blood, to the recipient head, using silicone tubes along one side.

Then, under a microscope, Dr. Ren and his team connect spinal nerves of the head and its new body, capping them with a coating of very stable molecules called polyethylene glycol. They are testing whether this substance improves fusion of the nerves.

Still working quickly, they next stabilize the head by affixing the bone from the vertebrae between the head and the new body using pins, screws and plates.

Finally, they use microscopic sutures to attach the blood vessels on the other side of the head to blood vessels of the donor body, as well as muscle and skin.

When he does an operation involving monkeys, Dr. Ren plans to connect just a tiny fraction of the roughly 100 billion spinal-nerve fibers. Throughout the procedure, the fibers will be electrically stimulated by electrical probes placed in the spinal cord of both the head and the new body, in an effort to keep the nerves functioning well.

If just 10% to 20% of them connect, the body can keep its basic functioning, including voluntary muscle movement, according to the team's hypothesis. But the team hopes to raise this percentage over time. And the percentage of functioning nerves would need to be improved dramatically for the procedure to have clinical value in humans.

Other organ-transplant experts are mixed in their views about this work. John H. Barker, a former colleague of Dr. Ren's at the University of Louisville, described him as a capable surgeon and said that a human head-body transplant was theoretically possible. From an immunologic and ethical standpoint, it would be similar to that of a hand or face, said Dr. Barker, now at J.W. Goethe-Universität in Frankfurt, Germany.

Peter Stern, a hand surgeon and a professor of orthopedic medicine at the University of Cincinnati who trained Dr. Ren, said the Chinese scientist's work "is interesting and extraordinarily futuristic. But it's a huge area of challenges from many, many standpoints: ethical issues, immune rejection -- the head being a very complex organ -- technical issues, particularly nerve regeneration."

Dr. Ren said he didn't know whether the head transplant would become a tool of human medical care in his lifetime. He hopes to at least make significant progress, so the next generation of scientists can build on it.

"Today it is not possible," he said. "But tomorrow, it may be possible."

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